Supplement to the Clinical Practice Guideline for the Management of Osteoarthritis of the Knee (Non-Arthroplasty)

e-Appendix 2

- Quality Evaluation
- Data Summary
- Detailed Data Tables

This supplementary material has been provided by the authors to give readers additional information about their work

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Strength of Recommendations

Strength Of Recommendation	Overall Strength Of Evidence	Description Of Evidence Quality
Strong	**Strong**	Evidence from two or more "High" quality studies with consistent findings for recommending for or against the intervention. Also requires no reasons to downgrade from the EtD framework
Moderate	**Moderate or Strong**	Evidence from two or more "Moderate" quality studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.
Limited	**Limited, Moderate or Strong**	Evidence from one or more "Low" quality studies with consistent findings or evidence from a single "Moderate" quality study recommending for or against the intervention. Also, higher strength evidence can be downgraded to limited due to major concerns addressed in the EtD Framework.
Consensus	**No Reliable Evidence**	There is no supporting evidence, or higher quality evidence was downgraded due to major concerns addressed in the EtD framework. In the absence of reliable evidence, the guideline work group is making a recommendation based on their clinical opinion.

Quality Evaluation – Randomized

Study	Random Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Reporting	Other Bias	Inclusion	Strength
Inal, E. E., 2016							Include	High Quality
Aamir, M., 2019							Include	High Quality
Afilalo, M., 2010							Include	High Quality
Ahmad, H. S., 2018							Include	Moderate Quality
Akan, O, 2018							Include	Moderate Quality
Al-Omran, A., 2014							Include	High Quality
Allen, K. D., 2010							Include	Moderate Quality
Allen, K. D., 2016							Include	Moderate Quality
Allen, K. D., 2017							Include	Moderate Quality
Allen, K. D., 2018							Include	Moderate Quality
Alpayci, M., 2013							Include	High Quality
Altinbilek, T., 2018							Include	High Quality
Altman, R., 2015							Include	High Quality
Ammar, T. A., 2014							Include	High Quality
Amorndoljai, P., 2017							Include	High Quality
Anz, A. W.,							Include	High Quality
Apparao, P., 2017							Include	High Quality
Apparao, P., 2017							Include	Moderate Quality
Arden, N. K., 2016							Include	Moderate Quality
Aree-Ue, S., 2017							Include	Low Quality
Armagan, O., 2015							Include	Moderate Quality
Askari, A.,							Include	High Quality
Askari, A., 2016							Include	High Quality
Atamaz, F. C., 2012							Include	High Quality
Azad, A. K., 2011							Include	High Quality
Azidah, A. K., 2017							Include	High Quality
Babaei-Ghazani, A., 2018							Include	High Quality
Babaskin, D. V.,							Include	High Quality
Bagnato, G. L., 2016							Include	High Quality
Baker, K., 2007							Include	High Quality
Baker, K., 2019							Include	High Quality
Banerjee, M., 2016							Include	Moderate Quality
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Bellare, N., 2014							Include	Moderate Quality

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Birbara, C., 2006							Include	Moderate Quality
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Bliddal, H., 2011							Include	High Quality
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Branco, M., 2016							Include	High Quality
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Cagnin, A.,							Include	High Quality
Cai, G., 2019							Include	High Quality
Callaghan, M. J., 2015							Include	High Quality
Campos, A. L. S., 2017							Include	High Quality
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Chen, H., 2020							Include	Moderate Quality
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Chen, R., 2012							Include	High Quality
Chen, R., 2015							Include	High Quality
Chen, S. M., 2019							Include	High Quality
Chen, T. W., 2014							Include	High Quality
Cherian, J. J., 2016							Include	Moderate Quality
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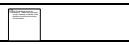
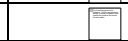
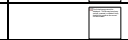
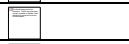
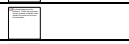
Chubick Jr, A., 1987							Include	High Quality
Ciani, O., 2017							Include	Moderate Quality
Cole, B. J., 2017							Include	High Quality
Coleman, S., 2012							Include	Moderate Quality
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Delgado-Enciso, I., 2019							Include	High Quality
Deng, K. F., 2020							Include	High Quality
Deyle, G. D.,							Include	High Quality
Di Martino, A., 2019							Include	High Quality
Dias, J. M., 2017							Include	High Quality
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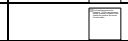
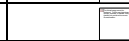
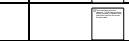
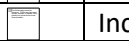
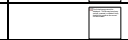
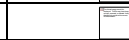
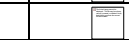
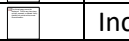
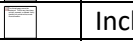
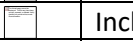
Essouiri, J., 2017							Include	Moderate Quality
Farr, J.,							Include	Moderate Quality
Fary, R. E., 2011							Include	High Quality
Fazaa, A., 2014							Include	Moderate Quality
Felson, D. T., 2019							Include	High Quality
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Sanchez Romero, E. A., 2019							Include	High Quality
Saccomanno, M. F., 2016							Include	Moderate Quality
Sadeghi, A., 2014							Include	High Quality
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Sanghi, D., 2013							Include	High Quality
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Sit, R. W. S., 2018							Include	High Quality
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Smith, M. T., 2015							Include	Moderate Quality
Somers, T. J., 2012							Include	High Quality
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Spakova, T., 2012							Include	Moderate Quality
Srikanth,, 2012							Include	High Quality
Srivastava, S., 2016							Include	High Quality
Stevens, R. M., 2019							Include	High Quality
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Sun, S. F., 2017							Include	High Quality
Sun, Y.,							Include	Moderate Quality
Suppan, V. K. L., 2017							Include	High Quality
Suppan, V. K. L., 2020							Include	High Quality
Takamura, J., 2018							Include	Moderate Quality
Tammachote, N., 2016							Include	High Quality
Tao, Q. W., 2009							Include	Moderate Quality
Thoumie, P., 2018							Include	Moderate Quality
Toda, Y., 2004							Include	Moderate Quality
Toda, Y., 2008							Include	High Quality
Topp, R., 2002							Include	High Quality
Torri, G., 1994							Include	High Quality
Tosun, B., 2017							Include	Moderate Quality
Trc, T., 2011							Include	Moderate Quality
Trock, D. H., 1994							Include	High Quality

Trueba Davalillo, C. A., 2015							Include	High Quality
Tuna, H. I., 2018							Include	Moderate Quality
Uchio, Y., 2018							Include	Moderate Quality
Uysal, A., 2020							Include	High Quality
Vaishya, R., 2017							Include	Moderate Quality
Vaittianadane, K, 2014							Include	High Quality
van de Graaf, V. A., 2018							Include	Moderate Quality
van Egmond, N., 2017							Include	Moderate Quality
Van Ginckel, A., 2019							Include	Moderate Quality
Vaquerizo, V., 2013							Include	High Quality
Vaquerizo, V., 2018							Include	Moderate Quality
Verkleij, S. P., 2015							Include	High Quality
Villadsen, A., 2014							Include	Moderate Quality
Wadsworth, L. T., 2016							Include	High Quality
Waller, B., 2017							Include	High Quality
Wang, C., 2016							Include	Moderate Quality
Wang, H., 2018							Include	Moderate Quality
Wang, J.,							Include	High Quality
Wang, P., 2016							Include	Moderate Quality
Wang, P., 2018							Include	High Quality
Wang, S. Z., 2018							Include	High Quality
Weiner, D. K., 2013							Include	High Quality
Williamson, L., 2007							Include	High Quality
Xiao, L., 2018							Include	Moderate Quality
Xin, Y., 2016							Include	High Quality
Xu, Y. Y., 2014							Include	High Quality
Yaligod, V., 2014							Include	Moderate Quality
Yang, P. F., 2011							Include	Moderate Quality
Yaradilmis, Y. U.,							Include	High Quality
Yavuz, U., 2012							Include	Moderate Quality
Yegin, T., 2017							Include	Moderate Quality
Yengkhom, JS, 2017							Include	High Quality
Yildiz, S. K., 2015							Include	High Quality
Yilmaz, E.,							Include	High Quality
Yilmaz, E., 2019							Include	High Quality
Yilmaz, M., 2019							Include	Moderate Quality

Yoo, M. C., 2014							Include	High Quality
Yu, Z., 2018							Include	Moderate Quality
Zakeri, Z., 2011							Include	High Quality
Zarringam, D., 2018							Include	Moderate Quality
Zegels, B., 2013							Include	High Quality
Zhang, J. Q., 2012							Include	Moderate Quality
Zhang, Y., 2016							Include	Moderate Quality
Zhang, Y., 2018							Include	Moderate Quality
Zhao, J., 2016							Include	High Quality
Zhao, L., 2014							Include	High Quality
Zhao, Z., 2013							Include	High Quality
Zhong, Z., 2019							Include	High Quality

Quality Evaluation – Observational

Study	Is this an observational study? (If no, exit form)	Participant Recruitment	Treatment recording	Confounding Variables	Outcome measurement bias	Incomplete Outcome Data	Adequate Reporting	Inclusion	Strength
Annaniemi, J. A., 2018								Include	Low Quality
Apparao, P., 2017								Include	Low Quality
Dell'Isola, A.,								Include	Low Quality
Evcik, Deniz, 2003								Include	Low Quality
Gil, H. Y., 2019								Include	Low Quality
Hungerford, D. S., 2013								Include	Low Quality
Kim, Y. S.,								Include	Low Quality
Korkmaz, M., 2013								Include	Low Quality
Lee, T., 2016								Include	Low Quality

Lu, L.,								Include	Low Quality
Mautner, K.,								Include	Low Quality
Ogawa, H., 2019								Include	Low Quality
Park, J. Y.,								Include	Low Quality
Qin, X., 2020								Include	Low Quality
Que, B., 2018								Include	Low Quality
Shewale, A. R., 2017								Include	Low Quality
van Outeren, M. V., 2017								Include	Low Quality
van Wulfften Palthe, A. F. Y., 2018								Include	Low Quality
Wu, C. C., 2017								Include	Low Quality
Xu, J.,								Include	Low Quality
Yu, S. P., 2016								Include	Low Quality
Zarringam, D., 2018								Include	Low Quality

Quality Evaluation – Prognostic

Study	Prognostic Study Design	Representative Population	Reason for Follow Up Loss	Prognostic Factor Measured	Outcome Measurement	Confounders	Appropriate Statistical Analysis	Inclusion	Strength
Legha, A.,								Include	Moderate Quality

Quality Evaluation – Included in Osteoarthritis on the Knee 2013 CPG

Study	Prospective	Random	Blinding	Group Comp	Treatment Integrity	Measurement	Investigator Bias	Quality
Baker(2007)	●	●	●	○	●	●	○	Moderate
Maillefert(2001)	●	○	●	○	○	●	●	Moderate
Toda(2004)	○	○	○	○	●	●	○	Low
Bennell(2011)	●	●	●	●	●	●	○	High
Pham(2004)	●	○	●	○	○	●	●	Moderate
Kirkley(1999)	●	●	●	●	●	●	○	High
Brouwer(2006)	●	●	●	●	●	●	●	High
Van Raaij(2010)	●	●	●	●	●	●	●	High
Cibere(2004)	●	●	●	●	○	●	●	High
Clegg(2006)	●	○	●	○	●	●	●	Moderate
Hughes(2002)	●	●	●	●	●	●	○	High
Rindone(2000)	●	○	●	●	●	●	○	Moderate
Pavelka(2002)	●	●	●	○	●	●	○	Moderate
McAlindon(2004)	●	●	●	●	●	●	●	High
Houpt(1999)	●	○	●	○	●	●	○	Moderate
Trc(2010)	●	○	●	●	●	●	○	Moderate
Giordano(2009)	●	○	●	○	●	●	○	Moderate
Noack(1994)	●	○	●	○	●	●	○	Moderate
Das(2000)	●	○	●	○	●	●	○	Moderate
Rai(2004)	●	○	●	○	●	●	○	Moderate
Reginster(2001)	●	●	●	○	●	●	●	High
Bourgeois(1998)	●	○	●	●	●	●	○	Moderate
Mazieres(2006)	●	○	●	●	○	●	○	Moderate
Bucsi(1998)	●	○	●	●	●	●	○	Moderate

Mazieres(2001)	●	○	●	●	●	●	○	Moderate
Moller(2010)	●	○	●	○	●	●	○	Moderate
Uebelhart(2004)	●	○	●	●	●	●	○	High
Kahan(2003)	●	●	●	●	●	●	○	High
Pavelka(2010)	●	○	●	○	●	●	○	Moderate
Azad(2011)	●	○	●	○	●	●	●	Moderate
Bennell(2010)	●	●	○	●	●	●	○	Moderate
Huang(2003)	●	●	○	●	●	●	○	Moderate
Jan(2008)	●	○	○	●	●	●	○	Moderate
Lin(2009)	●	●	○	●	●	●	●	High
Topp(2002)	●	○	○	○	●	●	○	Low
Maurer(1999)	●	○	●	○	●	●	●	Moderate
Shakoor(2010)	●	○	●	○	●	●	○	Moderate
Borjesson(1996)	●	○	○	○	●	●	○	Moderate
Deyle(2000)	●	○	●	○	●	●	○	Moderate
Bennell(2005)	●	●	●	●	●	●	●	Moderate
Diracoglu(2005)	●	○	●	●	●	●	○	Moderate
Fitzgerald(2011)	●	●	●	●	●	●	●	Moderate
Yip(2007)	●	○	●	○	●	●	○	Moderate
Coleman(2012)	●	●	●	●	●	●	●	Moderate
Allen(2010)	●	○	●	○	●	●	●	Moderate
Kovar(1992)	●	○	●	○	●	●	○	Moderate
Silva(2008)	●	○	●	●	●	●	○	Moderate
Rejeski(2002)	○	○	○	●	●	●	○	Moderate
Ettinger(1997)	●	○	○	○	●	●	●	Moderate
Focht(2005)	○	○	○	●	●	●	○	Moderate
Jan(2009)	●	○	●	○	●	●	●	Moderate
O'Reilly(1999)	●	●	○	●	●	●	●	High
McCarthy(2004)	●	●	●	●	●	●	○	High
Tunay(2010)	●	○	●	○	●	●	●	Moderate
Ravaud(2009)	●	●	●	●	○	●	○	Moderate
Hurley(2007)	●	○	●	○	○	●	●	Moderate
Ebnezar(2011)	○	○	○	○	●	●	○	Moderate
Ebnezar(2012)	○	○	○	○	●	●	○	Moderate

Rejeski(2002)	○	○	○	●	●	●	○	Low
Focht(2005)	○	○	○	●	●	●	○	Low
Miller(2006)	●	○	●	●	●	●	○	Moderate
Rejeski(2002)	○	○	○	●	●	●	○	Low
Christensen(2005)	●	○	●	○	●	●	○	Moderate
Riecke(2010)	○	○	○	○	●	●	○	Low
Bliddal(2011)	○	○	○	○	●	●	○	Low
Jenkinson(2009)	●	●	●	●	●	●	○	High
Berman(1999)	●	○	○	●	●	●	●	Moderate
Berman(2004)	●	●	●	●	●	●	●	High
Sandgee(2002)	●	○	●	○	●	●	●	Moderate
Suarez-Almazor(2010)	●	●	●	●	●	●	●	High
Taechaarpornkul(2009)	●	●	●	●	●	●	○	High
Vas(2004)	●	○	●	○	●	●	○	Moderate
Witt(2005)	●	○	●	○	●	●	○	Moderate
Williamson(2007)	●	●	○	●	●	●	●	High
Fary(2011)	○	○	○	○	●	●	○	Low
Trock(1994)	●	○	●	○	●	●	○	Moderate
Zizic(1995)	●	○	●	●	●	●	○	Moderate
Battisti(2004)	●	○	●	○	●	●	●	Moderate
Atamaz(2012)	●	○	●	●	○	●	●	Moderate
Perlman(2006)	●	○	○	○	○	●	●	Low
Huang(2005)	●	●	○	●	●	●	○	Moderate
Yang(2011)	●	○	●	○	●	●	●	Moderate
Ehrich(1999)	●	○	●	●	○	●	○	Moderate
Fleischmann(2006)	●	○	●	○	○	●	○	Low
Gibofsky(2003)	●	○	●	●	●	●	○	Moderate
Gottesdiener(2002)	●	●	●	●	●	●	○	High
Kivits(2002)	●	○	●	●	●	●	○	Moderate
Kivitz(2004)	●	●	●	●	●	●	○	High
Lehmann(2005)	●	○	●	○	●	●	○	Moderate
Luyten(2007)	●	○	●	●	○	●	○	Moderate
Mckenna(2001)	●	○	●	●	●	●	○	Moderate

Schnitzer(2005)	●	○	●	○	●	●	○	Moderate
Schnitzer(2009)	●	○	●	○	●	●	○	Moderate
Schnitzer(2010)	●	○	●	●	●	●	○	Moderate
Tannenbaum(2004)	●	○	●	●	●	●	○	Moderate
Williams(2000)	●	○	●	●	●	●	○	Moderate
Williams(2001)	●	○	●	●	●	●	○	Moderate
Fleischmann(2006)	●	○	●	○	○	●	○	Moderate
Williams(2001)	●	○	●	○	○	●	○	Low
Astorga(1991)	●	○	●	○	●	●	○	Moderate
Goregaonkar(2009)	●	○	●	●	●	●	○	Moderate
Ayral(2003)	●	○	●	○	●	●	○	Moderate
Bellamy(1993)	●	○	●	○	●	●	○	Moderate
Bradley(1991)	●	○	●	○	●	●	●	Moderate
Chubick(1987)	●	○	●	○	●	●	○	Moderate
Dick(1992)	●	○	●	○	●	●	○	Moderate
Evcik(2003)	●	○	○	○	●	●	○	Low
Herrera(2007)	●	○	●	○	●	●	○	Moderate
Karbowski(1991)	●	○	●	○	●	●	○	Moderate
Kogstad(1981)	●	○	●	○	●	●	○	Moderate
La Montagna(1998)	●	○	●	○	●	●	○	Moderate
Liang(2003)	●	○	●	○	●	●	○	Moderate
Lucker(1994)	●	○	●	●	●	●	○	Moderate
Queiros(1990)	●	○	●	○	●	●	○	Moderate
Schnitzer	●	○	●	○	●	●	○	Moderate
Tyson(1980)	●	○	●	○	●	●	○	Moderate
Bookman(2004)	●	●	●	●	●	●	○	High
Barthel(2009)	●	○	●	○	●	●	○	Moderate
Bookman(2004)	●	○	●	○	●	●	○	Moderate
Roth(2004)	●	●	●	●	●	●	○	High
Baer(2005)	●	●	●	●	●	●	○	High
Rother(2007)	●	○	●	○	●	●	○	Moderate
Ottillinger(2001)	●	○	●	●	●	●	○	Moderate
Torri(1994)	●	○	●	●	●	●	○	Moderate
Lee(1985)	●	○	●	●	●	●	○	Moderate

Lohmander(2005)	●	○	●	○	○	●	○	Low
Lohmander(2005)	●	○	●	○	○	●	○	Moderate
Gualda(2007)	●	●	●	●	●	●	○	High
Micelli(2004)	●	○	●	○	●	●	●	Moderate
Louthrenoo(2007)	●	○	●	○	●	●	○	Moderate
Pavelka(2007)	●	○	●	●	●	●	○	Moderate
Zheng(2006)	●	○	●	●	●	●	○	Moderate
Babul(2004)	●	○	●	○	●	●	○	Moderate
Beaulieu(2008)	●	○	●	○	●	●	○	Moderate
Burch(2007)	●	○	●	○	●	●	○	Moderate
Fishman(2007)	●	●	●	●	●	●	○	High
Fleischmann(2001)	●	●	●	●	●	●	○	High
Schnitzer(1999)	●	○	●	○	●	●	○	Moderate
McIlwain(1989)	●	○	●	●	●	●	○	Moderate
Jones(1996)	●	○	●	○	●	●	○	Moderate
Chao(2010)	●	○	●	●	●	●	○	Moderate
Gaffney(1995)	●	○	●	○	●	●	○	Moderate
Raynauld(2003)	●	○	●	○	●	●	●	Moderate
Caborn(2004)	●	○	●	○	●	●	○	Moderate
Arden(2008)	●	●	●	○	●	●	○	Moderate
Heybeli(2008)	●	○	●	●	●	●	○	Moderate
Lundsgaard(2008)	●	●	●	●	●	●	○	High
Altman(2009)	●	○	●	○	●	●	○	Moderate
Altman(2004)	●	○	●	○	●	●	○	Moderate
Day(2004)	●	○	●	○	○	●	○	Moderate
Jorgensen(2010)	●	○	●	○	●	●	●	Moderate
Kahan(2003)	●	○	○	●	●	●	○	Moderate
Karlsson(2002)	●	○	●	○	●	●	○	Moderate
Petrella(2006)	●	○	●	○	●	●	○	Moderate
Wobig(1998)	●	○	●	○	●	●	○	Moderate
Navarro-Sarabia(2011)	●	○	●	○	●	●	○	Moderate
Huang(2011)	●	○	●	●	●	●	●	High
Chevalier(2010)	●	○	●	○	●	●	○	Moderate
Puhl(1993)	●	●	●	●	●	●	○	High

Juni(2007)	●	●	●	●	●	●	●	High
Berenbaum(2012)	●	●	●	○	●	●	○	Moderate
Lee(2006)	●	○	●	○	○	●	○	Low
Raman(2008)	●	○	●	○	○	●	●	Moderate
Wobig(1999)	●	○	●	○	●	●	○	Moderate
Maheu(2011)	●	●	●	●	●	●	○	High
Pavelka(2011)	●	○	●	●	●	●	○	Moderate
Sanchez(2008)	○	○	○	○	●	●	○	Low
Sanchez(2012)	●	●	●	●	●	●	●	High
Spakova(2012)	●	○	●	●	●	●	○	Moderate
Bradley(2002)	●	●	●	●	●	●	●	High
Vad(2003)	●	○	●	○	●	●	●	Moderate
Moseley(2002)	●	●	●	●	●	●	●	High
Kalunian(2000)	●	○	●	○	○	●	●	Moderate
Kirkley(2008)	●	○	●	○	●	●	●	Moderate
Moseley(2000)	●	●	●	●	●	●	●	High
Herrlin(2007)	●	○	●	○	●	●	○	Moderate
Song(2012)	○	○	○	○	●	●	○	Low

PICO 1: Assisted Devices

Insoles vs Control

Table 1: Insole vs Control

Quality: H=High; M=Moderate; L=Low	H					
↑ Better Outcomes ↓ Worse Outcomes • Not Significant	Pham; 2004	Toda; 2008	Hatef; 2014	Bennell; 2011	Maillefert; 2001	Baker; 2007
Composite						
Global assessment	•					
Lequesne Index		•				
Function						
Physical Activity Scale for the Elderly				•		
Edinburgh Knee Function Scale			↑			
No. of Daily Steps				↑		
Pain						
VAS Pain Severe (61-80)			↑			
VAS Pain Very Severe (81-100)			↑			
calculable MID outcomes						
WOMAC Function	•			•		
WOMAC Stiffness	•			•	•	
WOMAC Pain	•			•	↓	•
WOMAC Physical function					•	
VAS Pain		↑		•		
VAS Pain (Walking)				•		
QOL						
AQoL				•		
NSAID use						
Number of NSAIDs used during last 2 weeks (1-3)			•			
Number of NSAIDs used during last 2 weeks (4-8)			•			
Number of NSAIDs used during last 2 weeks (9-12)			•			
Number of NSAIDs used during last 2 weeks (>12)			•			
Number of NSAIDs used during last 2 weeks (Total)			•			

Evidence Table 1: Insole vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Pain:VAS Pain	52 wks	89/90	3.1(2.1)/3.1(2.3)	Mean Diff	0(-0.65,0.65)	Not Sig.	clinically insignificant
Toda; 2008/High	1: Insoles-Strapped Insole w/ Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Pain:VAS Pain	12 wks	41/38	29.4(19.4)/46.5(15.3)	Mean Diff	-17.1(-24.9,-9.3)	Group 1	possibly clinically significant
Toda; 2008/High	1: Insoles-Strapped Insole w/o Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Pain:VAS Pain	12 wks	44/38	27.4(20)/46.5(15.3)	Mean Diff	-19.1(-26.87,-11.33)	Group 1	possibly clinically significant
Toda; 2008/High	1: Insoles-Inserted Insole w/o Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Pain:VAS Pain	12 wks	41/38	42(25.4)/46.5(15.3)	Mean Diff	-4.5(-13.84, 4.84)	Not Sig.	clinically insignificant
Toda; 2008/High	1: Insoles-Inserted Insole w/ Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Pain:VAS Pain	12 wks	43/38	41.9(23.1)/46.5(15.3)	Mean Diff	-4.6(-13.19, 3.99)	Not Sig.	clinically insignificant
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Pain:VAS Pain (Walking)	52 wks	89/90	3.2(2.1)/3(2.5)	Mean Diff	0.2(-0.48,0.88)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Pain:VAS Pain Mild (21-40)	8 wks	75/75	37.33%/5.33%	RR	7(2.58, 18.98)	Group 2	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Pain:VAS Pain Moderate (41-60)	8 wks	75/75	28%/26.67%	RR	1.05(0.62,1.77)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Pain:VAS Pain None to scant (0-20)	8 wks	75/75	9.33%/1.33%	RR	7(0.88, 55.51)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Pain:VAS Pain Severe (61-80)	8 wks	75/75	4%/24%	RR	0.17(0.05,0.54)	Group 1	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Pain:VAS Pain Very Severe (81-100)	8 wks	75/75	1.33%/24%	RR	0.06(0.01,0.41)	Group 1	na
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Pain:WOMAC Pain	52 wks	89/90	6.4(3.3)/6.2(3.2)	Mean Diff	0.2(-0.76,1.16)	Not Sig.	clinically insignificant
Baker; 2007/High	1: Insoles-Wedge sole to Neutral sole	1: Insoles-Neutral sole to Wedge sole	Pain:WOMAC Pain	12 wks	46/41	13.8(59.43)/14.5(119.28)	Mean Diff	-0.7(-41.92, 40.52)	Not Sig.	inconclusive
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Pain:WOMAC Pain	1 mos	82/74	54.1(19)/48.9(18)	Mean Diff	5.2(-0.65,11.05)	Not Sig.	inconclusive
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Pain:WOMAC Pain	3 mos	82/74	53.4(21)/48.2(17)	Mean Diff	5.2(-0.82,11.22)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Pain:WOMAC Pain	6 mos	82/74	52.8(22)/46.4(18)	Mean Diff	6.4(0.07,12.73)	Group 2	possibly clinically significant
Pham; 2004/High	1: Insoles-Lateral Wedge insole	1: Insoles-neutral insole	Pain:WOMAC pain	24 mos	74/82	51(26.7)/48.2(19.9)	Mean Diff	2.8(-4.72,10.32)	Not Sig.	inconclusive
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Function:Edinburgh Knee Function Scale (1-6)	8 wks	75/75	9.33%/2.67%	RR	3.5(0.75,16.3)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Function:Edinburgh Knee Function Scale (13-18)	8 wks	75/75	17.33%/25.33%	RR	0.68(0.36,1.28)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Function:Edinburgh Knee Function Scale (19-24)	8 wks	75/75	5.33%/21.33%	RR	0.25(0.09,0.71)	Group 1	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Function:Edinburgh Knee Function Scale (25-30)	8 wks	75/75	2.67%/14.67%	RR	0.18(0.04,0.79)	Group 1	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Function:Edinburgh Knee Function Scale (31-36)	8 wks	75/75	0%/1.33%	RD	-1.333(-6.328, 4.507)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	Function:Edinburgh Knee Function Scale (7-12)	8 wks	75/75	41.33%/16%	RR	2.58(1.44,4.63)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Function:No. of Daily Steps	52 wks	89/90	8059(4946)/6688(4106)	Mean Diff	1371(29,2713)	Group 1	na
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Function:Physical Activity Scale for the Elderly	52 wks	89/90	167(83)/167(88)	Mean Diff	0(-25.23, 25.23)	Not Sig.	na
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Function:WOMAC Function	52 wks	89/90	20.8(12.2)/20.1(11.6)	Mean Diff	0.7(-2.81,4.21)	Not Sig.	clinically insignificant
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Function:WOMAC Physical function	1 mos	82/74	51.6(18)/49(19)	Mean Diff	2.6(-3.27,8.47)	Not Sig.	inconclusive
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Function:WOMAC Physical function	3 mos	82/74	52.4(20)/47.2(18)	Mean Diff	5.2(-0.81,11.21)	Not Sig.	inconclusive
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Function:WOMAC Physical function	6 mos	82/74	53.3(20)/47.3(20)	Mean Diff	6(-0.34,12.34)	Not Sig.	inconclusive
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	Function:WOMAC Stiffness	52 wks	89/90	3(2)/3(2)	Mean Diff	0(-0.59,0.59)	Not Sig.	clinically insignificant
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Function:WOMAC Stiffness	3 mos	82/74	53(24)/48.8(18)	Mean Diff	4.2(-2.47,10.87)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Function:WOMAC Stiffness	6 mos	82/74	51.4(24)/47.1(22)	Mean Diff	4.3(-2.98,11.58)	Not Sig.	inconclusive
Maillefert; 2001/High	1: Insoles-Laterally wedged insole	1: Insoles-Neutrally wedged insole	Function:WOMAC Stiffness	1 mos	82/74	54(23)/48.5(23)	Mean Diff	5.5(-1.79,12.79)	Not Sig.	inconclusive
Pham; 2004/High	1: Insoles-Lateral Wedge insole	1: Insoles-neutral insole	Function:WOMAC function	24 mos	74/82	50(26.4)/50.4(21.1)	Mean Diff	-0.4(-8.02,7.22)	Not Sig.	inconclusive
Pham; 2004/High	1: Insoles-Lateral Wedge insole	1: Insoles-neutral insole	Function:WOMAC stiffness	24 mos	74/82	51.8(27.3)/50(19.7)	Mean Diff	1.8(-5.81,9.41)	Not Sig.	clinically insignificant
Pham; 2004/High	1: Insoles-Lateral Wedge insole	1: Insoles-neutral insole	Composite:Global assessment	24 wks	74/82	-4.7(22.5)/-5.8(26.1)	Mean Diff	1.1(-6.59,8.79)	Not Sig.	na
Toda; 2008/High	1: Insoles-Strapped Insole w/ Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Composite:Lequesne Index	12 wks	41/38	6.8(5.1)/8.1(5)	Mean Diff	-1.3(-3.56,0.96)	Not Sig.	na
Toda; 2008/High	1: Insoles-Strapped Insole w/o Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Composite:Lequesne Index	12 wks	44/38	6.2(5.3)/8.1(5)	Mean Diff	-1.9(-4.17,0.37)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Toda; 2008/High	1: Insoles-Inserted Insole w/o Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Composite:Lequesne Index	12 wks	41/38	8.4(5.8)/8.1(5)	Mean Diff	0.3(-2.12,2.72)	Not Sig.	na
Toda; 2008/High	1: Insoles-Inserted Insole w/ Shoes(5-10hrs/day)	1: Placebo/Control-Control (Placebo Insole w/ Shoes)(5-10hrs/day)	Composite:Lequesne Index	12 wks	43/38	9.1(5.3)/8.1(5)	Mean Diff	1(-1.28,3.28)	Not Sig.	na
Bennell; 2011/High	1: Insoles-Lateral Wedge Insole(everyday)	1: Placebo/Control-Placebo (Control Insole)(everyday)	QOL:AQoL	52 wks	89/90	0.7(0.2)/0.7(0.2)	Mean Diff	0(-0.06,0.06)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	NSAID use:Number of NSAIDs used during last 2 weeks (1-3)	8 wks	75/75	4%/5.33%	RR	0.75(0.17,3.24)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	NSAID use:Number of NSAIDs used during last 2 weeks (4-8)	8 wks	75/75	4%/10.67%	RR	0.38(0.1,1.36)	Not Sig.	na

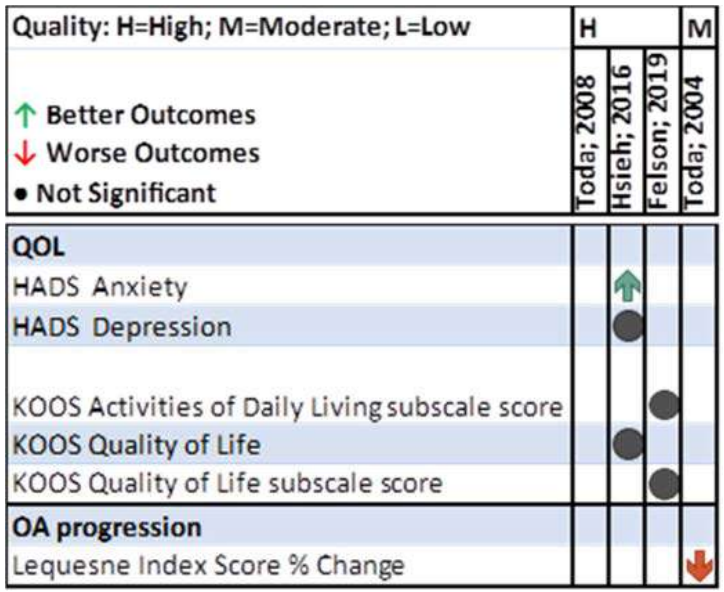
study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	NSAID use:Number of NSAIDs used during last 2 weeks (9-12)	8 wks	75/75	2.67%/5.33%	RR	0.5(0.09,2.65)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	NSAID use:Number of NSAIDs used during last 2 weeks (>12)	8 wks	75/75	2.67%/9.33%	RR	0.29(0.06,1.33)	Not Sig.	na
Hatef; 2014/High	1: Insoles-Lateral Wedged Insoles	1: Insoles-Neutral Wedged Insoles	NSAID use:Number of NSAIDs used during last 2 weeks (Total)	8 wks	75/75	62.67%/50.67%	RR	1.24(0.93,1.64)	Not Sig.	na

PICO 1: Assisted Devices

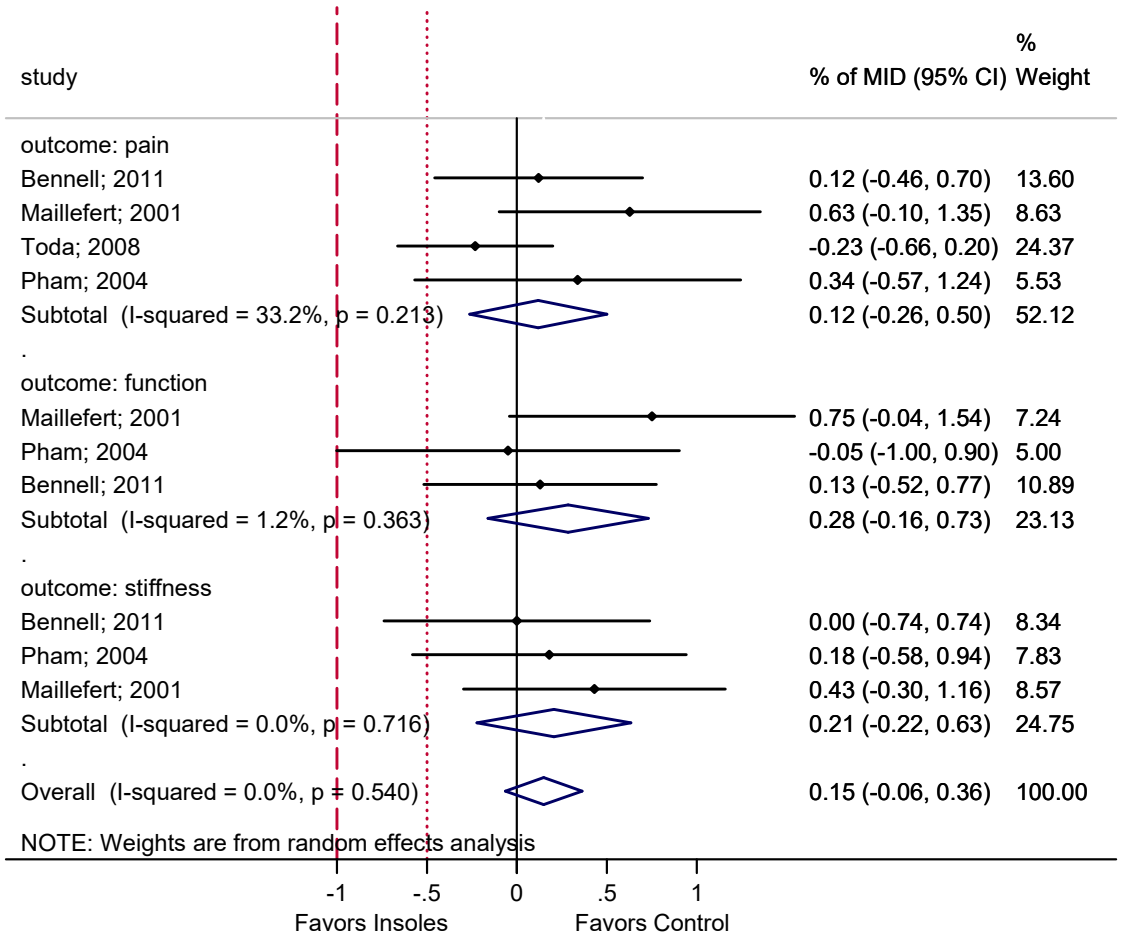
Insoles vs Insole

Table 2: Insole vs Insole

Quality: H=High; M=Moderate; L=Low	H			M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Toda; 2008	Hsieh; 2016	Felson; 2019	Toda; 2004
Composite				
Lequesne Index	↑			
Lequesne Index Score				↓
Function				
10m Walk Test (s)		●		
Chair Rising Time (s)		●		
Chronic Pain Grade Disability Points		●		
Chronic Pain Grade Disability Score		●		
Fall Risk Biodex Stability System Measurement		↑		
KOOS Activities of Daily Living		●		
KOOS Sports & Recreation subscale score			●	
KOOS Sports/Recreation		●		
KOOS Symptoms		●		
Limits of Stability Biodex Stability System Measurement		↓		
Postural Stability Biodex Stability System Measurement		●		
Stair Ascent Time (s)		↑		
Stair Descent Time (s)		↑		
Pain				
KOOS Pain		●		
KOOS Pain subscale score			●	
KOOS Symptom subscale score			●	
Pain in nominated activity			↑	
Pain in the last week			↑	
Adverse events				
Any Pain				↓
Foot Pain				●
Low Back Pain				●
Popliteal Pain				●
calculable MID outcomes				
VAS Pain	↓			



Meta-Analysis Figure 1: Laterally Wedged Insoles vs Control Insoles



Evidence Table 2: Acupressure vs Sham- Function

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Pain:KOOS Pain	3 mos	45/45	41.55(17.57)/47.68(14.42)	Mean Diff	-6.13(-12.87, 0.61)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Pain:KOOS Pain	2 mos	45/45	42.89(15.75)/42.83(14.91)	Mean Diff	0.06(-6.37,6.49)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Pain:KOOS Pain	1 mos	45/45	41.1(13.64)/38.2(15.77)	Mean Diff	2.9(-3.28,9.08)	Not Sig.	na
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	Pain:KOOS Pain subscale score	8 wks	83	none	Mean Diff	1.84(-2.62,6.31)	Not Sig.	na
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	Pain:KOOS Symptom subscale score	8 wks	83	none	Mean Diff	1.23(-2.65,5.11)	Not Sig.	na
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	Pain:Pain in nominated activity	8 wks	83	none	Mean Diff	-0.97(-1.61,-0.32)	Group 1	na
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	Pain:Pain in the last week	8 wks	83	none	Mean Diff	-0.7(-1.27,-0.12)	Group 1	na
Toda; 2008/High	1: Insoles-Strapped Insole w/ Shoes(5-10hrs/day)	1: Insoles-Inserted Insole w/ Shoes(5-10hrs/day)	Pain:VAS Pain	12 wks	41/43	29.4(19.4)/41.9(23.1)	Mean Diff	-12.5(-21.75,-3.25)	Group 1	possibly clinically significant
Toda; 2008/High	1: Insoles-Inserted Insole w/o Shoes(5-10hrs/day)	1: Insoles-Inserted Insole w/ Shoes(5-10hrs/day)	Pain:VAS Pain	12 wks	41/43	42(25.4)/41.9(23.1)	Mean Diff	0.1(-10.46, 10.66)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Toda; 2008/High	1: Insoles-Inserted Insole w/o Shoes(5-10hrs/day)	1: Insoles-Strapped Insole w/o Shoes(5-10hrs/day)	Pain:VAS Pain	12 wks	41/44	42(25.4)/27.4(20)	Mean Diff	14.6(4.68,24.52)	Group 2	possibly clinically significant
Toda; 2008/High	1: Insoles-Strapped Insole w/ Shoes(5-10hrs/day)	1: Insoles-Strapped Insole w/o Shoes(5-10hrs/day)	Pain:VAS Pain	12 wks	41/44	29.4(19.4)/27.4(20)	Mean Diff	2(-6.5,10.5)	Not Sig.	clinically insignificant
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:10 m Walk Test (s)	3 mos	45/45	8.03(1.43)/8.39(2.22)	Mean Diff	-0.36(-1.14,0.42)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:10 m Walk Test (s)	2 mos	45/45	7.97(1.45)/8.61(2.12)	Mean Diff	-0.64(-1.4,0.12)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:10 m Walk Test (s)	1 mos	45/45	7.96(1.73)/8.76(2.39)	Mean Diff	-0.8(-1.68,0.08)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chair Rising Time (s)	2 mos	45/45	15.34(4.32)/16.18(5.13)	Mean Diff	-0.84(-2.83,1.15)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chair Rising Time (s)	3 mos	45/45	14.36(3.65)/15.55(6.42)	Mean Diff	-1.19(-3.39,1.01)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chair Rising Time (s)	1 mos	45/45	15.58(4.95)/17.03(5.7)	Mean Diff	-1.45(-3.69,0.79)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chronic Pain Grade Disability Points	3 mos	45/45	2.98(1.76)/3.38(2.3)	Mean Diff	-0.4(-1.26,0.46)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chronic Pain Grade Disability Points	2 mos	45/45	3.44(2.08)/4.22(2.34)	Mean Diff	-0.78(-1.71,0.15)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chronic Pain Grade Disability Points	1 mos	45/45	3.38(2.23)/4.3(2.26)	Mean Diff	-0.92(-1.86,0.02)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chronic Pain Grade Disability Score	3 mos	45/45	29.72(16.72)/32.11(23.11)	Mean Diff	-2.39(-10.85, 6.07)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chronic Pain Grade Disability Score	2 mos	45/45	35.58(20.64)/40.41(22.68)	Mean Diff	-4.83(-13.92, 4.26)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Chronic Pain Grade Disability Score	1 mos	45/45	33.82(21.57)/38.94(23.15)	Mean Diff	-5.12(-14.49, 4.25)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Fall Risk Biodex Stability System Measurement	1 mos	45/45	2.19(1.76)/2.35(1.52)	Mean Diff	-0.16(-0.85,0.53)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Fall Risk Biodex Stability System Measurement	3 mos	45/45	2.24(1.65)/2.62(1.91)	Mean Diff	-0.38(-1.13,0.37)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Fall Risk Biodex Stability System Measurement	2 mos	45/45	1.9(1)/2.52(1.75)	Mean Diff	-0.62(-1.22,-0.02)	Group 1	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Activities of Daily Living	3 mos	45/45	44.8(16.3)/47.99(14.44)	Mean Diff	-3.19(-9.64,3.26)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Activities of Daily Living	2 mos	45/45	47.47(16.24)/44.56(14.27)	Mean Diff	2.91(-3.5,9.32)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Activities of Daily Living	1 mos	45/45	44.54(14.06)/40.85(14.34)	Mean Diff	3.69(-2.26,9.64)	Not Sig.	na
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	Function:KOOS Sports & Recreation subscale score	8 wks	83	none	Mean Diff	1.36(-4.26,6.97)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Sports/Recreation	2 mos	45/45	21.56(22.47)/26.18(21.89)	Mean Diff	-4.62(-13.91, 4.67)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Sports/Recreation	3 mos	45/45	23.07(23.73)/27.84(20.77)	Mean Diff	-4.77(-14.11, 4.57)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Sports/Recreation	1 mos	45/45	23.72(25.1)/16.09(22.31)	Mean Diff	7.63(-2.32,17.58)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Symptoms	1 mos	45/45	35.74(15.11)/37.52(16.47)	Mean Diff	-1.78(-8.4,4.84)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Symptoms	2 mos	45/45	36.98(17.18)/39.26(17.43)	Mean Diff	-2.28(-9.53,4.97)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:KOOS Symptoms	3 mos	45/45	36.23(15.48)/41.54(15.05)	Mean Diff	-5.31(-11.71, 1.09)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Limits of Stability Biodex Stability System Measurement	1 mos	45/45	46.81(13.24)/47.91(13.42)	Mean Diff	-1.1(-6.68,4.48)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Limits of Stability Biodex Stability System Measurement	2 mos	45/45	45.25(12.94)/50.07(13.86)	Mean Diff	-4.82(-10.44, 0.8)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Limits of Stability Biodex Stability System Measurement	3 mos	45/45	44.18(13.97)/49.97(11.73)	Mean Diff	-5.79(-11.2,-0.38)	Group 2	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Postural Stability Biodex Stability System Measurement	3 mos	45/45	0.63(0.35)/0.68(0.4)	Mean Diff	-0.05(-0.21,0.11)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Postural Stability Biodex Stability System Measurement	1 mos	45/45	0.73(0.36)/0.84(0.51)	Mean Diff	-0.11(-0.3,0.08)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Postural Stability Biodex Stability System Measurement	2 mos	45/45	0.66(0.3)/0.92(0.84)	Mean Diff	-0.26(-0.53,0.01)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Stair Ascent Time (s)	3 mos	45/45	10.76(3.3)/11.65(4.25)	Mean Diff	-0.89(-2.49,0.71)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Stair Ascent Time (s)	2 mos	45/45	10.8(2.54)/12.44(4.24)	Mean Diff	-1.64(-3.11,-0.17)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Stair Ascent Time (s)	1 mos	45/45	10.77(2.83)/13.14(5.04)	Mean Diff	-2.37(-4.09,-0.65)	Group 1	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Stair Descent Time (s)	3 mos	45/45	10.16(3)/10.95(4.07)	Mean Diff	-0.79(-2.29,0.71)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Stair Descent Time (s)	1 mos	45/45	10.2(3.15)/12.36(5.4)	Mean Diff	-2.16(-4.02,-0.3)	Group 1	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	Function:Stair Descent Time (s)	2 mos	45/45	10.28(3.22)/12.54(5.81)	Mean Diff	-2.26(-4.24,-0.28)	Group 1	na
Toda; 2008/High	1: Insoles-Inserted Insole w/o Shoes(5-10hrs/day)	1: Insoles-Inserted Insole w/ Shoes(5-10hrs/day)	Composite:Lequesne Index	12 wks	41/43	8.4(5.8)/9.1(5.3)	Mean Diff	-0.7(-3.12,1.72)	Not Sig.	na
Toda; 2008/High	1: Insoles-Strapped Insole w/ Shoes(5-10hrs/day)	1: Insoles-Inserted Insole w/ Shoes(5-10hrs/day)	Composite:Lequesne Index	12 wks	41/43	6.8(5.1)/9.1(5.3)	Mean Diff	-2.3(-4.56,-0.04)	Group 1	na
Toda; 2008/High	1: Insoles-Strapped Insole w/ Shoes(5-10hrs/day)	1: Insoles-Strapped Insole w/o Shoes(5-10hrs/day)	Composite:Lequesne Index	12 wks	41/44	6.8(5.1)/6.2(5.3)	Mean Diff	0.6(-1.64,2.84)	Not Sig.	na
Toda; 2008/High	1: Insoles-Inserted Insole w/o Shoes(5-10hrs/day)	1: Insoles-Strapped Insole w/o Shoes(5-10hrs/day)	Composite:Lequesne Index	12 wks	41/44	8.4(5.8)/6.2(5.3)	Mean Diff	2.2(-0.2,4.6)	Not Sig.	na
Toda; 2004/Moderate	1: Insoles-Rubber Insole(3-6 hr/day x 4wks)	1: Insoles-Urethane Insole(3-6 hr/day x 4wks)	Composite:Lequesne Index Score	4 wks	42/42	6.6(5.1)/4.4(4.7)	Mean Diff	2.2(0.07,4.33)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:HADS Anxiety	3 mos	45/45	6.84(3.45)/7.08(3.25)	Mean Diff	-0.24(-1.64,1.16)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:HADS Anxiety	1 mos	45/45	6.05(4.27)/7.52(3.87)	Mean Diff	-1.47(-3.18,0.24)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:HADS Anxiety	2 mos	45/45	5.98(3.64)/7.86(3.82)	Mean Diff	-1.88(-3.44,-0.32)	Group 1	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:HADS Depression	3 mos	45/45	7.08(3.03)/7.49(3.17)	Mean Diff	-0.41(-1.71,0.89)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:HADS Depression	2 mos	45/45	6.83(3)/7.86(3.06)	Mean Diff	-1.03(-2.3,0.24)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:HADS Depression	1 mos	45/45	6.9(2.72)/8.03(2.73)	Mean Diff	-1.13(-2.27,0.01)	Not Sig.	na
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	QOL:KOOS Activities of Daily Living subscale score	8 wks	83	none	Mean Diff	1.28(-2.62,5.19)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:KOOS Quality of Life	2 mos	45/45	21.61(22.07)/26.47(18.9)	Mean Diff	-4.86(-13.47, 3.75)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:KOOS Quality of Life	3 mos	45/45	24.62(20.89)/32.6(17.65)	Mean Diff	-7.98(-16.08, 0.12)	Not Sig.	na
Hsieh; 2016/High	P1: Insoles-Lateral Insole (Rigid)	P1: Insoles-Lateral Insole (Soft)	QOL:KOOS Quality of Life	1 mos	45/45	22.37(22.47)/20.22(19.87)	Mean Diff	2.15(-6.74,11.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Felson; 2019/High	1: Insoles-Neutral insole(4+ hours daily for 6 months)	1: Insoles-Lateral wedge(4+ hours daily for 8 weeks)	QOL:KOOS Quality of Life subscale score	8 wks	83	none	Mean Diff	0.09(-4.47,4.64)	Not Sig.	na
Toda; 2004/Moderate	1: Insoles-Rubber Insole(3-6 hr/day x 4wks)	1: Insoles-Urethane Insole(3-6 hr/day x 4wks)	OA progression:Lequesne Index Score % Change	4 wks	42/42	-24(51.9)/-58.4(34.9)	Mean Diff	34.4(15.16,53.64)	Group 2	na
Toda; 2004/Moderate	1: Insoles-Rubber Insole(3-6 hr/day x 4wks)	1: Insoles-Urethane Insole(3-6 hr/day x 4wks)	Adverse events:Any Pain	4 wks	42/42	40.48%/19.05%	RR	2.13(1.03,4.38)	Group 2	na
Toda; 2004/Moderate	1: Insoles-Rubber Insole(3-6 hr/day x 4wks)	1: Insoles-Urethane Insole(3-6 hr/day x 4wks)	Adverse events:Foot Pain	4 wks	42/42	19.05%/9.52%	RR	2(0.65, 6.14)	Not Sig.	na
Toda; 2004/Moderate	1: Insoles-Rubber Insole(3-6 hr/day x 4wks)	1: Insoles-Urethane Insole(3-6 hr/day x 4wks)	Adverse events:Low Back Pain	4 wks	42/42	7.14%/2.38%	RR	3(0.33, 27.69)	Not Sig.	na
Toda; 2004/Moderate	1: Insoles-Rubber Insole(3-6 hr/day x 4wks)	1: Insoles-Urethane Insole(3-6 hr/day x 4wks)	Adverse events:Popliteal Pain	4 wks	42/42	14.29%/7.14%	RR	2(0.54, 7.47)	Not Sig.	na

PICO 1: Assisted Devices

Canes vs Control

Table 3: Canes vs. Control

Quality: H=High; M=Moderate; L=Low	H	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Jones; 2012	van Ginckel; 2019
Composite		
Lequesne Index Score	↑	
Function		
Physical Activity Scale for the Elderly		●
6MWT (m)(With Cane)	↑	
6MWT (m)(Without Cane)	●	
Avg Step Count		●
SF-36 Role Physical	↑	
Pain		
NRS Avg Knee Pain		●
NRS Avg Walking Knee Pain		●
NRS Avg Walking Knee Pain (non-study knee)		●
calculable MID outcomes		
WOMAC Total	●	
WOMAC Function		●
WOMAC Pain		●
VAS Pain	↑	
SF-36 Physical Functioning	↑	
SF-36 Bodily Pain	↑	
QOL		
Assessment of QoL 6D		●
SF-36 Role Emotional	↑	
SF-36 Social Functioning	●	
SF-36 Vitality	↑	
SF-36 General Health	●	
SF-36 Mental Health	●	

Evidence Table 31: Canes vs. Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QoL:SF-36 General Health	60 days	30/29	58.87(24.13)/56.81(23.55)	Mean Diff	2.06(-10.37, 14.49)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QoL:SF-36 General Health	30 days	31/30	55.97(19.99)/51.7(18.97)	Mean Diff	4.27(-5.71,14.25)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QoL:SF-36 Mental Health	30 days	31/30	52(21.82)/46.1(18.42)	Mean Diff	5.9(-4.44,16.24)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QoL:SF-36 Mental Health	60 days	30/29	58.85(19.62)/51.1(20.79)	Mean Diff	7.75(-2.8,18.3)	Not Sig.	na
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Pain:NRS Avg Knee Pain	3 mos	40/38	4.1(2.2)/3.6(2.2)	Mean Diff	0.5(-0.49,1.49)	Not Sig.	na
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Pain:NRS Avg Walking Knee Pain	3 mos	40/38	4.4(2.3)/4.3(2.1)	Mean Diff	0.1(-0.89,1.09)	Not Sig.	na
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Pain:NRS Avg Walking Knee Pain (non-study knee)	3 mos	40/38	2.3(2)/2.1(2.4)	Mean Diff	0.2(-0.8,1.2)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Pain:SF-36 Bodily Pain	60 days	30/29	60.19(19.38)/46.03(20.34)	Mean Diff	14.16(3.79,24.53)	Group 1	possibly clinically significant
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Pain:SF-36 Bodily Pain	30 days	31/30	53.16(17.59)/47.7(23)	Mean Diff	5.46(-5.07,15.99)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Pain:VAS Pain	30 days	31/30	5.28(0.92)/6.05(1.35)	Mean Diff	-0.77(-1.37,-0.17)	Group 1	clinically insignificant
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Pain:VAS Pain	60 days	30/29	3.84(1.44)/5.95(1.4)	Mean Diff	-2.11(-2.85,-1.37)	Group 1	possibly clinically significant
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Pain:WOMAC Pain	3 mos	40/38	6.3(3.4)/5.8(2.8)	Mean Diff	0.5(-0.9,1.9)	Not Sig.	inconclusive
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:6MWT (m)(With Cane)	30 days	31/30	377.88(37.3)/326.63(35.52)	Mean Diff	51.25(32.59, 69.91)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:6MWT (m)(With Cane)	60 days	30/29	404.22(51.85)/320.94(25.12)	Mean Diff	83.28(61.99, 104.57)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:6MWT (m)(Without Cane)	60 days	30/29	399.59(43.13)/406.09(26.61)	Mean Diff	-6.5(-25.19, 12.19)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:6MWT (m)(Without Cane)	30 days	31/30	392.15(49.45)/401.65(24.74)	Mean Diff	-9.5(-29.58, 10.58)	Not Sig.	na
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Function:Avg Step Count	3 mos	40/38	5409(2773)/5549(2972)	Mean Diff	-140(-1438.23,1158.23)	Not Sig.	na
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Function:Physical Activity Scale for the Elderly	3 mos	40/38	175.5(99.1)/158.4(73.8)	Mean Diff	17.1(-22.21, 56.41)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:SF-36 Physical Functioning	30 days	31/30	37.13(14.78)/33.9(15.59)	Mean Diff	3.23(-4.56,11.02)	Not Sig.	inconclusive
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:SF-36 Physical Functioning	60 days	30/29	45(15.08)/35.94(18.94)	Mean Diff	9.06(0.1,18.02)	Group 1	possibly clinically significant
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:SF-36 Role Physical	60 days	30/29	42.81(30.21)/26.06(28.33)	Mean Diff	16.75(1.49,32.01)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Function:SF-36 Role Physical	30 days	31/30	32.97(29.64)/24.34(31.51)	Mean Diff	8.63(-7.06,24.32)	Not Sig.	na
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	Function:WOMAC Activities of Daily Living	3 mos	40/38	19.5(10)/20.5(7.1)	Mean Diff	-1(-4.9,2.9)	Not Sig.	clinically insignificant
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Composite:Lequesne Index Score	30 days	31/30	14.28(3.53)/14.6(3.53)	Mean Diff	-0.32(-2.13,1.49)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Composite:Lequesne Index Score	60 days	30/29	12.56(3.47)/15.09(3.6)	Mean Diff	-2.53(-4.37,-0.69)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Composite:WOMAC Total	60 days	30/29	46.22(15.88)/47.28(14.71)	Mean Diff	-1.06(-9.04,6.92)	Not Sig.	inconclusive
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	Composite:WOMAC Total	30 days	31/30	49.56(15.05)/47.7(15.36)	Mean Diff	1.86(-5.93,9.65)	Not Sig.	inconclusive
van Ginckel; 2019/Moderate	P1: Cane-Cane (generic "swan neck")(daily for 3 mo)	P1: Placebo/Control-Control (No Cane)	QOL:Assessment of QoL 6D	3 mos	40/38	0.8(0.1)/0.8(0.2)	Mean Diff	0(-0.07,0.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QOL:SF-36 Role Emotional	30 days	31/30	36.71(31.62)/19.3(23.9)	Mean Diff	17.41(3.06,31.76)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QOL:SF-36 Role Emotional	60 days	30/29	42.98(29.63)/24.9(29.37)	Mean Diff	18.08(2.7,33.46)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QOL:SF-36 Social Functioning	30 days	31/30	54.89(20.02)/49.5(20.8)	Mean Diff	5.39(-5.08,15.86)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QOL:SF-36 Social Functioning	60 days	30/29	57.16(17.29)/49.22(19.56)	Mean Diff	7.94(-1.7,17.58)	Not Sig.	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QOL:SF-36 Vitality	60 days	30/29	54.09(26.28)/38.59(28.4)	Mean Diff	15.5(1.22,29.78)	Group 1	na
Jones; 2012/High	1: Cane-Cane (wooden; T Handle)	1: Placebo/Control-Control (No Cane)	QOL:SF-36 Vitality	30 days	31/30	46.13(20.94)/41.6(22.7)	Mean Diff	4.53(-6.67,15.73)	Not Sig.	na

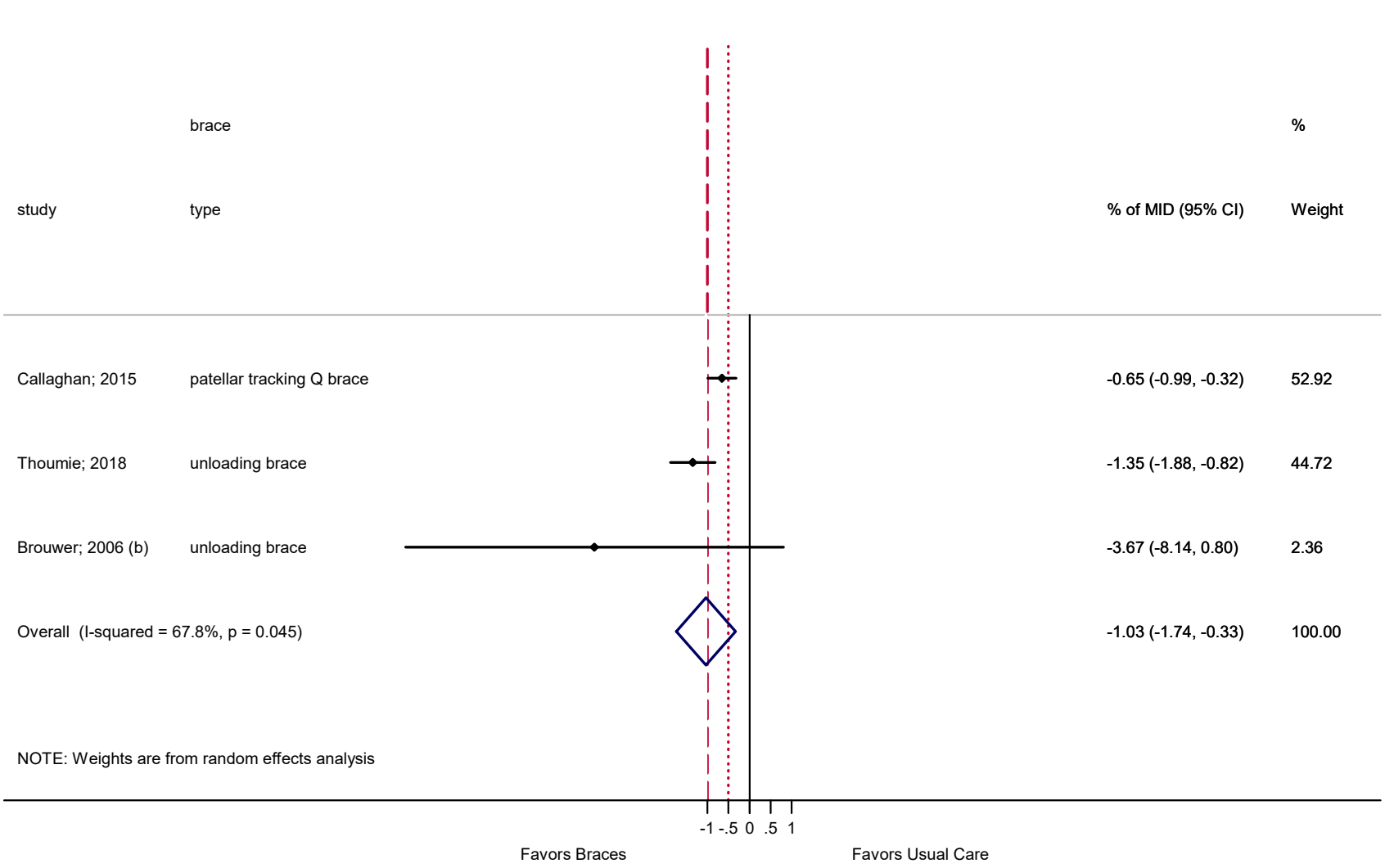
PICO 2: Braces

Braces vs Contol

Table 4: Brace vs Control

Quality: H=High; M=Moderate; L=Low	H			M		L	
↑ Better Outcomes ↓ Worse Outcomes • Not Significant	Brouwer; 2006 (b)	Kirkley ; 1999	Callaghan; 2015	Thoumie; 2018	Hjartarson; 2018	Hungerford; 2013	Yu; 2016
Composite							
WOMAC Total		↑					
Lequesne Index Score				↑			
EQ-5D	•						
KSS Score					↑		
MACTAR improvement		↑					
Patient Global Assessment						↑	
Physician Global Assessment						•	
Function							
WOMAC Function		↑					
WOMAC Stiffness		↑					
KOOS Activities of Daily Living			↑		↑		
KOOS Sports/Recreation					↑		
KOOS Symptoms					↑		
30 second stair climb improvement		↑					
6 minute walk distance- improvement		↑					
6MWT							↑
KSS Function					↑		
Timed Up and Go Test (sec)							↑
walking distance	↑						
Pain							
WOMAC Pain		↑					
VAS Pain	•						
KOOS Pain			↑		↑		
1cm improvement on VAS Pain after 6 minute walk		↑					
Pain While Sleeping at Night						•	
VAS Pain on 30 second stair climb improvement		↑					
VAS Pain on 6 minute walk- improvement		↑					
Adverse events							
Any Adverse Event				↓			
calculable MID outcomes							
VAS Pain			↑				
VAS Pain in Last 24 hrs				↑			
VAS Pain on Movement				↑			
QOL							
KOOS Quality of Life					↑		

Meta-Analysis Figure 2: Brace vs. Usual Care- Pain



Evidence Table 5 2: Brace vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Pain:1cm improvement on VAS Pain after 6 minute walk	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	Pain:KOOS Pain	12 mos	52/34	68.9(10.42)/63.7(10.17)	Mean Diff	5.2(0.68,9.72)	Group 1	na
Callaghan; 2015/High	P2: Brace/Device-Bioskin Patellar Tracking Q Brace	P2: Placebo/Control-No Brace	Pain:KOOS Pain	6 wks	56/61	57.5(14.94)/51.8(12.3)	Mean Diff	5.7(0.66,10.74)	Group 1	na
Hungerford; 2013/Low	2: Brace/Device-Transcutaneous Electrical Joint Stimulator w/ Unloading Brace(n/a)	1: Placebo/Control-Control (Transcutaneous Electrical Joint Stimulator w/o Unloading Brace(n/a)	Pain:Pain While Sleeping at Night	12 mos	225/289	-0.76(0.52)/-0.73(0.72)	Mean Diff	-0.03(-0.14,0.08)	Not Sig.	na
Thoumie; 2018/Moderate	P2: Brace/Device-Unloading Knee Brace(6h daily / 6 weeks)	P2: Placebo/Control-No Brace / Usual Care	Pain:VAS Pain in Last 24 hrs	6 wks	32/35	22.2(19.9)/49(23.4)	Mean Diff	-26.8(-37.37,-16.23)	Group 1	possibly clinically significant
Callaghan; 2015/High	P2: Brace/Device-Bioskin Patellar Tracking Q Brace	P2: Placebo/Control-No Brace	Pain:VAS Pain	6 wks	56/61	5(1.87)/6.3(1.76)	Mean Diff	-1.3(-1.97,-0.63)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Pain:VAS Pain on 30 second stair climb improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Pain:VAS Pain on 6 minute walk-improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Thoumie; 2018/Moderate	P2: Brace/Device-Unloading Knee Brace(6h daily / 6 weeks)	P2: Placebo/Control-No Brace / Usual Care	Pain:VAS Pain on Movement	6 wks	32/35	26.7(21.5)/59.7(22.4)	Mean Diff	-33(-43.71,-22.29)	Group 1	clinically significant
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Pain:WOMAC Pain improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Pain:vas pain	13 weeks		none	pvalue	NS	Not Sig.	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Pain:vas pain	26 weeks		none	pvalue	NS	Not Sig.	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Pain:vas pain	52 weeks		none	pvalue	NS	Not Sig.	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Function:30 second stair climb improvement	26 wks		none	pvalue	Sig (P<.05)	Unloader Br second stair climb improvement ;	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Function:6 minute walk distance-improvement	26 wks		none	pvalue	Sig (P<.05)	Unloader Br minute walk distance-improvemen	na
Yu; 2016/Low	2: Brace/Device-Tibiofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:6MWT	52 wks	86/68	428.88(127)/445.97(112.93)	Mean Diff	-17.09(-55.36, 21.18)	Not Sig.	na
Yu; 2016/Low	2: Brace/Device-Tibiofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:6MWT	12 wks	86/68	422.19(118.48)/421.37(110.04)	Mean Diff	0.82(-35.69, 37.33)	Not Sig.	na
Yu; 2016/Low	2: Brace/Device-Tibiofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:6MWT	26 wks	86/68	427.99(128.63)/426.7(121.34)	Mean Diff	1.29(-38.67, 41.25)	Not Sig.	na
Yu; 2016/Low	2: Brace/Device-Patellofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:6MWT	12 wks	50/68	470.32(125.33)/421.37(110.04)	Mean Diff	48.95(4.92,92.98)	Group 1	na
Yu; 2016/Low	2: Brace/Device-Patellofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:6MWT	52 wks	50/68	497.63(105.36)/445.97(112.93)	Mean Diff	51.66(11.55, 91.77)	Group 1	na
Yu; 2016/Low	2: Brace/Device-Patellofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:6MWT	26 wks	50/68	493.94(114.88)/426.7(121.34)	Mean Diff	67.24(23.8,110.68)	Group 1	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	Function:KOOS Activities of Daily Living	12 mos	52/34	75.2(10.06)/66.9(9.74)	Mean Diff	8.3(3.96,12.64)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Callaghan; 2015/High	P2: Brace/Device-Bioskin Patellar Tracking Q Brace	P2: Placebo/Control-No Brace	Function:KOOS Activities of Daily Living	6 wks	56/61	60.8(10.46)/56.3(11.32)	Mean Diff	4.5(0.51,8.49)	Group 1	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	Function:KOOS Sports/Recreation	12 mos	52/34	40.2(12.75)/27.8(12.47)	Mean Diff	12.4(6.87,17.93)	Group 1	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	Function:KOOS Symptoms	12 mos	52/34	72.4(11.49)/65.4(11.03)	Mean Diff	7(2.07,11.93)	Group 1	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	Function:KSS Function	12 mos	50/35	78.6(13.72)/70.8(13.25)	Mean Diff	7.8(1.9,13.7)	Group 1	na
Yu; 2016/Low	2: Brace/Device-Patellofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:Timed Up and Go Test (sec)	26 wks	50/68	8.53(4.09)/9.02(2.83)	Mean Diff	-0.49(-1.83,0.85)	Not Sig.	na
Yu; 2016/Low	2: Brace/Device-Patellofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:Timed Up and Go Test (sec)	52 wks	50/68	8.31(4.67)/8.93(3.07)	Mean Diff	-0.62(-2.13,0.89)	Not Sig.	na
Yu; 2016/Low	2: Brace/Device-Tibiofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:Timed Up and Go Test (sec)	12 wks	86/68	1.25(14.38)/9.46(2.77)	Mean Diff	-8.21(-11.36,-5.06)	Group 1	na
Yu; 2016/Low	2: Brace/Device-Tibiofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:Timed Up and Go Test (sec)	52 wks	86/68	9.44(3.8)/8.93(3.07)	Mean Diff	0.51(-0.58,1.6)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yu; 2016/Low	2: Brace/Device-Patellofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:Timed Up and Go Test (sec)	12 wks	50/68	10.26(5.22)/9.46(2.77)	Mean Diff	0.8(-0.82,2.42)	Not Sig.	na
Yu; 2016/Low	2: Brace/Device-Tibiofemoral Brace(4-6hrs/day)	2: Placebo/Control-Control (Unbraced)	Function:Timed Up and Go Test (sec)	26 wks	86/68	10.06(6.09)/9.02(2.83)	Mean Diff	1.04(-0.43,2.51)	Not Sig.	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Function:WOMAC Function improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Function:WOMAC Stiffness improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Function:walking distance	26 weeks		none	pvalue	NS	Not Sig.	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Function:walking distance	13 weeks		none	pvalue	Sig (p<0.05)	Brace favored over Usual Care	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Function:walking distance	52 weeks		none	pvalue	Sig (p<0.05)	Brace favored over Usual Care	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Composite:EQ-5D	13 weeks		none	pvalue	NS	Not Sig.	na
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Composite:EQ-5D	26 weeks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brouwer; 2006 (b)/high	2: Brace/Device-brace+ usual care	2: Placebo/Control-usual care	Composite:EQ-5D	52 weeks		none	pvalue	NS	Not Sig.	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	Composite:KSS Score	12 mos	50/35	84(15.83)/74.6(15.57)	Mean Diff	9.4(2.52,16.28)	Group 1	na
Thoumie; 2018/Moderate	P2: Brace/Device-Unloading Knee Brace(6h daily / 6 weeks)	P2: Placebo/Control-No Brace / Usual Care	Composite:Lequesne Index Score	6 wks	32/35	7.4(4.1)/10.6(3.7)	Mean Diff	-3.2(-5.11,-1.29)	Group 1	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Composite:MACTAR improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Hungerford; 2013/Low	2: Brace/Device-Transcutaneous Electrical Joint Stimulator w/ Unloading Brace(n/a)	1: Placebo/Control-Control (Transcutaneous Electrical Joint Stimulator w/o Unloading Brace(n/a)	Composite:Patient Global Assessment	12 mos	225/289	-0.83(0.48)/-0.63(0.72)	Mean Diff	-0.2(-0.3,-0.1)	Group 1	na
Hungerford; 2013/Low	2: Brace/Device-Transcutaneous Electrical Joint Stimulator w/ Unloading Brace(n/a)	1: Placebo/Control-Control (Transcutaneous Electrical Joint Stimulator w/o Unloading Brace(n/a)	Composite:Physician Global Assessment	12 mos	225/289	-0.84(0.46)/-0.75(0.72)	Mean Diff	-0.09(-0.19,0.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Placebo/Control-Usual care	Composite:WOMAC Total improvement	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Hjartarson; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace	P1: Placebo/Control-Placebo Unloader Knee Brace	QOL:KOOS Quality of Life	12 mos	52/34	55.7(11.85)/49.5(11.75)	Mean Diff	6.2(1.02,11.38)	Group 1	na
Thoumie; 2018/Moderate	P2: Brace/Device-Unloading Knee Brace(6h daily / 6 weeks)	P2: Placebo/Control-No Brace / Usual Care	Adverse events:Any Adverse Event	6 wks	32/35	31.25%/8.57%	RR	3.65(1.1,12.08)	Group 2	na

PICO 2: Braces

Braces vs Insole

Table 5: Brace vs Insole

Quality: H=High; M=Moderate; L=Low	H	M	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Van raaij; 2010	Petersen; 2018	Niazi; 2014
Function			
KOOS Activities of Daily Living		●	
KOOS Sports/Recreation		●	
KOOS Symptoms		●	
Lequesne Scale Walking Distance			↑
Pain			
VAS Pain while Walking		●	
KOOS Pain		●	
VAS Pain at Rest		●	
VAS Pain at Sports		●	
Adverse events			
Bruising		↓	
Pain			↑
calculable MID outcomes			
WOMAC Function	●		
vas pain change from baseline	↑		
QOL			
KOOS Quality of Life		●	

Evidence Table 6 3: Brace vs Insole

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:KOOS Pain	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:KOOS Pain	6 mos	121	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:VAS Pain at Rest	6 mos	121	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:VAS Pain at Rest	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:VAS Pain at Sports	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:VAS Pain at Sports	6 mos	121	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:VAS Pain while Walking	6 mos	121	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Pain:VAS Pain while Walking	8 wks	159	none	pvalue	NS	Not Sig.	na
Van raaij; 2010/High	2: Brace/Device-Valgus Brace	2: Non-arthro Tx-insole	Pain:vas pain change from baseline	26 wks	46/45	-10(22)/9(24)	Mean Diff	-19(-28.6,-9.4)	Group 1	possibly clinically significant
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Function:KOOS Activities of Daily Living	6 mos	121	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Function:KOOS Activities of Daily Living	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Function:KOOS Sports/Recreation	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Function:KOOS Sports/Recreation	6 mos	121	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Function:KOOS Symptoms	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Function:KOOS Symptoms	6 mos	121	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Niazi; 2014/Moderate	2: Brace/Device-Valgus Knee Braces	1: Insoles-Lateral Wedge	Function:Lequesne Scale Walking Distance	6 mos	60/60	1.93(0.8)/2.36(1.41)	Mean Diff	-0.43(-0.85,-0.01)	Group 1	na
Van raaij; 2010/High	2: Brace/Device-Valgus Brace	2: Non-arthro Tx-insole	Function:WOMAC Function	26 wks	46/45	4(18.9)/4.2(16.9)	Mean Diff	-0.2(-7.67,7.27)	Not Sig.	clinically insignificant
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	QOL:KOOS Quality of Life	6 mos	121	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	QOL:KOOS Quality of Life	8 wks	159	none	pvalue	NS	Not Sig.	na
Petersen; 2018/Moderate	P2: Brace/Device-Unloader Knee Brace(6+ hrs / day)	1: Insoles-Ankle/Foot Orthrosis(6+ hrs / day)	Adverse events:Bruising	6 mos	62/59	66.13%/23.73%	RR	2.79(1.71,4.55)	Group 2	na
Niazi; 2014/Moderate	2: Brace/Device-Valgus Knee Braces	1: Insoles-Lateral Wedge	Adverse events:Pain	6 mos	60/60	3.97(1.67)/4.53(1.41)	Mean Diff	-0.56(-1.12,0)	Group 1	na

PICO 2: Braces

Brace vs Sleeve

Table 6: Brace vs Sleeve

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Kirkley ; 1999**
Composite	
WOMAC Total	●
MACTAR	●
Function	
WOMAC Function	●
WOMAC Stiffness	●
30 second stair climb	●
6 minute walk distance	●
Pain	
WOMAC Pain	↑
1cm on VAS Pain after 6 minute walk	↑
VAS Pain on 30 second stair climb	↑
VAS Pain on 6 minute walk	↑

Evidence Table 7 4: Brace vs Sleeve

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Pain:1cm on VAS Pain after 6 minute walk	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Pain:VAS Pain on 30 second stair climb	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Pain:VAS Pain on 6 minute walk	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Pain:WOMAC Pain	26 wks		none	pvalue	Sig (p<0.05)	Unloader brace favored over Neoprene sleeve	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Function:30 second stair climb	26 wks		none	pvalue	NS	Unloader brace vs. (Unloader0Neoprbreraw aN	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Function:6 minute walk distance	26 wks		none	pvalue	NS	Unloader brace vs. s (UnloaderNeoprbrnraw kN	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Function:WOMAC Function	26 wks		none	pvalue	NS	Unloader brace vs. der braceONeoprbrCraw oNe	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Function:WOMAC Stiffness	26 wks		none	pvalue	NS	Unloader brace vs. ader braceONeoprbrCraw eN	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Composite:MACTAR	26 wks		none	pvalue	NS	Unloader brace vs. e vsANeoprbrAraw kNeoprr	na
Kirkley ; 1999/High	2: Brace/Device-Unloader brace	2: Brace/Device-Neoprene sleeve	Composite:WOMAC Total	26 wks		none	pvalue	NS	Unloader brace vs. braceONeoprbrCraw Neopr	na

PICO 2: Braces

Braces vs Brace

Table 7: Brace vs Brace

Quality: H=High; M=Moderate; L=Low	**M**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**van Egmond; 2017**
Function	
6MWT (m)	●
SF-12 Physical Component	●
Pain	
VAS	●
Adverse events	
Blisters	●
Bad Brace Fit	●
Not Comfortable	●
Other	●
Painful	●
Red Skin	●
Skin Lesions	●
calculable MID outcomes	
WOMAC Total	●
WOMAC Function	●
WOMAC Stiffness	●
WOMAC Pain	●
QOL	
SF-12 Mental Component Score	●
VAS Satisfaction	●

Evidence Table 8 5: Brace vs Brace

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Pain:VAS	12 wks	76	none	pvalue	NS	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Pain:WOMAC Pain	12 wks	76	none	Mean Diff.	0.2(-2,2.5)	Not Sig.	inconclusive
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Function:6MWT (m)	12 wks	76	none	Mean Diff.	4.2(-39.6,47.9)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Function:SF-12 Physical Component Score	12 wks	76	none	Mean Diff.	0(-4.3,4.2)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Function:WOMAC Activities of Daily Living	12 wks	76	none	Mean Diff.	1.7(-5.8,9.1)	Not Sig.	inconclusive
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Function:WOMAC Stiffness	12 wks	76	none	Mean Diff.	0(-0.9,1)	Not Sig.	inconclusive
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Composite:WOMAC Total	12 wks	76	none	Mean Diff.	1.9(-8.2,12)	Not Sig.	inconclusive
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	QOL:SF-12 Mental Component Score	12 wks	76	none	Mean Diff.	2.3(-6.6,2)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	QOL:VAS Satisfaction	12 wks	40/36	5.7(3.1)/5.5(2.7)	Mean Diff	0.2(-1.13,1.53)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Bad Brace Fit	12 wks	40/36	5%/2.78%	RR	1.8(0.17,19.02)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Blisters	12 wks	40/36	10%/22.22%	RR	0.45(0.15,1.37)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Not Comfortable	12 wks	40/36	12.5%/8.33%	RR	1.5(0.39,5.84)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Other	12 wks	40/36	22.5%/19.44%	RR	1.16(0.48,2.79)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Painful	12 wks	40/36	20%/11.11%	RR	1.8(0.59,5.48)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Red Skin	12 wks	40/36	37.5%/41.67%	RR	0.9(0.52,1.57)	Not Sig.	na
van Egmond; 2017/Moderate	P2: Brace/Device-Bledsoe Valgus Unloading Brace	P2: Brace/Device-SofTec Valgus Unloading Brace	Adverse events:Skin Lesions	12 wks	40/36	0%/2.78%	RD	-2.778(-11.833,8.614)	Not Sig.	na

PICO 3: Oral/Dietary Supplements

Turmeric Extract vs Control

Table 8: Turmeric Extract vs Control

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Srivastava; 2016**
Adverse events	
Joint Crepitation	↑
Joint Effusion	↑
Joint Stiffness	●
calculable MID outcomes	
WOMAC Function	↑
WOMAC Stiffness	●
WOMAC Pain	↑
VAS Pain	↑

Evidence Table 9 6: Turmeric Extract vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Pain:VAS Pain	60 days	78/82	4.96(0.62)/6(1)	Mean Diff	-1.04(-1.3,-0.78)	Group 1	some may benefit
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Pain:VAS Pain	120 days	78/82	4.03(0.71)/5.11(1.27)	Mean Diff	-1.08(-1.4,-0.76)	Group 1	some may benefit
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Pain:WOMAC Pain	120 days	78/82	9.48(1.5)/10.16(1.45)	Mean Diff	-0.68(-1.14,-0.22)	Group 1	clinically insignificant
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Pain:WOMAC Pain	60 days	78/82	11.19(2.3)/12.05(1.9)	Mean Diff	-0.86(-1.52,-0.2)	Group 1	some may benefit
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Function:WOMAC Function	120 days	78/82	32.14(3.53)/33.88(4.53)	Mean Diff	-1.74(-3.01,-0.47)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Function:WOMAC Function	60 days	78/82	41.28(4.5)/45.11(3.35)	Mean Diff	-3.83(-5.07,-2.59)	Group 1	some may benefit
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Function:WOMAC Stiffness	120 days	78/82	4.08(1.5)/4.16(1.63)	Mean Diff	-0.08(-0.57,0.41)	Not Sig.	clinically insignificant
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Function:WOMAC Stiffness	60 days	78/82	4.51(1.85)/4.7(2.08)	Mean Diff	-0.19(-0.8,0.42)	Not Sig.	inconclusive
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Adverse events:Joint Crepitation	120 days	78/82	15.38%/34.15%	RR	0.45(0.25,0.82)	Group 1	na
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Adverse events:Joint Crepitation	60 days	78/82	19.23%/39.02%	RR	0.49(0.29,0.84)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Adverse events:Joint Effusion	120 days	78/82	8.97%/20.73%	RR	0.43(0.19,0.99)	Group 1	na
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Adverse events:Joint Effusion	60 days	78/82	20.51%/25.61%	RR	0.8(0.45,1.42)	Not Sig.	na
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Adverse events:Joint Stiffness	120 days	78/82	11.54%/18.29%	RR	0.63(0.29,1.36)	Not Sig.	na
Srivastava; 2016/High	3: Oral Supplement-Curcumin (Turmeric Extract)(500mg 2x/day x 4mo)	3: Placebo/Control-Placebo(500mg 2x/day x 4mo)	Adverse events:Joint Stiffness	60 days	78/82	19.23%/23.17%	RR	0.83(0.45,1.52)	Not Sig.	na

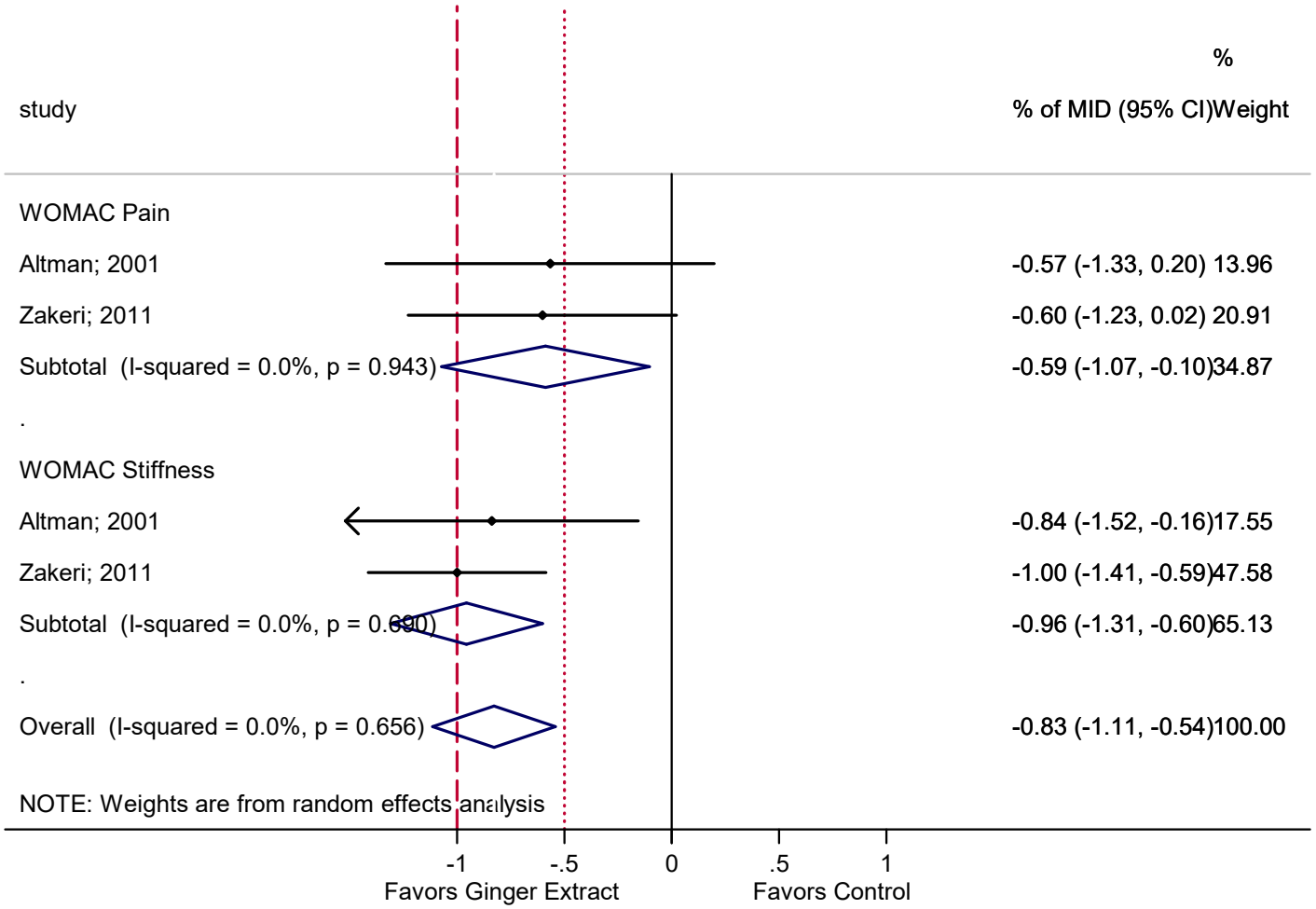
PICO 3: Oral/Dietary Supplements

Ginger Extract vs Control

Table 9: Ginger Extract vs Control

Quality: H=High; M=Moderate; L=Low	H	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Zakeri; 2011	Altman; 2001
Function		
SF-12 physical summary		●
Pain		
Improvement >= 25 mm VAS pain on standing		↑
Improvement >=20 mm VAS pain on standing		↑
improvement >=15 mm VAS pain on standing		↑
calculable MID outcomes		
WOMAC Total		↑
WOMAC Function		●
WOMAC Stiffness	↑	↑
WOMAC Pain	●	●
WOMAC Difficulty	↑	
VAS Pain after walking 50 m	●	
VAS Pain on standing	●	
pain after walking 5? ft (VAS)		●
adverse events		
adverse events		↓
QOL		
SF-12 mental summary		●
acetaminophen use; mean tablets daily		●

Meta-Analysis Figure 2: Ginger Extract vs Placebo- Pain and Stiffness



Evidence Table 10 7: Ginger Extract vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Pain:Improvement ?25 mm VAS pain on standing	6 weeks	124/123	52.42%/39.02%	RR	1.34(1.02,1.77)	Group 2	na
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Pain:Improvement ?2? mm VAS pain on standing	6 weeks	124/123	58.87%/45.53%	RR	1.29(1.01,1.65)	Group 2	na
Zakeri; 2011/High	3: Oral Supplement-Ginger extract(250 mg)	3: Placebo/Control-Placebo	Pain:VAS Pain after walking 50 m	6 wks	103/101	39.4(16.6)/46.5(18.8)	Mean Diff	-7.1(-12,-2.2)	Group 1	clinically insignificant
Zakeri; 2011/High	3: Oral Supplement-Ginger extract(250 mg)	3: Placebo/Control-Placebo	Pain:VAS Pain on standing	6 wks	103/101	38.7(18.5)/44.8(18.6)	Mean Diff	-6.1(-11.22,-0.98)	Group 1	clinically insignificant
Zakeri; 2011/High	3: Oral Supplement-Ginger extract(250 mg)	3: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	103/101	2.2(0.8)/2.4(0.7)	Mean Diff	-0.2(-0.41,0.01)	Not Sig.	inconclusive
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Pain:averaged WOMAC pain	6 weeks	123/124	7.22(5.24)/8.16(4.88)	Mean Diff	-0.94(-2.21,0.33)	Not Sig.	inconclusive
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Pain:improvement ?15 mm VAS pain on standing	6 weeks	124/123	62.9%/50.41%	RR	1.25(1,1.56)	Group 2	na
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Pain:pain after walking 5? ft (VAS)	6 weeks	123/124	34.6(29.5)/44.2(28.3)	Mean Diff	-9.6(-16.85,-2.35)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Function:SF-12 physical summary	6 weeks	123/124	36.9(9.7)/35.3(9.5)	Mean Diff	1.6(-0.81,4.01)	Not Sig.	na
Zakeri; 2011/High	3: Oral Supplement-Ginger extract(250 mg)	3: Placebo/Control-Placebo	Function:WOMAC Difficulty	6 wks	103/101	0.4(0.6)/2.2(0.6)	Mean Diff	-1.8(-1.97,-1.63)	Group 1	clinically significant
Zakeri; 2011/High	3: Oral Supplement-Ginger extract(250 mg)	3: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	103/101	1.4(0.6)/1.8(0.6)	Mean Diff	-0.4(-0.57,-0.23)	Group 1	possibly clinically significant
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Function:averaged WOMAC function	6 weeks	123/124	25.64(17.2)/29.51(16.12)	Mean Diff	-3.87(-8.05,0.31)	Not Sig.	inconclusive
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Function:averaged WOMAC stiffness	6 weeks	123/124	3.26(2.25)/3.93(2.1)	Mean Diff	-0.67(-1.22,-0.12)	Group 1	possibly clinically significant
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	Function:averaged WOMAC total	6 weeks	123/124	35.81(24.1)/41.76(22.37)	Mean Diff	-5.95(-11.78,-0.12)	Group 1	possibly clinically significant
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	QOL:SF-12 mental summary	6 weeks	123/124	53.4(10.9)/53(10.5)	Mean Diff	0.4(-2.28,3.08)	Not Sig.	na
Altman; 2001/Moderate	3: Oral Supplement-ginger extract(2x 255mg)	3: Placebo/Control-placebo(2x 255mg)	QOL:acetaminophen use; mean tablets daily	6 weeks	123/124	2(1.9)/2.2(2)	Mean Diff	-0.2(-0.69,0.29)	Not Sig.	na

PICO 3: Oral/Dietary Supplements

Glucosamine vs Control

Table 10: Glucosamine vs Control

Quality: H=High; M=Moderate; L=Low	H							M							L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Herrero-Beaumont; 2007	Reginster; 2001	Cibere ; 2004	McAlindon ; 2004	Hughes; 2002	Noack ; 1994	Shahine; 2014	Houpt ; 1999	Pavelka; 2002	Giordano ; 2009	Rindone ; 2000	Gang; 2019	
Composite															
Lequesne Index			↑					●							
20% womac decrease-mild sample		●													
20% womac decrease-severe sample		●													
20% womac decrease-whole sample		●													
Lysholm Knee Score														↑	
OARSI-A responder criteria			↑												
OARSI-B responder criteria			↑												
mean change in lequesne index											↓				
responder (3pt reduction in lequesne and positive investigator global assessment)								↑							
Function															
SF-12 Physical Component	●														
50 Foot Walk (s)	●														
WOMAC Function MCII(unclear threshold)			↑												
Other															
Daily consumption of NSAIDs												↑			
HAQ Alternative Disability score		●													
McGill affective AUC							●								
McGill sensory AUC							●								
No. of 500-mg tablets of acetaminophen		●													
OMERACT-OARSI response; % (n) -mild sample		●													
OMERACT-OARSI response; % (n) -severe sample		↑													
OMERACT-OARSI response; % (n) -whole sample		●													
Patient's global assessment of disease status score		●													
Patient's global assessment of response to therapy score		↑													
Physician's global assessment of disease status		●													
mean change in analgesic use (mg)						↓									

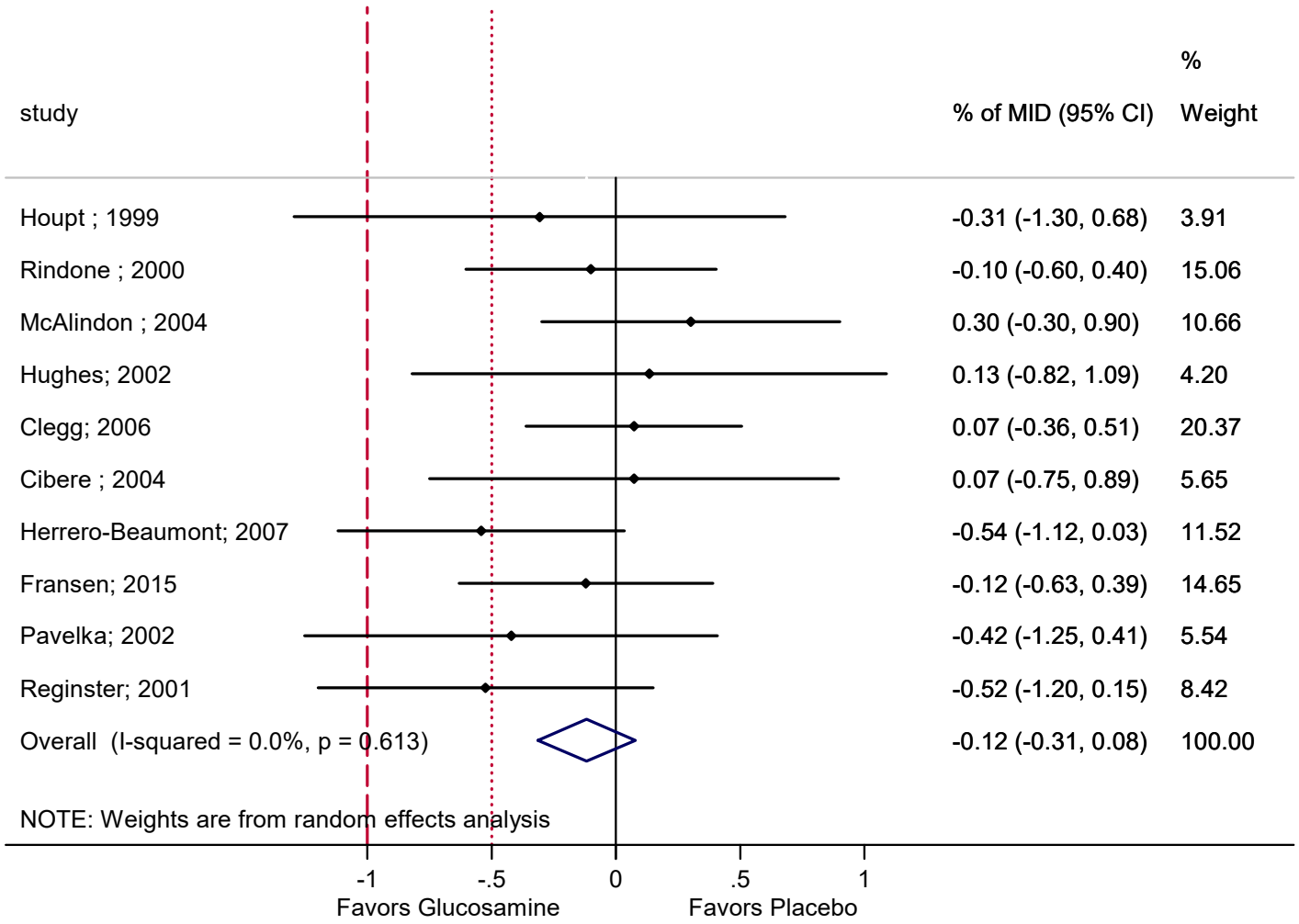
Table 10 Continued: Glucosamine vs Control

Quality: H=High; M=Moderate; L=Low	H							M						L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Herrero-Beaumont; 2007	Reginster; 2001	Cibere ; 2004	McAlindon ; 2004	Hughes; 2002	Noack ; 1994	Shahine; 2014	Houpt ; 1999	Pavelka; 2002	Giordano ; 2009	Rindone ; 2000	Gang; 2019
Pain														
WOMAC Pain					●									
50% decrease in WOMAC pain score; % (n) -mild sample		●												
50% decrease in WOMAC pain score; % (n) -severe sample		●												
50% decrease in WOMAC pain score; % (n) -whole sample		●												
HAQ Pain score		●												
WOMAC Pain MCII(unclear threshold)			↑											
global pain (VAS) AUC							●							
mean change in EQ-5D (VAS)					●									
pain at rest (VAS) AUC							●							
pain on movement (VAS)							●							
Adverse events														
Any Adverse Event														●
Circulatory disturbances								●						
Constipation														●
Gastrointestinal Reaction														●
Gastrointestinal disturbances								●						
Headache								●						
Inadequate Exercise	●													
Joint Pain and Swelling														●
Mild Abdominal Pain														●
Nausea														●
Pruritus or Skin reaction								●						
total adverse events								●						

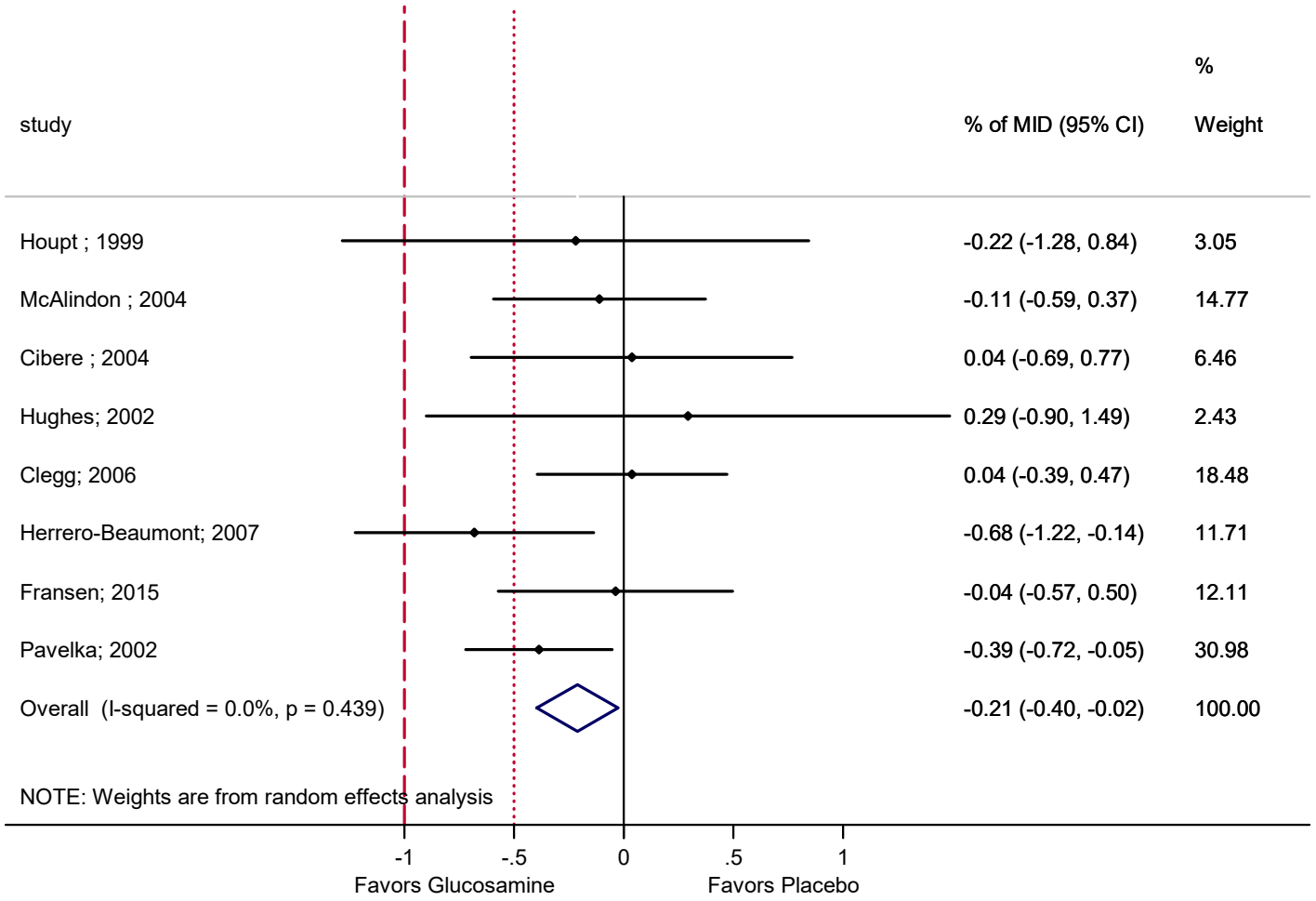
Table 10 Continued: Glucosamine vs Control

Quality: H=High; M=Moderate; L=Low	H							M							L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Herrero-Beaumont; 2007	Reginster; 2001	Cibere ; 2004	McAlindon ; 2004	Hughes; 2002	Noack ; 1994	Shahine; 2014	Houpt ; 1999	Pavelka; 2002	Giordano ; 2009	Rindone ; 2000	Gang; 2019
calculable MID outcomes														
WOMAC Total			↑	●	●	●			↑	●	●			
WOMAC Function	●	●	↑		●	●	●		↑	●	●			
WOMAC Stiffness		●			●	●	●		↑	●	↑			
WOMAC Pain	●	●	●	●	●	●	●		↑	●	●			
VAS Pain	●								↑					
Normalized WOMAC score		●												
mean change in pain intensity from baseline (VAS) at 30 days; resting													●	
mean change in pain intensity from baseline (VAS) at 30 days; walking													●	
mean change in pain intensity from baseline (VAS) at 60 days; resting													●	
mean change in pain intensity from baseline (VAS) at 60 days; walking													●	
pain intensity (VAS) at 30 days; resting													●	
pain intensity (VAS) at 30 days; walking													●	
pain intensity (VAS) at 60 days; resting													●	
pain intensity (VAS) at 60 days; walking													●	
QOL														
SF-12 Mental Component Score	●													

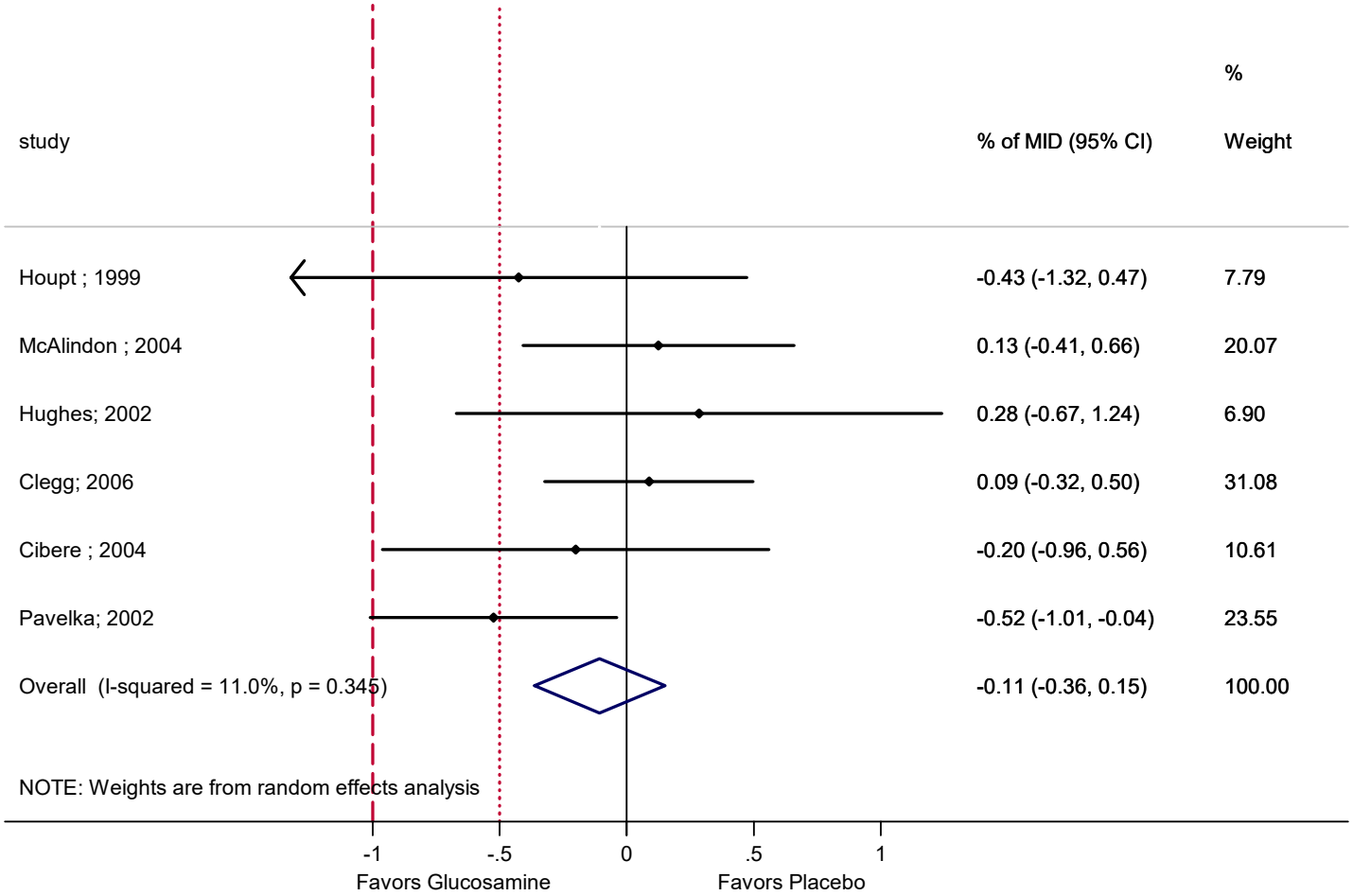
Meta-Analysis Figure 4: Glucosamine vs Placebo- Pain



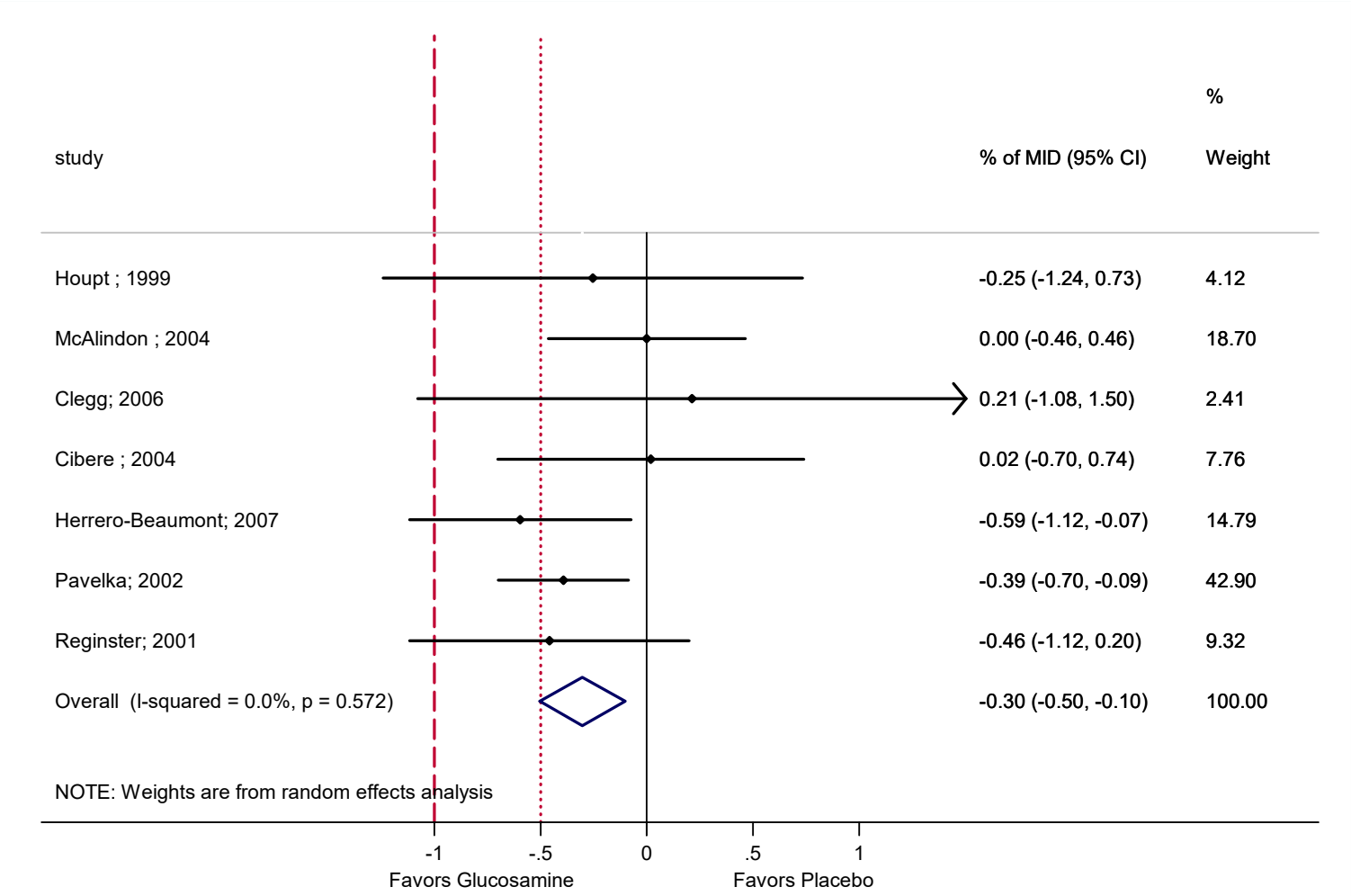
Meta-Analysis Figure 5: Glucosamine vs Placebo- Function



Meta-Analysis Figure 6: Glucosamine vs Placebo- Stiffness



Meta-Analysis Figure 7: Glucosamine vs Placebo- WOMAC total



Evidence Table 11 8: Glucomsamin vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Pain:50% decrease in WOMAC pain score; % (n) - mild sample	24 weeks	247/243	47.77%/44.86%	RR	1.07(0.88,1.29)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Pain:50% decrease in WOMAC pain score; % (n) - severe sample	24 weeks	70/70	41.43%/32.86%	RR	1.26(0.82,1.95)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Pain:50% decrease in WOMAC pain score; % (n) - whole sample	24 weeks	317/313	46.37%/42.17%	RR	1.1(0.92,1.31)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Pain:HAQ Pain score	24 weeks	313/317	-16(29.1)/-16.6(28)	Mean Diff	0.6(-3.87,5.07)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Pain:VAS Pain	1 yrs	151/151	3.94(2.57)/4.01(2.63)	Mean Diff	-0.07(-0.66,0.52)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:VAS Pain	1 yrs	152/151	4.02(2.75)/4.14(2.46)	Mean Diff	-0.12(-0.71,0.47)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:VAS Pain	2 yrs	152/151	3.86(2.52)/4.03(2.61)	Mean Diff	-0.17(-0.75,0.41)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Pain:VAS Pain	2 yrs	151/151	3.58(2.6)/3.76(2.66)	Mean Diff	-0.18(-0.78,0.42)	Not Sig.	clinically insignificant
Shahine; 2014/Moderate	3: Oral Supplement-Glucosamine Sulfate +Ibuprofen(500mg x3/day + 1200mg ibuprofen)	3: Placebo/Control-Control (Ibuprofen Alone)(1200mg/day)	Pain:VAS Pain	12 wks	30/30	-42.2(15.6)/-26.5(17.3)	Mean Diff	-15.7(-24.22,-7.18)	Group 1	possibly clinically significant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:WOMAC Pain	2 yrs	152/151	4.5(3.7)/4.6(3.5)	Mean Diff	-0.1(-0.91,0.71)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:WOMAC Pain	1 yrs	152/151	4.5(3.7)/4.7(3.8)	Mean Diff	-0.2(-1.05,0.65)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Pain:WOMAC Pain	1 yrs	151/151	4.9(3.5)/4.8(3.9)	Mean Diff	0.1(-0.74,0.94)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Pain:WOMAC Pain	2 yrs	151/151	4.7(3.7)/4.4(3.6)	Mean Diff	0.3(-0.53,1.13)	Not Sig.	clinically insignificant
Reginster; 2001/High	3: Oral Supplement-glucosamine sulfate	3: Placebo/Control-placebo	Pain:WOMAC Pain	156 wks	106/106	6.89(4.18)/7.76(4.08)	Mean Diff	-0.87(-1.99,0.25)	Not Sig.	inconclusive
Shahine; 2014/Moderate	3: Oral Supplement-Glucosamine Sulfate +Ibuprofen(500mg x3/day + 1200mg ibuprofen)	3: Placebo/Control-Control (Ibuprofen Alone)(1200mg/day)	Pain:WOMAC Pain	12 wks	30/30	-7.6(3.2)/-3.4(2.8)	Mean Diff	-4.2(-5.75,-2.65)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Pain:WOMAC Pain	180 days	106/104	-2.7(3.12)/-1.8(3.86)	Mean Diff	-0.9(-1.86,0.06)	Not Sig.	inconclusive
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Pain:WOMAC Pain MCII(unclear threshold)	180 days	106/104	48.11%/32.69%	RR	1.47(1.05,2.07)	Group 1	na
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:WOMAC pain (likert AUC)	24 weeks	37/38	184.88(98.79)/179.32(69.96)	Mean Diff	5.56(-34.01, 45.13)	Not Sig.	inconclusive
Houpt ; 1999/Moderate	3: Oral Supplement-glucosamine hydrochloride	3: Placebo/Control-placebo	Pain:WOMAC pain (likert)	8 weeks	53/45	7.14(4.01)/7.65(4.13)	Mean Diff	-0.51(-2.15,1.13)	Not Sig.	inconclusive
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Pain:WOMAC pain score	24 weeks	313/317	-3.32(4.62)/-3.44(4.57)	Mean Diff	0.12(-0.6,0.84)	Not Sig.	clinically insignificant
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:global pain (VAS) AUC	24 weeks	37/38	1081.28(577.69)/1065.45(398.07)	Mean Diff	15.83(-213.62,245.28)	Not Sig.	na
Cibere ; 2004/high	3: Oral Supplement-glucosamine sulfate(up to 1500mg)	3: Placebo/Control-placebo	Pain:mean change in EQ-5D (VAS)	24 weeks	66/71	0.1(16)/-2(12)	Mean Diff	2.1(-2.71,6.91)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Cibere ; 2004/high	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:mean change in WOMAC pain	24 weeks	66/71	-1(3.92)/-1.12(4.16)	Mean Diff	0.12(-1.25,1.49)	Not Sig.	clinically insignificant
McAlindon ; 2004/High	3: Oral Supplement-glucosamine sulfate/glucosamine hydrochloride(496/1500mg)	3: Placebo/Control-placebo	Pain:mean change in WOMAC pain (likert)	12 wks	104/101	-2(3.4)/-2.5(3.8)	Mean Diff	0.5(-0.49,1.49)	Not Sig.	clinically insignificant
Pavelka; 2002/Moderate	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:mean change in WOMAC pain (likert)	156 wks	101/101	-2(2.31)/-1.3(6.61)	Mean Diff	-0.7(-2.08,0.68)	Not Sig.	inconclusive
Cibere ; 2004/high	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:mean change in WOMAC pain on walking (VAS)	24 weeks	66/71	-0.2(0.84)/-0.32(1)	Mean Diff	0.12(-0.19,0.43)	Not Sig.	na
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x500mg)	3: Placebo/Control-placebo	Pain:mean change in pain intensity from baseline (VAS) at 30 days; resting	8.5 wks	49/49	0.71(2.3)/0.18(2.5)	Mean Diff	0.53(-0.43,1.49)	Not Sig.	clinically insignificant
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x500mg)	3: Placebo/Control-placebo	Pain:mean change in pain intensity from baseline (VAS) at 30 days; walking	8.5 wks	49/49	1.1(2)/1.2(2.6)	Mean Diff	-0.1(-1.03,0.83)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x 500mg)	3: Placebo/Control-placebo	Pain:mean change in pain intensity from baseline (VAS) at 60 days; resting	8.5 wks	49/49	0.73(2.7)/0.59(2.9)	Mean Diff	0.14(-0.98,1.26)	Not Sig.	clinically insignificant
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x 500mg)	3: Placebo/Control-placebo	Pain:mean change in pain intensity from baseline (VAS) at 60 days; walking	8.5 wks	49/49	1.4(3)/1.5(2.5)	Mean Diff	-0.1(-1.21,1.01)	Not Sig.	clinically insignificant
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:pain at rest (VAS) AUC	24 weeks	37/38	713.02(562.25)/561.75(361.76)	Mean Diff	151.27 (-67.65, 370.19)	Not Sig.	na
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x 500mg)	3: Placebo/Control-placebo	Pain:pain intensity (VAS) at 30 days; resting	8.5 wks	49/49	3.3(2.4)/3.5(2.7)	Mean Diff	-0.2(-1.22,0.82)	Not Sig.	clinically insignificant
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x 500mg)	3: Placebo/Control-placebo	Pain:pain intensity (VAS) at 30 days; walking	8.5 wks	49/49	5.3(2.4)/5.1(2.6)	Mean Diff	0.2(-0.8,1.2)	Not Sig.	clinically insignificant
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x 500mg)	3: Placebo/Control-placebo	Pain:pain intensity (VAS) at 60 days; resting	8.5 wks	49/49	3.2(2.5)/3.4(2.5)	Mean Diff	-0.2(-1.2,0.8)	Not Sig.	clinically insignificant
Rindone ; 2000/Moderate	3: Oral Supplement-glucosamine(3x 500mg)	3: Placebo/Control-placebo	Pain:pain intensity (VAS) at 60 days; walking	8.5 wks	49/49	4.9(2.8)/4.9(2.2)	Mean Diff	0(-1.01,1.01)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Pain:pain on movement (VAS)	24 weeks	37/38	1091.1(629.77)/1080.45(456.21)	Mean Diff	10.65(-243.47,264.77)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Function:50 Foot Walk (s)	1 yrs	151/151	8.5(1.9)/8.4(1.7)	Mean Diff	0.1(-0.31,0.51)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:50 Foot Walk (s)	2 yrs	152/151	8.5(2.1)/8.4(1.9)	Mean Diff	0.1(-0.35,0.55)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:50 Foot Walk (s)	1 yrs	152/151	8.6(2.2)/8.5(2)	Mean Diff	0.1(-0.38,0.58)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Function:50 Foot Walk (s)	2 yrs	151/151	8.7(2)/8.4(1.7)	Mean Diff	0.3(-0.12,0.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:SF-12 Physical Component Score	2 yrs	152/151	43.9(9.4)/44.2(9.7)	Mean Diff	-0.3(-2.46,1.86)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Function:SF-12 Physical Component Score	1 yrs	151/151	43.2(9.8)/44.7(8.9)	Mean Diff	-1.5(-3.62,0.62)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Function:SF-12 Physical Component Score	2 yrs	151/151	42.6(10)/44.1(9.4)	Mean Diff	-1.5(-3.7,0.7)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:SF-12 Physical Component Score	1 yrs	152/151	44.5(10.2)/44(9.5)	Mean Diff	0.5(-1.73,2.73)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:WOMAC Function	1 yrs	152/151	16.3(13)/16.5(12.7)	Mean Diff	-0.2(-3.11,2.71)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:WOMAC Function	2 yrs	152/151	17.8(13.5)/17.8(12.9)	Mean Diff	0(-2.99,2.99)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Function:WOMAC Function	2 yrs	151/151	17.8(13.7)/17.4(13.1)	Mean Diff	0.4(-2.64,3.44)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Function:WOMAC Function	1 yrs	151/151	17.2(12.5)/16.2(11.8)	Mean Diff	1(-1.75,3.75)	Not Sig.	clinically insignificant
Shahine; 2014/Moderate	3: Oral Supplement-Glucosamine Sulfate +Ibuprofen(500mg x3/day + 1200mg ibuprofen)	3: Placebo/Control-Control (Ibuprofen Alone)(1200mg/day)	Function:WOMAC Function	12 wks	30/30	-12.9(6.9)/-2.5(7.4)	Mean Diff	-10.4(-14.1,-6.7)	Group 1	clinically significant
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Function:WOMAC Function MCII(unclear threshold)	180 days	106/104	55.66%/37.5%	RR	1.48(1.1,2.01)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Shahine; 2014/Moderate	3: Oral Supplement-Glucosamine Sulfate +Ibuprofen(500mg x3/day + 1200mg ibuprofen)	3: Placebo/Control-Control (Ibuprofen Alone)(1200mg/day)	Function:WOMAC Stiffness	12 wks	30/30	-4.1(2.1)/-2.1(2.2)	Mean Diff	-2(-3.11,-0.89)	Group 1	clinically significant
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Function:WOMAC function	180 days	106/104	-9.2(10.38)/-5.5(11.31)	Mean Diff	-3.7(-6.65,-0.75)	Group 1	possibly clinically significant
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Function:WOMAC function (likert AUC)	24 weeks	37/38	665.1(394.42)/625.2(301.92)	Mean Diff	39.9(-122.28,202.08)	Not Sig.	inconclusive
Houpt ; 1999/Moderate	3: Oral Supplement-glucosamine hydrochloride	3: Placebo/Control-placebo	Function:WOMAC function (likert)	8 weeks	53/45	25.98(14.7)/27.17(14.1)	Mean Diff	-1.19(-6.98,4.6)	Not Sig.	inconclusive
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Function:WOMAC function score	24 weeks	313/317	-8.89(15.53)/-9.1(14.51)	Mean Diff	0.21(-2.14,2.56)	Not Sig.	clinically insignificant
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Function:WOMAC stiffness (likert AUC)	24 weeks	37/38	87.98(47.7)/82.28(33.88)	Mean Diff	5.7(-13.43, 24.83)	Not Sig.	inconclusive
Houpt ; 1999/Moderate	3: Oral Supplement-glucosamine hydrochloride	3: Placebo/Control-placebo	Function:WOMAC stiffness (likert)	8 weeks	53/45	3.39(1.81)/3.73(1.76)	Mean Diff	-0.34(-1.06,0.38)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Function:WOMAC stiffness score	24 weeks	313/317	-1.39(2.1)/-1.46(2.09)	Mean Diff	0.07(-0.26,0.4)	Not Sig.	clinically insignificant
Cibere ; 2004/high	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Function:mean change in WOMAC function	24 weeks	66/71	-2.32(10.8)/-2.52(12.72)	Mean Diff	0.2(-3.78,4.18)	Not Sig.	clinically insignificant
McAlindon ; 2004/High	3: Oral Supplement-glucosamine sulfate/glucosamine hydrochloride(496/1500mg)	3: Placebo/Control-placebo	Function:mean change in WOMAC function (likert)	12 wks	104/101	-5.2(9.5)/-4.6(9.6)	Mean Diff	-0.6(-3.23,2.03)	Not Sig.	clinically insignificant
Pavelka; 2002/Moderate	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Function:mean change in WOMAC function (likert)	156 wks	101/101	-5.8(6.92)/-3.7(6.15)	Mean Diff	-2.1(-3.92,-0.28)	Group 1	clinically insignificant
Cibere ; 2004/high	3: Oral Supplement-glucosamine sulfate(up to 1500mg)	3: Placebo/Control-placebo	Function:mean change in WOMAC stiffness	24 weeks	66/71	0.08(1.68)/0.24(1.92)	Mean Diff	-0.16(-0.77,0.45)	Not Sig.	clinically insignificant
McAlindon ; 2004/High	3: Oral Supplement-glucosamine sulfate/glucosamine hydrochloride(496/1500mg)	3: Placebo/Control-placebo	Function:mean change in WOMAC stiffness (likert)	12 wks	104/101	-0.7(1.6)/-0.8(1.5)	Mean Diff	0.1(-0.33,0.53)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2002/Moderate	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Function:mean change in WOMAC stiffness (likert)	156 wks	101/101	-0.31(1.59)/0.11(1.18)	Mean Diff	-0.42(-0.81,-0.03)	Group 1	possibly clinically significant
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Composite:20% womac decrease-mild sample	24 weeks	247/243	63.56%/61.73%	RR	1.03(0.9,1.18)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Composite:20% womac decrease-severe sample	24 weeks	70/70	65.71%/54.29%	RR	1.21(0.92,1.59)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Composite:20% womac decrease-whole sample	24 weeks	317/313	64.04%/60.06%	RR	1.07(0.94,1.2)	Not Sig.	na
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:Lequesne Index	180 days	106/104	-3.1(3.89)/-1.9(3.6)	Mean Diff	-1.2(-2.22,-0.18)	Group 1	na
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Composite:Lequesne index	4 wks	126/126	7.4(5.61)/8.4(4.49)	Mean Diff	-1(-2.26,0.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Composite:Lysholm Knee Score	8 wks	60/60	87.29(10.38)/75.63(9.15)	Mean Diff	11.66(8.12,15.2)	Group 1	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Composite:Normalized WOMAC score	24 weeks	313/317	-47.1(66.9)/-48.8(65.1)	Mean Diff	1.7(-8.63,12.03)	Not Sig.	inconclusive
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:OARSI-A responder criteria	180 days	106/104	39.62%/21.15%	RR	1.87(1.21,2.91)	Group 1	na
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:OARSI-B responder criteria	180 days	106/104	35.85%/19.23%	RR	1.86(1.17,2.98)	Group 1	na
Reginster; 2001/High	3: Oral Supplement-glucosamine sulfate	3: Placebo/Control-placebo	Composite:WOMAC Total	156 wks	106/106	37.59(19.39)/41.21(18.95)	Mean Diff	-3.62(-8.81,1.57)	Not Sig.	inconclusive
Shahine; 2014/Moderate	3: Oral Supplement-Glucosamine Sulfate +Ibuprofen(500mg x3/day + 1200mg ibuprofen)	3: Placebo/Control-Control (Ibuprofen Alone)(1200mg/day)	Composite:WOMAC Total	12 wks	30/30	-24.6(7.3)/-8.1(7.5)	Mean Diff	-16.5(-20.33,-12.67)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrero-Beaumont; 2007/High	3: Oral Supplement-glucosamine sulfate(1500mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:WOMAC Total	180 days	106/104	-12.9(14.28)/-8.2(15.94)	Mean Diff	-4.7(-8.82,-0.58)	Group 1	possibly clinically significant
Houpt ; 1999/Moderate	3: Oral Supplement-glucosamine hydrochloride	3: Placebo/Control-placebo	Composite:WOMAC total (likert)	8 weeks	53/45	36.57(19.5)/38.57(19.3)	Mean Diff	-2(-9.81,5.81)	Not Sig.	inconclusive
Cibere ; 2004/high	3: Oral Supplement-glucosamine sulfate(up to 1500mg)	3: Placebo/Control-placebo	Composite:mean change in WOMAC total	24 weeks	66/71	-3.24(15.52)/-3.4(18.12)	Mean Diff	0.16(-5.53,5.85)	Not Sig.	clinically insignificant
McAlindon ; 2004/High	3: Oral Supplement-glucosamine sulfate/glucosamine hydrochloride(496/1500mg)	3: Placebo/Control-placebo	Composite:mean change in WOMAC total (likert)	12 wks	104/101	-7.8(13.1)/-7.8(13.5)	Mean Diff	0(-3.66,3.66)	Not Sig.	clinically insignificant
Pavelka; 2002/Moderate	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Composite:mean change in WOMAC total (likert)	156 wks	101/101	-8(8.97)/-4.9(8.46)	Mean Diff	-3.1(-5.52,-0.68)	Group 1	clinically insignificant
Pavelka; 2002/Moderate	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Composite:mean change in lequesne index	156 wks	101/101	-1.7(2.56)/-0.82(1.51)	Mean Diff	-0.88(-1.46,-0.3)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Composite:responder (3pt reduction in lequesne and positive investigator global assessment)	4 wks	126/126	52.38%/36.51%	RR	1.43(1.08,1.91)	Group 1	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	QOL:SF-12 Mental Component Score	1 yrs	151/151	52.8(8)/52.4(9.2)	Mean Diff	0.4(-1.55,2.35)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	QOL:SF-12 Mental Component Score	2 yrs	151/151	54.6(7.6)/53.6(9.8)	Mean Diff	1(-0.99,2.99)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	QOL:SF-12 Mental Component Score	1 yrs	152/151	52.3(10)/51.3(10.6)	Mean Diff	1(-1.33,3.33)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	QOL:SF-12 Mental Component Score	2 yrs	152/151	53.1(10.3)/51.6(10)	Mean Diff	1.5(-0.8,3.8)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Giordano ; 2009/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:Daily consumption of NSAIDs	4 weeks	30/30	8.2(2.8)/9.8(2.9)	Mean Diff	-1.6(-3.07,-0.13)	Group 1	na
Giordano ; 2009/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:Daily consumption of NSAIDs	24 weeks	30/30	9.75(3.1)/12.25(2.9)	Mean Diff	-2.5(-4.05,-0.95)	Group 1	na
Giordano ; 2009/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:Daily consumption of NSAIDs	8 weeks	30/30	7.8(2.9)/10.4(2.8)	Mean Diff	-2.6(-4.07,-1.13)	Group 1	na
Giordano ; 2009/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:Daily consumption of NSAIDs	16 weeks	30/30	7.65(2.8)/10.85(2.8)	Mean Diff	-3.2(-4.65,-1.75)	Group 1	na
Giordano ; 2009/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:Daily consumption of NSAIDs	20 weeks	30/30	8.3(2.8)/11.6(2.9)	Mean Diff	-3.3(-4.77,-1.83)	Group 1	na
Giordano ; 2009/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:Daily consumption of NSAIDs	12 weeks	30/30	6.6(3.1)/10.3(2.8)	Mean Diff	-3.7(-5.23,-2.17)	Group 1	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Other:HAQ Alternative Disability score	24 weeks	313/317	-0.18(0.36)/-0.16(0.36)	Mean Diff	-0.02(-0.08,0.04)	Not Sig.	na
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Other:McGill affective AUC	24 weeks	37/38	63.3(56.87)/65.25(56.83)	Mean Diff	-1.95(-28.12, 24.22)	Not Sig.	na
Hughes; 2002/High	3: Oral Supplement-glucosamine sulfate(1500mg)	3: Placebo/Control-placebo	Other:McGill sensory AUC	24 weeks	37/38	342.75(191.33)/380.18(149.2)	Mean Diff	-37.43(-116.63,41.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Other:No. of 500-mg tablets of acetaminophen	24 weeks	313/317	1.7(1.7)/1.8(1.8)	Mean Diff	-0.1(-0.37,0.17)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:OMERACT-OARSI response; % (n) -mild sample	24 weeks	247/243	59.11%/59.26%	RR	1(0.86,1.16)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:OMERACT-OARSI response; % (n) -severe sample	24 weeks	70/70	65.71%/48.57%	RR	1.35(1.01,1.82)	Group 1	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-Placebo	Other:OMERACT-OARSI response; % (n) -whole sample	24 weeks	317/313	60.57%/56.87%	RR	1.07(0.93,1.21)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Other:Patient's global assessment of disease status score	24 weeks	313/317	-12.3(27.4)/-13.6(27.5)	Mean Diff	1.3(-3,5.6)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Other:Patient's global assessment of response to therapy score	24 weeks	313/317	45.3(31.8)/-45.2(30.5)	Mean Diff	90.5(85.62,95.38)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Other:Physician's global assessment of disease status	24 weeks	313/317	-12.1(26.3)/-14.6(23.4)	Mean Diff	2.5(-1.4,6.4)	Not Sig.	na
McAlindon ; 2004/High	3: Oral Supplement-glucosamine sulfate/glucosamine hydrochloride(496/1500mg)	3: Placebo/Control-placebo	Other:mean change in analgesic use (mg)	12 wks	104/101	133(553)/-88(755)	Mean Diff	221(38.2,403.8)	Group 2	na
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Adverse events:Any Adverse Event	8 wks	60/60	10%/21.67%	RR	0.46(0.19,1.13)	Not Sig.	na
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Adverse events:Circulatory disturbances	4 wks	126/126	0%/1.59%	RD	-1.587(-4.762, 2.428)	Not Sig.	na
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Adverse events:Constipation	8 wks	60/60	1.67%/1.67%	RR	1(0.06, 15.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Adverse events:Gastrointestinal Reaction	8 wks	60/60	3.33%/10%	RR	0.33(0.07,1.59)	Not Sig.	na
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Adverse events:Gastrointestinal disturbances	4 wks	126/126	3.97%/4.76%	RR	0.83(0.26,2.66)	Not Sig.	na
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Adverse events:Headache	4 wks	126/126	1.59%/1.59%	RR	1(0.14, 6.99)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Adverse events:Inadequate Exercise	1 yrs	151/148	54.97%/62.16%	RR	0.88(0.73,1.07)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	3: Placebo/Control-Placebo(2x/day)	Adverse events:Inadequate Exercise	2 yrs	152/148	61.18%/61.49%	RR	1(0.83, 1.19)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Adverse events:Inadequate Exercise	2 yrs	150/149	62%/61.74%	RR	1(0.84, 1.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	Adverse events:Inadequate Exercise	1 yrs	150/149	61.33%/55.03%	RR	1.11(0.92,1.35)	Not Sig.	na
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Adverse events:Joint Pain and Swelling	8 wks	60/60	3.33%/3.33%	RR	1(0.15, 6.87)	Not Sig.	na
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Adverse events:Mild Abdominal Pain	8 wks	60/60	0%/3.33%	RD	-3.333(-9.817, 4.697)	Not Sig.	na
Gang; 2019/Low	3: Oral Supplement-Glucosamine Sulfate + Celecoxib(500mg/kg x3/day + 200mg/kg/day celecoxib)	3: Placebo/Control-Control (Celecoxib Alone)(200mg/kg/day)	Adverse events:Nausea	8 wks	60/60	1.67%/3.33%	RR	0.5(0.05,5.37)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Adverse events:Pruritus or Skin reaction	4 wks	126/126	0.79%/2.38%	RR	0.33(0.04,3.16)	Not Sig.	na
Noack ; 1994/Moderate	3: Oral Supplement-Glucosamine	3: Placebo/Control-placebo	Adverse events:total adverse events	4 wks	126/126	6.35%/10.32%	RR	0.62(0.26,1.43)	Not Sig.	na

PICO 3: Oral/Dietary Supplements

Chondroitin vs Control

Table 11: Chondroitin vs Control

Quality: H=High; M=Moderate; L=Low	H								M					
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Uebelhart; 2004	Reginster; 2017	Morita; 2018	Zegels; 2013	Kahan ; 2009	Rondanelli; 2019	Mazieres ; 2006	Moller; 2010	Rondanelli; 2019	Bourgeois; 1998	Mazieres; 2001	Bucsi; 1998
Composite														
Lequesne Index									●	↓				
Lequesne Index Score				↑	●	↑								
Patient Global Assessment							↓							
20% womac decrease-mild sample		●												
20% womac decrease-severe sample		●												
20% womac decrease-whole sample		●												
Lequesne Index AFI			●											
Tegner Lysholm Knee Score								↑			↑			
mean Lequesne Index AFI												↑		
mean change in lequesne index AFI; completer population													↓	
mean change in lequesne index AFI; intention to treat population													●	
Function														
SF-12 Physical Component	●													
50 Foot Walk (s)	●													
Physical SF-12									●					
SF-36 Physical activity											●			
SF-36 Physical role								●			●			
Walking time (sec)			●											●

Table 11 Continued: Chondroitin vs Control

Quality: H=High; M=Moderate; L=Low	H								M					
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Uebelhart; 2004	Reginster; 2017	Morita; 2018	Zegels; 2013	Kahan ; 2009	Rondanelli; 2019	Mazieres ; 2006	Moller; 2010	Rondanelli; 2019	Bourgeois; 1998	Mazieres; 2001	Bucsi; 1998

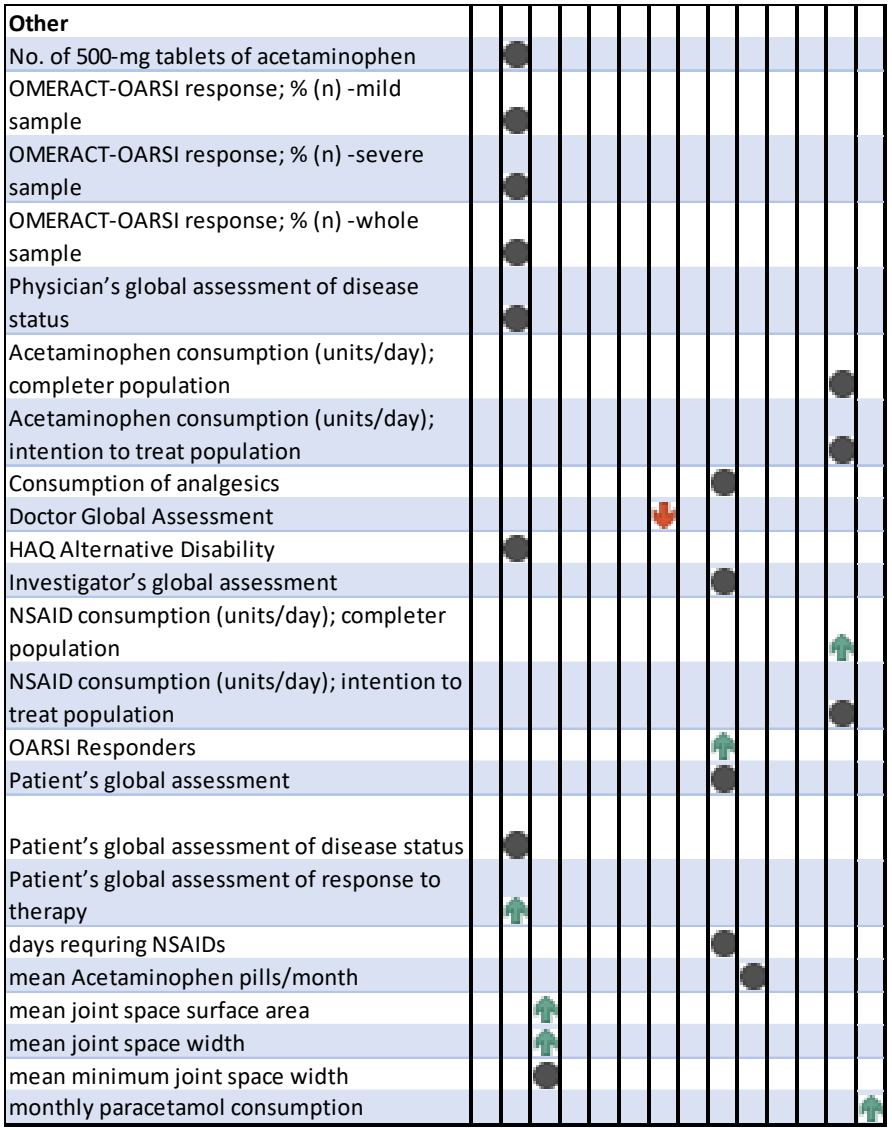

Other
No. of 500-mg tablets of acetaminophen
OMERACT-OARSI response; % (n) -mild sample
OMERACT-OARSI response; % (n) -severe sample
OMERACT-OARSI response; % (n) -whole sample
Physician's global assessment of disease status
Acetaminophen consumption (units/day); completer population
Acetaminophen consumption (units/day); intention to treat population
Consumption of analgesics
Doctor Global Assessment
HAQ Alternative Disability
Investigator's global assessment
NSAID consumption (units/day); completer population
NSAID consumption (units/day); intention to treat population
OARSI Responders
Patient's global assessment
Patient's global assessment of disease status
Patient's global assessment of response to therapy
days requring NSAIDs
mean Acetaminophen pills/month
mean joint space surface area
mean joint space width
mean minimum joint space width
monthly paracetamol consumption

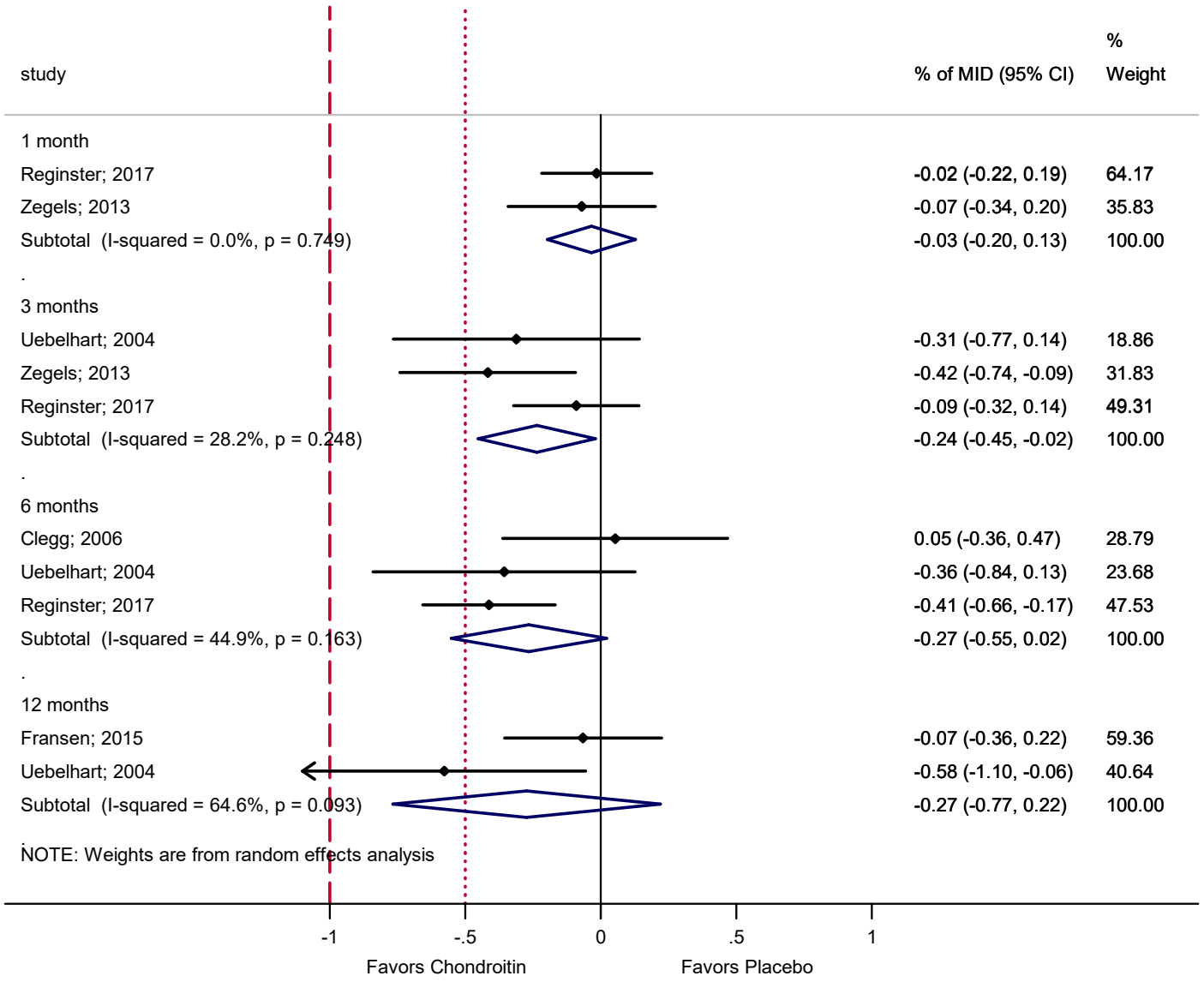
Table 11 Continued: Chondroitin vs Control

Quality: H=High; M=Moderate; L=Low	H								M					
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Uebelhart; 2004	Reginster; 2017	Monta; 2018	Zegels; 2013	Kahan ; 2009	Rondanelli; 2019	Mazieres ; 2006	Moller; 2010	Rondanelli; 2019	Bourgeois; 1998	Mazieres; 2001	Bucsi; 1998
Pain														
VAS Pain					●									
50% decrease in WOMAC pain score; % (n) - mild sample		●												
50% decrease in WOMAC pain score; % (n) - severe sample		●												
50% decrease in WOMAC pain score; % (n) - whole sample		●												
HAQ Pain		●												
Adverse events														
Inadequate Exercise	●													
Adverse Events									●					
calculable MID outcomes														
WOMAC Total								↓			↓			
WOMAC Function	●	●												
WOMAC Stiffness		●												
WOMAC Pain	●	●												
VAS Pain	●			●		●						↑		↑
Normalized WOMAC		●												
SF-36 Physical activity								●						
SF-36 Physical component										●				
Change in pain at rest (VAS; mm)									●					
SF-36 Physical Pain								↑			↑			
VAS pain Huskisson's			↑											
VAS pain during activity									●					
mean change in pain at rest (VAS); completer population													●	
mean change in pain at rest (VAS); intention to treat population													●	
mean change in pain with activity (VAS); completer population													●	
mean change in pain with activity (VAS); intention to treat population													●	
mean effect of OA on daily living (VAS); completer population													●	
mean effect of OA on daily living (VAS); intention to treat population													●	
vas pain intensity mean										↑				

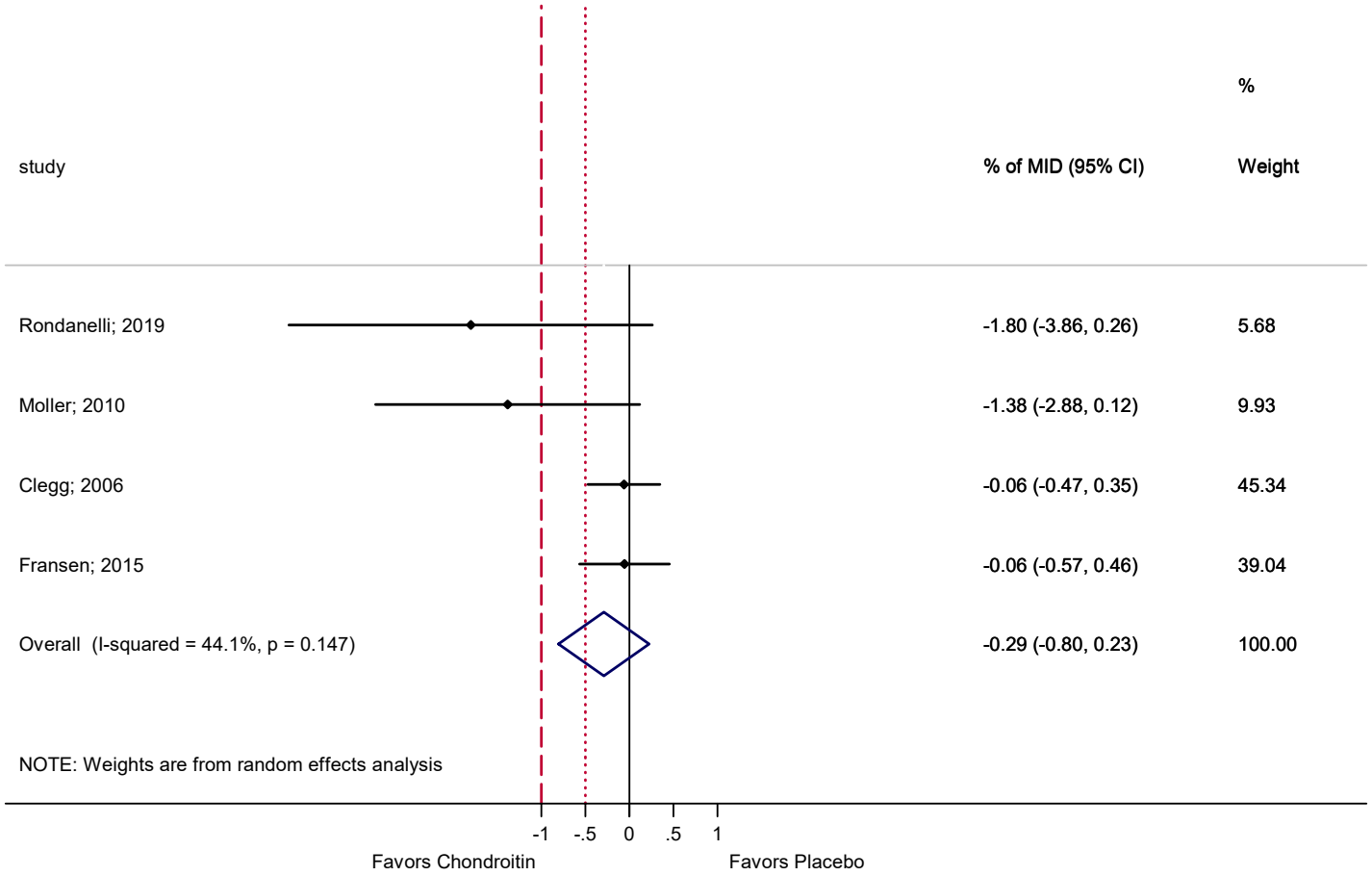
Table 11 Continued: Chondroitin vs Control

Quality: H=High; M=Moderate; L=Low	H								M					
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Fransen; 2015	Clegg; 2006	Uebelhart; 2004	Reginster; 2017	Morita; 2018	Zegels; 2013	Kahan ; 2009	Rondanelli; 2019	Mazieres ; 2006	Moller; 2010	Rondanelli; 2019	Bourgeois; 1998	Mazieres; 2001	Bucsi; 1998
QOL														
SF-36 Vitality								●			●			
SF-36 General Health								●			●			
SF-36 Mental Health								●			●			
SF-12 Mental Component Score	●													
Mental SF-12									●					
SF-36 Emotional role								●			●			
SF-36 Social activities								●			●			
SF-36 score; mental component										●				

Meta-Analysis Figure 8: Chondroitin vs Placebo- Pain Using subgroup of High-Quality Studies



Meta-Analysis Figure 9: Chondroitin vs Placebo- Function



Evidence Table 12 9: Chondroitin vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QoL:SF-36 General health	12 wks	30/30	-0.32(14.39)/0.06(16.54)	Mean Diff	-0.38(-8.4,7.64)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QoL:SF-36 General health	12 wks	30/30	-0.32(14.39)/0.06(16.54)	Mean Diff	-0.38(-8.4,7.64)	Not Sig.	na
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QoL:SF-36 Mental health	12 wks	30/30	-4.07(15.47)/-2(18.48)	Mean Diff	-2.07(-10.88, 6.74)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QoL:SF-36 Mental health	12 wks	30/30	-4.07(15.47)/-2(18.48)	Mean Diff	-2.07(-10.88, 6.74)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Pain:50% decrease in WOMAC pain score; % (n) - mild sample	24 weeks	248/243	43.95%/44.86%	RR	0.98(0.8,1.19)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Pain:50% decrease in WOMAC pain score; % (n) - severe sample	24 weeks	70/70	35.71%/32.86%	RR	1.09(0.69,1.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Pain:50% decrease in WOMAC pain score; % (n) - whole sample	24 weeks	318/313	42.14%/42.17%	RR	1(0.83, 1.2)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Pain:Change in pain at rest (VAS; mm)	24 wks	154/153	-18.8(23.8)/-16.6(24.2)	Mean Diff	-2.2(-7.59,3.19)	Not Sig.	clinically insignificant
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Pain:HAQ Pain	24 weeks	313/318	-15.4(25.5)/-16.6(28)	Mean Diff	1.2(-2.99,5.39)	Not Sig.	na
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Pain:SF-36 Physical Pain	12 wks	30/30	8.81(16.72)/-0.58(19.22)	Mean Diff	9.39(0.08,18.7)	Group 1	possibly clinically significant
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Pain:SF-36 Physical Pain	12 wks	30/30	8.81(16.72)/-0.58(19.22)	Mean Diff	9.39(0.08,18.7)	Group 1	possibly clinically significant
Reginster; 2017/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	30 days	195/204	49.4(20.95)/49.7(20)	Mean Diff	-0.3(-4.33,3.73)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reginster; 2017/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	91 days	179/188	39.4(22.74)/41.2(21.94)	Mean Diff	-1.8(-6.39,2.79)	Not Sig.	clinically insignificant
Reginster; 2017/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	182 days	160/172	28.6(22.77)/36.8(22.3)	Mean Diff	-8.2(-13.07,-3.33)	Group 1	clinically insignificant
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	9 mos	73	none	pvalue	NS	Not Sig.	na
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	3 mos	73	none	pvalue	NS	Not Sig.	na
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	12 mos	73	none	pvalue	NS	Not Sig.	na
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	6 mos	73	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Pain:VAS Pain	1 yrs	151/152	3.94(2.57)/4.02(2.75)	Mean Diff	-0.08(-0.68,0.52)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:VAS Pain	1 yrs	151/151	4.01(2.63)/4.14(2.46)	Mean Diff	-0.13(-0.71,0.45)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:VAS Pain	2 yrs	151/151	3.76(2.66)/4.03(2.61)	Mean Diff	-0.27(-0.87,0.33)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Pain:VAS Pain	2 yrs	151/152	3.58(2.6)/3.86(2.52)	Mean Diff	-0.28(-0.86,0.3)	Not Sig.	clinically insignificant
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Capsule)(400mg 3x/day)	3: Placebo/Control-Placebo	Pain:VAS Pain	1 mos	119/117	48.9(20.9)/50.3(21.2)	Mean Diff	-1.4(-6.8,4)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Capsule)(400mg 3x/day)	3: Placebo/Control-Placebo	Pain:VAS Pain	2 mos	119/117	43.1(23.5)/47.9(22.9)	Mean Diff	-4.8(-10.75, 1.15)	Not Sig.	clinically insignificant
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Gel Sachet)(1200mg x1/day)	3: Placebo/Control-Placebo	Pain:VAS Pain	2 mos	117/117	43(22.9)/47.9(22.9)	Mean Diff	-4.9(-10.8,1)	Not Sig.	clinically insignificant
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Gel Sachet)(1200mg x1/day)	3: Placebo/Control-Placebo	Pain:VAS Pain	3 mos	117/117	39.4(24.2)/47.1(24.8)	Mean Diff	-7.7(-14.01,-1.39)	Group 1	clinically insignificant
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Capsule)(400mg 3x/day)	3: Placebo/Control-Placebo	Pain:VAS Pain	3 mos	119/117	38.8(25.5)/47.1(24.8)	Mean Diff	-8.3(-14.75,-1.85)	Group 1	clinically insignificant
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Gel Sachet)(1200mg x1/day)	3: Placebo/Control-Placebo	Pain:VAS Pain	1 mos	117/117	52.5(21)/50.3(21.2)	Mean Diff	2.2(-3.24,7.64)	Not Sig.	clinically insignificant
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain	12 weeks	46/39	36(26)/52(24)	Mean Diff	-16(-26.8,-5.2)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain	24 weeks	46/39	32(23)/55(26)	Mean Diff	-23(-33.69,-12.31)	Group 1	possibly clinically significant
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain	4 weeks	46/39	43(19)/49(23)	Mean Diff	-6(-15.22, 3.22)	Not Sig.	clinically insignificant
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(3x 400mg)	3: Placebo/Control-placebo	Pain:VAS pain	6 weeks	44/43	37(18)/50(18)	Mean Diff	-13(-20.67,-5.33)	Group 1	possibly clinically significant
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(1200mg)	3: Placebo/Control-placebo	Pain:VAS pain	6 weeks	44/40	35(17)/50(18)	Mean Diff	-15(-22.62,-7.38)	Group 1	possibly clinically significant
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(1200mg)	3: Placebo/Control-placebo	Pain:VAS pain	13 weeks	44/40	29(16)/45(19)	Mean Diff	-16(-23.67,-8.33)	Group 1	possibly clinically significant
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(3x 400mg)	3: Placebo/Control-placebo	Pain:VAS pain	13 weeks	44/43	28(19)/45(19)	Mean Diff	-17(-25.1,-8.9)	Group 1	possibly clinically significant
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain Huskisson's	52 wks	56/54	34.3(27.4)/45.8(27.6)	Mean Diff	-11.5(-21.9,-1.1)	Group 1	possibly clinically significant
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain Huskisson's	39 wks	56/54	34(26.4)/46.1(27.2)	Mean Diff	-12.1(-22.24,-1.96)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain Huskisson's	13 wks	56/54	42.9(23.2)/49.1(24.5)	Mean Diff	-6.2(-15.23, 2.83)	Not Sig.	clinically insignificant
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:VAS pain Huskisson's	26 wks	56/54	40.5(23.9)/47.6(26.9)	Mean Diff	-7.1(-16.73, 2.53)	Not Sig.	clinically insignificant
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Pain:VAS pain during activity	12 wks	154/153	40(23)/42(21)	Mean Diff	-2(-6.95,2.95)	Not Sig.	clinically insignificant
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Pain:VAS pain during activity	4 wks	154/153	48(21)/51(23)	Mean Diff	-3(-7.95,1.95)	Not Sig.	clinically insignificant
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Pain:VAS pain during activity	24 wks	154/153	36(24)/41(23)	Mean Diff	-5(-10.28, 0.28)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:WOMAC Pain	2 yrs	151/151	4.4(3.6)/4.6(3.5)	Mean Diff	-0.2(-1,0.6)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Pain:WOMAC Pain	1 yrs	151/151	4.8(3.9)/4.7(3.8)	Mean Diff	0.1(-0.77,0.97)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Pain:WOMAC Pain	2 yrs	151/152	4.7(3.7)/4.5(3.7)	Mean Diff	0.2(-0.64,1.04)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Pain:WOMAC Pain	1 yrs	151/152	4.9(3.5)/4.5(3.7)	Mean Diff	0.4(-0.41,1.21)	Not Sig.	clinically insignificant
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Pain:WOMAC pain	24 weeks	313/318	-83.9(106.3)/-86.1(114.2)	Mean Diff	2.2(-15.04, 19.44)	Not Sig.	clinically insignificant
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Pain:mean change in pain at rest (VAS); completer population	12.85 wks	59/55	-16.9(21)/-8.8(21.9)	Mean Diff	-8.1(-16.07,-0.13)	Group 1	clinically insignificant
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Pain:mean change in pain at rest (VAS); intention to treat population	12.85 wks	67/63	-14.9(32.34)/-8(21.2)	Mean Diff	-6.9(-16.35, 2.55)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Pain:mean change in pain with activity (VAS); completer population	12.85 wks	59/55	-29.5(21.6)/-20.7(23.6)	Mean Diff	-8.8(-17.22,-0.38)	Group 1	clinically insignificant
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Pain:mean change in pain with activity (VAS); intention to treat population	12.85 wks	67/63	-26(2.78)/-19.7(22.8)	Mean Diff	-6.3(-12.08,-0.52)	Group 1	clinically insignificant
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Pain:mean effect of OA on daily living (VAS); completer population	12.85 wks	59/55	-27.1(23.1)/-19.2(25.8)	Mean Diff	-7.9(-17.01, 1.21)	Not Sig.	clinically insignificant
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Pain:mean effect of OA on daily living (VAS); intention to treat population	12.85 wks	67/63	-24.2(25.1)/-18.1(25)	Mean Diff	-6.1(-14.8,2.6)	Not Sig.	clinically insignificant
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:vas pain intensity mean	12 wks	56/60	31.3(2.8)/43.2(2.9)	Mean Diff	-11.9(-12.95,-10.85)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:vas pain intensity mean	8 wks	56/60	36.5(2.7)/42(2.8)	Mean Diff	-5.5(-6.51,-4.49)	Group 1	clinically insignificant
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Pain:vas pain intensity mean	4 wks	56/60	43.5(2.8)/50.3(2.4)	Mean Diff	-6.8(-7.76,-5.84)	Group 1	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:50 Foot Walk (s)	1 yrs	151/151	8.4(1.7)/8.5(2)	Mean Diff	-0.1(-0.52,0.32)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Function:50 Foot Walk (s)	1 yrs	151/152	8.5(1.9)/8.6(2.2)	Mean Diff	-0.1(-0.56,0.36)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:50 Foot Walk (s)	2 yrs	151/151	8.4(1.7)/8.4(1.9)	Mean Diff	0(-0.41,0.41)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Function:50 Foot Walk (s)	2 yrs	151/152	8.7(2)/8.5(2.1)	Mean Diff	0.2(-0.26,0.66)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Function:Physical SF-12	24 wks	154/153	5.8(9)/3.8(10.2)	Mean Diff	2(-0.16,4.16)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:SF-12 Physical Component Score	2 yrs	151/151	44.1(9.4)/44.2(9.7)	Mean Diff	-0.1(-2.26,2.06)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Function:SF-12 Physical Component Score	2 yrs	151/152	42.6(10)/43.9(9.4)	Mean Diff	-1.3(-3.49,0.89)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Function:SF-12 Physical Component Score	1 yrs	151/152	43.2(9.8)/44.5(10.2)	Mean Diff	-1.3(-3.56,0.96)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:SF-12 Physical Component Score	1 yrs	151/151	44.7(8.9)/44(9.5)	Mean Diff	0.7(-1.38,2.78)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Function:SF-36 Physical activity	12 wks	30/30	5.99(12.21)/0.05(14.02)	Mean Diff	5.94(-0.86,12.74)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Function:SF-36 Physical activity	12 wks	30/30	5.99(12.21)/0.05(14.02)	Mean Diff	5.94(-0.86,12.74)	Not Sig.	inconclusive
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Function:SF-36 Physical role	12 wks	30/30	6.14(35.63)/-4.19(40.92)	Mean Diff	10.33(-9.51,30.17)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Function:SF-36 Physical role	12 wks	30/30	6.14(35.63)/-4.19(40.92)	Mean Diff	10.33(-9.51,30.17)	Not Sig.	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:SF-36 score; physical component	12 wks	56/60	49.48(7.9)/46.72(8.4)	Mean Diff	2.76(-0.24,5.76)	Not Sig.	inconclusive
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:WOMAC Function	1 yrs	151/151	16.2(11.8)/16.5(12.7)	Mean Diff	-0.3(-3.08,2.48)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Function:WOMAC Function	2 yrs	151/151	17.4(13.1)/17.8(12.9)	Mean Diff	-0.4(-3.34,2.54)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Function:WOMAC Function	2 yrs	151/152	17.8(13.7)/17.8(13.5)	Mean Diff	0(-3.08,3.08)	Not Sig.	clinically insignificant
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Function:WOMAC Function	1 yrs	151/152	17.2(12.5)/16.3(13)	Mean Diff	0.9(-1.98,3.78)	Not Sig.	clinically insignificant
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Function:WOMAC function	24 weeks	313/318	-235.6(346.6)/-227.4(362.7)	Mean Diff	-8.2(-63.66, 47.26)	Not Sig.	clinically insignificant
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Function:WOMAC stiffness	24 weeks	313/318	-31.2(51.5)/-36.4(52.3)	Mean Diff	5.2(-2.91,13.31)	Not Sig.	clinically insignificant
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	12 wks	56/54	21.4(9)/22.4(8.3)	Mean Diff	-1(-4.27,2.27)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	24 wks	56/54	21.5(9.4)/23.1(8.5)	Mean Diff	-1.6(-4.98,1.78)	Not Sig.	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	36 wks	56/54	20.9(8)/22.7(7.5)	Mean Diff	-1.8(-4.73,1.13)	Not Sig.	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	48 wks	56/54	20.1(6.8)/22.7(7.7)	Mean Diff	-2.6(-5.35,0.15)	Not Sig.	na
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	12 weeks	46/39	23.2(7.2)/24.5(7.9)	Mean Diff	-1.3(-4.59,1.99)	Not Sig.	na
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	4 weeks	46/39	23.3(6.5)/24.8(8.2)	Mean Diff	-1.5(-4.74,1.74)	Not Sig.	na
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Function:Walking time (sec)	24 weeks	46/39	22.5(6.8)/25(7.9)	Mean Diff	-2.5(-5.72,0.72)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Composite:20% womac decrease-mild sample	24 weeks	248/243	66.53%/61.73%	RR	1.08(0.94,1.23)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Composite:20% womac decrease-severe sample	24 weeks	70/70	61.43%/54.29%	RR	1.13(0.85,1.5)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Composite:20% womac decrease-whole sample	24 weeks	318/313	65.41%/60.06%	RR	1.09(0.97,1.23)	Not Sig.	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index	8 wks	56/60	5.4(0.4)/6.3(0.4)	Mean Diff	-0.9(-1.05,-0.75)	Group 1	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index	12 wks	56/60	4.5(0.5)/6.1(0.4)	Mean Diff	-1.6(-1.77,-1.43)	Group 1	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index	4 wks	56/60	7.5(0.3)/7.3(0.3)	Mean Diff	0.2(0.09,0.31)	Group 2	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:Lequesne Index	4 wks	154/153	8.3(2.8)/8.4(2.4)	Mean Diff	-0.1(-0.69,0.49)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:Lequesne Index	12 wks	154/153	7.8(3.6)/7.9(3.1)	Mean Diff	-0.1(-0.85,0.65)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:Lequesne Index	24 wks	154/153	7.2(3.7)/7.7(3.3)	Mean Diff	-0.5(-1.29,0.29)	Not Sig.	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index AFI	13 wks	56/54	6.8(3.6)/7.4(4.2)	Mean Diff	-0.6(-2.08,0.88)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index AFI	26 wks	56/54	6.7(3.5)/7.5(4)	Mean Diff	-0.8(-2.22,0.62)	Not Sig.	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index AFI	39 wks	56/54	6(3.8)/7(3.9)	Mean Diff	-1(-2.46,0.46)	Not Sig.	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Composite:Lequesne Index AFI	52 wks	56/54	5.8(3.6)/7(3.9)	Mean Diff	-1.2(-2.62,0.22)	Not Sig.	na
Reginster; 2017/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	30 days	195/204	9.6(4.19)/9.8(4.28)	Mean Diff	-0.2(-1.03,0.63)	Not Sig.	na
Reginster; 2017/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	91 days	179/188	8.1(4.01)/8.8(4.11)	Mean Diff	-0.7(-1.53,0.13)	Not Sig.	na
Reginster; 2017/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	182 days	160/172	7.1(3.79)/8(3.93)	Mean Diff	-0.9(-1.73,-0.07)	Group 1	na
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	3 mos	73	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	12 mos	73	none	pvalue	NS	Not Sig.	na
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	9 mos	73	none	pvalue	NS	Not Sig.	na
Morita; 2018/High	3: Oral Supplement-Chondroitin Sulfate(800mg x1/day x6mo)	3: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	6 mos	73	none	pvalue	NS	Not Sig.	na
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Capsule)(400mg 3x/day)	3: Placebo/Control-Placebo	Composite:Lequesne Index Score	1 mos	119/117	9.4(3.1)/10.1(3.7)	Mean Diff	-0.7(-1.58,0.18)	Not Sig.	na
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Gel Sachet)(1200mg x1/day)	3: Placebo/Control-Placebo	Composite:Lequesne Index Score	1 mos	117/117	8.8(3.7)/10.1(3.7)	Mean Diff	-1.3(-2.25,-0.35)	Group 1	na
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Capsule)(400mg 3x/day)	3: Placebo/Control-Placebo	Composite:Lequesne Index Score	2 mos	119/117	8.4(3.6)/9.9(4.3)	Mean Diff	-1.5(-2.52,-0.48)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Gel Sachet)(1200mg x1/day)	3: Placebo/Control-Placebo	Composite:Lequesne Index Score	2 mos	117/117	8.4(3.8)/9.9(4.3)	Mean Diff	-1.5(-2.55,-0.45)	Group 1	na
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Gel Sachet)(1200mg x1/day)	3: Placebo/Control-Placebo	Composite:Lequesne Index Score	3 mos	117/117	7.8(4.2)/9.7(4.6)	Mean Diff	-1.9(-3.03,-0.77)	Group 1	na
Zegels; 2013/High	3: Oral Supplement-Chondroitin Sulfate (Capsule)(400mg 3x/day)	3: Placebo/Control-Placebo	Composite:Lequesne Index Score	3 mos	119/117	7.5(3.9)/9.7(4.6)	Mean Diff	-2.2(-3.29,-1.11)	Group 1	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Composite:Normalized WOMAC	24 weeks	313/318	-46.2(62.2)/-48.8(65.1)	Mean Diff	2.6(-7.35,12.55)	Not Sig.	inconclusive
Kahan ; 2009/High	3: Oral Supplement-chondroitin sulfate	3: Placebo/Control-Placebo	Composite:Patient Global Assessment	26 wks	309/313	42.2(31.85)/36.6(29.88)	Mean Diff	5.6(0.74,10.46)	Group 2	na
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:Tegner Lysholm Knee Score	12 wks	30/30	9.6(9)/-1.04(16.84)	Mean Diff	10.64(3.62,17.66)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:Tegner Lysholm Knee Score	12 wks	30/30	9.6(9)/-1.04(16.84)	Mean Diff	10.64(3.62,17.66)	Group 1	na
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:WOMAC Total	12 wks	30/30	-8.7(6.84)/3.54(7.73)	Mean Diff	-12.24(-16.01,-8.47)	Group 2	clinically significant
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	Composite:WOMAC Total	12 wks	30/30	-8.7(6.84)/3.54(7.73)	Mean Diff	-12.24(-16.01,-8.47)	Group 2	clinically significant
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(3x 400mg)	3: Placebo/Control-placebo	Composite:mean Lequesne Index AFI	6 weeks	44/43	7(2)/9(3)	Mean Diff	-2(-3.09,-0.91)	Group 1	na
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(1200mg)	3: Placebo/Control-placebo	Composite:mean Lequesne Index AFI	6 weeks	44/40	7(3)/9(3)	Mean Diff	-2(-3.3,-0.7)	Group 1	na
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(3x 400mg)	3: Placebo/Control-placebo	Composite:mean Lequesne Index AFI	13 weeks	44/43	6(3)/9(4)	Mean Diff	-3(-4.51,-1.49)	Group 1	na
Bourgeois; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(1200mg)	3: Placebo/Control-placebo	Composite:mean Lequesne Index AFI	13 weeks	44/40	6(3)/9(4)	Mean Diff	-3(-4.55,-1.45)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Composite:mean change in lequesne index AFI; completer population	12.85 wks	59/55	-2.9(2.5)/-1.7(3.1)	Mean Diff	-1.2(-2.25,-0.15)	Group 2	na
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Composite:mean change in lequesne index AFI; intention to treat population	12.85 wks	67/63	-2.4(2.76)/-1.6(3.1)	Mean Diff	-0.8(-1.82,0.22)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:Mental SF-12	24 wks	154/153	1.2(10.4)/0.3(11.3)	Mean Diff	0.9(-1.54,3.34)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	QOL:SF-12 Mental Component Score	1 yrs	151/152	52.8(8)/52.3(10)	Mean Diff	0.5(-1.55,2.55)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	QOL:SF-12 Mental Component Score	1 yrs	151/151	52.4(9.2)/51.3(10.6)	Mean Diff	1.1(-1.15,3.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	QOL:SF-12 Mental Component Score	2 yrs	151/152	54.6(7.6)/53.1(10.3)	Mean Diff	1.5(-0.55,3.55)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	QOL:SF-12 Mental Component Score	2 yrs	151/151	53.6(9.8)/51.6(10)	Mean Diff	2(-0.24,4.24)	Not Sig.	na
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:SF-36 Emotional role	12 wks	30/30	1.3(32.11)/-6.25(36.73)	Mean Diff	7.55(-10.29, 25.39)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:SF-36 Emotional role	12 wks	30/30	1.3(32.11)/-6.25(36.73)	Mean Diff	7.55(-10.29, 25.39)	Not Sig.	na
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:SF-36 Social activities	12 wks	30/30	-0.37(21.08)/-8.09(24.21)	Mean Diff	7.72(-4.02,19.46)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:SF-36 Social activities	12 wks	30/30	-0.37(21.08)/-8.09(24.21)	Mean Diff	7.72(-4.02,19.46)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rondanelli; 2019/Moderate	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:SF-36 Vitality	12 wks	30/30	0.53(16.43)/0.1(18.87)	Mean Diff	0.43(-8.72,9.58)	Not Sig.	na
Rondanelli; 2019/High	3: Oral Supplement-Non-Animal Chondroitin Sulfate	3: Placebo/Control-Placebo	QOL:SF-36 Vitality	12 wks	30/30	0.53(16.43)/0.1(18.87)	Mean Diff	0.43(-8.72,9.58)	Not Sig.	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	QOL:SF-36 score; mental component	12 wks	56/60	52.83(8.9)/53.42(8.6)	Mean Diff	-0.59(-3.81,2.63)	Not Sig.	na
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Other:Acetaminophen consumption (units/day); completer population	12.85 wks	56/50	594(697)/647(664)	Mean Diff	-53(-315.29,209.29)	Not Sig.	na
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Other:Acetaminophen consumption (units/day); intention to treat population	12.85 wks	63/58	544(664)/652(657)	Mean Diff	-108(-345.96,129.96)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Other:Consumption of analgesics	24 wks	154/153	28(29)/28(32)	Mean Diff	0(-6.86,6.86)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kahan ; 2009/High	3: Oral Supplement-chondroitin sulfate	3: Placebo/Control-Placebo	Other:Doctor Global Assessment	26 wks	309/313	39.6(28.31)/34.8(29.88)	Mean Diff	4.8(0.22,9.38)	Group 2	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Other:HAQ Alternative Disability	24 weeks	313/318	-0.17(0.34)/-0.16(0.36)	Mean Diff	-0.01(-0.06,0.04)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Other:Investigator's global assessment	24 wks	154/153	3.1(2.7)/2.5(3)	Mean Diff	0.6(-0.04,1.24)	Not Sig.	na
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Other:NSAID consumption (units/day); completer population	12.85 wks	24/29	0.2(12.6)/9.2(15.4)	Mean Diff	-9(-16.72,-1.28)	Group 1	na
Mazieres; 2001/Moderate	3: Oral Supplement-chondroitin sulfate(500mg)	3: Placebo/Control-placebo	Other:NSAID consumption (units/day); intention to treat population	12.85 wks	27/35	8.2(11.7)/13(22)	Mean Diff	-4.8(-13.52,3.92)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Other:No. of 500-mg tablets of acetaminophen	24 weeks	313/318	1.9(1.9)/1.8(1.8)	Mean Diff	0.1(-0.19,0.39)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Other:OARSI Responders	24 wks	154/153	67.53%/56.21%	RR	1.2(1.01,1.43)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Other:OMERACT-OARSI response; % (n) -mild sample	24 weeks	248/243	64.92%/59.26%	RR	1.1(0.95,1.26)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Other:OMERACT-OARSI response; % (n) -severe sample	24 weeks	70/70	58.57%/48.57%	RR	1.21(0.88,1.65)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin	3: Placebo/Control-Placebo	Other:OMERACT-OARSI response; % (n) -whole sample	24 weeks	318/313	63.52%/56.87%	RR	1.12(0.98,1.27)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Other:Patient's global assessment	24 wks	154/153	3.1(3)/2.5(3.1)	Mean Diff	0.6(-0.09,1.29)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Other:Patient's global assessment of disease status	24 weeks	313/318	-12.4(24.5)/-13.6(27.5)	Mean Diff	1.2(-2.87,5.27)	Not Sig.	na
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Other:Patient's global assessment of response to therapy	24 weeks	313/318	45.6(30.9)/-45.2(30.5)	Mean Diff	90.8(86,95.6)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-placebo	Other:Physician's global assessment of disease status	24 weeks	313/318	-13.7(23.2)/-14.6(23.4)	Mean Diff	0.9(-2.74,4.54)	Not Sig.	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Other:days requring NSAIDs	24 wks	154/153	6.9(20.2)/9.2(24.6)	Mean Diff	-2.3(-7.36,2.76)	Not Sig.	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:mean Acetaminophen pills/month	4 wks	56/60	29.5(31.4)/29.5(29.6)	Mean Diff	0(-11.24, 11.24)	Not Sig.	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:mean Acetaminophen pills/month	8 wks	56/60	32.3(33.9)/28.8(28.2)	Mean Diff	3.5(-8.02,15.02)	Not Sig.	na
Moller; 2010/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:mean Acetaminophen pills/month	12 wks	56/60	38.2(42.6)/30.2(33.8)	Mean Diff	8(-6.22,22.22)	Not Sig.	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:mean joint space surface area	48 wks	76/77	67.8(26.9)/58.7(20.9)	Mean Diff	9.1(1.39,16.81)	Group 1	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:mean joint space width	48 wks	76/77	4.2(1.58)/3.74(1.28)	Mean Diff	0.46(0, 0.92)	Group 1	na
Uebelhart; 2004/High	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:mean minimum joint space width	48 wks	76/77	3.61(1.51)/3.23(1.27)	Mean Diff	0.38(-0.07,0.83)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:monthly paracetamol consumption	12 weeks	46/39	7.5(10.7)/10.8(20)	Mean Diff	-3.3(-10.45, 3.85)	Not Sig.	na
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:monthly paracetamol consumption	4 weeks	46/39	7.6(12.4)/11.4(22.5)	Mean Diff	-3.8(-11.89, 4.29)	Not Sig.	na
Bucsi; 1998/Moderate	3: Oral Supplement-chondroitin sulfate(800mg)	3: Placebo/Control-placebo	Other:monthly paracetamol consumption	24 weeks	46/39	5.6(7)/10.3(12.7)	Mean Diff	-4.7(-9.27,-0.13)	Group 1	na
Mazieres ; 2006/Moderate	3: Oral Supplement-Chondroitin Sulfate	3: Placebo/Control-Placebo	Adverse events:Adverse Events	24 wks	154/153	48.7%/49.67%	RR	0.98(0.78,1.23)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Adverse events:Inadequate Exercise	1 yrs	149/148	55.03%/62.16%	RR	0.89(0.73,1.07)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Chondroitin Sulfate(400mg 2x/day)	3: Placebo/Control-Placebo(2x/day)	Adverse events:Inadequate Exercise	2 yrs	149/148	61.74%/61.49%	RR	1(0.84, 1.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Adverse events:Inadequate Exercise	2 yrs	150/152	62%/61.18%	RR	1.01(0.85,1.21)	Not Sig.	na
Fransen; 2015/High	3: Oral Supplement-Glucosamine Sulfate + Chondroitin Sulfate(753mg GS + 400mg CS 2x/day)	3: Oral Supplement-Glucosamine Sulfate(753mg GS 2x/day)	Adverse events:Inadequate Exercise	1 yrs	150/151	61.33%/54.97%	RR	1.12(0.92,1.35)	Not Sig.	na

PICO 3: Oral/Dietary Supplements

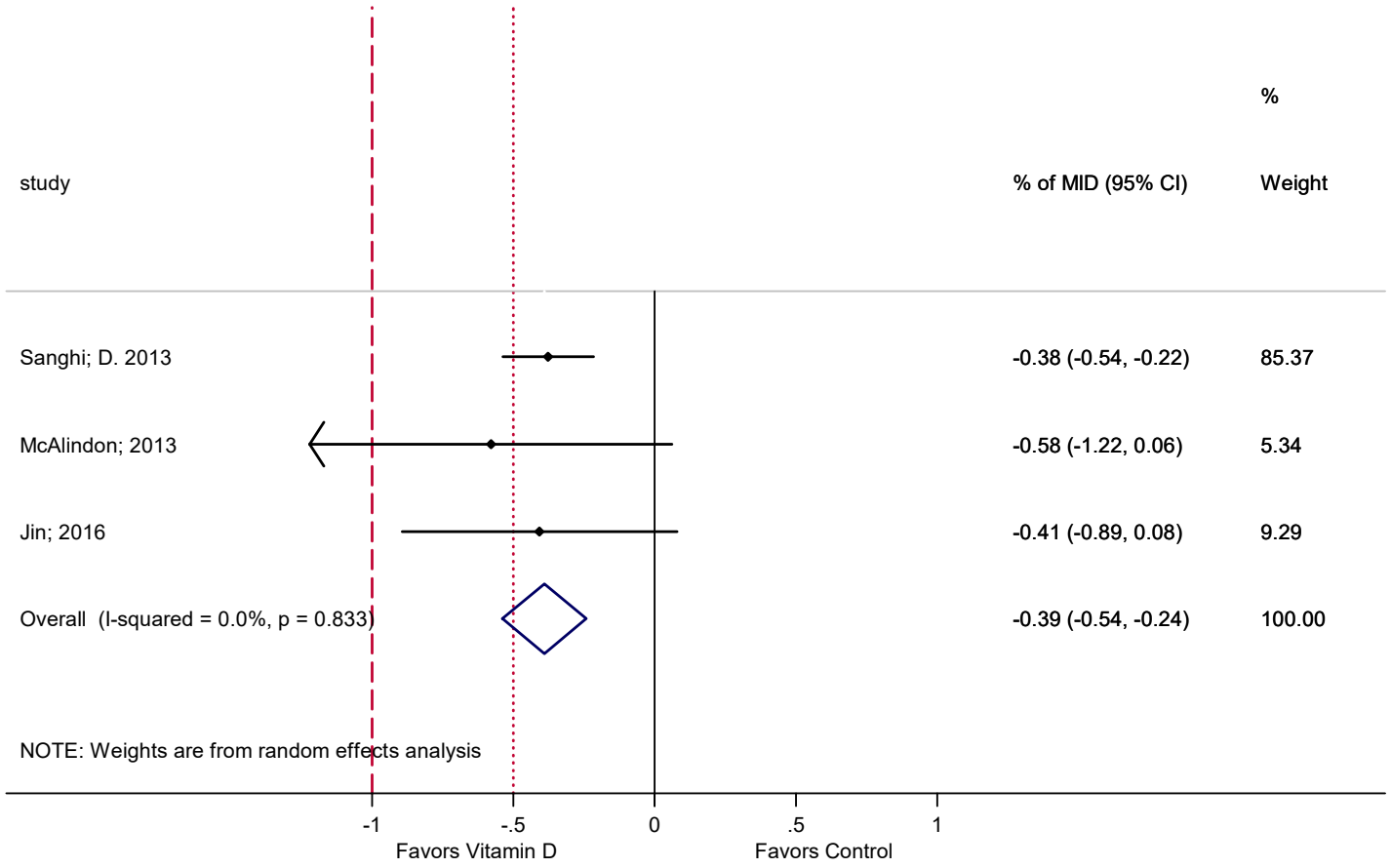
Vitamin D vs Control

Table 13: Vitamin D vs Control

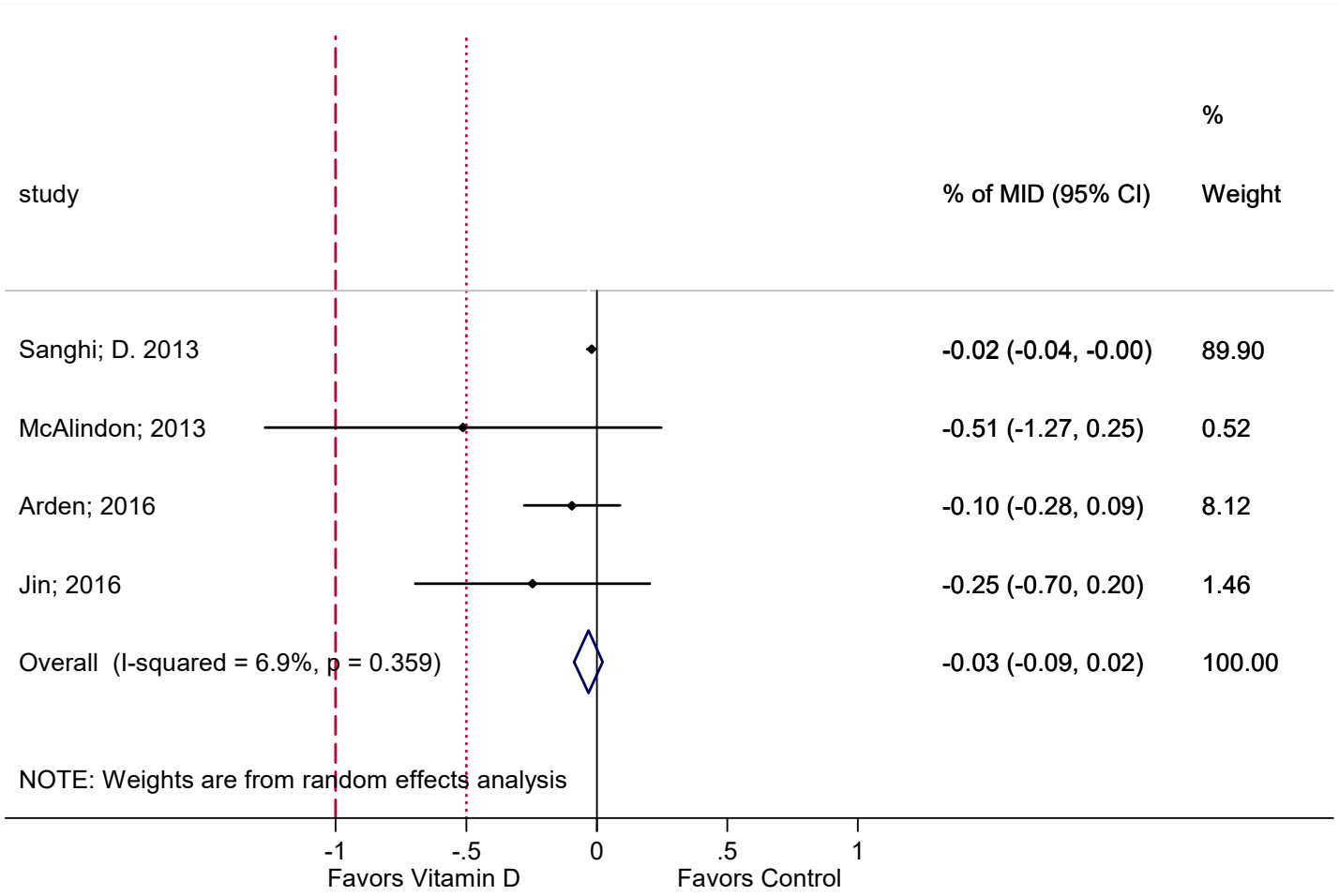
Quality: H=High; M=Moderate; L=Low	H			M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Jin; 2016	McAlindon; 2013	Sanghi; D. 2013	Arden; 2016
Function				
20-m Walk (s)(delta)		●		
Chair-stand (s)(delta)		●		
Odds of Higher Grade in Get Up and Go Test				●
Adverse events				
Any Adverse Event		●		
Pain	●			
Allergy/Immunology Adverse Events	●			
Cardiac Arrhythmia	●			
Chest Pain	●			
Coronary Artery Disease	●			
Death	●			
Falls	●			
Gastrointestinal Adverse Events	●			
Hospitalization	●			
Hypercalcemia	●			
Hyperparathyroidism	●			
Infection	●			
Major Depression	●			
Malignancy	●			
Musculoskeletal Adverse Events	●			
Nephrolithiasis	●			
Neurological Adverse Events	●			
Ocular Adverse Events	●			
Other Adverse Events(headache; lethargy; flu symptoms; and other events (neuroma; dysphonia; hypotension; lipoma; hypersensitivity; and Sjögren syndrome).)	●			
Renal Adverse Events	●			
Respiratory Adverse Events	●			
Severe Infection	●			

Quality: H=High; M=Moderate; L=Low	H			M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Jin; 2016	McAlindon; 2013	Sanghi; D. 2013	Arden; 2016
calculable MID outcomes				
WOMAC Total	●		●	●
WOMAC Function	●	●	●	●
WOMAC Stiffness	●		●	●
WOMAC Pain	●	●	↑	●
VAS Pain	●		●	
OA progression				
Higher K-L Grade Per Year (Contralateral Knee)				●
Higher K-L Grade Per Year (Index Knee)				●

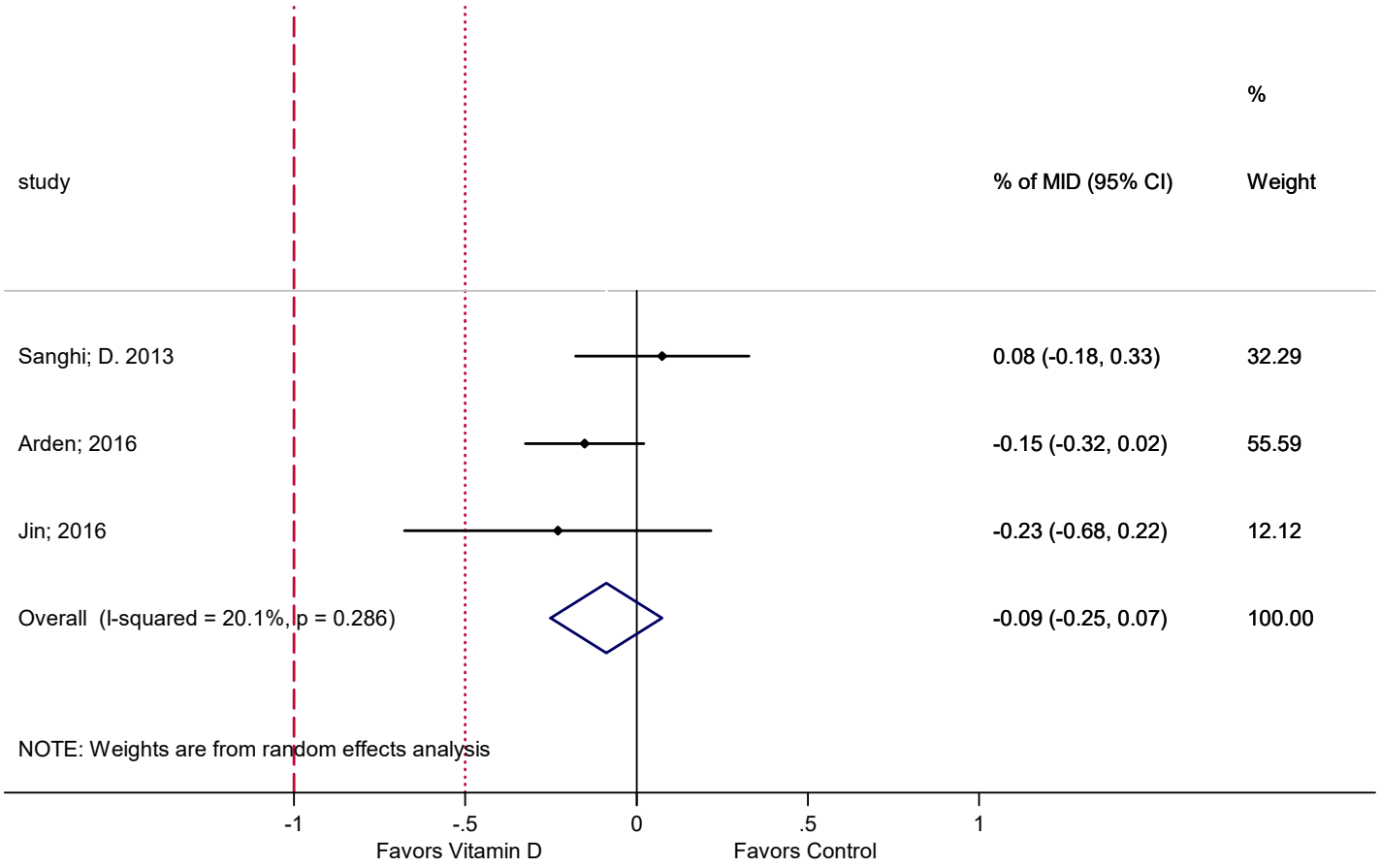
Meta-Analysis Figure 10: Vitamin D vs Placebo- Function Subgroup of High-Quality Studies



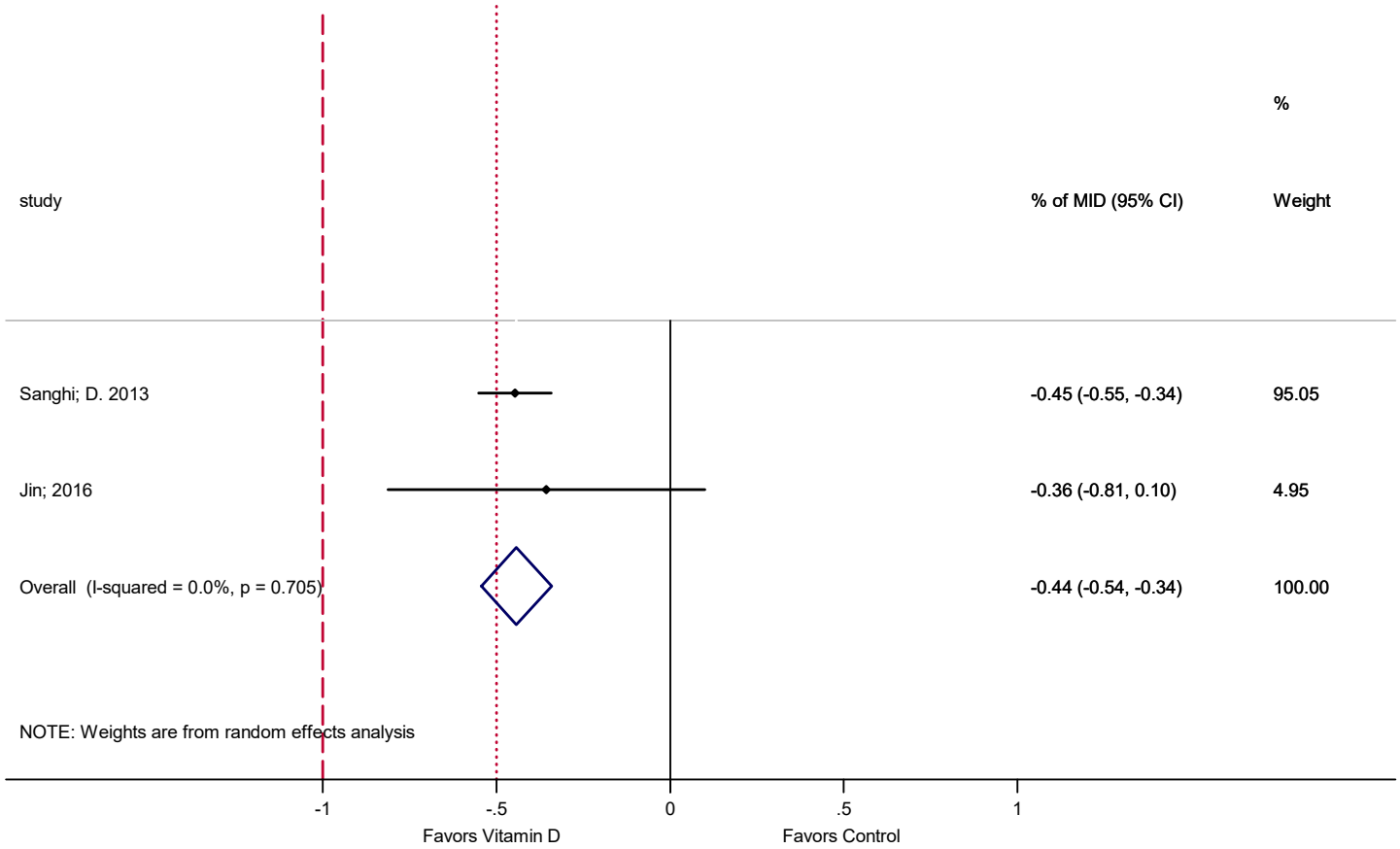
Meta-Analysis Figure 11: Vitamin D vs Placebo- Pain



Meta-Analysis Figure 12: Vitamin D vs Placebo- Stiffness



Meta-Analysis Figure 13: Vitamin D vs Placebo- WOMAC Total Subgroup of High-Quality Studies



Evidence Table 1014: Vitamin D vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Pain:VAS Pain	24 mos	182/167	33.7(27.1)/36.4(25.1)	Mean Diff	-2.7(-8.2,2.8)	Not Sig.	clinically insignificant
Sanghi; D. 2013/High	3: Oral Supplement-Vitamin D(Vitamin D group (experimental arm) received FDA-approved oral vitamin D (cholecalciferol granules) of 60;000 IU per day for 10 days followed by 60;000 IU once a month for 12 months)	3: Oral Supplement-Placebo(One placebo capsule per day for 10 days followed by one capsule once per month for 12 months)	Pain:VAS pain	1 yrs	52/51	-0.26(.)/0.13(.)	Mean Diff	-0.39 (-0.71,-0.08)	Group 1	clinically insignificant
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Pain:WOMAC Pain (0-500)	24 mos	183/168	87(90.1)/97.2(87.5)	Mean Diff	-10.2(-28.85, 8.45)	Not Sig.	clinically insignificant
McAlindon; 2013/High	3: Oral Supplement-Vitamin D (Cholecalciferol)(2000 IU 1x/day)	3: Placebo/Control-Placebo(1x/day)	Pain:WOMAC Pain(delta)	2 yrs	73/73	-2.31(3.99)/-1.46(3.71)	Mean Diff	-0.85(-2.11,0.41)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanghi; D. 2013/High	3: Oral Supplement-Vitamin D(Vitamin D group (experimental arm) received FDA-approved oral vitamin D (cholecalciferol granules) of 60;000 IU per day for 10 days followed by 60;000 IU once a month for 12 months)	3: Oral Supplement-Placebo(One placebo capsule per day for 10 days followed by one capsule once per month for 12 months)	Pain:WOMAC pain	1 yrs	52/51	-0.55(1.96)/1.16(1.19)	Mean Diff	-1.71(-2.34,-1.08)	Group 1	possibly clinically significant
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Pain:Yearly WOMAC Pain Reduction	3 yrs	474	none	Mean Difference	-0.79(-2.31,0.74)	Not Sig.	clinically insignificant
McAlindon; 2013/High	3: Oral Supplement-Vitamin D (Cholecalciferol)(2000 IU 1x/day)	3: Placebo/Control-Placebo(1x/day)	Function:20-m Walk (s)(delta)	2 yrs	73/73	0.09(2.81)/-0.24(3.39)	Mean Diff	0.33(-0.69,1.35)	Not Sig.	na
McAlindon; 2013/High	3: Oral Supplement-Vitamin D (Cholecalciferol)(2000 IU 1x/day)	3: Placebo/Control-Placebo(1x/day)	Function:Chair-stand (s)(delta)	2 yrs	73/73	-1.25(6.39)/-0.93(7.91)	Mean Diff	-0.32(-2.67,2.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Function:Odds of Higher Grade in Get Up and Go Test	3 yrs	474	none	OR	0.96(0.73,1.27)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Function:WOMAC Function	24 mos	181/168	306.4(303.7)/361.8(322.8)	Mean Diff	-55.4(-121.51,10.71)	Not Sig.	clinically insignificant
McAlindon; 2013/High	3: Oral Supplement-Vitamin D (Cholecalciferol)(2000 IU 1x/day)	3: Placebo/Control-Placebo(1x/day)	Function:WOMAC Function(delta)	2 yrs	73/73	-6.97(11.96)/-3.82(9.17)	Mean Diff	-3.15(-6.64,0.34)	Not Sig.	inconclusive
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Function:WOMAC Stiffness	24 mos	183/168	41.1(44.1)/45.7(41.1)	Mean Diff	-4.6(-13.54, 4.34)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanghi; D. 2013/High	3: Oral Supplement-Vitamin D(Vitamin D group (experimental arm) received FDA-approved oral vitamin D (cholecalciferol granules) of 60;000 IU per day for 10 days followed by 60;000 IU once a month for 12 months)	3: Oral Supplement-Placebo(One placebo capsule per day for 10 days followed by one capsule once per month for 12 months)	Function:WOMAC function	1 yrs	52/51	-1.36(1.83)/0.69(2.56)	Mean Diff	-2.05(-2.92,-1.18)	Group 1	clinically insignificant
Sanghi; D. 2013/High	3: Oral Supplement-Vitamin D(Vitamin D group (experimental arm) received FDA-approved oral vitamin D (cholecalciferol granules) of 60;000 IU per day for 10 days followed by 60;000 IU once a month for 12 months)	3: Oral Supplement-Placebo(One placebo capsule per day for 10 days followed by one capsule once per month for 12 months)	Function:WOMAC stiffness	1 yrs	52/51	0.15(0.43)/0.09(0.59)	Mean Diff	0.06(-0.14,0.26)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Function:Yearly WOMAC Function Reduction	3 yrs	474	none	Mean Difference	-0.65(-2.09,0.79)	Not Sig.	clinically insignificant
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Function:Yearly WOMAC Stiffness Reduction	3 yrs	474	none	Mean Difference	-1.52(-3.24,0.21)	Not Sig.	clinically insignificant
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Composite:WOMAC Total	24 mos	181/168	434.3(419.3)/504.7(435.7)	Mean Diff	-70.4(-160.56,19.76)	Not Sig.	clinically insignificant
Sanghi; D. 2013/High	3: Oral Supplement-Vitamin D(Vitamin D group (experimental arm) received FDA-approved oral vitamin D (cholecalciferol granules) of 60;000 IU per day for 10 days followed by 60;000 IU once a month for 12 months)	3: Oral Supplement-Placebo(One placebo capsule per day for 10 days followed by one capsule once per month for 12 months)	Composite:WOMAC total	1 yrs	52/51	-2.12(2.5)/1.41(1.62)	Mean Diff	-3.53(-4.35,-2.71)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Composite:Yearly WOMAC Total Reduction	3 yrs	474	none	Mean Difference	-0.72(-1.92,0.48)	Not Sig.	clinically insignificant
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	OA progression: Higher K-L Grade Per Year (Contralateral Knee)	3 yrs	474	none	OR	1.01(0.8,1.27)	Not Sig.	na
Arden; 2016/Moderate	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	OA progression: Higher K-L Grade Per Year (Index Knee)	3 yrs	474	none	OR	1.07(0.88,1.31)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Allergy/Immunology Adverse Events	24 mos	209/204	0%/0.98%	RD	-0.98(-2.92,1.543)	Not Sig.	na
McAlindon; 2013/High	3: Oral Supplement-Vitamin D (Cholecalciferol)(2000 IU 1x/day)	3: Placebo/Control-Placebo(1x/day)	Adverse events:Any Adverse Event	2 yrs	73/73	21.92%/21.92%	RR	1(0.54, 1.84)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Cardiac Arrhythmia	24 mos	209/204	1.44%/0%	RD	1.435(-1.264, 3.512)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Chest Pain	24 mos	209/204	1.91%/2.45%	RR	0.78(0.21,2.87)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Coronary Artery Disease	24 mos	209/204	0.48%/0.49%	RR	0.98(0.06,15.5)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Death	24 mos	209/204	0.48%/0%	RD	0.478(-1.703, 2.368)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Falls	24 mos	209/204	0.96%/0%	RD	0.957(-1.507, 2.931)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Events	24 mos	209/204	3.35%/2.45%	RR	1.37(0.44,4.24)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Hospitalization	24 mos	209/204	1.44%/0%	RD	1.435(-1.264, 3.512)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Hypercalcemia	24 mos	209/204	1.91%/0.98%	RR	1.95(0.36,10.54)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Hyperparathyroidism	24 mos	209/204	0.48%/0%	RD	0.478(-1.703, 2.368)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Infection	24 mos	209/204	2.87%/1.96%	RR	1.46(0.42,5.11)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Major Depression	24 mos	209/204	0.48%/0%	RD	0.478(-1.703, 2.368)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Malignancy	24 mos	209/204	1.91%/0.98%	RR	1.95(0.36,10.54)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Musculoskeletal Adverse Events	24 mos	209/204	0.48%/0.49%	RR	0.98(0.06,15.5)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Nephrolithiasis	24 mos	209/204	0.48%/0.49%	RR	0.98(0.06,15.5)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Neurological Adverse Events	24 mos	209/204	2.39%/1.96%	RR	1.22(0.33,4.48)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Ocular Adverse Events	24 mos	209/204	0.48%/0.98%	RR	0.49(0.04,5.34)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Other Adverse Events(headache; lethargy; flu symptoms; and other events (neuroma; dysphonia; hypotension; lipoma; hypersensitivity; and Sjögren syndrome).)	25 mos	209/204	4.31%/3.43%	RR	1.25(0.48,3.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Pain	24 mos	209/204	3.35%/0.98%	RR	3.42(0.72,16.25)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Renal Adverse Events	24 mos	209/204	0.96%/0%	RD	0.957(-1.507, 2.931)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Respiratory Adverse Events	24 mos	209/204	0.96%/0.98%	RR	0.98(0.14,6.86)	Not Sig.	na
Jin; 2016/High	3: Oral Supplement-Vitamin D(50000 IU (1.25mg) x1 /mo x24 mo)	3: Placebo/Control-Placebo	Adverse events:Severe Infection	24 mos	209/204	0%/1.47%	RD	-1.471(-3.519, 1.293)	Not Sig.	na

PICO 4: Topical Treatments

Topical vs Control

Table 12: Topical NSAID vs Control

Quality: H=High; M=Moderate; L=Low	H																M	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Baer; 2005	Roth; 2004	Conaghan; 2013	Simon; 2009	Kneer; 2013	Rother; 2013	Bookman; 2004	Wadsworth; 2019	Wadsworth; 2017	Wadsworth; 2018	Wadsworth; 2016	Sandelin; 1997	Dehghan; 2019	Dehghan; 2020	Rother; 2007	Barthel; 2009	Ottillinger ; 2001
Composite																	
Patient Global Assessment					↑			●									
Function																	
Lequesne Index(0-24)												↑					
WOMAC Daily Stiffness													↑				
WOMAC Daytime Stiffness														↑			
WOMAC Morning Stiffness													↑	↑			
Other																	
average tablets acetaminophen taken per day																●	
mean acetaminophen consumption (tablets)							↑										
mean patient global assessment							↑										
need for omeprazole for dyspepsia			●														
patient global assessment of overall health				↑													
patient global assessment of study knee				↑													
weeks with no rescue drug																↑	
Pain																	
WOMAC Pain		↑															
VAS Pain														●			
% Response to Tx(50+% reduction in WOMAC Pain vs. Baseline)			●			↓											
mean WOMAC pain on walking (Likert)							↑										
calculable MID outcomes																	
WOMAC Function	↑	↑			●	●	↑		●					↑	●		
WOMAC Stiffness	↑	↑		●		●	↑			●							
WOMAC Pain	↑	↑	●	↑	●	●	↑				●		↑		↑		
WOMAC Physical function				↑													
VAS Pain													↑				
VAS Pain in Last 24 hrs								●									
WOMAC Physical Performance													↑				
VAS Pain Evening								●									
VAS Pain Midday								●									
VAS Pain(0-100)												●					
mean global pain (VAS)																	●
QOL																	
change in patient global assessment		↑															
global evaluation of treatment																↓	
mean change in patient global assessment (Likert)	↑																
mean change in WOMAC pain on walking (Likert)	↑																

Table 12 Continued: Topical NSAID vs Control

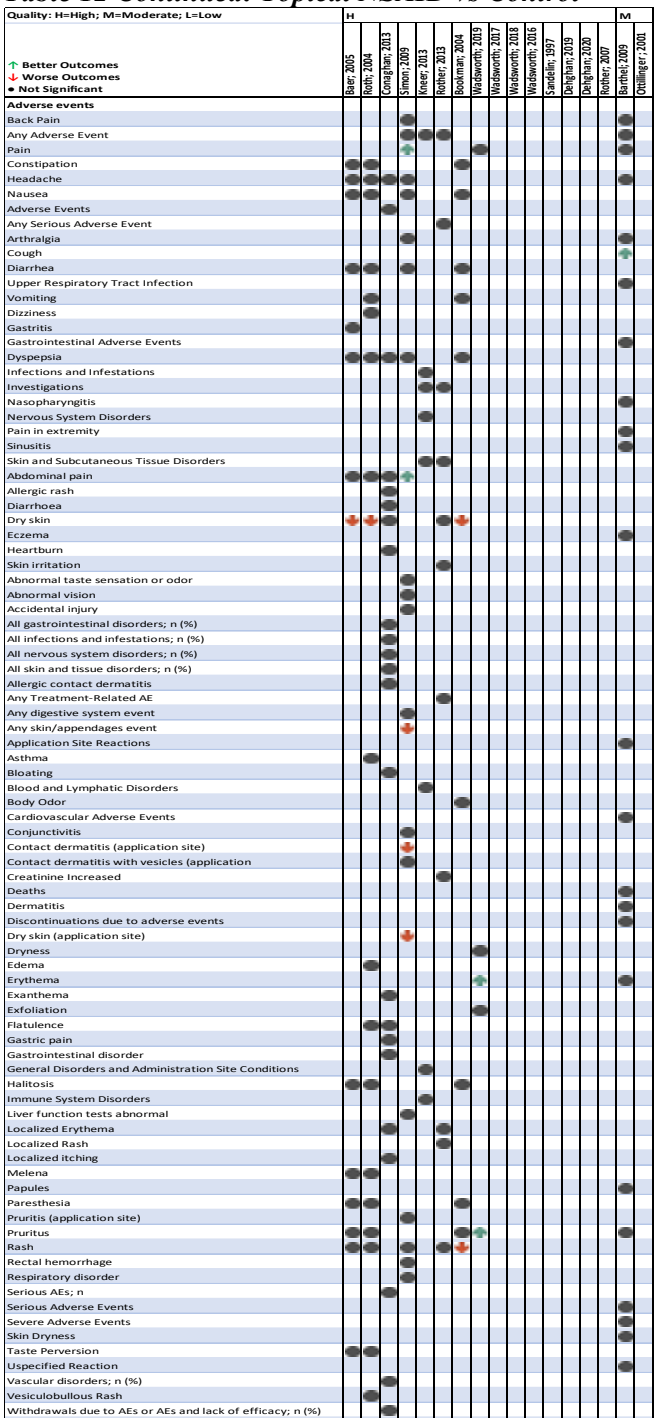
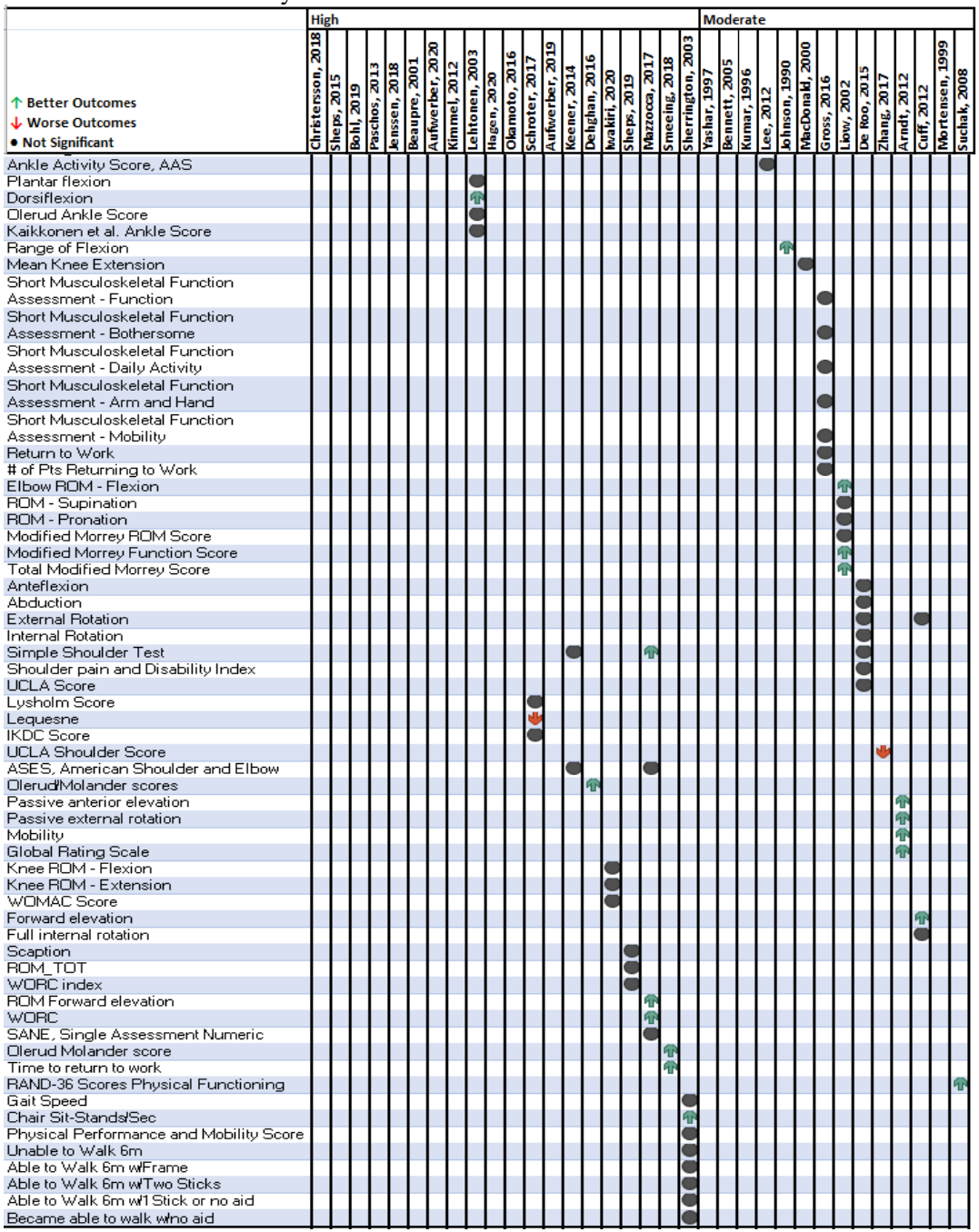


Table 8 Continued 2: Early Mobilization/Ambulation vs Control



Evidence Table 1511: Topical NSAID vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:% Response to Tx(50+% reduction in WOMAC Pain vs. Baseline)	12 wks	274/281	41.24%/50.53%	RR	0.816(0.68,0.98)	Group 2	na
Conaghan; 2013/High	4: Topical Supplement-Ketoprofen in Gel (high dose)(100mg 2x/day)	4: Placebo/Control-Placebo Gel (high dose)(2x/day)	Pain:% Response to Tx(50+% reduction in WOMAC Pain vs. Baseline)	12 wks	230/234	43.48%/40.6%	RR	1.071(0.865,1.326)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-Ketoprofen in Gel (low dose)(50mg 2x/day)	4: Placebo/Control-Placebo Gel (low dose)(2x/day)	Pain:% Response to Tx(50+% reduction in WOMAC Pain vs. Baseline)	12 wks	233/238	45.06%/40.76%	RR	1.106(0.897,1.362)	Not Sig.	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:VAS Pain in Last 24 hrs	4 wks	130/129	4.6(2.6)/5.1(2.5)	Mean Diff	-0.5(-1.12,0.12)	Not Sig.	clinically insignificant
Dehghan; 2019/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	40/40	3.68(2.3)/6.05(2.18)	Mean Diff	-2.37(-3.37,-1.37)	Group 1	possibly clinically significant
Dehghan; 2019/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	40/40	2.18(1.08)/6.05(2.18)	Mean Diff	-3.87(-4.64,-3.1)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Dehghan; 2020/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	49/48	2.57(1.08)/2.7(0.91)	Mean Diff	-0.13(-0.53,0.27)	Not Sig.	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:VAS Pain Evening	4 wks	130/129	4.5(2.5)/4.8(2.6)	Mean Diff	-0.3(-0.92,0.32)	Not Sig.	clinically insignificant
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:VAS Pain Midday	4 wks	130/129	4.5(2.6)/4.8(2.5)	Mean Diff	-0.3(-0.92,0.32)	Not Sig.	clinically insignificant
Sandelin; 1997/High	4: Topical Supplement-topical eltenac 1% gel and placebo tablet(3g applied 3 times daily)	9: Placebo/Control-Placebo (Oral)(once a day)	Pain:VAS Pain(0-100)	28 days	124/79	28(20.7)/32(24.1)	Mean Diff	-4(-10.5,2.5)	Not Sig.	clinically insignificant
Wadsworth; 2016/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:WOMAC Pain	4 wks	130/129	7.9(4.5)/8.9(4.4)	Mean Diff	-1(-2.09,0.09)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Pain:WOMAC Pain	12 wks	151/151	-7(4.8)/-6.4(4.1)	Mean Diff	-0.6(-1.61,0.41)	Not Sig.	clinically insignificant
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Pain:WOMAC Pain	12 wks	154/161	-6(4.5)/-4.7(4.3)	Mean Diff	-1.3(-2.28,-0.32)	Group 1	possibly clinically significant
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Pain:WOMAC Pain	12 wks	154/155	-6(4.5)/-4.7(4.4)	Mean Diff	-1.3(-2.3,-0.3)	Group 1	possibly clinically significant
Dehghan; 2019/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	40/40	3.57(2.6)/10.35(5.17)	Mean Diff	-6.78(-8.61,-4.95)	Group 1	clinically significant
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:WOMAC Pain (VAS Version)	12 wks	223/199	29.88(21.16)/32.57(32.33)	Mean Diff	-2.69(-7.99,2.61)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:WOMAC Pain (VAS Version)	12 wks	221/199	28.39(21)/32.57(32.33)	Mean Diff	-4.18(-9.48,1.12)	Not Sig.	inconclusive
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:WOMAC Pain (VAS Version)	12 wks	223/199	27.92(21.28)/32.57(32.33)	Mean Diff	-4.65(-9.96,0.66)	Not Sig.	inconclusive
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Pain:WOMAC Pain (VAS Version)	12 wks	274/281	3.2(2.1)/2.9(2.2)	Mean Diff	0.3(-0.06,0.66)	Not Sig.	clinically insignificant
Roth; 2004/High	9: NSAIDs (oral/IM)-Topical Diclofenac 40 drops 4times daily	9: Placebo/Control-vehicle control	Pain:change in WOMAC pain	12 wks	163/159	-5.9(4.7)/-4.3(4.4)	Mean Diff	-1.6(-2.6,-0.6)	Group 1	possibly clinically significant
Roth; 2004/High	9: NSAIDs (oral/IM)-Topical Diclofenac 40 drops 4times daily	9: Placebo/Control-vehicle control	Pain:change in WOMAC pain on walking	12 wks	163/159	-1.18(1.11)/-0.87(1.06)	Mean Diff	-0.31(-0.55,-0.07)	Group 1	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Pain:change in womac pain (lower is better)	84 days	230/234	-1.92(1.75)/-1.8(1.74)	Mean Diff	-0.12(-0.44,0.2)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Pain:change in womac pain (lower is better)	84 days	233/238	-1.88(1.59)/-1.93(1.61)	Mean Diff	0.05(-0.24,0.34)	Not Sig.	clinically insignificant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Pain:mean WOMAC pain (Likert)	4 weeks	84/79	5.2(4.6)/6.8(4.8)	Mean Diff	-1.6(-3.06,-0.14)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Pain:mean WOMAC pain (Likert)	4 weeks	84/79	5.2(4.6)/6.8(4.8)	Mean Diff	-1.6(-3.06,-0.14)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Pain:mean WOMAC pain (Likert)	4 weeks	84/84	5.2(4.6)/6.9(4.5)	Mean Diff	-1.7(-3.09,-0.31)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Pain:mean WOMAC pain (Likert)	4 weeks	84/84	5.2(4.6)/6.9(4.5)	Mean Diff	-1.7(-3.09,-0.31)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Pain:mean WOMAC pain on walking (Likert)	4 weeks	84/84	1(1)/1.4(1)	Mean Diff	-0.4(-0.7,-0.1)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Pain:mean WOMAC pain on walking (Likert)	4 weeks	84/84	1(1)/1.4(1)	Mean Diff	-0.4(-0.7,-0.1)	Group 1	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Pain:mean WOMAC pain on walking (Likert)	4 weeks	84/79	1(1)/1.5(1.1)	Mean Diff	-0.5(-0.83,-0.17)	Group 1	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Pain:mean WOMAC pain on walking (Likert)	4 weeks	84/79	1(1)/1.5(1.1)	Mean Diff	-0.5(-0.83,-0.17)	Group 1	na
Baer; 2005/High	9: NSAIDs (oral/IM)-Pennsaid (topical diclofenac solution) 40 drops 4times daily	9: Placebo/Control-vehicle control solution	Pain:mean change in WOMAC pain (Likert)	6 weeks	105/107	-5.2(5)/-3.3(4.3)	Mean Diff	-1.9(-3.16,-0.64)	Group 1	possibly clinically significant
Baer; 2005/High	9: NSAIDs (oral/IM)-Pennsaid (topical diclofenac solution) 40 drops 4times daily	9: Placebo/Control-vehicle control solution	Pain:mean change in WOMAC pain on walking (Likert)	6 weeks	105/107	-1.2(1.2)/-0.8(1.1)	Mean Diff	-0.4(-0.71,-0.09)	Group 1	na
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 0.3% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	6 wks	59/59	37.14(23.5)/37.97(22.3)	Mean Diff	-0.83(-9.18,7.52)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 1% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	5 wks	57/59	35.61(21.3)/38.37(22.6)	Mean Diff	-2.76(-10.84, 5.32)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 1% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	4 wks	57/59	38.4(21.7)/41.19(20.5)	Mean Diff	-2.79(-10.56, 4.98)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 1% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	6 wks	57/59	34.84(24)/37.97(22.3)	Mean Diff	-3.13(-11.66, 5.4)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 0.3% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	5 wks	59/59	38.41(23.8)/38.37(22.6)	Mean Diff	0.04(-8.42,8.5)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 0.3% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	4 wks	59/59	42.42(23.1)/41.19(20.5)	Mean Diff	1.23(-6.73,9.19)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 0.1% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	6 wks	59/59	39.39(22.1)/37.97(22.3)	Mean Diff	1.42(-6.68,9.52)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 0.1% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	5 wks	59/59	41.9(23)/38.37(22.6)	Mean Diff	3.53(-4.78,11.84)	Not Sig.	clinically insignificant
Ottillinger ; 2001/Moderate	9: NSAIDs (oral/IM)-Eltenac gel 0.1% 3g 3times daily	9: Placebo/Control-placebo gel	Pain:mean global pain (VAS)	4 wks	59/59	44.86(22.2)/41.19(20.5)	Mean Diff	3.67(-4.12,11.46)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2007/High	9: NSAIDs (oral/IM)-topical ketoprofen 119mg in 4.8g transersome	9: Placebo/Control-placebo	Pain:womac pain	6 wks	138/127	-19.4(21.2)/-12.4(20.8)	Mean Diff	-7(-12.08,-1.92)	Group 1	possibly clinically significant
Sandelin; 1997/High	4: Topical Supplement-topical eltenac 1% gel and placebo tablet(3g applied 3 times daily)	9: Placebo/Control-Placebo (Oral)(once a day)	Function:Lequesne Index(0-24)	28 days	124/79	6.3(3.11)/7.4(4.19)	Mean Diff	-1.1(-2.18,-0.02)	Group 1	na
Wadsworth; 2017/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Activities of Daily Living	4 wks	130/129	28.6(15.3)/31.8(15.1)	Mean Diff	-3.2(-6.92,0.52)	Not Sig.	inconclusive
Dehghan; 2019/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Function:WOMAC Daily Stiffness	6 wks	40/40	0.75(0.54)/2.1(1.1)	Mean Diff	-1.35(-1.74,-0.96)	Group 1	na
Dehghan; 2020/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Function:WOMAC Daytime Stiffness	6 wks	49/48	0.38(0.57)/0.81(0.67)	Mean Diff	-0.43(-0.68,-0.18)	Group 1	na
Dehghan; 2020/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Function:WOMAC Function	6 wks	49/48	26.43(21.94)/43.27(19.01)	Mean Diff	-16.84(-25.11,-8.57)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Function (VAS Version)	12 wks	223/199	32.12(19.62)/33.16(21.75)	Mean Diff	-1.04(-5.02,2.94)	Not Sig.	clinically insignificant
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Function (VAS Version)	12 wks	221/199	30.56(21.44)/33.16(21.75)	Mean Diff	-2.6(-6.75,1.55)	Not Sig.	clinically insignificant
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Function (VAS Version)	12 wks	223/199	29.07(21.2)/33.16(21.75)	Mean Diff	-4.09(-8.21,0.03)	Not Sig.	inconclusive
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Function (VAS Version)	12 wks	274/281	3.4(2.2)/3.1(2.2)	Mean Diff	0.3(-0.07,0.67)	Not Sig.	clinically insignificant
Dehghan; 2019/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Function:WOMAC Morning Stiffness	6 wks	40/40	0.75(0.54)/2.07(1.09)	Mean Diff	-1.32(-1.71,-0.93)	Group 1	na
Dehghan; 2020/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Function:WOMAC Morning Stiffness	6 wks	49/48	1(0.61)/1.41(0.64)	Mean Diff	-0.41(-0.66,-0.16)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Function:WOMAC Physical Function	12 wks	150/151	-18.7(14)/-17.5(14.3)	Mean Diff	-1.2(-4.41,2.01)	Not Sig.	clinically insignificant
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Function:WOMAC Physical Function	12 wks	154/153	-15.8(15.1)/-12.3(14.7)	Mean Diff	-3.5(-6.85,-0.15)	Group 1	possibly clinically significant
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Function:WOMAC Physical Function	12 wks	154/161	-15.8(15.1)/-12.1(14.6)	Mean Diff	-3.7(-7,-0.4)	Group 1	possibly clinically significant
Dehghan; 2019/High	4: Topical Supplement-Diclofenac gel	4: Placebo/Control-Placebo	Function:WOMAC Physical Performance	6 wks	40/40	12.85(9.2)/37.66(18.67)	Mean Diff	-24.81(-31.4,-18.22)	Group 1	clinically significant
Wadsworth; 2018/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Stiffness	4 wks	130/129	3.6(2)/4(1.9)	Mean Diff	-0.4(-0.88,0.08)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Function:WOMAC Stiffness	12 wks	150/151	-2.3(2)/-2.07(2.02)	Mean Diff	-0.23(-0.69,0.23)	Not Sig.	clinically insignificant
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Function:WOMAC Stiffness	12 wks	154/153	-1.93(2.01)/-1.52(2.05)	Mean Diff	-0.41(-0.87,0.05)	Not Sig.	inconclusive
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Function:WOMAC Stiffness	12 wks	154/161	-1.93(2.01)/-1.48(2.07)	Mean Diff	-0.45(-0.9,0)	Not Sig.	inconclusive
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Function:WOMAC Stiffness (VAS Version)	12 wks	274/281	3.6(2.3)/3.2(2.3)	Mean Diff	0.4(0.02,0.78)	Group 2	clinically insignificant
Roth; 2004/High	9: NSAIDs (oral/IM)-Topical Diclofenac 40 drops 4times daily	9: Placebo/Control-vehicle control	Function:change in WOMAC function	12 wks	162/159	-15.4(15.3)/-10.1(13.9)	Mean Diff	-5.3(-8.51,-2.09)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Roth; 2004/High	9: NSAIDs (oral/IM)-Topical Diclofenac 40 drops 4times daily	9: Placebo/Control-vehicle control	Function:change in WOMAC stiffness	12 wks	162/159	-1.8(2.1)/-1.3(2)	Mean Diff	-0.5(-0.95,-0.05)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Function:mean WOMAC function (Likert)	4 weeks	84/84	17.9(15.6)/23.7(15.9)	Mean Diff	-5.8(-10.6,-1)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Function:mean WOMAC function (Likert)	4 weeks	84/84	17.9(15.6)/23.7(15.9)	Mean Diff	-5.8(-10.6,-1)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Function:mean WOMAC function (Likert)	4 weeks	84/79	17.9(15.6)/24.7(16.2)	Mean Diff	-6.8(-11.73,-1.87)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Function:mean WOMAC function (Likert)	4 weeks	84/79	17.9(15.6)/24.7(16.2)	Mean Diff	-6.8(-11.73,-1.87)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Function:mean WOMAC stiffness (Likert)	4 weeks	84/79	2.2(1.9)/2.7(2)	Mean Diff	-0.5(-1.1,0.1)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Function:mean WOMAC stiffness (Likert)	4 weeks	84/79	2.2(1.9)/2.7(2)	Mean Diff	-0.5(-1.1,0.1)	Not Sig.	inconclusive
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Function:mean WOMAC stiffness (Likert)	4 weeks	84/84	2.2(1.9)/3(1.9)	Mean Diff	-0.8(-1.38,-0.22)	Group 1	possibly clinically significant
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Function:mean WOMAC stiffness (Likert)	4 weeks	84/84	2.2(1.9)/3(1.9)	Mean Diff	-0.8(-1.38,-0.22)	Group 1	possibly clinically significant
Baer; 2005/High	9: NSAIDs (oral/IM)-Pennsaid (topical diclofenac solution) 40 drops 4times daily	9: Placebo/Control-vehicle control solution	Function:mean change in WOMAC function (Likert)	6 weeks	105/107	-13.4(16.3)/-6.9(13.2)	Mean Diff	-6.5(-10.52,-2.48)	Group 1	possibly clinically significant
Baer; 2005/High	9: NSAIDs (oral/IM)-Pennsaid (topical diclofenac solution) 40 drops 4times daily	9: Placebo/Control-vehicle control solution	Function:mean change in WOMAC stiffness (Likert)	6 weeks	105/107	-1.8(2.1)/-0.9(2)	Mean Diff	-0.9(-1.46,-0.34)	Group 1	possibly clinically significant
Rother; 2007/High	9: NSAIDs (oral/IM)-topical ketoprofen 119mg in 4.8g transersome	9: Placebo/Control-placebo	Function:womac function	6 wks	138/127	-9.93(14.38)/-6.94(13.79)	Mean Diff	-2.99(-6.4,0.42)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Composite:Patient Global Assessment	12 wks	223/199	2.23(1.1)/2.11(1.21)	Mean Diff	0.12(-0.1,0.34)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Composite:Patient Global Assessment	12 wks	221/199	2.23(1.12)/2.11(1.21)	Mean Diff	0.12(-0.1,0.34)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Composite:Patient Global Assessment	12 wks	223/199	2.36(1.13)/2.11(1.21)	Mean Diff	0.25(0.03,0.47)	Group 1	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Composite:Patient Global Assessment	4 wks	130/129	2.9(1.1)/3.1(1.1)	Mean Diff	-0.2(-0.47,0.07)	Not Sig.	na
Roth; 2004/High	9: NSAIDs (oral/IM)-Topical Diclofenac 40 drops 4times daily	9: Placebo/Control-vehicle control	QOL:change in patient global assessment	12 wks	161/159	-1.3(1.2)/-0.9(1.2)	Mean Diff	-0.4(-0.66,-0.14)	Group 1	na
Roth; 2004/High	9: NSAIDs (oral/IM)-Topical Diclofenac 40 drops 4 times per day	9: Placebo/Control-vehicle control 40 drops 4 times per day	QOL:change in patient global assessment	12 wks	161/159	-1.3(1.2)/-0.9(1.2)	Mean Diff	-0.4(-0.66,-0.14)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	QOL:global evaluation of treatment	12 weeks	253/238	2.23(1.43)/1.86(1.43)	Mean Diff	0.37(0.12,0.62)	Group 2	na
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	QOL:global evaluation of treatment	12 weeks	253/238	2.23(1.43)/1.86(1.43)	Mean Diff	0.37(0.12,0.62)	Group 2	na
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	QOL:global evaluation of treatment	12 weeks	253/238	2.23(1.43)/1.86(1.43)	Mean Diff	0.37(0.12,0.62)	Group 2	na
Baer; 2005/High	9: NSAIDs (oral/IM)-Pennsaid (topical diclofenac solution) 40 drops 4 times per day	9: Placebo/Control-vehicle control solution 40 drops 4 times per day	QOL:mean change in patient global assessment (Likert)	6 weeks	105/107	-1.3(1.3)/-0.7(1.1)	Mean Diff	-0.6(-0.93,-0.27)	Group 1	na
Baer; 2005/High	9: NSAIDs (oral/IM)-Pennsaid (topical diclofenac solution) 40 drops 4times daily	9: Placebo/Control-vehicle control solution	QOL:mean change in patient global assessment (Likert)	6 weeks	105/107	-1.3(1.3)/-0.7(1.1)	Mean Diff	-0.6(-0.93,-0.27)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	Other:average tablets acetaminophen taken per day	12 weeks	253/238	1.4(1.74)/1.65(1.8)	Mean Diff	-0.25(-0.56,0.06)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	Other:average tablets acetaminophen taken per day	12 weeks	253/238	1.4(1.74)/1.65(1.8)	Mean Diff	-0.25(-0.56,0.06)	Not Sig.	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Other:mean acetaminophen consumption (tablets)	4 weeks	84/79	36.2(52.1)/49.5(63.4)	Mean Diff	-13.3(-31.32, 4.72)	Not Sig.	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Other:mean acetaminophen consumption (tablets)	4 weeks	84/79	36.2(52.1)/49.5(63.4)	Mean Diff	-13.3(-31.32, 4.72)	Not Sig.	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Other:mean acetaminophen consumption (tablets)	4 weeks	84/84	36.2(52.1)/54.9(69.2)	Mean Diff	-18.7(-37.37,-0.03)	Group 1	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Other:mean acetaminophen consumption (tablets)	4 weeks	84/84	36.2(52.1)/54.9(69.2)	Mean Diff	-18.7(-37.37,-0.03)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Other:mean patient global assessment	4 weeks	82/75	6.7(49.52)/7.8(1.21)	Mean Diff	-1.1(-11.98, 9.78)	Not Sig.	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Other:mean patient global assessment	4 weeks	82/83	6.7(54.81)/7.8(0.93)	Mean Diff	-1.1(-13.14, 10.94)	Not Sig.	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo	Other:mean patient global assessment	4 weeks	82/83	6.7(3)/7.8(3.02)	Mean Diff	-1.1(-2.03,-0.17)	Group 1	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-placebo 40 drops 4 times per day	Other:mean patient global assessment	4 weeks	82/83	6.7(3)/7.8(3.02)	Mean Diff	-1.1(-2.03,-0.17)	Group 1	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control	Other:mean patient global assessment	4 weeks	82/75	6.7(3)/7.8(3.76)	Mean Diff	-1.1(-2.18,-0.02)	Group 1	na
Bookman; 2004/high	4: Topical Supplement-Topical Diclofenac(40 drops x4/day)	4: Placebo/Control-vehicle control 40 drops 4 times per day	Other:mean patient global assessment	4 weeks	82/75	6.7(3)/7.8(3.76)	Mean Diff	-1.1(-2.18,-0.02)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Other:need for omeprazole for dyspepsia	84 days	233/238	2.58%/3.78%	RR	0.68(0.25,1.88)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Other:need for omeprazole for dyspepsia	84 days	230/234	4.78%/2.56%	RR	1.87(0.7,4.96)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Other:patient global assessment of overall health	12 wks	148/150	-0.95(1.21)/-0.88(1.31)	Mean Diff	-0.07(-0.36,0.22)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Other:patient global assessment of overall health	12 wks	154/160	-0.95(1.3)/-0.65(1.12)	Mean Diff	-0.3(-0.57,-0.03)	Group 1	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Other:patient global assessment of overall health	12 wks	154/152	-0.95(1.3)/-0.37(1.04)	Mean Diff	-0.58(-0.84,-0.32)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Other:patient global assessment of study knee	12 wks	150/151	-1.53(1.27)/-1.42(1.29)	Mean Diff	-0.11(-0.4,0.18)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Other:patient global assessment of study knee	12 wks	154/161	-1.36(1.19)/-1.07(1.1)	Mean Diff	-0.29(-0.54,-0.04)	Group 1	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Other:patient global assessment of study knee	12 wks	154/153	-1.36(1.19)/-1.01(1.18)	Mean Diff	-0.35(-0.62,-0.08)	Group 1	na
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	Other:weeks with no rescue drug	12 weeks	253/238	4.33(4.45)/3.46(4.21)	Mean Diff	0.87(0.1,1.64)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Barthel; 2009/Moderate	4: Topical Supplement-Diclofenac Sodium Gel(1% gel in DMSO 4g x4/day)	4: Placebo/Control-Placebo (DMSO vehicle)	Other:weeks with no rescue drug	12 weeks	253/238	4.33(4.45)/3.46(4.21)	Mean Diff	0.87(0.1,1.64)	Group 1	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Abdominal Pain	6 wks	107/109	3.74%/0.92%	RR	4.07(0.46,35.87)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Abdominal Pain	12 wks	164/162	3.05%/1.85%	RR	1.65(0.4,6.78)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Abdominal pain	84 days	230/234	0%/0%	RD	0(-1.643, 1.615)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Abdominal pain	84 days	233/238	1.29%/0%	RD	1.288(-1.141, 3.088)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Abdominal pain	12 wks	152/151	1.97%/7.28%	RR	0.27(0.08,0.95)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Abdominal pain	12 wks	154/161	3.25%/3.11%	RR	1.05(0.31,3.54)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abdominal pain	12 wks	161/157	3.11%/0.64%	RR	4.88(0.58,41.27)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abdominal pain	12 wks	154/157	3.25%/0.64%	RR	5.1(0.6,43.13)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Abnormal taste sensation or odor	12 wks	154/161	0%/0.62%	RD	-0.621(-3.108, 2.192)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abnormal taste sensation or odor	12 wks	154/157	0%/0.64%	RD	-0.637(-3.127, 2.245)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Abnormal taste sensation or odor	12 wks	152/151	0.66%/0%	RD	0.658(-2.316, 3.197)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abnormal taste sensation or odor	12 wks	161/157	0.62%/0.64%	RR	0.98(0.06,15.45)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Abnormal vision	12 wks	152/151	0.66%/2.65%	RR	0.25(0.03,2.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abnormal vision	12 wks	161/157	2.48%/3.18%	RR	0.78(0.21,2.85)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abnormal vision	12 wks	154/157	2.6%/3.18%	RR	0.82(0.22,2.98)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Abnormal vision	12 wks	154/161	2.6%/2.48%	RR	1.05(0.27,4.11)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Accidental injury	12 wks	154/161	2.6%/4.35%	RR	0.6(0.18,2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Accidental injury	12 wks	154/157	2.6%/3.82%	RR	0.68(0.2,2.36)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Accidental injury	12 wks	161/157	4.35%/3.82%	RR	1.14(0.39,3.31)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Accidental injury	12 wks	152/151	3.95%/2.65%	RR	1.49(0.43,5.17)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:All gastrointestinal disorders; n (%)	84 days	230/234	1.3%/2.99%	RR	0.44(0.11,1.67)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:All gastrointestinal disorders; n (%)	84 days	233/238	1.29%/0.84%	RR	1.53(0.26,9.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:All infections and infestations; n (%)	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:All infections and infestations; n (%)	84 days	230/234	0%/0%	RD	0(-1.643, 1.615)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:All nervous system disorders; n (%)	84 days	230/234	0%/0.43%	RD	-0.427(-2.107, 1.526)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:All nervous system disorders; n (%)	84 days	233/238	0%/1.26%	RD	-1.261(-3.083, 1.119)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:All skin and tissue disorders; n (%)	84 days	233/238	5.58%/5.88%	RR	0.95(0.46,1.97)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:All skin and tissue disorders; n (%)	84 days	230/234	12.17%/11.11%	RR	1.1(0.66,1.81)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Allergic contact dermatitis	84 days	233/238	0%/1.26%	RD	-1.261(-3.083, 1.119)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Allergic contact dermatitis	84 days	230/234	0.43%/0.43%	RR	1.02(0.06,16.17)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Allergic rash	84 days	233/238	0%/0.42%	RD	-0.42(-2.079, 1.501)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Allergic rash	84 days	230/234	1.3%/0%	RD	1.304(-1.155, 3.134)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Any Adverse Event	12 wks	223/199	13.9%/17.59%	RR	0.79(0.51,1.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Any Adverse Event	12 wks	223/199	19.28%/17.59%	RR	1.1(0.73,1.64)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Any Adverse Event	12 wks	221/199	22.62%/17.59%	RR	1.29(0.87,1.89)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Any Adverse Event	12 wks	274/281	39.42%/40.21%	RR	0.98(0.8,1.2)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Any Adverse Event	12 wks	254/238	60.24%/53.78%	RR	1.12(0.96,1.31)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Any Serious Adverse Event	12 wks	274/281	1.09%/1.42%	RR	0.77(0.17,3.4)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Any Treatment-Related AE	12 wks	274/281	24.45%/23.49%	RR	1.04(0.77,1.4)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Any adverse event	12 wks	154/161	62.34%/60.25%	RR	1.03(0.87,1.23)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Any adverse event	12 wks	152/151	64.47%/62.25%	RR	1.04(0.87,1.23)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any adverse event	12 wks	161/157	60.25%/57.32%	RR	1.05(0.87,1.26)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any adverse event	12 wks	154/157	62.34%/57.32%	RR	1.09(0.91,1.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Any digestive system event	12 wks	154/161	6.49%/11.18%	RR	0.58(0.28,1.22)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any digestive system event	12 wks	154/157	6.49%/9.55%	RR	0.68(0.32,1.47)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Any digestive system event	12 wks	152/151	25.66%/23.84%	RR	1.08(0.73,1.59)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Any skin/appendages event	12 wks	154/161	26.62%/16.77%	RR	1.59(1.03,2.45)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any skin/appendages event	12 wks	154/157	26.62%/7.64%	RR	3.48(1.9,6.37)	Group 2	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Any skin/appendages event	12 wks	152/151	30.92%/7.28%	RR	4.24(2.29,7.86)	Group 2	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Application Site Reactions	12 wks	254/238	5.12%/2.52%	RR	2.03(0.78,5.25)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Arthralgia	12 wks	152/151	4.61%/7.95%	RR	0.58(0.23,1.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Arthralgia	12 wks	154/161	9.09%/15.53%	RR	0.59(0.32,1.08)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Arthralgia	12 wks	154/157	9.09%/9.55%	RR	0.95(0.48,1.9)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Arthralgia	12 wks	254/238	13.39%/8.82%	RR	1.52(0.91,2.54)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Asthma	12 wks	164/162	1.83%/0.62%	RR	2.96(0.31,28.19)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Back Pain	12 wks	254/238	9.06%/6.72%	RR	1.35(0.73,2.49)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Back pain	12 wks	152/151	2.63%/7.28%	RR	0.36(0.12,1.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Back pain	12 wks	154/161	9.74%/9.32%	RR	1.05(0.53,2.07)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Back pain	12 wks	154/157	9.74%/6.37%	RR	1.53(0.71,3.3)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Bloating	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Bloating	84 days	230/234	0%/0%	RD	0(-1.643, 1.615)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Blood and Lymphatic Disorders	12 wks	223/199	0%/0%	RD	0(-1.693, 1.894)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Blood and Lymphatic Disorders	12 wks	221/199	0.9%/0%	RD	0.905(-1.429, 2.909)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Blood and Lymphatic Disorders	12 wks	223/199	1.35%/0%	RD	1.345(-1.189, 3.436)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Body Odor	4 wks	84/84	2.38%/0%	RD	2.381(-3.51,7.082)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Body Odor	4 wks	84/80	2.38%/0%	RD	2.381(-3.51,7.277)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Cardiovascular Adverse Events	12 wks	254/238	1.57%/0.42%	RR	3.75(0.42,33.29)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Conjunctivitis	12 wks	152/151	0%/1.99%	RD	-1.987(-4.778, 1.704)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Conjunctivitis	12 wks	154/161	2.6%/0%	RD	2.597(-1.293, 5.414)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Conjunctivitis	12 wks	154/157	2.6%/0.64%	RR	4.08(0.46,36.07)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Constipation	6 wks	107/109	0.93%/0.92%	RR	1.02(0.06,16.08)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Constipation	12 wks	164/162	1.22%/0.62%	RR	1.98(0.18,21.57)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Constipation	4 wks	84/80	1.19%/1.25%	RR	0.95(0.06,14.97)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Constipation	4 wks	84/84	1.19%/1.19%	RR	1(0.06, 15.73)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Contact dermatitis (application site)	12 wks	154/161	2.6%/3.11%	RR	0.84(0.23,3.06)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Contact dermatitis (application site)	12 wks	152/151	7.89%/0.66%	RR	11.92(1.57,90.54)	Group 2	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Contact dermatitis (application site)	12 wks	154/157	2.6%/0.64%	RR	4.08(0.46,36.07)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Contact dermatitis with vesicles (application	12 wks	154/161	1.95%/0%	RD	1.948(-1.674,4.608)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Contact dermatitis with vesicles (application	12 wks	154/157	1.95%/0%	RD	1.948(-1.674, 4.659)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Contact dermatitis with vesicles (application	12 wks	152/151	3.95%/0.66%	RR	5.96(0.73,48.92)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Cough	12 wks	254/238	0.39%/3.36%	RR	0.12(0.01,0.93)	Group 1	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Creatinine Increased	12 wks	274/281	1.09%/0.36%	RR	3.08(0.32,29.4)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Deaths	12 wks	254/238	0.39%/0%	RD	0.394(-1.409, 2.015)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Dermatitis	12 wks	254/238	4.33%/1.68%	RR	2.58(0.83,7.98)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Diarrhea	6 wks	107/109	0.93%/0%	RD	0.935(-3.236, 4.425)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Diarrhea	12 wks	154/157	1.3%/1.91%	RR	0.68(0.12,4.01)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Diarrhea	12 wks	154/161	1.3%/1.24%	RR	1.05(0.15,7.33)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Diarrhea	12 wks	152/151	7.89%/4.64%	RR	1.7(0.69,4.21)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Diarrhea	12 wks	164/162	0%/1.85%	RD	-1.852(-4.445, 1.599)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Diarrhea	4 wks	84/84	1.19%/3.57%	RR	0.33(0.04,3.14)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Diarrhea	4 wks	84/80	1.19%/2.5%	RR	0.48(0.04,5.15)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Diarrhoea	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Diarrhoea	84 days	230/234	0%/0%	RD	0(-1.643, 1.615)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Discontinuations due to adverse events	12 wks	254/238	5.12%/3.78%	RR	1.35(0.59,3.11)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Dizziness	12 wks	164/162	1.22%/0%	RD	1.22(-1.898, 3.699)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Dry Skin	12 wks	274/281	0.36%/1.78%	RR	0.21(0.02,1.74)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Dry Skin	6 wks	107/109	39.25%/21.1%	RR	1.86(1.21,2.87)	Group 2	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Dry Skin	12 wks	164/162	36.59%/25.31%	RR	1.45(1.04,2.02)	Group 2	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Dry Skin	4 wks	84/80	35.71%/13.75%	RR	2.6(1.4,4.82)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Dry Skin	4 wks	84/84	35.71%/1.19%	RR	30(4.19,214.96)	Group 2	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Dry skin	84 days	230/234	1.3%/2.99%	RR	0.44(0.11,1.67)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Dry skin	84 days	233/238	0.86%/1.68%	RR	0.51(0.09,2.76)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Dry skin (application site)	12 wks	154/161	18.18%/11.18%	RR	1.63(0.94,2.82)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Dry skin (application site)	12 wks	154/157	18.18%/3.18%	RR	5.71(2.26,14.4)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Dry skin (application site)	12 wks	152/151	19.74%/2.65%	RR	7.45(2.69,20.63)	Group 2	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Dryness	4 wks	130/129	20%/21.71%	RR	0.92(0.57,1.48)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Dyspepsia	84 days	230/234	0%/0.43%	RD	-0.427(-2.107, 1.526)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Dyspepsia	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Dyspepsia	6 wks	107/109	3.74%/0.92%	RR	4.07(0.46,35.87)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Dyspepsia	12 wks	154/157	2.6%/3.82%	RR	0.68(0.2,2.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Dyspepsia	12 wks	154/161	2.6%/3.73%	RR	0.7(0.2,2.42)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Dyspepsia	12 wks	152/151	3.29%/3.97%	RR	0.83(0.26,2.65)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Dyspepsia	12 wks	164/162	4.88%/3.7%	RR	1.32(0.47,3.71)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Dyspepsia	4 wks	84/84	7.14%/5.95%	RR	1.2(0.38,3.78)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Dyspepsia	4 wks	84/80	7.14%/5%	RR	1.43(0.42,4.88)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Eczema	12 wks	254/238	0%/0.42%	RD	-0.42(-1.95,1.501)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Edema	12 wks	164/162	2.44%/1.23%	RR	1.98(0.37,10.64)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Erythema	4 wks	130/129	3.08%/11.63%	RR	0.26(0.09,0.78)	Group 1	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Erythema	12 wks	254/238	0.39%/0.42%	RR	0.94(0.06,14.9)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Exanthema	84 days	230/234	0%/1.28%	RD	-1.282(-3.129, 1.137)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Exanthema	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Exfoliation	4 wks	130/129	6.15%/7.75%	RR	0.79(0.32,1.95)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Flatulence	84 days	230/234	0%/0.43%	RD	-0.427(-2.107, 1.526)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Flatulence	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Flatulence	12 wks	164/162	2.44%/1.23%	RR	1.98(0.37,10.64)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Gastric pain	84 days	233/238	0%/0.42%	RD	-0.42(-2.079, 1.501)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Gastric pain	84 days	230/234	0%/0.85%	RD	-0.855(-2.611, 1.353)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Gastritis	6 wks	107/109	0.93%/0%	RD	0.935(-3.236, 4.425)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Gastrointestinal Adverse Events	12 wks	254/238	5.91%/5.04%	RR	1.17(0.56,2.45)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Gastrointestinal disorder	84 days	230/234	0%/0.43%	RD	-0.427(-2.107, 1.526)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Gastrointestinal disorder	84 days	233/238	0%/0%	RD	0(-1.622, 1.588)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:General Disorders and Administration Site Conditions	12 wks	221/199	0%/0%	RD	0(-1.709, 1.894)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:General Disorders and Administration Site Conditions	12 wks	223/199	0.45%/0%	RD	0.448(-1.599, 2.378)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:General Disorders and Administration Site Conditions	12 wks	223/199	0.45%/0%	RD	0.448(-1.599, 2.378)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Halitosis	6 wks	107/109	1.87%/0%	RD	1.869(-2.822, 5.533)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Halitosis	12 wks	164/162	0%/1.23%	RD	-1.235(-3.692, 1.92)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Halitosis	4 wks	84/80	4.76%/1.25%	RR	3.81(0.44,33.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Halitosis	4 wks	84/84	4.76%/0%	RD	4.762(-2.09,10.006)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Headache	84 days	230/234	0%/0.43%	RD	-0.427(-2.107, 1.526)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Headache	84 days	233/238	0%/0.84%	RD	-0.84(-2.573, 1.331)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Headache	6 wks	107/109	5.61%/9.17%	RR	0.61(0.23,1.62)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Headache	12 wks	152/151	13.82%/17.22%	RR	0.8(0.47,1.36)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Headache	12 wks	154/161	17.53%/13.04%	RR	1.34(0.79,2.27)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Headache	12 wks	154/157	17.53%/11.46%	RR	1.53(0.88,2.66)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Headache	12 wks	164/162	5.49%/4.32%	RR	1.27(0.48,3.33)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Headache	12 wks	254/238	13.78%/14.29%	RR	0.96(0.62,1.49)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Heartburn	84 days	233/238	0.43%/0%	RD	0.429(-1.532, 2.056)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Heartburn	84 days	230/234	0.43%/0%	RD	0.435(-1.552, 2.089)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Immune System Disorders	12 wks	221/199	0%/0%	RD	0(-1.709, 1.894)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Immune System Disorders	12 wks	223/199	0.45%/0%	RD	0.448(-1.599, 2.378)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Immune System Disorders	12 wks	223/199	1.35%/0%	RD	1.345(-1.189, 3.436)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Infections and Infestations	12 wks	223/199	0%/0%	RD	0(-1.693, 1.894)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Infections and Infestations	12 wks	223/199	0%/0%	RD	0(-1.693, 1.894)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Infections and Infestations	12 wks	221/199	0.45%/0%	RD	0.452(-1.613, 2.383)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Investigations	12 wks	223/199	0.45%/0%	RD	0.448(-1.599, 2.378)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Investigations	12 wks	221/199	0.45%/0%	RD	0.452(-1.613, 2.383)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Investigations	12 wks	223/199	0.9%/0%	RD	0.897(-1.417, 2.899)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Investigations	12 wks	274/281	2.55%/0.71%	RR	3.59(0.75,17.13)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Liver function tests abnormal	12 wks	154/161	1.95%/3.73%	RR	0.52(0.13,2.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Liver function tests abnormal	12 wks	152/151	7.24%/7.95%	RR	0.91(0.41,2)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Liver function tests abnormal	12 wks	154/157	1.95%/0.64%	RR	3.06(0.32,29.08)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Localized Erythema	12 wks	274/281	3.28%/1.42%	RR	2.31(0.72,7.4)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Localized Rash	12 wks	274/281	1.09%/1.07%	RR	1.03(0.21,5.04)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Localized erythema	84 days	233/238	1.29%/1.26%	RR	1.02(0.21,5.01)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Localized erythema	84 days	230/234	2.61%/1.28%	RR	2.03(0.52,8.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Localized itching	84 days	230/234	0.43%/1.71%	RR	0.25(0.03,2.26)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Localized itching	84 days	233/238	0.86%/0.42%	RR	2.04(0.19,22.38)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Melena	6 wks	107/109	0%/0.92%	RD	-0.917(-4.465, 3.18)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Melena	12 wks	164/162	0%/1.23%	RD	-1.235(-3.692, 1.92)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Nasopharyngitis	12 wks	254/238	3.54%/5.88%	RR	0.6(0.27,1.37)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Nausea	6 wks	107/109	0.93%/1.83%	RR	0.51(0.05,5.53)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Nausea	12 wks	154/161	0%/0.62%	RD	-0.621(-3.108, 2.192)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Nausea	12 wks	154/157	0%/0%	RD	0(-2.434, 2.388)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Nausea	12 wks	152/151	3.29%/1.99%	RR	1.66(0.4,6.81)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Nausea	12 wks	164/162	2.44%/0.62%	RR	3.95(0.45,34.97)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Nausea	4 wks	84/84	0%/1.19%	RD	-1.19(-5.672, 4.059)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Nausea	4 wks	84/80	0%/5%	RD	-5(-10.325 ,2.162)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Nervous System Disorders	12 wks	223/199	0%/0%	RD	0(-1.693, 1.894)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Nervous System Disorders	12 wks	223/199	0%/0%	RD	0(-1.693, 1.894)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Nervous System Disorders	12 wks	221/199	0.45%/0%	RD	0.452(-1.613, 2.383)	Not Sig.	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Pain	4 wks	130/129	1.54%/3.1%	RR	0.5(0.09,2.66)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Pain	12 wks	152/151	0.66%/5.3%	RR	0.12(0.02,0.98)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Pain	12 wks	154/161	4.55%/6.83%	RR	0.67(0.26,1.67)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Pain	12 wks	154/157	4.55%/3.18%	RR	1.43(0.46,4.4)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Pain	12 wks	254/238	4.33%/2.94%	RR	1.47(0.58,3.74)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Pain in extremity	12 wks	254/238	3.94%/5.88%	RR	0.67(0.3,1.48)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Papules	12 wks	254/238	0.39%/0%	RD	0.394(-1.409, 2.015)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Paresthesia	6 wks	107/109	1.87%/1.83%	RR	1.02(0.15,7.1)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Paresthesia	12 wks	164/162	0.61%/2.47%	RR	0.25(0.03,2.19)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Paresthesia	4 wks	84/80	14.29%/22.5%	RR	0.63(0.33,1.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Parasthesia	4 wks	84/84	14.29%/5.95%	RR	2.4(0.88,6.51)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Pruritis (application site)	12 wks	152/151	0.66%/0%	RD	0.658(-2.316, 3.197)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Pruritis (application site)	12 wks	154/161	1.3%/0%	RD	1.299(-2.014, 3.812)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Pruritis (application site)	12 wks	154/157	1.3%/0%	RD	1.299(-2.014, 3.866)	Not Sig.	na
Wadsworth; 2019/High	4: Topical Supplement-Topical Diclofenac Sodium(2mL 2% 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Pruritus	4 wks	130/129	2.31%/13.95%	RR	0.17(0.05,0.55)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Pruritus	6 wks	107/109	0%/1.83%	RD	-1.835(-5.547, 2.775)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Pruritus	12 wks	164/162	0.61%/0%	RD	0.61(-2.153, 2.98)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Pruritus	12 wks	254/238	1.57%/0.42%	RR	3.75(0.42,33.29)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Pruritus	4 wks	84/80	10.71%/7.5%	RR	1.43(0.53,3.83)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Pruritus	4 wks	84/84	10.71%/3.57%	RR	3(0.84, 10.69)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Rash	12 wks	274/281	4.74%/2.85%	RR	1.67(0.7,3.96)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Rash	6 wks	107/109	1.87%/3.67%	RR	0.51(0.1,2.72)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Rash	12 wks	152/151	0%/0%	RD	0(-2.465, 2.481)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Rash	12 wks	154/161	2.6%/1.24%	RR	2.09(0.39,11.25)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Rash	12 wks	154/157	2.6%/0%	RD	2.597(-1.293, 5.463)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Rash	12 wks	164/162	10.98%/4.94%	RR	2.22(0.99,4.97)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Rash	4 wks	84/80	13.1%/7.5%	RR	1.75(0.68,4.5)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Rash	4 wks	84/84	13.1%/3.57%	RR	3.67(1.06,12.67)	Group 2	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Rectal hemorrhage	12 wks	154/161	0.65%/0%	RD	0.649(-2.287, 3.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Rectal hemorrhage	12 wks	154/157	0.65%/0%	RD	0.649(-2.287, 3.097)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Rectal hemorrhage	12 wks	152/151	3.29%/0%	RD	3.289(-0.89,6.4)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Respiratory disorder	12 wks	154/157	3.25%/3.82%	RR	0.85(0.26,2.73)	Not Sig.	na
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	4: Placebo/Control-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	Adverse events:Respiratory disorder	12 wks	152/151	4.61%/5.3%	RR	0.87(0.32,2.34)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	4: Topical Supplement-40 drops 4x daily of topical diclofenac + oral placebo	4: Topical Supplement-40 drops 4x daily of topical dmso vehicle (45.5% equal to 40 drops 4x daily of topical diclofenac dmso) + oral placebo	Adverse events:Respiratory disorder	12 wks	154/161	3.25%/2.48%	RR	1.31(0.36,4.78)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Serious AEs; n	84 days	233/238	0%/1.26%	RD	-1.261(-3.083, 1.119)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Serious AEs; n	84 days	230/234	1.3%/1.71%	RR	0.76(0.17,3.37)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Serious Adverse Events	12 wks	254/238	1.18%/0.84%	RR	1.41(0.24,8.34)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Severe Adverse Events	12 wks	254/238	5.12%/5.88%	RR	0.87(0.42,1.81)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Sinusitis	12 wks	254/238	3.54%/2.52%	RR	1.41(0.51,3.89)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Skin Dryness	12 wks	254/238	0.39%/0.84%	RR	0.47(0.04,5.13)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Skin Irritation	12 wks	274/281	0%/1.07%	RD	-1.068(-2.619, 0.956)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (low dose; 25 mg)(25mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Skin and Subcutaneous Tissue Disorders	12 wks	223/199	12.56%/17.59%	RR	0.71(0.45,1.13)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (middle dose; 50 mg)(50mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Skin and Subcutaneous Tissue Disorders	12 wks	223/199	17.94%/17.59%	RR	1.02(0.68,1.54)	Not Sig.	na
Kneer; 2013/High	4: Topical Supplement-Ketoprofen Gel (high dose; 100 mg)(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Skin and Subcutaneous Tissue Disorders	12 wks	221/199	21.72%/17.59%	RR	1.23(0.84,1.83)	Not Sig.	na
Rother; 2013/High	4: Topical Supplement-Ketoprofen in Gel(100mg 2x/day)	4: Placebo/Control-Placebo Gel(2x/day)	Adverse events:Skin and Subcutaneous Tissue Disorders	12 wks	274/281	10.58%/11.39%	RR	0.93(0.58,1.49)	Not Sig.	na
Baer; 2005/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Taste Perversion	6 wks	107/109	3.74%/1.83%	RR	2.04(0.38,10.89)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Taste Perversion	12 wks	164/162	1.83%/3.09%	RR	0.59(0.14,2.44)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Upper respiratory tract infection	12 wks	254/238	3.54%/5.46%	RR	0.65(0.28,1.49)	Not Sig.	na
Barthel; 2009/Moderate	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Uspecified Reaction	12 wks	254/238	0.39%/0%	RD	0.394(-1.409, 2.015)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Vascular disorders; n (%)	84 days	230/234	0%/0.43%	RD	-0.427(-2.107, 1.526)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Vascular disorders; n (%)	84 days	233/238	0.43%/0.84%	RR	0.51(0.05,5.59)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Vesiculobullous Rash	12 wks	164/162	0.61%/0%	RD	0.61(-2.153, 2.98)	Not Sig.	na
Roth; 2004/High	4: Topical Supplement-Topical diclofenac	9: Placebo/Control-Control	Adverse events:Vomiting	12 wks	164/162	0.61%/0%	RD	0.61(-2.153, 2.98)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Placebo	Adverse events:Vomiting	4 wks	84/84	0%/1.19%	RD	-1.19(-5.672, 4.059)	Not Sig.	na
Bookman; 2004/High	4: Topical Supplement-Topical diclofenac	4: Placebo/Control-Vehicle-Control	Adverse events:Vomiting	4 wks	84/80	0%/1.25%	RD	-1.25(-5.743, 4.246)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:Withdrawals due to AEs or AEs and lack of efficacy; n (%)	84 days	233/238	1.29%/2.52%	RR	0.51(0.13,2.02)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:Withdrawals due to AEs or AEs and lack of efficacy; n (%)	84 days	230/234	5.65%/3.85%	RR	1.47(0.64,3.37)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 50mg	4: Placebo/Control-2.2 g vehicle control	Adverse events:adverse events	84 days	233/238	39.48%/44.54%	RR	0.89(0.72,1.1)	Not Sig.	na
Conaghan; 2013/High	4: Topical Supplement-topical ketoprofen 100mg	4: Placebo/Control-4.4g vehicle control	Adverse events:adverse events	84 days	230/234	44.35%/45.73%	RR	0.97(0.79,1.19)	Not Sig.	na

PICO 5: Exercise and Activity

Supervised Exercise vs. Control

Table 13: Supervised Exercise vs Control

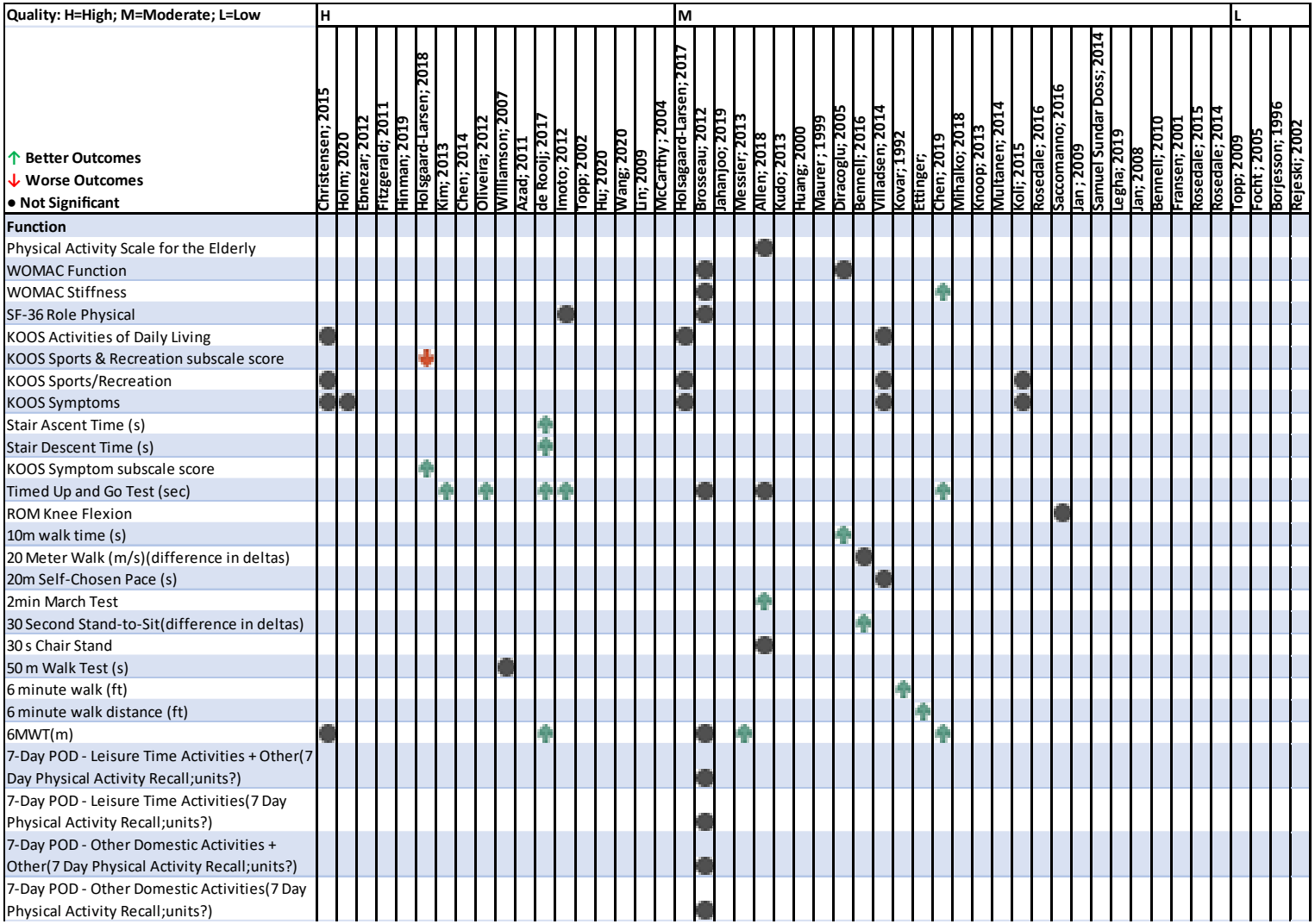


Table 13 Continued: Supervised Exercise vs Control

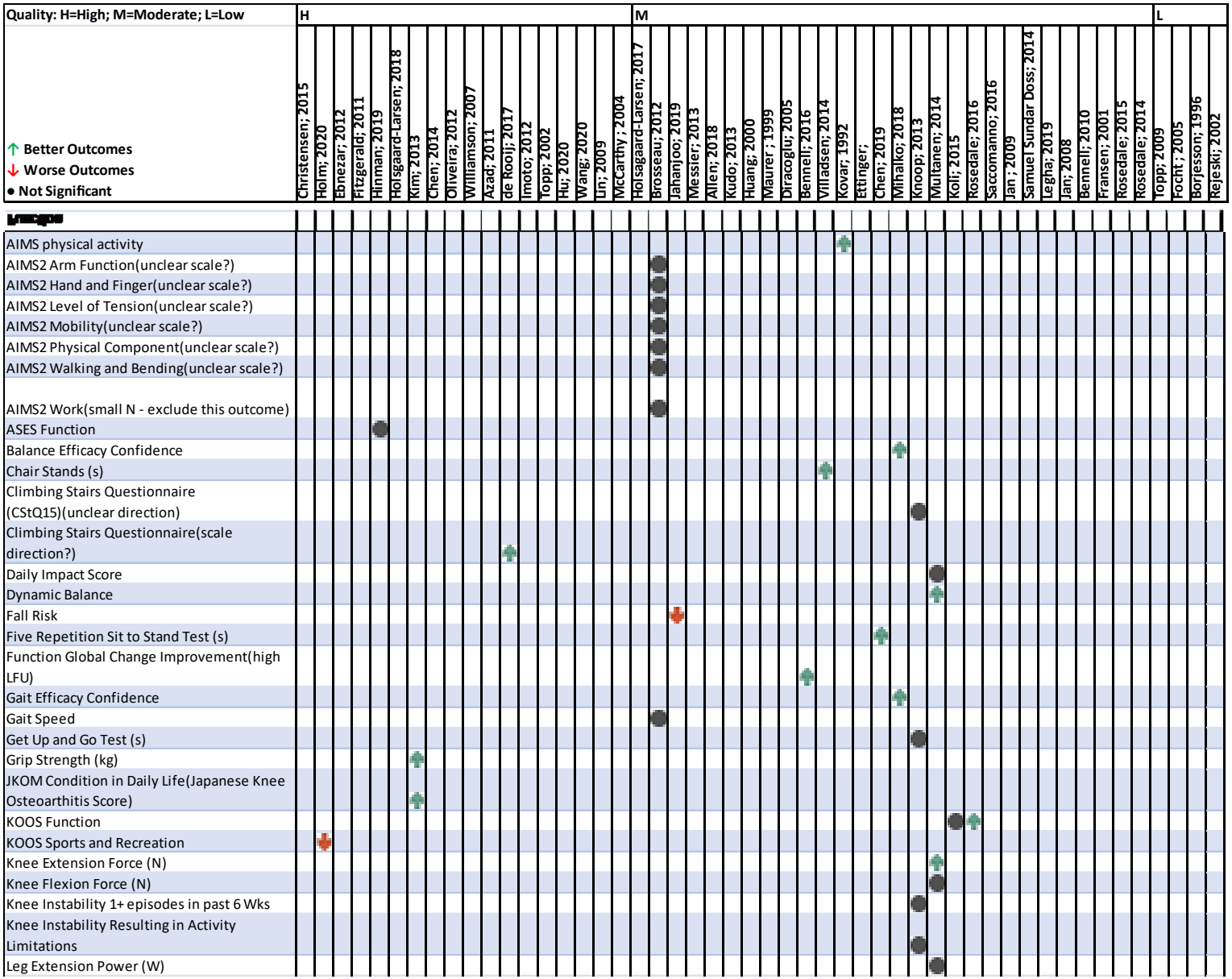


Table 13 Continued: Supervised Exercise vs Control

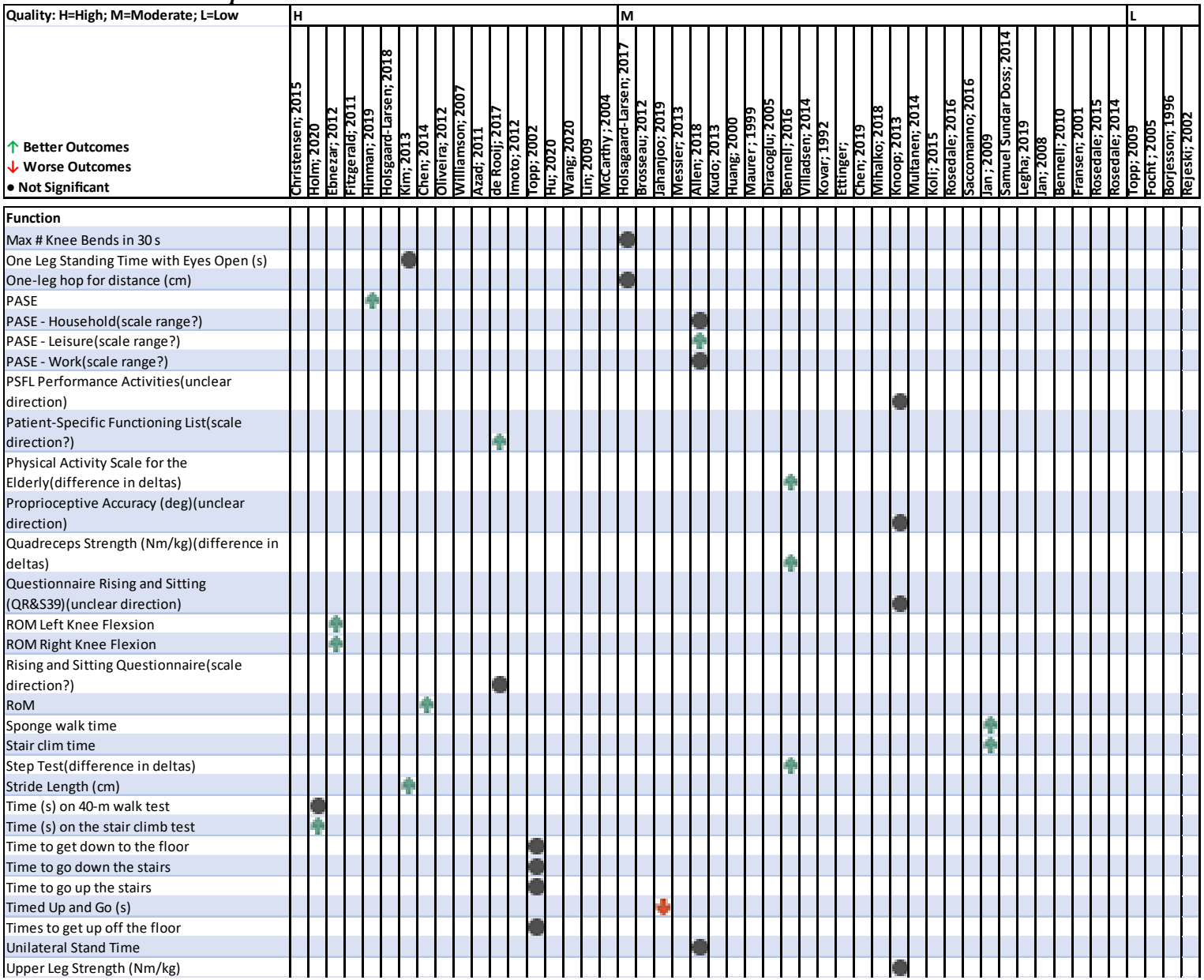


Table 13 Continued: Supervised Exercise vs Control

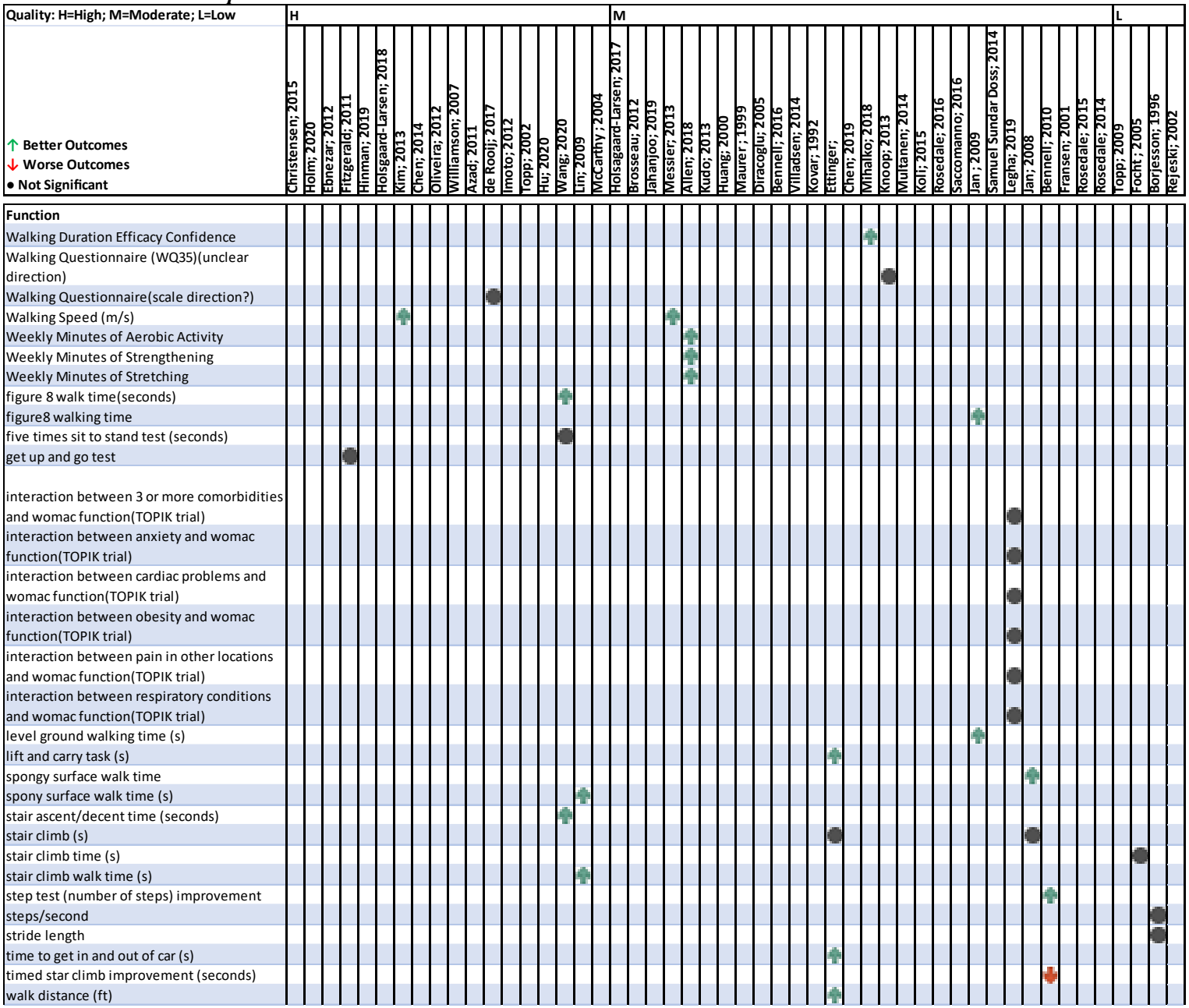


Table 13 Continued: Supervised Exercise vs Control

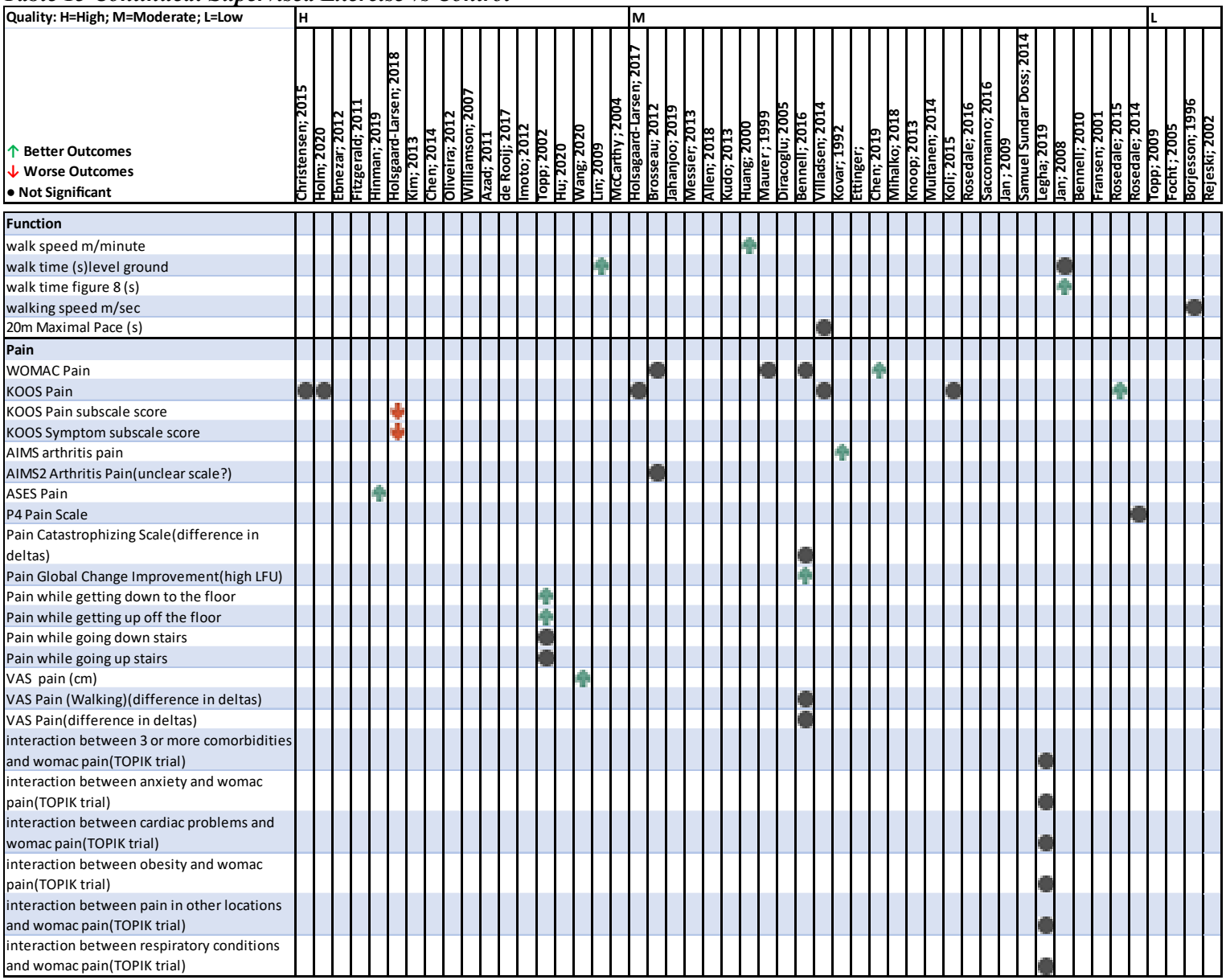


Table 13 Continued: Supervised Exercise vs Control

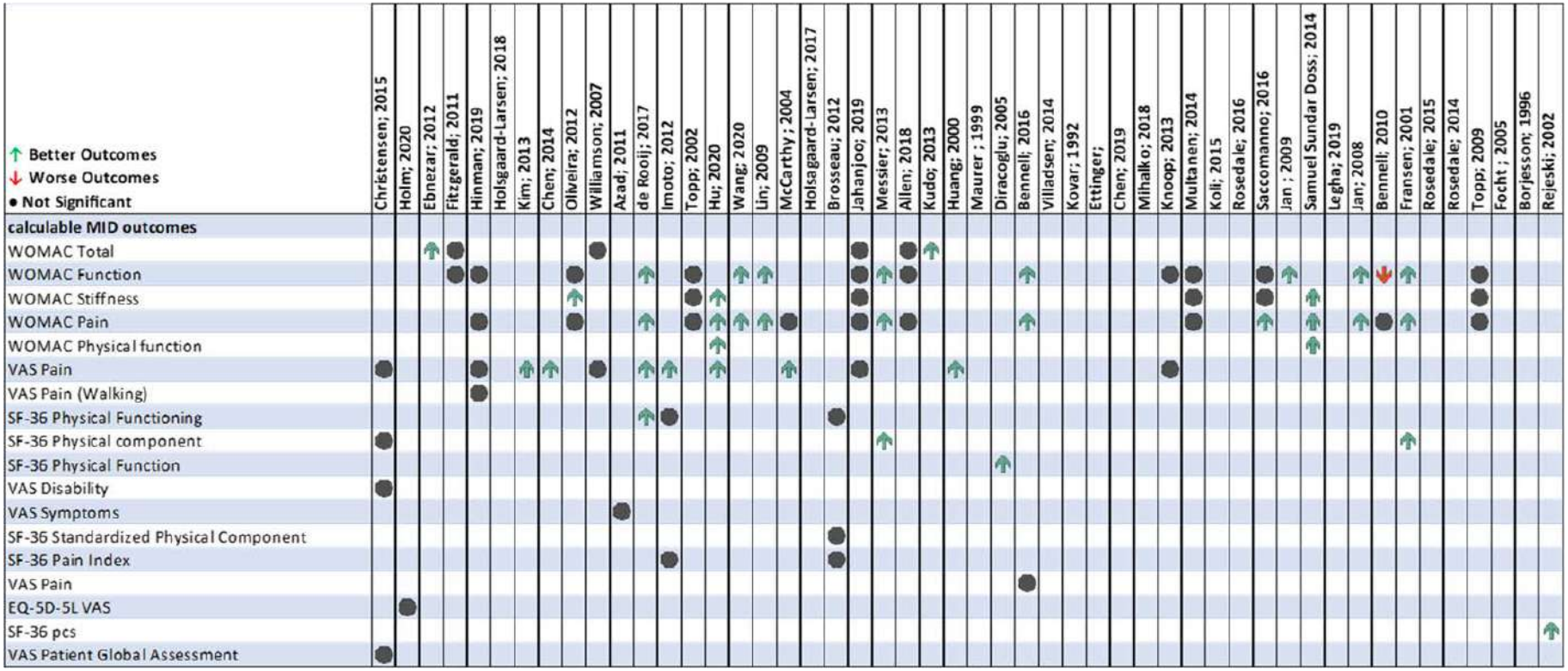


Table 13 Continued: Supervised Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H										M																L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Holm; 2020	Fitzgerald; 2011	Hinman; 2019	Holsgaard-Larsen; 2018	Kim; 2013	Chen; 2014	Oliveira; 2012	Williamson; 2007	Imoto; 2012	Holsagaard-Larsen; 2017	Brosseau; 2012	Jahanjoo; 2019	Messier; 2013	Allen; 2018	Huang; 2000	Maurer ; 1999	Diracoglu; 2005	Bennell; 2016	Villadsen; 2014	Kovar; 1992	Chen; 2019	Knoop; 2013	Koli; 2015	Fransen; 2001	Kigozi; 2018	Rejeski; 2002
Composite																											
WOMAC Total												●					●										
Lequesne Index							↑									↑											
Lequesne Index Score								↑					●														
AIMS2 Symptoms Component(unclear scale?)												●															
BoPAS				●																							
BtPAS				●																							
EQ Health State					↑																						
JKOM Pain/Stiffness(Japanese Knee Osteoarthitis Score)						↑																					
JKOM Total(Japanese Knee Osteoarthitis Score)						●																					
Oxford Knee Score									●																		
UCLA Activity Score					↑																						
Other																											
AIMS arthritis impact																					●						
AIMS medications use																					●						
OMERACT-OARSI Responder(Outcome Measures in Reumatorlogy; Osteoarthritis Research Society International)	●																										
global rating of change			●																								
sf-36 role limitations																		●									
sf36 vitality																		↑									
QOL																											
SF-36 Role Emotional										●		●															
SF-36 Social Functioning										↑		●															
SF-36 Vitality										●		●															
HADS Anxiety									↓																		
HADS Depression									●																		
KOOS Quality of Life	●										●									↑				●			

Table 13 Continued: Supervised Exercise vs Control

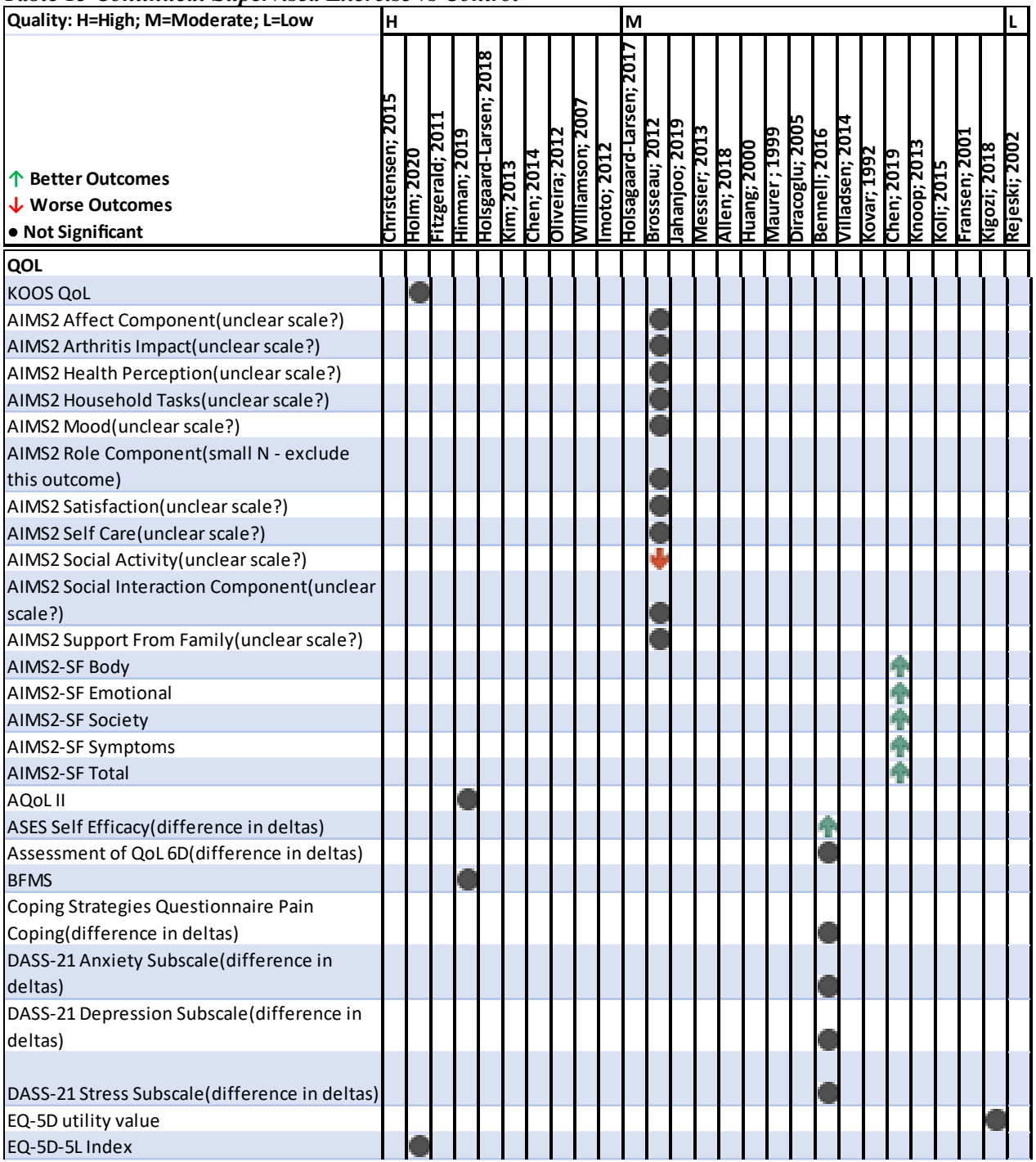


Table 13 Continued: Supervised Exercise vs Control

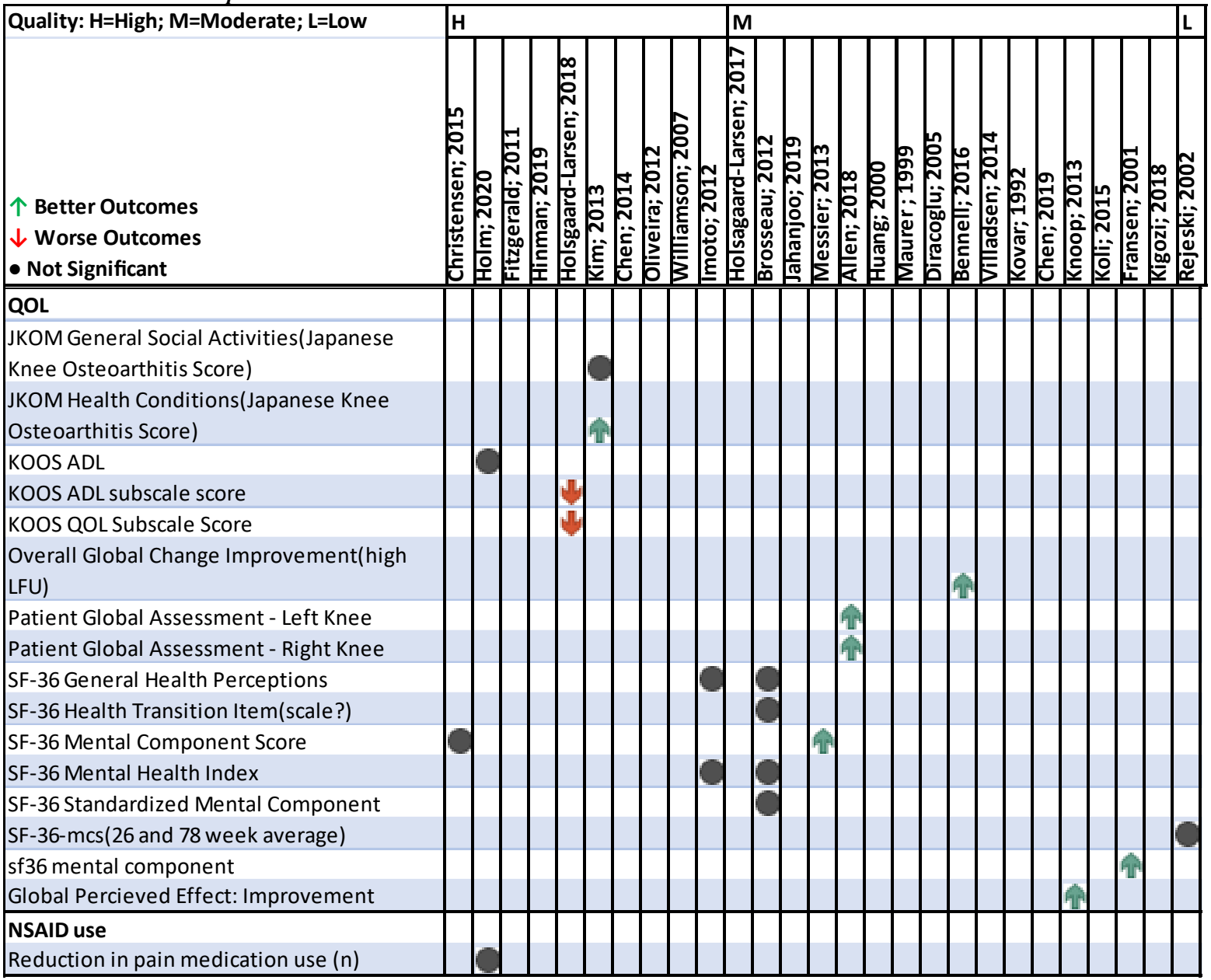


Table 13 Continued: Supervised Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H				M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Holm; 2020	Ebnezar; 2012	Fitzgerald; 2011	Holsagaard-Larsen; 2017
Adverse events					
Back Pain					●
Knee Pain				●	
Constipation					●
Headache					●
Nausea					●
Adverse Events		●			
Diarrhea					●
Dizziness					●
Infection		●			
Abdominal pain					●
Anxiety					●
Bad breath					●
Biliary symptoms					●
Cramps					●
Depressive tendencies					●
Dry skin					●
Eczema					●
Epigastric pain					●
Hair loss					●
Heartburn					●
Influenza					●
Joint pain					●
Mood changes					●
Perianal itching					●
Redness					●
Sciatic pain					●
Sensitive to cold					●
Skin irritation					●
Sleeplessness					●
Swollen joints					●
Toothache					●
Wind/flatulence					●

Table 13 Continued: Supervised Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H				M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Holm; 2020	Ebnezar; 2012	Fitzgerald; 2011	Holsagaard-Larsen; 2017
Adverse events					
Serious Adverse Events		●			
Abdominal Pain(Per Protocol Population; still >80% FU)	●				
Allergeic Rash					●
Allergic Rash(Per Protocol Population; still >80% FU)	●				
Anxiety(Per Protocol Population; still >80% FU)	●				
Back Pain(Per Protocol Population; still >80% FU)	●				
Bad Breath(Per Protocol Population; still >80% FU)	↓				
Biliary Symptoms(Per Protocol Population; still >80% FU)	●				
Constipation(Per Protocol Population; still >80% FU)	●				
Consultation in orthopedic outpatient clinic		●			
Cramps(Per Protocol Population; still >80% FU)	●				
Crepitus			↑		
DVT		●			
Depressive Tendencies(Per Protocol Population; still >80% FU)	●				
Diarrhea(Per Protocol Population; still >80% FU)	●				
Dizziness(Per Protocol Population; still >80% FU)	●				
Dry Skin(Per Protocol Population; still >80% FU)	●				
Eczema(Per Protocol Population; still >80% FU)	●				

Table 13 Continued: Supervised Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H				M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Holm; 2020	Ebnezar; 2012	Fitzgerald; 2011	Holsagaard-Larsen; 2017
Adverse events					
Epigasric Pain(Per Protocol Population; still >80% FU)	●				
Fatigue(Per Protocol Population; still >80% FU)	●				
Fatuigue					●
Flatulence(Per Protocol Population; still >80% FU)	●				
Gastrointestinal		●			
General practitioner consultation		●			
Hair Loss(Per Protocol Population; still >80% FU)	↓				
Headache(Per Protocol Population; still >80% FU)	●				
Heartburn(Per Protocol Population; still >80% FU)	●				
Influenza(Per Protocol Population; still >80% FU)	↓				
Joint Pain(Per Protocol Population; still >80% FU)	●				
Mood Changes(Per Protocol Population; still >80% FU)	↓				
Nausea(Per Protocol Population; still >80% FU)	↓				
Non-serious adverse events		●			
Non-serious adverse events involving index knee		●			
Other Serious Adverse Events		●			
Perianal Itching(Per Protocol Population; still >80% FU)	↓				
Redness(Per Protocol Population; still >80% FU)	●				
Renal system		●			
Sciatic Pain(Per Protocol Population; still >80% FU)	●				

Table 13 Continued: Supervised Exercise vs Control

Quality: H=High; M=Moderate; L=Low ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	H				M
	Christensen; 2015	Holm; 2020	Ebnezar; 2012	Fitzgerald; 2011	Holsagaard-Larsen; 2017
Adverse events					
Sensitive to Cold(Per Protocol Population; still >80% FU)	↓				
Serious Adverse Events involving index knee		●			
Serious Adverse Events involving other sites		●			
Skin Irritation(Per Protocol Population; still >80% FU)	●				
Sleeplessness(Per Protocol Population; still >80% FU)	●				
Swelling			↑		
Swollen Joints(Per Protocol Population; still >80% FU)	●				
Tenderness			↑		
Toothache(Per Protocol Population; still >80% FU)	↓				
Urticaria(Per Protocol Population; still >80% FU)	●				
Urticarial					●
Vomiting(Per Protocol Population; still >80% FU)	●				
Vomitting					●

Evidence Table 1612: Supervised Exercise vs. Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	QoL:Global Percieved Effect: Improvement	12 wks	80/79	86.25%/69.62%	RR	1.24(1.05,1.47)	Group 1	na
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	function:20m Maximal Pace (s)	9 wks	84/81	-0.5(4.583)/-0.4(4.5)	Mean Diff	-0.1(-1.5,1.3)	Not Sig.	na
Kovar; 1992/Moderate	5: Supervised exercise-supervised walking	5: Placebo/Control-control	Pain:AIMS arthritis pain	8 wks	47/45	3.77(1.73)/4.77(2.12)	Mean Diff	-1(-1.8,-0.2)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Pain:AIMS2 Arthritis Pain(unclear scale?)	12 mos	44/41	3.49(2.38)/3.49(2.38)	Mean Diff	0(-1.03,1.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Pain:AIMS2 Arthritis Pain(unclear scale?)	18 mos	44/35	4.4(2.41)/3.4(2.23)	Mean Diff	1(-0.04,2.04)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:ASES Pain	12 mos	82/76	7.3(2)/6.3(2.3)	Mean Diff	1(0.32,1.68)	Group 1	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:ASES Pain	6 mos	83/82	7.3(1.9)/6(2)	Mean Diff	1.3(0.7,1.9)	Group 1	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Pain:KOOS Pain	8 wks	47/46	7.23(10.49)/5.15(10.39)	Mean Diff	2.08(-2.22,6.38)	Not Sig.	na
Koli; 2015/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 3x/week x 12 mo)	5: Placebo/Control-Control (Usual Activities / Care)	Pain:KOOS Pain	12 mos	36/40	4.4(10.34)/1.8(7.82)	Mean Diff	2.6(-1.64,6.84)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Pain:KOOS Pain	68 wks	64/64	6.8(14.81)/8.7(15.01)	Mean Diff	-1.9(-7.12,3.32)	Not Sig.	na
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	Pain:KOOS Pain	9 wks	84/81	3(14.664)/0.8(14.4)	Mean Diff	2.2(-2.27,6.67)	Not Sig.	na
Rosedale; 2015/Moderate	5: Exercise-Exercise	5: Placebo/Control-Control (No Exercise)	Pain:KOOS Pain	3 mos	158	none	mean diff.	7(3,11)	Group 1	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Pain:KOOS Pain	12 wks	45/45	58.5(14.31)/61.2(13.31)	Mean Diff	-2.7(-8.49,3.09)	Not Sig.	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Pain:KOOS Pain subscale score	2 mos	46/47	5.2(2)/9.4(2.1)	Mean Diff	-4.2(-5.04,-3.36)	Group 2	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Pain:KOOS Pain subscale score	1 yrs	46/47	7.2(2.1)/13.6(2)	Mean Diff	-6.4(-7.25,-5.55)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Pain:KOOS Symptom subscale score	1 yrs	46/47	5.8(1.8)/10.9(1.8)	Mean Diff	-5.1(-5.84,-4.36)	Group 2	na
Rosedale; 2014/Moderate	5: Exercise-Exercise	5: Placebo/Control-Control (No Exercise)	Pain:P4 Pain Scale	3 mos	158	none	mean diff.	-2(-4,1)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	12 wks	73/74	-0.8(0.1)/-0.7(0.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	52 wks	73/74	-0.7(0.2)/-0.9(0.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	32 wks	73/74	-0.6(0.2)/-0.6(0.2)	Mean Diff	0(-0.07,0.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:Pain Global Change Improvement (high LFU)	52 wks	120	none	Relative Risk	Sig (p < 0.05)	exercise	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:Pain Global Change Improvement (high LFU)	32 wks	119	none	Relative Risk	1.2(0.9,1.5)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:Pain Global Change Improvement (high LFU)	12 wks	134	none	Relative Risk	1.3(1.1,1.6)	Group 1	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Pain:Pain while getting down to the floor	16 wks	35/35	2.86(3.31)/3.89(3.25)	Mean Diff	-1.03(-2.59,0.53)	Not Sig.	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Pain:Pain while getting down to the floor	16 wks	32/35	1.84(3.28)/3.89(3.25)	Mean Diff	-2.05(-3.65,-0.45)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Pain:Pain while getting up off the floor	16 wks	32/35	2.89(3.85)/5.03(3.96)	Mean Diff	-2.14(-4.05,-0.23)	Group 1	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Pain:Pain while getting up off the floor	16 wks	35/35	2.67(3.96)/5.03(3.96)	Mean Diff	-2.36(-4.25,-0.47)	Group 1	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Pain:Pain while going down stairs	16 wks	35/35	3.71(3.37)/4.4(3.37)	Mean Diff	-0.69(-2.3,0.92)	Not Sig.	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Pain:Pain while going down stairs	16 wks	32/35	2.78(3.39)/4.4(3.37)	Mean Diff	-1.62(-3.27,0.03)	Not Sig.	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Pain:Pain while going up stairs	16 wks	35/35	4.03(3.61)/4.66(3.61)	Mean Diff	-0.63(-2.35,1.09)	Not Sig.	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Pain:Pain while going up stairs	16 wks	32/35	2.98(3.62)/4.66(3.61)	Mean Diff	-1.68(-3.45,0.09)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Pain:SF-36 Pain Index	18 mos	44/36	65.05(18.88)/67.44(18.32)	Mean Diff	-2.39(-10.7,5.92)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Pain:SF-36 Pain Index	12 mos	44/41	63.82(19.13)/67.81(18.38)	Mean Diff	-3.99(-12.08, 4.1)	Not Sig.	inconclusive
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	Pain:SF-36 Pain Index	8 wks	50/50	46.98(25.3)/44(24.94)	Mean Diff	2.98(-6.99,12.95)	Not Sig.	inconclusive
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Pain:VAS pain (cm)	12 wks	35/37	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Pain:VAS pain (cm)	6 wks	35/37	none	mean difference	-0.66(-1.16,-0.17)	Group 1	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Pain:VAS Pain	10 wks	63/63	5.3(1.9)/5.7(2.3)	Mean Diff	-0.4(-1.14,0.34)	Not Sig.	clinically insignificant
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Pain:VAS Pain	32 wks	63/63	4.7(1.9)/6.2(2.1)	Mean Diff	-1.5(-2.21,-0.79)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Pain:VAS Pain	20 wks	63/63	4.3(2)/5.8(2.2)	Mean Diff	-1.5(-2.24,-0.76)	Group 1	possibly clinically significant
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	Pain:VAS Pain	8 wks	50/50	4.27(2.45)/5.74(3.14)	Mean Diff	-1.47(-2.59,-0.35)	Group 1	possibly clinically significant
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	68 wks	64/64	-5.6(19.82)/-5.5(20.02)	Mean Diff	-0.1(-7.07,6.87)	Not Sig.	clinically insignificant
Chen; 2014/High	8: Placebo/Control-Isokinetic Exercise(3x/wk)	8: Placebo/Control-Control (No Intervention)	Pain:VAS Pain	8 wks	30/30	4.2(0.9)/5.2(1.1)	Mean Diff	-1(-1.52,-0.48)	Group 1	some may benefit
Chen; 2014/High	8: Placebo/Control-Isokinetic Exercise(3x/wk)	8: Placebo/Control-Control (No Intervention)	Pain:VAS Pain	6 mos	30/30	4(1.4)/6.5(1.3)	Mean Diff	-2.5(-3.2,-1.8)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Pain:VAS Pain	3 mos	33/35	19.64(16.42)/34.06(24.54)	Mean Diff	-14.42(-24.5,-4.34)	Group 1	possibly clinically significant
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Pain:VAS Pain	3 mos	34/35	33.77(21.91)/37.86(22.58)	Mean Diff	-4.09(-14.78, 6.6)	Not Sig.	clinically insignificant
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Pain:VAS Pain	6 wks	80/79	3.7(2.1)/3.9(1.9)	Mean Diff	-0.2(-0.83,0.43)	Not Sig.	clinically insignificant
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Pain:VAS Pain	12 wks	80/79	2.8(2.1)/3.3(2.1)	Mean Diff	-0.5(-1.16,0.16)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Pain:VAS Pain	38 wks	80/79	3.1(2.5)/3.7(2.4)	Mean Diff	-0.6(-1.37,0.17)	Not Sig.	clinically insignificant
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Pain:VAS Pain	3 mos	60/61	3.86(2.59)/3.95(2.59)	Mean Diff	-0.09(-1.02,0.84)	Not Sig.	clinically insignificant
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Pain:VAS Pain	12 wks	60/61	6.36(2.6)/7.24(2.07)	Mean Diff	-0.88(-1.73,-0.03)	Group 1	clinically insignificant
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Pain:VAS Pain	7 wks	60/61	6.9(2.36)/6.89(2.29)	Mean Diff	0.01(-0.83,0.85)	Not Sig.	clinically insignificant
McCarthy ; 2004/High	5: Supervised exercise-home based + class based exercise	5: Placebo/Control-home based exercise alone	Pain:VAS Pain	6 mos	71/80	43(18.1)/ 54.6(21.8)	Mean Diff	11.6(5.1,18.1)	Group 1	some may benefit
McCarthy ; 2004/High	5: Supervised exercise-home based + class based exercise	5: Placebo/Control-home based exercise alone	Pain:VAS Pain	12 mos	71/80	44.1(18.6)/ 58.9(19.2)	Mean Diff	14.8(8.7,20.9)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Pain:VAS Pain	5 wks	30/30	3.83(1.15)/3.43(1.26)	Mean Diff	0.4(-0.22,1.02)	Not Sig.	clinically insignificant
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:VAS Pain	12 mos	82/76	3.9(2.4)/4(2.3)	Mean Diff	-0.1(-0.84,0.64)	Not Sig.	clinically insignificant
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:VAS Pain	6 mos	83/82	3.5(2.1)/4.2(2.2)	Mean Diff	-0.7(-1.36,-0.04)	Group 1	clinically insignificant
Hu; 2020/High	5: Supervised exercise-Taichi(three times a week for 60 minutes for 24 weeks)	5: Placebo/Control-Control(30 minute health education lecture)	Pain:VAS Pain	24 wks	52/40	2.53(1.61)/3.6(1.6)	Mean Diff	-1.07(-1.74,-0.4)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:VAS Pain (Walking)	6 mos	83/82	3.7(2.4)/4.4(2.4)	Mean Diff	-0.7(-1.44,0.04)	Not Sig.	clinically insignificant
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:VAS Pain (Walking)	12 mos	82/76	3.9(2.4)/3.8(2.5)	Mean Diff	0.1(-0.67,0.87)	Not Sig.	clinically insignificant
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:VAS Pain (Walking)(difference in deltas)	12 wks	73/74	-33.7(2.5)/-26.5(0)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:VAS Pain (Walking)(difference in deltas)	32 wks	73/74	-28.2(3.2)/-23.5(3.4)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:VAS Pain (Walking)(difference in deltas)	52 wks	73/74	-27.5(2.9)/-24.2(2.8)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:VAS Pain(difference in deltas)	12 wks	73/74	-31.4(2.5)/-24.9(2.6)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:VAS Pain(difference in deltas)	52 wks	73/74	-26.3(2.8)/-23.9(2.9)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:VAS Pain(difference in deltas)	32 wks	73/74	-30.6(2.9)/-22.3(3.2)	Mean Diff	-8.3(-9.3,-7.3)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Pain:WOMAC Pain	10 wks	63/63	8.4(3)/9.1(3.6)	Mean Diff	-0.7(-1.87,0.47)	Not Sig.	inconclusive
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Pain:WOMAC Pain	20 wks	63/63	6.9(3.4)/8.8(4.2)	Mean Diff	-1.9(-3.25,-0.55)	Group 1	possibly clinically significant
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Pain:WOMAC Pain	32 wks	63/63	6.6(3.6)/8.6(3.6)	Mean Diff	-2(-3.27,-0.73)	Group 1	possibly clinically significant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Pain:WOMAC Pain	12 mos	140/68	-0.71(3.26)/-0.65(3.06)	Mean Diff	-0.06(-0.97,0.85)	Not Sig.	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Pain:WOMAC Pain	4 mos	140/68	-1.12(3.23)/-0.65(3.1)	Mean Diff	-0.47(-1.39,0.45)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Pain:WOMAC Pain	12 mos	140/142	-0.71(3.26)/-1.12(3.22)	Mean Diff	0.41(-0.35,1.17)	Not Sig.	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Pain:WOMAC Pain	4 mos	140/142	-1.12(3.23)/-1.53(3.53)	Mean Diff	0.41(-0.38,1.2)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Pain:WOMAC Pain	6 mos	152/152	4.6(3.12)/4.9(2.81)	Mean Diff	-0.3(-0.97,0.37)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Pain:WOMAC Pain	18 mos	152/152	3.7(3.43)/4.8(3.43)	Mean Diff	-1.1(-1.87,-0.33)	Group 1	possibly clinically significant
Oliveira; 2012/High	5: Supervised exercise-Supervised Group Exercise + Instruction Manual(2x/wk x8 wks)	5: Placebo/Control-Control (Instruction Manual Alone)	Pain:WOMAC Pain	8 wks	50/50	6.29(3.96)/7.06(4.24)	Mean Diff	-0.77(-2.4,0.86)	Not Sig.	inconclusive
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Pain:WOMAC Pain	16 wks	35/35	10.71(3.14)/10.77(3.19)	Mean Diff	-0.06(-1.57,1.45)	Not Sig.	clinically insignificant
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Pain:WOMAC Pain	16 wks	32/35	10.38(3.17)/10.77(3.19)	Mean Diff	-0.39(-1.94,1.16)	Not Sig.	inconclusive
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	Pain:WOMAC Pain	12 wks	141	none	pvalue	Sig ($p < 0.05$)	Exercise favored over Control	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Pain:WOMAC Pain	5 wks	30/30	5.7(2.25)/5.3(2.3)	Mean Diff	0.4(-0.78,1.58)	Not Sig.	clinically insignificant
Samuel Sundar Doss; 2014/Moderate	5: Exercise-Strength training	5: Placebo/Control-Control	Pain:WOMAC Pain	4 wks	37/36	7.62(2.24)/13.42(2.91)	Mean Diff	-5.8(-7.02,-4.58)	Group 1	clinically significant
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:WOMAC Pain	12 mos	82/76	5.7(3.3)/6.2(3.3)	Mean Diff	-0.5(-1.54,0.54)	Not Sig.	clinically insignificant
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Pain:WOMAC Pain	6 mos	83/82	5.6(3)/6.5(3.4)	Mean Diff	-0.9(-1.89,0.09)	Not Sig.	inconclusive
Hu; 2020/High	5: Supervised exercise-Taichi(three times a week for 60 minutes for 24 weeks)	5: Placebo/Control-Control(30 minute health education lecture)	Pain:WOMAC Pain	24 wks	52/40	2.03(2.14)/9.4(9.5)	Mean Diff	-7.37(-10.46,-4.28)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Pain:WOMAC Pain (0-500)	3 mos	53/53	154.9(102.1)/177.7(100.5)	Mean Diff	-22.8(-61.82, 16.22)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Pain:WOMAC Pain (0-500)	1 mos	53/53	134.8(77.6)/177(98.2)	Mean Diff	-42.2(-76.31,-8.09)	Group 1	possibly clinically significant
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Pain:WOMAC Pain (0-500)	6 mos	53/53	173.7(101.6)/181.5(98)	Mean Diff	-7.8(-46.25, 30.65)	Not Sig.	inconclusive
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Pain:WOMAC Pain (VAS Version)	12 mos	36/40	-2(13.3)/0(7.82)	Mean Diff	-2(-7.09,3.09)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Pain:WOMAC Pain (VAS Version)(scale doesn't make sense?)	12 mos	43/41	24.65(15.78)/25(19.44)	Mean Diff	-0.35(-8.06,7.36)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Pain:WOMAC Pain (VAS Version)(scale doesn't make sense?)	18 mos	43/35	23.6(15.09)/23.5(17.78)	Mean Diff	0.1(-7.46,7.66)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:WOMAC Pain(difference in deltas)	52 wks	73/74	-3.5(0.5)/-3(0.5)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:WOMAC Pain(difference in deltas)	32 wks	73/74	-3.7(0)/-2.3(0.5)	Mean Diff	-1.4(-1.52,-1.28)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Pain:WOMAC Pain(difference in deltas)	12 wks	73/74	-4.3(0)/-2.6(0.5)	Mean Diff	-1.7(-1.82,-1.58)	Group 1	possibly clinically significant
Topp; 2009/Low	5: Exercise-dynamic strength training	5: Placebo/Control-control	Pain:WOMAC pain	16 wks	35/32	10.71(3.13)/10.77(3.05)	Mean Diff	-0.06(-1.57,1.45)	Not Sig.	clinically insignificant
Topp; 2009/Low	5: Exercise-isometric strength training	5: Placebo/Control-control	Pain:WOMAC pain	16 wks	35/32	10.38(3.31)/10.77(3.05)	Mean Diff	-0.39(-1.94,1.16)	Not Sig.	inconclusive
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Pain:WOMAC pain	12 wks	35/37	none	pvalue	NS	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Pain:WOMAC pain	6 wks	35/37	none	mean difference	-0.9(-1.7,-0.1)	Group 1	possibly clinically significant
Maurer ; 1999/Moderate	5: Exercise-isokinetic quadricepts exercise	5: Wellness education-education	Pain:Womac pain	8 wks	49/49	-43.54(.)/-28.49(.)	Mean Diff	-15.05	isokinetic quadricepts exercise quadricepts	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Pain:interaction between 3 or more comorbidities and womac pain(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Pain:interaction between anxiety and womac pain(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Pain:interaction between cardiac problems and womac pain(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Pain:interaction between obesity and womac pain(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Pain:interaction between pain in other locations and womac pain(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Pain:interaction between respiratory conditions and womac pain(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Huang; 2000/Moderate	5: Exercise-isokinetic strengthening	5: Placebo/Control-control	Pain:vas pain	8 weeks	58/66	31(12)/44(4)	Mean Diff	-13(-16.29,-9.71)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2000/Moderate	5: Exercise-isotonic strengthening	5: Placebo/Control-control	Pain:vas pain	8 weeks	62/66	26(7)/44(4)	Mean Diff	-18(-20.02,-15.98)	Group 1	possibly clinically significant
Huang; 2000/Moderate	5: Exercise-isometric strength training	5: Placebo/Control-control	Pain:vas pain	1 yrs	60/54	32(16)/61(13)	Mean Diff	-29(-34.39,-23.61)	Group 1	clinically significant
Huang; 2000/Moderate	5: Exercise-isokinetic strengthening	5: Placebo/Control-control	Pain:vas pain	1 yrs	56/54	25(18)/61(13)	Mean Diff	-36(-41.92,-30.08)	Group 1	clinically significant
Huang; 2000/Moderate	5: Exercise-isotonic strengthening	5: Placebo/Control-control	Pain:vas pain	1 yrs	58/54	20(14)/61(13)	Mean Diff	-41(-46.06,-35.94)	Group 1	clinically significant
Huang; 2000/Moderate	5: Exercise-isometric strength training	5: Placebo/Control-control	Pain:vas pain	8 weeks	62/66	36(6)/44(4)	Mean Diff	-8(-9.8,-6.2)	Group 1	clinically insignificant
McCarthy ; 2004/High	5: Supervised exercise-home based + class based exercise	5: Placebo/Control-home based exercise alone	Pain:womac Pain	6 mos	71/80	9.13(3.99)/8.04(3.6)	Mean Diff	1.09(-0.14,2.32)	Not Sig.	inconclusive
Lin; 2009/High	5: Exercise-Proprioceptive training (not strength)	5: Placebo/Control-control	Pain:womac pain	8 wks	36/36	4.3(2.3)/7.3(3.4)	Mean Diff	-3(-4.37,-1.63)	Group 1	possibly clinically significant
Lin; 2009/High	5: Exercise-strength training	5: Placebo/Control-control	Pain:womac pain	8 wks	36/36	4.2(3)/7.3(3.4)	Mean Diff	-3.1(-4.61,-1.59)	Group 1	possibly clinically significant
Jan; 2008/Moderate	5: Exercise-low resistance training	5: Placebo/Control-no exercise	Pain:womac pain	8 wks	34/30	4.8(2.7)/7.1(3.4)	Mean Diff	-2.3(-3.85,-0.75)	Group 1	possibly clinically significant
Jan; 2008/Moderate	5: Exercise-high resistance training	5: Placebo/Control-no exercise	Pain:womac pain	8 wks	34/30	4.8(3.5)/7.1(3.4)	Mean Diff	-2.3(-4.03,-0.57)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2010/Moderate	5: Exercise-hip strengthening	5: Placebo/Control-no exercise	Pain:womac pain improvement	13 weeks	39/37	4.9(20.6)/6.5(20.07)	Mean Diff	-1.6(-10.9,7.7)	Not Sig.	inconclusive
Fransen; 2001/Moderate	5: PT-physical therapy (individual or group)	5: Placebo/Control-waitlist control	Pain:womac pain improvement	8 weeks	83/43	10.6(3.14)/-1.5(5.18)	Mean Diff	12.1(10.38,13.82)	Group 1	clinically significant
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Function:10 m walk time (s)	8 weeks	30/30	5.21(1.1)/5.89(1.3)	Mean Diff	-0.68(-1.3,-0.06)	Group 1	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:20 Meter Walk (m/s)(difference in deltas)	12 wks	73/74	0.1(0)/0.1(0)	Mean Diff	0	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:20 Meter Walk (m/s)(difference in deltas)	52 wks	73/74	0.2(0)/0.2(0)	Mean Diff	0	Not Sig.	na
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	Function:20 m Self-Chosen Pace (s)	9 wks	84/81	-1.3(3.666)/-0.9(4.5)	Mean Diff	-0.4(-1.66,0.86)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:2min March Test	12 mos	140/142	1.06(28.34)/1.35(29.26)	Mean Diff	-0.29(-7.04,6.46)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:2min March Test	12 mos	140/68	1.06(28.34)/-0.09(27.2)	Mean Diff	1.15(-6.91,9.21)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:2min March Test	4 mos	140/142	0.14(25.97)/-2.38(27.09)	Mean Diff	2.52(-3.7,8.74)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:2min March Test	4 mos	140/68	0.14(25.97)/-8.83(25.45)	Mean Diff	8.97(1.48,16.46)	Group 1	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:30 Second Stand-to-Sit(difference in deltas)	52 wks	73/74	2.2(0.3)/1.5(0.5)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:30 Second Stand-to-Sit(difference in deltas)	12 wks	73/74	1.7(0.3)/0.7(0.3)	Mean Diff	1(0.9,1.1)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:30 s Chair Stand	4 mos	140/68	-0.06(4.43)/0.1(4.36)	Mean Diff	-0.16(-1.44,1.12)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:30 s Chair Stand	12 mos	140/68	0.13(4.01)/0.55(3.86)	Mean Diff	-0.42(-1.56,0.72)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:30 s Chair Stand	12 mos	140/142	0.13(4.01)/0.86(4.13)	Mean Diff	-0.73(-1.68,0.22)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:30 s Chair Stand	4 mos	140/142	-0.06(4.43)/0.67(4.61)	Mean Diff	-0.73(-1.79,0.33)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Function:50 m Walk Test (s)	12 wks	60/61	51.8(18.4)/57.4(26.7)	Mean Diff	-5.6(-13.85, 2.65)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Function:50 m Walk Test (s)	7 wks	60/61	50.3(17.7)/57.4(23.1)	Mean Diff	-7.1(-14.51, 0.31)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Function:50 m Walk Test (s)	3 mos	60/61	46.6(11.4)/44.1(6.91)	Mean Diff	2.5(-0.91,5.91)	Not Sig.	na
Kovar; 1992/Moderate	5: Supervised exercise-supervised walking	5: Placebo/Control-control	Function:6 minute walk (ft)	8 wks	47/45	1479.7(387.2)/1112.2(410.1)	Mean Diff	367.5(202.13,532.87)	Group 1	na
Ettinger;/Moderate	5: Exercise-resistance exercise	5: Wellness education-health education	Function:6 minute walk distance (ft)	18 weeks	127/132	1507(180.31)/1349(183.83)	Mean Diff	158(113.44,202.56)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:6MWT(m)	12 mos	44/40	524.86(106.52)/520.52(115.11)	Mean Diff	4.34(-43.97, 52.65)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:6MWT(m)	18 mos	42/35	492.91(86.95)/540.35(103.37)	study reported p value	NS	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:6MWT(m)	10 wks	63/63	440.6(96.7)/423.4(115.5)	Mean Diff	17.2(-20.37, 54.77)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:6MWT(m)	20 wks	63/63	448(102.5)/416.5(116.9)	Mean Diff	31.5(-7.28,70.28)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:6MWT(m)	32 wks	63/63	465.3(93.9)/423(114.8)	Mean Diff	42.3(5.3,79.3)	Group 1	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Function:6MWT(m)	68 wks	64/64	38.48(59.1)/22.89(60.03)	Mean Diff	15.59(-5.25,36.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:6MWT(m)	18 mos	152/152	537(102.96)/502(84.24)	Mean Diff	35(13.76,56.24)	Group 1	na
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:6MWT(m)	6 mos	152/152	537(93.6)/5.5(81.12)	Mean Diff	531.5(511.73,551.27)	Group 1	na
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	Function:6MWT(m)	12 wks	141	none	pvalue	Sig ($p < 0.05$)	Exercise favored over Control	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Leisure Time Activities + Other(7 Day Physical Activity Recall;units?)	18 mos	26/30	22.63(20.97)/17.99(37.28)	Mean Diff	4.64(-11.36, 20.64)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Leisure Time Activities + Other(7 Day Physical Activity Recall;units?)	12 mos	13-Sep	17.1(21.03)/11.05(8.39)	Mean Diff	6.05(-10.46, 22.56)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Leisure Time Activities(7 Day Physical Activity Recall;units?)	12 mos	42/38	12.22(7.86)/12.68(11.2)	Mean Diff	-0.46(-4.82,3.9)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Leisure Time Activities(7 Day Physical Activity Recall;units?)	18 mos	43/41	15.34(10.23)/16.01(14.14)	Mean Diff	-0.67(-6.06,4.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Other Domestic Activities + Other(7 Day Physical Activity Recall;units?)	18 mos	30/19	23.34(22.4)/26.13(15.64)	Mean Diff	-2.79(-13.74, 8.16)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Other Domestic Activities + Other(7 Day Physical Activity Recall;units?)	12 mos	13/8	22.33(26.1)/12.04(5.64)	Mean Diff	10.29(-5.84,26.42)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Other Domestic Activities(7 Day Physical Activity Recall;units?)	12 mos	40/32	12.2(9.9)/16.88(17.5)	Mean Diff	-4.68(-11.66, 2.3)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:7-Day POD - Other Domestic Activities(7 Day Physical Activity Recall;units?)	18 mos	41/33	16.46(13.17)/24.18(25.59)	Mean Diff	-7.72(-17.6,2.16)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kovar; 1992/Moderate	5: Supervised exercise-supervised walking	5: Placebo/Control-control	Function:AIMS physical activity	8 wks	47/45	3.74(2.69)/5.96(2.32)	Mean Diff	-2.22(-3.26,-1.18)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Arm Function(unclear scale?)	12 mos	44/41	0.3(0.73)/0.22(0.7)	Mean Diff	0.08(-0.23,0.39)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Arm Function(unclear scale?)	18 mos	43/36	0.58(1.17)/1.19(0.51)	study reported p value	NS	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Hand and Finger(unclear scale?)	12 mos	44/41	0.6(0.93)/0.74(1.94)	Mean Diff	-0.14(-0.81,0.53)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Hand and Finger(unclear scale?)	18 mos	44/36	0.62(1.2)/0.57(1.2)	Mean Diff	0.05(-0.49,0.59)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Level of Tension(unclear scale?)	12 mos	44/40	3.09(1.69)/2.97(1.9)	Mean Diff	0.12(-0.66,0.9)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Level of Tension(unclear scale?)	18 mos	44/36	3.31(1.97)/2.82(1.6)	Mean Diff	0.49(-0.3,1.28)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Mobility(unclear scale?)	12 mos	44/41	0.61(1.02)/0.72(1.09)	Mean Diff	-0.11(-0.57,0.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Mobility(unclear scale?)	18 mos	44/36	0.82(1.19)/0.49(0.9)	Mean Diff	0.33(-0.14,0.8)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Physical Component(unclear scale?)	12 mos	44/41	0.88(0.85)/0.86(0.77)	Mean Diff	0.02(-0.33,0.37)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Physical Component(unclear scale?)	18 mos	43/36	1.04(1.01)/0.68(0.61)	Mean Diff	0.36(-0.01,0.73)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Walking and Bending(unclear scale?)	12 mos	44/41	3.36(2.22)/3.09(2.49)	Mean Diff	0.27(-0.75,1.29)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Walking and Bending(unclear scale?)	18 mos	44/36	3.67(2.32)/2.71(2.11)	Mean Diff	0.96(-0.03,1.95)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Work(small N - exclude this outcome)	12 mos	15/18	1.54(1.83)/1.88(1.56)	Mean Diff	-0.34(-1.57,0.89)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:AIMS2 Work(small N - exclude this outcome)	18 mos	14-Dec	2.19(2.45)/1.83(1.83)	Mean Diff	0.36(-1.43,2.15)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Function:ASES Function	12 mos	82/76	8.3(1.6)/8.1(1.6)	Mean Diff	0.2(-0.3,0.7)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Function:ASES Function	6 mos	83/82	8.3(1.7)/8.1(1.6)	Mean Diff	0.2(-0.31,0.71)	Not Sig.	na
Mihalko; 2018/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Balance Efficacy Confidence	6 mos	152/152	85.39(13.04)/83.26(13.6)	Mean Diff	2.13(-0.88,5.14)	Not Sig.	na
Mihalko; 2018/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Balance Efficacy Confidence	18 mos	152/152	85.44(13.23)/80.82(13.29)	Mean Diff	4.62(1.63,7.61)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	Function:Chair Stands (s)	9 wks	84/81	-3(4.583)/-1.1(4.5)	Mean Diff	-1.9(-3.3,-0.5)	Group 1	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Climbing Stairs Questionnaire (CStQ15)(unclear direction)	12 wks	80/79	25.3(19.1)/27.4(18.8)	Mean Diff	-2.1(-8.04,3.84)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Climbing Stairs Questionnaire (CStQ15)(unclear direction)	38 wks	80/80	28.3(22.7)/30.8(22)	Mean Diff	-2.5(-9.48,4.48)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Climbing Stairs Questionnaire (CStQ15)(unclear direction)	6 wks	80/79	32.2(20.4)/36.2(21.8)	Mean Diff	-4(-10.62, 2.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Climbing Stairs Questionnaire(scale direction?)	20 wks	63/63	42.7(20.3)/48.8(18.2)	Mean Diff	-6.1(-12.9,0.7)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Climbing Stairs Questionnaire(scale direction?)	32 wks	63/63	40.3(22.6)/48.1(18.1)	Mean Diff	-7.8(-15.02,-0.58)	Group 1	na
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:Daily Impact Score	12 mos	34/40	163(43)/168(46)	Mean Diff	-5(-25.65, 15.65)	Not Sig.	na
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:Dynamic Balance	12 mos	36/40	-0.6(0.74)/-0.2(0.47)	Mean Diff	-0.4(-0.69,-0.11)	Group 1	na
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Function:Fall Risk	5 wks	30/30	3.79(1.37)/1.9(1.48)	Mean Diff	1.89(1.15,2.63)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	Function:Five Repetition Sit to Stand Test (s)	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Function Global Change Improvement (high LFU)	12 wks	134	none	Relative Risk	Sig (p < 0.05)	exercise	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Function Global Change Improvement (high LFU)	32 wks	119	none	Relative Risk	1.2(0.9,1.6)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Function Global Change Improvement (high LFU)	52 wks	120	none	Relative Risk	1.4(1.1,1.7)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mihalko; 2018/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Gait Efficacy Confidence	6 mos	152/152	86.46(16.38)/82.26(17.22)	Mean Diff	4.2(0.41,7.99)	Group 1	na
Mihalko; 2018/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Gait Efficacy Confidence	18 mos	152/152	86.49(16.57)/81.01(16.82)	Mean Diff	5.48(1.71,9.25)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:Gait Speed	12 mos	44/41	1.46(0.3)/1.45(0.32)	Mean Diff	0.01(-0.12,0.14)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:Gait Speed	18 mos	42/35	1.37(0.24)/1.5(0.29)	study reported p value	NS	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Get Up and Go Test (s)	38 wks	80/80	10(1.6)/9.9(2)	Mean Diff	0.1(-0.47,0.67)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Get Up and Go Test (s)	6 wks	80/79	10.2(1.8)/10.1(2.7)	Mean Diff	0.1(-0.62,0.82)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Get Up and Go Test (s)	12 wks	80/79	10.1(1.5)/9.7(2)	Mean Diff	0.4(-0.15,0.95)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Function:Grip Strength (kg)	3 mos	33/35	22.15(4.74)/20(4.67)	Mean Diff	2.15(-0.13,4.43)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Function:Grip Strength (kg)	3 mos	34/35	21.1(3.09)/18.88(3.83)	Mean Diff	2.22(0.55,3.89)	Group 1	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Function:JKOM Condition in Daily Life(Japanese Knee Osteoarthitis Score)	3 mos	33/35	15.11(4.18)/16.56(5.08)	Mean Diff	-1.45(-3.7,0.8)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Function:JKOM Condition in Daily Life(Japanese Knee Osteoarthitis Score)	3 mos	34/35	15.93(5.15)/18.94(7.06)	Mean Diff	-3.01(-5.98,-0.04)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Function:KOOS Activities of Daily Living	8 wks	47/46	6.96(10.9)/7.46(10.76)	Mean Diff	-0.5(-4.96,3.96)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Activities of Daily Living	68 wks	64/64	8.4(14.21)/6.2(14.21)	Mean Diff	2.2(-2.77,7.17)	Not Sig.	na
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	Function:KOOS Activities of Daily Living	9 wks	84/81	2.6(17.414)/-0.9(17.1)	Mean Diff	3.5(-1.81,8.81)	Not Sig.	na
Koli; 2015/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 3x/week x 12 mo)	5: Placebo/Control-Control (Usual Activities / Care)	Function:KOOS Function	12 mos	36/40	1(7.39)/-0.2(4.69)	Mean Diff	1.2(-1.68,4.08)	Not Sig.	na
Rosedale; 2016/Moderate	5: Exercise-Exercise	5: Placebo/Control-Control (No Exercise)	Function:KOOS Function	3 mos	158	none	mean diff.	5(1,9)	Group 1	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Function:KOOS Sports & Recreation subscale score	2 mos	46/47	5(2.9)/6.5(3.1)	Mean Diff	-1.5(-2.74,-0.26)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Function:KOOS Sports & Recreation subscale score	1 yrs	46/47	7.8(2.9)/9.4(2.9)	Mean Diff	-1.6(-2.79,-0.41)	Group 2	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Function:KOOS Sports and Recreation	12 wks	45/45	29.1(16.48)/35.8(15.31)	Mean Diff	-6.7(-13.36,-0.04)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Function:KOOS Sports/Recreation	8 wks	47/46	7.8(17.86)/4.97(18.03)	Mean Diff	2.83(-4.56,10.22)	Not Sig.	na
Koli; 2015/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 3x/week x 12 mo)	5: Placebo/Control-Control (Usual Activities / Care)	Function:KOOS Sports/Recreation	12 mos	36/40	4(16.26)/-1(12.51)	Mean Diff	5(-1.7,11.7)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Sports/Recreation	68 wks	64/64	6.4(17.61)/4.7(17.61)	Mean Diff	1.7(-4.46,7.86)	Not Sig.	na
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	Function:KOOS Sports/Recreation	9 wks	84/81	-1.7(19.247)/-2.8(20.7)	Mean Diff	1.1(-5.05,7.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Function:KOOS Symptom subscale score	2 mos	46/47	4.7(1.7)/3.3(1.8)	Mean Diff	1.4(0.68,2.12)	Group 1	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Function:KOOS Symptoms	8 wks	47/46	5.84(10.3)/4.71(10.05)	Mean Diff	1.13(-3.06,5.32)	Not Sig.	na
Koli; 2015/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 3x/week x 12 mo)	5: Placebo/Control-Control (Usual Activities / Care)	Function:KOOS Symptoms	12 mos	36/40	1.8(10.34)/1(10.94)	Mean Diff	0.8(-4.07,5.67)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Symptoms	68 wks	64/64	4.5(14.81)/5.9(14.81)	Mean Diff	-1.4(-6.58,3.78)	Not Sig.	na
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	Function:KOOS Symptoms	9 wks	84/81	4.9(17.414)/0.5(16.2)	Mean Diff	4.4(-0.77,9.57)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Function:KOOS Symptoms	12 wks	45/45	63.9(13.15)/63.2(12.15)	Mean Diff	0.7(-4.6,6)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:Knee Extension Force (N)	12 mos	36/40	21(66.5)/-14(46.9)	Mean Diff	35(8.34,61.66)	Group 1	na
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:Knee Flexion Force (N)	12 mos	36/40	8(41.38)/15(37.52)	Mean Diff	-7(-25.14, 11.14)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Knee Instability 1+ episodes in past 6 Wks	6 wks	80/79	66.25%/68.35%	RR	0.97(0.78,1.2)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Knee Instability 1+ episodes in past 6 Wks	12 wks	80/79	51.25%/51.9%	RR	0.99(0.73,1.33)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Knee Instability 1+ episodes in past 6 Wks	38 wks	80/79	51.25%/37.97%	RR	1.35(0.95,1.92)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Knee Instability Resulting in Activity Limitations	12 wks	80/79	22.5%/30.38%	RR	0.74(0.44,1.25)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Knee Instability Resulting in Activity Limitations	38 wks	80/79	27.5%/36.71%	RR	0.75(0.47,1.19)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Knee Instability Resulting in Activity Limitations	6 wks	80/79	33.75%/34.18%	RR	0.99(0.64,1.52)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:Leg Extension Power (W)	12 mos	36/40	47(161.08)/21(159.47)	Mean Diff	26(-47.4,99.4)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Function:Max # Knee Bends in 30 s	8 wks	47/46	4.03(8.67)/2.45(8.37)	Mean Diff	1.58(-1.93,5.09)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Function:One Leg Standing Time with Eyes Open (s)	3 mos	34/35	27.74(24.17)/28.09(22.19)	Mean Diff	-0.35(-11.51, 10.81)	Not Sig.	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Function:One Leg Standing Time with Eyes Open (s)	3 mos	33/35	33.46(22.88)/27.67(22.29)	Mean Diff	5.79(-5.16,16.74)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Function:One-leg hop for distance (cm)	8 wks	47/46	7.53(16.08)/6.12(15.51)	Mean Diff	1.41(-5.1,7.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Function:PASE	6 mos	83/82	190(91)/172(99)	Mean Diff	18(-11.24, 47.24)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Function:PASE	12 mos	82/76	193(115)/152(87)	Mean Diff	41(9.09,72.91)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:PASE - Household(scale range?)	4 mos	140/68	-2.05(37.67)/-5.65(37.29)	Mean Diff	3.6(-7.34,14.54)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:PASE - Household(scale range?)	12 mos	140/68	2.02(35.1)/-4.05(33.13)	Mean Diff	6.07(-3.8,15.94)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:PASE - Household(scale range?)	12 mos	140/142	2.02(35.1)/-4.12(39.57)	Mean Diff	6.14(-2.63,14.91)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:PASE - Household(scale range?)	4 mos	140/142	-2.05(37.67)/-8.83(40.87)	Mean Diff	6.78(-2.43,15.99)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:PASE - Leisure(scale range?)	12 mos	140/142	8.81(26.06)/7.69(27.7)	Mean Diff	1.12(-5.18,7.42)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:PASE - Leisure(scale range?)	4 mos	140/142	4.01(21.36)/-1(23.57)	Mean Diff	5.01(-0.26,10.28)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:PASE - Leisure(scale range?)	4 mos	140/68	4.01(21.36)/-2.73(22.39)	Mean Diff	6.74(0.29,13.19)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:PASE - Leisure(scale range?)	12 mos	140/68	8.81(26.06)/-0.23(25.86)	Mean Diff	9.04(1.46,16.62)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:PASE - Work(scale range?)	4 mos	140/68	1.45(44.64)/4.38(46.21)	Mean Diff	-2.93(-16.3,10.44)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:PASE - Work(scale range?)	12 mos	140/68	-2.76(41.14)/5.67(40.36)	Mean Diff	-8.43(-20.3,3.44)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:PASE - Work(scale range?)	12 mos	140/142	-2.76(41.14)/5.87(43.22)	Mean Diff	-8.63(-18.52, 1.26)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:PASE - Work(scale range?)	4 mos	140/142	1.45(44.64)/-1.32(49.37)	Mean Diff	2.77(-8.26,13.8)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:PSFL Performance Activities(unclear direction)	38 wks	80/80	31.3(22.1)/34.6(20.3)	Mean Diff	-3.3(-9.93,3.33)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:PSFL Performance Activities(unclear direction)	12 wks	80/79	29.5(18.1)/34.4(19.8)	Mean Diff	-4.9(-10.84, 1.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Patient-Specific Functioning List(scale direction?)	20 wks	63/63	4.2(2.1)/5.8(1.7)	Mean Diff	-1.6(-2.27,-0.93)	Group 1	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Patient-Specific Functioning List(scale direction?)	32 wks	63/63	4.1(2.2)/5.9(1.8)	Mean Diff	-1.8(-2.51,-1.09)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Physical Activity Scale for the Elderly	12 mos	140/142	7.91(64.48)/9.43(69.65)	Mean Diff	-1.52(-17.25, 14.21)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Physical Activity Scale for the Elderly	4 mos	140/142	2.49(69.27)/-11.25(79.11)	Mean Diff	13.74(-3.68,31.16)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Physical Activity Scale for the Elderly	4 mos	140/68	2.49(69.27)/-2.72(67.46)	Mean Diff	5.21(-14.68, 25.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Physical Activity Scale for the Elderly	12 mos	140/68	7.91(64.48)/1.96(61.52)	Mean Diff	5.95(-12.32, 24.22)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Physical Activity Scale for the Elderly(difference in deltas)	52 wks	73/74	36.6(9.1)/20.8(11)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Physical Activity Scale for the Elderly(difference in deltas)	12 wks	73/74	30(10.3)/16.6(8.6)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Physical Activity Scale for the Elderly(difference in deltas)	32 wks	73/74	37.6(10.6)/1.6(15.9)	Mean Diff	36(31.6,40.4)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Proprioceptive Accuracy (deg)(unclear direction)	6 wks	80/79	2.4(1.9)/2.5(1.6)	Mean Diff	-0.1(-0.65,0.45)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Proprioceptive Accuracy (deg)(unclear direction)	38 wks	80/80	1.9(1.4)/2.2(1.4)	Mean Diff	-0.3(-0.74,0.14)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Proprioceptive Accuracy (deg)(unclear direction)	12 wks	80/79	2(1.6)/2.5(1.8)	Mean Diff	-0.5(-1.03,0.03)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Quadreceps Strength (Nm/kg)(difference in deltas)	12 wks	73/74	0.1(0)/0.1(0)	Mean Diff	0	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Quadreceps Strength (Nm/kg)(difference in deltas)	52 wks	73/74	0.3(0.1)/0.1(0.1)	Mean Diff	0.2(0.17,0.23)	Group 1	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Questionnaire Rising and Sitting (QR&S39)(unclear direction)	6 wks	80/79	31.4(22.9)/32.2(25.5)	Mean Diff	-0.8(-8.4,6.8)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Questionnaire Rising and Sitting (QR&S39)(unclear direction)	12 wks	80/79	24.6(20.3)/26.6(23.1)	Mean Diff	-2(-8.82,4.82)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Questionnaire Rising and Sitting (QR&S39)(unclear direction)	38 wks	80/80	29.2(25.3)/26.9(24.6)	Mean Diff	2.3(-5.49,10.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:ROM Knee Flexion	1 mos	53/53	122.1(10)/124.5(10.4)	Mean Diff	-2.4(-6.33,1.53)	Not Sig.	na
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:ROM Knee Flexion	6 mos	53/53	119.5(13.6)/122.2(13.3)	Mean Diff	-2.7(-7.88,2.48)	Not Sig.	na
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:ROM Knee Flexion	3 mos	53/53	120.7(11.6)/123.7(11.1)	Mean Diff	-3(-7.37,1.37)	Not Sig.	na
Ebnezar; 2012/High	5: Exercise-Yoga(40 min daily)	5: Placebo/Control-Control	Function:ROM Left Knee Flexsion	90 days	118/125	112.53(10.26)/99.15(9.91)	Mean Diff	13.38(10.83, 15.93)	Group 1	na
Ebnezar; 2012/High	5: Exercise-Yoga(40 min daily)	5: Placebo/Control-Control	Function:ROM Right Knee Flexion	90 days	118/125	113.07(10.37)/100.46(10.9)	Mean Diff	12.61(9.92,15.3)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Rising and Sitting Questionnaire(scale direction?)	32 wks	63/63	38.5(26.7)/43.8(25.7)	Mean Diff	-5.3(-14.54, 3.94)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Rising and Sitting Questionnaire(scale direction?)	20 wks	63/63	39.2(26.1)/45.9(25.7)	Mean Diff	-6.7(-15.83, 2.43)	Not Sig.	na
Chen; 2014/High	8: Placebo/Control-Isokinetic Exercise(3x/wk)	8: Placebo/Control-Control (No Intervention)	Function:RoM	8 wks	30/30	105(17)/100(11)	Mean Diff	5(-2.43,12.43)	Not Sig.	na
Chen; 2014/High	8: Placebo/Control-Isokinetic Exercise(3x/wk)	8: Placebo/Control-Control (No Intervention)	Function:RoM	6 mos	30/30	109(13)/100(15)	Mean Diff	9(1.74, 16.26)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:SF-36 Physical Functioning	18 mos	44/36	68.16(21.31)/75.69(19.65)	Mean Diff	-7.53(-16.67, 1.61)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:SF-36 Physical Functioning	12 mos	44/41	70.09(18.82)/68.17(26.38)	Mean Diff	1.92(-8.05,11.89)	Not Sig.	inconclusive
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:SF-36 Physical Functioning	20 wks	63/63	20.8(4.5)/18.9(5)	Mean Diff	1.9(0.22,3.58)	Group 1	possibly clinically significant
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:SF-36 Physical Functioning	32 wks	63/63	21.4(4.5)/18.9(4.7)	Mean Diff	2.5(0.88,4.12)	Group 1	possibly clinically significant
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	Function:SF-36 Physical Functioning	8 wks	50/50	49.38(23.94)/41.55(26.66)	Mean Diff	7.83(-2.23,17.89)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:SF-36 Role Physical	18 mos	44/36	57.39(40.56)/68.52(39.35)	Mean Diff	-11.13(-28.99, 6.73)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:SF-36 Role Physical	12 mos	44/41	61.74(39.76)/65.85(42.48)	Mean Diff	-4.11(-21.9,13.68)	Not Sig.	na
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	Function:SF-36 Role Physical	8 wks	50/50	53.13(46.41)/39.66(47.49)	Mean Diff	13.47(-5.17,32.11)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:SF-36 Standardized Physical Component	12 mos	44/41	42.51(9.23)/43.46(9.41)	Mean Diff	-0.95(-4.98,3.08)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:SF-36 Standardized Physical Component	18 mos	44/36	42.82(9.24)/45.15(8.93)	Mean Diff	-2.33(-6.39,1.73)	Not Sig.	inconclusive
Jan ; 2009/Moderate	5: Exercise-non-Weight bearing exercise	5: Placebo/Control-Control	Function:Sponge walk time	8 wks	35/35	9.4(3.8)/11.7(3.7)	Mean Diff	-2.3(-4.09,-0.51)	Group 1	na
Jan ; 2009/Moderate	5: Exercise-Weight bearing exercise	5: Placebo/Control-Control	Function:Sponge walk time	8 wks	36/35	5.8(2.9)/11.7(3.7)	Mean Diff	-5.9(-7.48,-4.32)	Group 1	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Stair Ascent Time (s)	20 wks	63/63	7.7(4.3)/8.7(4.4)	Mean Diff	-1(-2.53,0.53)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Stair Ascent Time (s)	32 wks	63/63	7.4(3.8)/10(9.6)	Mean Diff	-2.6(-5.19,-0.01)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Stair Ascent Time (s)	10 wks	63/63	8.6(6.7)/11.4(14.7)	Mean Diff	-2.8(-6.85,1.25)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Stair Descent Time (s)	20 wks	63/63	8.3(4.4)/9.8(5.5)	Mean Diff	-1.5(-3.26,0.26)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Stair Descent Time (s)	10 wks	63/63	9.6(8.8)/11.6(12.5)	Mean Diff	-2(-5.82,1.82)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Stair Descent Time (s)	32 wks	63/63	7.6(3.8)/9.7(4.9)	Mean Diff	-2.1(-3.65,-0.55)	Group 1	na
Jan ; 2009/Moderate	5: Exercise-Weight bearing exercise	5: Placebo/Control-Control	Function:Stair clim time	8 wks	36/35	11.8(3)/15.4(4)	Mean Diff	-3.6(-5.28,-1.92)	Group 1	na
Jan ; 2009/Moderate	5: Exercise-non-Weight bearing exercise	5: Placebo/Control-Control	Function:Stair clim time	8 wks	35/35	10(3.1)/15.4(4)	Mean Diff	-5.4(-7.11,-3.69)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Step Test(difference in deltas)	52 wks	73/74	2.6(0.6)/1.8(0.5)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:Step Test(difference in deltas)	12 wks	73/74	2.1(0.6)/0.7(0.3)	Mean Diff	1.4(1.24,1.56)	Group 1	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Function:Stride Length (cm)	3 mos	34/35	114.42(12.06)/102.53(17.91)	Mean Diff	11.89(4.56,19.22)	Group 1	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Function:Stride Length (cm)	3 mos	33/35	114.76(14.21)/105.86(16.5)	Mean Diff	8.9(1.46,16.34)	Group 1	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Function:Time (s) on 40-m walk test	12 wks	45/45	24.2(2.33)/24.8(2)	Mean Diff	-0.6(-1.51,0.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Function:Time (s) on the stair climb test	12 wks	45/45	9.6(2.5)/10.7(2.33)	Mean Diff	-1.1(-2.11,-0.09)	Group 1	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Function:Time to get down to the floor	16 wks	32/35	4.31(3.62)/5.33(3.61)	Mean Diff	-1.02(-2.79,0.75)	Not Sig.	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Function:Time to get down to the floor	16 wks	35/35	3.89(3.67)/5.33(3.61)	Mean Diff	-1.44(-3.18,0.3)	Not Sig.	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Function:Time to go down the stairs	16 wks	35/35	15.96(6.8)/16.34(6.8)	Mean Diff	-0.38(-3.62,2.86)	Not Sig.	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Function:Time to go down the stairs	16 wks	32/35	13.95(6.84)/16.34(6.8)	Mean Diff	-2.39(-5.72,0.94)	Not Sig.	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Function:Time to go up the stairs	16 wks	35/35	16.33(7.04)/17.53(7.04)	Mean Diff	-1.2(-4.56,2.16)	Not Sig.	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Function:Time to go up the stairs	16 wks	32/35	15.15(7.01)/17.53(7.04)	Mean Diff	-2.38(-5.81,1.05)	Not Sig.	na
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Function:Timed Up and Go (s)	5 wks	30/30	9.54(1.64)/7.61(1.64)	Mean Diff	1.93(1.08,2.78)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:Timed Up and Go Test (sec)	12 mos	44/41	8.12(2.44)/7.65(1.79)	Mean Diff	0.47(-0.45,1.39)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:Timed Up and Go Test (sec)	18 mos	42/35	8.41(2.05)/7.88(1.89)	Mean Diff	0.53(-0.37,1.43)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Timed Up and Go Test (sec)	10 wks	63/63	12(3.4)/12.9(4.3)	Mean Diff	-0.9(-2.27,0.47)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Timed Up and Go Test (sec)	20 wks	63/63	11.9(3.6)/13(4.4)	Mean Diff	-1.1(-2.52,0.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Timed Up and Go Test (sec)	32 wks	63/63	11.4(3)/12.8(3.7)	Mean Diff	-1.4(-2.59,-0.21)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Timed Up and Go Test (sec)	4 mos	140/68	-0.56(4.4)/-0.11(4.23)	Mean Diff	-0.45(-1.7,0.8)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Timed Up and Go Test (sec)	12 mos	140/68	-0.94(4.85)/-0.31(4.61)	Mean Diff	-0.63(-2,0.74)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Timed Up and Go Test (sec)	4 mos	140/142	-0.56(4.4)/-0.9(5.06)	Mean Diff	0.34(-0.77,1.45)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Timed Up and Go Test (sec)	12 mos	140/142	-0.94(4.85)/-1.47(5.36)	Mean Diff	0.53(-0.67,1.73)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	Function:Timed Up and Go Test (sec)	8 wks	50/50	7.42(1.7)/9.22(3.1)	Mean Diff	-1.8(-2.8,-0.8)	Group 1	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Function:Timed Up and Go Test (sec)	3 mos	33/35	7(3)/7.28(2.06)	Mean Diff	-0.28(-1.54,0.98)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Function:Timed Up and Go Test (sec)	3 mos	34/35	6.21(1.22)/7.65(2.52)	Mean Diff	-1.44(-2.39,-0.49)	Group 1	na
Oliveira; 2012/High	5: Supervised exercise-Supervised Group Exercise + Instruction Manual(2x/wk x8 wks)	5: Placebo/Control-Control (Instruction Manual Alone)	Function:Timed Up and Go Test (sec)	8 wks	50/50	7.42(1.7)/9.22(3.31)	Mean Diff	-1.8(-2.85,-0.75)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	Function:Timed Up and Go Test (sec)	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Function:Times to get up off the floor	16 wks	32/35	6.37(6)/8.16(6.03)	Mean Diff	-1.79(-4.73,1.15)	Not Sig.	na
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Function:Times to get up off the floor	16 wks	35/35	5.71(6.21)/8.16(6.03)	Mean Diff	-2.45(-5.37,0.47)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Unilateral Stand Time	12 mos	140/142	-0.02(3.2)/0.02(3.38)	Mean Diff	-0.04(-0.81,0.73)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Unilateral Stand Time	4 mos	140/68	-0.53(3.29)/-0.12(3.22)	Mean Diff	-0.41(-1.36,0.54)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Unilateral Stand Time	4 mos	140/142	-0.53(3.29)/0.08(3.71)	Mean Diff	-0.61(-1.43,0.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Unilateral Stand Time	12 mos	140/68	-0.02(3.2)/-0.14(3.28)	Mean Diff	0.12(-0.83,1.07)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Upper Leg Strength (Nm/kg)	6 wks	80/79	0.92(0.35)/0.94(0.39)	Mean Diff	-0.02(-0.14,0.1)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Upper Leg Strength (Nm/kg)	38 wks	80/80	1(0.36)/1.04(0.4)	Mean Diff	-0.04(-0.16,0.08)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Upper Leg Strength (Nm/kg)	12 wks	80/79	0.97(0.32)/1.01(0.42)	Mean Diff	-0.04(-0.16,0.08)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Function:VAS Disability	68 wks	64/64	-7.6(21.62)/-9(21.62)	Mean Diff	1.4(-6.16,8.96)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:WOMAC Function	10 wks	63/63	30.4(11.6)/32.9(11.2)	Mean Diff	-2.5(-6.52,1.52)	Not Sig.	inconclusive
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:WOMAC Function	20 wks	63/63	26.3(12.7)/31.4(13.4)	Mean Diff	-5.1(-9.7,-0.5)	Group 1	possibly clinically significant
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:WOMAC Function	32 wks	63/63	23.5(13.1)/31.4(12.6)	Mean Diff	-7.9(-12.43,-3.37)	Group 1	possibly clinically significant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:WOMAC Function	4 mos	140/142	-4.97(9.19)/-3.97(9.64)	Mean Diff	-1(-3.21,1.21)	Not Sig.	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:WOMAC Function	12 mos	140/68	-3.39(9.84)/-1.63(9.56)	Mean Diff	-1.76(-4.58,1.06)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:WOMAC Function	4 mos	140/68	-4.97(9.19)/-2.31(8.84)	Mean Diff	-2.66(-5.28,-0.04)	Group 1	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:WOMAC Function	12 mos	140/142	-3.39(9.84)/-3.75(9.98)	Mean Diff	0.36(-1.96,2.68)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:WOMAC Function	6 mos	152/152	16.5(11.23)/18.3(10.61)	Mean Diff	-1.8(-4.27,0.67)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:WOMAC Function	18 mos	152/152	14.2(11.54)/17.7(12.79)	Mean Diff	-3.5(-6.25,-0.75)	Group 1	possibly clinically significant
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:WOMAC Function	6 wks	80/79	21.5(11.6)/21.8(10.4)	Mean Diff	-0.3(-3.75,3.15)	Not Sig.	clinically insignificant
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:WOMAC Function	38 wks	80/79	18.9(13.3)/19.2(13.2)	Mean Diff	-0.3(-4.45,3.85)	Not Sig.	clinically insignificant
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:WOMAC Function	12 wks	80/79	17.4(11.6)/19.3(11.4)	Mean Diff	-1.9(-5.5,1.7)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Oliveira; 2012/High	5: Supervised exercise-Supervised Group Exercise + Instruction Manual(2x/wk x8 wks)	5: Placebo/Control-Control (Instruction Manual Alone)	Function:WOMAC Function	8 wks	50/50	23.83(15.49)/29.44(15.45)	Mean Diff	-5.61(-11.75, 0.53)	Not Sig.	inconclusive
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Function:WOMAC Function	16 wks	32/35	35.97(10.8)/39.7(10.83)	Mean Diff	-3.73(-9.01,1.55)	Not Sig.	inconclusive
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Function:WOMAC Function	16 wks	35/35	35.3(10.83)/39.7(10.83)	Mean Diff	-4.4(-9.57,0.77)	Not Sig.	inconclusive
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Function:WOMAC Function	5 wks	30/30	21.17(6.79)/22.07(7.07)	Mean Diff	-0.9(-4.48,2.68)	Not Sig.	clinically insignificant
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Function:WOMAC Function	12 mos	82/76	18.1(11.4)/20.1(12.5)	Mean Diff	-2(-5.77,1.77)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Function:WOMAC Function	6 mos	83/82	18.4(11.3)/22(12.5)	Mean Diff	-3.6(-7.26,0.06)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:WOMAC Function (VAS Version)	6 mos	53/53	643.5(336.4)/691.4(363.8)	Mean Diff	-47.9(-182.88,87.08)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:WOMAC Function (VAS Version)	3 mos	53/53	625.8(327)/685.7(360)	Mean Diff	-59.9(-192.39,72.59)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:WOMAC Function (VAS Version)	1 mos	53/53	589.8(320.1)/675.8(342.7)	Mean Diff	-86(-213.74,41.74)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:WOMAC Function (VAS Version)	12 mos	36/40	-1(5.91)/1(4.69)	Mean Diff	-2(-4.46,0.46)	Not Sig.	clinically insignificant
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:WOMAC Function (VAS Version)(scale doesn't make sense?)	12 mos	44/40	24.48(13.79)/25.06(13.53)	Mean Diff	-0.58(-6.51,5.35)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:WOMAC Function (VAS Version)(scale doesn't make sense?)	18 mos	43/35	18.2(14.63)/19.4(17.08)	Mean Diff	-1.2(-8.48,6.08)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:WOMAC Function(difference in deltas)	52 wks	73/74	-18.9(1.3)/-13.1(1.5)	Mean Diff	-5.8(-6.26,-5.34)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:WOMAC Function(difference in deltas)	32 wks	73/74	-17.6(1.4)/-10.7(1.7)	Mean Diff	-6.9(-7.41,-6.39)	Group 1	clinically significant
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	Function:WOMAC Function(difference in deltas)	12 wks	73/74	-19.6(1.1)/-11.3(1.3)	Mean Diff	-8.3(-8.69,-7.91)	Group 1	clinically significant
Samuel Sundar Doss; 2014/Moderate	5: Exercise-Strength training	5: Placebo/Control-Control	Function:WOMAC Physical function	4 wks	37/36	28.81(6.21)/40.83(8.02)	Mean Diff	-12.02(-15.38,-8.66)	Group 1	clinically significant
Hu; 2020/High	5: Supervised exercise-Taichi(three times a week for 60 minutes for 24 weeks)	5: Placebo/Control-Control(30 minute health education lecture)	Function:WOMAC Physical function	24 wks	52/40	2.83(6.3)/20.3(15.2)	Mean Diff	-17.47(-22.61,-12.33)	Group 1	clinically significant
Oliveira; 2012/High	5: Supervised exercise-Supervised Group Exercise + Instruction Manual(2x/wk x8 wks)	5: Placebo/Control-Control (Instruction Manual Alone)	Function:WOMAC Stiffness	8 wks	50/50	2.1(2.26)/3.38(2.39)	Mean Diff	-1.28(-2.2,-0.36)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Topp; 2002/High	5: Exercise-Dynamic exercise	5: Placebo/Control-Control	Function:WOMAC Stiffness	16 wks	35/35	5.04(15.97)/5.5(1.54)	Mean Diff	-0.46(-5.97,5.05)	Not Sig.	inconclusive
Topp; 2002/High	5: Exercise-Isometric exercise	5: Placebo/Control-Control	Function:WOMAC Stiffness	16 wks	32/35	5.03(1.58)/5.5(1.54)	Mean Diff	-0.47(-1.23,0.29)	Not Sig.	inconclusive
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	Function:WOMAC Stiffness	12 wks	141	none	pvalue	Sig ($p < 0.05$)	Exercise favored over Control	na
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Function:WOMAC Stiffness	5 wks	30/30	1.4(1.7)/1.7(1.75)	Mean Diff	-0.3(-1.19,0.59)	Not Sig.	inconclusive
Samuel Sundar Doss; 2014/Moderate	5: Exercise-Strength training	5: Placebo/Control-Control	Function:WOMAC Stiffness	4 wks	37/36	2.35(0.97)/4.67(1.54)	Mean Diff	-2.32(-2.92,-1.72)	Group 1	clinically significant
Hu; 2020/High	5: Supervised exercise-Taichi(three times a week for 60 minutes for 24 weeks)	5: Placebo/Control-Control(30 minute health education lecture)	Function:WOMAC Stiffness	24 wks	52/40	1.34(1.2)/2.8(3.13)	Mean Diff	-1.46(-2.51,-0.41)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:WOMAC Stiffness (VAS Version)	1 mos	53/53	67.2(42.2)/70(41.9)	Mean Diff	-2.8(-19,13.4)	Not Sig.	clinically insignificant
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:WOMAC Stiffness (VAS Version)	6 mos	53/53	68.9(45.5)/72.5(47.4)	Mean Diff	-3.6(-21.5,14.3)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	5: Exercise-Exercise + IA HA(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	5: Placebo/Control-Control (IA HA Alone)(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	Function:WOMAC Stiffness (VAS Version)	3 mos	53/53	72.2(44.3)/69.8(44.5)	Mean Diff	2.4(-14.7,19.5)	Not Sig.	clinically insignificant
Multanen; 2014/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 2x/week x 12 mo; increased loading over time)	5: Placebo/Control-Control (Usual Activities / Care)	Function:WOMAC Stiffness (VAS Version)	12 mos	36/40	-4(14.78)/0(14.07)	Mean Diff	-4(-10.62, 2.62)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:WOMAC Stiffness (VAS Version)(scale doesn't make sense?)	12 mos	44/40	30.96(22.31)/28.43(20.41)	Mean Diff	2.53(-6.74,11.8)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Function:WOMAC Stiffness (VAS Version)(scale doesn't make sense?)	18 mos	43/35	29.94(20.43)/27.14(18.8)	Mean Diff	2.8(-6.07,11.67)	Not Sig.	na
Topp; 2009/Low	5: Exercise-isometric strength training	5: Placebo/Control-control	Function:WOMAC function	16 wks	35/32	35.97(11.3)/39.7(10.35)	Mean Diff	-3.73(-9.01,1.55)	Not Sig.	inconclusive
Topp; 2009/Low	5: Exercise-dynamic strength training	5: Placebo/Control-control	Function:WOMAC function	16 wks	35/32	35.3(10.82)/39.7(10.35)	Mean Diff	-4.4(-9.57,0.77)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:WOMAC function	6 wks	35/37	none	mean difference	-5.9(-8.4,-3.5)	Group 1	possibly clinically significant
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:WOMAC function	12 wks	35/37	none	mean difference	-5.9(-8.7,-3.1)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Topp; 2009/Low	5: Exercise-dynamic strength training	5: Placebo/Control-control	Function:WOMAC stiffness	16 wks	35/32	5.04(15.9)/5.5(1.49)	Mean Diff	-0.46(-5.94,5.02)	Not Sig.	inconclusive
Topp; 2009/Low	5: Exercise-isometric strength training	5: Placebo/Control-control	Function:WOMAC stiffness	16 wks	35/32	5.03(1.65)/5.5(1.49)	Mean Diff	-0.47(-1.24,0.3)	Not Sig.	inconclusive
Mihalko; 2018/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Walking Duration Efficacy Confidence	18 mos	152/152	74.1(25.68)/59.69(26.08)	Mean Diff	14.41(8.57,20.25)	Group 1	na
Mihalko; 2018/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Walking Duration Efficacy Confidence	6 mos	152/152	75.49(25.52)/59.3(26.43)	Mean Diff	16.19(10.33, 22.05)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Walking Questionnaire (WQ35)(unclear direction)	38 wks	80/80	17.7(20.4)/19.2(20.7)	Mean Diff	-1.5(-7.92,4.92)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Walking Questionnaire (WQ35)(unclear direction)	6 wks	80/79	19.8(16.8)/24.1(20.6)	Mean Diff	-4.3(-10.19, 1.59)	Not Sig.	na
Knoop; 2013/Moderate	5: Exercise-Joint Stability Exercise + Strength/Activities Exercise(60min x2/wk x12 wks)	5: Placebo/Control-Control (Strength/Activities Exercise alone)(60min x2/wk x12 wks)	Function:Walking Questionnaire (WQ35)(unclear direction)	12 wks	80/79	14.6(15.4)/19.4(20.3)	Mean Diff	-4.8(-10.45, 0.85)	Not Sig.	na
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Walking Questionnaire(scale direction?)	32 wks	63/63	29.9(25.4)/34.9(22.5)	Mean Diff	-5(-13.46, 3.46)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
de Rooij; 2017/High	5: Supervised exercise-Supervised Exercise(2 30-60min sessions/week x 20 weeks)	5: Placebo/Control-Control (No Supervised Exercise)	Function:Walking Questionnaire(scale direction?)	20 wks	63/63	30.9(25.2)/38.4(24.1)	Mean Diff	-7.5(-16.2,1.2)	Not Sig.	na
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Walking Speed (m/s)	18 mos	152/152	1.33(0.22)/1.27(0.16)	Mean Diff	0.06(0.02,0.1)	Group 1	na
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Function:Walking Speed (m/s)	6 mos	152/152	1.32(0.22)/1.25(0.19)	Mean Diff	0.07(0.02,0.12)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Function:Walking Speed (m/s)	3 mos	33/35	1.36(0.21)/1.23(0.19)	Mean Diff	0.13(0.03,0.23)	Group 1	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Function:Walking Speed (m/s)	3 mos	34/35	1.4(0.2)/1.18(0.27)	Mean Diff	0.22(0.11,0.33)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Weekly Minutes of Aerobic Activity	4 mos	140/142	0.98(6.04)/1.88(6.75)	Mean Diff	-0.9(-2.4,0.6)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Weekly Minutes of Aerobic Activity	12 mos	140/142	0.51(6.91)/0.49(7.56)	Mean Diff	0.02(-1.68,1.72)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Weekly Minutes of Aerobic Activity	4 mos	140/68	0.98(6.04)/-0.05(5.91)	Mean Diff	1.03(-0.71,2.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Weekly Minutes of Aerobic Activity	12 mos	140/68	0.51(6.91)/-1.68(6.75)	Mean Diff	2.19(0.2,4.18)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Weekly Minutes of Strengthening	12 mos	140/142	1.17(5.06)/1.32(5.67)	Mean Diff	-0.15(-1.41,1.11)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Weekly Minutes of Strengthening	4 mos	140/142	1.85(4.82)/1.47(4.1)	Mean Diff	0.38(-0.67,1.43)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Weekly Minutes of Strengthening	12 mos	140/68	1.17(5.06)/-0.1(4.87)	Mean Diff	1.27(-0.17,2.71)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Weekly Minutes of Strengthening	4 mos	140/68	1.85(4.82)/0.43(4.63)	Mean Diff	1.42(0.05,2.79)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Weekly Minutes of Stretching	12 mos	140/142	0.36(3.83)/0.8(1.84)	Mean Diff	-0.44(-1.15,0.27)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Function:Weekly Minutes of Stretching	4 mos	140/142	1.45(4.16)/1.08(4.64)	Mean Diff	0.37(-0.66,1.4)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Weekly Minutes of Stretching	12 mos	140/68	0.36(3.83)/-1.29(3.74)	Mean Diff	1.65(0.55,2.75)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Function:Weekly Minutes of Stretching	4 mos	140/68	1.45(4.16)/-0.36(4.15)	Mean Diff	1.81(0.6,3.02)	Group 1	na
Jan ; 2009/Moderate	5: Exercise-Weight bearing exercise	5: Placebo/Control-Control	Function:Womac function	8 wks	36/35	12.3(9.8)/25(11.8)	Mean Diff	-12.7(-17.85,-7.55)	Group 1	clinically significant
Jan ; 2009/Moderate	5: Exercise-non-Weight bearing exercise	5: Placebo/Control-Control	Function:Womac function	8 wks	35/35	10.1(10.3)/25(11.8)	Mean Diff	-14.9(-20.18,-9.62)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:figure 8 walk time(seconds)	12 wks	35/37	none	mean difference	-1.17(-1.8,-0.54)	Group 1	na
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:figure 8 walk time(seconds)	6 wks	35/37	none	mean difference	-1.29(-1.8,-0.78)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jan ; 2009/Moderate	5: Exercise-non-Weight bearing exercise	5: Placebo/Control-Control	Function:figure8 walking time	8 wks	35/35	7.4(2.6)/8.6(2.3)	Mean Diff	-1.2(-2.37,-0.03)	Group 1	na
Jan ; 2009/Moderate	5: Exercise-Weight bearing exercise	5: Placebo/Control-Control	Function:figure8 walking time	8 wks	36/35	6.3(2.4)/8.6(2.3)	Mean Diff	-2.3(-3.41,-1.19)	Group 1	na
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:five times sit to stand test (seconds)	6 wks	35/37	none	mean difference	-0.23(-1.74,1.28)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:five times sit to stand test (seconds)	12 wks	35/37	none	mean difference	-0.47(-2,1.07)	Not Sig.	na
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Function:get up and go test	1 yrs	92/91	11.1(6.36)/9.7(4.14)	Mean Diff	1.4(-0.17,2.97)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Function:interaction between 3 or more comorbidities and womac function(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Function:interaction between anxiety and womac function(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Function:interaction between cardiac problems and womac function(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Function:interaction between obesity and womac function(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Function:interaction between pain in other locations and womac function(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na
Legha; 2019/Moderate	5: Supervised exercise-community physical therapy(3–6 physiotherapist-led sessions of advice about activity and pacing; and an individualized exercise programme of strengthening; stretching and aerobic exercises)	5: Placebo/Control-Non-exercise control	Function:interaction between respiratory conditions and womac function(TOPIK trial)		217	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jan ; 2009/Moderate	5: Exercise-Weight bearing exercise	5: Placebo/Control-Control	Function:level ground walking time (s)	8 wks	36/35	36(5.7)/38.9(3.8)	Mean Diff	-2.9(-5.19,-0.61)	Group 1	na
Jan ; 2009/Moderate	5: Exercise-non-Weight bearing exercise	5: Placebo/Control-Control	Function:level ground walking time (s)	8 wks	35/35	34.6(6)/38.9(3.8)	Mean Diff	-4.3(-6.7,-1.9)	Group 1	na
Ettinger;/Moderate	5: Exercise-aerobic exercise	5: Wellness education-health education	Function:lift and carry task (s)	18 weeks	133/132	9.3(2.31)/10(1.15)	Mean Diff	-0.7(-1.14,-0.26)	Group 1	na
Ettinger;/Moderate	5: Exercise-resistance exercise	5: Wellness education-health education	Function:lift and carry task (s)	18 weeks	127/132	9.1(2.25)/10(1.15)	Mean Diff	-0.9(-1.34,-0.46)	Group 1	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Function:sf-36 physical function	8 weeks	30/30	69.33(17.8)/56.25(16.7)	Mean Diff	13.08(4.16,22)	Group 1	clinically significant
Jan; 2008/Moderate	5: Exercise-low resistance training	5: Placebo/Control-no exercise	Function:spongy surface walk time	8 wks	34/30	7.3(1.4)/12.5(12.5)	Mean Diff	-5.2(-9.89,-0.51)	Group 1	na
Jan; 2008/Moderate	5: Exercise-high resistance training	5: Placebo/Control-no exercise	Function:spongy surface walk time	8 wks	34/30	6.3(2.5)/12.5(12.5)	Mean Diff	-6.2(-10.94,-1.46)	Group 1	na
Lin; 2009/High	5: Exercise-strength training	5: Placebo/Control-control	Function:spony surface walk time (s)	8 wks	36/36	9(3.4)/12.1(3.2)	Mean Diff	-3.1(-4.65,-1.55)	Group 1	na
Lin; 2009/High	5: Exercise-Proprioceptive training (not strength)	5: Placebo/Control-control	Function:spony surface walk time (s)	8 wks	36/36	7.6(2.4)/12.1(3.2)	Mean Diff	-4.5(-5.83,-3.17)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:stair ascent/decent time (seconds)	12 wks	35/37	none	mean difference	-2.25(-3.68,-0.81)	Group 1	na
Wang; 2020/High	5: Supervised exercise-hip abductor training (pelvic lift training and lateral straight leg raise) + quadracepts training(a set of 10 repetitions of each exercise; and three sets were completed in each of the sessions. Sessions conducted once per day over 6 weeks)	5: Placebo/Control-qudracepts training only	Function:stair ascent/decent time (seconds)	6 wks	35/37	none	mean difference	-2.42(-3.82,-1.03)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jan; 2008/Moderate	5: Exercise-low resistance training	5: Placebo/Control-no exercise	Function:stair climb (s)	8 wks	34/30	14.2(4.1)/14.5(14.5)	Mean Diff	-0.3(-5.87,5.27)	Not Sig.	na
Jan; 2008/Moderate	5: Exercise-high resistance training	5: Placebo/Control-no exercise	Function:stair climb (s)	8 wks	34/30	13.5(4.4)/14.5(14.5)	Mean Diff	-1(-6.6,4.6)	Not Sig.	na
Ettinger;/Moderate	5: Exercise-aerobic exercise	5: Wellness education-health education	Function:stair climb (s)	18 weeks	133/132	13.2(4.61)/13.9(4.6)	Mean Diff	-0.7(-1.81,0.41)	Not Sig.	na
Focht ; 2005/Low	5: Self management-exercise	5: Wellness education-health education control	Function:stair climb time (s)	72 weeks	80/78	9.15(4.7)/9.86(5.56)	Mean Diff	-0.71(-2.33,0.91)	Not Sig.	na
Focht ; 2005/Low	5: Self management-exercise + diet	5: Self management-diet	Function:stair climb time (s)	72 weeks	162/82	8.85(5.35)/9.86(8.78)	Mean Diff	-1.01(-3.1,1.08)	Not Sig.	na
Lin; 2009/High	5: Exercise-Proprioceptive training (not strength)	5: Placebo/Control-control	Function:stair climb walk time (s)	8 wks	36/36	11(3.4)/16.2(4.5)	Mean Diff	-5.2(-7.08,-3.32)	Group 1	na
Lin; 2009/High	5: Exercise-strength training	5: Placebo/Control-control	Function:stair climb walk time (s)	8 wks	36/36	10.5(4.2)/16.2(4.5)	Mean Diff	-5.7(-7.75,-3.65)	Group 1	na
Bennell; 2010/Moderate	5: Exercise-hip strengthening	5: Placebo/Control-no exercise	Function:step test (number of steps) improvement	13 weeks	39/37	1.76(1.99)/0.8(1.95)	Mean Diff	0.96(0.06,1.86)	Group 1	na
Borjesson; 1996/Low	5: PT-physiotherapy	5: Placebo/Control-no treatment	Function:steps/second	5 weeks	34/34	1.73(0.12)/1.74(0.14)	Mean Diff	-0.01(-0.07,0.05)	Not Sig.	na
Borjesson; 1996/Low	5: PT-physiotherapy	5: Placebo/Control-no treatment	Function:stride length	5 weeks	34/34	1.38(0.18)/1.37(0.14)	Mean Diff	0.01(-0.07,0.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ettinger;/Moderate	5: Exercise-aerobic exercise	5: Wellness education-health education	Function:time to get in and out of car (s)	18 weeks	133/132	9(3.46)/10.6(3.45)	Mean Diff	-1.6(-2.44,-0.76)	Group 1	na
Ettinger;/Moderate	5: Exercise-resistance exercise	5: Wellness education-health education	Function:time to get in and out of car (s)	18 weeks	127/132	8.7(3.38)/10.6(3.45)	Mean Diff	-1.9(-2.74,-1.06)	Group 1	na
Bennell; 2010/Moderate	5: Exercise-hip strengthening	5: Placebo/Control-no exercise	Function:timed star climb improvement (seconds)	13 weeks	39/37	0.97(1.19)/0.25(1.14)	Mean Diff	0.72(0.19,1.25)	Group 2	na
Ettinger;/Moderate	5: Exercise-aerobic exercise	5: Wellness education-health education	Function:walk distance (ft)	18 weeks	133/132	1406(196.05)/1349(183.83)	Mean Diff	57(11.03,102.97)	Group 1	na
Huang; 2000/Moderate	5: Exercise-isotonic strengthening	5: Placebo/Control-control	Function:walk speed m/minute	8 weeks	31/33	85(4)/70(3)	Mean Diff	15(13.22,16.78)	Group 1	na
Huang; 2000/Moderate	5: Exercise-isometric strength training	5: Placebo/Control-control	Function:walk speed m/minute	1 yrs	31/33	78(5)/70(3)	Mean Diff	8(5.91, 10.09)	Group 1	na
Lin; 2009/High	5: Exercise-strength training	5: Placebo/Control-control	Function:walk time (s)level ground	8 wks	36/36	35.5(5.3)/38(3.8)	Mean Diff	-2.5(-4.67,-0.33)	Group 1	na
Lin; 2009/High	5: Exercise-Proprioceptive training (not strength)	5: Placebo/Control-control	Function:walk time (s)level ground	8 wks	36/36	34.8(7.2)/38(3.8)	Mean Diff	-3.2(-5.92,-0.48)	Group 1	na
Jan; 2008/Moderate	5: Exercise-high resistance training	5: Placebo/Control-no exercise	Function:walk time (s)level ground	8 wks	34/30	35.5(5.3)/38(38)	Mean Diff	-2.5(-16.79, 11.79)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jan; 2008/Moderate	5: Exercise-low resistance training	5: Placebo/Control-no exercise	Function:walk time (s)level ground	8 wks	34/30	33.9(5.1)/38(38)	Mean Diff	-4.1(-18.38, 10.18)	Not Sig.	na
Jan; 2008/Moderate	5: Exercise-low resistance training	5: Placebo/Control-no exercise	Function:walk time figure 8 (s)	8 wks	34/30	6.8(1.4)/12.1(12.1)	Mean Diff	-5.3(-9.84,-0.76)	Group 1	na
Jan; 2008/Moderate	5: Exercise-high resistance training	5: Placebo/Control-no exercise	Function:walk time figure 8 (s)	8 wks	34/30	6.1(2)/12.1(12.1)	Mean Diff	-6(-10.56,-1.44)	Group 1	na
Borjesson; 1996/Low	5: PT-physiotherapy	5: Placebo/Control-no treatment	Function:walking speed m/sec	5 weeks	34/34	65.4(10.2)/66.6(10.8)	Mean Diff	-1.2(-6.29,3.89)	Not Sig.	na
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Function:womac function	1 yrs	92/91	13.2(6.85)/15.9(12.9)	Mean Diff	-2.7(-5.72,0.32)	Not Sig.	inconclusive
Lin; 2009/High	5: Exercise-Proprioceptive training (not strength)	5: Placebo/Control-control	Function:womac function	8 wks	36/36	14.6(9.6)/24.9(11.8)	Mean Diff	-10.3(-15.36,-5.24)	Group 1	possibly clinically significant
Lin; 2009/High	5: Exercise-strength training	5: Placebo/Control-control	Function:womac function	8 wks	36/36	10.1(8.3)/24.9(11.8)	Mean Diff	-14.8(-19.61,-9.99)	Group 1	clinically significant
Jan; 2008/Moderate	5: Exercise-low resistance training	5: Placebo/Control-no exercise	Function:womac function	8 wks	34/30	14.8(9.2)/22.5(10.9)	Mean Diff	-7.7(-12.79,-2.61)	Group 1	possibly clinically significant
Jan; 2008/Moderate	5: Exercise-high resistance training	5: Placebo/Control-no exercise	Function:womac function	8 wks	34/30	14.7(8.5)/22.5(10.9)	Mean Diff	-7.8(-12.74,-2.86)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Function:womac function	8 weeks	30/30	13.6(10.88)/18.36(9.52)	Mean Diff	-4.76(-10.05, 0.53)	Not Sig.	na
Bennell; 2010/Moderate	5: Exercise-hip strengthening	5: Placebo/Control-no exercise	Function:womac function improvement	13 weeks	39/37	8.07(7.16)/1.9(7.05)	Mean Diff	6.17(2.92,9.42)	Group 2	possibly clinically significant
Fransen; 2001/Moderate	5: PT-physical therapy (individual or group)	5: Placebo/Control-waitlist control	Function:womac function improvement	8 weeks	83/43	7.7(2.53)/-0.1(12.72)	Mean Diff	7.8(3.85,11.75)	Group 1	possibly clinically significant
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Composite:AIMS2 Symptoms Component(unclear scale?)	12 mos	44/41	3.52(2.36)/3.49(2.38)	Mean Diff	0.03(-0.99,1.05)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Composite:AIMS2 Symptoms Component(unclear scale?)	18 mos	44/35	3.44(2.41)/3.4(2.23)	Mean Diff	0.04(-1,1.08)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Composite:BoPAS	6 mos	83/82	55.9(8.1)/56.1(9.2)	Mean Diff	-0.2(-2.87,2.47)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Composite:BoPAS	12 mos	82/76	56(9.2)/55.9(9.4)	Mean Diff	0.1(-2.83,3.03)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Composite:BtPAS	12 mos	82/76	25.7(14.1)/26.2(16.1)	Mean Diff	-0.5(-5.27,4.27)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	Composite:BtPAS	6 mos	83/82	26.6(13.3)/27.2(16.4)	Mean Diff	-0.6(-5.2,4)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Composite:EQ Health State	2 mos	46/47	4.1(1.9)/2.9(2)	Mean Diff	1.2(0.4,2)	Group 1	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Composite:EQ Health State	1 yrs	46/47	2(2)/0.3(1.9)	Mean Diff	1.7(0.9,2.5)	Group 1	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Composite:JKOM Pain/Stiffness (Japanese Knee Osteoarthitis Score)	3 mos	33/35	13.96(4.24)/15.41(5.19)	Mean Diff	-1.45(-3.74,0.84)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Composite:JKOM Pain/Stiffness (Japanese Knee Osteoarthitis Score)	3 mos	34/35	14(3.89)/17.42(5.93)	Mean Diff	-3.42(-5.83,-1.01)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	Composite:JKOM Total(Japanese Knee Osteoarthitis Score)	3 mos	33/35	42.29(9.1)/44.29(11.72)	Mean Diff	-2(-7.07,3.07)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	Composite:JKOM Total(Japanese Knee Osteoarthitis Score)	3 mos	34/35	42.72(11.55)/48.24(13.8)	Mean Diff	-5.52(-11.63, 0.59)	Not Sig.	na
Chen; 2014/High	8: Placebo/Control-Isokinetic Exercise(3x/wk)	8: Placebo/Control-Control (No Intervention)	Composite:Lequesne Index	6 mos	30/30	5.4(1.7)/7.6(1.6)	Mean Diff	-2.2(-3.05,-1.35)	Group 1	na
Chen; 2014/High	8: Placebo/Control-Isokinetic Exercise(3x/wk)	8: Placebo/Control-Control (No Intervention)	Composite:Lequesne Index	8 wks	30/30	5.1(0.9)/7.4(1.3)	Mean Diff	-2.3(-2.88,-1.72)	Group 1	na
Oliveira; 2012/High	5: Supervised exercise-Supervised Group Exercise + Instruction Manual(2x/wk x8 wks)	5: Placebo/Control-Control (Instruction Manual Alone)	Composite:Lequesne Index Score	8 wks	50/50	9.78(4.94)/11.76(4.04)	Mean Diff	-1.98(-3.77,-0.19)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Composite:Lequesne Index Score	5 wks	30/30	8.07(2.08)/7.73(2.08)	Mean Diff	0.34(-0.74,1.42)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Composite:Oxford Knee Score	7 wks	60/61	39.2(8.22)/40.5(8.62)	Mean Diff	-1.3(-4.33,1.73)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Composite:Oxford Knee Score	12 wks	60/61	38.8(8.71)/40.8(8.14)	Mean Diff	-2(-5.04,1.04)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Composite:Oxford Knee Score	3 mos	60/61	28.3(9.78)/26.7(7.45)	Mean Diff	1.6(-1.54,4.74)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Composite:SF-36 Physical Component Score	68 wks	64/64	3.8(7.61)/4.4(7.81)	Mean Diff	-0.6(-3.3,2.1)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Composite:SF-36 Physical Component Score	6 mos	152/152	43.5(9.67)/41.8(9.98)	Mean Diff	1.7(-0.52,3.92)	Not Sig.	inconclusive
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	Composite:SF-36 Physical Component Score	18 mos	152/152	44.7(9.67)/42(10.61)	Mean Diff	2.7(0.41,4.99)	Group 1	possibly clinically significant
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Composite:UCLA Activity Score	2 mos	46/47	0.1(0.2)/0.1(0.2)	Mean Diff	0(-0.08,0.08)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	Composite:UCLA Activity Score	1 yrs	46/47	0.4(0.24)/0(0.2)	Mean Diff	0.4(0.31,0.49)	Group 1	na
Azad; 2011/High	5: Exercise-Quadriceps muscle strengthening exercise	5: Placebo/Control-Control	Composite:VAS Symptoms	4 wks	52/54	21.75(12.7)/26.74(13.81)	Mean Diff	-4.99(-10.1,0.12)	Not Sig.	clinically insignificant
Azad; 2011/High	5: Exercise-Quadriceps muscle strengthening exercise	5: Placebo/Control-Control	Composite:VAS Symptoms	5 wks	52/54	16.97(11.21)/24.56(14.04)	Mean Diff	-7.59(-12.48,-2.7)	Group 1	clinically insignificant
Azad; 2011/High	5: Exercise-Quadriceps muscle strengthening exercise	5: Placebo/Control-Control	Composite:VAS Symptoms	6 wks	52/54	12.7(10.21)/22.6(14.77)	Mean Diff	-9.9(-14.78,-5.02)	Group 1	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Composite:WOMAC Total	4 mos	140/142	-6.85(12.93)/-6(13.17)	Mean Diff	-0.85(-3.91,2.21)	Not Sig.	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Composite:WOMAC Total	12 mos	140/68	-4.72(13.4)/-2.95(12.79)	Mean Diff	-1.77(-5.57,2.03)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	Composite:WOMAC Total	4 mos	140/68	-6.85(12.93)/-3.29(12.39)	Mean Diff	-3.56(-7.23,0.11)	Not Sig.	clinically insignificant
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	Composite:WOMAC Total	12 mos	140/142	-4.72(13.4)/-5.68(14.2)	Mean Diff	0.96(-2.28,4.2)	Not Sig.	clinically insignificant
Ebnezar; 2012/High	5: Exercise-Yoga(40 min daily)	5: Placebo/Control-Control	Composite:WOMAC Total	90 days	118/125	9.72(4.87)/27.66(13.78)	Mean Diff	-17.94(-20.53,-15.35)	Group 1	clinically significant
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Composite:WOMAC Total	7 wks	60/61	49.4(17.1)/51.1(16.4)	Mean Diff	-1.7(-7.73,4.33)	Not Sig.	clinically insignificant
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Composite:WOMAC Total	12 wks	60/61	49.4(17.3)/52.3(16.6)	Mean Diff	-2.9(-9.01,3.21)	Not Sig.	inconclusive
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	Composite:WOMAC Total	3 mos	60/61	26(17.7)/24.6(16.8)	Mean Diff	1.4(-4.81,7.61)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jahanjoo; 2019/Moderate	5: Exercise-Balance Exercise + PT(1h balance + 1 hr TENS; US; heat pack; x2/wk x5wks)	5: Placebo/Control-Control (PT Alone)(1 hr TENS; US; heat pack; x2/wk x5wks)	Composite:WOMAC Total	5 wks	30/30	28.27(8.33)/29.07(8.33)	Mean Diff	-0.8(-5.11,3.51)	Not Sig.	clinically insignificant
Kudo; 2013/Moderate	5: Exercise-Group Supervised Exercise	5: Exercise-Home Exercise	Composite:WOMAC Total (Normalized))	3 mos	81/128	-10.2(10.3)/-3.2(8.7)	Mean Diff	-7(-9.72,-4.28)	Group 1	possibly clinically significant
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Composite:WOMAC Total (VAS Version)(scale doesn't make sense?)	18 mos	43/35	20.3(13.97)/20.9(15.74)	Mean Diff	-0.6(-7.4,6.2)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	Composite:WOMAC Total (VAS Version)(scale doesn't make sense?)	12 mos	43/40	21.05(13.62)/22.32(17.77)	Mean Diff	-1.27(-8.23,5.69)	Not Sig.	na
Huang; 2000/Moderate	5: Exercise-isometric strength training	5: Placebo/Control-control	Composite:lequesne index	1 yrs	31/33	5.6(0.7)/6.9(1.1)	Mean Diff	-1.3(-1.76,-0.84)	Group 1	na
Huang; 2000/Moderate	5: Exercise-isotonic strengthening	5: Placebo/Control-control	Composite:lequesne index	8 weeks	31/33	5.3(1.3)/6.9(1.1)	Mean Diff	-1.6(-2.2,-1)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Composite:womac total	1 yrs	92/91	23.5(19.09)/23.9(17.03)	Mean Diff	-0.4(-5.68,4.88)	Not Sig.	clinically insignificant
Maurer ; 1999/Moderate	5: Exercise-isokinetic quadricepts exercise	5: Wellness education-education	Composite:womac total	8 wks	49/49	153(.)/156(.)	Mean Diff	-3	isokinetic quadricepts exercise c quadricept	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Affect Component(unclear scale?)	12 mos	44/40	2.44(1.5)/2.23(1.45)	Mean Diff	0.21(-0.43,0.85)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Affect Component(unclear scale?)	18 mos	44/36	2.55(1.81)/2.17(1.37)	Mean Diff	0.38(-0.33,1.09)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Arthritis Impact(unclear scale?)	18 mos	34/30	1.99(2.11)/2.25(1.9)	Mean Diff	-0.26(-1.26,0.74)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Arthritis Impact(unclear scale?)	12 mos	39/36	2.37(1.81)/2.22(1.96)	Mean Diff	0.15(-0.72,1.02)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Health Perception(unclear scale?)	18 mos	42/34	3.34(1.95)/3.44(1.93)	Mean Diff	-0.1(-0.99,0.79)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Health Perception(unclear scale?)	12 mos	44/39	3.64(2.37)/3.34(1.88)	Mean Diff	0.3(-0.63,1.23)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Household Tasks(unclear scale?)	12 mos	44/41	0.34(1)/0.27(0.71)	Mean Diff	0.07(-0.3,0.44)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Household Tasks(unclear scale?)	18 mos	44/36	0.41(0.93)/0.12(0.47)	Mean Diff	0.29(-0.03,0.61)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Mood(unclear scale?)	18 mos	44/36	1.8(1.91)/1.53(1.3)	Mean Diff	0.27(-0.45,0.99)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Mood(unclear scale?)	12 mos	44/40	1.8(1.64)/1.48(1.28)	Mean Diff	0.32(-0.32,0.96)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Role Component(small N - exclude this outcome)	12 mos	15/18	1.54(1.83)/1.88(1.56)	Mean Diff	-0.34(-1.57,0.89)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Role Component(small N - exclude this outcome)	18 mos	14-Dec	2.19(2.45)/1.83(1.83)	Mean Diff	0.36(-1.43,2.15)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Satisfaction(unclear scale?)	12 mos	43/41	2.11(18.18)/2.13(1.64)	Mean Diff	-0.02(-5.64,5.6)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Satisfaction(unclear scale?)	18 mos	44/36	2.18(2.08)/1.93(1.57)	Mean Diff	0.25(-0.56,1.06)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Self Care(unclear scale?)	12 mos	44/41	0.11(0.51)/0.09(0.36)	Mean Diff	0.02(-0.17,0.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Self Care(unclear scale?)	18 mos	43/36	0.87(0.57)/0(0)	study reported p value	NS	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Social Activity(unclear scale?)	18 mos	44/36	4.63(1.84)/4.28(2.14)	Mean Diff	0.35(-0.55,1.25)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Social Activity(unclear scale?)	12 mos	44/41	4.73(1.57)/3.73(2.19)	Mean Diff	1(0.17, 1.83)	Group 2	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Social Interaction Component(unclear scale?)	18 mos	44/36	3.28(1.91)/3.51(1.97)	Mean Diff	-0.23(-1.1,0.64)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Social Interaction Component(unclear scale?)	12 mos	44/40	3.36(1.51)/3.03(1.98)	Mean Diff	0.33(-0.44,1.1)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Support From Family(unclear scale?)	12 mos	44/40	1.99(2.27)/2.33(2.36)	Mean Diff	-0.34(-1.35,0.67)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:AIMS2 Support From Family(unclear scale?)	18 mos	44/36	1.93(2.44)/2.74(2.61)	Mean Diff	-0.81(-1.95,0.33)	Not Sig.	na
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	QOL:AIMS2-SF Body	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	QOL:AIMS2-SF Emotional	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	QOL:AIMS2-SF Society	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	QOL:AIMS2-SF Symptoms	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na
Chen; 2019/Moderate	5: Supervised exercise-Supervised and Home Exericse + Education(2h session x4 over 12 weeks)	5: Placebo/Control-Control (Education Only)	QOL:AIMS2-SF Total	12 wks	141	none	pvalue	Sig (p < 0.05)	Exercise favored over Control	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	QOL:AQoL II	12 mos	82/76	0.7(0.2)/0.7(0.2)	Mean Diff	0(-0.06,0.06)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	QOL:AQoL II	6 mos	83/82	0.7(0.2)/0.7(0.2)	Mean Diff	0(-0.06,0.06)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:ASES Self Efficacy(difference in deltas)	52 wks	73/74	4.5(0.5)/3.1(0.7)	Mean Diff	1.4(1.2,1.6)	Group 1	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:ASES Self Efficacy(difference in deltas)	32 wks	73/74	4.5(0.6)/3(0.6)	Mean Diff	1.5(1.3,1.7)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:ASES Self Efficacy(difference in deltas)	12 wks	73/74	4.8(0.4)/3.1(0.6)	Mean Diff	1.7(1.53,1.87)	Group 1	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Assessment of QoL 6D(difference in deltas)	52 wks	73/74	0.1(0)/0.1(0)	Mean Diff	0	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Assessment of QoL 6D(difference in deltas)	32 wks	73/74	0.1(0)/0.1(0)	Mean Diff	0	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Assessment of QoL 6D(difference in deltas)	12 wks	73/74	0.1(0)/0.1(0)	Mean Diff	0	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	QOL:BFMS	6 mos	83/82	11.6(2.8)/11.8(3.8)	Mean Diff	-0.2(-1.23,0.83)	Not Sig.	na
Hinman; 2019/High	5: Wellness education-Musculoskeletal Help Line Service w/ Physiotherapist Consultations(5-10x over 6mos)	5: Wellness education-Control (Musculoskeletal Help Line Service w/o Physiotherapist Consultations	QOL:BFMS	12 mos	82/76	12(3.5)/11.8(3.7)	Mean Diff	0.2(-0.93,1.33)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Coping Strategies Questionnaire Pain Coping(difference in deltas)	32 wks	73/74	0.2(0.1)/0.1(0.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Coping Strategies Questionnaire Pain Coping(difference in deltas)	52 wks	73/74	0.2(0.1)/0.1(0)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Coping Strategies Questionnaire Pain Coping(difference in deltas)	12 wks	73/74	0.3(0)/0.2(0)	Mean Diff	0.1	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Anxiety Subscale(difference in deltas)	52 wks	73/74	-1.8(0.6)/-2.7(0.7)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Anxiety Subscale(difference in deltas)	12 wks	73/74	-1(0.6)/-1.8(0.6)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Anxiety Subscale(difference in deltas)	32 wks	73/74	-0.9(0.9)/-1.8(1)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Depression Subscale(difference in deltas)	32 wks	73/74	-1.7(1)/0.1(1.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Depression Subscale(difference in deltas)	52 wks	73/74	-1.1(0.8)/-2.3(0.9)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Depression Subscale(difference in deltas)	12 wks	73/74	-1(0.6)/-1.2(0.9)	Mean Diff	0.2(-0.05,0.45)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Stress Subscale(difference in deltas)	52 wks	73/74	-2.1(0.8)/-3.2(1.1)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Stress Subscale(difference in deltas)	32 wks	73/74	0(1.2)/0.6(1.2)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:DASS-21 Stress Subscale(difference in deltas)	12 wks	73/74	-0.6(0.8)/-0.8(0.9)	Mean Diff	0.2(-0.08,0.48)	Not Sig.	na
Kigozi; 2018/Moderate	5: Exercise-targeted exercise adherance (TEA) with an aim to support progress to increasing general physical activity adherence over 6 months. It consisted of four individual face to-face treatments up to week 12; and a further 4–6 follow-up contacts (face-to-face or over the telephone)	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	3 mos	163/175	0.67(0.23)/0.69(0.2)	Mean Diff	-0.02(-0.07,0.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-targeted exercise adherance (TEA) with an aim to support progress to increasing general physical activity adherence over 6 months. It consisted of four individual face to-face treatments up to week 12; and a further 4–6 follow-up contacts (face-to-face or over the telephone)	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	18 mos	163/175	0.68(0.23)/0.7(0.22)	Mean Diff	-0.02(-0.07,0.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-individually tailored and progressed lower-limb exercise (ITE) programme provided in six to eight one-to-one treatment sessions over 12 weeks. Participants received a print-out of a specific exercise prescription individualized for them based on their progress on the programme.	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	9 mos	176/175	0.67(0.25)/0.7(0.22)	Mean Diff	-0.03(-0.08,0.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-targeted exercise adherance (TEA) with an aim to support progress to increasing general physical activity adherence over 6 months. It consisted of four individual face to-face treatments up to week 12; and a further 4–6 follow-up contacts (face-to-face or over the telephone)	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	9 mos	163/175	0.7(0.2)/0.7(0.22)	Mean Diff	0(-0.04,0.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-individually tailored and progressed lower-limb exercise (ITE) programme provided in six to eight one-to-one treatment sessions over 12 weeks. Participants received a print-out of a specific exercise prescription individualized for them based on their progress on the programme.	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	18 mos	176/175	0.7(0.21)/0.7(0.22)	Mean Diff	0(-0.05,0.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-individually tailored and progressed lower-limb exercise (ITE) programme provided in six to eight one-to-one treatment sessions over 12 weeks. Participants received a print-out of a specific exercise prescription individualized for them based on their progress on the programme.	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	6 mos	176/175	0.69(0.22)/0.69(0.23)	Mean Diff	0(-0.05,0.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-targeted exercise adherance (TEA) with an aim to support progress to increasing general physical activity adherence over 6 months. It consisted of four individual face to-face treatments up to week 12; and a further 4–6 follow-up contacts (face-to-face or over the telephone)	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	6 mos	163/175	0.69(0.22)/0.69(0.23)	Mean Diff	0(-0.05,0.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kigozi; 2018/Moderate	5: Exercise-individually tailored and progressed lower-limb exercise (ITE) programme provided in six to eight one-to-one treatment sessions over 12 weeks. Participants received a print-out of a specific exercise prescription individualized for them based on their progress on the programme.	4: Placebo/Control-advice and lower-limb exercise provided in up to four individual; one-to-one treatment sessions over 12 weeks; in line with usual physical therapy practice	QOL:EQ-5D utility value	3 mos	176/175	0.71(0.19)/0.69(0.2)	Mean Diff	0.02(-0.02,0.06)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	QOL:EQ-5D-5L Index	12 wks	45/45	0.72(0.12)/0.75(0.1)	Mean Diff	-0.03(-0.08,0.02)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	QOL:EQ-5D-5L VAS	12 wks	45/45	70.1(17.31)/69.9(16.14)	Mean Diff	0.2(-6.81,7.21)	Not Sig.	clinically insignificant
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	QOL:HADS Anxiety	7 wks	60/61	6.32(4.59)/6.69(3.63)	Mean Diff	-0.37(-1.86,1.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	QOL:HADS Anxiety	12 wks	60/61	7.08(5.16)/6.54(3.93)	Mean Diff	0.54(-1.11,2.19)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	QOL:HADS Anxiety	3 mos	60/61	4.26(4.04)/2.42(2.39)	Mean Diff	1.84(0.64,3.04)	Group 2	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	QOL:HADS Depression	3 mos	60/61	3.43(2.54)/3.68(2.93)	Mean Diff	-0.25(-1.24,0.74)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	QOL:HADS Depression	12 wks	60/61	6.75(3.84)/7.13(3.54)	Mean Diff	-0.38(-1.71,0.95)	Not Sig.	na
Williamson; 2007/High	5: PT-Physiotherapy(1/wk x6wks;)	5: Placebo/Control-Control (Standard Care)(educational pamphlet)	QOL:HADS Depression	7 wks	60/61	6.62(3.68)/7.43(3.4)	Mean Diff	-0.81(-2.09,0.47)	Not Sig.	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	QOL:JKOM General Social Activities(Japanese Knee Osteoarthitis Score)	3 mos	33/35	7.59(2.08)/8.19(2.66)	Mean Diff	-0.6(-1.75,0.55)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	QOL:JKOM General Social Activities(Japanese Knee Osteoarthitis Score)	3 mos	34/35	7.93(2.66)/8.94(3.03)	Mean Diff	-1.01(-2.38,0.36)	Not Sig.	na
Kim; 2013/High	5: Exercise-Supervised Group Exercise + Thermal Therapy(exercise 2x/week x 3 mo; 1 hr each + 6hr/day heat sheet)	5: Placebo/Control-Control (Thermal Therapy Heat Sheet Alone)(6hr/day)	QOL:JKOM Health Conditions(Japanese Knee Osteoarthitis Score)	3 mos	33/35	3.78(1.22)/4.09(1.57)	Mean Diff	-0.31(-0.99,0.37)	Not Sig.	na
Kim; 2013/High	5: Supervised exercise-Supervised Group Exercise(2x/week; 3 mo; 1 hr each)	5: Wellness education-Health Education(1hr class 1x/mo)	QOL:JKOM Health Conditions(Japanese Knee Osteoarthitis Score)	3 mos	34/35	3.6(1.25)/4.45(1.52)	Mean Diff	-0.85(-1.52,-0.18)	Group 1	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	QOL:KOOS ADL	12 wks	45/45	67(12.65)/68.1(13.65)	Mean Diff	-1.1(-6.61,4.41)	Not Sig.	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	QOL:KOOS ADL subscale score	2 mos	46/47	7.5(2)/7.9(2)	Mean Diff	-0.4(-1.22,0.42)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	QOL:KOOS ADL subscale score	1 yrs	46/47	7(2)/11.4(2)	Mean Diff	-4.4(-5.22,-3.58)	Group 2	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	QOL:KOOS QOL	12 wks	45/45	40.4(12.65)/42.9(11.65)	Mean Diff	-2.5(-7.6,2.6)	Not Sig.	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	QOL:KOOS QOL Subscale Score	2 mos	46/47	4.5(2.2)/8.7(2.3)	Mean Diff	-4.2(-5.13,-3.27)	Group 2	na
Holsgaard-Larsen; 2018/High	5: Exercise-NEMEX(8-week exercise program)	5: Wellness education-PHARMA(Analgesic use instructions)	QOL:KOOS QOL Subscale Score	1 yrs	46/47	3.1(2.2)/10(2.2)	Mean Diff	-6.9(-7.81,-5.99)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	QOL:KOOS Quality of Life	8 wks	47/46	3.14(12.43)/4.5(12.56)	Mean Diff	-1.36(-6.51,3.79)	Not Sig.	na
Koli; 2015/Moderate	5: Supervised exercise-Supervised Group Exercise(55 min 3x/week x 12 mo)	5: Placebo/Control-Control (Usual Activities / Care)	QOL:KOOS Quality of Life	12 mos	36/40	7(14.78)/4(12.66)	Mean Diff	3(-3.33,9.33)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:KOOS Quality of Life	68 wks	64/64	5.8(14.81)/5.4(15.01)	Mean Diff	0.4(-4.82,5.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Villadsen; 2014/Moderate	5: Supervised exercise-Neuromuscular Exercise + Educational Pamphlet(2x/wk x8 wks)	5: Placebo/Control-Control (Educational Pamphlet Alone)	QOL:KOOS Quality of Life	9 wks	84/81	3.8(17.414)/-2.5(17.1)	Mean Diff	6.3(0.99,11.61)	Group 1	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Overall Global Change Improvement (high LFU)	32 wks	119	none	Relative Risk	1.2(0.9,1.5)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Overall Global Change Improvement (high LFU)	12 wks	134	none	Relative Risk	1.2(1,1.5)	Not Sig.	na
Bennell; 2016/Moderate	5: Exercise-Exercise + Pain Coping Skills Training(25 min exercise + 45 min PCST x 10 sessions over 12 weeks)	5: Placebo/Control-Control (Pain Coping Skills Alone)(45 min PCST x 10 sessions over 12 weeks)	QOL:Overall Global Change Improvement (high LFU)	52 wks	120	none	Relative Risk	1.4(1.2,1.6)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	QOL:Patient Global Assessment - Left Knee	12 mos	140/142	0.16(2.57)/0.58(2.62)	Mean Diff	-0.42(-1.03,0.19)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	QOL:Patient Global Assessment - Left Knee	4 mos	140/142	0.94(2.3)/0.5(2.41)	Mean Diff	0.44(-0.11,0.99)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	QOL:Patient Global Assessment - Left Knee	12 mos	140/68	0.16(2.57)/-0.39(2.33)	Mean Diff	0.55(-0.15,1.25)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	QOL:Patient Global Assessment - Left Knee	4 mos	140/68	0.94(2.3)/-0.1(2.29)	Mean Diff	1.04(0.37,1.71)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	QOL:Patient Global Assessment - Right Knee	12 mos	140/142	0.6(2.42)/0.53(2.44)	Mean Diff	0.07(-0.5,0.64)	Not Sig.	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	QOL:Patient Global Assessment - Right Knee	12 mos	140/68	0.6(2.42)/-0.17(2.17)	Mean Diff	0.77(0.11,1.43)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Self management-Internet Based Exercise Training(constant access)	QOL:Patient Global Assessment - Right Knee	4 mos	140/142	1.36(2.3)/0.43(2.38)	Mean Diff	0.93(0.38,1.48)	Group 1	na
Allen; 2018/Moderate	5: PT-Traditional PT Intervention(up to 8 one-hr sessions)	5: Placebo/Control-Control (Put on Waitlist)	QOL:Patient Global Assessment - Right Knee	4 mos	140/68	1.36(2.3)/0.14(2.19)	Mean Diff	1.22(0.57,1.87)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 General Health Perceptions	18 mos	44/36	69.31(19.19)/69.92(18.24)	Mean Diff	-0.61(-8.97,7.75)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 General Health Perceptions	12 mos	44/41	67.62(17.48)/72(18.36)	Mean Diff	-4.38(-12.13, 3.37)	Not Sig.	na
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	QOL:SF-36 General Health Perceptions	8 wks	50/50	61.68(25.54)/59.31(22.28)	Mean Diff	2.37(-7.14,11.88)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Health Transition Item(scale?)	12 mos	43/41	2.42(0.85)/2.46(0.84)	Mean Diff	-0.04(-0.41,0.33)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Health Transition Item(scale?)	18 mos	44/36	2.73(0.92)/2.64(0.9)	Mean Diff	0.09(-0.32,0.5)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:SF-36 Mental Component Score	68 wks	64/64	0.1(7.41)/1.3(7.41)	Mean Diff	-1.2(-3.79,1.39)	Not Sig.	na
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	QOL:SF-36 Mental Component Score	18 mos	152/152	56.1(7.18)/54.9(7.8)	Mean Diff	1.2(-0.49,2.89)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	5: Supervised exercise-Supervised Exercise + Diet(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min); energy deficit 800-1k kcal;)	5: Placebo/Control-Control (Diet Alone)(energy deficit 800-1k kcal)	QOL:SF-36 Mental Component Score	6 mos	152/152	56.9(7.8)/55(8.74)	Mean Diff	1.9(0.03,3.77)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Mental Health Index	18 mos	44/36	77.11(17.93)/79.33(14.89)	Mean Diff	-2.22(-9.53,5.09)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Mental Health Index	12 mos	44/41	78.36(16.01)/81.37(14.41)	Mean Diff	-3.01(-9.57,3.55)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	QOL:SF-36 Mental Health Index	8 wks	50/50	64.3(24.35)/60.41(20.9)	Mean Diff	3.89(-5.12,12.9)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Role Emotional	18 mos	44/36	75(40.11)/82.41(33.32)	Mean Diff	-7.41(-23.75, 8.93)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Role Emotional	12 mos	44/41	85.61(30.84)/82.93(35.06)	Mean Diff	2.68(-11.62, 16.98)	Not Sig.	na
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	QOL:SF-36 Role Emotional	8 wks	50/50	64.18(46.78)/48.31(48.47)	Mean Diff	15.87(-3.04,34.78)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Social Functioning	18 mos	44/36	78.13(26.7)/79.17(21.55)	Mean Diff	-1.04(-11.78, 9.7)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Social Functioning	12 mos	44/41	79.55(22.89)/85.67(20.26)	Mean Diff	-6.12(-15.43, 3.19)	Not Sig.	na
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	QOL:SF-36 Social Functioning	8 wks	50/50	80.73(24.29)/67.76(32.27)	Mean Diff	12.97(1.62,24.32)	Group 1	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Standardized Mental Component	18 mos	44/36	51.99(11)/53.1(9.91)	Mean Diff	-1.11(-5.77,3.55)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Standardized Mental Component	12 mos	44/41	53.82(9.85)/55.16(8.54)	Mean Diff	-1.34(-5.31,2.63)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Vitality	12 mos	44/41	62.05(19.63)/64.76(18.27)	Mean Diff	-2.71(-10.89, 5.47)	Not Sig.	na
Brosseau; 2012/Moderate	5: Supervised exercise-Supervised Walking(65 minute supervised group weekly sessions; 12 months)	5: Placebo/Control-Control (Usual Care)(pamphlet)	QOL:SF-36 Vitality	18 mos	44/36	60.15(21.86)/66.16(17.84)	Mean Diff	-6.01(-14.85, 2.83)	Not Sig.	na
Imoto; 2012/High	5: Supervised exercise-Supervised Group Exercise + Orientation Manual(30-4- min 2x/week)	5: Placebo/Control-Control (Orientation Pamphlet Alone)	QOL:SF-36 Vitality	8 wks	50/50	63(21.95)/56.72(23)	Mean Diff	6.28(-2.64,15.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rejeski; 2002/Low	6: Weight loss-exercise	6: No weight loss-control	QOL:SF-36 pcs(26 and 78 week average)	78 wks	69/68	54.7(15.28)/49.56(15.1)	Mean Diff	5.14(0.01,10.27)	Group 1	possibly clinically significant
Rejeski; 2002/Low	6: Weight loss-exercise	6: No weight loss-control	QOL:SF-36-mcs(26 and 78 week average)	78 wks	69/68	79.33(9.97)/78.56(9.91)	Mean Diff	0.77(-2.59,4.13)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:VAS Patient Global Assessment	68 wks	64/64	-4.6(20.02)/-6.1(20.02)	Mean Diff	1.5(-5.5,8.5)	Not Sig.	clinically insignificant
Fransen; 2001/Moderate	5: PT-physical therapy (individual or group)	5: Placebo/Control-waitlist control	QOL:sf-36 physical component	8 weeks	83/43	3.6(1.22)/0.5(6.36)	Mean Diff	3.1(1.13,5.07)	Group 1	possibly clinically significant
Fransen; 2001/Moderate	5: PT-physical therapy (individual or group)	5: Placebo/Control-waitlist control	QOL:sf36 mental component	8 weeks	83/43	2(0.91)/-0.7(3.87)	Mean Diff	2.7(1.49,3.91)	Group 1	na
Kovar; 1992/Moderate	5: Supervised exercise-supervised walking	5: Placebo/Control-control	Other:AIMS arthritis impact	8 wks	47/45	2.86(1.88)/3.06(1.91)	Mean Diff	-0.2(-0.99,0.59)	Not Sig.	na
Kovar; 1992/Moderate	5: Supervised exercise-supervised walking	5: Placebo/Control-control	Other:AIMS medications use	8 wks	47/45	3.64(1.92)/2.9(2.02)	Mean Diff	0.74(-0.08,1.56)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Other:OMERACT-OARSI Responder(Outcome Measures in Reumatorlogy; Osteoarthritis Research Society International)	68 wks	64/64	40.63%/51.56%	RR	0.79(0.54,1.15)	Not Sig.	na
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Other:global rating of change	1 yrs	92/91	5.4(4.16)/5.4(3.41)	Mean Diff	0(-1.11,1.11)	Not Sig.	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Other:sf-36 role limitations	8 weeks	30/30	77.5(34.9)/57.14(45)	Mean Diff	20.36(-0.48,41.2)	Not Sig.	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Other:sf36 vitality	8 weeks	30/30	54(19.5)/43.5(18.3)	Mean Diff	10.5(0.73,20.27)	Group 1	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	NSAID use:Reduction in pain medication use (n)	12 wks	45/45	20%/15.56%	RR	1.29(0.52,3.15)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Abdominal Pain	8 wks	47/46	6.38%/8.7%	RR	0.73(0.17,3.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Abdominal Pain(Per Protocol Population; still >80% FU)	68 wks	52/52	11.54%/5.77%	RR	2(0.53, 7.57)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Adverse Events	12 wks	45/45	37.78%/28.89%	RR	1.31(0.72,2.36)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Allergeic Rash	8 wks	47/46	4.26%/2.17%	RR	1.96(0.18,20.85)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Allergic Rash(Per Protocol Population; still >80% FU)	68 wks	51/52	13.73%/7.69%	RR	1.78(0.56,5.73)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Anxiety	8 wks	47/46	2.13%/2.17%	RR	0.98(0.06,15.19)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Anxiety(Per Protocol Population; still >80% FU)	68 wks	50/52	10%/3.85%	RR	2.6(0.53,12.79)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Back Pain	8 wks	47/46	6.38%/6.52%	RR	0.98(0.21,4.6)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Back Pain(Per Protocol Population; still >80% FU)	68 wks	52/50	11.54%/20%	RR	0.58(0.23,1.47)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Bad Breath	8 wks	47/46	2.13%/2.17%	RR	0.98(0.06,15.19)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Bad Breath(Per Protocol Population; still >80% FU)	68 wks	51/52	35.29%/9.62%	RR	3.67(1.47,9.14)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Biliary Symptoms	8 wks	47/46	2.13%/0%	RD	2.128(-6.858, 10.031)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Biliary Symptoms(Per Protocol Population; still >80% FU)	68 wks	51/52	7.84%/0%	RD	7.843(-2.814, 16.203)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Constipation	8 wks	47/46	0%/4.35%	RD	-4.348(-12.533,5.837)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Constipation(Per Protocol Population; still >80% FU)	68 wks	52/52	13.46%/15.38%	RR	0.88(0.34,2.24)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Consultation in orthopedic outpatient clinic	12 wks	45/45	4.44%/6.67%	RR	0.67(0.12,3.8)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Cramps	8 wks	47/46	8.51%/8.7%	RR	0.98(0.26,3.68)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Cramps(Per Protocol Population; still >80% FU)	68 wks	52/49	13.46%/16.33%	RR	0.82(0.32,2.1)	Not Sig.	na
Ebnezar; 2012/High	5: Exercise-Yoga(40 min daily)	5: Placebo/Control-Control	Adverse events:Crepitus	90 days	118/125	0.68(0.85)/1.74(1)	Mean Diff	-1.06(-1.29,-0.83)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Deep venous thrombosis	12 wks	45/45	0%/2.22%	RD	-2.222(-10.297,7.122)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Depressive Tendencies	8 wks	47/46	2.13%/0%	RD	2.128(-6.858, 10.031)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Depressive Tendencies(Per Protocol Population; still >80% FU)	68 wks	51/52	9.8%/7.69%	RR	1.27(0.36,4.48)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Diarrhea	8 wks	47/46	4.26%/6.52%	RR	0.65(0.11,3.73)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Diarrhea(Per Protocol Population; still >80% FU)	68 wks	52/51	11.54%/7.84%	RR	1.47(0.44,4.91)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Dizziness	8 wks	47/46	2.13%/2.17%	RR	0.98(0.06,15.19)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Dizziness(Per Protocol Population; still >80% FU)	68 wks	52/52	19.23%/15.38%	RR	1.25(0.54,2.91)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Dry Skin	8 wks	47/46	0%/6.52%	RD	-6.522(-15.205,4.459)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Dry Skin(Per Protocol Population; still >80% FU)	68 wks	51/52	11.76%/11.54%	RR	1.02(0.35,2.95)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Eczema	8 wks	47/46	4.26%/4.35%	RR	0.98(0.14,6.66)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Eczema(Per Protocol Population; still >80% FU)	68 wks	51/51	9.8%/5.88%	RR	1.67(0.42,6.61)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Epigastric Pain(Per Protocol Population; still >80% FU)	68 wks	52/52	13.46%/1.92%	RR	7(0.89, 54.91)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Epigastric Pain	8 wks	47/46	8.51%/6.52%	RR	1.3(0.31,5.51)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Fatigue(Per Protocol Population; still >80% FU)	68 wks	51/52	25.49%/23.08%	RR	1.1(0.56,2.19)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Fatuigue	8 wks	47/46	10.64%/15.22%	RR	0.7(0.24,2.04)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Flatulence(Per Protocol Population; still >80% FU)	68 wks	52/52	19.23%/26.92%	RR	0.71(0.35,1.46)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Gastrointestinal	12 wks	45/45	2.22%/2.22%	RR	1(0.06, 15.5)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:General practitioner consultation	12 wks	45/45	2.22%/4.44%	RR	0.5(0.05,5.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Hair Loss	8 wks	47/46	0%/2.17%	RD	-2.174(-9.939, 6.987)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Hair Loss(Per Protocol Population; still >80% FU)	68 wks	51/52	27.45%/3.85%	RR	7.14(1.71,29.84)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Headache	8 wks	47/46	8.51%/8.7%	RR	0.98(0.26,3.68)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Headache(Per Protocol Population; still >80% FU)	68 wks	51/52	23.53%/9.62%	RR	2.45(0.93,6.45)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Heartburn	8 wks	47/46	2.13%/8.7%	RR	0.24(0.03,2.11)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Heartburn(Per Protocol Population; still >80% FU)	68 wks	52/51	17.31%/5.88%	RR	2.94(0.84,10.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Infection	12 wks	45/45	8.89%/0%	RD	8.889(-2.956, 18.417)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Influenza	8 wks	47/46	0%/2.17%	RD	-2.174(-9.939, 6.987)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Influenza(Per Protocol Population; still >80% FU)	68 wks	51/52	19.61%/3.85%	RR	5.1(1.17,22.13)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Joint Pain	8 wks	47/46	4.26%/8.7%	RR	0.49(0.09,2.54)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Joint Pain(Per Protocol Population; still >80% FU)	68 wks	52/51	23.08%/23.53%	RR	0.98(0.49,1.98)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Mood Changes	8 wks	47/46	6.38%/10.87%	RR	0.59(0.15,2.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Mood Changes(Per Protocol Population; still >80% FU)	68 wks	51/52	25.49%/9.62%	RR	2.65(1.02,6.9)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Nausea	8 wks	47/46	2.13%/4.35%	RR	0.49(0.05,5.21)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Nausea(Per Protocol Population; still >80% FU)	68 wks	52/52	15.38%/1.92%	RR	8(1.04, 61.71)	Group 2	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Non-serious adverse events	12 wks	45/45	31.11%/17.78%	RR	1.75(0.82,3.76)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Non-serious adverse events involving index knee	12 wks	45/45	6.67%/11.11%	RR	0.6(0.15,2.36)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Other Serious Adverse Events	12 wks	45/45	2.22%/6.67%	RR	0.33(0.04,3.08)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Perianal Itching	8 wks	47/46	0%/0%	RD	0(-7.556, 7.707)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Perianal Itching(Per Protocol Population; still >80% FU)	68 wks	51/52	21.57%/3.85%	RR	5.61(1.31,24.06)	Group 2	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Redness	8 wks	47/46	4.26%/4.35%	RR	0.98(0.14,6.66)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Redness(Per Protocol Population; still >80% FU)	68 wks	51/52	13.73%/3.85%	RR	3.57(0.78,16.37)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Renal system	12 wks	45/45	4.44%/2.22%	RR	2(0.19, 21.28)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Sciatic Pain	8 wks	47/46	4.26%/2.17%	RR	1.96(0.18,20.85)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Sciatic Pain(Per Protocol Population; still >80% FU)	68 wks	52/51	13.46%/17.65%	RR	0.76(0.31,1.89)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Sensitive to Cold	8 wks	47/46	2.13%/6.52%	RR	0.33(0.04,3.02)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Sensitive to Cold(Per Protocol Population; still >80% FU)	68 wks	51/52	31.37%/11.54%	RR	2.72(1.16,6.39)	Group 2	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Serious Adverse Events	12 wks	45/45	6.67%/11.11%	RR	0.6(0.15,2.36)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Serious Adverse Events involving index knee	12 wks	45/45	0%/0%	RD	0(-7.865, 7.865)	Not Sig.	na
Holm; 2020/High	5: Exercise-Strength training	5: Placebo/Control-Control	Adverse events:Serious Adverse Events involving other sites	12 wks	45/45	6.67%/11.11%	RR	0.6(0.15,2.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Skin Irritation	8 wks	47/46	6.38%/6.52%	RR	0.98(0.21,4.6)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Skin Irritation(Per Protocol Population; still >80% FU)	68 wks	51/52	15.69%/5.77%	RR	2.72(0.76,9.68)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Sleeplessness	8 wks	47/46	8.51%/6.52%	RR	1.3(0.31,5.51)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Sleeplessness(Per Protocol Population; still >80% FU)	68 wks	51/52	21.57%/21.15%	RR	1.02(0.49,2.14)	Not Sig.	na
Ebnezar; 2012/High	5: Exercise-Yoga(40 min daily)	5: Placebo/Control-Control	Adverse events:Swelling	90 days	118/125	0.4(0.57)/1.12(0.82)	Mean Diff	-0.72(-0.9,-0.54)	Group 1	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Swollen Joints	8 wks	47/46	21.28%/8.7%	RR	2.45(0.83,7.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Swollen Joints(Per Protocol Population; still >80% FU)	68 wks	52/51	19.23%/21.57%	RR	0.89(0.42,1.91)	Not Sig.	na
Ebnezar; 2012/High	5: Exercise-Yoga(40 min daily)	5: Placebo/Control-Control	Adverse events:Tenderness	90 days	118/125	0.49(0.63)/1.44(0.69)	Mean Diff	-0.95(-1.12,-0.78)	Group 1	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Toothache	8 wks	47/46	6.38%/6.52%	RR	0.98(0.21,4.6)	Not Sig.	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Toothache(Per Protocol Population; still >80% FU)	68 wks	51/52	23.53%/7.69%	RR	3.06(1.06,8.86)	Group 2	na
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Urticaria(Per Protocol Population; still >80% FU)	68 wks	51/52	5.88%/1.92%	RR	3.06(0.33,28.45)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Urticarial	8 wks	47/46	0%/2.17%	RD	-2.174(-9.939, 6.987)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	5: Exercise-Exercise Sessions 3x/week(1hr 3x/week x 52 weeks)	5: Placebo/Control-Control (Usual Care)	Adverse events:Vomiting(Per Protocol Population; still >80% FU)	68 wks	52/52	7.69%/1.92%	RR	4(0.46, 34.59)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Vomiting	8 wks	47/46	4.26%/2.17%	RR	1.96(0.18,20.85)	Not Sig.	na
Holsagaard-Larsen; 2017/Moderate	5: Exercise-Neuromuscular Exercise(60min 2x/week x8 weeks)	5: Wellness education-Education on Acetaminophen and NSAIDs	Adverse events:Wind/Flatulence	8 wks	47/46	12.77%/13.04%	RR	0.98(0.34,2.81)	Not Sig.	na
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Adverse events:knee pain	1 yrs	92/91	4.1(2.69)/3.8(2.92)	Mean Diff	0.3(-0.52,1.12)	Not Sig.	na

PICO 5: Exercise and Activity

Aquatic Exercise vs. Control

Table 14: Aquatic Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H				M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Kuptniratsaikul; 2019	Rewald; 2020	Waller; 2017	Dias; 2017	Munukka; 2020
Composite					
Patient Global Assessment		●			
Function					
WOMAC Function					●
WOMAC Stiffness					●
KOOS Activities of Daily Living			●		
KOOS Sports/Recreation			●		
KOOS Symptoms		●	●		
KOOS Sport and Recreation Function		●			
6MWT(m)	●				
Walking Speed (m/s)			●		
6 minute walk test		↓			
Lower Extremity Function Scale (LEFS)		↑			
Power Knee Extension				●	
Power Knee Flexion				●	
Resistance Knee Extension				●	
Resistance Knee Flexion				●	
Strength - Quadriceps	●				
Strength Knee Extension				●	
Strength Knee Flexsion				●	
Timed Up and Go test		↑			
Pain					
WOMAC Pain					●
KOOS Pain			●		
Pain Score	●				
Adverse events					
Any Adverse Event	●				
Joint pain	●				
Muscle Pain	●				
Other Adverse Event	●				

Table 14 Continued: Aquatic Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H				M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Kuptniratsaikul; 2019	Rewald; 2020	Waller; 2017	Dias; 2017	Munukka; 2020
calculable MID outcomes					
WOMAC Function				↑	
WOMAC Stiffness					↑
WOMAC Pain				↑	
QOL					
KOOS Quality of Life			●		
Global Assessment - Improved(direction?)	↑				
Global Assessment - Much Improved	↓				
Global Assessment - No Change	●				
KOOS Quality of Life (Follow-Up)		●			
KOOS Quality of Life (Post)		↑			
LTPA (MET/h)(Leisure Time Physical Activity)			↑		
Satisfaction Index - Satisfied(direction?)	↑				
Satisfaction Index - Unsatisfied	●				
Satisfaction Index - Very Satisfied	●				
all subscales of SF-36					●

Evidence Table 1713: Aquatic Exercise vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Pain:KOOS Pain	4 mos	43/44	84.3(10.5)/83.3(11.7)	Mean Diff	1(-3.74,5.74)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Pain:KOOS Pain	12 mos	43/44	86.8(10.5)/85.1(12.4)	Mean Diff	1.7(-3.2,6.6)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Pain:Pain Score	4 wks	40/40	4.8(1.6)/4.5(1.9)	Mean Diff	0.3(-0.48,1.08)	Not Sig.	na
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain (VAS Version)	6 wks	33/32	37.7(16.5)/48.6(22.1)	Mean Diff	-10.9(-20.61,-1.19)	Group 1	possibly clinically significant
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	Pain:womac pain	4 mos		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	Pain:womac pain	1 yrs		none	pvalue	NS	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	Function:6 minute walk test	24 wks	98	none	Mean diff	46.75(17.6,75.9)	Group 2	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Function:6MWT(m)	4 wks	40/40	338.8(71.8)/333.9(78.7)	Mean Diff	4.9(-28.64, 38.44)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Activities of Daily Living	12 mos	43/44	89.2(11.2)/88.3(11)	Mean Diff	0.9(-3.83,5.63)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Activities of Daily Living	4 mos	43/44	87.7(9.7)/86(14.6)	Mean Diff	1.7(-3.58,6.98)	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	Function:KOOS Sport and Recreation Function	24 wks	97	none	Mean diff	3.88(-4.55,12.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Sports/Recreation	12 mos	43/44	71(20.7)/68.7(24.6)	Mean Diff	2.3(-7.39,11.99)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Sports/Recreation	4 mos	43/44	70.6(21.7)/67.6(26.5)	Mean Diff	3(-7.32,13.32)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Symptoms	4 mos	43/44	80.9(12.1)/77.5(14.9)	Mean Diff	3.4(-2.38,9.18)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:KOOS Symptoms	12 mos	43/44	81.4(11.4)/77.9(14.5)	Mean Diff	3.5(-2.06,9.06)	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	Function:KOOS Symptoms	24 wks	101	none	Mean diff	5.52(-0.04,10.54)	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	Function:Lower Extremity Function Scale (LEFS)	24 wks	99	none	Mean diff	5.96(1.89,10.03)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Power Knee Extension	6 wks	33/32	64.5(14.4)/61.7(15.4)	Mean Diff	2.8(-4.6,10.2)	Not Sig.	na
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Power Knee Flexion	6 wks	33/32	25.9(9.6)/26.1(11.3)	Mean Diff	-0.2(-5.41,5.01)	Not Sig.	na
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Resistance Knee Extension	6 wks	33/32	27.6(9.1)/23.7(13.4)	Mean Diff	3.9(-1.81,9.61)	Not Sig.	na
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Resistance Knee Flexion	6 wks	33/32	27.8(14.8)/26(28.5)	Mean Diff	1.8(-9.59,13.19)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Function:Strength - Quadriceps	4 wks	40/40	9.3(2.5)/10.4(3)	Mean Diff	-1.1(-2.33,0.13)	Not Sig.	na
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Strength Knee Extension	6 wks	33/32	111.6(23.1)/106.7(34.3)	Mean Diff	4.9(-9.69,19.49)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Strength Knee Flexsion	6 wks	33/32	57.8(15.2)/52.8(19.6)	Mean Diff	5(-3.73,13.73)	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	Function:Timed Up and Go test	24 wks	98	none	Mean diff	-0.91(-1.45,-0.37)	Group 1	na
Dias; 2017/High	5: Exercise-Hydrotherapy Exercise(40 min 2x/week x6 weeks)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function (VAS Version)	6 wks	33/32	36.3(19)/50.2(22.7)	Mean Diff	-13.9(-24.3,-3.5)	Group 1	possibly clinically significant
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Walking Speed (m/s)	12 mos	43/44	1.82(0.14)/1.77(0.13)	Mean Diff	0.05(-0.01,0.11)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	Function:Walking Speed (m/s)	4 mos	43/44	1.83(0.16)/1.76(0.17)	Mean Diff	0.07(0,0.14)	Not Sig.	na
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	Function:womac function	4 mos		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	Function:womac function	1 yrs		none	pvalue	NS	Not Sig.	na
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	Function:womac stiffness	1 yrs		none	pvalue	NS	Not Sig.	na
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	Function:womac stiffness	4 mos	77	none	mean difference	-8.5(-14.9,-2)	Group 1	possibly clinically significant
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	Composite:Patient Global Assessment	24 wks	99	none	Mean diff	-0.62(-1.68,0.45)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	QOL:Global Assessment - Improved(direction?)	4 wks	40/40	75%/42.5%	RR	1.76(1.18,2.64)	Group 1	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	QOL:Global Assessment - Much Improved	4 wks	40/40	10%/32.5%	RR	0.31(0.11,0.86)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	QOL:Global Assessment - No Change	4 wks	40/40	7.5%/7.5%	RR	1(0.21, 4.66)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:KOOS Quality of Life	12 mos	43/44	75(18.2)/76.4(24.4)	Mean Diff	-1.4(-10.57, 7.77)	Not Sig.	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:KOOS Quality of Life	4 mos	43/44	72.6(18.1)/74.1(23.1)	Mean Diff	-1.5(-10.34, 7.34)	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	QOL:KOOS Quality of Life (Follow-Up)	24 wks	100	none	Mean diff	6.74(-0.57,14.05)	Not Sig.	na
Rewald; 2020/High	5: Supervised exercise-Aquatic Cycling	5: Placebo/Control-Usual Care	QOL:KOOS Quality of Life (Post)	12 wks	100	none	Mean diff	13.03(5.85,20.22)	Group 1	na
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:LTPA (MET/h)(Leisure Time Physical Activity)	12 mos	43/44	100(57)/107(56)	Mean Diff	-7(-31.09, 17.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Waller; 2017/High	5: Exercise-Aquatic Resistance Training(1h x3/week x16 weeks)	5: Placebo/Control-Control (Usual Care)	QOL:LTPA (MET/h)(Leisure Time Physical Activity)	4 mos	43/44	160(53)/104(63)	Mean Diff	56(31.2,80.8)	Group 1	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	QOL:Satisfaction Index - Satisfied(direction?)	4 wks	40/40	52.5%/22.5%	RR	2.33(1.22,4.45)	Group 1	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	QOL:Satisfaction Index - Unsatisfied	4 wks	40/40	0%/2.5%	RD	-2.5(-11.5,7.881)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	QOL:Satisfaction Index - Very Satisfied	4 wks	40/40	40%/57.5%	RR	0.7(0.44,1.11)	Not Sig.	na
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	QOL:all subscales of SF-36	4 mos		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Munukka; 2020/Moderate	5: Supervised exercise-48 supervised aquatic resistance training sessions over 4 months	5: Placebo/Control-maintain usual level of physical activity	QOL:all subscales of SF-36	1 yrs		none	pvalue	NS	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Adverse events:Any Adverse Event	4 wks	40/40	35%/20%	RR	1.75(0.83,3.7)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Adverse events:Joint Pain	4 wks	40/40	10%/7.5%	RR	1.33(0.32,5.58)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Adverse events:Muscle Pain	4 wks	40/40	17.5%/10%	RR	1.75(0.56,5.51)	Not Sig.	na
Kuptniratsaikul; 2019/High	5: Exercise-Underwater Treadmill (UTM)(30 min session 3x/week x4 weeks)	5: Self management-Exercise Education	Adverse events:Other Adverse Event	4 wks	40/40	12.5%/2.5%	RR	5(0.61, 40.91)	Not Sig.	na

PICO 5: Exercise and Activity

Supervised vs. Non-Supervised PT

Table 15: Supervised vs Non-Supervised PT

Quality: H=High; M=Moderate; L=Low	**M**			
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Yilmaz; 2019**	**Allen; 2016**	**Bennell; 2014**	**Tunay; 2010**
Function				
SF-36 Role Physical	↑			
6MWT(m)		↑		
Duration of All Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))		●		
Duration of Moderate or Greater Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))		●		
Duration of Moderate or Greater Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))		●		
Freq. of All Exercise (#/wk)(CHAMPS (Community Health Activities Model Program for Seniors))		●		
Freq. of Moderate or Greater Exercise (#/wk)(CHAMPS (Community Health Activities Model Program for Seniors))		●		
Hamstr. Strength Left	●			
Hamstr. Strength Right	●			
Quadri. Strength Left	●			
Quadri. Strength Right	●			
ROM (extension) Left Knee	↓			
ROM (extension) Right Knee	↓			
ROM (flexion) Left Knee	↑			
ROM (flexion) Right Knee	●			
Short Physical Perfmance Battery		●		
TUG (sec)				●
Other				
% Adherence to Home Exercise Program			●	
Adverse events				
Proprioception				●

Table 15 Continued: Supervised vs Non-Supervised PT

Quality: H=High; M=Moderate; L=Low	H	M			
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	McCarthy ; 2004	Yilmaz; 2019	Allen; 2016	Bennell; 2014	Tunay ; 2010
calculable MID outcomes					
WOMAC Total		↑	●		
WOMAC Function		↑	●	●	
WOMAC Stiffness		↑			
WOMAC Pain	●	●	●		
VAS Pain	↑	●		●	
SF-36 Physical Functioning		●			
SF-36 Pain Index		↑			
VAS Pain Activity		↑			
WOMAC					●
Left knee VAS Activity					↑
Left knee VAS Night					●
Left knee VAS rest					●
Right knee VAS Activity					●
Right knee VAS Night					●
Right knee VAS rest					●
QOL					
SF-36 Role Emotional		↑			
SF-36 Social Functioning		↓			
SF-36 Vitality		●			
SF-36 General Health Perceptions		↑			
SF-36 Mental Health Index		●			
Satisfaction with Function			●		

Evidence Table 1814: Supervised vs Non-Supervised PT

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Pain:SF-36 Pain Index	6 wks	41/39	74.1(12.63)/64.11(21.56)	Mean Diff	9.99(2.04,17.94)	Group 1	possibly clinically significant
Bennell; 2014/Moderate	5: Wellness education-Physiotherapist Booster Session + Home Exercise(30min discussion (progam content; dose; adherence; barries to home exercise) x2 (week 8; 16); home ex. X4/wk)	5: Placebo/Control-Control (Home Exercise Alone)(X4/wk)	Pain:VAS PAin	24 wks	38/36	37.1(20.5)/35.5(20.2)	Mean Diff	1.6(-7.83,11.03)	Not Sig.	clinically insignificant
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Pain:VAS Pain	6 wks	41/39	0.04(0.21)/0.63(1.21)	Mean Diff	-0.59(-0.99,-0.19)	Group 1	clinically insignificant
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Pain:VAS Pain Activity	6 wks	41/39	2.38(1.39)/3.78(1.81)	Mean Diff	-1.4(-2.12,-0.68)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Pain:WOMAC Pain	6 wks	41/39	5.95(3.2)/6.74(4.64)	Mean Diff	-0.79(-2.58,1)	Not Sig.	inconclusive
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Pain:WOMAC Pain	12 wks	320	none	mean diff.	-0.4(-1.1,0.2)	Not Sig.	clinically insignificant
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Pain:WOMAC Pain	24 wks	320	none	mean diff.	-0.4(-1.1,0.3)	Not Sig.	clinically insignificant
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:6MWT(m)	12 wks	320	none	mean diff.	17.5(3.4,31.6)	Group 1	na
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Duration of All Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	24 wks	320	none	Incidence Rate Ratio	1.1(0.9,1.3)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Duration of All Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	12 wks	320	none	Incidence Rate Ratio	1.1(1,1.3)	Not Sig.	na
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Duration of Moderate or Greater Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	12 wks	320	none	Incidence Rate Ratio	1(0.8,1.3)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Duration of Moderate or Greater Exercise (hr/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	24 wks	320	none	Incidence Rate Ratio	1.1(0.9,1.4)	Not Sig.	na
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Freq. of All Exercise (#/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	24 wks	320	none	Incidence Rate Ratio	1(0.8,1.1)	Not Sig.	na
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Freq. of All Exercise (#/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	12 wks	320	none	Incidence Rate Ratio	1(0.9,1.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Freq. of Moderate or Greater Exercise (#/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	24 wks	320	none	Incidence Rate Ratio	0.9(0.7,1.1)	Not Sig.	na
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Freq. of Moderate or Greater Exercise (#/wk)(CHAMPS (Community Health Activities Model Program for Seniors))	12 wks	320	none	Incidence Rate Ratio	1(0.8,1.2)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:Hamstr. Strength Left	6 wks	41/39	8.82(1.76)/8.93(25.31)	Mean Diff	-0.11(-8.33,8.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:Hamstr. Strength Right	6 wks	41/39	8.46(1.76)/8.97(2.09)	Mean Diff	-0.51(-1.37,0.35)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:Quadri. Strength Left	6 wks	41/39	8.76(1.57)/8.83(1.93)	Mean Diff	-0.07(-0.86,0.72)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:Quadri. Strength Right	6 wks	41/39	9.18(1.6)/9.24(1.5)	Mean Diff	-0.06(-0.75,0.63)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:ROM (extension) Left Knee	6 wks	41/39	0.66(1.42)/1.52(1.89)	Mean Diff	-0.86(-1.61,-0.11)	Group 2	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:ROM (extension) Right Knee	6 wks	41/39	0.33(0.96)/1.68(2.05)	Mean Diff	-1.35(-2.07,-0.63)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:ROM (flexion) Left Knee	6 wks	41/39	114.67(9.76)/106.05(14.01)	Mean Diff	8.62(3.21,14.03)	Group 1	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:ROM (flexion) Right Knee	6 wks	41/39	115.19(10.24)/111.79(10.73)	Mean Diff	3.4(-1.27,8.07)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:SF-36 Physical Functioning	6 wks	41/39	64.05(12.9)/60(15.36)	Mean Diff	4.05(-2.28,10.38)	Not Sig.	inconclusive
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:SF-36 Role Physical	6 wks	41/39	77.38(28.4)/61.84(32.66)	Mean Diff	15.54(1.88,29.2)	Group 1	na
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:Short Physical Perfmance Battery	12 wks	320	none	mean diff.	-0.1(-0.5,0.2)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:WOMAC Function	6 wks	41/39	13.71(9.01)/18.89(8.29)	Mean Diff	-5.18(-9.03,-1.33)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:WOMAC Function	24 wks	320	none	mean diff.	-0.9(-3.4,1.7)	Not Sig.	clinically insignificant
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Function:WOMAC Function	12 wks	320	none	mean diff.	-2(-4.5,0.5)	Not Sig.	clinically insignificant
Bennell; 2014/Moderate	5: Wellness education-Physiotherapist Booster Session + Home Exercise(30min discussion (progam content; dose; adherence; barries to home exercise) x2 (week 8; 16); home ex. X4/wk)	5: Placebo/Control-Control (Home Exercise Alone)(X4/wk)	Function:WOMAC Function	24 wks	38/36	20.2(12.4)/21(12.3)	Mean Diff	-0.8(-6.53,4.93)	Not Sig.	inconclusive
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Function:WOMAC Stiffness	6 wks	41/39	0.86(1.65)/2.32(2.45)	Mean Diff	-1.46(-2.4,-0.52)	Group 1	possibly clinically significant
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	Composite:WOMAC Total	6 wks	41/39	20.52(12.55)/27.95(13.14)	Mean Diff	-7.43(-13.16,-1.7)	Group 1	possibly clinically significant
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Composite:WOMAC Total	24 wks	320	none	mean diff.	-1.3(-4.6,2)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	Composite:WOMAC Total	12 wks	320	none	mean diff.	-2.7(-5.9,0.5)	Not Sig.	clinically insignificant
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	QOL:SF-36 General Health Perceptions	6 wks	41/39	67.62(15.4)/57.89(16)	Mean Diff	9.73(2.73,16.73)	Group 1	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	QOL:SF-36 Mental Health Index	6 wks	41/39	75.62(17.1)/75.62(17.1)	Mean Diff	0(-7.62,7.62)	Not Sig.	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	QOL:SF-36 Role Emotional	6 wks	41/39	87.19(24.83)/61.21(38.96)	Mean Diff	25.98(11.31,40.65)	Group 1	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	QOL:SF-36 Social Functioning	6 wks	41/39	5.95(16.31)/65.53(17.61)	Mean Diff	-59.58(-67.15,-52.01)	Group 2	na
Yilmaz; 2019/Moderate	5: Exercise-Home Exercise w/ PT trainer(PT trainer instructed once + exercises taught at hospital)	5: Exercise-Home Exercise via Brochure(pts only given brochure with exercises)	QOL:SF-36 Vitality	6 wks	41/39	51.67(23.41)/50(22.28)	Mean Diff	1.67(-8.5,11.84)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2016/Moderate	5: PT-Group PT(1hr x6)	5: PT-Individual PT(1hr x2)	QOL:Satisfaction with Function	12 wks	320	none	mean diff.	0.2(-0.1,0.6)	Not Sig.	na
Bennell; 2014/Moderate	5: Wellness education-Physiotherapist Booster Session + Home Exercise(30min discussion (progam content; dose; adherence; barries to home exercise) x2 (week 8; 16); home ex. X4/wk)	5: Placebo/Control-Control (Home Exercise Alone)(X4/wk)	Other:% Adherence to Home Exercise Program	24 wks	38/36	56(34)/51(37)	Mean Diff	5(-11.5,21.5)	Not Sig.	na
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Pain:Left knee VAS Activity	6 wks	30/30	1.46(2.04)/2.8(2.02)	MeanDiff	-1.34(-2.39,-0.29)	Group 1	possibly clinically significant
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Pain:Left knee VAS Night	6 wks	30/30	0.76(1.92)/1.4(2.26)	MeanDiff	-0.64(-1.72,0.44)	Not Sig.	clinically insignificant
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Pain:Left knee VAS rest	6 wks	30/30	0.73(1.7)/0.63(1.29)	MeanDiff	0.1(-0.68,0.88)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Pain:Right knee VAS Activity	6 wks	30/30	1.66(1.58)/2.4(1.58)	MeanDiff	-0.74(-1.56,0.08)	Not Sig.	clinically insignificant
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Pain:Right knee VAS Night	6 wks	30/30	0.53(1.3)/0.33(0.75)	MeanDiff	0.2(-0.35,0.75)	Not Sig.	clinically insignificant
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Pain:Right knee VAS rest	6 wks	30/30	0.3(0.83)/0.56(1.27)	MeanDiff	-0.26(-0.82,0.3)	Not Sig.	clinically insignificant
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Function:TUG (sec)	6 wks	30/30	5.19(1.05)/5.39(1.46)	MeanDiff	-0.2(-0.86,0.46)	Not Sig.	na
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Composite:WOMAC	6 wks	30/30	5.45(3.76)/5.69(2.84)	MeanDiff	-0.24(-1.96,1.48)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tunay ; 2010/Moderate	5: Supervised exercise-Hospital based proprioceptive and strength exercise	5: Self management-home based proprioceptive and strength exercise	Adverse events:Proprioception	6 wks	30/30	14.26(2.88)/13.03(2.97)	MeanDiff	1.23(-0.28,2.74)	Not Sig.	na
McCarthy ; 2004/High	5: Supervised exercise-home based + class based exercise	5: Placebo/Control-home based exercise alone	Pain:VAS Pain	6 mos	71/80	43(18.1)/ 54.6(21.8)	MeanDiff	11.6(5.1,18.1)	Group 1	some may benefit
McCarthy ; 2004/High	5: Supervised exercise-home based + class based exercise	5: Placebo/Control-home based exercise alone	Pain:VAS Pain	12 mos	71/80	44.1(18.6)/ 58.9(19.2)	MeanDiff	14.8(8.7,20.9)	Group 1	possibly clinically significant
McCarthy ; 2004/High	5: Supervised exercise-home based + class based exercise	5: Placebo/Control-home based exercise alone	Pain:womac Pain	6 mos	71/80	9.13(3.99)/8.04(3.6)	MeanDiff	1.09(-0.14,2.32)	Not Sig.	inconclusive

PICO 5: Exercise and Activity

Neuromuscular Exercise vs Control

Table 16a: Neuromuscular Exercise vs Control

Quality: H=High; M=Moderate; L=Low	High	Moderate
↑ Better Outcomes ↓ Worse Outcomes ● Not Si	Fitzgerald; 2011	Diracoglu; 2005
Composite		
womac total	●	
Function		
womac function	●	●
get up and go test	●	
10m walk time (s)		↑
sf-36 physical function		↑
Other		
global rating of change	●	
sf36 vitality		↑
sf-36 role limitations		●
Adverse events		
knee pain	●	

Evidence Table 19: Neuromuscular Exercise vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Function:get up and go test	1 yrs	92/91	11.1(6.36)/9.7(4.14)	Mean Diff	1.4(-0.17,2.97)	Not Sig.	na
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Function:womac function	1 yrs	92/91	13.2(6.85)/15.9(12.9)	Mean Diff	-2.7(-5.72,0.32)	Not Sig.	inconclusive
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Composite:womac total	1 yrs	92/91	23.5(19.09)/23.9(17.03)	Mean Diff	-0.4(-5.68,4.88)	Not Sig.	clinically insignificant
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Other:global rating of change	1 yrs	92/91	5.4(4.16)/5.4(3.41)	Mean Diff	0(-1.11,1.11)	Not Sig.	na
Fitzgerald; 2011/High	5: Exercise-agility and purbutation	5: Exercise-standard exercise	Adverse events:knee pain	1 yrs	92/91	4.1(2.69)/3.8(2.92)	Mean Diff	0.3(-0.52,1.12)	Not Sig.	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Function:10 m walk time (s)	8 weeks	30/30	5.21(1.1)/5.89(1.3)	Mean Diff	-0.68(-1.3,-0.06)	Group 1	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Function:sf-36 physical function	8 weeks	30/30	69.33(17.8)/56.25(16.7)	Mean Diff	13.08(4.16,22)	Group 1	clinically significant
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Function:womac function	8 weeks	30/30	13.6(10.88)/18.36(9.52)	Mean Diff	-4.76(-10.05, 0.53)	Not Sig.	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Other:sf-36 role limitations	8 weeks	30/30	77.5(34.9)/57.14(45)	Mean Diff	20.36(-0.48,41.2)	Not Sig.	na
Diracoglu; 2005/Moderate	5: PT-kinesthesia + balance+ strengthening	5: Placebo/Control-strengthening exercise	Other:sf36 vitality	8 weeks	30/30	54(19.5)/43.5(18.3)	Mean Diff	10.5(0.73,20.27)	Group 1	na

PICO 5: Exercise and Activity

Neuromuscular Exercise vs Proprioceptive Exercises

Table 16b: Neuromuscular Exercise vs Proprioceptive Exercises

Quality: H=High; M=Moderate; L=Low	**M**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Apparao; 2017**
Function	
KOOS Symptoms	●
Knee Extensors Strength	↑
Knee Flexors Strength	●
Pain	
KOOS Pain	●
calculable MID outcomes	
VAS Pain	●
QOL	
KOOS QoL	●
KOOS ADL	●

Evidence Table 2015: Neuromuscular Exercise vs Proprioceptive Exercise

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	Pain:KOOS Pain	8 wks	33/33	70.2(11.17)/69.7(3.02)	Mean Diff	0.5(-3.58,4.58)	Not Sig.	na
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	Pain:VAS Pain	8 wks	33/33	2.21(0.87)/1.98(0.88)	Mean Diff	0.23(-0.2,0.66)	Not Sig.	clinically insignificant
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	Function:KOOS Symptoms	8 wks	33/33	69.7(11.48)/70.6(4.86)	Mean Diff	-0.9(-5.28,3.48)	Not Sig.	na
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	Function:Knee Extensors Strength	8 wks	33/33	18.01(1.36)/17.08(1.7)	Mean Diff	0.93(0.17,1.69)	Group 1	na
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	Function:Knee Flexors Strength	8 wks	33/33	14.86(2.04)/14.21(0.93)	Mean Diff	0.65(-0.14,1.44)	Not Sig.	na
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	QOL:KOOS ADL	8 wks	33/33	60.7(10.97)/61.4(1.58)	Mean Diff	-0.7(-4.62,3.22)	Not Sig.	na
Apparao; 2017/Moderate	5: Exercise-Neuromuscular Training Exercises(n/a)	5: Exercise-Proprioceptive Exercises(n/a)	QOL:Koos QoL	8 wks	33/33	71.68(0.52)/71.64(2.12)	Mean Diff	0.04(-0.73,0.81)	Not Sig.	na

PICO 5: Exercise and Activity

Sensory Motor vs Resistance Training

Table 17: Sensory Motor vs Resistance Training

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Gomiero; 2018**
Function	
SF-36 Role Physical	●
Timed Up and Go Test (sec)	●
Maximal Voluntary Isometric Contraction	↑
Tinetti Balance Assessment Tool	●
calculable MID outcomes	
WOMAC Total	●
VAS Pain	●
SF-36 Physical Functioning	●
SF-36 Pain Index	●
QOL	
SF-36 Role Emotional	●
SF-36 Social Functioning	●
SF-36 Vitality	●
SF-36 General Health Perceptions	●
SF-36 Mental Health Index	●

Evidence Table 2116: Sensory Motor vs Resistance Training

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Pain:SF-36 Pain Index	16 wks	32/32	59.3(25.41)/54.8(25.1)	Mean Diff	4.5(-8.12,17.12)	Not Sig.	inconclusive
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Pain:VAS Pain	16 wks	32/32	4.6(2.11)/4.1(2.61)	Mean Diff	0.5(-0.69,1.69)	Not Sig.	clinically insignificant
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Function:Maximal Voluntary Isometric Contraction	16 wks	32/32	39.9(11.9)/33.4(14.01)	Mean Diff	6.5(0,13)	Group 1	na
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Function:SF-36 Physical Functioning	16 wks	32/32	57.5(41.6)/50.8(36.7)	Mean Diff	6.7(-12.91, 26.31)	Not Sig.	inconclusive
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Function:SF-36 Role Physical	16 wks	32/32	54.8(23.69)/51.4(24.49)	Mean Diff	3.4(-8.64,15.44)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Function:Timed Up and Go Test (sec)	16 wks	32/32	7.9(1.19)/8.7(2.8)	Mean Diff	-0.8(-1.89,0.29)	Not Sig.	na
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Function:Tinetti Balance Assessment Tool	16 wks	32/32	26(0.92)/26.5(2.11)	Mean Diff	-0.5(-1.32,0.32)	Not Sig.	na
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	Composite:WOMAC Total	16 wks	32/32	30.6(17.61)/29(15.89)	Mean Diff	1.6(-6.78,9.98)	Not Sig.	inconclusive
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	QOL:SF-36 General Health Perceptions	16 wks	32/32	60.8(19.19)/62(20.61)	Mean Diff	-1.2(-11.15, 8.75)	Not Sig.	na
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	QOL:SF-36 Mental Health Index	16 wks	32/32	74.1(16.31)/65.6(19)	Mean Diff	8.5(-0.35,17.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	QOL:SF-36 Role Emotional	16 wks	32/32	61.1(41.2)/64.6(40.61)	Mean Diff	-3.5(-23.94, 16.94)	Not Sig.	na
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	QOL:SF-36 Social Functioning	16 wks	32/32	74(22.8)/67.3(26.1)	Mean Diff	6.7(-5.55,18.95)	Not Sig.	na
Gomiero; 2018/High	5: Exercise-Sensory-Motor Training (agility; balance; etc)(2 sessions/week x 16 weeks)	5: Exercise-Resistance Training(2 sessions/week x 16 weeks)	QOL:SF-36 Vitality	16 wks	32/32	64.5(16.89)/60.3(19.89)	Mean Diff	4.2(-5.03,13.43)	Not Sig.	na

PICO 5: Exercise and Activity

Neuromuscular Exercise vs Strength Training

Table 18: Neuromuscular Exercise vs Strength Training

Quality: H=High; M=Moderate; L=Low	**M**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Bennell; 2014**
Function	
Physical Activity Scale for the Elderly	●
Walking Speed (m/s)	↑
30 Second Stand-to-Sit (repititions)	●
Four Square Step Test (s)	●
Step Test (repititions)	●
Strength Hamstrings (Nm/kg)	●
Strength Hip Abduction (Nm/kg)	●
Strength Hip Extension (Nm/kg)	●
Strength Hip External Rotation	●
Strength Hip Internal Rotation	●
Strength Quadriceps (Nm/kg)	●
Timed Stair Climb (s)	●
Adverse events	
Back Pain	●
Hip Pain	●
Any Adverse Event	●
Increased Knee Pain	●
Pain in Other Area	●
Stiffness	●
Swelling/Inflammation	●
calculable MID outcomes	
WOMAC Function	●
WOMAC Stiffness	●
VAS Pain while Walking	●
WOMAC Pain	●
VAS Pain	●
QOL	
Assessment of QoL 6D	●
Opioid use	
Any Opioid Use	●

Evidence Table 2217: Neuromuscular Exercise vs Strength Training

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Pain:VAS Pain	13 wks	50/50	34.1(23.6)/31.4(19.3)	Mean Diff	2.7(-5.86,11.26)	Not Sig.	clinically insignificant
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Pain:VAS Pain while Walking	13 wks	50/50	39.6(25.9)/40(22.9)	Mean Diff	-0.4(-10.1,9.3)	Not Sig.	clinically insignificant
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Pain:WOMAC Pain	13 wks	50/50	6.4(3.1)/6.4(2.9)	Mean Diff	0(-1.19,1.19)	Not Sig.	clinically insignificant
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:30 Second Stand-to-Sit (repititions)	13 wks	50/50	11.7(2.1)/12(2.5)	Mean Diff	-0.3(-1.22,0.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Four Square Step Test (s)	13 wks	50/50	8.1(1.8)/7.9(1.7)	Mean Diff	0.2(-0.49,0.89)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Physical Activity Scale for the Elderly	13 wks	50/50	174.9(112)/196.2(88.4)	Mean Diff	-21.3(-61.37, 18.77)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Step Test (repititions)	13 wks	50/50	14.1(3.2)/14.4(4.3)	Mean Diff	-0.3(-1.81,1.21)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Strength Hamstrings (Nm/kg)	13 wks	50/50	0.71(0.23)/0.79(0.26)	Mean Diff	-0.08(-0.18,0.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Strength Hip Abduction (Nm/kg)	13 wks	50/50	1.2(0.45)/1.23(0.41)	Mean Diff	-0.03(-0.2,0.14)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Strength Hip Extension (Nm/kg)	13 wks	50/50	1.75(0.54)/1.86(0.7)	Mean Diff	-0.11(-0.36,0.14)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Strength Hip External Rotation	13 wks	50/50	0.41(0.12)/0.45(0.14)	Mean Diff	-0.04(-0.09,0.01)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Strength Hip Internal Rotation	13 wks	50/50	0.5(0.17)/0.56(0.17)	Mean Diff	-0.06(-0.13,0.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Strength Quadriceps (Nm/kg)	13 wks	50/50	1.59(0.47)/1.62(0.51)	Mean Diff	-0.03(-0.22,0.16)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Timed Stair Climb (s)	13 wks	50/50	7.11(2.23)/6.84(1.88)	Mean Diff	0.27(-0.55,1.09)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:WOMAC Function	13 wks	50/50	18.3(9.6)/20.1(9.8)	Mean Diff	-1.8(-5.65,2.05)	Not Sig.	inconclusive
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:WOMAC Stiffness	13 wks	50/50	3.6(1.4)/3.9(1.8)	Mean Diff	-0.3(-0.94,0.34)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Function:Walking Speed (m/s)	13 wks	50/50	1.5(0.2)/1.24(0.21)	Mean Diff	0.26(0.18,0.34)	Group 1	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	QOL:Assessment of QoL 6D	13 wks	50/50	0.78(0.14)/0.78(0.16)	Mean Diff	0(-0.06,0.06)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Opioid use:Any Opioid Use	13 wks	46/44	4.35%/0%	RD	4.348(-5.837, 12.972)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Any Adverse Event	13 wks	46/44	30.43%/22.73%	RR	1.34(0.67,2.69)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Back Pain	13 wks	46/44	2.17%/2.27%	RR	0.96(0.06,14.83)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Hip Pain	13 wks	46/44	4.35%/2.27%	RR	1.91(0.18,20.35)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Increased Knee Pain	13 wks	46/44	21.74%/18.18%	RR	1.2(0.52,2.75)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Pain in Other Area	13 wks	46/44	4.35%/2.27%	RR	1.91(0.18,20.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Stiffness	13 wks	46/44	2.17%/0%	RD	2.174(-6.987, 10.4)	Not Sig.	na
Bennell; 2014/Moderate	5: Exercise-Neuromuscular Exercise (NEXA)(30-40min 2x/week (wk1;2) 1x/week (wk3;12))	5: Exercise-Quadriceps Strengthening	Adverse events:Swelling/Inflammation	13 wks	46/44	6.52%/2.27%	RR	2.87(0.31,26.56)	Not Sig.	na

PICO 5: Exercise and Activity

Self-Management vs. Control

Table 20 Continued: Self-Management vs Control

Quality: H=High; M=Moderate; L=Low	H		M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Hurley; 2007	Omidi; 2018	Coleman; 2012
Composite			
EQ-5D	●		
Function			
Aggregated Functional Performance Time	●		
Quadriceps Maximum Voluntary Contraction (N) - Left	●		
Quadriceps Maximum Voluntary Contraction (N) - Right	●		
ROM Left Knee Extension(EM: difference of deltas)			↓
ROM Left Knee Flexion(EM: difference of deltas)			↑
ROM Right Knee Extension(EM: difference of deltas)			●
ROM Right Knee Flexion(EM: difference of deltas)			●
SF-36 Role Physical(EM: difference of deltas)			↑
Strength Left Hamstring(EM: difference of deltas)			↑
Strength Left Quadriceps(EM: difference of deltas)			↑
Strength Right Hamstring(EM: difference of deltas)			↑
Strength Right Quadriceps(EM: difference of deltas)			↑
Timed Up and Go Test (sec)(EM: difference of deltas)			↑
Pain			
Pain intensity score		↑	
calculable MID outcomes			
WOMAC Total	↑		↑
WOMAC Function	↑		↑
WOMAC Stiffness			↑
WOMAC Pain	↑		↑
SF-36 Physical Functioning(EM: difference of deltas)			↑
SF-36 Pain Index(EM: difference of deltas)			↑
QOL			
HADS Anxiety	↑		
HADS Depression	●		
MACTAR (McMaster Toronto Arthritis Patient Preference Questionnaire)	↑		
SF - 36 Emotional Well-Being(EM: difference of deltas)			●
SF-36 General Health Perceptions(EM: difference of deltas)			●
SF-36 Role Emotional(EM: difference of deltas)			●
SF-36 Social Functioning(EM: difference of deltas)			↑
SF-36 Vitality(EM: difference of deltas)			↑

Evidence Table 25 18: Self-Management vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Pain:SF-36 Pain Index(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	6.06(0.04,12.07)	Group 1	possibly clinically significant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Pain:SF-36 Pain Index(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	7.19(1.93,12.44)	Group 1	possibly clinically significant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Pain:WOMAC Pain(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-0.49(-1.26,0.28)	Not Sig.	clinically insignificant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Pain:WOMAC Pain(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	-1.46(-2.18,-0.73)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Left Knee Extension(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-1.39(-2.71,-0.06)	Group 2	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Left Knee Extension(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	0.1(-0.72,0.88)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Left Knee Flexion(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	2.26(-0.32,4.86)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Left Knee Flexion(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	2.8(0.58,5.02)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Right Knee Extension(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-1.18(-2.63,0.26)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Right Knee Extension(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	0.9(-0.03,1.78)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Right Knee Flexion(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	0.02(-2.53,2.57)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:ROM Right Knee Flexion(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	1.56(-0.9,4.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:SF-36 Physical Functioning(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	5.61(1.84,9.37)	Group 1	possibly clinically significant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:SF-36 Physical Functioning(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	5.67(0.4,10.93)	Group 1	possibly clinically significant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:SF-36 Role Physical(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	17.06(5.9,28.21)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:SF-36 Role Physical(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	7.37(-5.93,20.67)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Left Hamstring(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	0.74(-0.31,1.79)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Left Hamstring(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	1.47(0.63,2.3)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Left Quadriceps(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	1.58(-0.31,3.47)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Left Quadriceps(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	1.65(0.34,2.95)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Right Hamstring(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	1.18(0.06,2.29)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Right Hamstring(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	1.8(0.89,2.7)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Right Quadriceps(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	0.66(-1.37,2.69)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Strength Right Quadriceps(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	1.79(0.33,3.24)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Timed Up and Go Test (sec)(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-0.72(-1.35,-0.08)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:Timed Up and Go Test (sec)(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	-1.3(-1.81,-0.86)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:WOMAC Function(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-4.35(-6.2,-0.91)	Group 1	possibly clinically significant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:WOMAC Function(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	-5.55(-7.38,-3.31)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:WOMAC Stiffness(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-0.29(-0.73,0.15)	Not Sig.	clinically insignificant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Function:WOMAC Stiffness(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	-0.5(-0.91,-0.08)	Group 1	possibly clinically significant
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Composite:WOMAC Total(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	-4.08(-7.47,-0.68)	Group 1	some may benefit
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	Composite:WOMAC Total(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	-7.23(-9.98,-4.49)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF - 36 Emotional Well-Being(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	2.08(-1.42,5.58)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF - 36 Emotional Well-Being(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	3.85(-0.21,7.91)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 General Health Perceptions(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	2.11(-1.45,5.67)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 General Health Perceptions(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	3.59(-1.19,8.37)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 Role Emotional(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	1.35(-11.06,13.76)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 Role Emotional(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	5.18(-5.64,16)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 Social Functioning(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	10.72(4.81,16.62)	Group 1	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 Social Functioning(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	4.07(-2.08,12.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 Vitality(EM: difference of deltas)	6 mos	146	none	mean diff. of deltas	4.72(-0.11,9.55)	Not Sig.	na
Coleman; 2012/Moderate	5: Self management -Self-Management (group sessions 2.5 hr/wk x6)	5: Placebo/Control-Control	QOL:SF-36 Vitality(EM: difference of deltas)	8 wks	146	none	mean diff. of deltas	6.02(1.87,10.16)	Group 1	na
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Pain:WOMAC Pain	6 mos	229/113	5.7(3.46)/6.7(3.49)	MeanDiff	-1(-1.79,-0.21)	Group 1	possibly clinically significant
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Function:Aggregated Functional Performance Time	6 mos	229/113	57.6(20.35)/61(20.66)	MeanDiff	-3.4(-8.06,1.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Function:Quadriceps Maximum Voluntary Contraction (N) - Left	6 mos	229/113	210.8(85.25)/203(82.35)	MeanDiff	7.8(-11.07,26.67)	Not Sig.	na
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Function:Quadriceps Maximum Voluntary Contraction (N) - Right	6 mos	229/113	237.4(66.05)/230.2(67.06)	MeanDiff	7.2(-7.92,22.32)	Not Sig.	na
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Function:WOMAC Function	6 mos	229/113	21.6(11.14)/25(11.27)	MeanDiff	-3.4(-5.94,-0.86)	Group 1	possibly clinically significant
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Composite:EQ-5D	6 mos	229/113	0.64(0.27)/0.66(0.3)	MeanDiff	-0.02(-0.09,0.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	Composite:WOMAC Total	6 mos	229/113	30.4(16.51)/35(16.1)	MeanDiff	-4.6(-8.28,-0.92)	Group 1	possibly clinically significant
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	QOL:HADS Anxiety	6 mos	229/113	5.32(2.76)/5.97(2.76)	MeanDiff	-0.65(-1.28,-0.02)	Group 1	na
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	QOL:HADS Depression	6 mos	229/113	3.93(2.23)/4.28(2.2)	MeanDiff	-0.35(-0.85,0.15)	Not Sig.	na
Hurley; 2007/High	5: Self management -ESCAPE-Knee Pain(12 sessions: combine self-mgt; coping; exercise)	5: Placebo/Control-Control (Usual Primary Care)	QOL:MACTAR (McMaster Toronto Arthritis Patient Preference Questionnaire)	6 mos	229/113	44(8.06)/41.8(8.05)	MeanDiff	2.2(0.38,4.02)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Omidi; 2018/High	5: Self management -Self-management training	5: Placebo/Control-Control	Pain:Pain intensity score	2 mos	54/54	2.77(1.03)/3.64(1.08)	MeanDiff	-0.87(-1.27,-0.47)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Pain:OAKHQOL Pain	3 mos	53/54	54.2(10.8)/42(14.9)	MeanDiff	12.2(7.21,17.19)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Pain:SF-12 Bodily Pain	3 mos	53/54	59.2(13.8)/45.8(17.3)	MeanDiff	13.4(7.4,19.4)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:6MWT(m)	3 mos	53/54	458(99.3)/410(98.6)	MeanDiff	48(10.06,85.94)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:OAK HQOL Physical Activity	3 mos	53/54	64.7(9.11)/55(13.6)	MeanDiff	9.7(5.26,14.14)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:ROM (flexion)	3 mos	53/54	119.3(19.6)/118.6(21.1)	MeanDiff	0.7(-7.1,8.5)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:SF-12 Physical Component Score	3 mos	53/54	50(5.2)/46.4(6)	MeanDiff	3.6(1.45,5.75)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:SF-12 Physical Function	3 mos	53/54	49.6(12.6)/38.7(25)	MeanDiff	10.9(3.3,18.5)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:SF-12 Role Physical	3 mos	53/54	92.5(22.2)/45(37.6)	MeanDiff	47.5(35.66,59.34)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:Strength - Hamstring	3 mos	53/54	54.9(7.7)/51.6(8.1)	MeanDiff	3.3(0.27,6.33)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:Strength - Quadriceps	3 mos	53/54	58.4(8.3)/54.5(7.9)	MeanDiff	3.9(0.79,7.01)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Composite:EuroQoL-5D-3L	3 mos	53/54	0.66(0.13)/0.53(0.28)	MeanDiff	0.13(0.05,0.21)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:EuroQoL - VAS	3 mos	53/54	60.7(10.9)/52.2(13)	MeanDiff	8.5(3.9,13.1)	Group 1	clinically insignificant
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:OAKHQOL Mental Health	3 mos	53/54	66.6(11.7)/55.5(15.1)	MeanDiff	11.1(5.92,16.28)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:SF-12 General Health	3 mos	53/54	48.3(9.1)/40.4(16)	MeanDiff	7.9(2.91,12.89)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:SF-12 Mental Component Score	3 mos	53/54	42.29(3.2)/37(6.6)	MeanDiff	5.29(3.3,7.28)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:SF-12 Mental Health	3 mos	53/54	63.5(12.7)/55.8(10.6)	MeanDiff	7.7(3.21,12.19)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:OAKHQOL Social Functioning	3 mos	53/54	45.3(9.8)/41.6(13.5)	MeanDiff	3.7(-0.82,8.22)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:OAKHQOL Social Support	3 mos	53/54	59.8(12.2)/50.9(15.6)	MeanDiff	8.9(3.53,14.27)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:SF-12 Role Emotional	3 mos	53/54	92.5(24)/49.2(40.6)	MeanDiff	43.3(30.51,56.09)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:SF-12 Social Function	3 mos	53/54	73.7(21.8)/60.4(16.1)	MeanDiff	13.3(5.93,20.67)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:SF-12 Vitality	3 mos	53/54	54.7(15.1)/54.3(18.1)	MeanDiff	0.4(-5.99,6.79)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Adverse events:Joint Swelling	3 mos	53/54	37.74%/46.3%	RR	0.82(0.52,1.28)	Not Sig.	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Pain:AIMS Pain	2 yrs	62/60	4(1.18)/4.4(1.35)	MeanDiff	-0.4(-0.86,0.06)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Pain:AIMS Pain	2 yrs	62/59	4(1.18)/4.7(1.53)	MeanDiff	-0.7(-1.19,-0.21)	Group 1	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Pain:Pain Catastrophizing	2 yrs	62/60	3.8(3.15)/4.9(3.48)	MeanDiff	-1.1(-2.29,0.09)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Pain:Pain Catastrophizing	2 yrs	62/59	3.8(3.15)/5.6(3.45)	MeanDiff	-1.8(-2.99,-0.61)	Group 1	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Pain:WOMAC Pain (VAS Version)	2 yrs	62/60	27.2(12.8)/34.5(14.32)	MeanDiff	-7.3(-12.18,-2.42)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Pain:WOMAC Pain (VAS Version)	2 yrs	62/59	27.2(12.8)/35.5(13.62)	MeanDiff	-8.3(-13.06,-3.54)	Group 1	possibly clinically significant
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:AIMS Physical	2 yrs	62/59	1(0.59)/1.5(0.58)	MeanDiff	-0.5(-0.71,-0.29)	Group 1	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:Fast Gait Velocity	2 yrs	62/59	1.6(.)/1.5(.)	p value	p>.05	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:Normal Gait Velocity	2 yrs	62/59	1.2(0.2)/1.2(0.19)	MeanDiff	0(-0.07,0.07)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:Normal Gait Velocity	2 yrs	62/60	1.2(.)/1.1(.)	MeanDiff	p>.05	Not Sig.	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Function:WOMAC Activities of Daily Living (VAS Version)	2 yrs	62/60	25.1(12.21)/35.2(13.16)	MeanDiff	-10.1(-14.65,-5.55)	Group 1	possibly clinically significant
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:WOMAC Activities of Daily Living (VAS Version)	2 yrs	62/59	25.1(12.21)/36(12.85)	MeanDiff	-10.9(-15.42,-6.38)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:WOMAC Stiffness (VAS Version)	2 yrs	62/59	35.4(16.54)/45.7(17.27)	MeanDiff	-10.3(-16.39,-4.21)	Group 1	possibly clinically significant
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Function:WOMAC Stiffness (VAS Version)	2 yrs	62/60	35.4(16.54)/44.5(18.39)	MeanDiff	-9.1(-15.38,-2.82)	Group 1	possibly clinically significant
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Composite:Arthritis Self-Efficacy	2 yrs	62/60	243.25(27.17)/225.7(30.97)	MeanDiff	17.55(7.09,28.01)	Group 1	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Composite:Arthritis Self-Efficacy	2 yrs	62/59	243.25(27.17)/222.3(28.97)	MeanDiff	20.95(10.83, 31.07)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Composite:Weight Self-Efficacy	2 yrs	62/60	6.5(1.18)/6(0.97)	MeanDiff	0.5(0.11,0.89)	Group 1	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Composite:Weight Self-Efficacy	2 yrs	62/59	6.5(1.18)/5.9(1.15)	MeanDiff	0.6(0.18,1.02)	Group 1	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management (6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	QOL:AIMS Psychological	2 yrs	62/59	2.2(0.79)/2.5(0.96)	MeanDiff	-0.3(-0.62,0.02)	Not Sig.	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	QOL:AIMS Psychological	2 yrs	62/60	2.2(0.79)/2.6(0.77)	MeanDiff	-0.4(-0.68,-0.12)	Group 1	na

PICO 5: Exercise and Activity

Self-Management and Exercise vs. Control

Table 21: Self-Management and Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H	M		
↑ Better Outcomes ↓ Worse Outcomes● Not Significant	Marconcin; 2018	Bennell; 2016	Yip; 2007	Kao; 2012
Composite				
Health assessment Questionnaire improvement			●	
Function				
WOMAC Function		●		
20 Meter Walk (m/s)(difference in deltas)		●		
30 Second Stand-to-Sit(difference in deltas)		●		
Physical Activity Scale for the Elderly(difference in deltas)		●		
hours of light exercize per week improvement			↑	
Quadreceps Strength (Nm/kg)(difference in deltas)		●		
Step Test(difference in deltas)		●		
improvement in arthritis self efficacy other symptoms score			↑	
KOOS Activities of Daily Living	●			
KOOS Sports/Recreation	●			
KOOS Symptoms	●			
Back Stretch Test - Left (cm)(scale direction?)	●			
Five Repetition Sit to Stand Test (s)(scale direction?)	↑			
Chair Sit and Reach - Less Painful Knee (cm)(scale direction?)	●			
Chair Sit and Reach - Most Painful Knee (cm)(scale direction?)	●			
Handgrip Test (kg)(scale direction?)	●			
6MWT change in meters walked	↑			
SF-36 Role Physical(deltas)				●
Pain				
WOMAC Pain		●		
Pain Catastrophizing Scale(difference in deltas)		●		
improvement in arthritis self efficacy pain score			↑	
VAS Pain (Walking)(difference in deltas)		●		
VAS Pain(difference in deltas)		●		
KOOS Pain	●			
calculable MID outcomes				
WOMAC Function		↑		●
VAS pain improvement			↑	
SF-36 Physical component				●
VAS Pain(difference in deltas)		●		
SF-36 Physical Functioning(deltas)				●
SF-36 Pain Index(deltas)				●
QOL				
DASS-21 Depression Subscale(difference in deltas)		●		
SF-36 Emotional Well-Being(deltas)				●
SF-36 General Health Perceptions(deltas)				↑
SF-36 Mental Component Score(deltas)				↑
SF-36 Role Emotional(deltas)				●
SF-36 Social Functioning(deltas)				↑
SF-36 Vitality(deltas)				●
EQ-5D-5F VAS	●			
KOOS Quality of Life	●			

Evidence Table 26 19: Self-Management and Exercise vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Pain:KOOS Pain	3 mos	35/32	68.2(17.4)/67.4(18.2)	Mean Diff	0.8(-7.91,9.51)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:Back Stretch Test - Left (cm)(scale direction?)	3 mos	35/32	-16.1(11.4)/-16.8(12.3)	Mean Diff	0.7(-5.11,6.51)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:Chair Sit and Reach - Less Painful Knee (cm)(scale direction?)	3 mos	35/32	-7.6(14.1)/-6.5(11.53)	Mean Diff	-1.1(-7.36,5.16)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:Chair Sit and Reach - Most Painful Knee (cm)(scale direction?)	3 mos	35/32	-6.6(14.4)/-5.6(12.8)	Mean Diff	-1(-7.64,5.64)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:Handgrip Test (kg)(scale direction?)	3 mos	35/32	28.65(9.5)/30.07(8.1)	Mean Diff	-1.42(-5.72,2.88)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:KOOS Activities of Daily Living	3 mos	35/32	65.7(18.8)/73.6(18.5)	Mean Diff	-7.9(-17.01,1.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:KOOS Sports/Recreation	3 mos	35/32	35.3(28.3)/42.9(29.6)	Mean Diff	-7.6(-21.76, 6.56)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Function:KOOS Symptoms	3 mos	35/32	72.1(17.5)/71.6(21.3)	Mean Diff	0.5(-9.08,10.08)	Not Sig.	na
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	Composite:EQ-5D-5F VAS	3 mos	35/32	79(14.9)/80(13.2)	Mean Diff	-1(-7.86,5.86)	Not Sig.	clinically insignificant
Marconcin; 2018/High	5: Self management-Self Management + Exercise	5: Wellness education-Education	QOL:KOOS Quality of Life	3 mos	35/32	48.9(22.8)/55(24.5)	Mean Diff	-6.1(-17.68, 5.48)	Not Sig.	na
Yip; 2007/Moderate	5: Self management-self management + exercise + usual care	5: Placebo/Control-control (usual care)	Pain:VAS pain improvement	16 wks	86/90	11.88(18.91)/1.76(13.47)	Mean Diff	10.12(5.21,15.03)	Group 2	some may benefit
Yip; 2007/Moderate	5: Self management-self management + exercise + usual care	5: Placebo/Control-control (usual care)	Pain:improvement in arthritis self efficacy other symptoms score	16 wks	86/90	6.46(8.21)/2.54(7.11)	Mean Diff	3.92(1.63,6.21)	Group 1	na
Yip; 2007/Moderate	5: Self management-self management + exercise + usual care	5: Placebo/Control-control (usual care)	Pain:improvement in arthritis self efficacy pain score	16 wks	86/90	6.89(12.64)/1.54(6.05)	Mean Diff	5.35(2.37,8.33)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yip; 2007/Moderate	5: Self management-self management + exercise + usual care	5: Placebo/Control-control (usual care)	Function:hours of light exercize per week improvement	16 wks	86/90	2.11(3.78)/0.34(2.23)	Mean Diff	1.77(0.84,2.7)	Group 1	na
Yip; 2007/Moderate	5: Self management-self management + exercise + usual care	5: Placebo/Control-control (usual care)	Composite:Health assessment Questionnaire improvement	16 wks	86/90	0.85(2.17)/0.6(1.9)	Mean Diff	0.25(-0.36,0.86)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	52 wks	73/75	-0.7(0.2)/-0.6(0.3)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	52 wks	73/75	-0.7(0.2)/-0.6(0.3)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	12 wks	73/75	-0.8(0.1)/-0.6(0.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Catastrophizing Scale(difference in deltas)	32 wks	73/75	-0.6(0.2)/-0.5(0.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Global Change Improvement (high LFU)	52 wks	122	none	Relative Risk	Sig ($p < 0.05$)	PCST	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Global Change Improvement (high LFU)	32 wks	121	none	Relative Risk	1.1(0.8,1.4)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:Pain Global Change Improvement (high LFU)	12 wks	135	none	Relative Risk	1.3(0.9,1.7)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:VAS Pain (Walking)(difference in deltas)	52 wks	73/75	-27.5(2.9)/-22.2(3.7)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:VAS Pain (Walking)(difference in deltas)	32 wks	73/75	-28.2(3.2)/-17.4(3.7)	Mean Diff	-10.8(-11.92,-9.68)	Group 1	some may benefit
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:VAS Pain (Walking)(difference in deltas)	12 wks	73/75	-33.7(2.5)/-25.4(3.2)	Mean Diff	-8.3(-9.23,-7.37)	Group 1	clinically insignificant
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:VAS Pain(difference in deltas)	12 wks	73/75	-31.4(2.5)/-26(2.9)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:VAS Pain(difference in deltas)	52 wks	73/75	-26.3(2.8)/-24.1(3.2)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:VAS Pain(difference in deltas)	32 wks	73/75	-30.6(2.9)/-21.7(3.3)	Mean Diff	-8.9(-9.91,-7.89)	Group 1	clinically insignificant
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:WOMAC Pain(difference in deltas)	12 wks	73/75	-4.3(0)/-3.4(0.4)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:WOMAC Pain(difference in deltas)	52 wks	73/75	-3.5(0.5)/-3.3(0.5)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Pain:WOMAC Pain(difference in deltas)	32 wks	73/75	-3.7(0)/-2.4(0.4)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:20 Meter Walk (m/s)(difference in deltas)	12 wks	73/75	0.1(0)/0.2(0)	Mean Diff	-0.1	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:20 Meter Walk (m/s)(difference in deltas)	52 wks	73/75	0.2(0)/0.2(0.1)	Mean Diff	0(-0.02,0.02)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:30 Second Stand-to-Sit(difference in deltas)	12 wks	73/75	1.7(0.3)/2.1(0.3)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:30 Second Stand-to-Sit(difference in deltas)	52 wks	73/75	2.2(0.3)/2.7(0.4)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Function Global Change Improvement (high LFU)	32 wks	121	none	Relative Risk	1.1(0.9,1.5)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Function Global Change Improvement (high LFU)	12 wks	135	none	Relative Risk	1.3(1,1.7)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Function Global Change Improvement (high LFU)	52 wks	122	none	Relative Risk	1.3(1.1,1.7)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Physical Activity Scale for the Elderly(difference in deltas)	12 wks	73/75	30(10.3)/17.8(8.6)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Physical Activity Scale for the Elderly(difference in deltas)	52 wks	73/75	36.6(9.1)/27.1(11.4)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Physical Activity Scale for the Elderly(difference in deltas)	32 wks	73/75	37.6(10.6)/15(11.5)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Quadreceps Strength (Nm/kg)(difference in deltas)	52 wks	73/75	0.3(0.1)/0.2(0.1)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Quadreceps Strength (Nm/kg)(difference in deltas)	12 wks	73/75	0.1(0)/0.1(0.1)	Mean Diff	0(-0.02,0.02)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Step Test(difference in deltas)	52 wks	73/75	2.6(0.6)/2.4(0.5)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:Step Test(difference in deltas)	12 wks	73/75	2.1(0.6)/2.2(0.4)	Mean Diff	-0.1(-0.27,0.07)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:WOMAC Function(difference in deltas)	52 wks	73/75	-18.9(1.3)/-15.3(1.6)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:WOMAC Function(difference in deltas)	12 wks	73/75	-19.6(1.1)/-15.3(1.3)	Mean Diff	-4.3(-4.69,-3.91)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	Function:WOMAC Function(difference in deltas)	32 wks	73/75	-17.6(1.4)/-12.5(1.6)	Mean Diff	-5.1(-5.59,-4.61)	Group 1	possibly clinically significant
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:ASES Self Efficacy(difference in deltas)	12 wks	73/75	4.8(0.4)/3.8(0.5)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:ASES Self Efficacy(difference in deltas)	52 wks	73/75	4.5(0.5)/2.9(0.7)	Mean Diff	1.6(1.4,1.8)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:ASES Self Efficacy(difference in deltas)	32 wks	73/75	4.5(0.6)/1.7(0.7)	Mean Diff	2.8(2.59,3.01)	Group 1	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Assessment of QoL 6D(difference in deltas)	12 wks	73/75	0.1(0)/0.1(0)	Mean Diff	0	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Assessment of QoL 6D(difference in deltas)	32 wks	73/75	0.1(0)/0(0)	Mean Diff	0.1	PCST	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Assessment of QoL 6D(difference in deltas)	52 wks	73/75	0.1(0)/0(0)	Mean Diff	0.1	PCST	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Coping Strategies Questionnaire Pain Coping(difference in deltas)	52 wks	73/75	0.2(0.1)/0(0.1)	Mean Diff	0.2(0.17,0.23)	Group 1	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Coping Strategies Questionnaire Pain Coping(difference in deltas)	32 wks	73/75	0.2(0.1)/-0.2(0.1)	Mean Diff	0.4(0.37,0.43)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Coping Strategies Questionnaire Pain Coping(difference in deltas)	12 wks	73/75	0.3(0)/-0.1(0.1)	Mean Diff	0.4(0.38,0.42)	Group 1	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Anxiety Subscale(difference in deltas)	32 wks	73/75	-0.9(0.9)/0.6(0.9)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Anxiety Subscale(difference in deltas)	52 wks	73/75	-1.8(0.6)/0(1.1)	Mean Diff	-1.8(-2.09,-1.51)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Anxiety Subscale(difference in deltas)	12 wks	73/75	-1(0.6)/-1.1(0.5)	Mean Diff	0.1(-0.08,0.28)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Depression Subscale(difference in deltas)	52 wks	73/75	-1.1(0.8)/0.4(0.9)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Depression Subscale(difference in deltas)	32 wks	73/75	-1.7(1)/1(1.2)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Depression Subscale(difference in deltas)	12 wks	73/75	-1(0.6)/-0.9(0.8)	Mean Diff	-0.1(-0.33,0.13)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Stress Subscale(difference in deltas)	32 wks	73/75	0(1.2)/-1.7(1.3)	Mean Diff	NS	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Stress Subscale(difference in deltas)	12 wks	73/75	-0.6(0.8)/-1.3(1)	Mean Diff	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:DASS-21 Stress Subscale(difference in deltas)	52 wks	73/75	-2.1(0.8)/0.9(1.5)	Mean Diff	-3(-3.39,-2.61)	Group 1	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Overall Global Change Improvement (high LFU)	32 wks	121	none	Relative Risk	1.2(1,1.6)	Not Sig.	na
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Overall Global Change Improvement (high LFU)	12 wks	135	none	Relative Risk	1.3(1,18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2016/Moderate	5: Self management-Pain Coping Skills Training + Exercise(45 min PCST + 25 min exercise x10 sessions over 12 weeks)	5: Placebo/Control-Control (Exercise Alone)(25 min exercise x10 sessions over 12 weeks)	QOL:Overall Global Change Improvement (high LFU)	52 wks	122	none	Relative Risk	1.3(1.1,1.6)	Group 1	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Pain:SF-36 Pain Index(deltas)	4 wks	114/91	-0.44(19.2)/0.62(15.7)	Mean Diff	-1.06(-5.87,3.75)	Not Sig.	clinically insignificant
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Pain:SF-36 Pain Index(deltas)	8 wks	114/91	-0.44(19.2)/-3.35(12.68)	Mean Diff	2.91(-1.5,7.32)	Not Sig.	clinically insignificant
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Function:SF-36 Physical Functioning(deltas)	4 wks	114/91	-3.1(20.9)/-2.2(19.4)	Mean Diff	-0.9(-6.47,4.67)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Function:SF-36 Physical Functioning(deltas)	8 wks	114/91	-3.1(20.9)/0.62(9.5)	Mean Diff	-3.72(-8.06,0.62)	Not Sig.	inconclusive
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Function:SF-36 Role Physical(deltas)	8 wks	114/91	3.5(45.5)/0.82(25.1)	Mean Diff	2.68(-7.2,12.56)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Function:SF-36 Role Physical(deltas)	4 wks	114/91	3.5(45.5)/-4(43.5)	Mean Diff	7.5(-4.81,19.81)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Composite:WOMAC function (Taiwanese Version)(deltas)	8 wks	114/91	2.7(33)/2.5(7.8)	Mean Diff	0.2(-6.13,6.53)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	Composite:WOMAC function (Taiwanese Version)(deltas)	4 wks	114/91	3.2(34)/1.5(20.3)	Mean Diff	1.7(-5.85,9.25)	Not Sig.	clinically insignificant
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Emotional Well-Being(deltas)	4 wks	114/91	0.49(16.2)/-0.7(12.6)	Mean Diff	1.19(-2.78,5.16)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Emotional Well-Being(deltas)	8 wks	114/91	0.49(16.2)/-3.3(13.5)	Mean Diff	3.79(-0.3,7.88)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 General Health Perceptions(deltas)	8 wks	114/91	2.6(18.7)/-3.9(12.2)	Mean Diff	6.5(2.22,10.78)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 General Health Perceptions(deltas)	4 wks	114/91	3.2(17.5)/-3.5(16.5)	Mean Diff	6.7(2,11.4)	Group 1	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Mental Component Score(deltas)	4 wks	114/91	2.1(9.3)/-0.33(7.9)	Mean Diff	2.43(0.06,4.8)	Group 1	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Mental Component Score(deltas)	8 wks	114/91	0.86(8.5)/-1.7(6)	Mean Diff	2.56(0.56,4.56)	Group 1	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Physical Component Score(deltas)	8 wks	114/91	0.19(10.7)/-0.76(6.2)	Mean Diff	0.95(-1.41,3.31)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Physical Component Score(deltas)	4 wks	114/91	0.06(9.8)/-1.2(9.7)	Mean Diff	1.26(-1.44,3.96)	Not Sig.	inconclusive
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Role Emotional(deltas)	4 wks	114/91	2.9(45.1)/-7.3(36.7)	Mean Diff	10.2(-1.07,21.47)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Role Emotional(deltas)	8 wks	114/91	2.9(45.1)/-0.73(22.8)	Mean Diff	3.63(-5.95,13.21)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Social Functioning(deltas)	4 wks	114/91	-0.77(18.6)/-0.37(20.8)	Mean Diff	-0.4(-5.91,5.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Social Functioning(deltas)	8 wks	114/91	-0.77(18.6)/-6(18.5)	Mean Diff	5.23(0.09,10.37)	Group 1	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Vitality(deltas)	4 wks	114/91	2(15.9)/1.7(15.1)	Mean Diff	0.3(-3.99,4.59)	Not Sig.	na
Kao; 2012/Moderate	5: Self management-Self-Management(20 minedu; 20 min exercise; 40 min discussion sessions; x1/wk)	5: Placebo/Control-Control	QOL:SF-36 Vitality(deltas)	8 wks	114/91	2.3(16.6)/-0.27(12.1)	Mean Diff	2.57(-1.39,6.53)	Not Sig.	na

PICO 5: Exercise and Activity

Cognitive Behavior vs. Control

Table 22: Cognitive Behavioral Therapy vs Control

Quality: H=High; M=Moderate; L=Low	H	M			
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Heiminen; 2015	Focht; 2012	Focht; 2017	Smith; 2015	Lerman; 2017
Function					
SF-36 Role Physical	●				
400-m Walk Time (s)		●			
Mobility-Related Self-Efficacy(unclear range)			●		
Satisfaction with Physical Function			●		
Weekly MVPA (min)(Moderate to Vigorous Physical Activity)		↑			
Weekly Total Physical Activity (min)		↑			
Other					
Insomnia Severity Index				↑	
Sleep Efficiency - Actigraphy				●	
Sleep Efficiency - PDF Diary				↑	
Sleep Efficiency - Polysomnography				●	
Sleep Latency - Actigraphy(scale direction?)				●	
Sleep Latency - PDF Diary(scale direction?)				↑	
Sleep Latency - Polysomnography(scale direction?)				●	
Total Sleep Time - Actigraphy				↓	
Total Sleep Time - PDA Diary				●	
Total Sleep Time - Polysomnography				●	
Wake After Sleep Onset - Actigraphy				●	
Wake After Sleep Onset - PDA Diary				↑	
Wake After Sleep Onset - Polysomnography				●	
Pain					
Conditioned Pain Modulation				●	
Daytime Catastrophizing (Diary)					●
Nocturnal Catastrophizing (Diary)					●
Pain Catastrophizing Scale					●
Pain Catastrophizing(unclear scale direction)	●				
Pain Self-Efficacy(unclear scale direction)	●				

Table 22 Continued: Cognitive Behavioral Therapy vs Control

Quality: H=High; M=Moderate; L=Low	H	M			
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Heiminen; 2015	Focht; 2012	Focht; 2017	Smith; 2015	Lerman; 2017
calculable MID outcomes					
WOMAC Function	●				
WOMAC Stiffness	●				
WOMAC Pain	●			●	
VAS Pain				●	
SF-36 Physical Functioning	●				
SF-36 Pain Index	●				
VAS Pain (Average; 3 mo)	●				
VAS Pain (Average; last week)	●				
VAS Pain (Worst; 3 mo)	●				
VAS Pain (Worst; last week)	●				
QOL					
SF-36 Role Emotional	●				
SF-36 Social Functioning	●				
SF-36 Vitality	●				
SF-36 General Health Perceptions	●				
Beck Anxiety Inventory(unclear scale direction)	●				
Beck Depression Inventory(unclear scale direction)	●				
Global Assessment of Change	●				
HRQoL 15D(unclear scale)	●				
Life Satisfaction(unclear scale direction)	●				
SF - 36 Emotional Well-Being	●				
SF-36 Health Change	●				
Self-Regulatory Self-Efficacy(unclear range)			↑		
Sense of Coherenece(unclear scale direction)	●				
Tampa Scale of Kinesiophobia(unclear scale direction)	●				

Evidence Table 27 20: Cognitive Behavioral Therapy vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Conditioned Pain Modulation	6 mos	35/38	1.14(0.19)/1.12(0.21)	Mean Diff	0.02(-0.07,0.11)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Conditioned Pain Modulation	3 mos	32/42	1.26(0.28)/1.15(0.23)	Mean Diff	0.11(-0.01,0.23)	Not Sig.	na
Lerman; 2017/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Daytime Catastrophizing (Diary)	3 mos	36/42	21.7(22.26)/23.12(24.06)	Mean Diff	-1.42(-11.87, 9.03)	Not Sig.	na
Lerman; 2017/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Daytime Catastrophizing (Diary)	6 mos	32/39	20.89(23.77)/19.93(22.89)	Mean Diff	0.96(-10.18, 12.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lerman; 2017/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Nocturnal Catastrophizing (Diary)	3 mos	32/42	16.83(17.45)/18.89(21.46)	Mean Diff	-2.06(-11.08, 6.96)	Not Sig.	na
Lerman; 2017/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Nocturnal Catastrophizing (Diary)	6 mos	32/38	17.12(21.41)/15.8(20.36)	Mean Diff	1.32(-8.71,11.35)	Not Sig.	na
Lerman; 2017/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Pain Catastrophizing Scale	6 mos	36/41	10.51(9.77)/11.31(11.33)	Mean Diff	-0.8(-5.59,3.99)	Not Sig.	na
Lerman; 2017/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:Pain Catastrophizing Scale	3 mos	35/41	10.87(9.47)/9.95(11.06)	Mean Diff	0.92(-3.77,5.61)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:Pain Catastrophizing(unclear scale direction)	12 mos	55/56	15.5(9.06)/12.2(9.34)	Mean Diff	3.3(-0.16,6.76)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:Pain Self-Efficacy(unclear scale direction)	12 mos	55/56	43.1(11.28)/46.2(10.64)	Mean Diff	-3.1(-7.23,1.03)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:SF-36 Pain Index	12 mos	55/56	57.3(21.27)/57.4(20.16)	Mean Diff	-0.1(-7.9,7.7)	Not Sig.	inconclusive
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:VAS Pain	3 mos	32/42	35.59(20.87)/39.79(22.6)	Mean Diff	-4.2(-14.33, 5.93)	Not Sig.	clinically insignificant
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:VAS Pain	6 mos	35/38	37.52(22.5)/36.64(22.35)	Mean Diff	0.88(-9.6,11.36)	Not Sig.	clinically insignificant
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:VAS Pain (Average; 3 mo)	12 mos	55/56	5.2(2.22)/5.4(2.24)	Mean Diff	-0.2(-1.04,0.64)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:VAS Pain (Average; last week)	12 mos	55/56	5(2.4)/4.9(2.24)	Mean Diff	0.1(-0.77,0.97)	Not Sig.	clinically insignificant
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:VAS Pain (Worst; 3 mo)	12 mos	55/56	6.4(2.03)/6.6(2.05)	Mean Diff	-0.2(-0.97,0.57)	Not Sig.	clinically insignificant
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:VAS Pain (Worst; last week)	12 mos	55/56	6.1(2.4)/5.9(2.24)	Mean Diff	0.2(-0.67,1.07)	Not Sig.	clinically insignificant
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:WOMAC Pain	3 mos	32/42	3.53(2.34)/3.61(2.81)	Mean Diff	-0.08(-1.27,1.11)	Not Sig.	inconclusive
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Pain:WOMAC Pain	6 mos	35/38	4.03(2.38)/3.54(2.75)	Mean Diff	0.49(-0.71,1.69)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Pain:WOMAC Pain (VAS Version)	12 mos	55/56	35.6(20.53)/39.5(21.47)	Mean Diff	-3.9(-11.8,4)	Not Sig.	inconclusive
Focht; 2012/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:400-m Walk Time (s)	3 mos	40/40	347(95.6)/382.3(112.2)	Mean Diff	-35.3(-81.72, 11.12)	Not Sig.	na
Focht; 2012/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:400-m Walk Time (s)	12 mos	40/40	351.3(95.5)/419.4(196.9)	Mean Diff	-68.1(-137.4, 1.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Focht; 2017/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Mobility-Related Self-Efficacy(unclear range)	3 mos	40/40	81.42(26.28)/74.17(27.05)	Mean Diff	7.25(-4.62,19.12)	Not Sig.	na
Focht; 2017/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Mobility-Related Self-Efficacy(unclear range)	12 mos	40/40	81.54(27)/71.63(28.25)	Mean Diff	9.91(-2.39,22.21)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Function:SF-36 Physical Functioning	12 mos	55/56	48(24.23)/49.4(21.66)	Mean Diff	-1.4(-10.05, 7.25)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Function:SF-36 Role Physical	12 mos	55/56	44.4(36.81)/44.5(39.58)	Mean Diff	-0.1(-14.48, 14.28)	Not Sig.	na
Focht; 2017/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Satisfaction with Physical Function	3 mos	40/40	1.33(1.25)/1.38(1.02)	Mean Diff	-0.05(-0.56,0.46)	Not Sig.	na
Focht; 2017/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Satisfaction with Physical Function	12 mos	40/40	1.22(1.11)/0.8(1.37)	Mean Diff	0.42(-0.14,0.98)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Function:WOMAC Function (VAS Version)	12 mos	55/56	36.5(21.64)/36.7(21.28)	Mean Diff	-0.2(-8.28,7.88)	Not Sig.	inconclusive
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	Function:WOMAC Stiffness (VAS Version)	12 mos	55/56	46.2(24.6)/49(21.28)	Mean Diff	-2.8(-11.46, 5.86)	Not Sig.	inconclusive
Focht; 2012/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Weekly MVPA (min)(Moderate to Vigorous Physical Activity)	3 mos	40/40	83.4(77)/44.8(62.3)	Mean Diff	38.6(7.4,69.8)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Focht; 2012/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Weekly MVPA (min)(Moderate to Vigorous Physical Activity)	12 mos	40/40	81.1(82)/33(48.9)	Mean Diff	48.1(17.94,78.26)	Group 1	na
Focht; 2012/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Weekly Total Physical Activity (min)	3 mos	40/40	410.3(246.4)/299.1(179.2)	Mean Diff	111.2(15.15, 207.25)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Focht; 2012/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	Function:Weekly Total Physical Activity (min)	12 mos	40/40	404.5(251.8)/278.3(179.2)	Mean Diff	126.2(28.75, 223.65)	Group 1	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:Beck Anxiety Inventory(unclear scale direction)	12 mos	55/56	8(5.55)/7.1(6.35)	Mean Diff	0.9(-1.34,3.14)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:Beck Depression Inventory(unclear scale direction)	12 mos	55/56	5.8(3.88)/5.9(6.72)	Mean Diff	-0.1(-2.17,1.97)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:Global Assessment of Change	12 mos	55/56	-0.3(3.51)/-0.8(3.17)	Mean Diff	0.5(-0.76,1.76)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:HRQoL 15D(unclear scale)	12 mos	55/56	0.82(0.09)/0.85(0.09)	Mean Diff	-0.03(-0.06,0)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:Life Satisfaction(unclear scale direction)	12 mos	55/56	7.9(2.59)/7.7(3.36)	Mean Diff	0.2(-0.93,1.33)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:SF - 36 Emotional Well-Being	12 mos	55/56	75.3(15.54)/78.5(17.92)	Mean Diff	-3.2(-9.51,3.11)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:SF-36 General Health Perceptions	12 mos	55/56	53.1(16.83)/58.2(22.22)	Mean Diff	-5.1(-12.51, 2.31)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:SF-36 Health Change	12 mos	55/56	46.6(22.19)/47.4(22.03)	Mean Diff	-0.8(-9.12,7.52)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:SF-36 Role Emotional	12 mos	55/56	67.9(36.44)/74.7(34.91)	Mean Diff	-6.8(-20.23, 6.63)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:SF-36 Social Functioning	12 mos	55/56	75(25.15)/82.8(19.42)	Mean Diff	-7.8(-16.27, 0.67)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:SF-36 Vitality	12 mos	55/56	62.7(20.34)/67.5(21.47)	Mean Diff	-4.8(-12.67, 3.07)	Not Sig.	na
Focht; 2017/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	QOL:Self-Regulatory Self-Efficacy(unclear range)	3 mos	40/40	63.5(18.77)/52.5(19.98)	Mean Diff	11(2.37,19.63)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Focht; 2017/Moderate	5: Cognitive therapy-Group-mediated Cognitive Behavioral Exercise + Traditional Supervised Exercise(36 contact hrs; 27 sessions (80 minutes (60 traditional + 20 GMCB))	5: Placebo/Control-Control (Traditional Supervised Exercise Alone)(36 contact hrs; 36 sessions (60 minutes exercise))	QOL:Self-Regulatory Self-Efficacy(unclear range)	12 mos	40/40	62.25(16.09)/46.94(22.5)	Mean Diff	15.31(6.59,24.03)	Group 1	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:Sense of Coherenece(unclear scale direction)	12 mos	55/56	59.4(5.18)/59.4(5.6)	Mean Diff	0(-2.03,2.03)	Not Sig.	na
Heiminen; 2015/High	5: Cognitive therapy-Cognitive Behavioural Therapy(2h session 1x/week x 6 weeks)	5: Placebo/Control-Control (No CBT)	QOL:Tampa Scale of Kinesiophobia(unclear scale direction)	12 mos	55/56	33(7.58)/32.8(10.83)	Mean Diff	0.2(-3.32,3.72)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Insomnia Severity Index	3 mos	32/42	10.26(5.91)/10.93(5.82)	Mean Diff	-0.67(-3.42,2.08)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Insomnia Severity Index	6 mos	35/38	8.9(5.99)/12.3(6.54)	Mean Diff	-3.4(-6.32,-0.48)	Group 1	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Efficiency - Actigraphy	6 mos	35/38	0.67(0.15)/0.67(0.14)	Mean Diff	0(-0.07,0.07)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Efficiency - Actigraphy	3 mos	32/42	0.69(0.16)/0.67(0.14)	Mean Diff	0.02(-0.05,0.09)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Efficiency - PDF Diary	6 mos	35/38	0.85(0.08)/0.82(0.09)	Mean Diff	0.03(-0.01,0.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Efficiency - PDF Diary	3 mos	32/42	0.88(0.06)/0.81(0.12)	Mean Diff	0.07(0.03,0.11)	Group 1	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Efficiency - Polysomnography	3 mos	32/42	0.81(0.12)/0.8(0.12)	Mean Diff	0.01(-0.05,0.07)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Efficiency - Polysomnography	6 mos	35/38	0.82(0.11)/0.79(0.13)	Mean Diff	0.03(-0.03,0.09)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Latency - Actigraphy(scale direction?)	6 mos	35/38	22.16(17.59)/22.31(19.76)	Mean Diff	-0.15(-8.87,8.57)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Latency - Actigraphy(scale direction?)	3 mos	32/42	30.18(57.63)/22.6(17.08)	Mean Diff	7.58(-13.78, 28.94)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Latency - PDF Diary(scale direction?)	3 mos	32/42	15.75(9.32)/29.11(24.2)	Mean Diff	-13.36(-21.54,-5.18)	Group 1	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Latency - PDF Diary(scale direction?)	6 mos	35/38	20.57(13.85)/26.86(23.69)	Mean Diff	-6.29(-15.29, 2.71)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Latency - Polysomnography(scale direction?)	6 mos	35/38	26.25(36.24)/28.98(58.85)	Mean Diff	-2.73(-25.4,19.94)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Sleep Latency - Polysomnography(scale direction?)	3 mos	32/42	16.4(17.17)/25.15(24.12)	Mean Diff	-8.75(-18.32, 0.82)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Total Sleep Time - Actigraphy	6 mos	35/38	297.43(76.76)/333.83(77.98)	Mean Diff	-36.4(-72.54,-0.26)	Group 2	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Total Sleep Time - Actigraphy	3 mos	32/42	300.75(80.61)/306.4(82.17)	Mean Diff	-5.65(-43.72, 32.42)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Total Sleep Time - PDA Diary	3 mos	32/42	385.93(57.93)/386.04(72)	Mean Diff	-0.11(-30.23, 30.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Total Sleep Time - PDA Diary	6 mos	35/38	382.94(65.84)/388.89(62.43)	Mean Diff	-5.95(-35.96, 24.06)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Total Sleep Time - Polysomnography	6 mos	35/38	356.6(74.67)/375.12(69.65)	Mean Diff	-18.52(-52.31, 15.27)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Total Sleep Time - Polysomnography	3 mos	32/42	361.14(60.34)/360.47(85.38)	Mean Diff	0.67(-33.12, 34.46)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Wake After Sleep Onset - Actigraphy	3 mos	32/42	89.98(50.76)/105.01(68.44)	Mean Diff	-15.03(-42.66, 12.6)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Wake After Sleep Onset - Actigraphy	6 mos	35/38	101.83(72.8)/106.07(61.49)	Mean Diff	-4.24(-35.86, 27.38)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Wake After Sleep Onset - PDA Diary	3 mos	32/42	22.57(20.03)/42.25(31.69)	Mean Diff	-19.68(-31.72,-7.64)	Group 1	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Wake After Sleep Onset - PDA Diary	6 mos	35/38	31.54(27.46)/37.48(30.81)	Mean Diff	-5.94(-19.54, 7.66)	Not Sig.	na
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Wake After Sleep Onset - Polysomnography	6 mos	35/38	58.01(46.84)/74.22(55.43)	Mean Diff	-16.21(-40.1,7.68)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smith; 2015/Moderate	5: Cognitive therapy-CBT-Insomnia Specific(45min/session x8 sessions)	5: Placebo/Control-Placebo (Behavioral Desensitization)(45min/session x8 sessions)	Other:Wake After Sleep Onset - Polysomnography	3 mos	32/42	70.45(60.21)/62.25(46.74)	Mean Diff	8.2(-17.55, 33.95)	Not Sig.	na

PICO 5: Exercise and Activity

Patient Education vs Control

Table 23: Patient Education vs Control

Quality: H=High; M=Moderate; L=Low	H						M													L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Saffari; 2018	Somers; 2012	Cagnin; 2019	Gilbert; 2018	Baker; 2019	Berman; 2004	Brosseau; 2012	Allen; 2017	O'Brien; 2018	Allen; 2010	Bennell; 2017	Marra; 2012	Rezende; 2017	Sadeghi; 2019	Rodrigues da Silva; 2017	Rini; 2015	Moseng; 2020	Chen; 2020	Ravaud; 2009	Saraboon; 2015	Aree-Ue; 2017
Function																					
WOMAC Function							●					↑									
WOMAC Stiffness							●					●									
SF-36 Physical Functioning							↓														
SF-36 Role Physical							↓														
KOOS Activities of Daily Living			↑																		
KOOS Symptoms			↑																		
Timed Up and Go Test (sec)							●						●		↑					↓	↑
SF-12 Physical Component Score	↑								↓												
6MWT(m)	↑						●								●						
7-Day POD - Leisure Time Activities + Other(7 Day Physical Activity Recall;units?)							↑														
7-Day POD - Leisure Time Activities(7 Day Physical Activity Recall;units?)							●														
7-Day POD - Other Domestic Activities + Other(7 Day Physical Activity Recall;units?)							↑														
7-Day POD - Other Domestic Activities(7 Day Physical Activity Recall;units?)							●														
AIMS2 Arm Function(unclear scale?)							●														
AIMS2 Hand and Finger(unclear scale?)							●														
AIMS2 Level of Tension(unclear scale?)							●														
AIMS2 Mobility(unclear scale?)							●														
AIMS2 Physical Component(unclear scale?)							↓														
AIMS2 Walking and Bending(unclear scale?)							●														
AIMS2 Work(small N - exclude this outcome)							●														
Five Repetition Sit to Stand Test (s)															↑						
Gait Speed							●														
KOOS Sports and Recreation			●																		
SF-36 Standardized Physical Component							↓														

Table 23 Continued: Patient Education vs Control

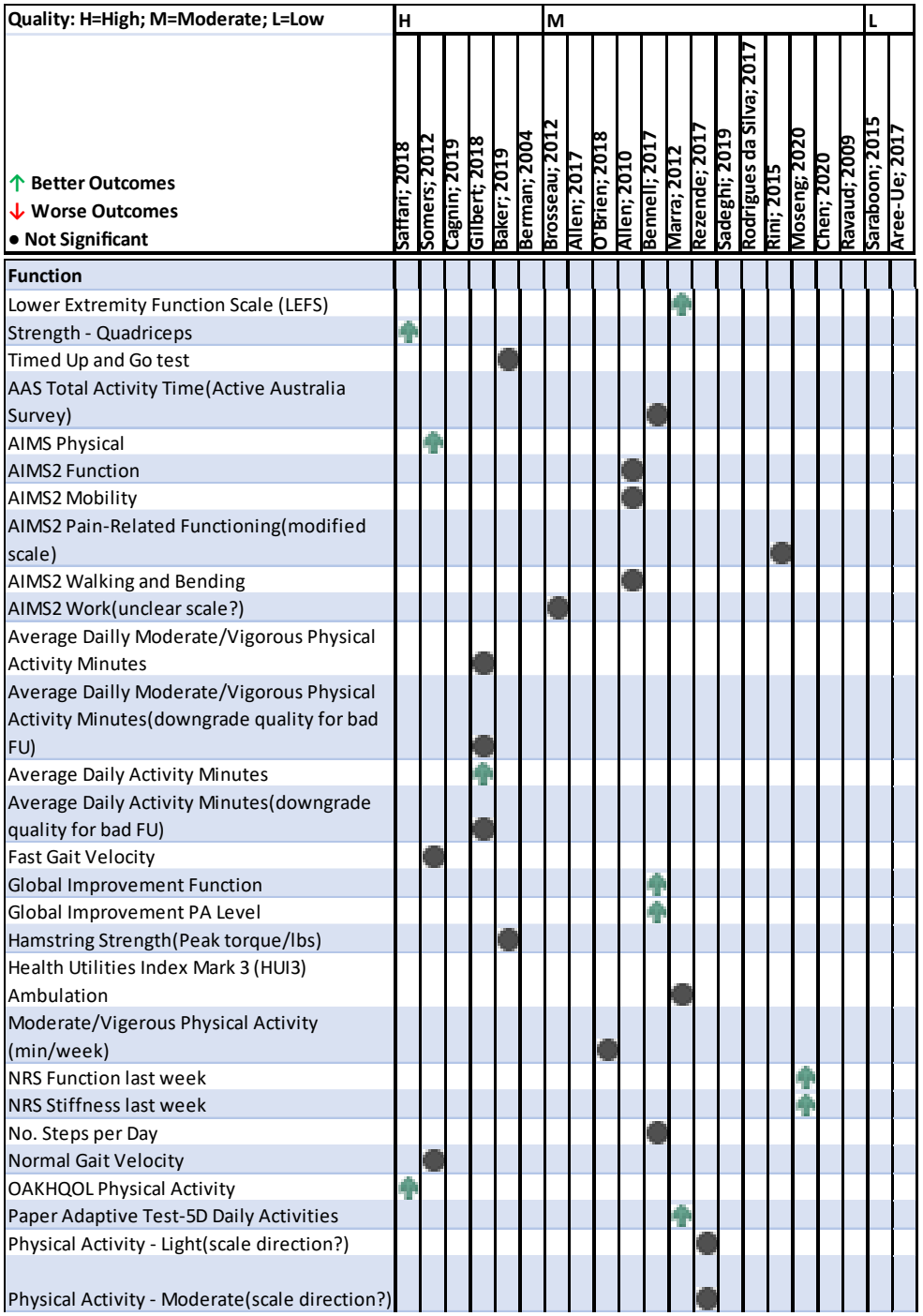


Table 23 Continued: Patient Education vs Control

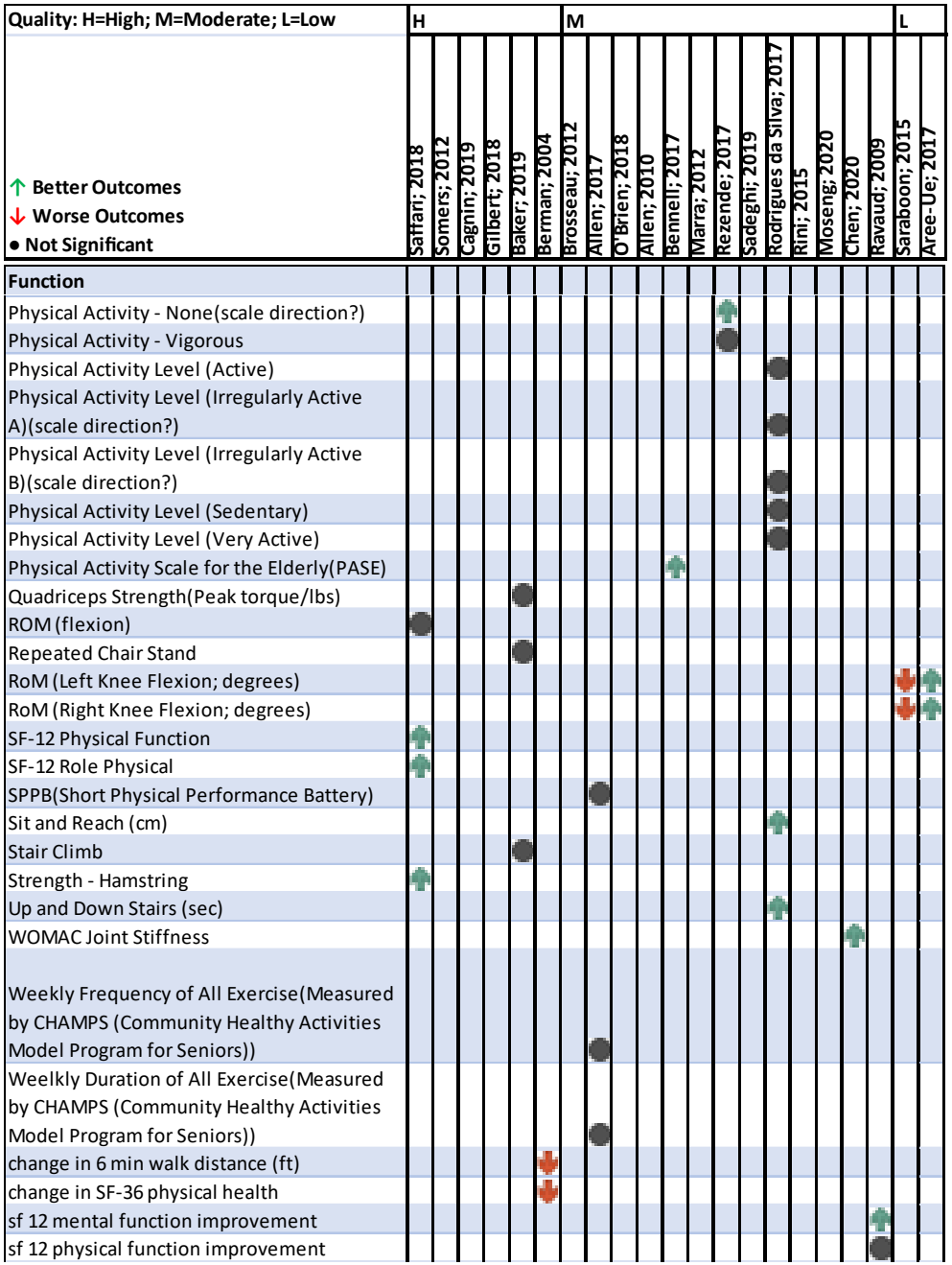


Table 23 Continued: Patient Education vs Control

Quality: H=High; M=Moderate; L=Low	H						M												L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Saffari; 2018	Somers; 2012	Cagnin; 2019	Gilbert; 2018	Baker; 2019	Berman; 2004	Brosseau; 2012	Allen; 2017	O'Brien; 2018	Allen; 2010	Bennell; 2017	Marra; 2012	Rezende; 2017	Sadeghi; 2019	Rodrigues da Silva; 2017	Rini; 2015	Moseng; 2020	Chen; 2020	Ravaud; 2009	Saraboon; 2015	Aree-Ue; 2017
Function																					
Five Times Sit to Stand													↑								
calculable MID outcomes																					
WOMAC Total								●	●				●	●							
WOMAC Function		↑		↑	●	↓		●	●		●			●					●		
WOMAC Stiffness		↑							●					●							
WOMAC Pain		↑		↑	●	↓		●	●		●		●	●							
VAS Pain									●		●		●	●						↓	
SF-36 Physical Functioning							●														
SF-36 Physical component				●																	
VAS Pain Walking											●										
SF-36 Standardized Physical Component							●														
SF-36 Pain Index							●														
VAS Pain (Left Knee)																				↓	↑
VAS Pain (Right Knee)																				↓	↑
EuroQoL- VAS	●																				

Table 23 Continued: Patient Education vs Control

Quality: H=High; M=Moderate; L=Low	H				M									
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Saffari; 2018	Somers; 2012	Cagnin; 2019	Gilbert; 2018	Brosseau; 2012	Allen; 2017	O'Brien; 2018	Allen; 2010	Bennell; 2017	Marra; 2012	Rezende; 2017	Rini; 2015	Moseng; 2020	Chen; 2020
Composite														
WOMAC Total					↓					↑				
Lequesne Index Score											●			
AIMS2 Symptoms Component(unclear scale?)					↓									
Arthritis Self-Efficacy		↑						●						
EuroQoL-5D-3L	↑													
Global Improvement Overall									↑					
Health Utilities Index Mark 3 (HUI3) Total										●				
KOOS Overall score			↑											
Overall Quality of Care Pass Rate (%)										↑				
Weight Self-Efficacy		↑												
Other														
Daily hours in sitting position													●	
NRS Disease activity last week													↑	
OAKHQOL Social Functioning	●													
OAKHQOL Social Support	↑													
SF-12 Role Emotional	↑													
SF-12 Social Function	↑													
SF-12 Vitality	●													
Pain														
WOMAC Pain					●					↑				↑
VAS Pain								↑						
KOOS Pain			↑											
AIMS2 Arthritis Pain(unclear scale?)					↑									
AIMS Pain		↑												
AIMS2 Pain								●						
AIMS2 Pain Subscale												●		
Global Improvement Pain									●					
Health Utilities Index Mark 3 (HUI3) Pain										↑				
NRS Pain last week													↑	
OAKHQOL Pain	↑													
Pain Catastrophizing		↑												
Paper Adaptive Test-5D Pain										↑				
SF-12 Bodily Pain	↑													
VAS Pain - Area Under the Curve							●							

Table 23 Continued: Patient Education vs Control

Quality: H=High; M=Moderate; L=Low	H				M									
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Saffari; 2018	Somers; 2012	Cagnin; 2019	Gilbert; 2018	Brosseau; 2012	Allen; 2017	O'Brien; 2018	Allen; 2010	Bennell; 2017	Marra; 2012	Rezende; 2017	Rini; 2015	Moseng; 2020	Chen; 2020
Adverse events														
Joint Replacement Surgery						●								
Joint Swelling	●													
Poor Sleep Quality							●							
Received Surgery of Knee Pain							●							
QOL														
SF-36 Role Emotional					●									
SF-36 Social Functioning					●									
SF-36 Vitality					●									
KOOS Quality of Life			●											
SF-12 Mental Component Score	↑						↑							
AIMS2 Affect Component(unclear scale?)					●									
AIMS2 Arthritis Impact(unclear scale?)					↓									
AIMS2 Health Perception(unclear scale?)					●									
AIMS2 Household Tasks(unclear scale?)					●									
AIMS2 Mood(unclear scale?)					●									
AIMS2 Role Component(small N - exclude this outcome)					●									
AIMS2 Satisfaction(unclear scale?)					●									
AIMS2 Self Care(unclear scale?)					●									
AIMS2 Social Activity(unclear scale?)					●									
AIMS2 Social Interaction Component(unclear scale?)					●									
AIMS2 Support From Family(unclear scale?)					●									
SF-36 General Health Perceptions					●									
SF-36 Health Transition Item(scale?)					●									
SF-36 Mental Component Score				↑										
SF-36 Mental Health Index					●									
SF-36 Standardized Mental Component					●									
AIMS Psychological		↑												
AIMS2 Affect								●						
AIMS2 Pain-Related Anxiety												●		
Assessment of QoL									●					
DASS-21 Anxiety Subscale							●							
DASS-21 Depression Subscale							●							
DASS-21 Stress Subscale							●							
Fear Avoidance Beliefs (FABQ)(Fear Avoidance Beliefs Quesionnaire)							↓							

Table 23 Continued: Patient Education vs Control

Quality: H=High; M=Moderate; L=Low	H				M									
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Saffari; 2018	Somers; 2012	Cagnin; 2019	Gilbert; 2018	Brosseau; 2012	Allen; 2017	O'Brien; 2018	Allen; 2010	Bennell; 2017	Marra; 2012	Rezende; 2017	Rini; 2015	Moseng; 2020	Chen; 2020
QOL														
Global Percieved Effect(Change from Baseline)							●							
H/KOOS QoL subscale mean													●	
Negative Effect(20-Item Positive and Negative Effect Scale)												●		
OAKHQOL Mental Health	↑													
PHQ-8(8 Item Patient Health Questionnaire)						●								
Pain Attitude (SOPA)(Survey of Pain Attitudes)							●							
Positive Effect(20-Item Positive and Negative Effect Scale)												↓		
SF-12 General Health	↑													
SF-12 Mental Health	↑													
SF-36 Mental Component Score(downgrade quality for bad FU)				●										
Self-Efficacy for Pain Management												↑		
Sleep Time (hr/day)									●					

Evidence Table 2821: Patient Education vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	function:Five Times Sit to Stand	1 yrs	150/48	18.17(5.96)/19.66(10.26)	Mean Diff	-1.49(-4.61,1.63)	Not Sig.	na
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	function:Five Times Sit to Stand	2 yrs	148/47	19.43(6.65)/23.24(10.49)	Mean Diff	-3.81(-7.06,-0.56)	Group 1	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Pain:AIMS Pain	2 yrs	62/60	4(1.18)/4.4(1.35)	Mean Diff	-0.4(-0.86,0.06)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Pain:AIMS Pain	2 yrs	62/59	4(1.18)/4.7(1.53)	Mean Diff	-0.7(-1.19,-0.21)	Group 1	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Pain:AIMS2 Arthritis Pain(unclear scale?)	12 mos	44/44	3.79(2.29)/3.49(2.38)	Mean Diff	0.3(-0.69,1.29)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Pain:AIMS2 Arthritis Pain(unclear scale?)	18 mos	42/44	3.64(2.16)/4.4(2.41)	study reported p value	p <.05	Behavioral Intervention + Supervised Walking	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	Pain:AIMS2 Pain	12 mos	343	none	Mean Diff.	-0.4(-0.8,0.1)	Not Sig.	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	Pain:AIMS2 Pain	12 mos	344	none	Mean Diff.	-0.6(-1,0.2)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	Pain:AIMS2 Pain Subscale	9 wks	58/55	4.07(1.99)/4.62(1.79)	Mean Diff	-0.55(-1.25,0.15)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	Pain:AIMS2 Pain Subscale	5 wks	58/55	4.2(1.68)/4.75(2.07)	Mean Diff	-0.55(-1.26,0.16)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:Global Improvement Pain	18 mos	168	none	odds ratio	1.1(0.5,2.1)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:Global Improvement Pain	6 mos	168	none	odds ratio	1.7(0.8,3.5)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:Global Improvement Pain	12 mos	168	none	odds ratio	2.3(1,5.2)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Pain:Health Utilities Index Mark 3 (HUI3) Pain	6 mos	139	none	Mean Difference	0.08(0,0.15)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Pain:Health Utilities Index Mark 3 (HUI3) Pain	3 mos	139	none	Mean Difference	0.09(0.02,0.15)	Group 1	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Knee Kinesiography Exam + Current Medical Management	Pain:KOOS Pain	6 mos	134/102	6.3(16.09)/6.9(14.51)	Mean Diff	-0.6(-4.54,3.34)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Pain:KOOS Pain	6 mos	134/213	6.3(16.09)/2.9(14.44)	Mean Diff	3.4(0.04,6.76)	Group 1	na
Cagnin; 2019/High	5: Wellness education-Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Pain:KOOS Pain	6 mos	102/213	6.9(14.51)/2.9(14.44)	Mean Diff	4(0.56,7.44)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Pain:NRS Pain last week	3 mos	242/106	4.4(2)/4.7(2.2)	Mean Diff	-0.3(-0.79,0.19)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Pain:NRS Pain last week	6 mos	239/106	4.2(2.1)/4.7(2.1)	Mean Diff	-0.5(-0.98,-0.02)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Pain:OAKHQOL Pain	3 mos	53/54	54.2(10.8)/42(14.9)	Mean Diff	12.2(7.21,17.19)	Group 1	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Pain:Pain Catastrophizing	2 yrs	62/60	3.8(3.15)/4.9(3.48)	Mean Diff	-1.1(-2.29,0.09)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Pain:Pain Catastrophizing	2 yrs	62/59	3.8(3.15)/5.6(3.45)	Mean Diff	-1.8(-2.99,-0.61)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Pain:Paper Adaptive Test-5D Pain	3 mos	139	none	Mean Difference	2.88(-0.26,6.02)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Pain:Paper Adaptive Test-5D Pain	6 mos	139	none	Mean Difference	3.65(0.4,6.91)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Pain:SF-12 Bodily Pain	3 mos	53/54	59.2(13.8)/45.8(17.3)	Mean Diff	13.4(7.4,19.4)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Pain:SF-36 Pain Index	12 mos	44/44	63.8(21.12)/63.82(19.13)	Mean Diff	-0.02(-8.56,8.52)	Not Sig.	inconclusive
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Pain:SF-36 Pain Index	18 mos	42/44	61.17(18.32)/65.05(18.88)	Mean Diff	-3.88(-11.86, 4.1)	Not Sig.	inconclusive
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:VAS Pain	12 mos	84/84	3.2(2.4)/3.7(2.2)	Mean Diff	-0.5(-1.2,0.2)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:VAS Pain	18 mos	84/84	3.6(2)/4.1(2.8)	Mean Diff	-0.5(-1.24,0.24)	Not Sig.	clinically insignificant
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:VAS Pain	6 mos	84/84	3.2(2.2)/3.8(2.3)	Mean Diff	-0.6(-1.29,0.09)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	22 wks	59/60	6.3(2.4)/6.6(2.3)	Mean Diff	-0.3(-1.15,0.55)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	14 wks	59/60	6.5(2.2)/7(1.8)	Mean Diff	-0.5(-1.23,0.23)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	10 wks	59/60	6.2(2.6)/6.7(2.1)	Mean Diff	-0.5(-1.36,0.36)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	6 wks	59/60	6.3(2.3)/6.3(1.9)	Mean Diff	0(-0.77,0.77)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	18 wks	59/60	6.5(2.2)/6.4(2.6)	Mean Diff	0.1(-0.77,0.97)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	26 wks	59/60	6.6(2.5)/5.9(2.8)	Mean Diff	0.7(-0.26,1.66)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Pain:VAS Pain	2 yrs	148/47	55.31(21.42)/62.35(18.45)	Mean Diff	-7.04(-13.43,-0.65)	Group 1	clinically insignificant
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Pain:VAS Pain	1 yrs	150/48	53.39(23.47)/60.89(23.96)	Mean Diff	-7.5(-15.37, 0.37)	Not Sig.	clinically insignificant
Saraboon; 2015/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain	8 wks	40/43	6.32(1.63)/1.84(1.61)	Mean Diff	4.48(3.77,5.19)	Group 2	clinically significant
Sadeghi; 2019/Moderate	5: Wellness education-Wellness Education for Diet	5: Placebo/Control-Control (No Wellness Education)	Pain:VAS Pain	3 mos	31/31	44.35(20.9)/48.12(21.39)	Mean Diff	-3.77(-14.51, 6.97)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	Pain:VAS Pain	12 mos	344	none	Mean Diff.	-1(-1.5,-0.5)	Group 1	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain	12 mos	343	none	Mean Diff.	-1.1(-1.6,-0.6)	Group 1	na
Saraboon; 2015/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain (Left Knee)	8 wks	40/41	5.29(2.81)/2.5(2.17)	Mean Diff	2.79(1.68,3.9)	Group 2	possibly clinically significant
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain (Left Knee)	6 mos	38/36	1.6(1.2)/3.9(2.8)	Mean Diff	-2.3(-3.32,-1.28)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain (Left Knee)	12 mos	38/36	1.1(1)/4.2(2.7)	Mean Diff	-3.1(-4.06,-2.14)	Group 1	clinically significant
Saraboon; 2015/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain (Right Knee)	8 wks	40/42	5.63(0.91)/2.86(2.11)	Mean Diff	2.77(2.06,3.48)	Group 2	clinically significant
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain (Right Knee)	6 mos	38/36	1.9(1.8)/4.1(2.9)	Mean Diff	-2.2(-3.33,-1.07)	Group 1	possibly clinically significant
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Pain:VAS Pain (Right Knee)	12 mos	38/36	0.8(0.9)/4.5(3.2)	Mean Diff	-3.7(-4.82,-2.58)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:VAS Pain - Area Under the Curve	26 wks	59/60	163.6(55.64)/169(48.19)	Mean Diff	-5.4(-24.32, 13.52)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:VAS Pain Walking	18 mos	84/84	3.2(2.6)/3.5(3.2)	Mean Diff	-0.3(-1.19,0.59)	Not Sig.	clinically insignificant
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:VAS Pain Walking	6 mos	84/84	2.8(2.5)/3.2(2.4)	Mean Diff	-0.4(-1.15,0.35)	Not Sig.	clinically insignificant
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:VAS Pain Walking	12 mos	84/84	3(2.5)/3.7(2.6)	Mean Diff	-0.7(-1.48,0.08)	Not Sig.	clinically insignificant
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Pain:WOMAC Pain	6 mos	57/66	5.31(2.58)/5.49(2.26)	Mean Diff	-0.18(-1.05,0.69)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Pain:WOMAC Pain	3 mos	65/60	5.17(2.44)/6.14(2.17)	Mean Diff	-0.97(-1.79,-0.15)	Group 1	possibly clinically significant
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain	6 mos	128/129	-1.5(3.43)/-1.9(3.73)	Mean Diff	0.4(-0.48,1.28)	Not Sig.	clinically insignificant
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain	12 mos	128/129	-1(3.72)/-1.5(4.02)	Mean Diff	0.5(-0.45,1.45)	Not Sig.	clinically insignificant
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:WOMAC Pain	18 mos	84/84	4.4(3.4)/4.3(3.5)	Mean Diff	0.1(-0.95,1.15)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain	6 wks	50/54	9.2(3.5)/9.8(3.7)	Mean Diff	-0.6(-2,0.8)	Not Sig.	inconclusive
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain	26 wks	37/52	9.5(3.5)/9.5(4.1)	Mean Diff	0(-1.61,1.61)	Not Sig.	clinically insignificant
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Pain:WOMAC Pain	2 yrs	148/47	8.47(3.91)/9(3.33)	Mean Diff	-0.53(-1.69,0.63)	Not Sig.	inconclusive
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Pain:WOMAC Pain	1 yrs	150/48	8.23(3.67)/9(4.17)	Mean Diff	-0.77(-2.11,0.57)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sadeghi; 2019/Moderate	5: Wellness education-Wellness Education for Diet	5: Placebo/Control-Control (No Wellness Education)	Pain:WOMAC Pain	3 mos	31/31	213.5(96.6)/232.01(117)	Mean Diff	-18.51(-73.06, 36.04)	Not Sig.	inconclusive
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Pain:WOMAC Pain	24 mos	52/52	4.63(3.83)/4.46(3.93)	Mean Diff	0.17(-1.34,1.68)	Not Sig.	inconclusive
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain (0-10)	3 mos	139	none	Mean Difference	-0.78(-1.4,-0.16)	Group 1	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Pain:WOMAC Pain (0-10)	6 mos	139	none	Mean Difference	-0.93(-1.59,-0.28)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Pain:WOMAC Pain (VAS Version)	2 yrs	62/60	27.2(12.8)/34.5(14.32)	Mean Diff	-7.3(-12.18,-2.42)	Group 1	possibly clinically significant
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Pain:WOMAC Pain (VAS Version)	2 yrs	62/59	27.2(12.8)/35.5(13.62)	Mean Diff	-8.3(-13.06,-3.54)	Group 1	possibly clinically significant
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Pain:WOMAC Pain (VAS Version)(scale doesn't make sense?)	12 mos	42/43	25.32(15.98)/24.65(15.78)	Mean Diff	0.67(-6.18,7.52)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Pain:WOMAC Pain (VAS Version)(scale doesn't make sense?)	18 mos	42/43	26.16(17.97)/23.6(15.09)	Mean Diff	2.56(-4.61,9.73)	Not Sig.	na
Chen; 2020/Moderate	5: Exercise-Exercise adherance education	5: Placebo/Control-Control	Pain:WOMAC Pain Intensity	24 wks	89/72	16.18(15.94)/22.71(19.57)	Mean Diff	-6.53(-12.18,-0.88)	Group 1	na
Chen; 2020/Moderate	5: Exercise-Exercise adherance education	5: Placebo/Control-Control	Pain:WOMAC Pain Intensity	12 wks	89/72	16.85(15.08)/23.47(17.11)	Mean Diff	-6.62(-11.71,-1.53)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:WOMAC Pain level of improvement	6 mos	84/84	4.2(3)/5.7(3.6)	Mean Diff	.8(-.5, 2)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Pain:WOMAC Pain level of improvement	12 mos	84/84	4.3(3.3)/5.4(3.4)	Mean Diff	1.5(-.3,3.4)	Not Sig.	inconclusive
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Pain:WOMAC Pain(downgrade quality for bad FU)	24 mos	35/40	3.96(2.21)/4.71(2.94)	Mean Diff	-0.75(-1.94,0.44)	Not Sig.	inconclusive
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Pain:WOMAC Pain(downgrade quality for bad FU)	12 mos	50/54	4.76(2.59)/5.66(2.55)	Mean Diff	-0.9(-1.9,0.1)	Not Sig.	inconclusive
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Pain:change in WOMAC pain	14 weeks	113/157	-1.54(3.72)/-2.68(4.13)	Mean Diff	1.14(0.19,2.09)	Group 2	possibly clinically significant
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Pain:change in WOMAC pain	4 weeks	124/163	-0.84(2.9)/-1.98(3.19)	Mean Diff	1.14(0.43,1.85)	Group 2	possibly clinically significant
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Pain:change in WOMAC pain	26 weeks	108/141	-1.69(3.43)/-2.92(3.56)	Mean Diff	1.23(0.35,2.11)	Group 2	possibly clinically significant
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Pain:change in WOMAC pain	8 weeks	125/161	-1.25(3.35)/-2.66(3.3)	Mean Diff	1.41(0.63,2.19)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:6MWT(m)	3 mos	53/54	458(99.3)/410(98.6)	Mean Diff	48(10.06,85.94)	Group 1	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:6MWT(m)	12 mos	41/44	509.41(82.43)/524.86(106.52)	Mean Diff	-15.45(-56.41, 25.51)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:6MWT(m)	18 mos	39/42	500.15(77.46)/492.91(86.95)	Mean Diff	7.24(-29.13, 43.61)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:6MWT(m)	6 mos	112/127	375.9(103.713)/379.1(85.648)	Mean Diff	-3.2(-27.64, 21.24)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:6MWT(m)	12 mos	112/127	385.6(98.422)/366.1(99.171)	Mean Diff	19.5(-5.73,44.73)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Leisure Time Activities + Other(7 Day Physical Activity Recall;units?)	12 mos	9-Nov	33(70.75)/17.1(21.03)	Mean Diff	15.9(-32.98, 64.78)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Leisure Time Activities + Other(7 Day Physical Activity Recall;units?)	18 mos	24/26	41.48(61.94)/22.63(20.97)	study reported p value	p <.05	Behavioral Intervention + Supervised Walking	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Leisure Time Activities(7 Day Physical Activity Recall;units?)	12 mos	37/42	13.89(12.4)/12.22(7.86)	Mean Diff	1.67(-3.08,6.42)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Leisure Time Activities(7 Day Physical Activity Recall;units?)	18 mos	38/43	19.77(15.85)/15.34(10.23)	Mean Diff	4.43(-1.58,10.44)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Other Domestic Activities + Other(7 Day Physical Activity Recall;units?)	12 mos	14/13	33.07(39.04)/22.33(26.1)	Mean Diff	10.74(-15.54, 37.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Other Domestic Activities + Other(7 Day Physical Activity Recall;units?)	18 mos	24/30	27.97(33.15)/23.34(22.4)	study reported p value	p <.05	Behavioral Intervention + Supervised Walking	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Other Domestic Activities(7 Day Physical Activity Recall;units?)	12 mos	33/40	16.4(18.72)/12.2(9.9)	Mean Diff	4.2(-3.08,11.48)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:7-Day POD - Other Domestic Activities(7 Day Physical Activity Recall;units?)	18 mos	35/41	22.15(21.21)/16.46(13.17)	Mean Diff	5.69(-2.59,13.97)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:AAS Total Activity Time(Active Australia Survey)	12 mos	84/84	336(354)/394(447)	Mean Diff	-58(-180.88,64.88)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:AAS Total Activity Time(Active Australia Survey)	18 mos	84/84	427(599)/284(344)	Mean Diff	143(-6.08,292.08)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:AAS Total Activity Time(Active Australia Survey)	6 mos	84/84	392(378)/325(303)	Mean Diff	67(-37.4,171.4)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:AIMS Physical	2 yrs	62/59	1(0.59)/1.5(0.58)	Mean Diff	-0.5(-0.71,-0.29)	Group 1	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Arm Function(unclear scale?)	18 mos	42/43	0.41(0.84)/0.58(1.17)	Mean Diff	-0.17(-0.61,0.27)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Arm Function(unclear scale?)	12 mos	44/44	0.59(1.45)/0.3(0.73)	Mean Diff	0.29(-0.2,0.78)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	Function:AIMS2 Function	12 mos	343	none	Mean Diff.	-0.1(-0.3,0.2)	Not Sig.	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	Function:AIMS2 Function	12 mos	344	none	Mean Diff.	-0.2(-0.5,0)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Hand and Finger(unclear scale?)	12 mos	44/44	0.46(0.69)/0.6(0.93)	Mean Diff	-0.14(-0.49,0.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Hand and Finger(unclear scale?)	18 mos	42/44	0.69(0.92)/0.62(1.2)	Mean Diff	0.07(-0.39,0.53)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Level of Tension(unclear scale?)	12 mos	43/44	3.08(1.73)/3.09(1.69)	Mean Diff	-0.01(-0.74,0.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Level of Tension(unclear scale?)	18 mos	42/44	3.01(1.8)/3.31(1.97)	Mean Diff	-0.3(-1.11,0.51)	Not Sig.	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	Function:AIMS2 Mobility	12 mos	344	none	Mean Diff.	-0.2(-0.5,0.1)	Not Sig.	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	Function:AIMS2 Mobility	12 mos	343	none	Mean Diff.	0(-0.3,0.3)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Mobility(unclear scale?)	18 mos	42/44	0.87(1.22)/0.82(1.19)	Mean Diff	0.05(-0.47,0.57)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Mobility(unclear scale?)	12 mos	44/44	0.77(0.87)/0.61(1.02)	Mean Diff	0.16(-0.24,0.56)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	Function:AIMS2 Pain-Related Functioning(modified scale)	5 wks	58/55	1.74(1.25)/1.82(1.09)	Mean Diff	-0.08(-0.52,0.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	Function:AIMS2 Pain-Related Functioning(modified scale)	9 wks	58/55	1.62(1.19)/1.75(1.24)	Mean Diff	-0.13(-0.58,0.32)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Physical Component(unclear scale?)	12 mos	44/44	0.94(0.55)/0.88(0.85)	Mean Diff	0.06(-0.24,0.36)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Physical Component(unclear scale?)	18 mos	42/43	1.06(0.75)/1.04(1.01)	study reported p value	p <.05	Supervised Walking Alone (Control)	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	Function:AIMS2 Walking and Bending	12 mos	343	none	Mean Diff.	-0.2(-0.7,0.3)	Not Sig.	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	Function:AIMS2 Walking and Bending	12 mos	344	none	Mean Diff.	-0.5(-1,0)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Walking and Bending(unclear scale?)	18 mos	42/44	3.7(2.4)/3.67(2.32)	Mean Diff	0.03(-0.98,1.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Walking and Bending(unclear scale?)	12 mos	44/44	3.7(2.25)/3.36(2.22)	Mean Diff	0.34(-0.61,1.29)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Work(small N - exclude this outcome)	12 mos	15-Nov	0.63(0.79)/1.54(1.83)	Mean Diff	-0.91(-2.01,0.19)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:AIMS2 Work(unclear scale?)	18 mos	12-Sep	2.08(1.85)/2.19(2.45)	Mean Diff	-0.11(-2.07,1.85)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Dailly Moderate/Vigorous Physical Activity Minutes	3 mos	65/60	15.63(8.41)/16.18(8.52)	Mean Diff	-0.55(-3.55,2.45)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Dailly Moderate/Vigorous Physical Activity Minutes	6 mos	57/66	18.51(14.38)/15.95(11.13)	Mean Diff	2.56(-2.09,7.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Dailly Moderate/Vigorous Physical Activity Minutes(downgrade quality for bad FU)	12 mos	50/54	15.03(11.51)/17.74(10.33)	Mean Diff	-2.71(-6.98,1.56)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Dailly Moderate/Vigorous Physical Activity Minutes(downgrade quality for bad FU)	24 mos	35/40	11.41(14.1)/15.88(9.76)	Mean Diff	-4.47(-10.15, 1.21)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Daily Activity Minutes	3 mos	65/60	495.31(75.29)/489.94(66.37)	Mean Diff	5.37(-19.72, 30.46)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Daily Activity Minutes	6 mos	57/66	524.17(153.48)/472.27(73.34)	Mean Diff	51.9(7.61,96.19)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Daily Activity Minutes(downgrade quality for bad FU)	24 mos	35/40	472.06(85.19)/484.14(89.08)	Mean Diff	-12.08(-52.23, 28.07)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:Average Daily Activity Minutes(downgrade quality for bad FU)	12 mos	50/54	484.91(71.45)/474.1(83.81)	Mean Diff	10.81(-19.42, 41.04)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:Fast Gait Velocity	2 yrs	62/59	1.6(.)/1.5(.)	p value	p>.05	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Five Repetition Sit to Stand Test (s)	12 mos	112/127	18.4(11.641)/22.8(15.777)	Mean Diff	-4.4(-7.91,-0.89)	Group 1	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Five Repetition Sit to Stand Test (s)	6 mos	112/127	17.1(9.525)/24.9(11.269)	Mean Diff	-7.8(-10.45,-5.15)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:Gait Speed	12 mos	41/44	1.42(0.23)/1.46(0.3)	Mean Diff	-0.04(-0.15,0.07)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:Gait Speed	18 mos	39/42	1.39(0.22)/1.37(0.24)	Mean Diff	0.02(-0.08,0.12)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Global Improvement Function	18 mos	168	none	odds ratio	2.2(1,4.5)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Global Improvement Function	12 mos	168	none	odds ratio	2.3(1.2,4.7)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Global Improvement Function	6 mos	168	none	odds ratio	3.3(1.5,7.1)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Global Improvement PA Level	12 mos	168	none	odds ratio	1.4(0.6,3.1)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Global Improvement PA Level	6 mos	168	none	odds ratio	2.1(1,4.4)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Global Improvement PA Level	18 mos	168	none	odds ratio	2.1(1,4.4)	Group 1	na
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Function:Hamstring Strength(Peak torque/lbs)	24 mos	52/52	0.15(0.07)/0.16(0.07)	Mean Diff	-0.01(-0.04,0.02)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:Health Utilities Index Mark 3 (HUI3) Ambulation	3 mos	139	none	Mean Difference	0.02(-0.03,0.07)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:Health Utilities Index Mark 3 (HUI3) Ambulation	6 mos	139	none	Mean Difference	0.02(-0.04,0.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Knee Kinesiography Exam + Current Medical Management	Function:KOOS Activities of daily living	6 mos	134/102	4.8(15.22)/5.6(14.26)	Mean Diff	-0.8(-4.6,3)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Function:KOOS Activities of daily living	6 mos	134/213	4.8(15.22)/1.5(14.07)	Mean Diff	3.3(0.09,6.51)	Group 1	na
Cagnin; 2019/High	5: Wellness education-Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Function:KOOS Activities of daily living	6 mos	102/213	5.6(14.26)/1.5(14.07)	Mean Diff	4.1(0.73,7.47)	Group 1	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Knee Kinesiography Exam + Current Medical Management	Function:KOOS Sports and Recreation	6 mos	134/102	2.9(22.82)/1.9(24.18)	Mean Diff	1(-5.11,7.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Cagnin; 2019/High	5: Wellness education-Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Function:KOOS Sports and Recreation	6 mos	102/213	1.9(24.18)/-0.1(22.58)	Mean Diff	2(-3.62,7.62)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Function:KOOS Sports and Recreation	6 mos	134/213	2.9(22.82)/-0.1(22.58)	Mean Diff	3(-1.93,7.93)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Knee Kinesiography Exam + Current Medical Management	Function:KOOS Symptoms	6 mos	134/102	4.6(15.22)/4.6(16.04)	Mean Diff	0(-4.06,4.06)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Function:KOOS Symptoms	6 mos	102/213	4.6(16.04)/0.7(13.7)	Mean Diff	3.9(0.26,7.54)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Function:KOOS Symptoms	6 mos	134/213	4.6(15.22)/0.7(13.7)	Mean Diff	3.9(0.72,7.08)	Group 1	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:Lower Extremity Function Scale (LEFS)	3 mos	139	none	Mean Difference	4.14(-1.06,9.35)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:Lower Extremity Function Scale (LEFS)	6 mos	139	none	Mean Difference	6.59(1.24,11.94)	Group 1	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:Moderate/Vigerous Physical Activity (min/week)	26 wks	37/52	179.7(324.8)/185.3(383.6)	Mean Diff	-5.6(-155.48,144.28)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:Moderate/Vigerous Physical Activity (min/week)	6 wks	50/55	235.9(486.2)/116.8(204)	Mean Diff	119.1(-28.83, 267.03)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Function:NRS Function last week	3 mos	242/106	4.4(1.9)/4.6(2.3)	Mean Diff	-0.2(-0.7,0.3)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Function:NRS Function last week	6 mos	239/106	4.1(2.1)/4.7(2.1)	Mean Diff	-0.6(-1.08,-0.12)	Group 1	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Function:NRS Stiffness last week	3 mos	242/106	4.5(2.1)/4.6(2.1)	Mean Diff	-0.1(-0.58,0.38)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Function:NRS Stiffness last week	6 mos	239/106	4.3(2.1)/4.9(2.1)	Mean Diff	-0.6(-1.08,-0.12)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:No. Steps per Day	6 mos	84/84	9148(3175)/8504(3180)	Mean Diff	644(-324.03,1612.03)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:Normal Gait Velocity	2 yrs	62/59	1.2(0.2)/1.2(0.19)	Mean Diff	0(-0.07,0.07)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:Normal Gait Velocity	2 yrs	62/60	1.2(.)/1.1(.)	Mean Diff	p>.05	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:OAK HQOL Physical Activity	3 mos	53/54	64.7(9.11)/55(13.6)	Mean Diff	9.7(5.26,14.14)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:Paper Adaptive Test-5D Daily Activities	3 mos	139	none	Mean Difference	3.28(0.38,6.19)	Group 1	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:Paper Adaptive Test-5D Daily Activities	6 mos	139	none	Mean Difference	4.09(0.95,7.23)	Group 1	na
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Function:Physical Activity - Light(scale direction?)	2 yrs	148/47	40.54%/29.79%	RR	1.36(0.84,2.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Function:Physical Activity - Moderate(scale direction?)	2 yrs	148/47	22.3%/14.89%	RR	1.5(0.71,3.16)	Not Sig.	na
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Function:Physical Activity - None(scale direction?)	2 yrs	148/47	25.68%/46.81%	RR	0.55(0.36,0.83)	Group 1	na
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Function:Physical Activity - Vigorous	2 yrs	148/47	5.41%/2.13%	RR	2.54(0.33,19.79)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Active)	12 mos	112/127	42.86%/39.37%	RR	1.09(0.8,1.48)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Active)	6 mos	112/127	42.86%/38.58%	RR	1.11(0.82,1.51)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Irregularly Active A)(scale direction?)	12 mos	112/127	15.18%/18.11%	RR	0.84(0.47,1.49)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Irregularly Active A)(scale direction?)	6 mos	112/127	18.75%/15.75%	RR	1.19(0.68,2.08)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Irregularly Active B)(scale direction?)	6 mos	112/127	13.39%/18.11%	RR	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Irregularly Active B)(scale direction?)	12 mos	112/127	14.29%/11.81%	RR	1.21(0.63,2.33)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Sedentary)	6 mos	112/127	8.93%/6.3%	RR	1.42(0.58,3.47)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Sedentary)	12 mos	112/127	8.93%/6.3%	RR	1.42(0.58,3.47)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Very Active)	6 mos	112/127	16.07%/22.05%	RR	0.73(0.43,1.24)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Physical Activity Level (Very Active)	12 mos	112/127	18.75%/25.2%	RR	0.74(0.46,1.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Physical Activity Scale for the Elderly(PASE)	18 mos	84/84	180(94)/162(70)	Mean Diff	18(-7.26,43.26)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Physical Activity Scale for the Elderly(PASE)	6 mos	84/84	189(85)/158(63)	Mean Diff	31(8.19,53.81)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:Physical Activity Scale for the Elderly(PASE)	12 mos	84/84	172(80)/166(77)	Mean Diff	6(-17.92, 29.92)	Not Sig.	na
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Function:Quadriceps Strength(Peak torque/lbs)	24 mos	52/52	0.3(0.13)/0.32(0.13)	Mean Diff	-0.02(-0.07,0.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:ROM (flexion)	3 mos	53/54	119.3(19.6)/118.6(21.1)	Mean Diff	0.7(-7.1,8.5)	Not Sig.	na
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Function:Repeated Chair Stand	24 mos	52/52	13.43(3.68)/13.4(3.25)	Mean Diff	0.03(-1.32,1.38)	Not Sig.	na
Saraboon; 2015/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:ROM (Left Knee Flexion; degrees)	8 wks	40/44	128.05(4.65)/138.05(4.28)	Mean Diff	-10(-11.95,-8.05)	Group 2	na
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:ROM (Left Knee Flexion; degrees)	6 mos	38/36	142.5(5.2)/127.8(5.1)	Mean Diff	14.7(12.31,17.09)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:ROM (Left Knee Flexion; degrees)	12 mos	38/36	145.2(5.8)/127.9(7.5)	Mean Diff	17.3(14.18,20.42)	Group 1	na
Saraboon; 2015/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:ROM (Right Knee Flexion; degrees)	8 wks	40/45	128.65(6.9)/140.25(4.6)	Mean Diff	-11.6(-14.17,-9.03)	Group 2	na
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:ROM (Right Knee Flexion; degrees)	6 mos	38/36	143.3(5.7)/125.9(5.9)	Mean Diff	17.4(14.71,20.09)	Group 1	na
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:ROM (Right Knee Flexion; degrees)	12 mos	38/36	145.9(6.1)/126(8.4)	Mean Diff	19.9(16.47,23.33)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:SF-12 Physical Component Score	3 mos	53/54	50(5.2)/46.4(6)	Mean Diff	3.6(1.45,5.75)	Group 1	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:SF-12 Physical Component Score	6 wks	49/53	31.7(10.9)/32.3(9.7)	Mean Diff	-0.6(-4.67,3.47)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:SF-12 Physical Component Score	26 wks	37/49	29.4(9.4)/33.4(8.9)	Mean Diff	-4(-7.99,-0.01)	Group 2	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:SF-12 Physical Function	3 mos	53/54	49.6(12.6)/38.7(25)	Mean Diff	10.9(3.3,18.5)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:SF-12 Role Physical	3 mos	53/54	92.5(22.2)/45(37.6)	Mean Diff	47.5(35.66,59.34)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:SF-36 Physical Functioning	12 mos	43/44	68.13(19.69)/70.09(18.82)	Mean Diff	-1.96(-10.17, 6.25)	Not Sig.	inconclusive
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:SF-36 Physical Functioning	18 mos	42/44	63.25(25.71)/68.16(21.31)	study reported p value	p <.05	Supervised Walking Alone (Control)	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:SF-36 Role Physical	18 mos	42/44	60.12(40.97)/57.39(40.56)	Mean Diff	2.73(-14.76, 20.22)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:SF-36 Role Physical	12 mos	44/44	59.66(41.14)/61.74(39.76)	study reported p value	p <.05	Supervised Walking Alone (Control)	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:SF-36 Standardized Physical Component	12 mos	43/44	42.19(10.07)/42.51(9.23)	Mean Diff	-0.32(-4.44,3.8)	Not Sig.	inconclusive
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:SF-36 Standardized Physical Component	18 mos	42/44	40.91(11.04)/42.82(9.24)	study reported p value	p <.05	Supervised Walking Alone (Control)	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Function:SPPB(Short Physical Performance Battery)	12 mos	117/118	0(1.91)/-0.3(2.19)	Mean Diff	0.3(-0.23,0.83)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Sit and Reach (cm)	12 mos	112/127	17.9(9.525)/13.2(11.269)	Mean Diff	4.7(2.05,7.35)	Group 1	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Sit and Reach (cm)	6 mos	112/127	17.6(9.525)/11.9(9.016)	Mean Diff	5.7(3.33,8.07)	Group 1	na
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Function:Stair Climb	24 mos	52/52	13.72(5.68)/13.53(8.67)	Mean Diff	0.19(-2.67,3.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:Strength - Hamstring	3 mos	53/54	54.9(7.7)/51.6(8.1)	Mean Diff	3.3(0.27,6.33)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Function:Strength - Quadriceps	3 mos	53/54	58.4(8.3)/54.5(7.9)	Mean Diff	3.9(0.79,7.01)	Group 1	na
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Function:Timed Up and Go Test	24 mos	52/52	7.45(1.96)/7.71(3.59)	Mean Diff	-0.26(-1.39,0.87)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:Timed Up and Go Test (sec)	18 mos	39/42	8.4(1.36)/8.41(2.05)	Mean Diff	-0.01(-0.78,0.76)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:Timed Up and Go Test (sec)	12 mos	41/44	8.1(1.54)/8.12(2.44)	Mean Diff	-0.02(-0.9,0.86)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Timed Up and Go Test (sec)	6 mos	112/127	11.5(5.292)/12.5(4.508)	Mean Diff	-1(-2.26,0.26)	Not Sig.	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Timed Up and Go Test (sec)	12 mos	112/127	10.4(7.408)/12.6(5.635)	Mean Diff	-2.2(-3.9,-0.5)	Group 1	na
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Function:Timed Up and Go Test (sec)	1 yrs	150/48	12.08(4.37)/12.6(4.73)	Mean Diff	-0.52(-2.05,1.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Function:Timed Up and Go Test (sec)	2 yrs	148/47	11.79(4.87)/12.6(5.2)	Mean Diff	-0.81(-2.52,0.9)	Not Sig.	na
Saraboon; 2015/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:Timed Up and Go Test (sec)	8 wks	40/46	12.1(2.59)/10.07(2.18)	Mean Diff	2.03(0.99,3.07)	Group 2	na
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:Timed Up and Go Test (sec)	6 mos	38/36	9.9(1.7)/12.6(2.9)	Mean Diff	-2.7(-3.81,-1.59)	Group 1	na
Aree-Ue; 2017/Low	5: Wellness education-Multifactorial Intervention Programs(first wk 2 hrs/day x 3 days; then 2 hrs/wk x 6wks)	5: Placebo/Control-Control (No Multifactorial Intervention Programs)	Function:Timed Up and Go Test (sec)	12 mos	38/36	9(1.7)/13.3(2.9)	Mean Diff	-4.3(-5.41,-3.19)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Up and Down Stairs (sec)	6 mos	112/127	24.3(25.399)/30.2(14.65)	Mean Diff	-5.9(-11.29,-0.51)	Group 1	na
Rodrigues da Silva; 2017/Moderate	5: Wellness education-Education Promoting Home Exercise(single day program)	5: Placebo/Control-Control (Usual Care)	Function:Up and Down Stairs (sec)	12 mos	112/127	24.4(16.933)/32.2(21.412)	Mean Diff	-7.8(-12.69,-2.91)	Group 1	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Function:WOMAC Activities of Daily Living (VAS Version)	2 yrs	62/60	25.1(12.21)/35.2(13.16)	Mean Diff	-10.1(-14.65,-5.55)	Group 1	possibly clinically significant
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:WOMAC Activities of Daily Living (VAS Version)	2 yrs	62/59	25.1(12.21)/36(12.85)	Mean Diff	-10.9(-15.42,-6.38)	Group 1	possibly clinically significant
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:WOMAC Function	3 mos	65/60	16.51(7.47)/17.8(6.02)	Mean Diff	-1.29(-3.68,1.1)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:WOMAC Function	6 mos	57/66	15.13(7.74)/16.69(6.59)	Mean Diff	-1.56(-4.15,1.03)	Not Sig.	clinically insignificant
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function	6 mos	127/129	-4.3(9.97)/-5(10.62)	Mean Diff	0.7(-1.84,3.24)	Not Sig.	clinically insignificant
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function	12 mos	128/129	-4.6(10.01)/-5.6(10.62)	Mean Diff	1(-1.54,3.54)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function	6 wks	50/55	34(13.8)/34.3(13.7)	Mean Diff	-0.3(-5.63,5.03)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function	26 wks	37/51	36.5(13.2)/32.8(15.1)	Mean Diff	3.7(-2.33,9.73)	Not Sig.	inconclusive
Sadeghi; 2019/Moderate	5: Wellness education-Wellness Education for Diet	5: Placebo/Control-Control (No Wellness Education)	Function:WOMAC Function	3 mos	31/31	631.94(361.2)/655.35(409.26)	Mean Diff	-23.41(-219.58,172.76)	Not Sig.	inconclusive
Baker; 2019/High	5: Wellness education-Telephone counseling for motivational strength training(24 months)	5: Placebo/Control-Control (Phone message reminder w/o motivational program)(24 months)	Function:WOMAC Function	24 mos	52/52	12.74(10.61)/13.09(11.98)	Mean Diff	-0.35(-4.75,4.05)	Not Sig.	clinically insignificant
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function (0-10)	3 mos	139	none	Mean Difference	-0.65(-1.2,-0.1)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Function (0-10)	6 mos	139	none	Mean Difference	-0.84(-1.45,-0.24)	Group 1	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:WOMAC Function (VAS Version)(scale doesn't make sense?)	12 mos	38/44	25.27(15.7)/24.48(13.79)	Mean Diff	0.79(-5.76,7.34)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:WOMAC Function (VAS Version)(scale doesn't make sense?)	18 mos	42/43	24.15(17.24)/18.2(14.63)	Mean Diff	5.95(-0.96,12.86)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:WOMAC Function level of improvement	6 mos	84/84	14.7(10.6)/18.2(11.7)	Mean Diff	1.8 (-1.9, 5.5)	Not Sig.	inconclusive
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:WOMAC Function level of improvement	12 mos	84/84	13.3(10.5)/17.4(11.9)	Mean Diff	3.9(-.3, 8.2)	Not Sig.	inconclusive
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Function:WOMAC Function level of improvement	18 mos	84/84	12.2(10.5)/16.4(11.7)	Mean Diff	3.9(-1, 8.7)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:WOMAC Function(downgrade quality for bad FU)	24 mos	35/40	12.53(7.03)/15.33(8.63)	Mean Diff	-2.8(-6.41,0.81)	Not Sig.	inconclusive
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Function:WOMAC Function(downgrade quality for bad FU)	12 mos	50/54	13.51(8.06)/16.6(7.44)	Mean Diff	-3.09(-6.11,-0.07)	Group 1	possibly clinically significant
Chen; 2020/Moderate	5: Exercise-Exercise adherance education	5: Placebo/Control-Control	Function:WOMAC Joint Stiffness	12 wks	89/72	19.1(20.91)/22.92(22.2)	Mean Diff	-3.82(-10.6,2.96)	Not Sig.	na
Chen; 2020/Moderate	5: Exercise-Exercise adherance education	5: Placebo/Control-Control	Function:WOMAC Joint Stiffness	24 wks	89/72	10.41(12.52)/19.62(19.88)	Mean Diff	-9.21(-14.54,-3.88)	Group 1	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Stiffness	26 wks	37/52	4(2)/4.2(1.9)	Mean Diff	-0.2(-1.04,0.64)	Not Sig.	inconclusive
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Stiffness	6 wks	50/55	4.2(1.8)/4.6(1.9)	Mean Diff	-0.4(-1.12,0.32)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sadeghi; 2019/Moderate	5: Wellness education-Wellness Education for Diet	5: Placebo/Control-Control (No Wellness Education)	Function:WOMAC Stiffness	3 mos	31/31	65.48(50.1)/79.03(61.9)	Mean Diff	-13.55(-42.19, 15.09)	Not Sig.	inconclusive
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Stiffness (0-10)	3 mos	139	none	Mean Difference	-0.54(-1.12,0.05)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Function:WOMAC Stiffness (0-10)	6 mos	139	none	Mean Difference	-0.59(-1.3,0.11)	Not Sig.	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Function:WOMAC Stiffness (VAS Version)	2 yrs	62/59	35.4(16.54)/45.7(17.27)	Mean Diff	-10.3(-16.39,-4.21)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Function:WOMAC Stiffness (VAS Version)	2 yrs	62/60	35.4(16.54)/44.5(18.39)	Mean Diff	-9.1(-15.38,-2.82)	Group 1	possibly clinically significant
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:WOMAC Stiffness (VAS Version)(scale doesn't make sense?)	12 mos	41/44	30.79(19.58)/30.96(22.31)	Mean Diff	-0.17(-9.21,8.87)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Function:WOMAC Stiffness (VAS Version)(scale doesn't make sense?)	18 mos	42/43	31.4(20.75)/29.94(20.43)	Mean Diff	1.46(-7.43,10.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Function:Weekly Frequency of All Exercise(Measured by CHAMPS (Community Healthy Activities Model Program for Seniors))	12 mos	125/126	-1.2(8.19)/-0.7(8.51)	Mean Diff	-0.5(-2.58,1.58)	Not Sig.	na
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Function:Weelkly Duration of All Exercise(Measured by CHAMPS (Community Healthy Activities Model Program for Seniors))	12 mos	125/126	-0.6(8.76)/-0.7(7.37)	Mean Diff	0.1(-1.91,2.11)	Not Sig.	na
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in 6 min walk distance (ft)	26 weeks	75/129	-3.6(353.34)/105(243.06)	Mean Diff	-108.6(-199.86,-17.34)	Group 2	na
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in 6 min walk distance (ft)	8 weeks	89/156	-1(290.57)/67.7(232.31)	Mean Diff	-68.7(-139.79,2.39)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in SF-36 physical health	8 weeks	126/169	4.3(14.59)/7.6(15.6)	Mean Diff	-3.3(-6.78,0.18)	Not Sig.	na
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in SF-36 physical health	26 weeks	108/141	4(15.59)/8.2(17.81)	Mean Diff	-4.2(-8.38,-0.02)	Group 2	na
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in WOMAC function	4 weeks	124/163	-4.65(9.02)/-5.9(8.43)	Mean Diff	1.25(-0.81,3.31)	Not Sig.	clinically insignificant
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in WOMAC function	8 weeks	125/161	-5.3(10.62)/-7.84(9.64)	Mean Diff	2.54(0.14,4.94)	Group 2	clinically insignificant
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in WOMAC function	26 weeks	108/141	-7.17(11.12)/-9.88(11.04)	Mean Diff	2.71(-0.08,5.5)	Not Sig.	inconclusive
Berman; 2004/high	8: Placebo/Control-education control	8: Physical agents-sham acupuncture	Function:change in WOMAC function	14 weeks	113/157	-5.62(11.16)/-9.4(11.78)	Mean Diff	3.78(1,6.56)	Group 2	possibly clinically significant
Ravaud; 2009/Moderate	5: Wellness education-education	5: Placebo/Control-control (usual care)	Function:sf 12 mental function improvement	4 mos	146/181	3.6(8.91)/0.86(9.51)	Mean Diff	2.74(0.73,4.75)	Group 1	na
Ravaud; 2009/Moderate	5: Wellness education-education	5: Placebo/Control-control (usual care)	Function:sf 12 physical function improvement	4 mos	146/181	3.02(6.97)/1.83(7.93)	Mean Diff	1.19(-0.43,2.81)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ravaud; 2009/Moderate	5: Wellness education-education	5: Placebo/Control-control (usual care)	Function:womac function improvement	4 mos	146/181	3.9(7.24)/2.74(7.71)	Mean Diff	1.16(-0.47,2.79)	Not Sig.	clinically insignificant
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Composite:AIMS2 Symptoms Component(unclear scale?)	12 mos	44/44	3.79(2.29)/3.52(2.36)	Mean Diff	0.27(-0.72,1.26)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Composite:AIMS2 Symptoms Component(unclear scale?)	18 mos	42/44	3.64(2.16)/3.44(2.41)	study reported p value	p <.05	Supervised Walking Alone (Control)	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Composite:Arthritis Self-Efficacy	2 yrs	62/60	243.25(27.17)/225.7(30.97)	Mean Diff	17.55(7.09,28.01)	Group 1	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Composite:Arthritis Self-Efficacy	2 yrs	62/59	243.25(27.17)/222.3(28.97)	Mean Diff	20.95(10.83, 31.07)	Group 1	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	Composite:Arthritis Self-Efficacy	12 mos	343	none	Mean Diff.	0.4(0,0.7)	Not Sig.	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	Composite:Arthritis Self-Efficacy	12 mos	344	none	Mean Diff.	0.4(0,0.8)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Composite:EuroQoL-5D-3L	3 mos	53/54	0.66(0.13)/0.53(0.28)	Mean Diff	0.13(0.05,0.21)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Composite:Global Improvement Overall	18 mos	168	none	odds ratio	2.1(1,4.4)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Composite:Global Improvement Overall	6 mos	168	none	odds ratio	2.2(1.1,4.4)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	Composite:Global Improvement Overall	12 mos	168	none	odds ratio	2.7(1.2,5.6)	Group 1	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Composite:Health Utilities Index Mark 3 (HUI3) Total	6 mos	139	none	Mean Difference	0.02(-0.06,0.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Composite:Health Utilities Index Mark 3 (HUI3) Total	3 mos	139	none	Mean Difference	0.05(-0.03,0.12)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Knee Kinesiography Exam + Current Medical Management	Composite:KOOS Overall score	6 mos	134/102	5(12.88)/5.5(12.98)	Mean Diff	-0.5(-3.85,2.85)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Composite:KOOS Overall score	6 mos	134/213	5(12.88)/1.8(12.22)	Mean Diff	3.2(0.46,5.94)	Group 1	na
Cagnin; 2019/High	5: Wellness education-Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	Composite:KOOS Overall score	6 mos	102/213	5.5(12.98)/1.8(12.22)	Mean Diff	3.7(0.67,6.73)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Composite:Lequesne Index Score	1 yrs	150/48	11.76(4.02)/12.26(4.06)	Mean Diff	-0.5(-1.84,0.84)	Not Sig.	na
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Composite:Lequesne Index Score	2 yrs	148/47	11.51(4.39)/12.16(4.13)	Mean Diff	-0.65(-2.05,0.75)	Not Sig.	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Composite:Overall Quality of Care Pass Rate (%)	6 mos	139	none	Mean Difference	45.2(34.5,55.9)	Group 1	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Composite:SF-36 Physical Component Score	6 mos	57/66	45.04(78.99)/44.81(5.55)	Mean Diff	0.23(-20.77, 21.23)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Composite:SF-36 Physical Component Score	3 mos	65/60	46.03(5.77)/44.67(5.85)	Mean Diff	1.36(-0.7,3.42)	Not Sig.	inconclusive
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Composite:SF-36 Physical Component Score(downgrade quality for bad FU)	24 mos	35/40	45.44(5.98)/44.66(7.32)	Mean Diff	0.78(-2.28,3.84)	Not Sig.	inconclusive
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	Composite:SF-36 Physical Component Score(downgrade quality for bad FU)	12 mos	50/54	46.03(5.03)/44.32(6.17)	Mean Diff	1.71(-0.47,3.89)	Not Sig.	inconclusive
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Composite:WOMAC Total	6 mos	128/129	-6.2(13.44)/-7.3(14.35)	Mean Diff	1.1(-2.32,4.52)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Composite:WOMAC Total	12 mos	128/129	-6.1(14.01)/-7.7(14.92)	Mean Diff	1.6(-1.96,5.16)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Composite:WOMAC Total	6 wks	50/54	47.4(17.9)/48.2(18.3)	Mean Diff	-0.8(-7.84,6.24)	Not Sig.	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Composite:WOMAC Total	26 wks	37/51	49.9(17)/46.6(20.3)	Mean Diff	3.3(-4.63,11.23)	Not Sig.	inconclusive
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Composite:WOMAC Total	2 yrs	148/47	42.01(18.32)/43.91(15.02)	Mean Diff	-1.9(-7.18,3.38)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rezende; 2017/Moderate	5: Wellness education-Wellness Education Classes + Material(not all educated get same amount (subgroup analysis available in text))	5: Placebo/Control-Control (Wellness Education Material Only)	Composite:WOMAC Total	1 yrs	150/48	42.85(17.22)/46.15(19.42)	Mean Diff	-3.3(-9.55,2.95)	Not Sig.	inconclusive
Sadeghi; 2019/Moderate	5: Wellness education-Wellness Education for Diet	5: Placebo/Control-Control (No Wellness Education)	Composite:WOMAC Total	3 mos	31/31	910.9(457.3)/966.4(558)	Mean Diff	-55.5(-314.9, 203.9)	Not Sig.	inconclusive
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Composite:WOMAC Total (0-30)	3 mos	139	none	Mean Difference	-1.99(-3.45,-0.54)	Group 1	na
Marra; 2012/Moderate	5: Wellness education-Education + Training(edu; medication review; referral to PT; PT assessment; training x2/wk x6wks)	5: Placebo/Control-Control (Usual Care)	Composite:WOMAC Total (0-30)	6 mos	139	none	Mean Difference	-2.4(-4.1,-0.71)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Composite:WOMAC Total (VAS Version)(scale doesn't make sense?)	12 mos	41/43	23.6(13.61)/21.05(13.62)	Mean Diff	2.55(-3.36,8.46)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	Composite:WOMAC Total (VAS Version)(scale doesn't make sense?)	18 mos	42/43	25.58(16.6)/20.3(13.97)	study reported p value	p <.05	Supervised Walking Alone (Control)	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	Composite:Weight Self-Efficacy	2 yrs	62/60	6.5(1.18)/6(0.97)	Mean Diff	0.5(0.11,0.89)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	Composite:Weight Self-Efficacy	2 yrs	62/59	6.5(1.18)/5.9(1.15)	Mean Diff	0.6(0.18,1.02)	Group 1	na
Somers; 2012/High	5: Wellness education-Pain Coping Skills Training + Behavioral Weight Management(6 mo program)	5: Placebo/Control-Control (Behavioral Weight Management Alone)(6 mo program)	QOL:AIMS Psychological	2 yrs	62/59	2.2(0.79)/2.5(0.96)	Mean Diff	-0.3(-0.62,0.02)	Not Sig.	na
Somers; 2012/High	6: Weight loss-Behavioral Weight Management + Pain Coping Skills(6 mo program)	6: No weight loss-Control (Pain Coping Skills Alone)(6 mo program)	QOL:AIMS Psychological	2 yrs	62/60	2.2(0.79)/2.6(0.77)	Mean Diff	-0.4(-0.68,-0.12)	Group 1	na
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Placebo/Control-Control (Usual Care)	QOL:AIMS2 Affect	12 mos	343	none	Mean Diff.	0(-0.3,0.4)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Allen; 2010/Moderate	5: Wellness education-Osteoarthritis Self-Management(1x/mos)	5: Wellness education-Health Education(1x/mos)	QOL:AIMS2 Affect	12 mos	344	none	Mean Diff.	0.1(-0.3,0.4)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Affect Component(unclear scale?)	18 mos	42/44	2.45(1.42)/2.55(1.81)	Mean Diff	-0.1(-0.8,0.6)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Affect Component(unclear scale?)	12 mos	42/44	2.44(1.44)/2.44(1.5)	Mean Diff	0(-0.63,0.63)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Arthritis Impact(unclear scale?)	12 mos	40/39	2.5(2.33)/2.37(1.81)	Mean Diff	0.13(-0.8,1.06)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Arthritis Impact(unclear scale?)	18 mos	39/34	3.01(2.51)/1.99(2.11)	study reported p value	p <.05	Supervised Walking Alone (Control)	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Health Perception(unclear scale?)	12 mos	43/44	3.5(1.78)/3.64(2.37)	Mean Diff	-0.14(-1.03,0.75)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Health Perception(unclear scale?)	18 mos	42/42	3.66(2.31)/3.34(1.95)	Mean Diff	0.32(-0.61,1.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Household Tasks(unclear scale?)	12 mos	44/44	0.11(0.28)/0.34(1)	Mean Diff	-0.23(-0.54,0.08)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Household Tasks(unclear scale?)	18 mos	42/44	0.57(1.38)/0.41(0.93)	Mean Diff	0.16(-0.35,0.67)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Mood(unclear scale?)	12 mos	42/44	1.82(1.32)/1.8(1.64)	Mean Diff	0.02(-0.62,0.66)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Mood(unclear scale?)	18 mos	42/44	1.89(1.29)/1.8(1.91)	Mean Diff	0.09(-0.61,0.79)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:AIMS2 Pain-Related Anxiety	5 wks	58/55	27.73(18.65)/30.48(17.68)	Mean Diff	-2.75(-9.52,4.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:AIMS2 Pain-Related Anxiety	9 wks	58/55	23.21(17.29)/27.39(17.06)	Mean Diff	-4.18(-10.58, 2.22)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Role Component(small N - exclude this outcome)	18 mos	12-Sep	2.08(1.85)/2.19(2.45)	Mean Diff	-0.11(-2.07,1.85)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Role Component(small N - exclude this outcome)	12 mos	15-Nov	0.63(0.79)/1.54(1.83)	Mean Diff	-0.91(-2.01,0.19)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Satisfaction(unclear scale?)	12 mos	44/43	2.33(1.73)/2.11(18.18)	Mean Diff	0.22(-5.4,5.84)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Satisfaction(unclear scale?)	18 mos	42/44	2.66(1.89)/2.18(2.08)	Mean Diff	0.48(-0.37,1.33)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Self Care(unclear scale?)	12 mos	44/44	0.03(0.13)/0.11(0.51)	Mean Diff	-0.08(-0.24,0.08)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Self Care(unclear scale?)	18 mos	42/43	0.1(0.44)/0.87(0.57)	study reported p value	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Social Activity(unclear scale?)	12 mos	43/44	4.45(1.89)/4.73(1.57)	Mean Diff	-0.28(-1.02,0.46)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Social Activity(unclear scale?)	18 mos	42/44	4.72(1.86)/4.63(1.84)	Mean Diff	0.09(-0.7,0.88)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Social Interaction Component(unclear scale?)	12 mos	43/44	3.35(1.7)/3.36(1.51)	Mean Diff	-0.01(-0.7,0.68)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Social Interaction Component(unclear scale?)	18 mos	42/44	3.35(1.56)/3.28(1.91)	Mean Diff	0.07(-0.68,0.82)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Support From Family(unclear scale?)	18 mos	42/44	1.98(2.05)/1.93(2.44)	Mean Diff	0.05(-0.91,1.01)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:AIMS2 Support From Family(unclear scale?)	12 mos	43/44	2.25(2.38)/1.99(2.27)	Mean Diff	0.26(-0.73,1.25)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	QOL:Assessment of QoL	6 mos	84/84	0.8(0.1)/0.8(0.1)	Mean Diff	0(-0.03,0.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	QOL:Assessment of QoL	12 mos	84/84	0.8(0.2)/0.8(0.1)	Mean Diff	0(-0.05,0.05)	Not Sig.	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	QOL:Assessment of QoL	18 mos	84/84	0.8(0.1)/0.8(0.2)	Mean Diff	0(-0.05,0.05)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:DASS-21 Anxiety Subscale	26 wks	37/52	6.4(6.6)/7(8.2)	Mean Diff	-0.6(-3.72,2.52)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:DASS-21 Depression Subscale	26 wks	37/52	8.7(7.5)/9.8(9.8)	Mean Diff	-1.1(-4.75,2.55)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:DASS-21 Stress Subscale	26 wks	37/52	10.9(9.3)/10.5(9.8)	Mean Diff	0.4(-3.67,4.47)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:EuroQoL - VAS	3 mos	53/54	60.7(10.9)/52.2(13)	Mean Diff	8.5(3.9,13.1)	Group 1	clinically insignificant
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:Fear Avoidance Beliefs (FABQ)(Fear Avoidance Beliefs Quesionnaire)	26 wks	37/52	17.4(5.6)/13.9(7.1)	Mean Diff	3.5(0.82,6.18)	Group 2	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:Global Percieved Effect(Change from Baseline)	26 wks	34/48	4.3(2.4)/4.6(2.2)	Mean Diff	-0.3(-1.34,0.74)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:Global Percieved Effect(Change from Baseline)	6 wks	50/55	4.1(2)/3.9(1.8)	Mean Diff	0.2(-0.54,0.94)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	QOL:H/KOOS QoL subscale mean	6 mos	239/106	49.7(15.8)/47.2(17.5)	Mean Diff	2.5(-1.41,6.41)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	QOL:H/KOOS QoL subscale mean	3 mos	242/106	47.8(14.9)/45.3(18.2)	Mean Diff	2.5(-1.47,6.47)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Knee Kinesiography Exam + Current Medical Management	QOL:KOOS Quality of Life	6 mos	134/102	6.5(19.9)/8.4(21.38)	Mean Diff	-1.9(-7.28,3.48)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Cagnin; 2019/High	5: Wellness education-Education program + Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	QOL:KOOS Quality of Life	6 mos	134/213	6.5(19.9)/4.3(18.51)	Mean Diff	2.2(-2.01,6.41)	Not Sig.	na
Cagnin; 2019/High	5: Wellness education-Knee Kinesiography Exam + Current Medical Management	5: Placebo/Control-Control/Current Medical Management	QOL:KOOS Quality of Life	6 mos	102/213	8.4(21.38)/4.3(18.51)	Mean Diff	4.1(-0.77,8.97)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:Negative Effect(20-Item Positive and Negative Effect Scale)	5 wks	58/55	9.11(6.38)/9.17(8.39)	Mean Diff	-0.06(-2.85,2.73)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:Negative Effect(20-Item Positive and Negative Effect Scale)	9 wks	58/55	8.2(6.26)/8.9(8.6)	Mean Diff	-0.7(-3.52,2.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:OAKHQOL Mental Health	3 mos	53/54	66.6(11.7)/55.5(15.1)	Mean Diff	11.1(5.92,16.28)	Group 1	na
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	QOL:PHQ-8(8 Item Patient Health Questionnaire)	12 mos	125/126	-0.7(3.39)/-0.4(3.4)	Mean Diff	-0.3(-1.14,0.54)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:Pain Attitude (SOPA)(Survey of Pain Attitudes)	6 wks	50/55	16.9(4.4)/15.9(5.7)	Mean Diff	1(-0.96,2.96)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:Pain Attitude (SOPA)(Survey of Pain Attitudes)	26 wks	37/51	16.5(4.9)/14.8(5.7)	Mean Diff	1.7(-0.56,3.96)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:Positive Effect(20-Item Positive and Negative Effect Scale)	5 wks	58/55	26.15(7.18)/33.29(9.08)	Mean Diff	-7.14(-10.2,-4.08)	Group 2	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:Positive Effect(20-Item Positive and Negative Effect Scale)	9 wks	58/55	36.34(8.65)/34.27(10.17)	Mean Diff	2.07(-1.46,5.6)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:SF-12 General Health	3 mos	53/54	48.3(9.1)/40.4(16)	Mean Diff	7.9(2.91,12.89)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:SF-12 Mental Component Score	3 mos	53/54	42.29(3.2)/37(6.6)	Mean Diff	5.29(3.3,7.28)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:SF-12 Mental Component Score	6 wks	49/53	48.6(14.8)/49.1(12.7)	Mean Diff	-0.5(-5.94,4.94)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	QOL:SF-12 Mental Component Score	26 wks	37/49	53.4(12.4)/47.4(12.3)	Mean Diff	6(0.64, 11.36)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	QOL:SF-12 Mental Health	3 mos	53/54	63.5(12.7)/55.8(10.6)	Mean Diff	7.7(3.21,12.19)	Group 1	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 General Health Perceptions	18 mos	42/44	66.14(20.48)/69.31(19.19)	Mean Diff	-3.17(-11.69, 5.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 General Health Perceptions	12 mos	44/44	68.93(19.01)/67.62(17.48)	Mean Diff	1.31(-6.43,9.05)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Health Transition Item(scale?)	12 mos	43/43	2.7(0.91)/2.42(0.85)	Mean Diff	0.28(-0.1,0.66)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Health Transition Item(scale?)	18 mos	42/44	3.02(1.02)/2.73(0.92)	Mean Diff	0.29(-0.13,0.71)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	QOL:SF-36 Mental Component Score	6 mos	57/66	54.32(6.71)/54.05(7.55)	Mean Diff	0.27(-2.28,2.82)	Not Sig.	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	QOL:SF-36 Mental Component Score	3 mos	65/60	53.96(6.74)/47.59(7.03)	Mean Diff	6.37(3.93,8.81)	Group 1	na
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	QOL:SF-36 Mental Component Score(downgrade quality for bad FU)	12 mos	50/54	54.06(7.51)/54.68(6.47)	Mean Diff	-0.62(-3.36,2.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gilbert; 2018/High	5: Wellness education-Motivational Interviewing during Education	5: Placebo/Control-Standard Education	QOL:SF-36 Mental Component Score(downgrade quality for bad FU)	24 mos	35/40	54.18(6.3)/52.84(8.76)	Mean Diff	1.34(-2.14,4.82)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Mental Health Index	18 mos	42/44	77.41(15.76)/77.11(17.93)	Mean Diff	0.3(-6.93,7.53)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Mental Health Index	12 mos	44/44	80(14.82)/78.36(16.01)	Mean Diff	1.64(-4.9,8.18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Role Emotional	12 mos	44/44	81.6(32.47)/85.61(30.84)	Mean Diff	-4.01(-17.43, 9.41)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Role Emotional	18 mos	42/44	80.16(31.29)/75(40.11)	Mean Diff	5.16(-10.24, 20.56)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Social Functioning	12 mos	44/44	84.38(18.31)/79.55(22.89)	Mean Diff	4.83(-3.96,13.62)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Social Functioning	18 mos	42/44	84.23(19.53)/78.13(26.7)	Mean Diff	6.1(-3.91,16.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Standardized Mental Component	12 mos	43/44	54.48(7.33)/53.82(9.85)	Mean Diff	0.66(-3.04,4.36)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Standardized Mental Component	18 mos	42/44	53.92(9.02)/51.99(11)	Mean Diff	1.93(-2.38,6.24)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Vitality	18 mos	42/44	58.93(18.79)/60.15(21.86)	Mean Diff	-1.22(-9.95,7.51)	Not Sig.	na
Brosseau; 2012/Moderate	5: Wellness education-Behavioral Intervention + Supervised Walking(goal setting classes; edu by instructor; counseling + [65 minute supervised group weekly sessions; 12 months])	5: Placebo/Control-Control (Supervised Walking Alone)(65 minute supervised group weekly sessions; 12 months)	QOL:SF-36 Vitality	12 mos	44/44	60.34(19.78)/62.05(19.63)	Mean Diff	-1.71(-10.06, 6.64)	Not Sig.	na
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:Self-Efficacy for Pain Management	5 wks	58/55	7.2(1.81)/6.38(1.97)	Mean Diff	0.82(0.11,1.53)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rini; 2015/Moderate	5: Wellness education-Internet-Based Pain Coping Skills Training (PainCOACH)(1 coaching session/week x 8 weeks)	5: Placebo/Control-Control (No Coaching)	QOL:Self-Efficacy for Pain Management	9 wks	58/55	7.56(2)/6.67(2.02)	Mean Diff	0.89(0.14,1.64)	Group 1	na
Bennell; 2017/Moderate	5: Wellness education-Coaching + PT & Edcuation(6 coaching calls + 30minPTx5 & Education)	5: Placebo/Control-Control (PT & Education Alone)(30minPTx5 & Education)	QOL:Sleep Time (hr/day)	6 mos	84/84	2(0.7)/1.9(0.7)	Mean Diff	0.1(-0.11,0.31)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Other:Daily hours in sitting position	6 mos	239/106	5.9(2.6)/6.2(3)	Mean Diff	-0.3(-0.96,0.36)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Other:Daily hours in sitting position	3 mos	242/106	6.1(2.8)/6.4(3.2)	Mean Diff	-0.3(-1.01,0.41)	Not Sig.	na
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Other:NRS Disease activity last week	3 mos	242/106	4.3(2)/4.7(2.3)	Mean Diff	-0.4(-0.91,0.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseng; 2020/Moderate	5: Wellness education-OA Education program and indiviually tailored exercises	5: Non-arthro Tx-Usual care	Other:NRS Disease activity last week	6 mos	239/106	4.2(2.1)/4.7(2.2)	Mean Diff	-0.5(-1,0)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:OAKH QOL Social Functioning	3 mos	53/54	45.3(9.8)/41.6(13.5)	Mean Diff	3.7(-0.82,8.22)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:OAKH QOL Social Support	3 mos	53/54	59.8(12.2)/50.9(15.6)	Mean Diff	8.9(3.53,14.27)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:SF-12 Role Emotional	3 mos	53/54	92.5(24)/49.2(40.6)	Mean Diff	43.3(30.51,56.09)	Group 1	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:SF-12 Social Function	3 mos	53/54	73.7(21.8)/60.4(16.1)	Mean Diff	13.3(5.93,20.67)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Other:SF-12 Vitality	3 mos	53/54	54.7(15.1)/54.3(18.1)	Mean Diff	0.4(-5.99,6.79)	Not Sig.	na
Allen; 2017/Moderate	5: Wellness education-Behavioral Intervention(goal setting; action planning; motivational interviewing; telephone call 2x/mo for 6 mo; 1x/mo for 6 mo)	5: Placebo/Control-Control (Usual Care)	Adverse events:Joint Replacement Surgery	12 mos	128/129	3.91%/3.1%	RR	1.26(0.35,4.58)	Not Sig.	na
Saffari; 2018/High	5: Wellness education-Theory of Planned Behavior (TPB) Education(1 mo course)	5: Placebo/Control-No Education	Adverse events:Joint Swelling	3 mos	53/54	37.74%/46.3%	RR	0.82(0.52,1.28)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Adverse events:Poor Sleep Quality	26 wks	37/51	10.81%/9.8%	RR	1.1(0.32,3.83)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Adverse events:Poor Sleep Quality	6 wks	50/55	16%/10.91%	RR	1.47(0.55,3.93)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Adverse events:Received Surgery of Knee Pain	6 wks	50/55	0%/0%	RD	0(-7.135, 6.528)	Not Sig.	na
O'Brien; 2018/Moderate	5: Wellness education-Telephone-Based Weight Management and Healthy Lifestyle Service	5: Placebo/Control-Control (Usual Care)	Adverse events:Received Surgery of Knee Pain	26 wks	33/44	3.03%/2.27%	RR	1.33(0.09,20.54)	Not Sig.	na

PICO 6: Weight Loss

Diet and Exercise vs. Control

Table 24: Diet and Exercise vs Control

Quality: H=High; M=Moderate; L=Low	H	M	L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Jenkinson et al ; 2009	Miller; 2006	Focht ; 2005	Rejeski; 2002
Function				
stair climb time (s)			●	
6 minute walk distance (ft_			↑	
SF-36 mental function(26 and 78 week average)				●
Pain				
womac pain 30% recuction	↑			
calculable MID outcomes				
WOMAC Total		↑		
WOMAC Function		↑		
WOMAC Stiffness		●		
WOMAC Pain		↑		
SF-36-physical function(26 and 78 week average)				↑

Evidence Table 29 22: Diet and Exercise vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Miller; 2006/Moderate	5: Self management-diet + weight loss	5: Wellness education-education	Pain:womac pain	6 mos	39/35	4.1(2.5)/6.1(2.96)	Mean Diff	-2(-3.28,-0.72)	Group 1	possibly clinically significant
Jenkinson et al ; 2009/High	5: Self management-diet or diet + exercise risk difference	5: Wellness education-exercise or leaflet	Pain:womac pain 30% recuction	104 wks	231/158	38.1%/38.61%	RR	0.99(0.76,1.27)	Not Sig.	na
Jenkinson et al ; 2009/High	5: Self management-exercise or exercise and diet	5: Wellness education-diet or leaflet	Pain:womac pain 30% recuction	104 wks	191/198	43.98%/32.83%	RR	1.34(1.04,1.73)	Group 1	na
Focht ; 2005/Low	5: Self management-diet + exercise	5: Wellness education-health education control	Function:6 minute walk distance (ft_	78 weeks	162/78	1524(316)/1411(261)	Mean Diff	113(36.84,189.16)	Group 1	na
Rejeski; 2002/Low	6: Weight loss-diet + exercise	6: No weight loss-control	Function:SF-36 mental function(26 and 78 week average)	78 wks	68/68	79.68(10.14)/78.56(9.91)	Mean Diff	1.12(-2.28,4.52)	Not Sig.	na
Rejeski; 2002/Low	6: Weight loss-diet + exercise	6: No weight loss-control	Function:SF-36-physical function(26 and 78 week average)	78 wks	68/68	59.03(15.5)/49.56(15.1)	Mean Diff	9.47(4.28,14.66)	Group 1	clinically significant
Focht ; 2005/Low	5: Self management-diet + exercise	5: Wellness education-health education control	Function:stair climb time (s)	72 weeks	162/78	8.85(5.35)/9.86(5.56)	Mean Diff	-1.01(-2.51,0.49)	Not Sig.	na
Miller; 2006/Moderate	5: Self management-diet + weight loss	5: Wellness education-education	Function:womac function	6 mos	39/35	15.2(9.4)/23.8(11.8)	Mean Diff	-8.6(-13.59,-3.61)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Miller; 2006/Moderate	5: Self management-diet + weight loss	5: Wellness education-education	Function:womac stiffness	6 mos	39/35	3(1.25)/3.1(1.78)	Mean Diff	-0.1(-0.82,0.62)	Not Sig.	inconclusive
Miller; 2006/Moderate	5: Self management-diet + weight loss	5: Wellness education-education	Composite:WOMAC total	6 mos	39/35	22.3(11.9)/33(15.38)	Mean Diff	-10.7(-17.14,-4.26)	Group 1	possibly clinically significant

PICO 6: Weight Loss

Diet vs. Control

Table 25: Diet vs Control

Quality: H=High; M=Moderate; L=Low	H		M		L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Bliddal; 2011	Messier; 2013	Mihalko; 2018	Focht ; 2005	Rejeski; 2002
Function						
KOOS Activities of Daily Living	●					
KOOS Sports/Recreation	●					
KOOS Symptoms	●					
6MWT(m)	●		↑			
Balance Efficacy Confidence				↑		
Gait Efficacy Confidence				↑		
Walking Duration Efficacy Confidence				↑		
Walking Speed (m/s)			↑			
stair climb time (s)					●	
SF-36 mental function(26 and 78 week average)						●
?HAQ		●				
Other						
OMERACT-OARSI Responder(Outcome Measures in Reumatorlogy; Osteoarthritis Research Society International)	●					
Pain						
KOOS Pain	●					
Adverse events						
Abdominal Pain(Per Protocol Population; still >80% FU)	●					
Allergic Rash(Per Protocol Population; still >80% FU)	●					
Anxiety(Per Protocol Population; still >80% FU)	●					
Back Pain(Per Protocol Population; still >80% FU)	●					
Bad Breath(Per Protocol Population; still >80% FU)	●					
Biliary Symptoms(Per Protocol Population; still >80% FU)	●					
Constipation(Per Protocol Population; still >80% FU)	●					
Cramps(Per Protocol Population; still >80% FU)	●					

Table 25: Continued: Diet vs Control

Quality: H=High; M=Moderate; L=Low	H		M		L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Bliddal; 2011	Messier; 2013	Mihalko; 2018	Focht ; 2005	Rejeski; 2002
Adverse events						
Depressive Tendencies(Per Protocol Population; still >80% FU)	●					
Diarrhea(Per Protocol Population; still >80% FU)	●					
Dizziness(Per Protocol Population; still >80% FU)	●					
Dry Skin(Per Protocol Population; still >80% FU)	●					
Eczema(Per Protocol Population; still >80% FU)	●					
Epigasric Pain(Per Protocol Population; still >80% FU)	●					
Fatigue(Per Protocol Population; still >80% FU)	●					
Flatulence(Per Protocol Population; still >80% FU)	●					
Hair Loss(Per Protocol Population; still >80% FU)	●					
Headache(Per Protocol Population; still >80% FU)	●					
Heartburn(Per Protocol Population; still >80% FU)	●					
Influenza(Per Protocol Population; still >80% FU)	●					
Joint Pain(Per Protocol Population; still >80% FU)	●					
Mood Changes(Per Protocol Population; still >80% FU)	●					
Nausea(Per Protocol Population; still >80% FU)	●					
Perianal Itching(Per Protocol Population; still >80% FU)	●					
Redness(Per Protocol Population; still >80% FU)	●					

Table 25: Continued: Diet vs Control

Quality: H=High; M=Moderate; L=Low	H		M		L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Christensen; 2015	Bliddal; 2011	Messier; 2013	Mihalko; 2018	Focht ; 2005	Rejeski; 2002
Adverse events						
Sciatic Pain(Per Protocol Population; still >80% FU)	●					
Sensitive to Cold(Per Protocol Population; still >80% FU)	●					
Skin Irritation(Per Protocol Population; still >80% FU)	●					
Sleeplessness(Per Protocol Population; still >80% FU)	●					
Swollen Joints(Per Protocol Population; still >80% FU)	●					
Toothache(Per Protocol Population; still >80% FU)	●					
Urticaria(Per Protocol Population; still >80% FU)	●					
Vomiting(Per Protocol Population; still >80% FU)	●					
calculable MID outcomes						
WOMAC Total		●				
WOMAC Function		●	↑			
WOMAC Stiffness		●				
WOMAC Pain		↑	●			
VAS Pain	●					
SF-36 Physical component	●		↑			
VAS Disability	●					
VAS Patient Global Assessment	●					
SF-36-physical function(26 and 78 week average)						↑
QOL						
KOOS Quality of Life	●					
SF-36 Mental Component Score	●		●			

Evidence Table 3023: Diet vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bliddal; 2011/High	6: Weight loss-Low-Energy Diet w/ Instruction(Formula 6x/day x 8wks; then Instruction 1x/wk x 24wks; then Formula 6x/day x 4wks; then Instruction 1x/2wks x 16wks)	6: Weight loss-Control (Instruction)(Instruction at baseline; wk 8;32;36; and 52)	Pain:?WOMAC Pain(weird scale)	52 wks	44/45	-7.7(14.59)/-0.5(14.76)	Mean Diff	-7.2(-13.38,-1.02)	Group 1	possibly clinically significant
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Pain:KOOS Pain	68 wks	64/64	7.6(15.01)/8.7(15.01)	Mean Diff	-1.1(-6.35,4.15)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Pain:VAS Pain	68 wks	64/64	-6.1(20.02)/-5.5(20.02)	Mean Diff	-0.6(-7.6,6.4)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Pain:WOMAC Pain	18 mos	152/150	3.7(3.43)/4.4(3.1)	adjusted mean difference	Sig (p < 0.05)	Diet favored over control	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Pain:WOMAC Pain	6 mos	152/150	4.6(3.12)/4.5(3.41)	Mean Diff	0.1(-0.64,0.84)	Not Sig.	clinically insignificant
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Function:6M WT(m)	68 wks	64/64	37.52(59.1)/22.89(60.03)	Mean Diff	14.63(-6.21,35.47)	Not Sig.	na
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:6M WT(m)	18 mos	152/150	537(102.96)/525(89.87)	adjusted mean difference	Sig ($p < 0.05$)	Diet favored over control	na
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:6M WT(m)	6 mos	152/150	537(93.6)/533(89.87)	Mean Diff	4(-16.78, 24.78)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bliddal; 2011/High	6: Weight loss-Low-Energy Diet w/ Instruction(Formula 6x/day x 8wks; then Instruction 1x/wk x 24wks; then Formula 6x/day x 4wks; then Instruction 1x/2wks x 16wks)	6: Weight loss-Control (Instruction)(Instruction at baseline; wk 8;32;36; and 52)	Function:?HAQ	52 wks	44/45	-0.12(0.2)/-0.04(0.2)	Mean Diff	-0.08(-0.16,0)	Not Sig.	na
Bliddal; 2011/High	6: Weight loss-Low-Energy Diet w/ Instruction(Formula 6x/day x 8wks; then Instruction 1x/wk x 24wks; then Formula 6x/day x 4wks; then Instruction 1x/2wks x 16wks)	6: Weight loss-Control (Instruction)(Instruction at baseline; wk 8;32;36; and 52)	Function:?WOMAC Function(weird scale)	52 wks	44/45	-7.5(13.27)/-3.9(13.42)	Mean Diff	-3.6(-9.22,2.02)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bliddal; 2011/High	6: Weight loss-Low-Energy Diet w/ Instruction(Formula 6x/day x 8wks; then Instruction 1x/wk x 24wks; then Formula 6x/day x 4wks; then Instruction 1x/2wks x 16wks)	6: Weight loss-Control (Instruction)(Instruction at baseline; wk 8;32;36; and 52)	Function:?WOMAC Stiffness(weird scale)	52 wks	44/45	-6.2(17.91)/-3.9(18.11)	Mean Diff	-2.3(-9.89,5.29)	Not Sig.	clinically insignificant
Mihalko; 2018/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Balance Efficacy Confidence	6 mos	152/150	85.39(13.04)/83.76(13.51)	Mean Diff	1.63(-1.38,4.64)	Not Sig.	na
Mihalko; 2018/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Balance Efficacy Confidence	18 mos	152/150	85.44(13.23)/80.9(13.2)	Mean Diff	4.54(1.55,7.53)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mihalko; 2018/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Gait Efficacy Confidence	6 mos	152/150	86.46(16.38)/82.17(16.77)	Mean Diff	4.29(0.54,8.04)	Group 1	na
Mihalko; 2018/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Gait Efficacy Confidence	18 mos	152/150	86.49(16.57)/81.18(16.52)	Mean Diff	5.31(1.56,9.06)	Group 1	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Function:KOOS Activities of Daily Living	68 wks	64/64	8.3(14.21)/6.2(14.21)	Mean Diff	2.1(-2.87,7.07)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Function:KOOS Sports/Recreation	68 wks	64/64	5.8(17.61)/4.7(17.61)	Mean Diff	1.1(-5.06,7.26)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Function:KOOS Symptoms	68 wks	64/64	7.4(15.01)/5.9(14.81)	Mean Diff	1.5(-3.72,6.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rejeski; 2002/Low	6: Weight loss-diet	6: No weight loss-control	Function:SF-36 mental function(26 and 78 week average)	78 wks	73/68	79.21(9.81)/78.56(9.91)	Mean Diff	0.65(-2.64,3.94)	Not Sig.	na
Rejeski; 2002/Low	6: Weight loss-diet	6: No weight loss-control	Function:SF-36-physical function(26 and 78 week average)	78 wks	73/68	57.32(15.1)/49.56(15.1)	Mean Diff	7.76(2.73,12.79)	Group 1	possibly clinically significant
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Function:VAS Disability	68 wks	64/64	-7.5(21.42)/-9(21.62)	Mean Diff	1.5(-6.03,9.03)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:WOMAC Function	6 mos	152/150	16.5(11.23)/17.7(11.16)	Mean Diff	-1.2(-3.74,1.34)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:WOMAC Function	18 mos	152/150	14.2(11.54)/17.6(11.16)	Mean Diff	-3.4(-5.97,-0.83)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mihalko; 2018/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Duration Efficacy Confidence	6 mos	152/150	75.49(25.52)/69.03(26.12)	Mean Diff	6.46(0.61,12.31)	Group 1	na
Mihalko; 2018/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Duration Efficacy Confidence	18 mos	152/150	74.1(25.68)/65.97(25.75)	Mean Diff	8.13(2.31,13.95)	Group 1	na
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Speed (m/s)	18 mos	152/150	1.33(0.22)/1.3(0.19)	adjusted mean difference	Sig ($p < 0.05$)	Diet favored over control	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Speed (m/s)	6 mos	152/150	1.32(0.22)/1.32(0.19)	Mean Diff	0(-0.05,0.05)	Not Sig.	na
Focht ; 2005/Low	5: Self management-exercise + diet	5: Exercise-exercise	Function:stair climb time (s)	72 weeks	162/80	8.85(5.35)/9.15(4.7)	Mean Diff	-0.3(-1.63,1.03)	Not Sig.	na
Focht ; 2005/Low	5: Self management-diet	5: Wellness education-health education control	Function:stair climb time (s)	72 weeks	82/78	9.86(8.78)/9.86(5.56)	Mean Diff	0(-2.29,2.29)	Not Sig.	na
Bliddal; 2011/High	6: Weight loss-Low-Energy Diet w/ Instruction(Formula 6x/day x 8wks; then Instruction 1x/wk x 24wks; then Formula 6x/day x 4wks; then Instruction 1x/2wks x 16wks)	6: Weight loss-Control (Instruction)(Instruction at baseline; wk 8;32;36; and 52)	Composite:?WOMAC Total(weird scale)	52 wks	44/45	-7.3(12.6)/-3(12.75)	Mean Diff	-4.3(-9.64,1.04)	Not Sig.	inconclusive
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Composite:SF-36 Physical Component Score	68 wks	64/64	5.5(7.81)/4.4(7.81)	Mean Diff	1.1(-1.63,3.83)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Composite:SF-36 Physical Component Score	6 mos	152/150	43.5(9.67)/41.5(9.92)	Mean Diff	2(-0.22,4.22)	Not Sig.	inconclusive
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Composite:SF-36 Physical Component Score	18 mos	152/150	44.7(9.67)/42(10.23)	Mean Diff	2.7(0.45,4.95)	Group 1	possibly clinically significant
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	QOL:KOOS Quality of Life	68 wks	64/64	8.2(14.81)/5.4(15.01)	Mean Diff	2.8(-2.42,8.02)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	QOL:SF-36 Mental Component Score	68 wks	64/64	-0.3(7.41)/1.3(7.41)	Mean Diff	-1.6(-4.19,0.99)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	QOL:SF-36 Mental Component Score	18 mos	152/150	56.1(7.18)/55.4(8.68)	Mean Diff	0.7(-1.11,2.51)	Not Sig.	na
Messier; 2013/Moderate	6: Weight loss-Diet + Exercise(energy deficit 800-1k kcal; + exercise)	6: No weight loss-Control (Exercise Alone)(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	QOL:SF-36 Mental Component Score	6 mos	152/150	56.9(7.8)/56.1(8.37)	Mean Diff	0.8(-1.03,2.63)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	QOL:VAS Patient Global Assessment	68 wks	64/64	-5.1(20.02)/-6.1(20.02)	Mean Diff	1(-6,8)	Not Sig.	clinically insignificant
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Other:OMERACT-OARSI Responder(Outcome Measures in Reumatorlogy; Osteoarthritis Research Society International)	68 wks	64/64	50%/51.56%	RR	0.97(0.69,1.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Abdominal Pain(Per Protocol Population; still >80% FU)	68 wks	55/52	10.91%/5.77%	RR	1.89(0.5,7.17)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Allergic Rash(Per Protocol Population; still >80% FU)	68 wks	53/52	9.43%/7.69%	RR	1.23(0.35,4.31)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Anxiety(Per Protocol Population; still >80% FU)	68 wks	53/52	5.66%/3.85%	RR	1.47(0.26,8.45)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Back Pain(Per Protocol Population; still >80% FU)	68 wks	54/50	20.37%/20%	RR	1.02(0.47,2.19)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Bad Breath(Per Protocol Population; still >80% FU)	68 wks	53/52	11.32%/9.62%	RR	1.18(0.38,3.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Biliary Symptoms(Per Protocol Population; still >80% FU)	68 wks	54/52	3.7%/0%	RD	3.704(-5.128, 11.087)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Constipation(Per Protocol Population; still >80% FU)	68 wks	55/52	16.36%/15.38%	RR	1.06(0.44,2.55)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Cramps(Per Protocol Population; still >80% FU)	68 wks	54/49	11.11%/16.33%	RR	0.68(0.25,1.82)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Depressive Tendencies(Per Protocol Population; still >80% FU)	68 wks	53/52	11.32%/7.69%	RR	1.47(0.44,4.92)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Diarrhea(Per Protocol Population; still >80% FU)	68 wks	55/51	5.45%/7.84%	RR	0.7(0.16,2.96)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Dizziness(Per Protocol Population; still >80% FU)	68 wks	55/52	12.73%/15.38%	RR	0.83(0.32,2.12)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Dry Skin(Per Protocol Population; still >80% FU)	68 wks	53/52	7.55%/11.54%	RR	0.65(0.2,2.18)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Eczema(Per Protocol Population; still >80% FU)	68 wks	53/51	7.55%/5.88%	RR	1.28(0.3,5.45)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Epigastric Pain(Per Protocol Population; still >80% FU)	68 wks	55/52	10.91%/1.92%	RR	5.67(0.71,45.53)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Fatigue(Per Protocol Population; still >80% FU)	68 wks	53/52	15.09%/23.08%	RR	0.65(0.29,1.47)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Flatulence(Per Protocol Population; still >80% FU)	68 wks	55/52	34.55%/26.92%	RR	1.28(0.72,2.28)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Hair Loss(Per Protocol Population; still >80% FU)	68 wks	53/52	9.43%/3.85%	RR	2.45(0.5,12.08)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Headache(Per Protocol Population; still >80% FU)	68 wks	53/52	11.32%/9.62%	RR	1.18(0.38,3.62)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Heartburn(Per Protocol Population; still >80% FU)	68 wks	55/51	5.45%/5.88%	RR	0.93(0.2,4.39)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Influenza(Per Protocol Population; still >80% FU)	68 wks	53/52	13.21%/3.85%	RR	3.43(0.75,15.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Joint Pain(Per Protocol Population; still >80% FU)	68 wks	55/51	27.27%/23.53%	RR	1.16(0.6,2.23)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Mood Changes(Per Protocol Population; still >80% FU)	68 wks	53/52	9.43%/9.62%	RR	0.98(0.3,3.19)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Nausea(Per Protocol Population; still >80% FU)	68 wks	55/52	5.45%/1.92%	RR	2.84(0.3,26.41)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Perianal Itching(Per Protocol Population; still >80% FU)	68 wks	53/52	9.43%/3.85%	RR	2.45(0.5,12.08)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Redness(Per Protocol Population; still >80% FU)	68 wks	53/52	7.55%/3.85%	RR	1.96(0.38,10.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Sciatic Pain(Per Protocol Population; still >80% FU)	68 wks	55/51	7.27%/17.65%	RR	0.41(0.14,1.26)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Sensitive to Cold(Per Protocol Population; still >80% FU)	68 wks	53/52	16.98%/11.54%	RR	1.47(0.56,3.84)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Skin Irritation(Per Protocol Population; still >80% FU)	68 wks	53/52	9.43%/5.77%	RR	1.64(0.41,6.5)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Sleeplessness(Per Protocol Population; still >80% FU)	68 wks	53/52	11.32%/21.15%	RR	0.54(0.21,1.34)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Swollen Joints(Per Protocol Population; still >80% FU)	68 wks	55/51	20%/21.57%	RR	0.93(0.44,1.95)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Toothache(Per Protocol Population; still >80% FU)	68 wks	52/52	7.69%/7.69%	RR	1(0.26, 3.79)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Urticaria(Per Protocol Population; still >80% FU)	68 wks	52/52	5.77%/1.92%	RR	3(0.32, 27.91)	Not Sig.	na
Christensen; 2015/High	6: Weight loss-Diet With Weekly Sessions(1 hr weekly sessions x 52 weeks)	6: No weight loss-Control (Usual Care)	Adverse events:Vomiting(Per Protocol Population; still >80% FU)	68 wks	55/52	5.45%/1.92%	RR	2.84(0.3,26.41)	Not Sig.	na

PICO 6: Weight Loss

Diet vs. Exercise

Table 25: Diet vs Exercise

Quality: H=High; M=Moderate; L=Low	M	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Messier; 2013	Mihalko; 2018
Function		
6MWT(m)	↓	
Balance Efficacy Confidence		●
Gait Efficacy Confidence		●
Walking Duration Efficacy Confidence		↓
Walking Speed (m/s)	↓	
calculable MID outcomes		
WOMAC Function	●	
WOMAC Pain	●	
SF-36 Physical component	●	
QOL		
SF-36 Mental Component Score	●	

Evidence Table 3124: Diet vs Exercise

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Pain:WOMAC Pain	6 mos	152/150	4.9(2.81)/4.5(3.41)	Mean Diff	0.4(-0.31,1.11)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Pain:WOMAC Pain	18 mos	152/150	4.8(3.43)/4.4(3.1)	Mean Diff	0.4(-0.34,1.14)	Not Sig.	clinically insignificant
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:6M WT(m)	18 mos	152/150	502(84.24)/525(89.87)	Mean Diff	-23(-42.73,-3.27)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:6MWT(m)	6 mos	152/150	5.5(81.12)/533(89.87)	Mean Diff	-527.5(-546.9,-508.1)	Group 2	na
Mihalko; 2018/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Balance Efficacy Confidence	18 mos	152/150	80.82(13.29)/80.9(13.2)	Mean Diff	-0.08(-3.08,2.92)	Not Sig.	na
Mihalko; 2018/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Balance Efficacy Confidence	6 mos	152/150	83.26(13.6)/83.76(13.51)	Mean Diff	-0.5(-3.57,2.57)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mihalko; 2018/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Gait Efficacy Confidence	18 mos	152/150	81.01(16.82)/81.18(16.52)	Mean Diff	-0.17(-3.95,3.61)	Not Sig.	na
Mihalko; 2018/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Gait Efficacy Confidence	6 mos	152/150	82.26(17.22)/82.17(16.77)	Mean Diff	0.09(-3.76,3.94)	Not Sig.	na
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:WOMAC Function	18 mos	152/150	17.7(12.79)/17.6(11.16)	Mean Diff	0.1(-2.62,2.82)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:WOMAC Function	6 mos	152/150	18.3(10.61)/17.7(11.16)	Mean Diff	0.6(-1.87,3.07)	Not Sig.	clinically insignificant
Mihalko; 2018/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Duration Efficacy Confidence	18 mos	152/150	59.69(26.08)/65.97(25.75)	Mean Diff	-6.28(-12.15,-0.41)	Group 2	na
Mihalko; 2018/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Duration Efficacy Confidence	6 mos	152/150	59.3(26.43)/69.03(26.12)	Mean Diff	-9.73(-15.68,-3.78)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Speed (m/s)	18 mos	152/150	1.27(0.16)/1.3(0.19)	Mean Diff	-0.03(-0.07,0.01)	Not Sig.	na
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Function:Walking Speed (m/s)	6 mos	152/150	1.25(0.19)/1.32(0.19)	Mean Diff	-0.07(-0.11,-0.03)	Group 2	na
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Composite:SF-36 Physical Component Score	18 mos	152/150	42(10.61)/42(10.23)	Mean Diff	0(-2.36,2.36)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	Composite:SF-36 Physical Component Score	6 mos	152/150	41.8(9.98)/41.5(9.92)	Mean Diff	0.3(-1.95,2.55)	Not Sig.	inconclusive
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	QOL:SF-36 Mental Component Score	18 mos	152/150	54.9(7.8)/55.4(8.68)	Mean Diff	-0.5(-2.37,1.37)	Not Sig.	na
Messier; 2013/Moderate	6: Weight loss-Diet(energy deficit 800-1k kcal)	6: Non-arthro Tx-Supervised Exercise(1hr x3/week x 18mo (aerobic walking (15min) strength (20min) aerobic (15 min) cool down (10 min))	QOL:SF-36 Mental Component Score	6 mos	152/150	55(8.74)/56.1(8.37)	Mean Diff	-1.1(-3.04,0.84)	Not Sig.	na

PICO 7: Manual Therapy

Manual Therapy vs. Control

Table 26: Manual Therapy vs Control

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Fitzgerald; 2016**
Function	
40 m walk	↑
Timed Chair Rise	●
Timed up and go; s	↑
Pain	
Knee Pain Rating	↑
calculable MID outcomes	
WOMAC Total	●

Evidence Table 3225: Manual Therapy vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Pain:Knee Pain Rating	1 yrs	75/75	3.9(0.5)/4.1(0.5)	Mean Diff	-0.2(-0.36,-0.04)	Group 1	na
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Pain:Knee Pain Rating	9 wks	75/75	3.3(0.5)/3.2(0.5)	Mean Diff	0.1(-0.06,0.26)	Not Sig.	na
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Function:40 m walk	9 wks	75/75	26.1(1.5)/26.6(1.4)	Mean Diff	-0.5(-0.97,-0.03)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Function:40 m walk	1 yrs	75/75	26.1(1.5)/26.9(1.4)	Mean Diff	-0.8(-1.27,-0.33)	Group 1	na
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Function:Timed Chair Rise	1 yrs	75/75	12.8(1.6)/12.9(1.7)	Mean Diff	-0.1(-0.63,0.43)	Not Sig.	na
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Function:Timed Chair Rise	9 wks	75/75	12.2(1.6)/12(1.7)	Mean Diff	0.2(-0.33,0.73)	Not Sig.	na
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Function:Timed up and go; s	9 wks	75/75	7.3(0.5)/7.5(0.5)	Mean Diff	-0.2(-0.36,-0.04)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Function:Timed up and go; s	1 yrs	75/75	7.2(0.5)/7.5(0.5)	Mean Diff	-0.3(-0.46,-0.14)	Group 1	na
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Composite:WOMAC Total(0-240)	9 wks	75/75	42.4(12.8)/46.9(13.2)	Mean Diff	-4.5(-8.7,-0.3)	Group 1	clinically insignificant
Fitzgerald; 2016/High	7: Manual therapy-Manual Therapy + Exercise(12 Therapy Sessions + Home exercise 2x per week or more)	7: Placebo/Control-Exercise Only (Control)(Home exercise 2x per week or more)	Composite:WOMAC Total(0-240)	1 yrs	75/75	57.4(12.8)/55.4(13.2)	Mean Diff	2(-2.2,6.2)	Not Sig.	clinically insignificant

PICO 7: Manual Therapy

Supervised Exercise and Manual Therapy vs. Control

Table 27: Supervised Exercise and Manual Therapy vs Control

Quality: H=High; M=Moderate; L=Low ↑ **Better Outcomes** ↓ **Worse Outcomes** ● **Not Significant**	**M** **Deyle; 2000**
Function	
6 minute walk distance (m)	↑
6minute walk distance (m)	↑
calculable MID outcomes	
WOMAC Total	↑

Evidence Table 3326: Supervised Exercise and Manual Therapy vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Deyle; 2000/Moderate	5: PT-exercise + physical therapy	5: Placebo/Control-placebo (non-theraputic intensity ultrasound)	Function:6 minute walk distance (m)	4 weeks	33/36	484(121.05)/402.1(129.1)	Mean Diff	81.9(21.79,142.01)	Group 1	na
Deyle; 2000/Moderate	5: PT-exercise + physical therapy	5: Placebo/Control-placebo (non-theraputic intensity ultrasound)	Function:6minute walk distance (m)	8 weeks	33/36	487.4(116.6)/409.7(133.8)	Mean Diff	77.7(17.51,137.89)	Group 1	na
Deyle; 2000/Moderate	5: PT-exercise + physical therapy	5: Placebo/Control-placebo (non-theraputic intensity ultrasound)	Composite:Womac Total	4 weeks	33/36	505.2(189.52)/921.2(563.47)	Mean Diff	-416(-616.68,-215.32)	Group 1	clinically significant
Deyle; 2000/Moderate	5: PT-exercise + physical therapy	5: Placebo/Control-placebo (non-theraputic intensity ultrasound)	Composite:Womac Total	8 weeks	33/36	462.4(421.62)/934.3(631)	Mean Diff	-471.9(-728.3,-215.5)	Group 1	clinically significant

PICO 7: Manual Therapy

Massage vs. Control

Table 28: Manual Therapy vs Control

Quality: H=High; M=Moderate; L=Low	H		M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Sansila; 2019	Pehlivan; 2018	Perlman; 2018
Composite			
Index of severity for OA of the knee	↑		
Function			
QOL Physical Activity		●	
Range of motion	↑		
Time up-and-go test	↑		
Timed Walk (ft/s)			↑
Pain			
VAS Pain			↑
PROMIS-PI T-score(range?)			↑
Pain Intensity	↓		
QOL Pain		↑	
calculable MID outcomes			
WOMAC Function		●	↑
WOMAC Stiffness		↑	↑
WOMAC Pain		↑	↑
VAS Pain	●		
VAS Global	●		
WOMAC Global (VAS Version)			↑
VAS Functionality	●		
VAS Stiffness	●		
QOL			
QOL Mental Health		●	
QOL Social Functionality		●	
QOL Social Support		●	

Evidence Table 3427: Massage vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Pain:PROMIS-PI T-score(range?)	8 wks	148	none	Mean Diff	-1.3(-3.04,0.45)	Not Sig.	na
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Pain:PROMIS-PI T-score(range?)	8 wks	149	none	Mean Diff	-2.09(-3.73,-0.45)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Pain:Pain Intensity	12 wks	30/30	2.62(1.87)/2.63(0.1)	Mean Diff	-0.01(-0.71,0.69)	Not Sig.	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Pain:Pain Intensity	6 wks	30/30	4.37(0.1)/4.31(0.11)	Mean Diff	0.06(0.01,0.11)	Group 2	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Pain:QOL Pain	4 wks	30/30	67.5(16.6)/80.33(12.97)	Mean Diff	-12.83(-20.54,-5.12)	Group 2	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Pain:QOL Pain	8 wks	30/30	56(17.01)/69.83(16.08)	Mean Diff	-13.83(-22.39,-5.27)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Pain:VAS Pain	8 wks	149	none	Mean Diff	-11.2(-18.53,-3.88)	Group 1	na
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Pain:VAS Pain	8 wks	148	none	Mean Diff	-4(-11.77, 3.77)	Not Sig.	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Pain:VAS Pain	6 wks	30/30	3.34(0.11)/4.08(0.1)	Mean Diff	-0.74(-0.79,-0.69)	Group 1	clinically insignificant
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Pain:VAS Pain	12 wks	30/30	1.47(0.07)/2.41(0.08)	Mean Diff	-0.94(-0.98,-0.9)	Group 1	clinically insignificant
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Pain:WOMAC Pain	4 wks	30/30	7.64(2.98)/5.96(2.7)	Mean Diff	1.68(0.21,3.15)	Group 2	possibly clinically significant
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Pain:WOMAC Pain	8 wks	30/30	9.18(2.67)/7.21(3.13)	Mean Diff	1.97(0.47,3.47)	Group 2	possibly clinically significant
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Pain:WOMAC Pain Subscale (VAS Version)	8 wks	149	none	Mean Diff	-10.83(-16.23,-5.43)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Pain:WOMAC Pain Subscale (VAS Version)	8 wks	148	none	Mean Diff	0.15(-5.57,5.86)	Not Sig.	clinically insignificant
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Function:QOL Physical Activity	4 wks	30/30	37.93(13.36)/40.4(14.16)	Mean Diff	-2.47(-9.59,4.65)	Not Sig.	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Function:QOL Physical Activity	8 wks	30/30	35.08(13.56)/38.31(14.33)	Mean Diff	-3.23(-10.44, 3.98)	Not Sig.	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:Range of motion	6 wks	30/30	106.12(1.85)/102.62(2)	Mean Diff	3.5(2.5,4.5)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:Range of motion	12 wks	30/30	124.5(1.87)/118.85(2.03)	Mean Diff	5.65(4.64,6.66)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:Time up-and-go test	6 wks	30/30	6.15(0.13)/6.26(0.11)	Mean Diff	-0.11(-0.17,-0.05)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:Time up-and-go test	12 wks	30/30	5.01(0.16)/5.13(0.14)	Mean Diff	-0.12(-0.2,-0.04)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Function:Timed Walk (ft/s)	8 wks	148	none	Mean Diff	0.03(-0.11,0.17)	Not Sig.	na
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Function:Timed Walk (ft/s)	8 wks	149	none	Mean Diff	0.16(0.03,0.29)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:VAS Functionality	6 wks	30/30	2.46(0.07)/2.86(0.07)	Mean Diff	-0.4(-0.44,-0.36)	Group 1	clinically insignificant
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:VAS Functionality	12 wks	30/30	1.15(0.05)/1.58(0.05)	Mean Diff	-0.43(-0.46,-0.4)	Group 1	clinically insignificant
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:VAS Stiffness	6 wks	30/30	3.42(0.12)/4.08(0.12)	Mean Diff	-0.66(-0.72,-0.6)	Group 1	clinically insignificant
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Function:VAS Stiffness	12 wks	30/30	1.53(0.08)/2.24(0.08)	Mean Diff	-0.71(-0.75,-0.67)	Group 1	clinically insignificant
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Function:WOMAC Function	8 wks	30/30	35.73(11)/31.98(9.78)	Mean Diff	3.75(-1.63,9.13)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Function:WOMAC Function	4 wks	30/30	33.58(14.26)/29.53(9.5)	Mean Diff	4.05(-2.23,10.33)	Not Sig.	inconclusive
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Function:WOMAC Function Subscale (VAS Version)	8 wks	148	none	Mean Diff	-1.91(-7.24,3.43)	Not Sig.	clinically insignificant
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Function:WOMAC Function Subscale (VAS Version)	8 wks	149	none	Mean Diff	-8.15(-13.16,-3.14)	Group 1	possibly clinically significant
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Function:WOMAC Stiffness	4 wks	30/30	1.68(1.41)/1.25(1.08)	Mean Diff	0.43(-0.22,1.08)	Not Sig.	inconclusive
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	Function:WOMAC Stiffness	8 wks	30/30	2.34(1.4)/1.65(1.25)	Mean Diff	0.69(0,1.38)	Group 2	possibly clinically significant
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Function:WOMAC Stiffness Subscale (VAS Version)	8 wks	149	none	Mean Diff	-10.53(-17.23,-3.84)	Group 1	possibly clinically significant
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Function:WOMAC Stiffness Subscale (VAS Version)	8 wks	148	none	Mean Diff	-3.01(-10.07,4.06)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Composite:Index of severity for OA of the knee	6 wks	30/30	3.33(0.06)/3.55(0.05)	Mean Diff	-0.22(-0.25,-0.19)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Composite:Index of severity for OA of the knee	12 wks	30/30	2.54(0.06)/2.89(0.06)	Mean Diff	-0.35(-0.38,-0.32)	Group 1	na
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Composite:VAS Global	6 wks	30/30	2.72(0.08)/3.22(0.08)	Mean Diff	-0.5(-0.54,-0.46)	Group 1	clinically insignificant
Sansila; 2019/High	7: Manual therapy-Court-type Traditional Thai Massage	7: Placebo/Control-Control	Composite:VAS Global	12 wks	30/30	1.23(0.05)/1.81(0.05)	Mean Diff	-0.58(-0.61,-0.55)	Group 1	clinically insignificant
Perlman; 2018/Moderate	7: Manual therapy-Light-touch(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Composite:WOMAC Global (VAS Version)	8 wks	148	none	Mean Diff	-1.4(-6.81,4.01)	Not Sig.	clinically insignificant
Perlman; 2018/Moderate	7: Manual therapy-Swedish massage(Weekly for 60 min)	7: Placebo/Control-Usual Care(Weekly for 60 min)	Composite:WOMAC Global (VAS Version)	8 wks	149	none	Mean Diff	-9.55(-14.66,-4.45)	Group 1	possibly clinically significant
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	QOL:QOL Mental Health	4 wks	30/30	58.48(12.66)/62.46(11.34)	Mean Diff	-3.98(-10.19, 2.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	QOL:QOL Mental Health	8 wks	30/30	56.41(12.75)/60.97(11.15)	Mean Diff	-4.56(-10.75, 1.63)	Not Sig.	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	QOL:QOL Social Functionality	4 wks	30/30	49.44(9.67)/52.55(10.19)	Mean Diff	-3.11(-8.24,2.02)	Not Sig.	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	QOL:QOL Social Functionality	8 wks	30/30	48.66(9.81)/53.77(10.16)	Mean Diff	-5.11(-10.27, 0.05)	Not Sig.	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	QOL:QOL Social Support	4 wks	30/30	51.75(16.57)/51.16(10.84)	Mean Diff	0.59(-6.67,7.85)	Not Sig.	na
Pehlivan; 2018/High	7: Manual therapy-Massage	7: Placebo/Control-Control	QOL:QOL Social Support	8 wks	30/30	51.58(16.4)/50.83(10.71)	Mean Diff	0.75(-6.43,7.93)	Not Sig.	na

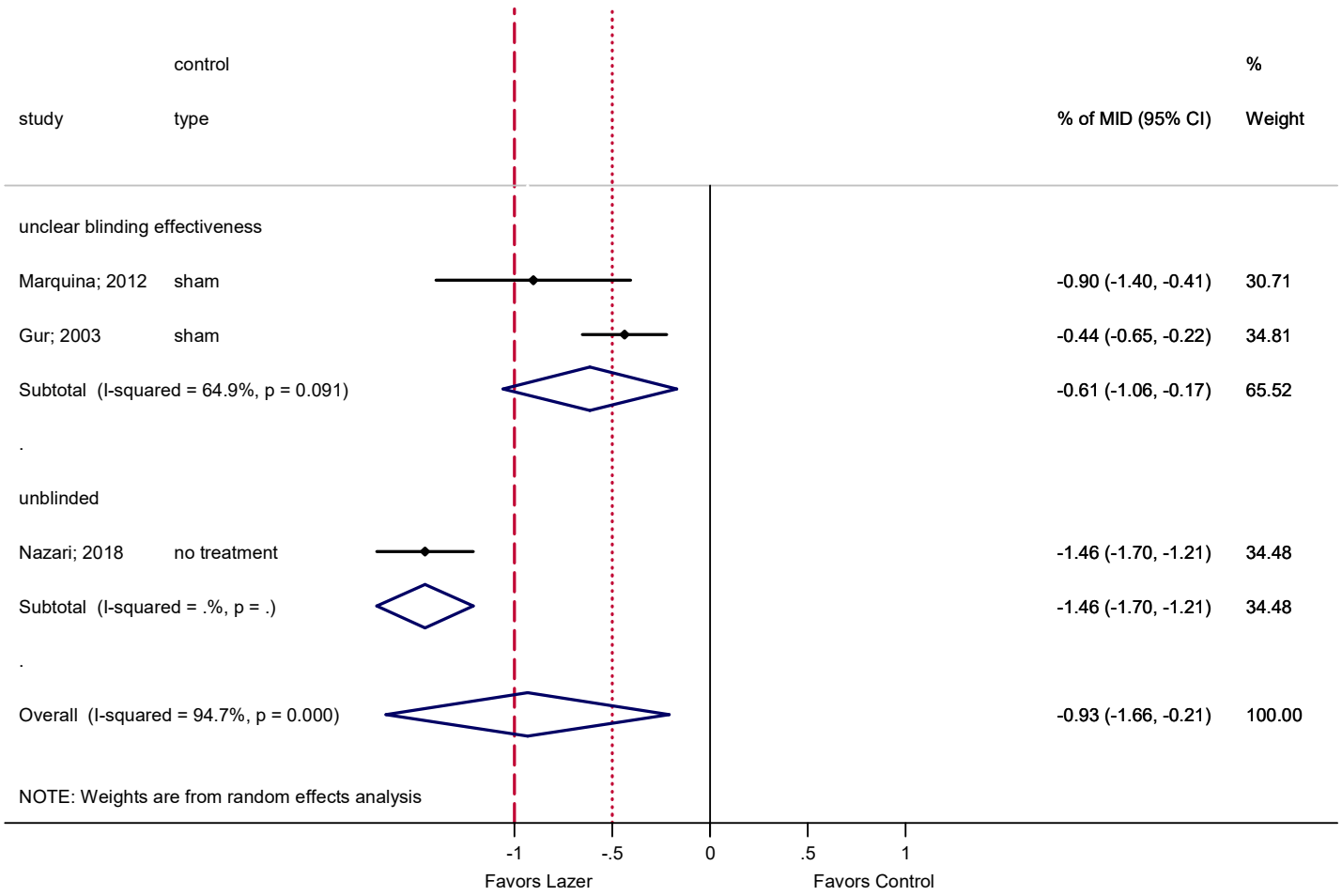
PICO 8: Physical/Electrotherapeutic Agents

Laser Treatment vs. Control

Table 29: Laser Treatment vs Control

Quality: H=High; M=Moderate; L=Low	H		M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Nazari; 2018	Gur; 2003	Marquina; 2012
Function			
Timed Up and Go test	↑		
6-m Walk Test	↑		
Flexion range of motion	↑		
Morning stiffness (minute)		↑	
Pain			
Painless walking distance (m)		↑	
Painless walking duration (minute)		↑	
calculable MID outcomes			
WOMAC Total	↑		
WOMAC Function	↑		
WOMAC Stiffness	↑		
WOMAC Pain	↑		
VAS Pain	↑		↑
pain at rest (VAS)		↑	
WOMAC		↑	
Pain at flexion (VAS)		↑	
Pain at movement (VAS		↑	

Meta-Analysis Figure 10: Laser Treatment vs Control- Pain by Blinding Effectiveness



Evidence Table 3528: Laser Treatment vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at flexion (VAS)	8 wks	30/30	3.24(1.63)/4.34(1.21)	Mean Diff	-1.1(-1.84,-0.36)	Group 1	some may benefit
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at flexion (VAS)	4 wks	30/30	4.2(2.3)/5.42(1.52)	Mean Diff	-1.22(-2.23,-0.21)	Group 1	possibly clinically significant
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at flexion (VAS)	12 wks	30/30	2.68(1.21)/4.02(1.29)	Mean Diff	-1.34(-1.99,-0.69)	Group 1	some may benefit
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at movement (VAS	12 wks	30/30	3.58(1.12)/4.3(1.38)	Mean Diff	-0.72(-1.37,-0.07)	Group 1	clinically insignificant
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at movement (VAS	8 wks	30/30	3.61(1.42)/4.58(1.36)	Mean Diff	-0.97(-1.69,-0.25)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at movement (VAS	4 wks	30/30	4.42(1.76)/5.58(1.62)	Mean Diff	-1.16(-2.03,-0.29)	Group 1	possibly clinically significant
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at rest (VAS)	12 wks	30/30	0.71(0.65)/1.58(0.97)	Mean Diff	-0.87(-1.3,-0.44)	Group 1	clinically insignificant
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at rest (VAS)	4 wks	30/30	1.08(1.41)/2.3(1.52)	Mean Diff	-1.22(-1.98,-0.46)	Group 1	some may benefit
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Pain at rest (VAS)	8 wks	30/30	0.54(0.93)/1.86(1.22)	Mean Diff	-1.32(-1.88,-0.76)	Group 1	some may benefit
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Painless walking distance (m)	4 wks	30/30	520(506.6)/402.1(310.3)	Mean Diff	117.9(-100.17,335.97)	Not Sig.	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Painless walking distance (m)	8 wks	30/30	644(602.1)/398.1(317.2)	Mean Diff	245.9(-4.52,496.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Painless walking distance (m)	12 wks	30/30	644(449.1)/380(284.3)	Mean Diff	264(68.99,459.01)	Group 2	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Painless walking duration (minute)	8 wks	30/30	28.8(28.9)/17.4(10.44)	Mean Diff	11.4(0.03,22.77)	Group 2	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Painless walking duration (minute)	12 wks	30/30	29.4(28.23)/17.72(10.17)	Mean Diff	11.68(0.57,22.79)	Group 2	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Pain:Painless walking duration (minute)	4 wks	30/30	25.68(29.89)/18.64(11.69)	Mean Diff	7.04(-4.83,18.91)	Not Sig.	na
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-Physical Therapy	Pain:VAS Pain	12 wks	30/30	4.14(0.68)/5.21(0.59)	Mean Diff	-1.07(-1.4,-0.74)	Group 1	some may benefit
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Pain:VAS Pain	12 wks	30/30	4.14(0.68)/5.64(0.5)	Mean Diff	-1.5(-1.81,-1.19)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Marquina; 2012/Moderate	8: Electrotherapeutic agents-Laser Therapy	8: Placebo/Control-Placebo	Pain:VAS Pain	30 days	53/48	2.8(2.4)/4.6(2.6)	Mean Diff	-1.8(-2.79,-0.81)	Group 1	possibly clinically significant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-Physical Therapy	Pain:WOMAC Pain	12 wks	30/30	5.36(0.66)/5.66(0.92)	Mean Diff	-0.3(-0.71,0.11)	Not Sig.	clinically insignificant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Pain:WOMAC Pain	12 wks	30/30	5.36(0.66)/7.78(0.9)	Mean Diff	-2.42(-2.83,-2.01)	Group 1	clinically significant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Function:6-m Walk Test	12 wks	30/30	415.93(21.29)/402.37(20.36)	Mean Diff	13.56(2.79,24.33)	Group 2	na
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-conventional pt-TENS and ultrasound	Function:6-m Walk Test	12 wks	30/30	415.93(21.29)/406.03(20.05)	Mean Diff	9.9(-0.79,20.59)	Not Sig.	na
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-Physical Therapy	Function:Flexion range of motion	12 wks	30/30	130.6(2.59)/129.16(2.24)	Mean Diff	1.44(0.19,2.69)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Function:Flexion range of motion	12 wks	30/30	130.6(2.59)/126.34(2.07)	Mean Diff	4.26(3.05,5.47)	Group 1	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Function:Morning stiffness (minute)	8 wks	30/30	3.48(2.85)/6.2(5.25)	Mean Diff	-2.72(-4.92,-0.52)	Group 1	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Function:Morning stiffness (minute)	12 wks	30/30	3.44(2.87)/7.09(4.18)	Mean Diff	-3.65(-5.51,-1.79)	Group 1	na
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Function:Morning stiffness (minute)	4 wks	30/30	4.16(2.8)/8.32(4.74)	Mean Diff	-4.16(-6.18,-2.14)	Group 1	na
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-Physical Therapy	Function:Timed Up and Go Test	12 wks	30/30	8.6(0.81)/9.01(0.71)	Mean Diff	-0.41(-0.8,-0.02)	Group 1	na
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Function:Timed Up and Go Test	12 wks	30/30	8.6(0.81)/9.22(0.65)	Mean Diff	-0.62(-1,-0.24)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-conventional pt-TENS and ultrasound	Function:WOMAC Function	12 wks	30/30	16.43(1.22)/18.56(1.19)	Mean Diff	-2.13(-2.75,-1.51)	Group 1	clinically insignificant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Function:WOMAC Function	12 wks	30/30	16.43(1.22)/25.83(1.25)	Mean Diff	-9.4(-10.04,-8.76)	Group 1	clinically significant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-conventional pt-TENS and ultrasound	Function:WOMAC Stiffness	12 wks	30/30	2.56(0.62)/3.13(0.77)	Mean Diff	-0.57(-0.93,-0.21)	Group 1	possibly clinically significant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Function:WOMAC Stiffness	12 wks	30/30	2.56(0.62)/3.32(0.78)	Mean Diff	-0.76(-1.12,-0.4)	Group 1	possibly clinically significant
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Composite:WOMAC	4 wks	30/30	31.88(12.82)/43.64(11.64)	Mean Diff	-11.76(-18.09,-5.43)	Group 1	possibly clinically significant
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Composite:WOMAC	12 wks	30/30	29.56(8.81)/34.96(7.19)	Mean Diff	-5.4(-9.56,-1.24)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gur; 2003/High	8: Electrotherapeutic agents-Actual laser therapy for 5 minutes	8: Placebo/Control-Placebo	Composite:WOMAC	8 wks	30/30	28.6(9.75)/35.32(9.77)	Mean Diff	-6.72(-11.76,-1.68)	Group 1	possibly clinically significant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: Exercise-Exercise Therapy	Composite:WOMAC Total	12 wks	30/30	24.36(1.84)/36.93(1.68)	Mean Diff	-12.57(-13.48,-11.66)	Group 1	clinically significant
Nazari; 2018/High	8: Electrotherapeutic agents-High Intensity Laser Therapy	5: PT-Physical Therapy	Composite:WOMAC Total	12 wks	30/30	24.36(1.84)/27.36(2.2)	Mean Diff	-3(-4.05,-1.95)	Group 1	clinically insignificant

PICO 8: Physical/Electrotherapeutic Agents

Acupuncture vs. Control

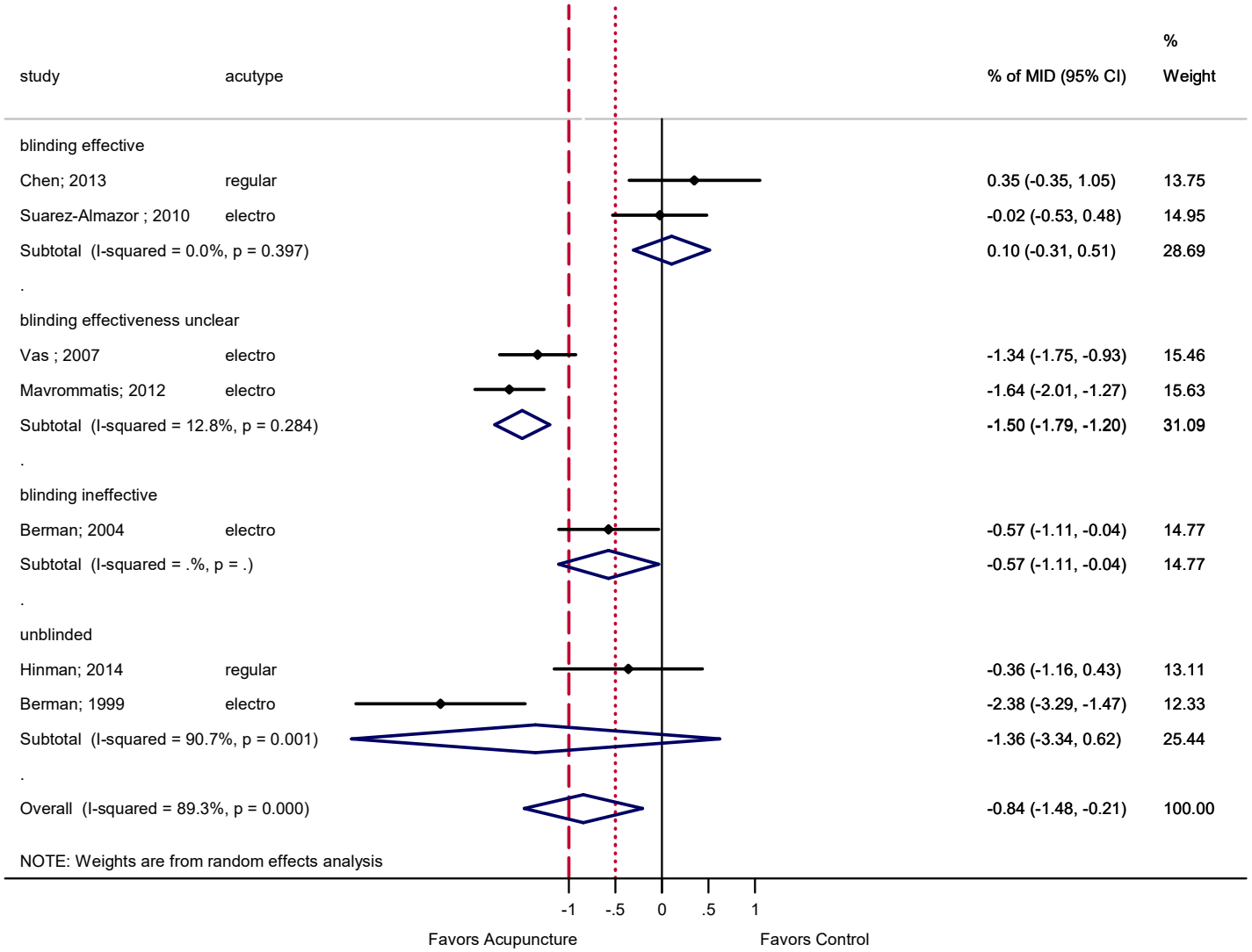
Table 30: Acupuncture vs Control

Quality: H=High; M=Moderate; L=Low	H						M			
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Berman; 2004	Chen; 2013	Mavrommatis; 2012	Sandgee; 2002	Hinman; 2014	Suarez-Almazor ; 2010	Berman; 1999	Witt; 2005	Vas ; 2007	Dai ; 2003
Composite										
Lequesne Index							↑			
Function										
SF-12 Physical Component Score					●	●				
SF-36 Physical health	●							↑		
6MWT(m)		●								
change in 6 min walk distance (ft)	●									
PLQC physical capability									●	
PLQC psychological functioning									●	
PLQC social functioning									●	
Timed get up and go (sec)						●				
change in 50 feet walk time (sec)				●						
change in Lequesne's functional index				↑						
knee joint function (VAS)										↓
Other										
JOA improvement										↑
change in number of paracetamol take (tablets/wk)				●						
total accumulated # diclofenac tablets									↑	
Pain										
Alogmeter(unclear direction)			↑							
Adverse events										
Bruising		●								
Other		●								
Fatigue		●								
Swelling		●								
Agitation		●								
Increased Pain		●								
Muscle Soreness		●								
Redness/Infection		●								
Tearfulness		●								
Weakness		●								

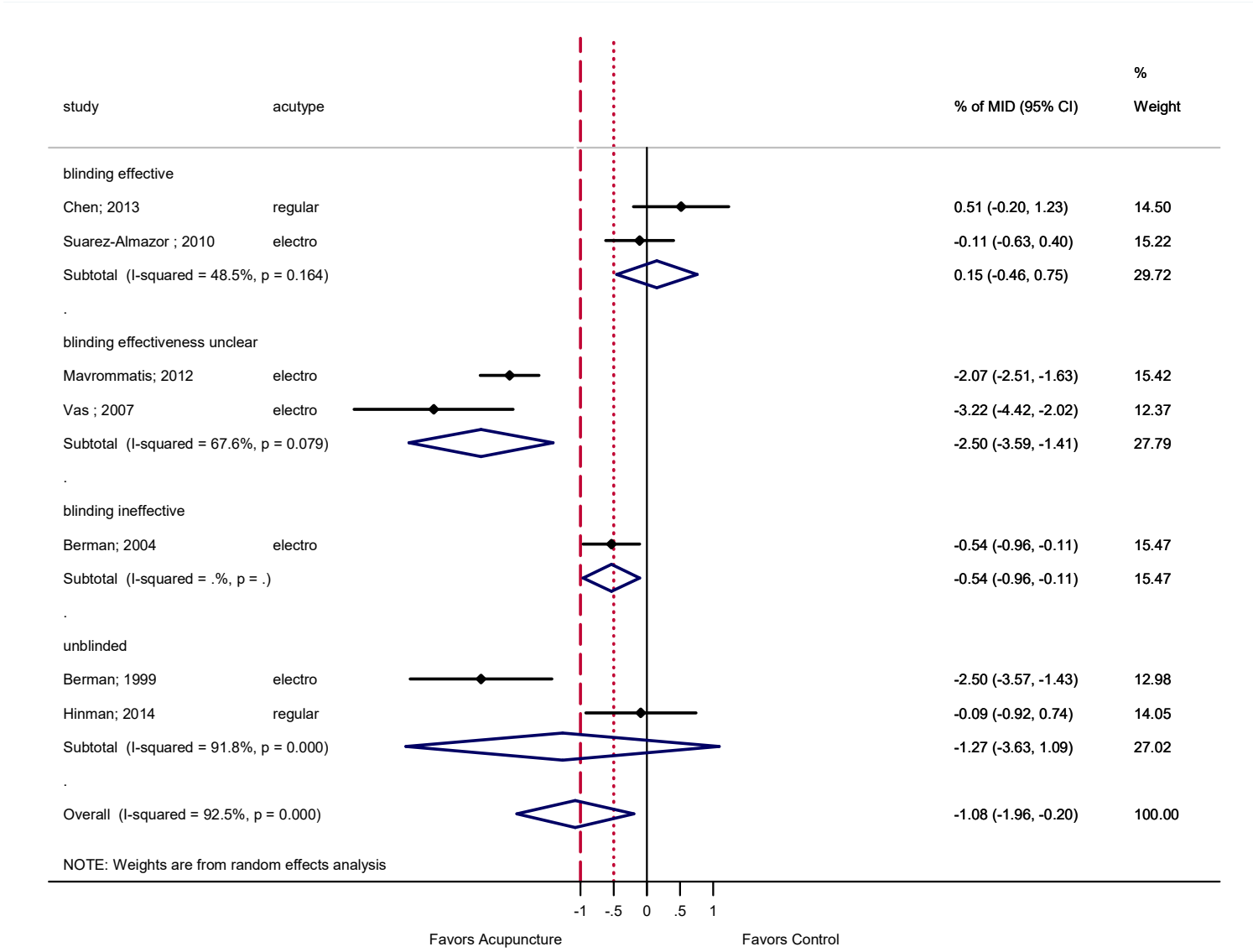
Table 30 Continued: Acupuncture vs Control

Quality: H=High; M=Moderate; L=Low	H						M			
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Berman; 2004	Chen; 2013	Mavrommatis; 2012	Sandgee; 2002	Hinman; 2014	Suarez-Almazor ; 2010	Berman; 1999	Witt; 2005	Vas ; 2007	Dai ; 2003
calculable MID outcomes										
WOMAC Total		●	↑	↑			↑	↑	↑	
WOMAC Function	↑	●	↑		●	●	↑		↑	
WOMAC Stiffness		●	↑	●				↑	↑	
WOMAC Pain	↑	●	↑		●	●	↑			
VAS Pain			↑		↑					
VAS Pain (Walking)					●					
SF-36 Physical component		●	↑							
Activity Restriction (VAS)					●					
change in WOMAC disability				●						
VAS Pain (Standing)					●					
VAS pain score						●				
final pain (VAS)									↑	
QOL										
SF-36 Mental Health								↑		
SF-12 Mental Component Score					↓	●				
SF-36 Mental Component		●	●							
PLQC negative mood									●	
PLQC social wellbeing									●	
AQoL-6D					●					
Patient Global Assessment "Better"(unclear direction)		●								
Patient Global Assessment "Much Better"		●								
Patient Global Assessment "Slightly Better"(unclear direction)		●								

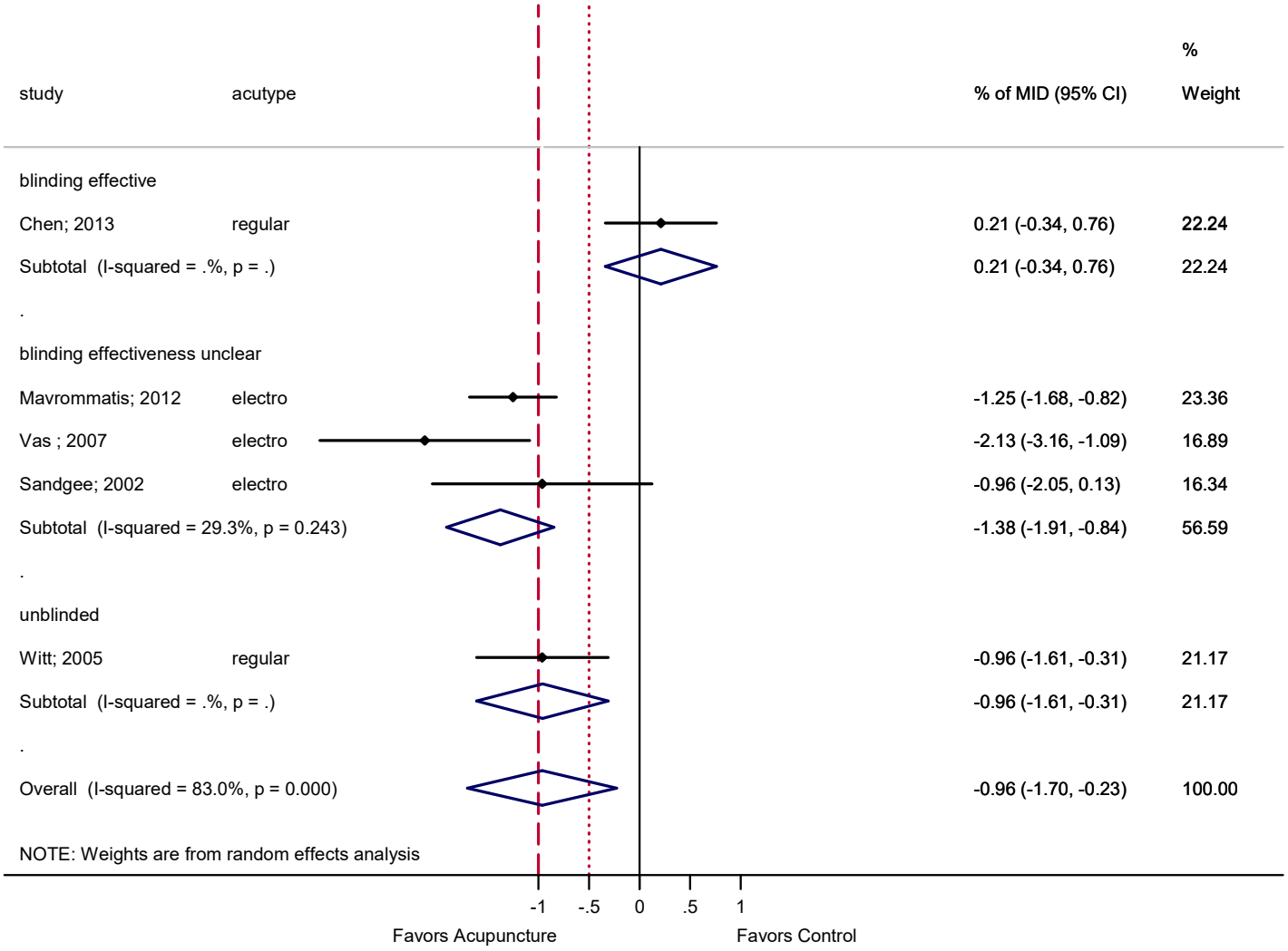
Meta-Analysis Figure 11: Acupuncture vs Control- Pain by Blinding Effectiveness



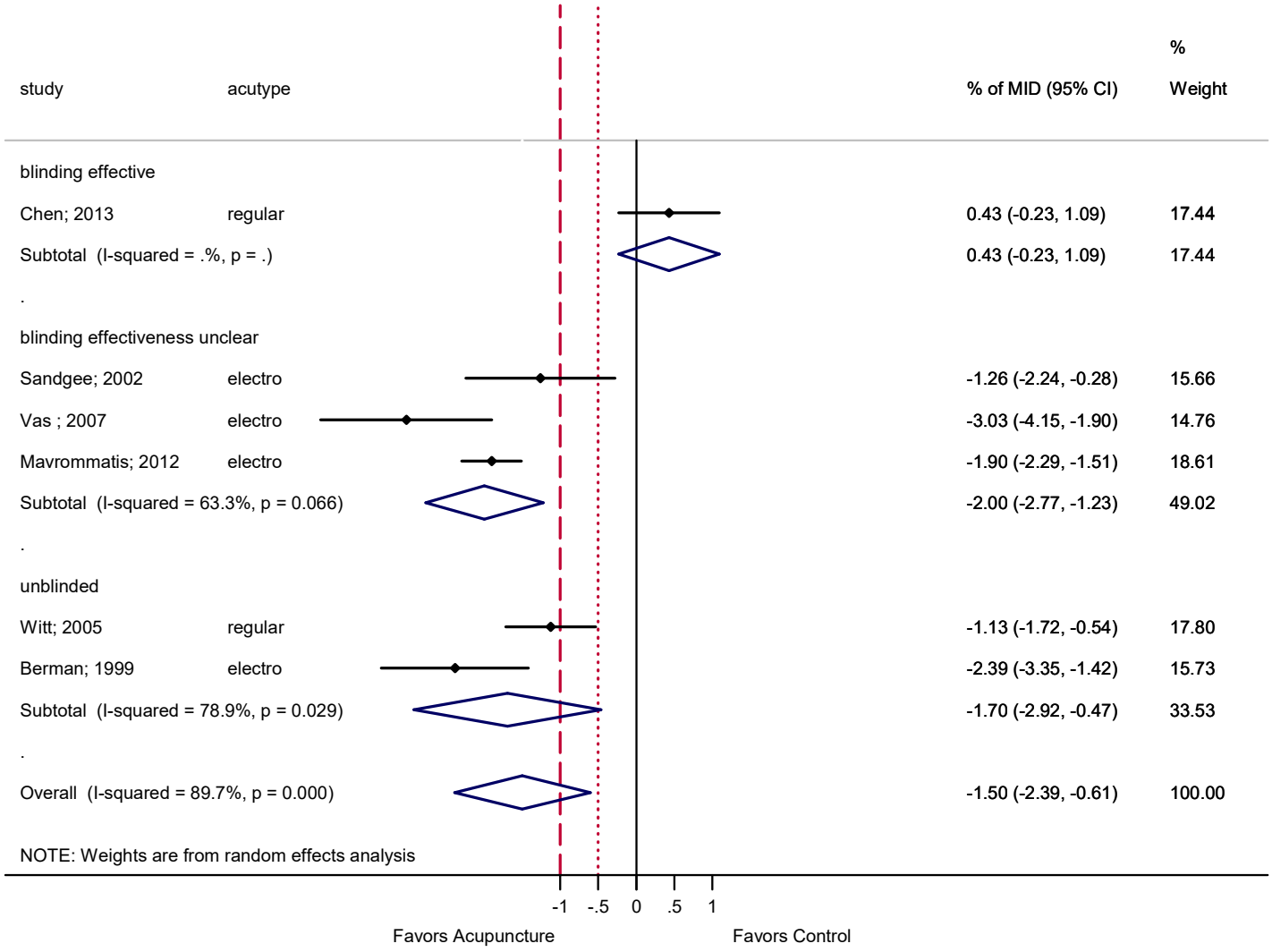
Meta-Analysis Figure 12: Acupuncture vs Control- Function by Blinding Effectiveness



Meta-Analysis Figure 13: Acupuncture vs Control- Stiffness by Blinding Effectiveness



Meta-Analysis Figure 14: Acupuncture vs Control- WOMAC Total by Blinding Effectiveness



Evidence Table 3629: Acupuncture vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	QoL:AQoL-6D	1 yrs	58/51	0.73(0.17)/0.74(0.16)	Mean Diff	-0.01(-0.07,0.05)	Not Sig.	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	QoL:AQoL-6D	1 yrs	59/62	0.74(0.17)/0.77(0.16)	Mean Diff	-0.03(-0.09,0.03)	Not Sig.	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	QoL:AQoL-6D	12 wks	64/69	0.75(0.18)/0.79(0.16)	Mean Diff	-0.04(-0.1,0.02)	Not Sig.	na
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	QoL:AQoL-6D	12 wks	65/58	0.73(0.17)/0.78(0.12)	Mean Diff	-0.05(-0.1,0)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment "Better"(unclear direction)	12 wks	104/109	34.62%/40.37%	RR	0.86(0.6,1.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment "Better"(unclear direction)	26 wks	104/109	23.08%/24.77%	RR	0.93(0.58,1.51)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment "Much Better"	12 wks	104/109	10.58%/15.6%	RR	0.68(0.33,1.38)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment "Much Better"	26 wks	104/109	8.65%/11.01%	RR	0.79(0.35,1.79)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment "Slightly Better"(unclear direction)	12 wks	104/109	75%/72.48%	RR	1.03(0.88,1.21)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment "Slightly Better"(unclear direction)	26 wks	104/109	50%/47.71%	RR	1.05(0.8,1.38)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	QoL:SF-36 Mental Component	12 wks	104/109	52(13.11)/53.9(11.06)	Mean Diff	-1.9(-5.18,1.38)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	QoL:SF-36 Mental Component	8 wks	39/40	52.2(8)/51.5(6.1)	Mean Diff	0.7(-2.5,3.9)	Not Sig.	na
Witt; 2005/Moderate	8: Physical agents-minimal acupuncture	8: Placebo/Control-waiting list	QoL:SF-36 mental health	8 wks	76/74	51.9(8.72)/50.7(8.6)	Mean Diff	1.2(-1.59,3.99)	Not Sig.	na
Witt; 2005/Moderate	8: Physical agents-manual acupuncture (Chinese)	8: Placebo/Control-waiting list	QoL:SF-36 mental health	8 wks	150/74	53.6(8.57)/50.7(8.6)	Mean Diff	2.9(0.49,5.31)	Group 1	na
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:Alogmeter(unclear direction)	4 wks	40/40	3(0.4)/2.8(0.3)	Mean Diff	0.2(0.04,0.36)	Group 1	na
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:Alogmeter(unclear direction)	8 wks	39/40	3.8(0.5)/3.3(0.3)	Mean Diff	0.5(0.31,0.69)	Group 1	na
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:Alogmeter(unclear direction)	12 wks	39/39	3.6(0.4)/3(0.3)	Mean Diff	0.6(0.44,0.76)	Group 1	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:VAS Pain	1 yrs	59/62	4(2.7)/4.6(2.6)	Mean Diff	-0.6(-1.56,0.36)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:VAS Pain	12 wks	64/69	3.3(2.2)/4.4(2.4)	Mean Diff	-1.1(-1.89,-0.31)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Pain:VAS Pain	12 wks	65/58	3.4(2.2)/3.4(2.3)	Mean Diff	0(-0.81,0.81)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Pain:VAS Pain	1 yrs	58/51	4(2.5)/3.9(2.5)	Mean Diff	0.1(-0.85,1.05)	Not Sig.	clinically insignificant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:VAS Pain	4 wks	40/40	33.3(14.8)/48.2(7.6)	Mean Diff	-14.9(-20.17,-9.63)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:VAS Pain	8 wks	39/40	15.2(9.6)/35.5(6.7)	Mean Diff	-20.3(-24.03,-16.57)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:VAS Pain	12 wks	39/39	19.9(11.1)/43.1(8.4)	Mean Diff	-23.2(-27.64,-18.76)	Group 1	possibly clinically significant
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:VAS Pain (Standing)	1 yrs	59/62	3.7(2.9)/4(2.6)	Mean Diff	-0.3(-1.29,0.69)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:VAS Pain (Standing)	12 wks	64/69	3.2(2.3)/3.8(2.5)	Mean Diff	-0.6(-1.42,0.22)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	Pain:VAS Pain (Standing)	1 yrs	58/51	3.8(2.6)/3.5(2.9)	Mean Diff	0.3(-0.75,1.35)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	Pain:VAS Pain (Standing)	12 wks	65/58	3.3(2.4)/2.9(2.4)	Mean Diff	0.4(-0.46,1.26)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	Pain:VAS Pain (Walking)	12 wks	65/58	3.6(2.4)/3.7(2.6)	Mean Diff	-0.1(-1,0.8)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	Pain:VAS Pain (Walking)	1 yrs	58/51	4.1(2.6)/4.2(2.6)	Mean Diff	-0.1(-1.09,0.89)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:VAS Pain (Walking)	1 yrs	59/62	4.1(2.9)/4.4(2.6)	Mean Diff	-0.3(-1.29,0.69)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:VAS Pain (Walking)	12 wks	64/69	3.4(2.2)/4.3(2.4)	Mean Diff	-0.9(-1.69,-0.11)	Group 1	clinically insignificant
Suarez-Almazor ; 2010/high	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Pain:VAS pain score	13 wks	150/151	36.2(28.5)/36.7(29)	Mean Diff	-0.5(-7.02,6.02)	Not Sig.	clinically insignificant
Suarez-Almazor ; 2010/high	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Pain:VAS pain score	4 wks	150/151	34.8(25.29)/38.2(25.4)	Mean Diff	-3.4(-9.15,2.35)	Not Sig.	clinically insignificant
Suarez-Almazor ; 2010/high	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Pain:VAS pain score	6 wks	150/151	29(26.3)/32.5(27.8)	Mean Diff	-3.5(-9.64,2.64)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:WOMAC Pain	12 wks	64/69	6.7(3.8)/7.3(3.9)	Mean Diff	-0.6(-1.92,0.72)	Not Sig.	inconclusive
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Pain:WOMAC Pain	1 yrs	59/62	6.7(4)/7.4(4.1)	Mean Diff	-0.7(-2.16,0.76)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Pain:WOMAC Pain	12 wks	65/58	6.6(3.9)/6.6(3.9)	Mean Diff	0(-1.39,1.39)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Pain:WOMAC Pain	1 yrs	58/51	7.1(4.1)/6.9(4)	Mean Diff	0.2(-1.34,1.74)	Not Sig.	inconclusive
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Pain:WOMAC Pain	12 wks	104/109	7.51(4.53)/6.93(4.06)	Mean Diff	0.58(-0.58,1.74)	Not Sig.	inconclusive
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Pain:WOMAC Pain	26 wks	104/109	8.56(4.06)/7.79(5.06)	Mean Diff	0.77(-0.47,2.01)	Not Sig.	inconclusive
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Pain:WOMAC Pain	4 wks	150/151	6.36(3.5)/6.52(3.44)	Mean Diff	-0.16(-0.95,0.63)	Not Sig.	clinically insignificant
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Pain:WOMAC Pain	6 wks	150/151	5.62(3.68)/6.28(3.7)	Mean Diff	-0.66(-1.5,0.18)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:WOMAC Pain (0-500)	8 wks	39/40	61(28.7)/177(28.5)	Mean Diff	-116(-128.82,-103.18)	Group 1	clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:WOMAC Pain (0-500)	4 wks	40/40	123.4(38.4)/164.9(37)	Mean Diff	-41.5(-58.29,-24.71)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Pain:WOMAC Pain (0-500)	12 wks	39/39	77.9(32.9)/145.9(35.5)	Mean Diff	-68(-83.44,-52.56)	Group 1	clinically significant
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Pain:WOMAC Pain (VAS Scale)	13 wks	150/151	30.8(17.9)/31(19.1)	Mean Diff	-0.2(-4.4,4)	Not Sig.	clinically insignificant
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Pain:change in WOMAC pain	4 weeks	173/163	-2.22(3.16)/-1.98(3.19)	Mean Diff	-0.24(-0.92,0.44)	Not Sig.	clinically insignificant
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Pain:change in WOMAC pain	8 weeks	169/161	-3.15(3.77)/-2.66(3.3)	Mean Diff	-0.49(-1.26,0.28)	Not Sig.	clinically insignificant
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Pain:change in WOMAC pain	26 weeks	142/141	-3.79(3.93)/-2.92(3.56)	Mean Diff	-0.87(-1.75,0.01)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Pain:change in WOMAC pain	12 weeks	158/157	-3.63(3.9)/-2.68(4.13)	Mean Diff	-0.95(-1.84,-0.06)	Group 1	possibly clinically significant
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Pain:final pain (VAS)	13 wks	48/49	10.6(10.8)/37.2(26.3)	Mean Diff	-26.6(-34.73,-18.47)	Group 1	possibly clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Pain:womac pain	4 weeks	36/37	6.25(3.46)/9.46(3.5)	Mean Diff	-3.21(-4.83,-1.59)	Group 1	possibly clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Pain:womac pain	12 weeks	36/37	5.56(3.44)/9.51(3.01)	Mean Diff	-3.95(-5.46,-2.44)	Group 1	clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Pain:womac pain	8 weeks	36/37	5.34(3.62)/9.46(3.56)	Mean Diff	-4.12(-5.8,-2.44)	Group 1	clinically significant
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Function:6MWT(m)	12 wks	104/109	1119(383.08)/1147(323.93)	Mean Diff	-28(-124.07,68.07)	Not Sig.	na
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	Function:Activity Restriction (VAS)	1 yrs	58/51	3.7(2.8)/3.9(2.6)	Mean Diff	-0.2(-1.23,0.83)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Function:Activity Restriction (VAS)	12 wks	64/69	3.3(2.5)/3.8(2.6)	Mean Diff	-0.5(-1.37,0.37)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Function:Activity Restriction (VAS)	1 yrs	59/62	3.4(2.9)/4.1(2.7)	Mean Diff	-0.7(-1.71,0.31)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Function:Activity Restriction (VAS)	12 wks	65/58	3(2.5)/2.8(2.5)	Mean Diff	0.2(-0.69,1.09)	Not Sig.	clinically insignificant
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Function:PLQC physical capability	13 wks	47/41	2.8(0.7)/2.5(0.8)	Mean Diff	.3(-.021, .62)	Not Sig.	na
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Function:PLQC psychological functioning	13 wks	48/49	2.7(0.4)/2.5(0.6)	Mean Diff	0.2(-0.01,0.41)	Not Sig.	na
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Function:PLQC social functioning	13 wks	48/49	2.8(0.5)/2.7(0.7)	Mean Diff	0.1(-0.15,0.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Function:SF-12 Physical Component Score	12 wks	65/58	39.4(9.5)/40.2(10.1)	Mean Diff	-0.8(-4.31,2.71)	Not Sig.	na
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Function:SF-12 Physical Component Score	1 yrs	58/51	38.8(10.2)/38.2(9.9)	Mean Diff	0.6(-3.22,4.42)	Not Sig.	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Function:SF-12 Physical Component Score	12 wks	64/69	40.7(9.6)/39.5(10.7)	Mean Diff	1.2(-2.28,4.68)	Not Sig.	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Function:SF-12 Physical Component Score	1 yrs	59/62	41.7(10.8)/38.9(11.2)	Mean Diff	2.8(-1.16,6.76)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Function:SF-36 Physical Component	12 wks	104/109	35.4(9.77)/36.9(10.8)	Mean Diff	-1.5(-4.28,1.28)	Not Sig.	inconclusive
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:SF-36 Physical Component	8 wks	39/40	45.8(6.9)/35.2(5.4)	Mean Diff	10.6(7.82,13.38)	Group 1	clinically significant
Witt; 2005/Moderate	8: Physical agents-minimal acupuncture	8: Placebo/Control-waiting list	Function:SF-36 physical health	8 wks	76/74	33.1(6.97)/31.8(7.74)	Mean Diff	1.3(-1.08,3.68)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Witt; 2005/Moderate	8: Physical agents-manual acupuncture (Chinese)	8: Placebo/Control-waiting list	Function:SF-36 physical health	8 wks	150/74	36.2(7.35)/31.8(7.74)	Mean Diff	4.4(2.26,6.54)	Group 1	na
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:SF-36 physical health	8 weeks	169/169	9.2(18.2)/7.6(15.6)	Mean Diff	1.6(-2.03,5.23)	Not Sig.	na
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:SF-36 physical health	26 weeks	142/141	10.7(19.07)/8.2(17.81)	Mean Diff	2.5(-1.82,6.82)	Not Sig.	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:Timed get up and go (sec)	13 wks	150/151	11.9(4.1)/12.1(5.4)	Mean Diff	-0.2(-1.29,0.89)	Not Sig.	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:Timed get up and go (sec)	6 wks	150/151	12.2(4.3)/12.2(5)	Mean Diff	0(-1.06,1.06)	Not Sig.	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Function:WOMAC Function	12 wks	64/69	22.5(13.1)/23(13.2)	Mean Diff	-0.5(-5.01,4.01)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	Function:WOMAC Function	1 yrs	59/62	22.4(14.1)/23.6(13.4)	Mean Diff	-1.2(-6.16,3.76)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Function:WOMAC Function	12 wks	65/58	21.9(12.3)/21.7(12)	Mean Diff	0.2(-4.14,4.54)	Not Sig.	clinically insignificant
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20 min/1-2wks)	Function:WOMAC Function	1 yrs	58/51	22.6(13.1)/21.6(13.6)	Mean Diff	1(-4.09,6.09)	Not Sig.	inconclusive
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Function	12 wks	104/109	26(14.65)/23.2(14.22)	Mean Diff	2.8(-1.1,6.7)	Not Sig.	inconclusive
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Function	26 wks	104/109	29(14.91)/25.7(17.12)	Mean Diff	3.3(-1.03,7.63)	Not Sig.	inconclusive
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:WOMAC Function	4 wks	40/40	522.6(200)/685.5(133)	Mean Diff	-162.9(-238.68,-87.12)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:WOMAC Function	8 wks	39/40	267(120)/504.1(109)	Mean Diff	-237.1(-288.51,-185.69)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:WOMAC Function	12 wks	39/39	321.6(141)/603.2(126)	Mean Diff	-281.6(-341.92,-221.28)	Group 1	clinically significant
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:WOMAC Function	13 wks	150/151	21.22(12.17)/21.83(12.44)	Mean Diff	-0.61(-3.4,2.18)	Not Sig.	clinically insignificant
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:WOMAC Function	4 wks	150/151	21.96(12.04)/23.19(11.63)	Mean Diff	-1.23(-3.92,1.46)	Not Sig.	clinically insignificant
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:WOMAC Function	6 wks	150/151	20.06(12.1)/21.35(12.58)	Mean Diff	-1.29(-4.09,1.51)	Not Sig.	clinically insignificant
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Stiffness	12 wks	104/109	3.57(1.7)/3.4(1.55)	Mean Diff	0.17(-0.27,0.61)	Not Sig.	clinically insignificant
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Stiffness	26 wks	104/109	3.99(2.03)/3.78(2.13)	Mean Diff	0.21(-0.35,0.77)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:WOMAC Stiffness	4 wks	40/40	32.3(24.7)/47.3(22.1)	Mean Diff	-15(-25.43,-4.57)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:WOMAC Stiffness	8 wks	39/40	13.2(14.1)/33.2(17.7)	Mean Diff	-20(-27.16,-12.84)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Function:WOMAC Stiffness	12 wks	39/39	15.4(15.7)/40.4(21.9)	Mean Diff	-25(-33.61,-16.39)	Group 1	possibly clinically significant
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Function:WOMAC function	13 wks	48/49	7.4(10.3)/24.9(20.4)	Mean Diff	-17.5(-24.02,-10.98)	Group 1	clinically significant
Witt; 2005/Moderate	8: Physical agents-minimal acupuncture	8: Placebo/Control-waiting list	Function:WOMAC stiffness	8 wks	76/74	42.3(23.54)/55(24.09)	Mean Diff	-12.7(-20.39,-5.01)	Group 1	possibly clinically significant
Witt; 2005/Moderate	8: Physical agents-manual acupuncture (Chinese)	8: Placebo/Control-waiting list	Function:WOMAC stiffness	8 wks	150/74	32.7(23.27)/55(24.09)	Mean Diff	-22.3(-28.99,-15.61)	Group 1	clinically significant
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Function:WOMAC stiffness	13 wks	48/49	0.4(1.3)/2.1(2.6)	Mean Diff	-1.7(-2.53,-0.87)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-Diclofenac (diclofenac + placebo electroacupuncture)	Function:change in 50 feet walk time (sec)	4 wks	46/49	-4.13(3.66)/-3.52(3.22)	Mean Diff	-0.61(-2.02,0.8)	Not Sig.	na
Sandgee; 2002/High	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in 50 feet walk time (sec)	4 wks	46/45	-4.41(4.75)/-2.7(3.49)	Mean Diff	-1.71(-3.45,0.03)	Not Sig.	na
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:change in 6 min walk distance (ft)	8 weeks	163/156	64.1(229.81)/67.7(232.31)	Mean Diff	-3.6(-54.53, 47.33)	Not Sig.	na
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:change in 6 min walk distance (ft)	26 weeks	136/129	74.2(235.57)/105(243.06)	Mean Diff	-30.8(-88.75, 27.15)	Not Sig.	na
Sandgee; 2002/High	8: Electrotherapeutic agents-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-Diclofenac (diclofenac + placebo electroacupuncture)	Function:change in Lequesne's functional index	4 wks	46/49	-5.39(3.53)/-4.8(4.27)	Mean Diff	-0.59(-2.18,1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in Lequesne's functional index	4 wks	46/45	-6.44(4)/-3.82(3.42)	Mean Diff	-2.62(-4.17,-1.07)	Group 1	na
Sandgee; 2002/High	8: Electrotherapeutic agents-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-Diclofenac (diclofenac + placebo electroacupuncture)	Function:change in WOMAC disability	4 wks	46/49	-18.98(13.02)/-14.39(12.39)	Mean Diff	-4.59(-9.78,0.6)	Not Sig.	inconclusive
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:change in WOMAC function	4 weeks	173/163	-7.56(10.26)/-5.9(8.43)	Mean Diff	-1.66(-3.67,0.35)	Not Sig.	clinically insignificant
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:change in WOMAC function	26 weeks	142/141	-12.42(13.35)/-9.88(11.04)	Mean Diff	-2.54(-5.41,0.33)	Not Sig.	clinically insignificant
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:change in WOMAC function	14 weeks	158/157	-12.18(12.07)/-9.4(11.78)	Mean Diff	-2.78(-5.42,-0.14)	Group 1	some may benefit
Berman; 2004/high	8: Physical agents-electroacupuncture (Chinese)	8: Placebo/Control-sham acupuncture	Function:change in WOMAC function	8 weeks	169/161	-10.77(11.7)/-7.84(9.64)	Mean Diff	-2.93(-5.25,-0.61)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-Diclofenac (diclofenac + placebo electroacupuncture)	Function:change in WOMAC stiffness	4 wks	46/49	-2.02(1.9)/-1.55(1.89)	Mean Diff	-0.47(-1.24,0.3)	Not Sig.	inconclusive
Sandgee; 2002/High	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in WOMAC stiffness	4 wks	46/45	-2.24(2.1)/-1.47(2.08)	Mean Diff	-0.77(-1.64,0.1)	Not Sig.	inconclusive
Dai ; 2003/Moderate	8: Physical agents-electroacupuncture	8: Non-arthro Tx-Ritalin	Function:knee joint function (VAS)	52 weeks	60/60	59(9.06)/56(8.87)	Mean Diff	3(-0.24,6.24)	Not Sig.	na
Dai ; 2003/Moderate	8: Physical agents-electroacupuncture	8: Non-arthro Tx-Ritalin	Function:knee joint function (VAS)	4 weeks	60/60	71.33(9.99)/67.67(7.33)	Mean Diff	3.66(0.49,6.83)	Group 2	na
Dai ; 2003/Moderate	8: Physical agents-electroacupuncture	8: Non-arthro Tx-Ritalin	Function:knee joint function (VAS)	12 weeks	60/60	62.67(10.06)/59(8.67)	Mean Diff	3.67(0.27,7.07)	Group 2	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:sf-12 physical component score	4 wks	150/151	38.5(10)/37.7(9.1)	Mean Diff	0.8(-1.37,2.97)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:sf-12 physical component score	13 wks	150/151	39.5(9.7)/38.7(10.1)	Mean Diff	0.8(-1.45,3.05)	Not Sig.	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	Function:sf-12 physical component score	6 wks	150/151	40.5(10)/39(9.9)	Mean Diff	1.5(-0.76,3.76)	Not Sig.	na
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Function:womac function	4 weeks	36/37	24.11(13.17)/36.11(10.04)	Mean Diff	-12(-17.48,-6.52)	Group 1	clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Function:womac function	12 weeks	36/37	23.17(13.92)/36.78(10.71)	Mean Diff	-13.61(-19.43,-7.79)	Group 1	clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Function:womac function	8 weeks	36/37	20.31(13.26)/36.14(10.55)	Mean Diff	-15.83(-21.44,-10.22)	Group 1	clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Composite:Lequesne index	4 weeks	36/37	10.17(3.85)/12.65(3.32)	Mean Diff	-2.48(-4.16,-0.8)	Group 1	na
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Composite:Lequesne index	12 weeks	36/37	9.34(4.09)/12.41(3.47)	Mean Diff	-3.07(-4.84,-1.3)	Group 1	na
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Composite:Lequesne index	8 weeks	36/37	8.89(4.32)/12.62(3.12)	Mean Diff	-3.73(-5.5,-1.96)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Composite:WOMAC Total	12 wks	104/109	37(19.8)/33.6(18.96)	Mean Diff	3.4(-1.84,8.64)	Not Sig.	inconclusive
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Composite:WOMAC Total	26 wks	104/109	41.5(20.05)/37.2(23.18)	Mean Diff	4.3(-1.55,10.15)	Not Sig.	inconclusive
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Composite:WOMAC Total	4 wks	40/40	671.4(259.1)/896.9(170.2)	Mean Diff	-225.5(-323.33,-127.67)	Group 1	possibly clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Composite:WOMAC Total	8 wks	39/40	341.5(153.8)/654.4(138)	Mean Diff	-312.9(-378.44,-247.36)	Group 1	clinically significant
Mavrommatis; 2012/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham Acupuncture)	Composite:WOMAC Total	12 wks	39/39	415.6(177.9)/791.2(166.1)	Mean Diff	-375.6(-453.23,-297.97)	Group 1	clinically significant
Witt; 2005/Moderate	8: Physical agents-minimal acupuncture	8: Placebo/Control-waiting list	Composite:WOMAC total	8 wks	76/74	35.8(16.56)/49.6(17.2)	Mean Diff	-13.8(-19.25,-8.35)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Witt; 2005/Moderate	8: Physical agents-manual acupuncture (Chinese)	8: Placebo/Control-waiting list	Composite:WOMAC total	8 wks	150/74	26.9(17.15)/49.6(17.2)	Mean Diff	-22.7(-27.52,-17.88)	Group 1	clinically significant
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Composite:WOMAC total	13 wks	48/49	9.5(13.7)/33.4(28)	Mean Diff	-23.9(-32.8,-15)	Group 1	clinically significant
Sandgee; 2002/High	8: Electrotherapeutic agents-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-Diclofenac (diclofenac + placebo electroacupuncture)	Composite:change in WOMAC total	4 wks	46/49	-27.28(18.92)/-20.84(17.01)	Mean Diff	-6.44(-13.79, 0.91)	Not Sig.	inconclusive
Sandgee; 2002/High	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Composite:change in WOMAC total	4 wks	46/45	-27.07(18.85)/-17.11(18.31)	Mean Diff	-9.96(-17.7,-2.22)	Group 1	possibly clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Composite:womac total	4 weeks	36/37	33.36(17.16)/50.5(14.03)	Mean Diff	-17.14(-24.47,-9.81)	Group 1	clinically significant
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Composite:womac total	12 weeks	36/37	31.58(18.27)/50.43(14.1)	Mean Diff	-18.85(-26.49,-11.21)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Berman; 1999/Moderate	8: Physical agents-acupuncture	8: Placebo/Control-usual care	Composite:womac total	8 weeks	36/37	28.08(17.96)/50.11(14.52)	Mean Diff	-22.03(-29.67,-14.39)	Group 1	clinically significant
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	QOL:PLQC negative mood	13 wks	48/49	3.2(0.7)/3.1(0.7)	Mean Diff	0.1(-0.18,0.38)	Not Sig.	na
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	QOL:PLQC social wellbeing	13 wks	48/49	3.2(0.5)/3.2(0.5)	Mean Diff	0(-0.2,0.2)	Not Sig.	na
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	QOL:SF-12 Mental Component Score	12 wks	65/58	53(9.9)/53.2(10.4)	Mean Diff	-0.2(-3.84,3.44)	Not Sig.	na
Hinman; 2014/High	8: Electrotherapeutic agents-Laser Acupuncture(20min/1-2wks)	8: Placebo/Control-Placebo (Sham Laser Acupuncture)(20min/1-2wks)	QOL:SF-12 Mental Component Score	1 yrs	58/51	52.1(9.8)/52.8(9.1)	Mean Diff	-0.7(-4.29,2.89)	Not Sig.	na
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	QOL:SF-12 Mental Component Score	1 yrs	59/62	51.1(11)/54.4(10.2)	Mean Diff	-3.3(-7.12,0.52)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hinman; 2014/High	8: Physical agents-Needle Acupuncture(20min/1-2wks)	8: Placebo/Control-Control (No Acupuncture)	QOL:SF-12 Mental Component Score	12 wks	64/69	51.5(11)/55.8(9.1)	Mean Diff	-4.3(-7.78,-0.82)	Group 2	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	QOL:sf-12 mental component score	4 wks	150/151	53.9(8.3)/54.2(8.9)	Mean Diff	-0.3(-2.25,1.65)	Not Sig.	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	QOL:sf-12 mental component score	6 wks	150/151	53.4(7.9)/54(8.7)	Mean Diff	-0.6(-2.48,1.28)	Not Sig.	na
Suarez-Almazor ; 2010/High	8: Physical agents-Traditiional Chinese acupuncture	8: Placebo/Control-sham	QOL:sf-12 mental component score	13 wks	150/151	54.1(8.2)/53.2(8.9)	Mean Diff	0.9(-1.04,2.84)	Not Sig.	na
Dai ; 2003/Moderate	8: Physical agents-electroacupuncture	8: Non-arthro Tx-Ritalin	Other:JOA improvement	4 weeks	60/60	56(4)/48(12)	Mean Diff	8(4.74, 11.26)	Group 1	na
Sandgee; 2002/High	8: Electrotherapeutic agents-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-Diclofenac (diclofenac + placebo electroacupuncture)	Other:change in number of paracetamol take (tablets/wk)	4 wks	46/49	-5.13(13.97)/-4.43(13.3)	Mean Diff	-0.7(-6.27,4.87)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Other:change in number of paracetamol take (tablets/wk)	4 wks	46/45	-7.89(14.18)/-5.16(15.63)	Mean Diff	-2.73(-8.95,3.49)	Not Sig.	na
Vas ; 2007/Moderate	8: Physical agents-manual acupuncture + diclofenac	8: Placebo/Control-placebo acupuncture + diclofenac	Other:total accumulated # diclofenac tablets	13 wks	48/49	85.4(48.9)/139.3(89.6)	Mean Diff	-53.9(-83.02,-24.78)	Group 1	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Agitation	26 wks	104/109	1.92%/0%	RD	1.923(-2.896, 5.602)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Bruising	26 wks	104/109	0.96%/0.92%	RR	1.05(0.07,16.54)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Fatigue	26 wks	104/109	0.96%/0.92%	RR	1.05(0.07,16.54)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Increased Pain	26 wks	104/109	21.15%/14.68%	RR	1.44(0.8,2.59)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Muscle Soreness	26 wks	104/109	5.77%/1.83%	RR	3.14(0.65,15.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Other	26 wks	104/109	6.73%/4.59%	RR	1.47(0.48,4.48)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Redness/Infection	26 wks	104/109	0.96%/0%	RD	0.962(-3.324, 4.457)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Swelling	26 wks	104/109	5.77%/4.59%	RR	1.26(0.4,4)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Tearfulness	26 wks	104/109	0%/0.92%	RD	-0.917(-4.559, 3.18)	Not Sig.	na
Chen; 2013/High	8: Physical agents-Acupuncture	8: Placebo/Control-Placebo(Sham TENS)	Adverse events:Weakness	26 wks	104/109	0.96%/0%	RD	0.962(-3.324, 4.457)	Not Sig.	na

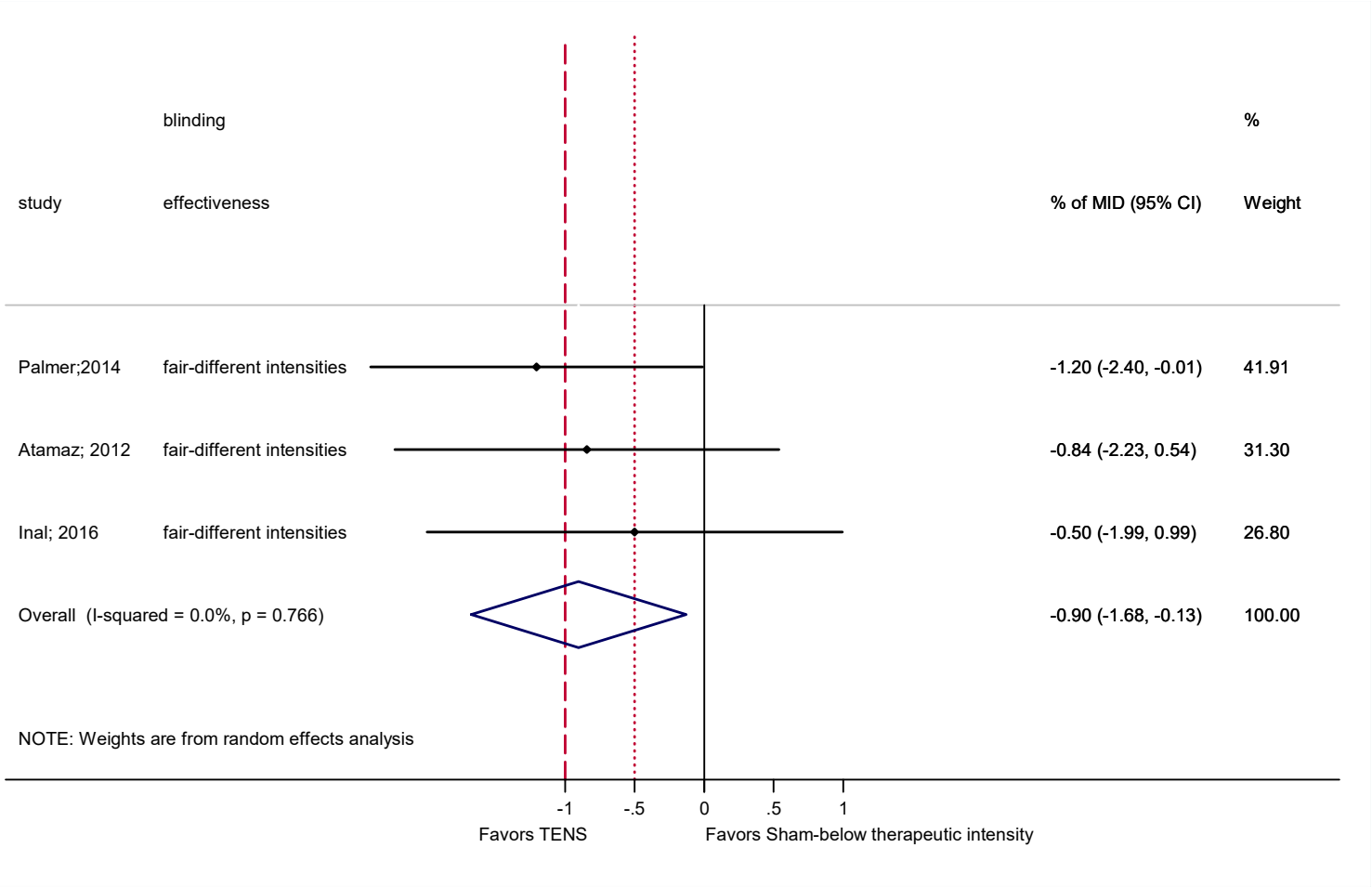
PICO 8: Physical/Electrotherapeutic Agents

Transcutaneous Electrical Nerve Stimulation vs. Control

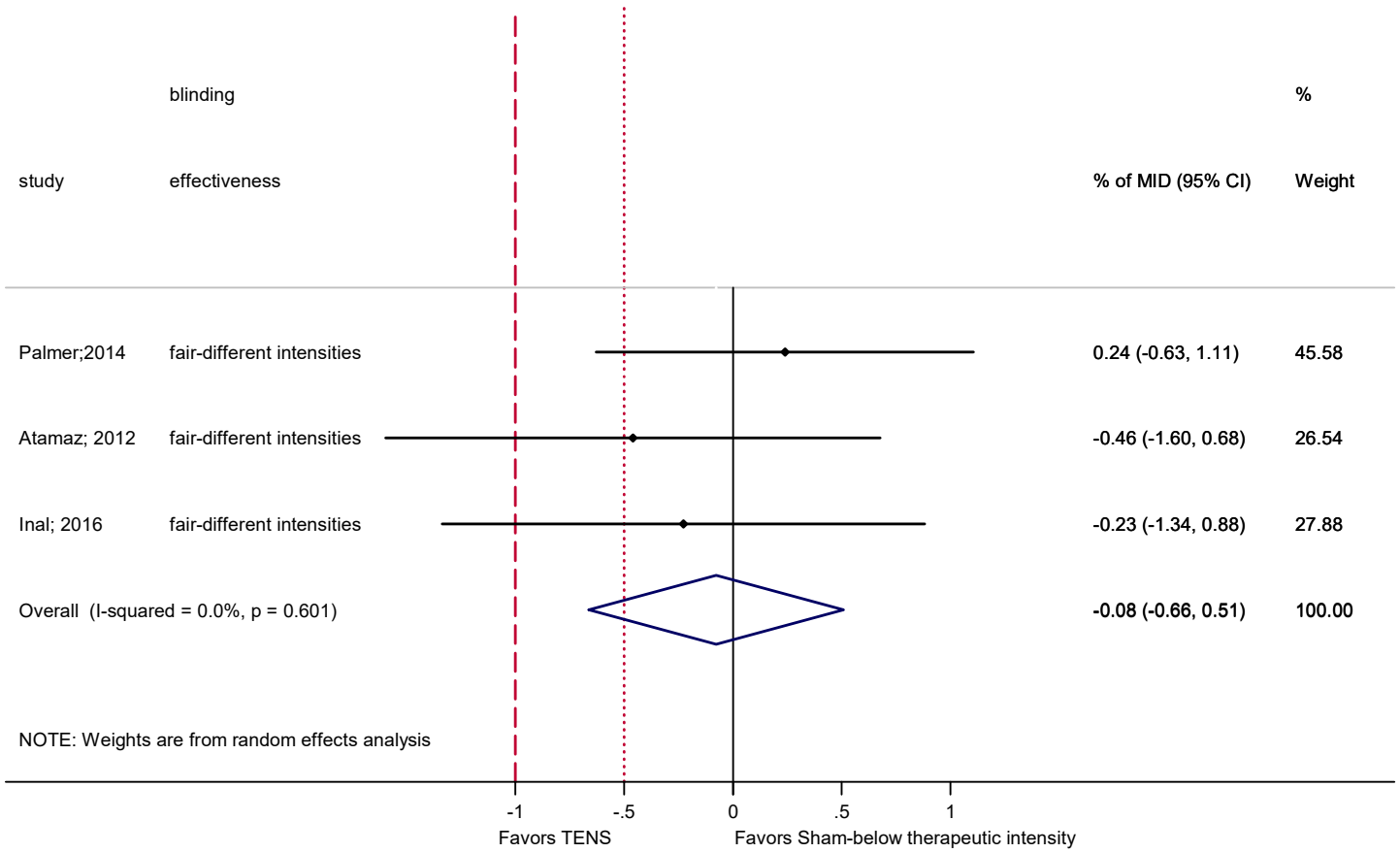
Table 31: Transcutaneous Electrical Nerve Stimulation vs Control

Quality: H=High; M=Moderate; L=Low	H		M	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Palmer;2014	Inal; 2016	Cherian; 2016	Atamaz; 2012
Composite				
Knee Society Scale			●	
Function				
Extensor Torque (Nm)	●			
Lower Extremity Function Scale			●	
Nottingham Health Profile-physical				●
Timed Walk				●
Pain				
VAS Pain			●	
Nottingham Health Profile-pain				●
calculable MID outcomes				
WOMAC Total	●	●		
WOMAC Function	●	●		●
WOMAC Stiffness	↑	●		
WOMAC Pain	↑	●		●
VAS Pain				●
VAS Pain in motion		●		
VAS Pain in rest		●		
QOL				
SF-36 Mental			●	
SF-36 Physical			●	
Patient Global Assessment of Change	●			
Return to activity				
Exercise Self-Efficacy	●			

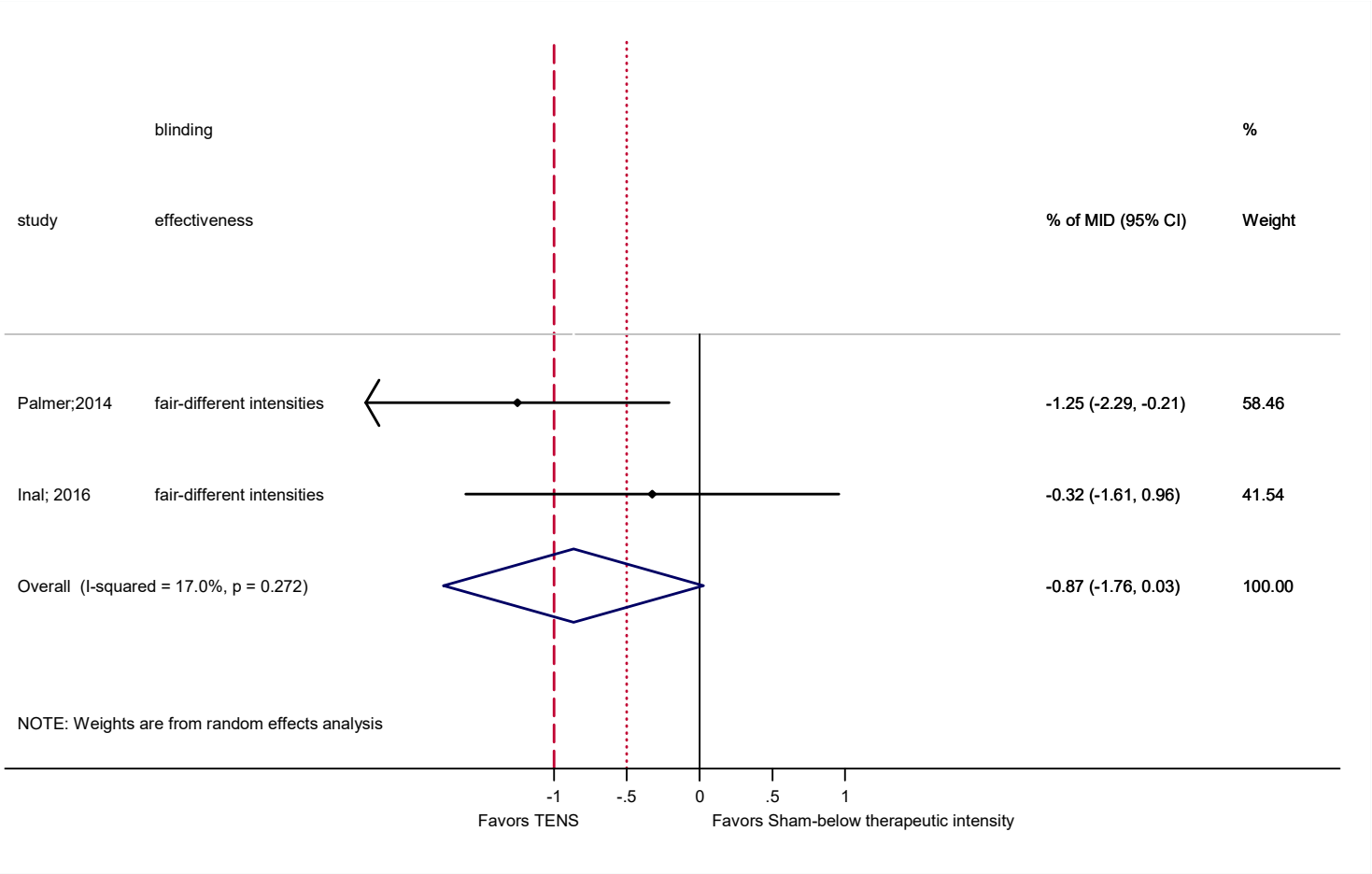
Meta-Analysis Figure 15: Transcutaneous Electrical Nerve Stimulation vs Sham-Pain



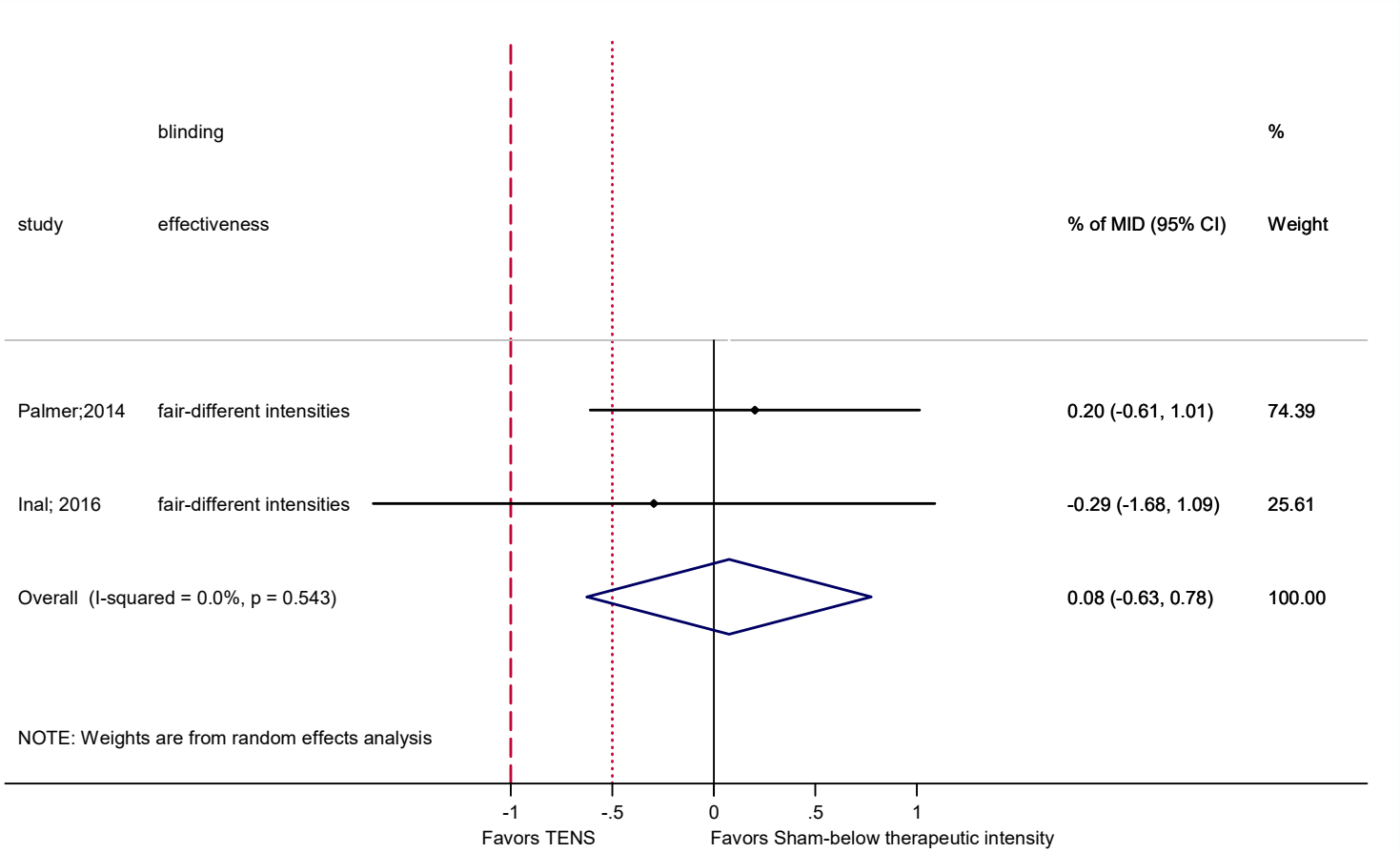
Meta-Analysis Figure 16: Transcutaneous Electrical Nerve Stimulation vs Sham- Function



Meta-Analysis Figure 17: Transcutaneous Electrical Nerve Stimulation vs Sham- Stiffness



Meta-Analysis Figure 18: Transcutaneous Electrical Nerve Stimulation vs Sham- WOMAC Total



Evidence Table 3730: Transcutaneous Electrical Nerve Stimulation vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment of Change	24 wks	73/74	2.8(5.8)/2.9(6.4)	Mean Diff	-0.1(-2.09,1.89)	Not Sig.	na
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment of Change	12 wks	73/74	2(5.6)/2.7(5.4)	Mean Diff	-0.7(-2.49,1.09)	Not Sig.	na
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	QoL:Patient Global Assessment of Change	6 wks	73/74	3(3.5)/2.9(4.4)	Mean Diff	0.1(-1.2,1.4)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:Nottingham Health Profile-pain	4 weeks	37/37	45.1(22.2)/48.4(25.6)	Mean Diff	-3.3(-14.41, 7.81)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:Nottingham Health Profile-pain	13 weeks	37/37	41.8(25.4)/41.4(25.7)	Mean Diff	0.4(-11.44, 12.24)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:Nottingham Health Profile-pain	26 weeks	37/37	40.8(25.8)/40.1(25.4)	Mean Diff	0.7(-11.17, 12.57)	Not Sig.	na
Cherian; 2016/Moderate	8: Electrotherapeutic agents-Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Control	Pain:VAS Pain	1 yrs		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Inal; 2016/High	8: Electrotherapeutic agents-100 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Pain:VAS Pain in motion	6 wks	30/30	4.9(3.72)/5.03(3.45)	Mean Diff	-0.13(-1.98,1.72)	Not Sig.	clinically insignificant
Inal; 2016/High	8: Electrotherapeutic agents-4 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Pain:VAS Pain in motion	6 wks	30/30	5.2(3.89)/5.03(3.45)	Mean Diff	0.17(-1.73,2.07)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-4 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Pain:VAS Pain in rest	6 wks	30/30	2.33(3.72)/2.07(3.56)	Mean Diff	0.26(-1.62,2.14)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-100 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Pain:VAS Pain in rest	6 wks	30/30	2.33(4)/2.07(3.56)	Mean Diff	0.26(-1.7,2.22)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:VAS pain	26 weeks	37/37	48.6(23.1)/48.4(22.7)	Mean Diff	0.2(-10.41,10.81)	Not Sig.	clinically insignificant
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:VAS pain	13 weeks	37/37	51.5(24.8)/47.3(22.6)	Mean Diff	4.2(-6.8,15.2)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:VAS pain	4 weeks	37/37	54.7(24.1)/50.4(20.3)	Mean Diff	4.3(-6.03,14.63)	Not Sig.	clinically insignificant
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Pain:WOMAC Pain	6 wks	73/74	6(5)/8(7)	Mean Diff	-2(-3.98,-0.02)	Group 1	possibly clinically significant
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Pain:WOMAC Pain	12 wks	73/74	7(7.8)/7(7)	Mean Diff	0(-2.42,2.42)	Not Sig.	inconclusive
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Pain:WOMAC Pain	24 wks	73/74	7(8)/6(8)	Mean Diff	1(-1.61,3.61)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:WOMAC Pain	26 weeks	37/37	10.2(5)/11.5(5.4)	Mean Diff	-1.3(-3.71,1.11)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:WOMAC Pain	13 weeks	37/37	10.4(4.9)/11.7(5.6)	Mean Diff	-1.3(-3.74,1.14)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Pain:WOMAC Pain	4 weeks	37/37	10.9(4.9)/12.3(5)	Mean Diff	-1.4(-3.69,0.89)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-4 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	30/30	6.7(4.71)/7.1(4.66)	Mean Diff	-0.4(-2.82,2.02)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Inal; 2016/High	8: Electrotherapeutic agents-100 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	30/30	6.27(4.93)/7.1(4.66)	Mean Diff	-0.83(-3.31,1.65)	Not Sig.	inconclusive
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:Extensor Torque (Nm)	12 wks	73/74	51.5(45.2)/53.9(44.4)	Mean Diff	-2.4(-17.01, 12.21)	Not Sig.	na
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:Extensor Torque (Nm)	24 wks	73/74	53.9(44.6)/58.9(39.7)	Mean Diff	-5(-18.77, 8.77)	Not Sig.	na
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:Extensor Torque (Nm)	6 wks	73/74	49.2(51.5)/56.6(35.8)	Mean Diff	-7.4(-21.89, 7.09)	Not Sig.	na
Cherian; 2016/Moderate	8: Electrotherapeutic agents-Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Control	Function:Lower Extremity Function Scale	1 yrs		none	pvalue	NS	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:Nottingham Health Profile-physical	26 weeks	37/37	36.1(18.1)/37.1(20.6)	Mean Diff	-1(-9.99,7.99)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:Nottingham Health Profile-physical	4 weeks	37/37	34.9(17.7)/36.7(23.2)	Mean Diff	-1.8(-11.37, 7.77)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:Nottingham Health Profile-physical	13 weeks	37/37	36.6(16.8)/36.3(23.2)	Mean Diff	0.3(-9.1,9.7)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:Timed Walk	13 weeks	37/37	14.7(3.6)/14.8(4.4)	Mean Diff	-0.1(-1.96,1.76)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:Timed Walk	26 weeks	37/37	14.4(3.5)/14.8(3)	Mean Diff	-0.4(-1.91,1.11)	Not Sig.	na
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:Timed Walk	4 weeks	37/37	14.3(3.3)/14.9(4.4)	Mean Diff	-0.6(-2.4,1.2)	Not Sig.	na
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Function	12 wks	73/74	25.3(14.1)/25.7(14.1)	Mean Diff	-0.4(-5,4.2)	Not Sig.	clinically insignificant
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Function	24 wks	73/74	25.8(13.8)/25.3(15)	Mean Diff	0.5(-4.2,5.2)	Not Sig.	clinically insignificant
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Function	6 wks	73/74	26.4(15)/25.1(13.9)	Mean Diff	1.3(-3.42,6.02)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Inal; 2016/High	8: Electrotherapeutic agents-4 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Function:WOMAC Function	6 wks	30/30	25.07(15.61)/25.67(4.93)	Mean Diff	-0.6(-6.67,5.47)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-100 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Function:WOMAC Function	6 wks	30/30	24.43(15.5)/25.67(4.93)	Mean Diff	-1.24(-7.27,4.79)	Not Sig.	inconclusive
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Stiffness	6 wks	73/74	3(3)/4(2)	Mean Diff	-1(-1.83,-0.17)	Group 1	possibly clinically significant
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Stiffness	12 wks	73/74	4(3)/4(3)	Mean Diff	0(-0.98,0.98)	Not Sig.	inconclusive
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Function:WOMAC Stiffness	24 wks	73/74	3.5(3)/3(3)	Mean Diff	0.5(-0.48,1.48)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-4 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	30/30	2.4(2.08)/2.53(1.81)	Mean Diff	-0.13(-1.14,0.88)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Inal; 2016/High	8: Electrotherapeutic agents-100 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	30/30	2.27(2.14)/2.53(1.81)	Mean Diff	-0.26(-1.28,0.76)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:WOMAC function	13 weeks	37/37	32.6(13.8)/34(13.8)	Mean Diff	-1.4(-7.8,5)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:WOMAC function	4 weeks	37/37	33.9(14.2)/36.4(12.4)	Mean Diff	-2.5(-8.68,3.68)	Not Sig.	inconclusive
Atamaz; 2012/Moderate	8: Electrotherapeutic agents-Tens	8: Placebo/Control-tens sham	Function:WOMAC function	26 weeks	37/37	31.8(14.9)/34.3(14)	Mean Diff	-2.5(-9.2,4.2)	Not Sig.	inconclusive
Cherian; 2016/Moderate	8: Electrotherapeutic agents-Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Control	Composite:Knee Society Scale	1 yrs		none	pvalue	NS	Not Sig.	na
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Composite:WOMAC Total	12 wks	73/74	36.2(19.4)/36.4(19.5)	Mean Diff	-0.2(-6.54,6.14)	Not Sig.	clinically insignificant
Palmer;2014/High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Composite:WOMAC Total	24 wks	73/74	36.7(19.5)/35.7(20.6)	Mean Diff	1(-5.54,7.54)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Composite:WOMAC Total	6 wks	73/74	37.3(20.4)/35.7(18.9)	Mean Diff	1.6(-4.81,8.01)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-4 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	30/30	34.17(21.69)/35.3(19.99)	Mean Diff	-1.13(-11.91, 9.65)	Not Sig.	inconclusive
Inal; 2016/High	8: Electrotherapeutic agents-100 Hz Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	30/30	32.97(22.24)/35.3(19.99)	Mean Diff	-2.33(-13.26, 8.6)	Not Sig.	inconclusive
Cherian; 2016/Moderate	8: Electrotherapeutic agents-Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Control	QOL:SF-36 Mental	1 yrs		none	pvalue	NS	Not Sig.	na
Cherian; 2016/Moderate	8: Electrotherapeutic agents-Transcutaneous Electrical Nerve Stimulation	8: Placebo/Control-Control	QOL:SF-36 Physical	1 yrs		none	pvalue	NS	Not Sig.	na
Palmer;2014/ High	8: Electrotherapeutic agents-TENS(at pt discretion)	8: Placebo/Control-Placebo(Sham TENS)	Return to activity:Exercise Self-Efficacy	24 wks	73/74	15.8(4.5)/16(4.1)	Mean Diff	-0.2(-1.6,1.2)	Not Sig.	na

PICO 8: Physical/Electrotherapeutic Agents

Percutaneous Electrical Nerve Stimulation vs. Control

Table 32: Percutaneous Electrical Nerve Stimulation vs Control

Quality: H=High; M=Moderate; L=Low ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	H He; 2019
Composite	
WOMAC Total	↑
SF-36 MCS	↑
SF-36 PCS	↑
Function	
WOMAC Function	↑
WOMAC Stiffness	↑
Pain	
WOMAC Pain	↑
NRS	↑

Evidence Table 3831: Percutaneous Electrical Nerve Stimulation vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Pain:NRS	8 wks	36/36	-2.1(.)/-0.5(.)	Mean Diff	-1.6	PENS group	na
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Pain:WOMAC Pain (0-500)	8 wks	36/36	157.2(.)/66.4(.)	Mean Diff	90.8	PENS group	na
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Function:WOMAC Function (0-1700)	8 wks	36/36	658.6(.)/321.7(.)	Mean Diff	336.9	PENS group	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Function:WOMAC Stiffness (0-200)	8 wks	36/36	53.1(.)/34.6(.)	Mean Diff	18.5	PENS group	na
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Composite:SF-36 MCS	8 wks	36/36	-9.4(.)/-9.4(.)	Mean Diff	0	PENS group	na
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Composite:SF-36 PCS	8 wks	36/36	-17.5(.)/-7.7(.)	Mean Diff	-9.8	PENS group	na
He; 2019/High	8: Electrotherapeutic agents-Percutaneous Electrical Nerve Stimulation (PENS)(3x/wk for 8 wks)	8: Placebo/Control-Sham PENS(3x/wk for 8 wks)	Composite:WOMAC Total (0-2400)	8 wks	36/36	789.4(.)/392.1(.)	Mean Diff	397.3	PENS group	na

PICO 8: Physical/Electrotherapeutic Agents

Pulsed Electromagnetic Field Therapy vs. Control

Table 33: Pulsed Electromagnetic Field Therapy vs Control

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Bagnato; 2016**
Function	
SF-36 Physical health	●
Pain	
Pressure-Pain Threshold (PPT) DIP	●
Pressure-Pain Threshold (PPT) Quadriceps	●
calculable MID outcomes	
WOMAC Total	↑
WOMAC Function	●
WOMAC Stiffness	●
WOMAC Pain	↑
VAS Pain	↑
QOL	
SF-36 Mental Health	●

Evidence Table 3932: Pulsed Electromagnetic Field Therapy vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	QoL:SF-36 Mental Health	1 mos	30/30	43.8(3.6)/43.6(4.7)	Mean Diff	0.2(-1.97,2.37)	Not Sig.	na
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Pain:Pressure-Pain Threshold (PPT) DIP	1 mos	30/30	4(1.6)/3.4(1.2)	Mean Diff	0.6(-0.13,1.33)	Not Sig.	na
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Pain:Pressure-Pain Threshold (PPT) Quadriceps	1 mos	30/30	13.5(6.2)/12(5.3)	Mean Diff	1.5(-1.48,4.48)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Pain:VAS Pain	1 mos	30/30	50(16.1)/61.3(15)	Mean Diff	-11.3(-19.34,-3.26)	Group 1	some may benefit
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Pain:WOMAC Pain (0-50)	1 mos	30/30	21.6(9.6)/26.8(8.2)	Mean Diff	-5.2(-9.82,-0.58)	Group 1	possibly clinically significant
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Function:SF-36 Physical Health	1 mos	30/30	55.8(6.1)/53.1(6.2)	Mean Diff	2.7(-0.48,5.88)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Function:WOMAC Function (0-170)	1 mos	30/30	81.7(37.9)/89.7(34.4)	Mean Diff	-8(-26.71, 10.71)	Not Sig.	inconclusive
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Function:WOMAC Stiffness (0-20)	1 mos	30/30	8.1(3.8)/9.6(3.1)	Mean Diff	-1.5(-3.29,0.29)	Not Sig.	inconclusive
Bagnato; 2016/High	8: Electrotherapeutic agents-Pulsed Electromagnetic Fields (PEMF)(1000Hz pulse rate; 100us burst width; 0.098 W/103cm2)	8: Placebo/Control-Placebo(sham)	Composite:WOMAC Total (0-240)	1 mos	30/30	111.5(48)/126.2(39)	adjusted mean difference	-20.8(-32.6, -8.9)	Group 1	possibly clinically significant

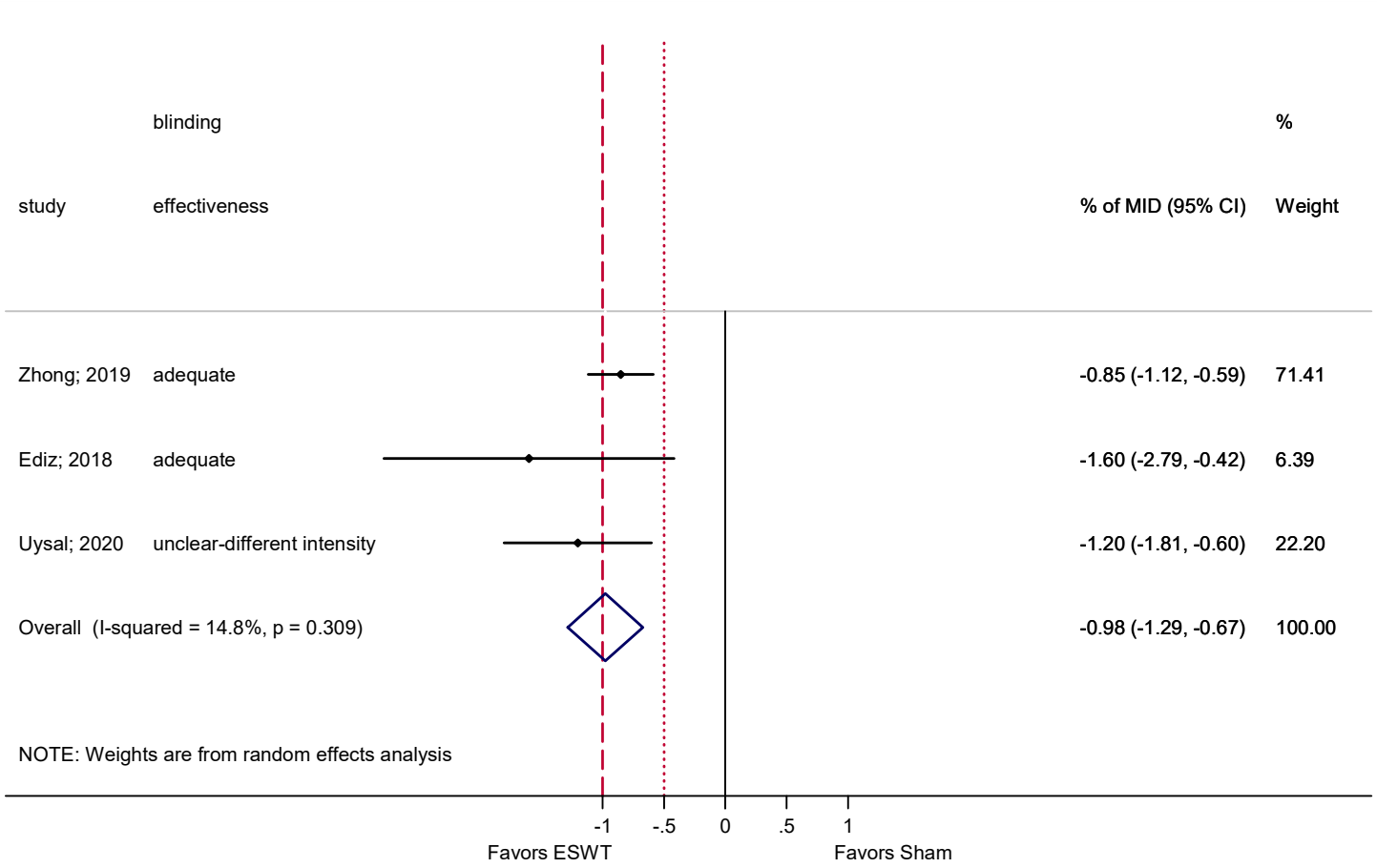
PICO 8: Physical/Electrotherapeutic Agents

Extracorporeal Shockwave Therapy vs. Control

Table 34: Extracorporeal Shockwave vs Control

Quality: H=High; M=Moderate; L=Low	H				
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Zhong; 2019	Zhao; 2013	Ediz; 2018	Uysal; 2020	Imamura; 2017
Composite					
Lequesne Index	↑				
Lequesne Index Score		↑	●		
Lequesne Total(scale not provided)				↑	
Function					
180°/s Angular Velocity (Nm)				↑	
20m Walking Test (sec)				↑	
Knee RoM (degrees)				↑	
Lequesne Distance(scale not provided)				↑	
Lequesne Function(scale not provided)				↑	
Quadriceps Peak Torque (Nm)				↑	
Pain					
WOMAC Pain					↑
VAS Pain					●
Lequesne Pain(scale not provided)				↑	
Adverse events					
Pain	●				
Burning Sensation	●				
Swelling	●				
Hypesthesia	●				
Petechiae	●				
Reddening of Skin	●				
Tremor	●				
calculable MID outcomes					
WOMAC Total		↑	●	↑	
WOMAC Function	↑	↑	↑	↑	
WOMAC Stiffness	↑	●	●	●	
WOMAC Pain	↑	↑	↑	↑	
VAS Pain	↑		●		
VAS Pain (Activity)(scale not provided)				↑	
VAS Pain (Rest)(scale not provided)				●	
QOL					
Patient Perception (Likert Higher Better)		↓			

Meta-Analysis Figure 19: Extracorporeal Shockwave vs Sham- Pain



Evidence Table 4033: Extracorporeal Shockwave vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhao; 2013/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy(4000 pulses 0.25mJ/mm2 6Hz)	8: Placebo/Control-Placebo(Sham)	QoL:Patient Perception (Likert Higher Better)	12 wks	34/36	-0.9(0.72)/-0.3(0.59)	Mean Diff	-0.6(-0.92,-0.28)	Group 2	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:Lequesne Pain(scale not provided)	1 mos	52/52	1.8(1.2)/2.7(1.3)	Mean Diff	-0.9(-1.39,-0.41)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:Lequesne Pain(scale not provided)	3 mos	52/52	1.6(1)/2.8(1.7)	Mean Diff	-1.2(-1.74,-0.66)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Imamura; 2017/High	8: Physical agents-Radial Extracorporeal Shock Wave Therapy	8: Placebo/Control-Placebo	Pain:VAS Pain	3 mos		none	pvalue	NS	Not Sig.	na
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Pain:VAS Pain	5 wks	32/31	3.1(1)/4.8(1.1)	Mean Diff	-1.7(-2.23,-1.17)	Group 1	possibly clinically significant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Pain:VAS Pain	12 wks	32/31	2.3(1.2)/4.3(1.1)	Mean Diff	-2(-2.58,-1.42)	Group 1	possibly clinically significant
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Pain:VAS Pain	1 mos	38/35	5.16(1.34)/5.43(1.22)	Mean Diff	-0.27(-0.87,0.33)	Not Sig.	clinically insignificant
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Pain:VAS Pain	12 mos	38/35	5.27(1.53)/5.98(1.91)	Mean Diff	-0.71(-1.52,0.1)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:VAS Pain (Activity)(scale not provided)	1 mos	52/52	3(1.2)/4.1(1.4)	Mean Diff	-1.1(-1.61,-0.59)	Group 1	some may benefit
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:VAS Pain (Activity)(scale not provided)	3 mos	52/52	2.9(1.4)/4.4(1.8)	Mean Diff	-1.5(-2.13,-0.87)	Group 1	possibly clinically significant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:VAS Pain (Rest)(scale not provided)	1 mos	52/52	1.2(0.9)/1.9(1.2)	Mean Diff	-0.7(-1.11,-0.29)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:VAS Pain (Rest)(scale not provided)	3 mos	52/52	1(0.8)/1.9(1.3)	Mean Diff	-0.9(-1.32,-0.48)	Group 1	clinically insignificant
Imamura; 2017/High	8: Physical agents-Radial Extracorporeal Shock Wave Therapy	8: Placebo/Control-Placebo	Pain:WOMAC Pain	3 mos		none	pvalue	Sig (p < 0.05)	Radial Extracorporeal Shock Wave Therapy fav	na
Zhao; 2013/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy(4000 pulses 0.25mJ/mm2 6Hz)	8: Placebo/Control-Placebo(Sham)	Pain:WOMAC Pain	12 wks	34/36	-4.5(2.58)/-2.2(2.96)	Mean Diff	-2.3(-3.62,-0.98)	Group 1	possibly clinically significant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Pain:WOMAC Pain	12 wks	32/31	2.4(1.4)/5.1(2.2)	Mean Diff	-2.7(-3.64,-1.76)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Pain:WOMAC Pain	5 wks	32/31	3(1.4)/6.1(2)	Mean Diff	-3.1(-3.97,-2.23)	Group 1	clinically significant
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Pain:WOMAC Pain	12 mos	38/35	9.82(4.42)/11.56(4.76)	Mean Diff	-1.74(-3.89,0.41)	Not Sig.	inconclusive
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Pain:WOMAC Pain	1 mos	38/35	9.27(5.15)/11.93(3.06)	Mean Diff	-2.66(-4.62,-0.7)	Group 1	possibly clinically significant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:WOMAC Pain(scale not provided)	1 mos	52/52	3.9(2.3)/5.9(2.8)	Mean Diff	-2(-3,-1)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Pain:WOMAC Pain(scale not provided)	3 mos	52/52	3.5(1.7)/6.5(3.6)	Mean Diff	-3(-4.1,-1.9)	Group 1	clinically significant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:180 °/s Angular Velocity (Nm)	3 mos	52/52	26(7.4)/21.8(6.6)	Mean Diff	4.2(1.47,6.93)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:180 °/s Angular Velocity (Nm)	1 mos	52/52	26.8(7.4)/22.3(5.8)	Mean Diff	4.5(1.91,7.09)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:20 m Walking Test (sec)	1 mos	52/52	16.7(2.2)/18.7(2.2)	Mean Diff	-2(-2.86,-1.14)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:20 m Walking Test (sec)	3 mos	52/52	16.4(2)/19.2(3.2)	Mean Diff	-2.8(-3.84,-1.76)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Knee RoM (degrees)	1 mos	52/52	129.6(7.9)/125.8(6.3)	Mean Diff	3.8(1.02,6.58)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Knee RoM (degrees)	3 mos	52/52	131.3(7)/126(6)	Mean Diff	5.3(2.76,7.84)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Lequesne Distance(scale not provided)	1 mos	52/52	2(0.5)/2.4(0.6)	Mean Diff	-0.4(-0.61,-0.19)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Lequesne Distance(scale not provided)	3 mos	52/52	1.8(0.6)/2.3(0.8)	Mean Diff	-0.5(-0.78,-0.22)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Lequesne Function(scale not provided)	1 mos	52/52	2.1(0.7)/2.5(0.7)	Mean Diff	-0.4(-0.67,-0.13)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Lequesne Function(scale not provided)	3 mos	52/52	1.8(0.8)/2.6(0.9)	Mean Diff	-0.8(-1.13,-0.47)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Quadriceps Peak Torque (Nm)	1 mos	52/52	48.1(13.8)/41(12.3)	Mean Diff	7.1(2.01,12.19)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:Quadriceps Peak Torque (Nm)	3 mos	52/52	49.8(14.9)/42.2(12.2)	Mean Diff	7.6(2.3,12.9)	Group 1	na
Zhao; 2013/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy(4000 pulses 0.25mJ/mm2 6Hz)	8: Placebo/Control-Placebo(Sham)	Function:WOMAC Function	12 wks	34/36	-13.9(9.46)/-6(9.46)	Mean Diff	-7.9(-12.41,-3.39)	Group 1	possibly clinically significant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Function:WOMAC Function	5 wks	32/31	10.3(4.9)/20.5(6.7)	Mean Diff	-10.2(-13.17,-7.23)	Group 1	clinically significant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Function:WOMAC Function	12 wks	32/31	7.9(4.9)/17.3(7.2)	Mean Diff	-9.4(-12.52,-6.28)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Function:WOMAC Function	12 mos	38/35	22.75(5.43)/24.46(5.12)	Mean Diff	-1.71(-4.17,0.75)	Not Sig.	clinically insignificant
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Function:WOMAC Function	1 mos	38/35	20.61(4.06)/24.27(5.87)	Mean Diff	-3.66(-6.04,-1.28)	Group 1	possibly clinically significant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:WOMAC Function(scale not provided)	1 mos	52/52	19.9(9.4)/25.7(9.1)	Mean Diff	-5.8(-9.4,-2.2)	Group 1	possibly clinically significant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:WOMAC Function(scale not provided)	3 mos	52/52	18.3(8.1)/27.8(1.4)	Mean Diff	-9.5(-11.79,-7.21)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhao; 2013/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy(4000 pulses 0.25mJ/mm2 6Hz)	8: Placebo/Control-Placebo(Sham)	Function:WOMAC Stiffness	12 wks	34/36	-0.7(0.86)/-0.3(1.48)	Mean Diff	-0.4(-0.98,0.18)	Not Sig.	inconclusive
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Function:WOMAC Stiffness	12 wks	32/31	1(0.6)/2.1(0.8)	Mean Diff	-1.1(-1.46,-0.74)	Group 1	possibly clinically significant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Function:WOMAC Stiffness	5 wks	32/31	1.2(0.5)/2.5(0.9)	Mean Diff	-1.3(-1.67,-0.93)	Group 1	clinically significant
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Function:WOMAC Stiffness	12 mos	38/35	4.02(1.22)/4.25(1.18)	Mean Diff	-0.23(-0.79,0.33)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Function:WOMAC Stiffness	1 mos	38/35	3.9(0.95)/4.27(1.42)	Mean Diff	-0.37(-0.94,0.2)	Not Sig.	inconclusive
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:WOMAC Stiffness(scale not provided)	3 mos	52/52	0.9(1.1)/1(1)	Mean Diff	-0.1(-0.51,0.31)	Not Sig.	clinically insignificant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Function:WOMAC Stiffness(scale not provided)	1 mos	52/52	1(1.1)/1(0.8)	Mean Diff	0(-0.37,0.37)	Not Sig.	clinically insignificant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Composite:Lequesne Index	12 wks	32/31	3.9(2.7)/8.7(3.5)	Mean Diff	-4.8(-6.38,-3.22)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Composite:Lequesne Index	5 wks	32/31	5(2.1)/10.5(3.3)	Mean Diff	-5.5(-6.9,-4.1)	Group 1	na
Zhao; 2013/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy(4000 pulses 0.25mJ/mm2 6Hz)	8: Placebo/Control-Placebo(Sham)	Composite:Lequesne Index Score	12 wks	34/36	-4.1(2.29)/-2(2.81)	Mean Diff	-2.1(-3.32,-0.88)	Group 1	na
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Composite:Lequesne Index Score	12 mos	38/35	9.43(2.27)/10.02(2.14)	Mean Diff	-0.59(-1.62,0.44)	Not Sig.	na
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Composite:Lequesne Index Score	1 mos	38/35	9.31(2.52)/9.96(2.45)	Mean Diff	-0.65(-1.81,0.51)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Composite:Lequesne Total(scale not provided)	1 mos	52/52	6(2.3)/7.6(2.5)	Mean Diff	-1.6(-2.53,-0.67)	Group 1	na
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Composite:Lequesne Total(scale not provided)	3 mos	52/52	5.3(2.1)/7.8(3.2)	Mean Diff	-2.5(-3.55,-1.45)	Group 1	na
Zhao; 2013/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy(4000 pulses 0.25mJ/mm2 6Hz)	8: Placebo/Control-Placebo(Sham)	Composite:WOMAC Total	12 wks	34/36	-19.1(10.17)/-8.5(11.53)	Mean Diff	-10.6(-15.78,-5.42)	Group 1	possibly clinically significant
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Composite:WOMAC Total	12 mos	38/35	38.43(7.65)/40.54(6.97)	Mean Diff	-2.11(-5.52,1.3)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ediz; 2018/High	8: Electrotherapeutic agents-Extracorporeal Shockwave Therapy + TENS	8: Placebo/Control-Placebo + TENS(Sham ESWT)	Composite:WOMAC Total	1 mos	38/35	37.08(7.04)/40.33(7.51)	Mean Diff	-3.25(-6.66,0.16)	Not Sig.	clinically insignificant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Composite:WOMAC Total(scale not provided)	3 mos	52/52	23(10.5)/35.4(15.7)	Mean Diff	-12.4(-17.6,-7.2)	Group 1	possibly clinically significant
Uysal; 2020/High	8: Electrotherapeutic agents-Extracorporeal Shock Wave Therapy(1x/wk x 3wks (2000 shocks; 10Hz; 2-3 bar))	8: Placebo/Control-Placebo (Sham Extracorporeal Shock Wave Therapy)(1x/wk x 3wks (0 shocks; 10Hz; 0.1 bar)	Composite:WOMAC Total(scale not provided)	1 mos	52/52	24.8(12.4)/32.7(12.4)	Mean Diff	-7.9(-12.72,-3.08)	Group 1	possibly clinically significant
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Burning Sensation	12 wks	32/31	15.63%/6.45%	RR	2.42(0.51,11.57)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Hypesthesia	12 wks	32/31	6.25%/0%	RD	6.25(-7.647, 18.166)	Not Sig.	na
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Pain	12 wks	32/31	34.38%/19.35%	RR	1.78(0.75,4.21)	Not Sig.	na
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Petechiae	12 wks	32/31	3.13%/0%	RD	3.125(-9.494, 14.446)	Not Sig.	na
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Reddening of Skin	12 wks	32/31	31.25%/9.68%	RR	3.23(0.98,10.63)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Swelling	12 wks	32/31	9.38%/3.23%	RR	2.91(0.32,26.46)	Not Sig.	na
Zhong; 2019/High	8: Electrotherapeutic agents-Low-Dose Extracorporeal Shockwave Therapy	8: Placebo/Control-Placebo	Adverse events:Tremor	12 wks	32/31	6.25%/3.23%	RR	1.94(0.18,20.3)	Not Sig.	na

PICO 8: Physical/Electrotherapeutic Agents

Dry Needling vs. Control

Table 35: Dry Needling vs Control

Quality: H=High; M=Moderate; L=Low	H	
↑ Better Outcomes ↓ Worse Outcomes● Not Significant	Sanchez; 2019	Dunning; 2018
Composite		
EQ-5D	●	
Function		
Timed Up and Go (s)	●	
Barthel Index	●	
WOAMC Stiffness		↑
Adverse events		
No. of Falls	●	
calculable MID outcomes		
WOMAC Total	●	↑
WOMAC Function	●	
WOMAC Stiffness	●	↑
WOMAC Pain	●	↑
WOMAC Physical function		↑
VAS Pain	●	
QOL		
Global Rating of Change Scale	●	

Evidence Table 4134: Dry Needling vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:VAS Pain	12 mos	31/31	3.58(1.68)/3.61(2.74)	Mean Diff	-0.03(-1.19,1.13)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:VAS Pain	9 mos	31/31	3.06(2.72)/3.23(2.41)	Mean Diff	-0.17(-1.48,1.14)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:VAS Pain	3 mos	31/31	2.49(1.99)/2.94(2.55)	Mean Diff	-0.45(-1.61,0.71)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:VAS Pain	6 mos	31/31	2.74(1.75)/3.39(2.72)	Mean Diff	-0.65(-1.82,0.52)	Not Sig.	clinically insignificant
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Pain:WOMAC Pain	6 wks	118/117	3.4(2.6)/4.8(2.8)	Mean Diff	-1.4(-2.09,-0.71)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Pain:WOMAC Pain	3 mos	118/117	2.8(2.5)/5.2(3.2)	Mean Diff	-2.4(-3.14,-1.66)	Group 1	clinically significant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:WOMAC Pain	9 mos	31/31	3.45(2.54)/3.77(4.09)	Mean Diff	-0.32(-2.06,1.42)	Not Sig.	inconclusive
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:WOMAC Pain	6 mos	31/31	3.35(2.73)/3.71(3.68)	Mean Diff	-0.36(-2.01,1.29)	Not Sig.	inconclusive
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:WOMAC Pain	3 mos	31/31	2.81(2.48)/3.68(3.12)	Mean Diff	-0.87(-2.3,0.56)	Not Sig.	inconclusive
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Pain:WOMAC Pain	12 mos	31/31	4.23(2.46)/4.03(4.25)	Mean Diff	0.2(-1.57,1.97)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Barthel Index	12 mos	31/31	97.16(3.47)/97.65(5.57)	Mean Diff	-0.49(-2.86,1.88)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Barthel Index	3 mos	31/31	97.61(4.07)/98.13(3.57)	Mean Diff	-0.52(-2.47,1.43)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Barthel Index	6 mos	31/31	97.9(4.04)/97.55(6.05)	Mean Diff	0.35(-2.27,2.97)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Barthel Index	9 mos	31/31	98.13(3.15)/97.74(5.34)	Mean Diff	0.39(-1.85,2.63)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Timed Up and Go (s)	6 mos	31/31	9.35(5.01)/9.52(3.54)	Mean Diff	-0.17(-2.38,2.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Timed Up and Go (s)	3 mos	31/31	9.29(4.08)/9.52(3.11)	Mean Diff	-0.23(-2.08,1.62)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Timed Up and Go (s)	12 mos	31/31	9.35(3.69)/9.81(4.28)	Mean Diff	-0.46(-2.49,1.57)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:Timed Up and Go (s)	9 mos	31/31	9.13(3.34)/9.71(3.94)	Mean Diff	-0.58(-2.44,1.28)	Not Sig.	na
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Function:WOAMC Stiffness	6 wks	118/117	1.7(1.4)/2.4(1.5)	Mean Diff	-0.7(-1.07,-0.33)	Group 1	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Function	3 mos	31/31	9.74(6.96)/10.03(8.4)	Mean Diff	-0.29(-4.21,3.63)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Function	12 mos	31/31	11.71(7.71)/12.1(10.25)	Mean Diff	-0.39(-5.01,4.23)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Function	6 mos	31/31	11.7(9.52)/12.45(11.7)	Mean Diff	-0.75(-6.17,4.67)	Not Sig.	inconclusive
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Function	9 mos	31/31	11.61(7.76)/12.45(10.71)	Mean Diff	-0.84(-5.6,3.92)	Not Sig.	inconclusive
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Function:WOMAC Physical Function	6 wks	118/117	12.1(9.8)/18.7(10.9)	Mean Diff	-6.6(-9.26,-3.94)	Group 1	possibly clinically significant
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Function:WOMAC Physical Function	3 mos	118/117	10.1(9.3)/18.7(11.7)	Mean Diff	-8.6(-11.32,-5.88)	Group 1	clinically significant
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Function:WOMAC Stiffness	3 mos	118/117	1.3(1.3)/2.4(1.5)	Mean Diff	-1.1(-1.46,-0.74)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Stiffness	6 mos	31/31	1.23(1.1)/1.26(1.5)	Mean Diff	-0.03(-0.7,0.64)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Stiffness	12 mos	31/31	1.19(1.25)/1.29(1.4)	Mean Diff	-0.1(-0.77,0.57)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Stiffness	3 mos	31/31	1.13(1.1)/1.29(1.46)	Mean Diff	-0.16(-0.82,0.5)	Not Sig.	inconclusive
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Function:WOMAC Stiffness	9 mos	31/31	1.48(0.96)/1.35(1.33)	Mean Diff	0.13(-0.46,0.72)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:EQ-5D	9 mos	31/31	5.81(0.83)/5.87(0.92)	Mean Diff	-0.06(-0.51,0.39)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:EQ-5D	6 mos	31/31	5.84(1.16)/5.9(1.02)	Mean Diff	-0.06(-0.62,0.5)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:EQ-5D	3 mos	31/31	6(1.6)/5.87(1.12)	Mean Diff	0.13(-0.57,0.83)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:EQ-5D	12 mos	31/31	6.35(1.56)/6.2(1.36)	Mean Diff	0.15(-0.59,0.89)	Not Sig.	na
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Composite:WOMAC Total	3 mos	118/117	14.2(12.5)/26.4(15.6)	Mean Diff	-12.2(-15.84,-8.56)	Group 1	clinically significant
Dunning; 2018/High	8: Electrotherapeutic agents-Electrical Dry Needling	8: Placebo/Control-Control	Composite:WOMAC Total	6 wks	118/117	17.2(13.1)/25.9(14.3)	Mean Diff	-8.7(-12.23,-5.17)	Group 1	possibly clinically significant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:WOMAC Total	12 mos	31/31	17.13(10.18)/17.42(14.82)	Mean Diff	-0.29(-6.77,6.19)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:WOMAC Total	9 mos	31/31	16.55(10.48)/17.6(14.97)	Mean Diff	-1.05(-7.63,5.53)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:WOMAC Total	6 mos	31/31	16.23(12.34)/17.42(15.55)	Mean Diff	-1.19(-8.33,5.95)	Not Sig.	inconclusive
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Composite:WOMAC Total	3 mos	31/31	13.7(9.4)/15(11.7)	Mean Diff	-1.3(-6.7,4.1)	Not Sig.	clinically insignificant
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	QOL:Global Rating of Change Scale	12 mos	31/31	3.1(1.7)/3.23(3.17)	Mean Diff	-0.13(-1.43,1.17)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	QOL:Global Rating of Change Scale	3 mos	31/31	3.84(2.66)/4.16(1.93)	Mean Diff	-0.32(-1.5,0.86)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	QOL:Global Rating of Change Scale	9 mos	31/31	3.32(2.01)/3.32(2.7)	Mean Diff	0(-1.21,1.21)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	QOL:Global Rating of Change Scale	6 mos	31/31	3.87(2.26)/3.48(2.87)	Mean Diff	0.39(-0.92,1.7)	Not Sig.	na
Sanchez; 2019/High	8: Physical agents-Dry Needling(1 session/week x6wks)	8: Placebo/Control-Placebo (Sham Dry Needling)(1 session/week x6wks)	Adverse events:No. of Falls	12 mos	31/31	0.22(0.49)/0.41(0.62)	Mean Diff	-0.19(-0.47,0.09)	Not Sig.	na

PICO 9: Systemic Treatment

NSAID vs. Control

Table 36: NSAIDs vs Control

Quality: H=High; M=Moderate; L=Low	H																								M											
↑ Better Outcomes ↓ Worse Outcomes • Not Significant	Simon; 2009	Sandelin; 1997	Ishijima; 2014	Sandgee; 2002	Elsaman; 2016	Strand; 2017	Gibofsky; 2014	Gordo; 2017	Essex; 2014	Essex; 2016	Essex; 2012	Singh; 2012	Fleischmann; 1997	Bensen; 1999	Schnitzer; 2010	Kivits; 2002	Kivitz; 2004	Puopolo; 2007	Lee; 1986	Doherty; 2011	Kongtharvonskul; 2016	Davies; 1999	Schnitzer; 2011	Svensson; 2006	Mckenna; 2001 (b)	Schnitzer; 2005b	Pavelka; 2007	Bolten; 2015	Lee; 1985	Ontori; 2013	Selvan; 2012	Ekman; 2014	Dwicandra; 2018	Schnitzer ; 1999	Micelli ; 2004	Altman; 1998
Composite																																				
WOMAC Total																					•							↑		↑						
SF-36 General Health						↑																														
Improved Patient Global Score																													↑							
JKOM Total			•																																	
Lequesne Functional Index Total Scores																												•								
Likert Pain/Function														↑																						
Patient global score improvement																			↑																	
Unchanged or Worse Patient Global Score																													↑							
change in likert Pain/Function(0-24)														↑																						
patient overall rating of disease status improvement (lower=better)															↑																					
sf-36 mcs improvement															•																					
Function																																				
WOMAC Function																					•							↑								
WOMAC Stiffness																					•							•		↑						
WOMAC Physical function																														↑						
SF-36 Role Physical						↑																														
Lequesne Index(0-24)		•																																		
change in 50 feet walk time (sec)				•																																
change in Lequesne's functional index				•																																
Inactivity stiffness													•																							
Sit-to-stand test; seconds; mean;SD (n)																				↑																
Other																																				
patient global assessment of overall health	↑																																			
patient global assessment of study knee	↑																																			
change in number of paracetamol take (tablets/wk)				•																																
Minimum Effective Naproxen Dose (among non responders)																																		•		
Minimum Effective Naproxen Dose (among responders)																																		↑		
PGART (0-4 Likert scale change from baseline)																		↑																		
Patient global assessment†; patients rating treatment as excellent or good; n/N (%)																				↑																
Patients with sleep loss													•																							
Sleep loss with joint pain as a contributing factor													↑																							
improved global assessment														•																						
paracetamol intake pills per day																											↑									
patient global assessment of improvement																									↑											
patient global assessment of response to therapy																										↑										
phyician global assessment of improvement																									↑											
physician global assessment of arthritis improvement (5 = very poor)																↑																				
rescue acetaminophen															↑																					
Pain																																				
WOMAC Pain																					•							•		↑						
VAS Pain																					•									↑	↑					
VAS Pain Walking																	↑																			
walking pain													•																							
?30% Reduction in WOMAC Pain Subscale Scores							↑																													
?50% Reduction in WOMAC Pain Subscale Scores							↑																													
Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)																				•																
Joint tenderness													•																							
Linear pain score																			↑																	
Nighttime pain													•																							
Weight bearing pain																			↑																	
calculable MID outcomes																																				
WOMAC Total				•			↑		↑		•	↑		↑	↑	↑				↑					↑		↑				↑					
sf36 physical function						↑																														
WOMAC Function															↑					↑		•	↑	↑	↑		↑				↑	↑				
WOMAC Stiffness	–			–					–		–					–				–	–				–		–				–					
WOMAC Pain	–						–		–		–				–					–	–	–	–	–	–	–	–				–	–				
WOMAC Physical function	↑								↑		•																						↑			
VAS Pain			•		↑			•	↑	•		↑			↑	•					•				↑											
SF-36 Bodily Pain						↑																														
VAS Pain(0-100)		•																																		
VAS pain improvement																																			•	
change in WOMAC disability				•																																
WOMAC composite(0-100)																						•														
change in WOMAC composite(0-96)														↑																						
womac (vas change from baseline) total																		↑																		
VAS function(SF-36 Physical Function scale; 0-100)																						•														
womac (vas change from baseline)-Function (0-100 VAS change from baseline)																		↑																		
PGADS (0-100 VAS change from baseline)																		•																		
womac (vas change from baseline) questionnaire overall score average (0-100 VAS change from baseline)																		↑																		
Patient's Assessment of Arthris Pain (VAS)											•																									
VAS Pain(SF-36 pain scale; 0-100)																						•														
Walking VAS pain(0-100)																																				•
vas pain at rest improvement															•																					
vas pain during walking improvement															↑																					
womac (vas change from baseline)- Pain (0-100 VAS change from baseline)																		↑																		
womac (vas change from baseline) stiffness subscale (0-100 VAS change from baseline)																		↑																		
QOL																																				
SF-36 Social Functioning						↑																														
SF-36 Vitality						↑																														
SF-36 Mental Health						•																														
Fair Global Efficacy Judgement by Patient												•																								
Good Global Efficacy Judgement by Patient												↑																								
Patient Global Response: Good/Excellent																	↑																			
Poor Global Efficacy Judgement by Patient												•																								
SF-36 Role Emotion						•																														
Very Good Global Efficacy Judgement by Patient												↑																								
Very Poor Global Efficacy Judgement by Patient												•																								

Table 36 Continued: NSAIDs vs Control

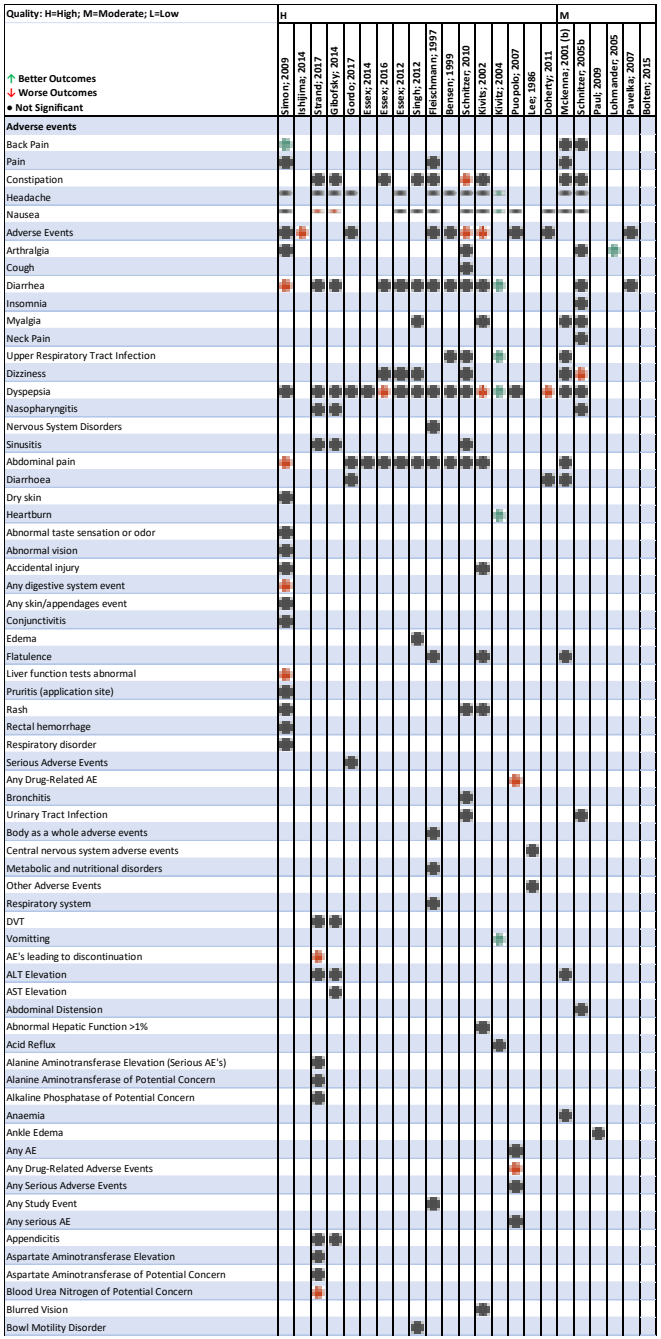
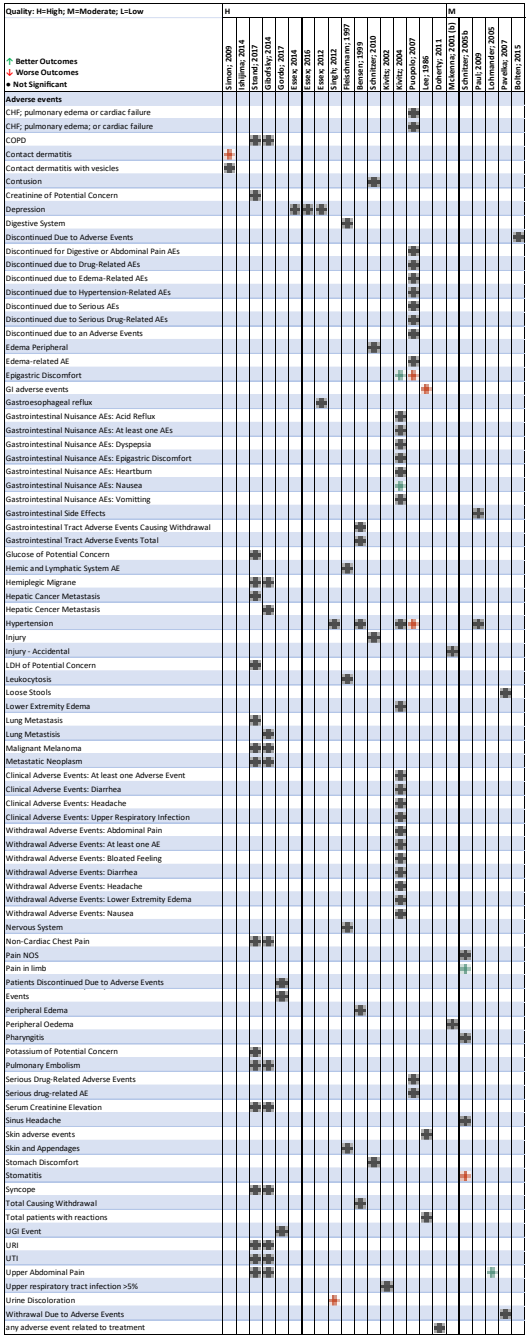
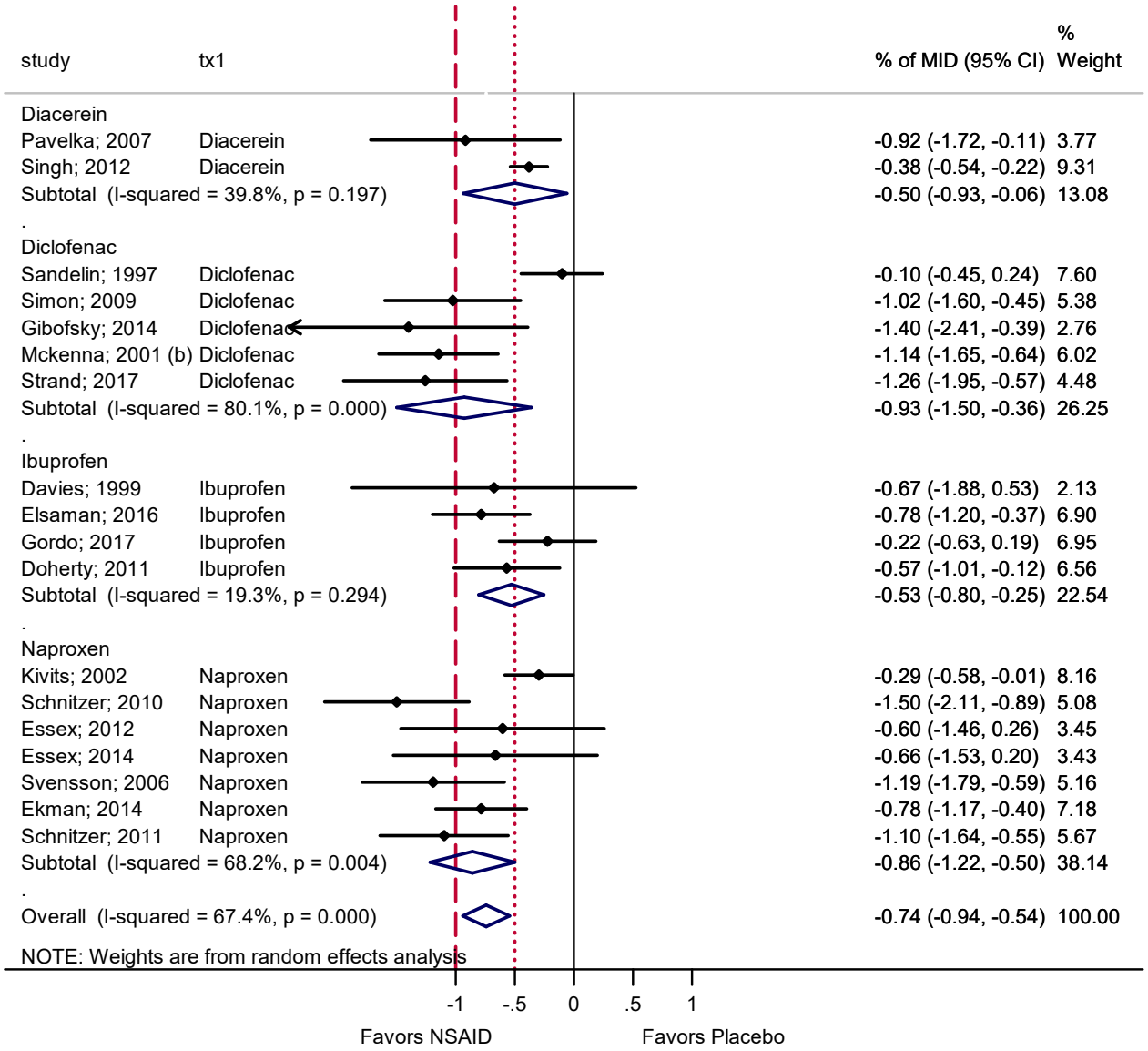


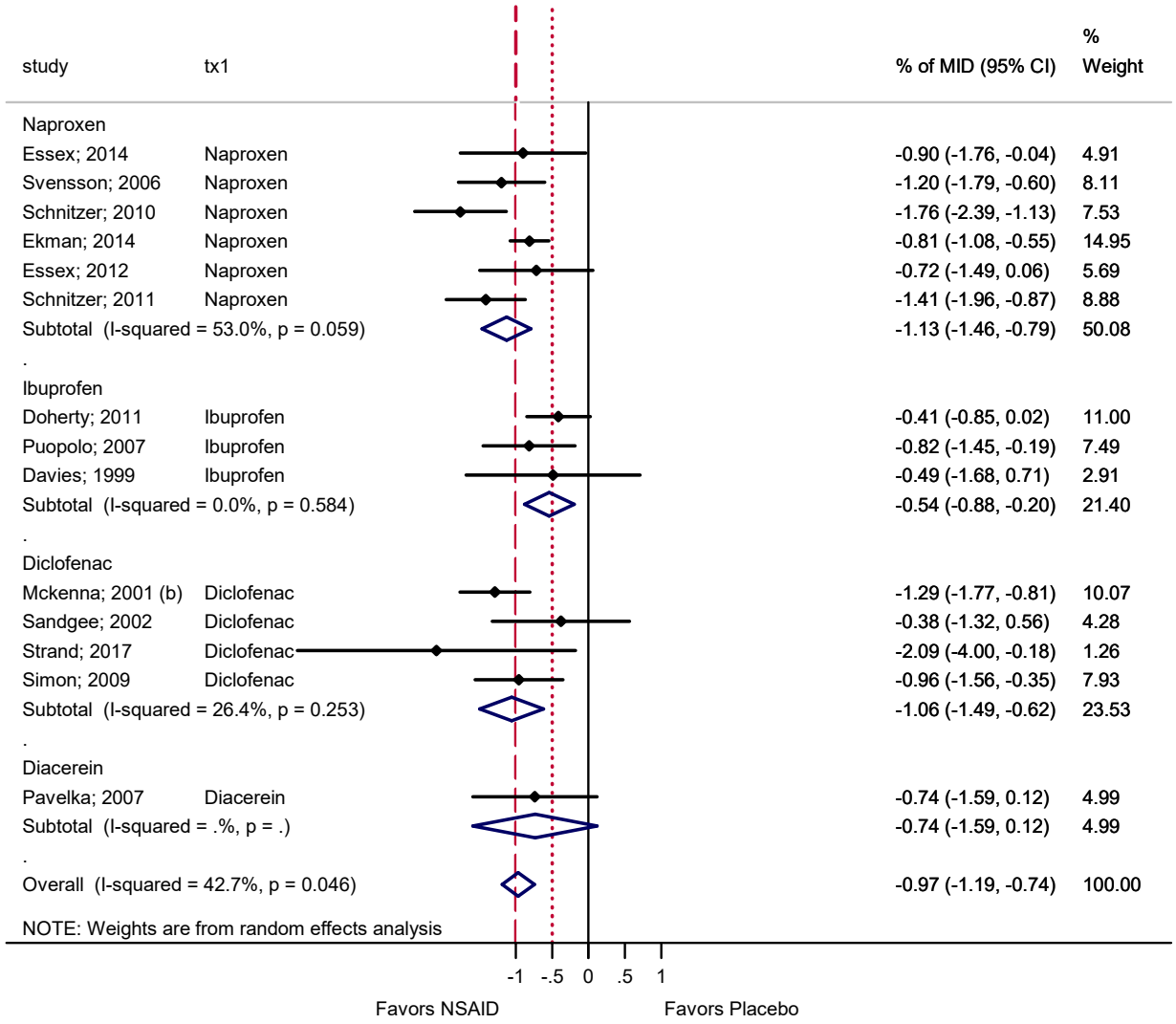
Table 36 Continued: NSAIDs vs Control



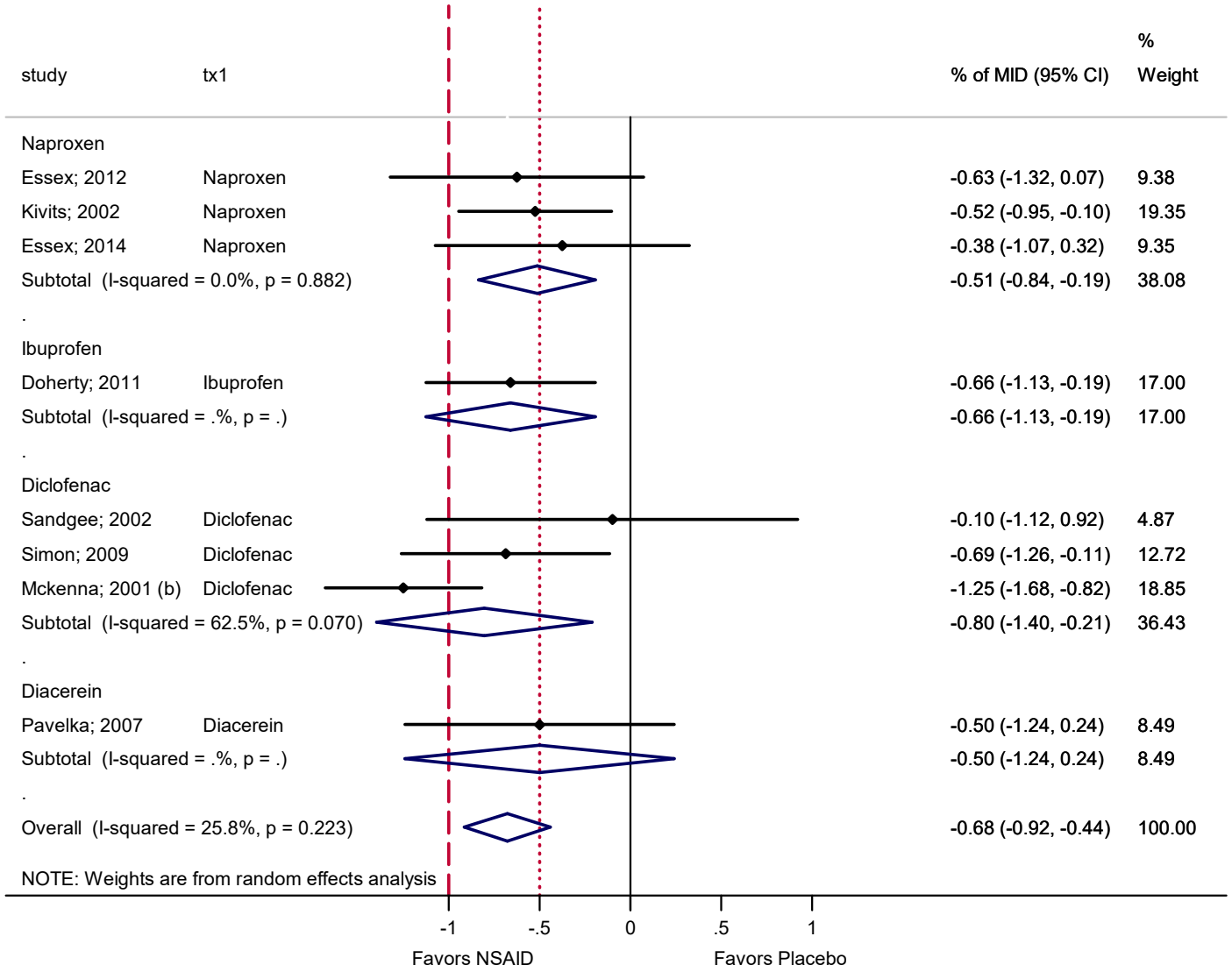
Meta-Analysis Figure 20: NSAID vs Placebo- Pain



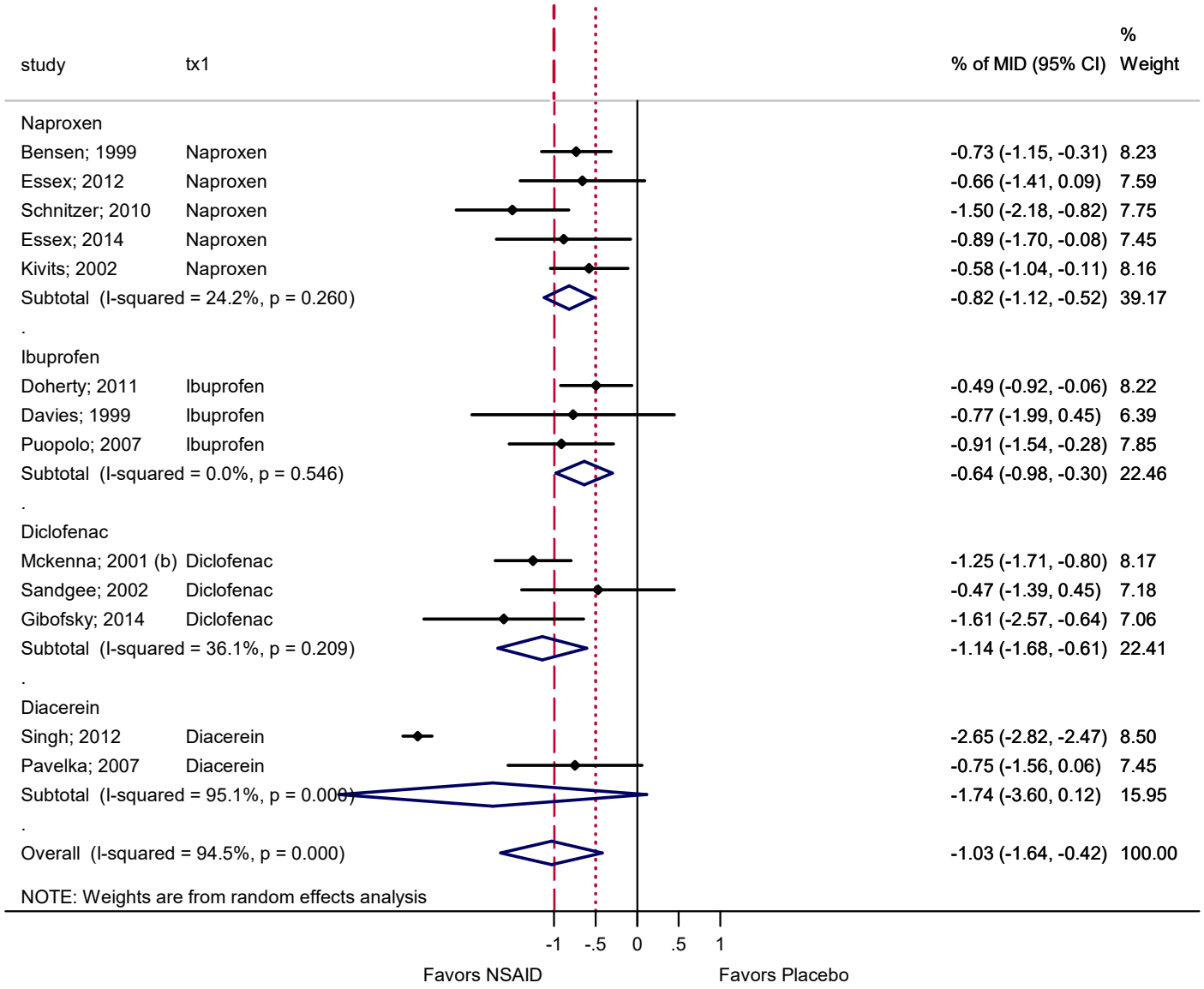
Meta-Analysis Figure 21: NSAID vs Placebo- Function



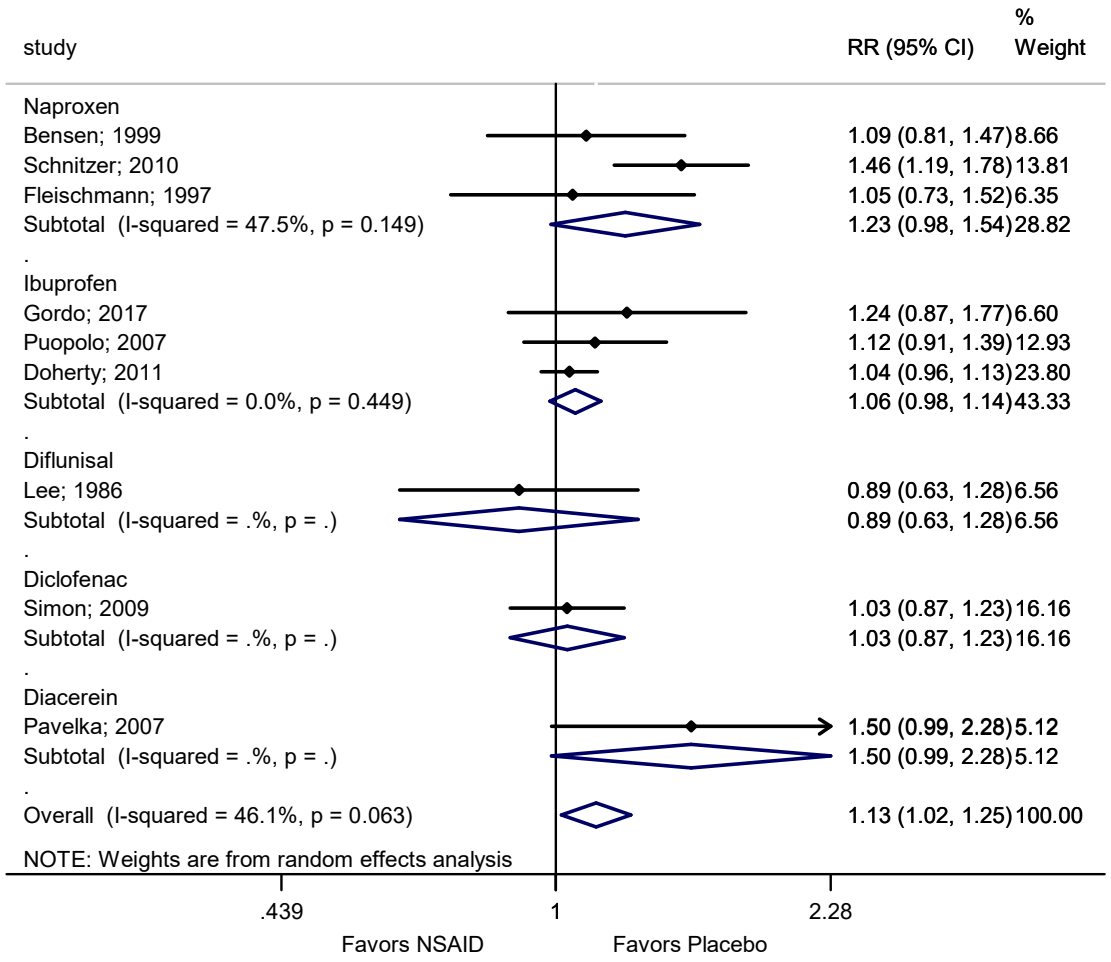
Meta-Analysis Figure 22: NSAID vs Placebo- Stiffness



Meta-Analysis Figure 23: NSAID vs Placebo- WOMAC Total Score



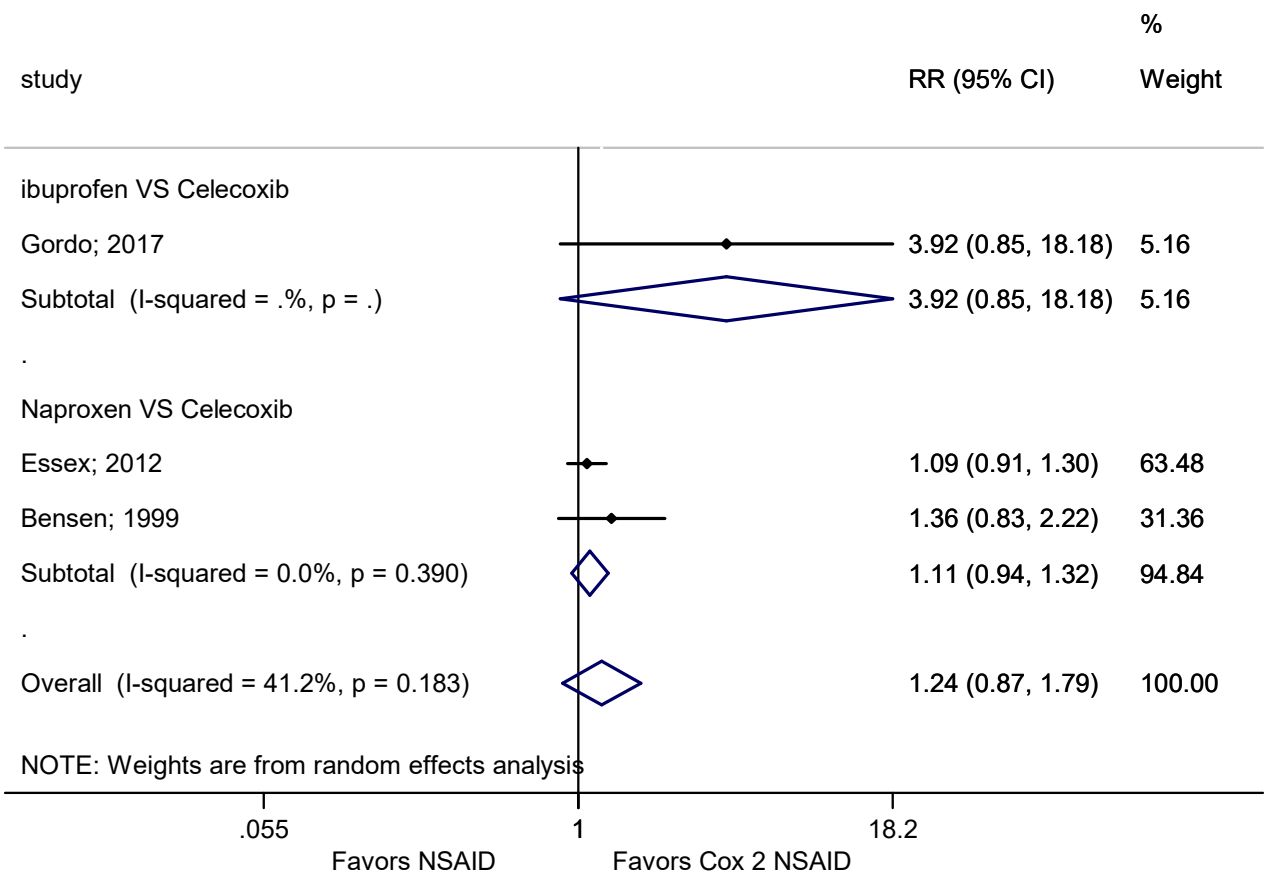
Meta-Analysis Figure 24: NSAID vs Placebo- Overall Adverse Events



NNTH=21

number of excess AEs per 1000=50(6.2,97.9)

Meta-Analysis Figure 24: NSAID vs Placebo- GI Adverse Events



NNTH=34

number of excess AEs per 1000=30(-16,94)

Evidence Table 4235: NSAID vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Pain:?30% Reduction in WOMAC Pain Subscale Scores	12 wks	104/103	67.31%/56.31%	RR	1.2(0.96,1.48)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Pain:?30% Reduction in WOMAC Pain Subscale Scores	6 wks	104/103	60.58%/45.63%	RR	1.33(1.02,1.72)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Pain:?30% Reduction in WOMAC Pain Subscale Scores	12 wks	98/103	76.53%/56.31%	RR	1.36(1.11,1.66)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Pain:?30% Reduction in WOMAC Pain Subscale Scores	6 wks	98/103	66.33%/45.63%	RR	1.45(1.13,1.87)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Pain:?50% Reduction in WOMAC Pain Subscale Scores	12 wks	104/103	54.81%/42.72%	RR	1.28(0.97,1.7)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Pain:?50% Reduction in WOMAC Pain Subscale Scores	6 wks	104/103	50%/34.95%	RR	1.43(1.03,1.98)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Pain:?50% Reduction in WOMAC Pain Subscale Scores	12 wks	98/103	61.22%/42.72%	RR	1.43(1.09,1.88)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Pain:?50% Reduction in WOMAC Pain Subscale Scores	6 wks	98/103	53.06%/34.95%	RR	1.52(1.1,2.1)	Group 2	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	7 weeks	158/149	68.99%/72.48%	RR	0.95(0.82,1.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	13 weeks	220/219	64.09%/63.01%	RR	1.02(0.88,1.17)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	13 weeks	220/219	65.45%/63.01%	RR	1.04(0.9,1.19)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	7 weeks	177/149	75.14%/72.48%	RR	1.04(0.91,1.18)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Pain:Joint tenderness	4 wks	92/94	1.12(.)/1.32(.)	Mean Diff	-0.2	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Pain:Joint tenderness	4 wks	93/94	1.36(.)/1.32(.)	Mean Diff	0.04	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Pain:Linear pain score	6 wks	88/70	4(2.7)/4.7(2.9)	Mean Diff	-0.7(-1.59,0.19)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Pain:Linear pain score	6 wks	69/70	3.5(2.6)/4.7(2.9)	Mean Diff	-1.2(-2.12,-0.28)	Group 1	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Pain:Nighttime pain	4 wks	92/94	0.87(.)/1.14(.)	Mean Diff	-0.27	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Pain:Nighttime pain	4 wks	93/94	1.27(.)/1.14(.)	Mean Diff	0.13	Not Sig.	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Pain:Patient's Assessment of Arthris Pain (VAS)	6 wks	106/46	29.9(24.71)/36.5(28.49)	Mean Diff	-6.6(-16.24, 3.04)	Not Sig.	clinically insignificant
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Pain:SF-36 Bodily Pain	12 wks	104/103	56(21.9)/48(20.81)	Mean Diff	8(2.15, 13.85)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Pain:SF-36 Bodily Pain	12 wks	98/103	57.8(17.88)/48(20.81)	Mean Diff	9.8(4.41,15.19)	Group 2	possibly clinically significant
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	123/56	-32.8(25.29)/-28.4(25.52)	Mean Diff	-4.4(-12.53, 3.73)	Not Sig.	clinically insignificant
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	96/47	25.2(23.52)/35.4(26.74)	Mean Diff	-10.2(-19.31,-1.09)	Group 1	some may benefit
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:VAS Pain	5 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:VAS Pain	4 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:VAS Pain	1 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:VAS Pain	2 mos	148	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:VAS Pain	3 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 mos	74/74	2.97(2.55)/2.88(2.55)	Mean Diff	0.09(-0.74,0.92)	Not Sig.	clinically insignificant
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	107/58	21.9(20.69)/25.6(23.61)	Mean Diff	-3.7(-11.02, 3.62)	Not Sig.	clinically insignificant
Ishijima; 2014/High	9: NSAIDs (oral/IM)-NSAID [Oral](60mg; x3/day; x5 weeks)	9: Non-arthro Tx-Hyaluronic Acid [IA](2700 kDa (25mg); 1x/wk x5wks)	Pain:VAS Pain	5 wks	85/97	31.9(23.9)/31.8(24.1)	Mean Diff	0.1(-6.93,7.13)	Not Sig.	clinically insignificant
Ohtori; 2013/Moderate	9: NSAIDs (oral/IM)-Meloxicam + Pregabalin(10 mg Meloxicam after breakfast + 25 mg pregabalin before sleep)	9: Placebo/Control-Control (Pregabalin Alone)(25 mg before sleep)	Pain:VAS Pain	4 wks		none	pvalue	Sig (p < 0.05)	Meloxicam + Pregabalin favored over Pregabal	na
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Pain:VAS Pain	4 wks	43	none	Mean Diff	-0.79(-1.02,-0.56)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Pain:VAS Pain	8 wks	43	none	Mean Diff	-0.89(-1.02,-0.58)	Group 1	na
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Pain:VAS Pain	12 wks	43	none	Mean Diff	-1.13(-1.41,-0.84)	Group 1	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Pain:VAS Pain	4 mos	30/30	14.83(5.16)/33(7.72)	Mean Diff	-18.17(-21.57,-14.77)	Group 1	possibly clinically significant
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	30/30	26.5(6.45)/33(8.8)	Mean Diff	-6.5(-10.5,-2.5)	Group 1	clinically insignificant
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Pain:VAS Pain	3 mos	30/30	15.3(5.07)/22.83(6.9)	Mean Diff	-7.53(-10.67,-4.39)	Group 1	clinically insignificant
Elsaman; 2016/High	9: NSAIDs (oral/IM)-Ibuprofen(1200 mg daily for two weeks)	8: Placebo/Control-Placebo	Pain:VAS Pain	4 wks	50/50	2.44(2.28)/4(1.85)	Mean Diff	-1.56(-2.38,-0.74)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Pain:VAS Pain	12 wks	205/204	-31.83(29.66)/-25.97(29.59)	Mean Diff	-5.86(-11.62,-0.1)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Pain:VAS Pain	6 wks	205/204	-31.84(27.84)/-23.92(27.76)	Mean Diff	-7.92(-13.32,-2.52)	Group 1	clinically insignificant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid)	9: Placebo/Control-placebo	Pain:VAS Pain	6 wks	200/199	-36.8(28.7)/-23.1(28)	Mean Diff	-13.7(-19.28,-8.12)	Group 1	some may benefit
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Pain:VAS Pain	12 wks	144/189	-40.51(24.33)/-29.71(24.38)	Mean Diff	-10.8(-16.1,-5.5)	Group 1	some may benefit
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Pain:VAS Pain Walking	6 wks	618	none	Mean Difference	-11.4(-15.5,-7.3)	Group 1	na
Micelli ; 2004/Moderate	9: NSAIDs (oral/IM)-paracetamol	9: Placebo/Control-placebo	Pain:VAS Pain improvement	6 wks	405/374	23(27)/23(26)	Mean Diff	0(-3.73,3.73)	Not Sig.	clinically insignificant
Sandelin; 1997/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(50mg twice a day)	9: Placebo/Control-Placebo (Oral)(once a day)	Pain:VAS Pain(0-100)	28 days	78/79	30(19.2)/32(24.1)	Mean Diff	-2(-8.87,4.87)	Not Sig.	clinically insignificant
Davies; 1999/High	9: NSAIDs (oral/IM)-Ibuprofen (Oral)(800mg ibuprofen 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:VAS Pain(SF-36 pain scale; 0-100)	28 days	54/50	61.5(23.7)/55.3(21.4)	Mean Diff	6.2(-2.57,14.97)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bolten; 2015/Moderate	9: NSAIDs (oral/IM)-Diclofenac Sodium(50 mg three times daily)	9: Placebo/Control-Placebo(2 tablets three times daily)	Pain:WOMAC Pain	12 wks	46/52	15(.)/21(.)	median difference	-6	Not Sig.	na
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	96/47	-5.1(3.92)/-4(4.11)	Mean Diff	-1.1(-2.53,0.33)	Not Sig.	inconclusive
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	1 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	4 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	5 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	2 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	3 mos	148	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	6 mos	74/74	12.02(10.77)/11.76(10.83)	Mean Diff	0.26(-3.25,3.77)	Not Sig.	clinically insignificant
Ohtori; 2013/Moderate	9: NSAIDs (oral/IM)-Meloxicam + Pregabalin(10 mg Meloxicam after breakfast + 25 mg pregabalin before sleep)	9: Placebo/Control-Control (Pregabalin Alone)(25 mg before sleep)	Pain:WOMAC Pain	4 wks	3.6/6.6	none	pvalue	Sig ($p < 0.05$)	Meloxicam + Pregabalin favored over Pregabal	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	125/65	-5.7(4.47)/-4.7(4.84)	Mean Diff	-1(-2.43,0.43)	Not Sig.	inconclusive
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Pain:WOMAC Pain	4 wks	43	none	Mean Diff	-4.2(-5.08,-3.33)	Group 1	clinically significant
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Pain:WOMAC Pain	8 wks	43	none	Mean Diff	-4.37(-5.03,-3.71)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Pain:WOMAC Pain	12 wks	43	none	Mean Diff	-5.38(-5.78,-4.97)	Group 1	clinically significant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid)	9: Placebo/Control-placebo	Pain:WOMAC Pain	6 wks	200/199	-4.3(4.3)/-2.4(4.2)	Mean Diff	-1.9(-2.74,-1.06)	Group 1	possibly clinically significant
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Pain:WOMAC Pain	12 wks	151/154	-7(4.8)/-6(4.5)	Mean Diff	-1(-2.05,0.05)	Not Sig.	inconclusive
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Pain:WOMAC Pain	12 wks	151/155	-6.4(4.1)/-4.7(4.4)	Mean Diff	-1.7(-2.66,-0.74)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Pain:WOMAC Pain	12 wks	226/221	-36.51(27.19)/-24.08(27.4)	Mean Diff	-12.43(-17.51,-7.35)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	112 days	206/207	-2.67(2.87)/-2.23(2.88)	Mean Diff	-0.44(-1,0.12)	Not Sig.	inconclusive
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	112 days	207/209	-2.26(3.17)/-1.81(3.18)	Mean Diff	-0.45(-1.06,0.16)	Not Sig.	inconclusive
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	56 days	207/209	-2.6(1.47)/-2(1.48)	Mean Diff	-0.6(-0.88,-0.32)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	28 days	207/209	-2.76(1.47)/-2.15(1.48)	Mean Diff	-0.61(-0.89,-0.33)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	84 days	207/209	-2.45(1.47)/-1.8(1.84)	Mean Diff	-0.65(-0.97,-0.33)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	84 days	206/207	-2.95(1.46)/-2.25(1.47)	Mean Diff	-0.7(-0.98,-0.42)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	14 days	207/209	-2.75(1.47)/-2(1.48)	Mean Diff	-0.75(-1.03,-0.47)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	14 days	206/207	-3.13(1.28)/-2.3(1.1)	Mean Diff	-0.83(-1.06,-0.6)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	56 days	206/207	-3.13(1.28)/-2.3(1.47)	Mean Diff	-0.83(-1.1,-0.56)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Pain:WOMAC Pain (0-10)	28 days	206/207	-3.25(1.28)/-2.35(1.1)	Mean Diff	-0.9(-1.13,-0.67)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg three times daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	84 days	98/103	-44.1(30.39)/-32.5(29.84)	Mean Diff	-11.6(-19.98,-3.22)	Group 1	possibly clinically significant
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg three times daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	42 days	98/103	-43.5(30.19)/-31.1(29.63)	Mean Diff	-12.4(-20.73,-4.07)	Group 1	possibly clinically significant
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg three times daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	14 days	98/103	-37.4(28.81)/-21.6(28.32)	Mean Diff	-15.8(-23.75,-7.85)	Group 1	possibly clinically significant
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	42 days	104/103	-36.8(30.59)/-31.1(29.63)	Mean Diff	-5.7(-13.95, 2.55)	Not Sig.	inconclusive
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	84 days	104/103	-39(29.68)/-32.5(29.84)	Mean Diff	-6.5(-14.66, 1.66)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	14 days	104/103	-31.4(27.94)/-21.6(28.32)	Mean Diff	-9.8(-17.51,-2.09)	Group 1	possibly clinically significant
Schnitzer; 2011/High	9: NSAIDs (oral/IM)-Naproxcinod(750 mg bid)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day)	Pain:WOMAC Pain (VAS Version)	91 days	241/256	-31.3(25.93)/-20.4(25.92)	Mean Diff	-10.9(-15.47,-6.33)	Group 1	possibly clinically significant
Schnitzer; 2011/High	9: NSAIDs (oral/IM)-Naproxcinod(350 mg bid)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day)	Pain:WOMAC Pain (VAS Version)	91 days	247/256	-28.1(25.77)/-20.4(25.92)	Mean Diff	-7.7(-12.23,-3.17)	Group 1	possibly clinically significant
Schnitzer; 2011/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500 mg 2x/day)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day)	Pain:WOMAC Pain (VAS Version)	91 days	254/255	-29.5(25.82)/-20.4(25.87)	Mean Diff	-9.1(-13.6,-4.6)	Group 1	possibly clinically significant
Davies; 1999/High	9: NSAIDs (oral/IM)-Ibuprofen (Oral)(800mg ibuprofen 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	28 days	54/50	75.9(23)/70.3(27.8)	Mean Diff	5.6(-4.38,15.58)	Not Sig.	inconclusive
Svensson; 2006/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain (VAS Version)	42 days	280/75	-16.62(20.5)/-6.75(19.12)	Mean Diff	-9.87(-14.87,-4.87)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 1998/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice daily and saline injections 5 times weekly)	9: Placebo/Control-Placebo (Intra-articular)(Placebo pill twice daily and saline injections 5 times weekly)	Pain:Walking VAS pain(0-100)	28 days	147/156	25(25)/28(27)	Mean Diff	-3(-8.88,2.88)	Not Sig.	clinically insignificant
Altman; 1998/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice daily and saline injections 5 times weekly)	9: Placebo/Control-Placebo (Intra-articular)(Placebo pill twice daily and saline injections 5 times weekly)	Pain:Walking VAS pain(0-100)	182 days	160/163	25(28)/28(30)	Mean Diff	-3(-9.35,3.35)	Not Sig.	clinically insignificant
Altman; 1998/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice daily and saline injections 5 times weekly)	9: Placebo/Control-Placebo (Oral)(Placebo pill twice daily and saline injections 5 times weekly)	Pain:Walking VAS pain(0-100)	35 days	143/149	25(27)/25(25)	Mean Diff	0(-6,6)	Not Sig.	clinically insignificant
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Pain:Walking pain	4 wks	92/94	1.41(.)/1.62(.)	Mean Diff	-0.21	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Pain:Walking pain	4 wks	93/94	1.73(.)/1.62(.)	Mean Diff	0.11	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Pain:Weight bearing pain	6 wks	88/70	2(1)/2.4(1)	Mean Diff	-0.4(-0.72,-0.08)	Group 1	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Pain:Weight bearing pain	6 wks	69/70	2(1.1)/2.4(1)	Mean Diff	-0.4(-0.75,-0.05)	Group 1	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod(125 mg)	9: Placebo/Control-	Pain:change in WOMAC pain (VAS)	6 weeks	209	none	adusted mean difference	-1(-7,5)	Not Sig.	clinically insignificant
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod(375 mg)	9: Placebo/Control-	Pain:change in WOMAC pain (VAS)	6 weeks	211	none	adusted mean difference	-12(-18,-6)	Group 1	possibly clinically significant
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod(750 mg)	9: Placebo/Control-	Pain:change in WOMAC pain (VAS)	6 weeks	218	none	adusted mean difference	-13(-19,-7)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 375 mg(bid)	9: Placebo/Control-placebo	Pain:vas pain at rest improvement	13 wks	144/197	-35.92(24.42)/-29.71(24.38)	Mean Diff	-6.21(-11.47,-0.95)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(375 mg bic)	9: Placebo/Control-placebo	Pain:vas pain at rest improvement	13 wks	197/144	-35.92(24.42)/-29.71(24.38)	Mean Diff	-6.21(-11.47,-0.95)	Group 1	clinically insignificant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 750mg(bid)	9: Placebo/Control-placebo	Pain:vas pain at rest improvement	13 wks	144/186	-37.84(24.41)/-29.71(24.38)	Mean Diff	-8.13(-13.46,-2.8)	Group 1	clinically insignificant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(750 mg bid)	9: Placebo/Control-placebo	Pain:vas pain at rest improvement	13 wks	186/144	-37.84(24.41)/-29.71(24.38)	Mean Diff	-8.13(-13.46,-2.8)	Group 1	clinically insignificant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Pain:vas pain during walking improvement	12 wks	144/189	-46.04(25.98)/-34.52(25.97)	Mean Diff	-11.52(-17.17,-5.87)	Group 1	some may benefit
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(375 mg bic)	9: Placebo/Control-placebo	Pain:vas pain during walking improvement	13 wks	197/144	-41.82(25.97)/-34.52(25.97)	Mean Diff	-7.3(-12.9,-1.7)	Group 1	clinically insignificant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 375 mg(bid)	9: Placebo/Control-placebo	Pain:vas pain during walking improvement	13 wks	144/197	-41.82(25.97)/-34.52(25.97)	Mean Diff	-7.3(-12.9,-1.7)	Group 1	clinically insignificant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(750 mg bid)	9: Placebo/Control-placebo	Pain:vas pain during walking improvement	13 wks	186/144	-44.49(25.97)/-34.52(25.97)	Mean Diff	-9.97(-15.64,-4.3)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 750mg(bid)	9: Placebo/Control-placebo	Pain:vas pain during walking improvement	13 wks	144/186	-44.49(25.97)/-34.52(25.97)	Mean Diff	-9.97(-15.64,-4.3)	Group 1	some may benefit
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Pain:womac (vas change from baseline)-Pain (0-100 VAS change from baseline)	12 weeks	211/109	-24.1(22.88)/-16.47(21.46)	Mean Diff	-7.63(-12.73,-2.53)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Pain:womac pain	8 wks	82/83	6.96(4.37)/7.84(4)	Mean Diff	-0.88(-2.17,0.41)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Pain:womac pain	12 wks	82/83	6.12(4.16)/7.64(4.49)	Mean Diff	-1.52(-2.85,-0.19)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Pain:womac pain	16 wks	82/83	5.84(4.15)/7.52(4.29)	Mean Diff	-1.68(-2.98,-0.38)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Pain:womac pain	24 wks	82/83	5.92(4.39)/7.68(4.52)	Mean Diff	-1.76(-3.13,-0.39)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Pain:womac pain	20 wks	82/83	5.76(4.23)/7.64(4.33)	Mean Diff	-1.88(-3.2,-0.56)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Pain:womac pain	4 wks	82/83	8.52(3.65)/8.32(3.82)	Mean Diff	0.2(-0.95,1.35)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:womac pain	7 weeks	161/148	-17.1(18.8)/-14.7(17.8)	Mean Diff	-2.4(-6.5,1.7)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:womac pain	7 weeks	173/148	-18(20.3)/-14.7(17.8)	Mean Diff	-3.3(-7.48,0.88)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:womac pain	13 weeks	220/215	-14.7(18.7)/-10.8(18.6)	Mean Diff	-3.9(-7.42,-0.38)	Group 1	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Pain:womac pain	13 weeks	218/215	-15.5(20.7)/-10.8(18.6)	Mean Diff	-4.7(-8.42,-0.98)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(750 mg bid)	9: Placebo/Control-placebo	Pain:womac pain likert	13 wks	229/221	-35.29(27.85)/-24.08(27.4)	Mean Diff	-11.21(-16.33,-6.09)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(375 mg bic)	9: Placebo/Control-placebo	Pain:womac pain likert	13 wks	240/221	-34.62(27.91)/-24.08(27.4)	Mean Diff	58.7(53.64,63.76)	Group 2	clinically significant
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Function:Inactivity stiffness	4 wks	93/94	1.76(.)/1.81(.)	Mean Diff	-0.05	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Function:Inactivity stiffness	4 wks	92/94	1.71(.)/1.81(.)	Mean Diff	-0.1	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandelin; 1997/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(50mg twice a day)	9: Placebo/Control-Placebo (Oral)(once a day)	Function:Lequesne Index(0-24)	28 days	78/79	6.9(3.57)/7.4(4.19)	Mean Diff	-0.5(-1.73,0.73)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Function:SF-36 Role Physical	12 wks	104/103	60.5(23.52)/56.5(23.04)	Mean Diff	4(-2.38,10.38)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Function:SF-36 Role Physical	12 wks	98/103	63.6(24.61)/56.5(23.04)	Mean Diff	7.1(0.46,13.74)	Group 2	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	7 weeks	152/139	15.3(6)/15.6(8.5)	Mean Diff	-0.3(-2.01,1.41)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	13 weeks	204/199	16(7.1)/16.7(9.4)	Mean Diff	-0.7(-2.33,0.93)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	7 weeks	171/139	14.1(6.2)/15.6(8.5)	Mean Diff	-1.5(-3.2,0.2)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	13 weeks	207/199	14.5(6)/16.7(9.4)	Mean Diff	-2.2(-3.75,-0.65)	Group 2	na
Davies; 1999/High	9: NSAIDs (oral/IM)-Ibuprofen (Oral)(800mg ibuprofen 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Function:VAS function(SF-36 Physical Function scale; 0-100)	28 days	54/50	52.1(25.7)/50.5(24.7)	Mean Diff	1.6(-8.2,11.4)	Not Sig.	inconclusive
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Function:WOMAC Function	12 wks	104/103	50.2(21.88)/44.6(22.38)	Mean Diff	5.6(-0.47,11.67)	Not Sig.	inconclusive
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Function:WOMAC Function	12 wks	98/103	51.5(22.93)/44.6(22.38)	Mean Diff	6.9(0.59,13.21)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bolten; 2015/Moderate	9: NSAIDs (oral/IM)-Diclofenac Sodium(50 mg three times daily)	9: Placebo/Control-Placebo(2 tablets three times daily)	Function:WOMAC Function	12 wks	46/52	53(.)/75(.)	median difference	-22	Group 1	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Function	4 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Function	1 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Function	3 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Function	5 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Function	2 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Function	6 mos	74/74	32.74(30.41)/32.74(30.56)	Mean Diff	0(-9.9,9.9)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Function:WOMAC Function	8 wks	43	none	Mean Diff	-5.9(-6.75,-5.05)	Group 1	possibly clinically significant
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Function:WOMAC Function	4 wks	43	none	Mean Diff	-7.56(-16.96,-1.83)	Group 1	possibly clinically significant
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Function:WOMAC Function	12 wks	43	none	Mean Diff	-8.2(-8.89,-7.51)	Group 1	clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	112 days	206/206	-2.3(2.73)/-1.84(2.73)	Mean Diff	-0.46(-0.99,0.07)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	112 days	207/209	-1.91(3.02)/-1.45(3.04)	Mean Diff	-0.46(-1.04,0.12)	Not Sig.	inconclusive
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	56 days	207/209	-2.2(1.47)/-1.58(1.48)	Mean Diff	-0.62(-0.9,-0.34)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	84 days	206/206	-2.6(1.1)/-1.95(1.1)	Mean Diff	-0.65(-0.86,-0.44)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	84 days	207/209	-2.18(1.47)/-1.45(1.48)	Mean Diff	-0.73(-1.01,-0.45)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	14 days	206/206	-2.65(1.1)/-1.9(1.1)	Mean Diff	-0.75(-0.96,-0.54)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	56 days	206/206	-2.7(1.46)/-1.95(1.1)	Mean Diff	-0.75(-1,-0.5)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	28 days	207/209	-2.35(1.47)/-1.6(1.48)	Mean Diff	-0.75(-1.03,-0.47)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	14 days	207/209	-2.36(1.47)/-1.53(1.48)	Mean Diff	-0.83(-1.11,-0.55)	Group 1	possibly clinically significant
Ekman; 2014/Moderate	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg 2x/day with placebo IV)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day with placebo IV)	Function:WOMAC Function (0-10)	28 days	206/206	-2.88(1.1)/-1.95(1.1)	Mean Diff	-0.93(-1.14,-0.72)	Group 1	possibly clinically significant
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Function:WOMAC Physical Function	6 wks	96/47	-16(13.72)/-11.1(13.03)	Mean Diff	-4.9(-9.59,-0.21)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ohtori; 2013/Moderate	9: NSAIDs (oral/IM)-Meloxicam + Pregabalin(10 mg Meloxicam after breakfast + 25 mg pregabalin before sleep)	9: Placebo/Control-Control (Pregabalin Alone)(25 mg before sleep)	Function:WOMAC Physical Function	4 wks	18.3/29.3	none	pvalue	Sig (p < 0.05)	Meloxicam + Pregabalin favored over Pregabal	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Function:WOMAC Physical Function	6 wks	125/65	-18.3(14.53)/-14.4(13.71)	Mean Diff	-3.9(-8.13,0.33)	Not Sig.	inconclusive
Dwicandra; 2018/Moderate	9: Other Systemic Tx-Diacerein and Meloxicam(50 mg diacerein and 15 mg meloxicam once daily)	9: Placebo/Control-Control (Meloxicam Alone)(15 mg once daily)	Function:WOMAC Physical Function	4 wks	30/32	17.07(8.18)/21.81(8.9)	Mean Diff	-4.74(-9.08,-0.4)	Group 1	possibly clinically significant
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Function:WOMAC Physical Function	12 wks	150/154	-18.7(14)/-15.8(15.1)	Mean Diff	-2.9(-6.19,0.39)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Function:WOMAC Physical Function	12 wks	151/153	-17.5(14.3)/-12.3(14.7)	Mean Diff	-5.2(-8.47,-1.93)	Group 1	possibly clinically significant
Bolten; 2015/Moderate	9: NSAIDs (oral/IM)-Diclofenac Sodium(50 mg three times daily)	9: Placebo/Control-Placebo(2 tablets three times daily)	Function:WOMAC Stiffness	12 wks	46/52	6(.)/8(.)	median difference	-2	Not Sig.	na
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	96/47	-1.9(1.96)/-1.6(1.37)	Mean Diff	-0.3(-0.86,0.26)	Not Sig.	inconclusive
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	4 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	5 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	2 mos	148	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	3 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	1 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 mos	74/74	3.85(4.58)/4.16(4.73)	Mean Diff	-0.31(-1.82,1.2)	Not Sig.	clinically insignificant
Ohtori; 2013/Moderate	9: NSAIDs (oral/IM)-Meloxicam + Pregabalin(10 mg Meloxicam after breakfast + 25 mg pregabalin before sleep)	9: Placebo/Control-Control (Pregabalin Alone)(25 mg before sleep)	Function:WOMAC Stiffness	4 wks	2.5/4.5	none	pvalue	Sig (p < 0.05)	Meloxicam + Pregabalin favored over Pregabal	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	125/65	-2(2.24)/-1.5(1.61)	Mean Diff	-0.5(-1.06,0.06)	Not Sig.	inconclusive
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Function:WOMAC Stiffness	4 wks	43	none	Mean Diff	-1.36(-1.16,-1.1)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Function:WOMAC Stiffness	8 wks	43	none	Mean Diff	-1.7(-1.98,-1.14)	Group 1	clinically significant
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Function:WOMAC Stiffness	12 wks	43	none	Mean Diff	-2.23(-2.44,-2.21)	Group 1	clinically significant
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Function:WOMAC Stiffness	12 wks	150/154	-2.3(2)/-1.93(2.01)	Mean Diff	-0.37(-0.82,0.08)	Not Sig.	inconclusive
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Function:WOMAC Stiffness	12 wks	151/153	-2.07(2.02)/-1.52(2.05)	Mean Diff	-0.55(-1.01,-0.09)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2011/High	9: NSAIDs (oral/IM)-Naproxcinod(350 mg bid)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day)	Function:WOMAC function	91 days	247/255	-23.8(24.83)/-14.9(24.91)	Mean Diff	-8.9(-13.26,-4.54)	Group 1	possibly clinically significant
Schnitzer; 2011/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500 mg 2x/day)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day)	Function:WOMAC function(0-100)	91 days	252/255	-26.2(24.92)/-14.9(24.91)	Mean Diff	-11.3(-15.65,-6.95)	Group 1	possibly clinically significant
Schnitzer; 2011/High	9: NSAIDs (oral/IM)-Naproxcinod(750 mg bid)	9: Placebo/Control-Placebo (Oral)(placebo 2x/day)	Function:WOMAC function(0-100)	91 days	242/255	-27.8(24.89)/-14.9(24.91)	Mean Diff	-12.9(-17.29,-8.51)	Group 1	clinically significant
Davies; 1999/High	9: NSAIDs (oral/IM)-Ibuprofen (Oral)(800mg ibuprofen 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Function:WOMAC function(0-100)	28 days	54/50	72.8(22.8)/68.9(26.1)	Mean Diff	3.9(-5.67,13.47)	Not Sig.	inconclusive
Svensson; 2006/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Function:WOMAC function(0-100)	42 days	278/72	-16.31(17.89)/-6.75(18.05)	Mean Diff	-9.56(-14.28,-4.84)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-Diclofenac (diclofenac + placebo electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in 50 feet walk time (sec)	4 wks	49/45	-3.52(3.22)/-2.7(3.49)	Mean Diff	-0.82(-2.2,0.56)	Not Sig.	na
Sandgee; 2002/High	9: NSAIDs (oral/IM)-Combined (diclofenac + electroacupuncture)	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	Function:change in 50 feet walk time (sec)	4 wks	46/46	-4.13(3.66)/-4.41(4.75)	Mean Diff	0.28(-1.48,2.04)	Not Sig.	na
Sandgee; 2002/High	8: Electrotherapeutic agents-Diclofenac (diclofenac + placebo electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in Lequesne's functional index	4 wks	49/45	-4.8(4.27)/-3.82(3.42)	Mean Diff	-0.98(-2.56,0.6)	Not Sig.	na
Sandgee; 2002/High	9: NSAIDs (oral/IM)-Combined (diclofenac + electroacupuncture)	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	Function:change in Lequesne's functional index	4 wks	46/46	-5.39(3.53)/-6.44(4)	Mean Diff	1.05(-0.51,2.61)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-Diclofenac (diclofenac + placebo electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in WOMAC disability	4 wks	49/45	-14.39(12.39)/-12.33(12.61)	Mean Diff	-2.06(-7.19,3.07)	Not Sig.	inconclusive
Sandgee; 2002/High	8: Electrotherapeutic agents-Diclofenac (diclofenac + placebo electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Function:change in WOMAC stiffness	4 wks	49/45	-1.55(1.89)/-1.47(2.08)	Mean Diff	-0.08(-0.9,0.74)	Not Sig.	inconclusive
Sandgee; 2002/High	9: NSAIDs (oral/IM)-Combined (diclofenac + electroacupuncture)	8: Placebo/Control-EA (placebo tablet + electroacupuncture)	Function:change in WOMAC stiffness	4 wks	46/46	-2.02(1.9)/-2.24(2.1)	Mean Diff	0.22(-0.61,1.05)	Not Sig.	inconclusive
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Function:womac (vas change from baseline)-Function (0-100 VAS change from baseline)	12 weeks	209/109	-20.09(22.55)/-13.56(21.2)	Mean Diff	-6.53(-11.57,-1.49)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac function	8 wks	82/83	25.88(15.5)/29.2(14.11)	Mean Diff	-3.32(-7.88,1.24)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac function	4 wks	82/83	28.4(13.25)/32.12(12.89)	Mean Diff	-3.72(-7.74,0.3)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac function	12 wks	82/83	24.24(14.75)/28.24(15.41)	Mean Diff	-4(-8.64,0.64)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac function	16 wks	82/83	22.12(14.84)/28.04(14.91)	Mean Diff	-5.92(-10.49,-1.35)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac function	24 wks	82/83	21.76(14.64)/28.2(15.68)	Mean Diff	-6.44(-11.1,-1.78)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac function	20 wks	82/83	21.04(14.39)/29(14.94)	Mean Diff	-7.96(-12.47,-3.45)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 750mg bid	9: Placebo/Control-placebo	Function:womac function	13 wks	229/221	-31.05(27.32)/-20(27.18)	Mean Diff	-11.05(-16.1,-6)	Group 1	possibly clinically significant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac function	13 weeks	216/211	-10.9(17.4)/-9.2(17.8)	Mean Diff	-1.7(-5.05,1.65)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac function	7 weeks	154/145	-14.1(16.2)/-11.2(16.8)	Mean Diff	-2.9(-6.66,0.86)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac function	13 weeks	217/211	-12.5(18.8)/-9.2(17.8)	Mean Diff	-3.3(-6.78,0.18)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac function	7 weeks	171/145	-16(19.1)/-11.2(16.8)	Mean Diff	-4.8(-8.77,-0.83)	Group 2	possibly clinically significant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid) 100 mg	9: Placebo/Control-placebo	Function:womac function improvement	6 wks	200/199	-15.1(13.8)/-8.1(12.7)	Mean Diff	-7(-9.61,-4.39)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid) 500mg bid	9: Placebo/Control-placebo	Function:womac function improvement	12 wks	226/226	-34.07(27.16)/-20(27.18)	Mean Diff	-14.07(-19.09,-9.05)	Group 1	clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 350mg bid	9: Placebo/Control-placebo	Function:womac function likert	13 wks	239/221	-30.19(27.97)/-20(27.18)	Mean Diff	-10.19(-15.24,-5.14)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac stiffness	4 wks	82/83	3.72(1.87)/4(1.79)	Mean Diff	-0.28(-0.84,0.28)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac stiffness	8 wks	82/83	3.2(1.81)/3.52(1.74)	Mean Diff	-0.32(-0.87,0.23)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac stiffness	12 wks	82/83	3(1.9)/3.4(1.96)	Mean Diff	-0.4(-0.99,0.19)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac stiffness	16 wks	82/83	2.72(1.91)/3.56(1.96)	Mean Diff	-0.84(-1.43,-0.25)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac stiffness	24 wks	82/83	2.68(1.87)/3.52(2.06)	Mean Diff	-0.84(-1.44,-0.24)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Function:womac stiffness	20 wks	82/83	2.56(1.83)/3.8(1.94)	Mean Diff	-1.24(-1.82,-0.66)	Group 1	possibly clinically significant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac stiffness	7 weeks	160/147	-21.7(24.1)/-16.4(21.7)	Mean Diff	-5.3(-10.44,-0.16)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac stiffness	13 weeks	219/218	-18.2(25.1)/-12.8(23.7)	Mean Diff	-5.4(-9.99,-0.81)	Group 1	some may benefit
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac stiffness	13 weeks	217/218	-19.4(25.8)/-12.8(23.7)	Mean Diff	-6.6(-11.27,-1.93)	Group 2	possibly clinically significant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Function:womac stiffness	7 weeks	173/147	-23.1(23.6)/-16.4(21.7)	Mean Diff	-6.7(-11.69,-1.71)	Group 2	possibly clinically significant
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Function:womac stiffness improvement	6 wks	205/204	-1.4(1.64)/-1.04(1.64)	Mean Diff	-0.36(-0.68,-0.04)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Function:womac stiffness improvement	12 wks	205/204	-1.54(1.75)/-1.12(1.72)	Mean Diff	-0.42(-0.76,-0.08)	Group 1	some may benefit
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid)	9: Placebo/Control-placebo	Function:womac stiffness improvement	6 wks	200/199	-1.9(1.8)/-0.9(1.7)	Mean Diff	-1(-1.34,-0.66)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Stiffness:womac (vas change from baseline) stiffness subscale (0-100 VAS change from baseline)	12 weeks	209/109	-22.92(24.35)/-16.26(22.91)	Mean Diff	-6.66(-12.11,-1.21)	Group 1	possibly clinically significant
Lee; 1985/Moderate	9: NSAIDs (oral/IM)-Diflunisal Low Dose(750 mg/day)	9: Placebo/Control-Placebo	Composite:Improved Patient Global Score	6 wks	88/70	59.09%/50%	RR	1.18(0.88,1.58)	Not Sig.	na
Lee; 1985/Moderate	9: NSAIDs (oral/IM)-Diflunisal High Dose(1000 mg/day)	9: Placebo/Control-Placebo	Composite:Improved Patient Global Score	6 wks	69/70	69.57%/50%	RR	1.39(1.05,1.84)	Group 1	na
Ishijima; 2014/High	9: NSAIDs (oral/IM)-NSAID [Oral](60mg; x3/day; x5 weeks)	9: Non-arthro Tx-Hyaluronic Acid [IA](2700 kDa (25mg); 1x/wk x5wks)	Composite:JKOM Total	5 wks	86/98	22(15.5)/21.5(14.6)	Mean Diff	0.5(-3.9,4.9)	Not Sig.	na
Bolten; 2015/Moderate	9: NSAIDs (oral/IM)-Diclofenac Sodium(50 mg three times daily)	9: Placebo/Control-Placebo(2 tablets three times daily)	Composite:Lequesne Functional Index Total Scores	12 wks	46/52	8.3(5.05)/9.8(4.49)	Mean Diff	-1.5(-3.43,0.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:Likert Pain/Function	84 days	198/203	-3.1(4.22)/-2(4.13)	Mean Diff	-1.1(-1.92,-0.28)	Group 1	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Composite:Patient global score improvement	6 wks	88/70	59.09%/50%	RR	1.18(0.88,1.58)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Composite:Patient global score improvement	6 wks	69/70	69.57%/50%	RR	1.39(1.05,1.84)	Group 2	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Composite:SF-36 General Health	12 wks	98/103	72.6(18.49)/66.9(18.49)	Mean Diff	5.7(0.55,10.85)	Group 2	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Composite:SF-36 General Health	12 wks	104/103	72.8(19.25)/66.9(18.49)	Mean Diff	5.9(0.73,11.07)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 1985/Moderate	9: NSAIDs (oral/IM)-Diflunisal High Dose(1000 mg/day)	9: Placebo/Control-Placebo	Composite:Unchanged or Worse Patient Global Score	6 wks	69/70	30.43%/48.57%	RR	0.63(0.41,0.96)	Group 2	na
Lee; 1985/Moderate	9: NSAIDs (oral/IM)-Diflunisal Low Dose(750 mg/day)	9: Placebo/Control-Placebo	Composite:Unchanged or Worse Patient Global Score	6 wks	88/70	39.77%/48.57%	RR	0.82(0.58,1.16)	Not Sig.	na
Bolten; 2015/Moderate	9: NSAIDs (oral/IM)-Diclofenac Sodium(50 mg three times daily)	9: Placebo/Control-Placebo(2 tablets three times daily)	Composite:WOMAC Total	12 wks	46/52	74(.)/101.5(.)	median difference	-27.5	Group 1	na
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	96/47	-23(18.62)/-16(17.82)	Mean Diff	-7(-13.39,-0.61)	Group 1	possibly clinically significant
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Composite:WOMAC Total	2 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Composite:WOMAC Total	5 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Composite:WOMAC Total	3 mos	148	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Composite:WOMAC Total	4 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Composite:WOMAC Total	1 mos	148	none	pvalue	NS	Not Sig.	na
Kongtharvonskul; 2016/High	9: Other Systemic Tx-Diacerein(50mg x1/day x6mo)	9: Placebo/Control-Placebo	Composite:WOMAC Total	6 mos	74/74	48.59(44.44)/48.69(44.7)	Mean Diff	-0.1(-14.58, 14.38)	Not Sig.	na
Ohtori; 2013/Moderate	9: NSAIDs (oral/IM)-Meloxicam + Pregabalin(10 mg Meloxicam after breakfast + 25 mg pregabalin before sleep)	9: Placebo/Control-Control (Pregabalin Alone)(25 mg before sleep)	Composite:WOMAC Total	4 wks	24.4/40.4	none	pvalue	Sig (p < 0.05)	Meloxicam + Pregabalin favored over Pregabal	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	125/65	-26(20.12)/-20.8(19.35)	Mean Diff	-5.2(-11.13, 0.73)	Not Sig.	inconclusive
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Composite:WOMAC Total	8 wks	43	none	Mean Diff	-11.79(-13.12,-10.45)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Composite:WOMAC Total	12 wks	43	none	Mean Diff	-15.79(-16.89,-14.68)	Group 1	clinically significant
Selvan; 2012/Moderate	9: Other Systemic Tx-Glucosamine Sulfate with NSAID (Ibuprofen or Piroxicam)(500 mg three times daily)	3: Oral Supplement-Glucosamine Sulfate(500 mg three times daily)	Composite:WOMAC Total	4 wks	43	none	Mean Diff	-8.45(-9.99,-6.91)	Group 1	possibly clinically significant
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	30/30	32.4(3.05)/47.66(3.29)	Mean Diff	-15.26(-16.9,-13.62)	Group 1	clinically significant
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Composite:WOMAC Total	3 mos	30/30	15.9(2.44)/36.8(2.92)	Mean Diff	-20.9(-22.29,-19.51)	Group 1	clinically significant
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Composite:WOMAC Total	4 mos	30/30	16(2.56)/48.26(3.5)	Mean Diff	-32.26(-33.85,-30.67)	Group 1	clinically significant
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:WOMAC Total	84 days	198/203	-11.9(18.15)/-6.1(15.53)	Mean Diff	-5.8(-9.12,-2.48)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg three times daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total (VAS Version)	84 days	98/103	-35.9(27.72)/-23.2(27)	Mean Diff	-12.7(-20.32,-5.08)	Group 1	possibly clinically significant
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Diclofenac (Oral)(submicron; 35mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total (VAS Version)	84 days	104/103	-30.3(26.82)/-23.2(27)	Mean Diff	-7.1(-14.48, 0.28)	Not Sig.	inconclusive
Davies; 1999/High	9: NSAIDs (oral/IM)-Ibuprofen (Oral)(800mg ibuprofen 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC composite(0-100)	28 days	54/50	73.1(22.4)/67(26.7)	Mean Diff	6.1(-3.53,15.73)	Not Sig.	inconclusive
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in WOMAC composite(0-96)	12 weeks	198/203	-11.9(18.15)/-6.1(15.53)	Mean Diff	-5.8(-9.12,-2.48)	Group 1	possibly clinically significant
Sandgee; 2002/High	9: NSAIDs (oral/IM)-Combined (diclofenac + electroacupuncture)	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	Composite:change in WOMAC total	4 wks	46/46	-27.28(18.92)/-27.07(18.85)	Mean Diff	-0.21(-8.03,7.61)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-Diclofenac (diclofenac + placebo electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Composite:change in WOMAC total	4 wks	49/45	-20.84(17.01)/-17.11(18.31)	Mean Diff	-3.73(-10.99, 3.53)	Not Sig.	inconclusive
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in likert Pain/Function(0-24)	12 weeks	198/203	-3.1(4.22)/-2(4.13)	Mean Diff	-1.1(-1.92,-0.28)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 375mg (Cox 2) 375mg times per day	9: Placebo/Control-placebo	Composite:patient overall rating of disease status improvement (lower=better)	13 wks	240/221	-1.16(1.05)/-0.72(1.06)	Mean Diff	-0.44(-0.63,-0.25)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 750mg (Cox 2) 750mg times per day	9: Placebo/Control-placebo	Composite:patient overall rating of disease status improvement (lower=better)	13 wks	229/221	-1.23(1.06)/-0.72(1.06)	Mean Diff	-0.51(-0.71,-0.31)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Composite:patient overall rating of disease status improvement (lower=better)	13 wks	225/221	-1.39(12.77)/-0.72(1.06)	Mean Diff	-0.67(-2.35,1.01)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Composite:sf-36 mcs improvement	12 wks	142/185	2.58(8.38)/1.99(8.39)	Mean Diff	0.59(-1.25,2.43)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(750 mg bid)	9: Placebo/Control-placebo	Composite:sf-36 mcs improvement	13 wks	184/142	2.78(8.38)/1.99(8.39)	Mean Diff	0.79(-1.05,2.63)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 750mg	9: Placebo/Control-placebo	Composite:sf-36 mcs improvement	13 wks	142/184	2.78(8.38)/1.99(8.39)	Mean Diff	0.79(-1.05,2.63)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(375 mg bic)	9: Placebo/Control-placebo	Composite:sf-36 mcs improvement	13 wks	195/142	2.92(8.38)/1.99(8.39)	Mean Diff	0.93(-0.89,2.75)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 375 mg	9: Placebo/Control-placebo	Composite:sf-36 mcs improvement	13 wks	142/195	2.92(8.38)/1.99(8.39)	Mean Diff	0.93(-0.89,2.75)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Composite:womac (vas change from baseline) total	12 weeks	209/109	-22.74(22.26)/-15.53(20.94)	Mean Diff	-7.21(-12.19,-2.23)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Composite:womac total	20 wks	82/83	29.32(19.94)/40.44(20.55)	Mean Diff	-11.12(-17.34,-4.9)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Composite:womac total	4 wks	82/83	40.6(18.16)/44.48(17.51)	Mean Diff	-3.88(-9.37,1.61)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Composite:womac total	8 wks	82/83	36.08(21.13)/40.52(19.18)	Mean Diff	-4.44(-10.65, 1.77)	Not Sig.	inconclusive
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Composite:womac total	12 wks	82/83	33.36(20.3)/39.28(21.2)	Mean Diff	-5.92(-12.3,0.46)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Composite:womac total	16 wks	82/83	30.72(20.44)/39.12(20.63)	Mean Diff	-8.4(-14.71,-2.09)	Group 1	possibly clinically significant
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Composite:womac total	24 wks	82/83	30.36(20.45)/39.4(21.87)	Mean Diff	-9.04(-15.55,-2.53)	Group 1	possibly clinically significant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Composite:womac total	13 weeks	220/215	-12.2(16.8)/-9.8(17.2)	Mean Diff	-2.4(-5.6,0.8)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Composite:womac total	7 weeks	160/147	-15(16)/-12.5(15.8)	Mean Diff	-2.5(-6.07,1.07)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Composite:womac total	13 weeks	218/215	-13.7(18.7)/-9.8(17.2)	Mean Diff	-3.9(-7.29,-0.51)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Composite:womac total	7 weeks	173/147	-17(18.6)/-12.5(15.8)	Mean Diff	-4.5(-8.28,-0.72)	Group 2	possibly clinically significant
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Composite:womac total improvement	6 wks	205/204	-16.99(18.11)/-12.98(18.04)	Mean Diff	-4.01(-7.52,-0.5)	Group 1	some may benefit
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Composite:womac total improvement	12 wks	205/204	-18.04(18.95)/-13.48(18.92)	Mean Diff	-4.56(-8.24,-0.88)	Group 1	possibly clinically significant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid)	9: Placebo/Control-placebo	Composite:womac total improvement	6 wks	200/199	-21.4(18.9)/-11.5(17.8)	Mean Diff	-9.9(-13.51,-6.29)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Composite:womac total improvement	12 wks	187/145	-39.9(24.6)/-28.03(24.61)	Mean Diff	-11.87(-17.22,-6.51)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(375 mg bic)	9: Placebo/Control-placebo	Composite:womac total likert	13 wks	198/145	-35.06(24.62)/-28.03(24.61)	Mean Diff	-7.03(-12.32,-1.73)	Group 1	possibly clinically significant
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(750 mg bid)	9: Placebo/Control-placebo	Composite:womac total likert	13 wks	188/145	-36.81(24.61)/-28.03(24.61)	Mean Diff	-8.78(-14.13,-3.42)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Fair Global Efficacy Judgement by Patient	4 mos	30/30	3.33%/20%	RR	0.17(0.02,1.3)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Fair Global Efficacy Judgement by Patient	3 mos	30/30	6.67%/26.67%	RR	0.25(0.06,1.08)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Fair Global Efficacy Judgement by Patient	6 wks	30/30	36.67%/23.33%	RR	1.57(0.71,3.5)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Good Global Efficacy Judgement by Patient	3 mos	30/30	6.67%/23.33%	RR	0.29(0.06,1.26)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Good Global Efficacy Judgement by Patient	6 wks	30/30	6.67%/13.33%	RR	0.5(0.1,2.53)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Good Global Efficacy Judgement by Patient	4 mos	30/30	53.33%/23.33%	RR	2.29(1.1,4.74)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	QOL:Patient Global Response: Good/Excellent	6 wks	618	none	Odds Ratio	2.43(1.68,3.51)	Group 1	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Poor Global Efficacy Judgement by Patient	6 wks	30/30	0%/6.67%	RD	-6.667(-18.999,7.99)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Poor Global Efficacy Judgement by Patient	4 mos	30/30	20%/16.67%	RR	1.2(0.41,3.51)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Mental Health	12 wks	104/103	78.5(16.84)/76(16.62)	Mean Diff	2.5(-2.09,7.09)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Mental Health	12 wks	98/103	78.5(17.4)/76(16.62)	Mean Diff	2.5(-2.24,7.24)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Role Emotion	12 wks	104/103	75(24.94)/72.3(22.44)	Mean Diff	2.7(-3.8,9.2)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Role Emotion	12 wks	98/103	76.7(25.5)/72.3(22.44)	Mean Diff	4.4(-2.3,11.1)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Social Functioning	12 wks	104/103	76.1(21.77)/73.6(23.22)	Mean Diff	2.5(-3.67,8.67)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Social Functioning	12 wks	98/103	80.7(22.65)/73.6(23.22)	Mean Diff	7.1(0.72,13.48)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Vitality	12 wks	104/103	55.5(18.01)/51.3(17.25)	Mean Diff	4.2(-0.63,9.03)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	QOL:SF-36 Vitality	12 wks	98/103	59.3(18)/51.3(17.25)	Mean Diff	8(3.09, 12.91)	Group 2	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Very Good Global Efficacy Judgement by Patient	4 mos	30/30	13.33%/16.67%	RR	0.8(0.24,2.69)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Very Good Global Efficacy Judgement by Patient	3 mos	30/30	30%/30%	RR	1(0.46, 2.17)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Very Good Global Efficacy Judgement by Patient	6 wks	30/30	43.33%/16.67%	RR	2.6(1.06,6.39)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Very Poor Global Efficacy Judgement by Patient	4 mos	30/30	3.33%/10%	RR	0.33(0.04,3.03)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Very Poor Global Efficacy Judgement by Patient	6 wks	30/30	30%/50%	RR	0.6(0.31,1.15)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	QOL:Very Poor Global Efficacy Judgement by Patient	3 mos	30/30	6.67%/10%	RR	0.67(0.12,3.71)	Not Sig.	na
Schnitzer ; 1999/Moderate	9: NSAIDs (oral/IM)-tramadol 200mg/day	9: Placebo/Control-placebo	Other:Minimum Effective Naproxen Dose (among non responders)	8 wks		none	pvalue	NS	tramadol 200mg/day se (amongivnsmd cvr Place	na
Schnitzer ; 1999/Moderate	9: NSAIDs (oral/IM)-tramadol 200mg/day	9: Placebo/Control-placebo	Other:Minimum Effective Naproxen Dose (among responders)	8 wks		none	pvalue	Sig (p<0.05)	tramadol 200mg/day se (amongivnsmd cvr Place	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Other:PGADS (0-100 VAS change from baseline)	12 weeks	211/107	-25.97(25.24)/-17.85(23.79)	Mean Diff	-8.12(-13.8,-2.44)	Group 2	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Other:PGART (0-4 Likert scale change from baseline)	12 weeks	210/108	1.72(1.1)/2.29(1.05)	Mean Diff	-0.57(-0.82,-0.32)	Group 2	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	7 weeks	161/149	59.63%/54.36%	RR	1.1(0.9,1.33)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	13 weeks	220/220	54.09%/45.45%	RR	1.19(0.98,1.44)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	7 weeks	178/149	66.85%/54.36%	RR	1.23(1.03,1.47)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	13 weeks	221/220	60.18%/45.45%	RR	1.32(1.11,1.59)	Group 2	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Other:Patients with sleep loss	4 wks	92/94	30.43%/31.91%	RR	0.95(0.62,1.46)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Other:Patients with sleep loss	4 wks	93/94	37.63%/31.91%	RR	1.18(0.79,1.75)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Other:Sleep loss with joint pain as a contributing factor	4 wks	92/94	52.17%/68.09%	RR	0.77(0.6,0.97)	Group 1	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Other:Sleep loss with joint pain as a contributing factor	4 wks	93/94	67.74%/68.09%	RR	0.99(0.82,1.21)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sandgee; 2002/High	8: Electrotherapeutic agents-Diclofenac (diclofenac + placebo electroacupuncture)	8: Placebo/Control-placebo (placebo tablet + placebo electroacupuncture)	Other:change in number of paracetamol take (tablets/wk)	4 wks	49/45	-4.43(13.3)/-5.16(15.63)	Mean Diff	0.73(-5.25,6.71)	Not Sig.	na
Sandgee; 2002/High	9: NSAIDs (oral/IM)-Combined (diclofenac + electroacupuncture)	8: Electrotherapeutic agents-EA (placebo tablet + electroacupuncture)	Other:change in number of paracetamol take (tablets/wk)	4 wks	46/46	-5.13(13.97)/-7.89(14.18)	Mean Diff	2.76(-3.07,8.59)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen (Oral)(500mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Other:improved global assessment	12 weeks	198/203	14.65%/11.82%	pvalue	1.24(.75, 2.051)	Not Sig.	na
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Other:paracetamol intake pills per day	8 wks	82/83	1.3(1.01)/1.4(1.41)	Mean Diff	-0.1(-0.48,0.28)	Not Sig.	na
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Other:paracetamol intake pills per day	12 wks	82/83	1.3(1.18)/1.4(1.36)	Mean Diff	-0.1(-0.49,0.29)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Other:paracetamol intake pills per day	4 wks	82/83	1.3(1.2)/1.5(1.5)	Mean Diff	-0.2(-0.62,0.22)	Not Sig.	na
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Other:paracetamol intake pills per day	16 wks	82/83	1.1(1.23)/1.5(1.32)	Mean Diff	-0.4(-0.79,-0.01)	Group 1	na
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Other:paracetamol intake pills per day	24 wks	82/83	1(1.07)/1.5(1.35)	Mean Diff	-0.5(-0.87,-0.13)	Group 1	na
Pavelka; 2007/Moderate	9: NSAIDs (oral/IM)-diacerein (interleukin) 50mg 2 times per day	9: Placebo/Control-placebo	Other:paracetamol intake pills per day	20 wks	82/83	1(1.11)/1.5(1.34)	Mean Diff	-0.5(-0.88,-0.12)	Group 1	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid)	9: Placebo/Control-placebo	Other:patient global assessment of improvement	6 wks	199/200	1.5(1.1)/0.9(1.2)	Mean Diff	0.6(0.37,0.83)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Other:patient global assessment of overall health	12 wks	150/152	-0.88(1.31)/-0.37(1.04)	Mean Diff	-0.51(-0.78,-0.24)	Group 1	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Other:patient global assessment of overall health	12 wks	148/154	-0.95(1.21)/-0.95(1.3)	Mean Diff	0(-0.28,0.28)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-placebo	Other:patient global assessment of response to therapy	6 weeks	105/104	40.95%/31.73%	RR	1.29(0.9,1.86)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-placebo	Other:patient global assessment of response to therapy	6 weeks	107/104	55.14%/31.73%	RR	1.74(1.25,2.42)	Group 1	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-placebo	Other:patient global assessment of response to therapy	6 weeks	114/104	62.28%/31.73%	RR	1.96(1.43,2.69)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-placebo	Other:patient global assessment of response to therapy	6 weeks	117/104	65.81%/31.73%	RR	2.07(1.52,2.83)	Group 1	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Other:patient global assessment of study knee	12 wks	150/154	-1.53(1.27)/-1.36(1.19)	Mean Diff	-0.17(-0.45,0.11)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Other:patient global assessment of study knee	12 wks	151/153	-1.42(1.29)/-1.01(1.18)	Mean Diff	-0.41(-0.69,-0.13)	Group 1	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-diclofenac (nsaid)	9: Placebo/Control-placebo	Other:phyician global assessment of improvement	6 wks	199/200	1.5(1.04)/0.9(1.1)	Mean Diff	0.6(0.39,0.81)	Group 2	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	12 wks	204/205	-1.43(1.06)/-1.22(1.02)	Mean Diff	-0.21(-0.41,-0.01)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-naproxen (nsaid)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	6 wks	204/205	-1.45(0.98)/-1.22(0.99)	Mean Diff	-0.23(-0.42,-0.04)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 750 mg	9: Placebo/Control-placebo	Other:rescue acetaminophen	13 wks	210/222	1.43(1.58)/1.77(1.57)	Mean Diff	-0.34(-0.64,-0.04)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(750 mg bid)	9: Placebo/Control-placebo	Other:rescue acetaminophen	13 wks	222/210	1.43(1.58)/1.77(1.57)	Mean Diff	-0.34(-0.64,-0.04)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxen (nsaid)(500mg bid)	9: Placebo/Control-placebo	Other:rescue acetaminophen	12 wks	210/219	1.34(1.57)/1.77(1.57)	Mean Diff	-0.43(-0.73,-0.13)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod(375 mg bic)	9: Placebo/Control-placebo	Other:rescue acetaminophen	13 wks	232/210	1.33(1.57)/1.77(1.57)	Mean Diff	-0.44(-0.73,-0.15)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-naproxcinod 375 mg	9: Placebo/Control-placebo	Other:rescue acetaminophen	13 wks	210/232	1.33(1.57)/1.77(1.57)	Mean Diff	-0.44(-0.73,-0.15)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400mg	9: Placebo/Control-placebo	Other:womac (vas change from baseline) questionnaire overall score average (0-100 VAS change from baseline)	12 weeks	209/109	-21.73(22.15)/-14.43(20.83)	Mean Diff	-7.3(-12.26,-2.34)	Group 1	possibly clinically significant
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:AE's leading to discontinuation	12 wks	104/103	8.65%/3.88%	RR	2.23(0.71,7.01)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:AE's leading to discontinuation	12 wks	98/103	12.24%/3.88%	RR	3.15(1.05,9.45)	Group 2	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:ALT Elevation	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:ALT Elevation	12 wks	98/103	3.06%/0%	RD	3.061(-2.495, 7.183)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:ALT Elevation	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:ALT Elevation	12 wks	98/103	3.06%/0%	RD	3.061(-2.495, 7.183)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:ALT Elevation (Serious Aes)	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:ALT Elevation (Serious Aes)	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:ALT Increased	6 wks	199/200	2.51%/2.5%	RR	1.01(0.3,3.42)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:AST Elevation	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:AST Elevation	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Distension	6 wks	111/107	0%/0%	RD	0(-3.345, 3.466)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal Distension	6 wks	121/107	3.31%/0%	RD	3.306(-1.581, 7.314)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Distension	6 wks	118/107	3.39%/0%	RD	3.39(-1.613, 7.424)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Distension	6 wks	111/107	4.5%/0%	RD	4.505(-1.104, 8.816)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	156/79	5.13%/1.27%	RR	4.05(0.52,31.82)	Not Sig.	na
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	129/61	3.1%/0%	RD	3.101(-1.5,9.319)	Not Sig.	na
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	141/76	10.64%/3.95%	RR	2.7(0.81,9.02)	Not Sig.	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	125/66	2.4%/4.55%	RR	0.53(0.11,2.54)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	4 mos	30/30	20%/16.67%	RR	1.2(0.41,3.51)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	4 wks	93/94	2.15%/9.57%	RR	0.22(0.05,1.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	4 wks	92/94	9.78%/9.57%	RR	1.02(0.42,2.46)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	12 wks	198/203	3.03%/1.97%	RR	1.54(0.44,5.37)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	199/200	7.04%/7%	RR	1.01(0.49,2.05)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	13 wks	240/222	0%/0%	RD	0(-1.575, 1.701)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	13 wks	225/222	1.78%/0%	RD	1.778(-0.926, 3.795)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	13 wks	229/222	2.18%/0%	RD	2.183(-0.642, 4.293)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >1%	12 wks	183/178	3.28%/2.25%	RR	1.46(0.42,5.08)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >5%	12 wks	183/178	12.57%/9.55%	RR	1.32(0.73,2.38)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Abdominal distension	6 weeks	111/107	0%/0%	RD	0(-3.345, 3.466)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Abdominal distension	6 weeks	121/107	3.31%/0%	RD	3.306(-1.581, 7.314)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Abdominal distension	6 weeks	118/107	3.39%/0%	RD	3.39(-1.613, 7.424)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Abdominal distension	6 weeks	111/107	4.5%/0%	RD	4.505(-1.104, 8.816)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal pain	4 wks	93/94	2.15%/9.57%	RR	0.22(0.05,1.01)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal pain	4 wks	92/94	9.78%/9.57%	RR	1.02(0.42,2.46)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Abdominal pain	12 wks	152/154	1.97%/3.25%	RR	0.61(0.15,2.5)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abdominal pain	12 wks	151/157	7.28%/0.64%	RR	11.44(1.49,87.51)	Group 2	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Abnormal Hepatic Function >1%	12 wks	183/178	0%/0%	RD	0(-2.056, 2.113)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abnormal taste sensation or odor	12 wks	151/157	0%/0.64%	RD	-0.637(-3.173, 2.245)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Abnormal taste sensation or odor	12 wks	152/154	0.66%/0%	RD	0.658(-2.316, 3.151)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Abnormal vision	12 wks	152/154	0.66%/2.6%	RR	0.25(0.03,2.24)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Abnormal vision	12 wks	151/157	2.65%/3.18%	RR	0.83(0.23,3.04)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Accidental Injury >1%	12 wks	183/178	0.55%/1.12%	RR	0.49(0.04,5.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Accidental injury	12 wks	151/157	2.65%/3.82%	RR	0.69(0.2,2.41)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Accidental injury	12 wks	152/154	3.95%/2.6%	RR	1.52(0.44,5.28)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Accidential Injury >5%	12 wks	183/178	4.37%/5.62%	RR	0.78(0.31,1.93)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Acid Reflux	6 wks	410/208	0.24%/0.96%	RR	0.25(0.02,2.78)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Adverse Events - Body as a whole	4 wks	93/94	11.83%/22.34%	RR	0.53(0.27,1.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Adverse Events - Body as a whole	4 wks	92/94	15.22%/22.34%	RR	0.68(0.37,1.26)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase Elevation (Serious AE's)	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase Elevation (Serious AE's)	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase of Potential Concern	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase of Potential Concern	12 wks	98/103	4.08%/0%	RD	4.082(-1.866, 8.451)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Alkaline Phosphatase of Potential Concern	12 wks	104/103	0.96%/0.97%	RR	0.99(0.06,15.62)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Alkaline Phosphatase of Potential Concern	12 wks	98/103	1.02%/0.97%	RR	1.05(0.07,16.57)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Anaemia	6 wks	199/200	3.52%/3.5%	RR	1.01(0.36,2.81)	Not Sig.	na
Paul; 2009/Moderate	9: NSAIDs (oral/IM)-Nabumetone(750 mg twice per day)	9: Placebo/Control-Placebo	Adverse events:Ankle Edema	4 wks	118/89	1.69%/0%	RD	1.695(-2.58,6.011)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Paul; 2009/Moderate	9: NSAIDs (oral/IM)-Aceclofenac(100 mg twice per day)	9: Placebo/Control-Placebo	Adverse events:Ankle Edema	4 wks	108/89	2.78%/0%	RD	2.778(-2.295, 7.302)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Any AE	12 weeks	213/111	57.75%/51.35%	RR	1.12(0.91,1.39)	Not Sig.	na
Ishijima; 2014/High	9: NSAIDs (oral/IM)-NSAID [Oral](60mg; x3/day; x5 weeks)	9: Non-arthro Tx-Hyaluronic Acid [IA](2700 kDa (25mg); 1x/wk x5wks)	Adverse events:Any Adverse Event	5 wks	83/99	12.05%/1.01%	RR	11.93(1.56,91.26)	Group 2	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	12 wks	213/111	57.75%/51.35%	RR	1.12(0.91,1.39)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Any Adverse Events	13 wks	240/222	40.83%/38.74%	RR	1.05(0.84,1.32)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Any Adverse Events	13 wks	229/222	47.16%/38.74%	RR	1.22(0.98,1.51)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Events	13 wks	225/222	56.44%/38.74%	RR	1.46(1.19,1.78)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Any Drug-Related Adverse Events	12 wks	213/111	33.33%/21.62%	RR	1.54(1.03,2.3)	Group 2	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Any Serious Adverse Events	12 wks	213/111	2.35%/0.9%	RR	2.61(0.31,22.03)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Any Study Event	4 wks	93/94	35.48%/37.23%	RR	0.95(0.65,1.39)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Any Study Event	4 wks	92/94	39.13%/37.23%	RR	1.05(0.73,1.52)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Any adverse event	12 wks	152/154	64.47%/62.34%	RR	1.03(0.87,1.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any adverse event	12 wks	151/157	62.25%/57.32%	RR	1.09(0.9,1.3)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Any adverse events	4 wks	93/94	35.48%/37.23%	RR	0.95(0.65,1.39)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Any adverse events	4 wks	92/94	39.13%/37.23%	RR	1.05(0.73,1.52)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any digestive system event	12 wks	151/157	23.84%/9.55%	RR	2.5(1.43,4.37)	Group 2	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Any digestive system event	12 wks	152/154	25.66%/6.49%	RR	3.95(2.05,7.63)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Any drug-related AE	12 weeks	213/111	33.33%/21.62%	RR	1.54(1.03,2.3)	Group 2	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Any serious AE	12 weeks	213/111	2.35%/0.9%	RR	2.61(0.31,22.03)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Any skin/appendages event	12 wks	151/157	7.28%/7.64%	RR	0.95(0.43,2.09)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Any skin/appendages event	12 wks	152/154	30.92%/26.62%	RR	1.16(0.82,1.65)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Appendicitis	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Appendicitis	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Appendicitis	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Appendicitis	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Arthralgia	12 wks	152/154	4.61%/9.09%	RR	0.51(0.21,1.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Arthralgia	12 wks	151/157	7.95%/9.55%	RR	0.83(0.4,1.72)	Not Sig.	na
Lohmander; 2005/Moderate	9: NSAIDs (oral/IM)-Naproxcinod(750 mg)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	437/116	5.49%/11.21%	RR	0.49(0.26,0.93)	Group 1	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	13 wks	225/222	1.33%/0.45%	RR	2.96(0.31,28.24)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Arthralgia	13 wks	229/222	2.18%/0.45%	RR	4.85(0.57,41.16)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Arthralgia	13 wks	240/222	3.33%/0.45%	RR	7.4(0.93,58.69)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Arthralgia	6 weeks	111/107	7.21%/13.08%	RR	0.55(0.24,1.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	111/107	7.21%/13.08%	RR	0.55(0.24,1.26)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Arthralgia	6 weeks	121/107	9.09%/13.08%	RR	0.69(0.33,1.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	121/107	9.09%/13.08%	RR	0.69(0.33,1.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	111/107	10.81%/13.08%	RR	0.83(0.4,1.7)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Arthralgia	6 weeks	111/107	10.81%/13.08%	RR	0.83(0.4,1.7)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Arthralgia	6 weeks	118/107	13.56%/13.08%	RR	1.04(0.53,2.02)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	118/107	13.56%/13.08%	RR	1.04(0.53,2.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Aspartate Aminotransferase Elevation (Serious AEs)	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Aspartate Aminotransferase Elevation (Serious AEs)	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Aspartate Aminotransferase of Potential Concern	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Aspartate Aminotransferase of Potential Concern	12 wks	98/103	2.04%/0%	RD	2.041(-3.057, 5.929)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	199/200	0.5%/0.5%	RR	1.01(0.06,15.96)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	121/107	4.13%/10.28%	RR	0.4(0.14,1.12)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	111/107	11.71%/10.28%	RR	1.14(0.53,2.43)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	111/107	11.71%/10.28%	RR	1.14(0.53,2.43)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	118/107	11.86%/10.28%	RR	1.15(0.55,2.43)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Back pain	12 wks	152/154	2.63%/9.74%	RR	0.27(0.09,0.8)	Group 1	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Back pain	12 wks	151/157	7.28%/6.37%	RR	1.14(0.5,2.61)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Back pain	6 weeks	121/107	4.13%/10.28%	RR	0.4(0.14,1.12)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Back pain	6 weeks	111/107	11.71%/10.28%	RR	1.14(0.53,2.43)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Back pain	6 weeks	111/107	11.71%/10.28%	RR	1.14(0.53,2.43)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Back pain	6 weeks	118/107	11.86%/10.28%	RR	1.15(0.55,2.43)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Blood Urea Nitrogen of Potential Concern	12 wks	104/103	16.35%/9.71%	RR	1.68(0.81,3.5)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Blood Urea Nitrogen of Potential Concern	12 wks	98/103	32.65%/9.71%	RR	3.36(1.75,6.47)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Blurred Vision >1%	12 wks	183/178	0%/1.12%	RD	-1.124(-3.335, 1.756)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Body as a whole adverse events	4 wks	93/94	11.83%/22.34%	RR	0.53(0.27,1.04)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Body as a whole adverse events	4 wks	92/94	15.22%/22.34%	RR	0.68(0.37,1.26)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Bowl Motility Disorder	4 mos	30/30	13.33%/10%	RR	1.33(0.33,5.45)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Bronchitis	13 wks	225/222	1.33%/0.9%	RR	1.48(0.25,8.77)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Bronchitis	13 wks	240/222	2.08%/0.9%	RR	2.31(0.45,11.8)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Bronchitis	13 wks	229/222	2.18%/0.9%	RR	2.42(0.48,12.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:CHF; pulmonary edema or cardiac failure	12 weeks	213/111	0.47%/0%	RD	0.469(-1.672, 3.837)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:CHF; pulmonary edema; or cardiac failure	12 wks	213/111	0.47%/0%	RD	0.469(-1.672, 3.837)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:COPD	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:COPD	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:COPD	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:COPD	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Central nervous system adverse events	6 wks	88/70	13.64%/24.29%	RR	0.56(0.29,1.1)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Central nervous system adverse events	6 wks	69/70	23.19%/24.29%	RR	0.95(0.53,1.73)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Conjunctivitis	12 wks	152/154	0%/2.6%	RD	-2.597(-5.527, 1.293)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Conjunctivitis	12 wks	151/157	1.99%/0.64%	RR	3.12(0.33,29.66)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Constipation	12 wks	104/103	2.88%/3.88%	RR	0.74(0.17,3.24)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Constipation	12 wks	98/103	4.08%/3.88%	RR	1.05(0.27,4.09)	Not Sig.	na
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	141/76	2.13%/0%	RD	2.128(-1.813, 7.139)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Constipation	12 wks	104/103	2.88%/3.88%	RR	0.74(0.17,3.24)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Constipation	12 wks	98/103	4.08%/3.88%	RR	1.05(0.27,4.09)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Constipation	4 mos	30/30	3.33%/3.33%	RR	1(0.07, 15.26)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	4 wks	93/94	0%/2.13%	RD	-2.128(-6.384, 3.174)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	4 wks	93/94	0%/2.13%	RD	-2.128(-6.384, 3.174)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	4 wks	92/94	3.26%/2.13%	RR	1.53(0.26,8.96)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	4 wks	92/94	3.26%/2.13%	RR	1.53(0.26,8.96)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	199/200	4.02%/4%	RR	1.01(0.38,2.63)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	13 wks	225/222	4.89%/0.45%	RR	10.85(1.41,83.36)	Group 2	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Constipation	13 wks	229/222	1.75%/0.45%	RR	3.88(0.44,34.42)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Constipation	13 wks	240/222	2.08%/0.45%	RR	4.63(0.54,39.28)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Constipation	6 weeks	111/107	2.7%/1.87%	RR	1.45(0.25,8.48)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	111/107	2.7%/1.87%	RR	1.45(0.25,8.48)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Constipation	6 weeks	121/107	3.31%/1.87%	RR	1.77(0.33,9.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	121/107	3.31%/1.87%	RR	1.77(0.33,9.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Constipation	6 weeks	118/107	4.24%/1.87%	RR	2.27(0.45,11.44)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	118/107	4.24%/1.87%	RR	2.27(0.45,11.44)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	111/107	5.41%/1.87%	RR	2.89(0.6,14.01)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Constipation	6 weeks	111/107	5.41%/1.87%	RR	2.89(0.6,14.01)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Constipation >5%	12 wks	183/178	6.01%/2.81%	RR	2.14(0.76,6.03)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Contact dermatitis (application site)	12 wks	151/157	0.66%/0.64%	RR	1.04(0.07,16.47)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Contact dermatitis (application site)	12 wks	152/154	7.89%/2.6%	RR	3.04(1,9.22)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Contact dermatitis with vesicles (application	12 wks	151/157	0.66%/0%	RD	0.662(-2.331, 3.112)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Contact dermatitis with vesicles (application	12 wks	152/154	3.95%/1.95%	RR	2.03(0.52,7.96)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Contusion	13 wks	229/222	0.44%/0.9%	RR	0.48(0.04,5.31)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Contusion	13 wks	240/222	2.08%/0.9%	RR	2.31(0.45,11.8)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Contusion	13 wks	225/222	2.22%/0.9%	RR	2.47(0.48,12.58)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Cough	13 wks	240/222	0.83%/1.35%	RR	0.62(0.1,3.66)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Cough	13 wks	229/222	0.87%/1.35%	RR	0.65(0.11,3.83)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Cough	13 wks	225/222	2.22%/1.35%	RR	1.64(0.4,6.8)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Creatinine of Potential Concern	12 wks	104/103	0.96%/0.97%	RR	0.99(0.06,15.62)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Creatinine of Potential Concern	12 wks	98/103	1.02%/0.97%	RR	1.05(0.07,16.57)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:DVT	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:DVT	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Deep Vein Thrombosis	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Deep Vein Thrombosis	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Adverse events:Depression	6 wks	129/61	3.1%/4.92%	RR	0.63(0.15,2.73)	Not Sig.	na
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Adverse events:Depression	6 wks	141/76	1.42%/2.63%	RR	0.54(0.08,3.75)	Not Sig.	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Depression	6 wks	125/66	3.2%/4.55%	RR	0.7(0.16,3.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	104/103	4.81%/2.91%	RR	1.65(0.4,6.73)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	98/103	7.14%/2.91%	RR	2.45(0.65,9.22)	Not Sig.	na
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	141/76	2.13%/0%	RD	2.128(-1.813, 7.139)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	104/103	4.81%/2.91%	RR	1.65(0.4,6.73)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	98/103	7.14%/2.91%	RR	2.45(0.65,9.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	125/66	1.6%/1.52%	RR	1.06(0.1,11.43)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	4 mos	30/30	36.67%/13.33%	RR	2.75(0.99,7.68)	Not Sig.	na
Pavelka; 2007/Moderate	9: Other Systemic Tx-Diacerein(50 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 mos	82/83	15.85%/8.43%	RR	1.88(0.79,4.47)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	410/208	3.41%/21.15%	RR	0.16(0.09,0.29)	Group 1	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	4 wks	92/94	5.43%/7.45%	RR	0.73(0.24,2.22)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	4 wks	92/94	5.43%/7.45%	RR	0.73(0.24,2.22)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	4 wks	93/94	7.53%/7.45%	RR	1.01(0.37,2.77)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	4 wks	93/94	7.53%/7.45%	RR	1.01(0.37,2.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	198/203	3.03%/2.46%	RR	1.23(0.38,3.97)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Diarrhea	12 wks	151/157	4.64%/1.91%	RR	2.43(0.64,9.21)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Diarrhea	12 wks	152/154	7.89%/1.3%	RR	6.08(1.38,26.71)	Group 2	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	13 wks	240/222	1.67%/2.25%	RR	0.74(0.2,2.72)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	13 wks	229/222	2.62%/2.25%	RR	1.16(0.36,3.76)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	13 wks	225/222	4%/2.25%	RR	1.78(0.6,5.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	121/107	2.48%/4.67%	RR	0.53(0.13,2.17)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Diarrhea	6 weeks	121/107	2.48%/4.67%	RR	0.53(0.13,2.17)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	111/107	5.41%/4.67%	RR	1.16(0.36,3.68)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Diarrhea	6 weeks	111/107	5.41%/4.67%	RR	1.16(0.36,3.68)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Diarrhea	6 weeks	111/107	7.21%/4.67%	RR	1.54(0.52,4.57)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	111/107	7.21%/4.67%	RR	1.54(0.52,4.57)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Diarrhea	6 weeks	118/107	7.63%/4.67%	RR	1.63(0.56,4.72)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	118/107	7.63%/4.67%	RR	1.63(0.56,4.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >1%	12 wks	183/178	1.64%/0%	RD	1.639(-1.43,4.012)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >5%	12 wks	183/178	6.01%/5.06%	RR	1.19(0.5,2.8)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea	6 wks	156/79	0.64%/1.27%	RR	0.51(0.03,7.99)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea	6 wks	199/200	6.53%/6.5%	RR	1.01(0.48,2.11)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:Diarrhoea	13 weeks	222/222	4.95%/5.86%	RR	0.85(0.39,1.85)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:Diarrhoea	13 weeks	224/222	9.38%/5.86%	RR	1.6(0.82,3.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Digestive System	4 wks	93/94	17.2%/18.09%	RR	0.95(0.51,1.77)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Digestive System	4 wks	92/94	19.57%/18.09%	RR	1.08(0.6,1.97)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Digestive system	4 wks	93/94	17.2%/18.09%	RR	0.95(0.51,1.77)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Digestive system	4 wks	92/94	19.57%/18.09%	RR	1.08(0.6,1.97)	Not Sig.	na
Bolten; 2015/Moderate	9: NSAIDs (oral/IM)-Diclofenac Sodium(50 mg three times daily)	9: Placebo/Control-Placebo(2 tablets three times daily)	Adverse events:Discontinued Due to Adverse Events	12 wks	46/52	13.04%/11.54%	RR	1.13(0.39,3.26)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Digestive or Abdominal Pain Adverse Events	12 wks	213/111	4.69%/3.6%	RR	1.3(0.42,4.06)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Drug-Related Adverse Events	12 wks	213/111	6.1%/4.5%	RR	1.35(0.5,3.7)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Edema-Related Adverse Events	12 wks	213/111	0.47%/0%	RD	0.469(-1.672, 3.837)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Hypertension-Related Adverse Events	12 wks	213/111	0.94%/0%	RD	0.939(-1.48,4.353)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Serious Adverse Events	12 wks	213/111	1.88%/0%	RD	1.878(-0.972, 5.414)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Serious Drug-Related Adverse Events	12 wks	213/111	0.47%/0%	RD	0.469(-1.672, 3.837)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to an Adverse Events	12 wks	213/111	8.45%/4.5%	RR	1.88(0.72,4.92)	Not Sig.	na
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	141/76	2.13%/0%	RD	2.128(-1.813, 7.139)	Not Sig.	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	125/66	0%/0%	RD	0(-2.982, 5.5)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Dizziness	4 mos	30/30	3.33%/3.33%	RR	1(0.07, 15.26)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	199/200	2.01%/2%	RR	1.01(0.25,3.96)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	13 wks	240/222	1.25%/2.7%	RR	0.46(0.12,1.83)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Dizziness	13 wks	225/222	1.33%/2.7%	RR	0.49(0.12,1.95)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	13 wks	229/222	5.24%/2.7%	RR	1.94(0.74,5.08)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	121/107	1.65%/0.93%	RR	1.77(0.16,19.23)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Dizziness	6 weeks	121/107	1.65%/0.93%	RR	1.77(0.16,19.23)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Dizziness	6 weeks	111/107	2.7%/0.93%	RR	2.89(0.31,27.37)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	111/107	2.7%/0.93%	RR	2.89(0.31,27.37)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Dizziness	6 weeks	118/107	5.08%/0.93%	RR	5.44(0.67,44.46)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	118/107	5.08%/0.93%	RR	5.44(0.67,44.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	111/107	8.11%/0.93%	RR	8.68(1.12,67.31)	Group 2	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Dizziness	6 weeks	111/107	8.11%/0.93%	RR	8.68(1.12,67.31)	Group 2	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Dry skin (application site)	12 wks	151/157	2.65%/3.18%	RR	0.83(0.23,3.04)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Dry skin (application site)	12 wks	152/154	19.74%/18.18%	RR	1.09(0.68,1.73)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	156/79	4.49%/2.53%	RR	1.77(0.38,8.33)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	104/103	0.96%/0.97%	RR	0.99(0.06,15.62)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	98/103	3.06%/0.97%	RR	3.15(0.33,29.8)	Not Sig.	na
Essex; 2014/High	9: NSAIDs (oral/IM)-Naproxen(500 md twice daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	129/61	3.88%/1.64%	RR	2.36(0.28,19.8)	Not Sig.	na
Essex; 2016/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	141/76	4.96%/0%	RD	4.965(0.037,10.405)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	104/103	0.96%/0.97%	RR	0.99(0.06,15.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	98/103	3.06%/0.97%	RR	3.15(0.33,29.8)	Not Sig.	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	125/66	3.2%/1.52%	RR	2.11(0.24,18.51)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	4 mos	30/30	40%/46.67%	RR	0.86(0.48,1.53)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	410/208	1.22%/4.33%	RR	0.28(0.1,0.83)	Group 1	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	4 wks	92/94	2.17%/0%	RD	2.174(-3.236, 6.405)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	4 wks	92/94	2.17%/0%	RD	2.174(-3.236, 6.405)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	4 wks	93/94	5.38%/0%	RD	5.376(-1.222, 10.353)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	4 wks	93/94	5.38%/0%	RD	5.376(-1.222, 10.353)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Dyspepsia	12 weeks	213/111	3.29%/3.6%	RR	0.91(0.27,3.05)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	213/111	3.29%/3.6%	RR	0.91(0.27,3.05)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	198/203	6.06%/3.94%	RR	1.54(0.64,3.68)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	199/200	7.54%/7.5%	RR	1.01(0.5,2)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Dyspepsia	12 wks	151/157	3.97%/3.82%	RR	1.04(0.34,3.15)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Dyspepsia	12 wks	152/154	3.29%/2.6%	RR	1.27(0.35,4.63)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	240/222	2.92%/3.6%	RR	0.81(0.3,2.2)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	225/222	4%/3.6%	RR	1.11(0.44,2.83)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	229/222	5.24%/3.6%	RR	1.45(0.61,3.49)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Dyspepsia	6 weeks	111/107	5.41%/5.61%	RR	0.96(0.32,2.9)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Dyspepsia	6 weeks	111/107	5.41%/5.61%	RR	0.96(0.32,2.9)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	111/107	5.41%/5.61%	RR	0.96(0.32,2.9)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	111/107	5.41%/5.61%	RR	0.96(0.32,2.9)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Dyspepsia	6 weeks	121/107	5.79%/5.61%	RR	1.03(0.36,2.97)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	121/107	5.79%/5.61%	RR	1.03(0.36,2.97)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Dyspepsia	6 weeks	118/107	7.63%/5.61%	RR	1.36(0.5,3.69)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	118/107	7.63%/5.61%	RR	1.36(0.5,3.69)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:Dyspepsia	13 weeks	224/222	11.16%/6.31%	RR	1.77(0.95,3.31)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:Dyspepsia	13 weeks	222/222	17.12%/6.31%	RR	2.71(1.51,4.87)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >1%	12 wks	183/178	4.37%/1.12%	RR	3.89(0.84,18.07)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >5%	12 wks	183/178	16.94%/7.3%	RR	2.32(1.26,4.29)	Group 2	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Edema	4 mos	30/30	6.67%/6.67%	RR	1(0.15,6.64)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Edema Peripheral	13 wks	240/222	0.83%/1.8%	RR	0.46(0.09,2.5)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Edema Peripheral	13 wks	229/222	2.62%/1.8%	RR	1.45(0.42,5.08)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Edema Peripheral	13 wks	225/222	4%/1.8%	RR	2.22(0.69,7.1)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Edema-Related Adverse Events	12 wks	213/111	3.29%/1.8%	RR	1.82(0.39,8.63)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Edema-related AE	12 weeks	213/111	3.29%/1.8%	RR	1.82(0.39,8.63)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Epigastric Discomfort	6 wks	410/208	0.49%/6.25%	RR	0.08(0.02,0.34)	Group 1	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Epigastric Discomfort	12 wks	213/111	9.39%/1.8%	RR	5.21(1.24,21.89)	Group 2	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Epigastric discomfort	12 weeks	213/111	9.39%/1.8%	RR	5.21(1.24,21.89)	Group 2	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Flatulence	4 wks	93/94	1.08%/1.06%	RR	1.01(0.06,15.92)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Flatulence	4 wks	93/94	1.08%/1.06%	RR	1.01(0.06,15.92)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Flatulence	4 wks	92/94	3.26%/1.06%	RR	3.07(0.32,28.93)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Flatulence	4 wks	92/94	3.26%/1.06%	RR	3.07(0.32,28.93)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Flatulence	6 wks	199/200	1.51%/1.5%	RR	1.01(0.21,4.92)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Flatulence >5%	12 wks	183/178	7.1%/6.18%	RR	1.15(0.53,2.5)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:GI adverse events	6 wks	88/70	28.41%/30%	RR	0.95(0.58,1.54)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:GI adverse events	6 wks	69/70	53.62%/30%	RR	1.79(1.17,2.72)	Group 2	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Gastroesophageal reflux	6 wks	125/66	0%/1.52%	RD	-1.515(-4.747, 5.066)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Acid Reflux	6 wks	410/208	0.24%/0%	RD	0.244(-0.881, 2.068)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: At least one Adverse Event	6 wks	410/208	5.12%/6.73%	RR	0.76(0.4,1.47)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Dyspepsia	6 wks	410/208	1.22%/0.48%	RR	2.54(0.3,21.57)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Epigastric Discomfort	6 wks	410/208	0.49%/0.96%	RR	0.51(0.07,3.58)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Heartburn	6 wks	410/208	2.44%/0.96%	RR	2.54(0.56,11.47)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Nausea	6 wks	410/208	1.22%/4.33%	RR	0.28(0.1,0.83)	Group 1	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Vomitting	6 wks	410/208	0.24%/0.48%	RR	0.51(0.03,8.07)	Not Sig.	na
Paul; 2009/Moderate	9: NSAIDs (oral/IM)-Nabumetone(750 mg twice per day)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Side Effects	4 wks	118/89	5.93%/3.37%	RR	1.76(0.47,6.62)	Not Sig.	na
Paul; 2009/Moderate	9: NSAIDs (oral/IM)-Aceclofenac(100 mg twice per day)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Side Effects	4 wks	108/89	10.19%/3.37%	RR	3.02(0.87,10.5)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Causing Withdrawal	12 wks	198/203	2.53%/0.49%	RR	5.13(0.6,43.49)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Total	12 wks	198/203	16.16%/10.84%	RR	1.49(0.9,2.47)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Glucose of Potential Concern	12 wks	104/103	2.88%/4.85%	RR	0.59(0.15,2.42)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Glucose of Potential Concern	12 wks	98/103	6.12%/4.85%	RR	1.26(0.4,4)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	156/79	0.64%/2.53%	RR	0.25(0.02,2.75)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	104/103	1.92%/2.91%	RR	0.66(0.11,3.87)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	98/103	6.12%/2.91%	RR	2.1(0.54,8.17)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	104/103	1.92%/2.91%	RR	0.66(0.11,3.87)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	98/103	6.12%/2.91%	RR	2.1(0.54,8.17)	Not Sig.	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Headache	6 wks	125/66	0%/3.03%	RD	-3.03(-6.733, 4.332)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	410/208	8.78%/51.92%	RR	0.17(0.12,0.24)	Group 1	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	4 wks	92/94	3.26%/9.57%	RR	0.34(0.1,1.22)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	4 wks	92/94	3.26%/9.57%	RR	0.34(0.1,1.22)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	4 wks	93/94	5.38%/9.57%	RR	0.56(0.2,1.61)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	4 wks	93/94	5.38%/9.57%	RR	0.56(0.2,1.61)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	198/203	7.07%/10.84%	RR	0.65(0.34,1.24)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	199/200	8.04%/8%	RR	1.01(0.52,1.95)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Headache	12 wks	152/154	13.82%/17.53%	RR	0.79(0.47,1.33)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Headache	12 wks	151/157	17.22%/11.46%	RR	1.5(0.86,2.62)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Headache	13 wks	229/222	0.87%/2.7%	RR	0.32(0.07,1.58)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	13 wks	225/222	2.67%/2.7%	RR	0.99(0.32,3.01)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Headache	13 wks	240/222	4.58%/2.7%	RR	1.7(0.64,4.51)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Headache	6 weeks	121/107	26.45%/30.84%	RR	0.86(0.57,1.29)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	121/107	26.45%/30.84%	RR	0.86(0.57,1.29)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Headache	6 weeks	111/107	28.83%/30.84%	RR	0.93(0.62,1.4)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Headache	6 weeks	111/107	28.83%/30.84%	RR	0.93(0.62,1.4)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	111/107	28.83%/30.84%	RR	0.93(0.62,1.4)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	111/107	28.83%/30.84%	RR	0.93(0.62,1.4)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	118/107	30.51%/30.84%	RR	0.99(0.67,1.47)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Headache	6 weeks	118/107	30.51%/30.84%	RR	0.99(0.67,1.47)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Headache >5%	12 wks	183/178	4.37%/5.62%	RR	0.78(0.31,1.93)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Heartburn	6 wks	410/208	2.44%/8.65%	RR	0.28(0.13,0.6)	Group 1	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Hemic and Lymphatic System	4 wks	92/94	2.17%/0%	RD	2.174(-3.236, 6.405)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Hemic and Lymphatic System	4 wks	93/94	4.3%/0%	RD	4.301(-1.94,9.019)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Hemic and lymphatic system adverse events	4 wks	92/94	2.17%/0%	RD	2.174(-3.236, 6.405)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Hemic and lymphatic system adverse events	4 wks	93/94	4.3%/0%	RD	4.301(-1.94,9.019)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Hemiplegic Migrane	12 wks	104/103	0%/0.97%	RD	-0.971(-4.622, 3.354)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Hemiplegic Migrane	12 wks	98/103	0%/0.97%	RD	-0.971(-4.827, 3.354)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Hemiplegic Migrane	12 wks	104/103	0%/0.97%	RD	-0.971(-4.622, 3.354)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Hemiplegic Migrane	12 wks	98/103	0%/0.97%	RD	-0.971(-4.827, 3.354)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Hepatic Cancer Metastasis	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Hepatic Cancer Metastasis	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Hepatic Cencer Metastasis	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Hepatic Cencer Metastasis	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Paul; 2009/Moderate	9: NSAIDs (oral/IM)-Nabumetone(750 mg twice per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension	4 wks	118/89	1.69%/2.25%	RR	0.75(0.11,5.25)	Not Sig.	na
Paul; 2009/Moderate	9: NSAIDs (oral/IM)-Aceclofenac(100 mg twice per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension	4 wks	108/89	1.85%/2.25%	RR	0.82(0.12,5.73)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension	4 mos	30/30	6.67%/3.33%	RR	2(0.19, 20.9)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Hypertension	6 wks	410/208	0.98%/0.96%	RR	1.01(0.19,5.49)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Hypertension	12 weeks	213/111	6.57%/0.9%	RR	7.3(0.97,54.76)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	213/111	6.57%/0.9%	RR	7.3(0.97,54.76)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	198/203	0%/0.49%	RD	-0.493(-2.439, 1.752)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Hypertension-Related Adverse Events	12 wks	213/111	8.92%/0.9%	RR	9.9(1.34,73)	Group 2	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Hypertension-related AE	12 weeks	213/111	8.92%/0.9%	RR	9.9(1.34,73)	Group 2	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Injury	13 wks	229/222	0.44%/0.9%	RR	0.48(0.04,5.31)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Injury	13 wks	225/222	1.33%/0.9%	RR	1.48(0.25,8.77)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Injury	13 wks	240/222	2.92%/0.9%	RR	3.24(0.68,15.42)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Injury - Accidental	6 wks	199/200	1.51%/1.5%	RR	1.01(0.21,4.92)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Insomnia	6 weeks	111/107	0%/0%	RD	0(-3.345, 3.466)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Insomnia	6 wks	111/107	0%/0%	RD	0(-3.345, 3.466)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Insomnia	6 weeks	121/107	0.83%/0%	RD	0.826(-2.88,4.358)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Insomnia	6 wks	121/107	0.83%/0%	RD	0.826(-2.88,4.358)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Insomnia	6 weeks	111/107	2.7%/0%	RD	2.703(-2.241, 6.599)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Insomnia	6 wks	111/107	2.7%/0%	RD	2.703(-2.241, 6.599)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Insomnia	6 weeks	118/107	5.08%/0%	RD	5.085(-0.481, 9.499)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Insomnia	6 wks	118/107	5.08%/0%	RD	5.085(-0.481, 9.499)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:LDH of Potential Concern	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:LDH of Potential Concern	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Leukocytosis	4 wks	92/94	0%/0%	RD	0(-4.008, 3.926)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Leukocytosis	4 wks	92/94	0%/0%	RD	0(-4.008, 3.926)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Leukocytosis	4 wks	93/94	3.23%/0%	RD	3.226(-2.608, 7.689)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Leukocytosis	4 wks	93/94	3.23%/0%	RD	3.226(-2.608, 7.689)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Liver function tests abnormal	12 wks	151/157	7.95%/0.64%	RR	12.48(1.64,94.78)	Group 2	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Liver function tests abnormal	12 wks	152/154	7.24%/1.95%	RR	3.71(1.06,13.05)	Group 2	na
Pavelka; 2007/Moderate	9: Other Systemic Tx-Diacerein(50 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Loose Stools	6 mos	82/83	14.63%/8.43%	RR	1.74(0.72,4.19)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Lower Extremity Edema	6 wks	410/208	1.71%/0.96%	RR	1.78(0.37,8.47)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Lung Metastasis	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Lung Metastasis	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Lung Metastisis	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Lung Metastisis	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Malignant Melanoma	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Malignant Melanoma	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Malignant Melanoma	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Malignant Melanoma	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Metabolic and Nutritional Disorders	4 wks	93/94	5.38%/3.19%	RR	1.68(0.41,6.85)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Metabolic and Nutritional Disorders	4 wks	92/94	5.43%/3.19%	RR	1.7(0.42,6.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Metabolic and nutritional disorders	4 wks	93/94	5.38%/3.19%	RR	1.68(0.41,6.85)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Metabolic and nutritional disorders	4 wks	92/94	5.43%/3.19%	RR	1.7(0.42,6.92)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Metastatic Neoplasm	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Metastatic Neoplasm	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Metastatic Neoplasm	12 wks	98/103	0%/0%	RD	0(-3.772, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Metastatic Neoplasm	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: At least one Adverse Event	6 wks	410/208	48.05%/50%	RR	0.96(0.81,1.14)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: Diarrhea	6 wks	410/208	3.41%/5.29%	RR	0.65(0.3,1.4)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: Headache	6 wks	410/208	8.78%/13.46%	RR	0.65(0.41,1.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: Upper Respiratory Infection	6 wks	410/208	8.78%/8.17%	RR	1.07(0.62,1.87)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Abdominal Pain	6 wks	410/208	0.49%/0%	RD	0.488(-0.785, 2.335)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: At least one Adverse Event	6 wks	410/208	5.85%/3.85%	RR	1.52(0.7,3.33)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Bloated Feeling	6 wks	410/208	0.49%/0%	RD	0.488(-0.785, 2.335)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Diarrhea	6 wks	410/208	0.73%/0%	RD	0.732(-0.666, 2.608)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Headache	6 wks	410/208	0.73%/0%	RD	0.732(-0.666, 2.608)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Lower Extremity Edema	6 wks	410/208	0.49%/0.48%	RR	1.01(0.09,11.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Nausea	6 wks	410/208	0.49%/0%	RD	0.488(-0.785, 2.335)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Myalgia	4 mos	30/30	3.33%/3.33%	RR	1(0.07, 15.26)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	199/200	2.51%/2.5%	RR	1.01(0.3,3.42)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Myalgia	6 weeks	121/107	0%/2.8%	RD	-2.804(-6.392, 2.313)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	121/107	0%/2.8%	RD	-2.804(-6.392, 2.313)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	118/107	1.69%/2.8%	RR	0.6(0.1,3.55)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Myalgia	6 weeks	118/107	1.69%/2.8%	RR	0.6(0.1,3.55)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Myalgia	6 weeks	111/107	2.7%/2.8%	RR	0.96(0.2,4.67)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	111/107	2.7%/2.8%	RR	0.96(0.2,4.67)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Myalgia	6 weeks	111/107	7.21%/2.8%	RR	2.57(0.7,9.43)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	111/107	7.21%/2.8%	RR	2.57(0.7,9.43)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Myalgia >5%	12 wks	183/178	0.55%/0%	RD	0.546(-1.937, 2.706)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	12 wks	98/103	1.02%/4.85%	RR	0.21(0.03,1.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	12 wks	104/103	4.81%/4.85%	RR	0.99(0.3,3.32)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	12 wks	98/103	1.02%/4.85%	RR	0.21(0.03,1.77)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	12 wks	104/103	4.81%/4.85%	RR	0.99(0.3,3.32)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	6 wks	121/107	4.13%/4.67%	RR	0.88(0.26,2.97)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Nasopharyngitis	6 weeks	121/107	4.13%/4.67%	RR	0.88(0.26,2.97)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	6 wks	111/107	4.5%/4.67%	RR	0.96(0.29,3.24)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Nasopharyngitis	6 weeks	111/107	4.5%/4.67%	RR	0.96(0.29,3.24)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	6 wks	118/107	6.78%/4.67%	RR	1.45(0.49,4.3)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Nasopharyngitis	6 weeks	118/107	6.78%/4.67%	RR	1.45(0.49,4.3)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	6 wks	111/107	9.01%/4.67%	RR	1.93(0.68,5.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Nasopharyngitis	6 weeks	111/107	9.01%/4.67%	RR	1.93(0.68,5.46)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	104/103	4.81%/1.94%	RR	2.48(0.49,12.47)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	98/103	9.18%/1.94%	RR	4.73(1.05,21.35)	Group 2	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	104/103	4.81%/1.94%	RR	2.48(0.49,12.47)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	98/103	9.18%/1.94%	RR	4.73(1.05,21.35)	Group 2	na
Essex; 2012/High	9: NSAIDs (oral/IM)-Naproxen(500 mg twice a day)	1: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	125/66	2.4%/3.03%	RR	0.79(0.14,4.62)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Nausea	4 mos	30/30	3.33%/6.67%	RR	0.5(0.05,5.22)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	410/208	1.22%/11.54%	RR	0.11(0.04,0.27)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	4 wks	93/94	1.08%/7.45%	RR	0.14(0.02,1.15)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	4 wks	93/94	1.08%/7.45%	RR	0.14(0.02,1.15)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	4 wks	92/94	7.61%/7.45%	RR	1.02(0.37,2.8)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	4 wks	92/94	7.61%/7.45%	RR	1.02(0.37,2.8)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	213/111	4.23%/2.7%	RR	1.56(0.43,5.66)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Nausea	12 weeks	213/111	4.23%/2.7%	RR	1.56(0.43,5.66)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	199/200	3.52%/3.5%	RR	1.01(0.36,2.81)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Nausea	12 wks	151/157	1.99%/0%	RD	1.987(-1.704, 4.71)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Nausea	12 wks	152/154	3.29%/0%	RD	3.289(-0.89,6.363)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	13 wks	240/222	2.5%/2.25%	RR	1.11(0.34,3.59)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	13 wks	229/222	3.49%/2.25%	RR	1.55(0.52,4.67)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	13 wks	225/222	5.78%/2.25%	RR	2.57(0.93,7.08)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	121/107	1.65%/0.93%	RR	1.77(0.16,19.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Nausea	6 weeks	121/107	1.65%/0.93%	RR	1.77(0.16,19.23)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	118/107	1.69%/0.93%	RR	1.81(0.17,19.72)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Nausea	6 weeks	118/107	1.69%/0.93%	RR	1.81(0.17,19.72)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	111/107	4.5%/0.93%	RR	4.82(0.57,40.58)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Nausea	6 weeks	111/107	4.5%/0.93%	RR	4.82(0.57,40.58)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	111/107	6.31%/0.93%	RR	6.75(0.84,53.93)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Nausea	6 weeks	111/107	6.31%/0.93%	RR	6.75(0.84,53.93)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:Nausea	13 weeks	224/222	5.36%/5.41%	RR	0.99(0.46,2.16)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:Nausea	13 weeks	222/222	6.76%/5.41%	RR	1.25(0.6,2.61)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Nausea >5%	12 wks	183/178	4.92%/5.06%	RR	0.97(0.4,2.39)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Nausea >1%	12 wks	183/178	1.09%/1.12%	RR	0.97(0.14,6.83)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Neck Pain	6 wks	111/107	0%/1.87%	RD	-1.869(-5.478, 2.822)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Neck Pain	6 wks	121/107	0.83%/1.87%	RR	0.44(0.04,4.81)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Neck Pain	6 wks	118/107	3.39%/1.87%	RR	1.81(0.34,9.7)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Neck Pain	6 wks	111/107	4.5%/1.87%	RR	2.41(0.48,12.16)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Neck pain	6 weeks	111/107	0%/1.87%	RD	-1.869(-5.478, 2.822)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Neck pain	6 weeks	121/107	0.83%/1.87%	RR	0.44(0.04,4.81)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Neck pain	6 weeks	118/107	3.39%/1.87%	RR	1.81(0.34,9.7)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Neck pain	6 weeks	111/107	4.5%/1.87%	RR	2.41(0.48,12.16)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Nervous System	4 wks	93/94	2.15%/5.32%	RR	0.4(0.08,2.03)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Nervous System	4 wks	92/94	3.26%/5.32%	RR	0.61(0.15,2.49)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Nervous System Disorders	4 wks	93/94	2.15%/5.32%	RR	0.4(0.08,2.03)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Nervous System Disorders	4 wks	92/94	3.26%/5.32%	RR	0.61(0.15,2.49)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Non-Cardiac Chest Pain	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Non-Cardiac Chest Pain	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Non-Cardiac Chest Pain	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Non-Cardiac Chest Pain	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Other Adverse Events	6 wks	88/70	6.82%/8.57%	RR	0.8(0.27,2.36)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Other Adverse Events	6 wks	69/70	17.39%/8.57%	RR	2.03(0.81,5.1)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Pain	4 wks	93/94	0%/3.19%	RD	-3.191(-7.68,2.584)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Pain	4 wks	93/94	0%/3.19%	RD	-3.191(-7.68,2.584)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Pain	4 wks	92/94	0%/3.19%	RD	-3.191(-7.717, 2.584)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Pain	4 wks	92/94	0%/3.19%	RD	-3.191(-7.717, 2.584)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Pain	6 wks	199/200	0%/0%	RD	0(-1.894, 1.885)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Pain	12 wks	152/154	0.66%/4.55%	RR	0.14(0.02,1.16)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Pain	12 wks	151/157	5.3%/3.18%	RR	1.66(0.56,4.97)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Pain NOS	6 weeks	121/107	0.83%/3.74%	RR	0.22(0.03,1.95)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Pain NOS	6 wks	121/107	0.83%/3.74%	RR	0.22(0.03,1.95)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Pain NOS	6 wks	111/107	2.7%/3.74%	RR	0.72(0.17,3.15)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Pain NOS	6 wks	111/107	2.7%/3.74%	RR	0.72(0.17,3.15)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Pain NOS	6 weeks	111/107	2.7%/3.74%	RR	0.72(0.17,3.15)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Pain NOS	6 weeks	111/107	2.7%/3.74%	RR	0.72(0.17,3.15)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Pain NOS	6 wks	118/107	4.24%/3.74%	RR	1.13(0.31,4.11)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Pain NOS	6 weeks	118/107	4.24%/3.74%	RR	1.13(0.31,4.11)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Pain in limb	6 weeks	121/107	1.65%/9.35%	RR	0.18(0.04,0.79)	Group 1	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Pain in limb	6 wks	121/107	1.65%/9.35%	RR	0.18(0.04,0.79)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Pain in limb	6 weeks	111/107	2.7%/9.35%	RR	0.29(0.08,1.02)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Pain in limb	6 wks	111/107	2.7%/9.35%	RR	0.29(0.08,1.02)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Pain in limb	6 weeks	111/107	7.21%/9.35%	RR	0.77(0.32,1.88)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Pain in limb	6 wks	111/107	7.21%/9.35%	RR	0.77(0.32,1.88)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Pain in limb	6 weeks	118/107	8.47%/9.35%	RR	0.91(0.39,2.09)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Pain in limb	6 wks	118/107	8.47%/9.35%	RR	0.91(0.39,2.09)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients Discontinued Due to Adverse Events	6 wks	156/79	6.41%/6.33%	RR	1.01(0.36,2.86)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	6 wks	156/79	30.77%/26.58%	RR	1.16(0.75,1.79)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Dose Reduced or Temporary Discontinuation Due to Adverse Events	6 wks	156/79	3.21%/1.27%	RR	2.53(0.3,21.3)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	6 wks	156/79	0.64%/0%	RD	0.641(-2.259, 5.308)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Severe Adverse Events	6 wks	156/79	3.21%/3.8%	RR	0.84(0.21,3.44)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	12 wks	198/203	1.01%/0.49%	RR	2.05(0.19,22.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Peripheral Oedema	6 wks	199/200	2.51%/2.5%	RR	1.01(0.3,3.42)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Pharyngitis	6 weeks	111/107	1.8%/2.8%	RR	0.64(0.11,3.77)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Pharyngitis	6 wks	111/107	1.8%/2.8%	RR	0.64(0.11,3.77)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Pharyngitis	6 weeks	121/107	2.48%/2.8%	RR	0.88(0.18,4.29)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Pharyngitis	6 wks	121/107	2.48%/2.8%	RR	0.88(0.18,4.29)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Pharyngitis	6 weeks	111/107	5.41%/2.8%	RR	1.93(0.49,7.51)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Pharyngitis	6 wks	111/107	5.41%/2.8%	RR	1.93(0.49,7.51)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Pharyngitis	6 weeks	118/107	5.93%/2.8%	RR	2.12(0.56,7.98)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Pharyngitis	6 wks	118/107	5.93%/2.8%	RR	2.12(0.56,7.98)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Potassium of Potential Concern	12 wks	104/103	4.81%/2.91%	RR	1.65(0.4,6.73)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Potassium of Potential Concern	12 wks	98/103	5.1%/2.91%	RR	1.75(0.43,7.13)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Pruritis (application site)	12 wks	151/157	0%/0%	RD	0(-2.481, 2.388)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Pruritis (application site)	12 wks	152/154	0.66%/1.3%	RR	0.51(0.05,5.53)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Pulmonary Embolism	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Pulmonary Embolism	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Pulmonary Embolism	12 wks	104/103	0%/0%	RD	0(-3.562, 3.595)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Pulmonary Embolism	12 wks	98/103	1.02%/0%	RD	1.02(-3.515, 4.713)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Rash	12 wks	152/154	0%/2.6%	RD	-2.597(-5.527, 1.293)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Rash	12 wks	151/157	0%/0%	RD	0(-2.481, 2.388)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Rash	13 wks	240/222	0.83%/0%	RD	0.833(-1.32,2.639)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Rash	13 wks	225/222	0.89%/0%	RD	0.889(-1.405, 2.708)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Rash	13 wks	229/222	2.18%/0%	RD	2.183(-0.642, 4.293)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Rash >1%	12 wks	183/178	0%/0%	RD	0(-2.056, 2.113)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Rectal hemorrhage	12 wks	151/157	0%/0%	RD	0(-2.481, 2.388)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Rectal hemorrhage	12 wks	152/154	3.29%/0.65%	RR	5.07(0.6,42.85)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Respiratory System	4 wks	92/94	1.09%/1.06%	RR	1.02(0.06,16.09)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Respiratory System	4 wks	93/94	4.3%/1.06%	RR	4.04(0.46,35.5)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Simon; 2009/High	9: NSAIDs (oral/IM)-oral diclofenac 100mg slow release once daily + 40 drops 4x daily of topical placebo (with 2.3% dmso)	9: Placebo/Control-40 drops 4x daily of topical placebo (with 2.3% dmso) + oral placebo	Adverse events:Respiratory disorder	12 wks	151/157	5.3%/3.82%	RR	1.39(0.49,3.9)	Not Sig.	na
Simon; 2009/High	9: NSAIDs (oral/IM)-40 drops 4x daily of topical diclofenac + oral diclofenac 100mg slow release once daily	9: Placebo/Control-40 drops 4x daily of topical diclofenac + oral placebo	Adverse events:Respiratory disorder	12 wks	152/154	4.61%/3.25%	RR	1.42(0.46,4.37)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Respiratory system	4 wks	92/94	1.09%/1.06%	RR	1.02(0.06,16.09)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Respiratory system	4 wks	93/94	4.3%/1.06%	RR	4.04(0.46,35.5)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen(800 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Serious Drug-Related Adverse Events	12 wks	213/111	0.47%/0%	RD	0.469(-1.672, 3.837)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-Ibuprofen 2400 mg	9: Placebo/Control-placebo	Adverse events:Serious drug-related AE	12 weeks	213/111	0.47%/0%	RD	0.469(-1.672, 3.837)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Serum Creatinine Elevation	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Serum Creatinine Elevation	12 wks	98/103	3.06%/0%	RD	3.061(-2.495, 7.183)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Serum Creatinine Elevation	12 wks	104/103	0.96%/0%	RD	0.962(-3.324, 4.643)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Serum Creatinine Elevation	12 wks	98/103	3.06%/0%	RD	3.061(-2.495, 7.183)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Sinus Headache	6 wks	121/107	0%/1.87%	RD	-1.869(-5.231, 2.822)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Sinus Headache	6 wks	118/107	1.69%/1.87%	RR	0.91(0.13,6.33)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Sinus Headache	6 wks	111/107	3.6%/1.87%	RR	1.93(0.36,10.31)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Sinus Headache	6 wks	111/107	4.5%/1.87%	RR	2.41(0.48,12.16)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Sinus headache	6 weeks	121/107	0%/1.87%	RD	-1.869(-5.231, 2.822)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Sinus headache	6 weeks	118/107	1.69%/1.87%	RR	0.91(0.13,6.33)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Sinus headache	6 weeks	111/107	3.6%/1.87%	RR	1.93(0.36,10.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Sinus headache	6 weeks	111/107	4.5%/1.87%	RR	2.41(0.48,12.16)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	12 wks	104/103	1.92%/0.97%	RR	1.98(0.18,21.51)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	12 wks	98/103	3.06%/0.97%	RR	3.15(0.33,29.8)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	12 wks	104/103	1.92%/0.97%	RR	1.98(0.18,21.51)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	12 wks	98/103	3.06%/0.97%	RR	3.15(0.33,29.8)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Sinusitis	13 wks	240/222	0%/1.35%	RD	-1.351(-3.161, 1.194)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Sinusitis	13 wks	229/222	1.31%/1.35%	RR	0.97(0.2,4.75)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	13 wks	225/222	2.67%/1.35%	RR	1.97(0.5,7.79)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Skin adverse events	6 wks	88/70	7.95%/10%	RR	0.8(0.29,2.16)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Skin adverse events	6 wks	69/70	11.59%/10%	RR	1.16(0.44,3.02)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Skin and Appendages	4 wks	93/94	1.08%/4.26%	RR	0.25(0.03,2.22)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Skin and Appendages	4 wks	92/94	1.09%/4.26%	RR	0.26(0.03,2.24)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Nabumetone(1500 mg)	9: Placebo/Control-Placebo	Adverse events:Skin and appendages	4 wks	93/94	1.08%/4.26%	RR	0.25(0.03,2.22)	Not Sig.	na
Fleischmann; 1997/High	9: NSAIDs (oral/IM)-Naprelan(1000 mg)	9: Placebo/Control-Placebo	Adverse events:Skin and appendages	4 wks	92/94	1.09%/4.26%	RR	0.26(0.03,2.24)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Stomach Discomfort	13 wks	240/222	0.42%/0.45%	RR	0.93(0.06,14.7)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Stomach Discomfort	13 wks	229/222	1.75%/0.45%	RR	3.88(0.44,34.42)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Stomach Discomfort	13 wks	225/222	2.22%/0.45%	RR	4.93(0.58,41.89)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Stomatitis	6 weeks	111/107	3.6%/0.93%	RR	3.86(0.44,33.95)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Stomatitis	6 wks	111/107	3.6%/0.93%	RR	3.86(0.44,33.95)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Stomatitis	6 wks	121/107	4.13%/0.93%	RR	4.42(0.52,37.25)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Stomatitis	6 weeks	121/107	4.13%/0.93%	RR	4.42(0.52,37.25)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Stomatitis	6 weeks	111/107	7.21%/0.93%	RR	7.71(0.98,60.62)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Stomatitis	6 wks	111/107	7.21%/0.93%	RR	7.71(0.98,60.62)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Stomatitis	6 wks	118/107	9.32%/0.93%	RR	9.97(1.31,75.97)	Group 2	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Stomatitis	6 weeks	118/107	9.32%/0.93%	RR	9.97(1.31,75.97)	Group 2	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Syncope	12 wks	104/103	0%/0.97%	RD	-0.971(-4.622,3.354)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Syncope	12 wks	98/103	0%/0.97%	RD	-0.971(-4.827, 3.354)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Syncope	12 wks	104/103	0%/0.97%	RD	-0.971(-4.622, 3.354)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Syncope	12 wks	98/103	0%/0.97%	RD	-0.971(-4.827, 3.354)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	6 wks	156/79	42.31%/34.18%	RR	1.24(0.87,1.77)	Not Sig.	na
Pavelka; 2007/Moderate	9: Other Systemic Tx-Diacerein(50 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	6 mos	84/84	42.86%/28.57%	RR	1.5(0.99,2.28)	Not Sig.	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	12 wks	198/203	31.82%/29.06%	RR	1.09(0.81,1.47)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >1%	12 wks	183/178	12.57%/8.43%	RR	1.49(0.8,2.76)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >5%	12 wks	183/178	68.31%/53.37%	RR	1.28(1.08,1.52)	Group 2	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Total Causing Withdrawal	12 wks	198/203	4.04%/3.94%	RR	1.03(0.39,2.68)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal low dose(375 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Total patients with reactions	6 wks	88/70	40.91%/45.71%	RR	0.89(0.63,1.28)	Not Sig.	na
Lee; 1986/High	9: NSAIDs (oral/IM)-Diflunisal high dose(500 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Total patients with reactions	6 wks	69/70	56.52%/45.71%	RR	1.24(0.89,1.72)	Not Sig.	na
Gordo; 2017/High	9: NSAIDs (oral/IM)-Ibuprofen(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:UGI Event	6 wks	156/79	5.13%/2.53%	RR	2.03(0.44,9.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:URI	12 wks	104/103	2.88%/5.83%	RR	0.5(0.13,1.93)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:URI	12 wks	98/103	3.06%/5.83%	RR	0.53(0.14,2.04)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:URI	12 wks	104/103	2.88%/5.83%	RR	0.5(0.13,1.93)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:URI	12 wks	98/103	3.06%/5.83%	RR	0.53(0.14,2.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:UTI	12 wks	104/103	0%/3.88%	RD	-3.883(-8.158, 1.796)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:UTI	12 wks	98/103	2.04%/3.88%	RR	0.53(0.1,2.8)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:UTI	12 wks	104/103	0%/3.88%	RD	-3.883(-8.158, 1.796)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:UTI	12 wks	98/103	2.04%/3.88%	RR	0.53(0.1,2.8)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (BID)(35 mg twice daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Upper Abdominal Pain	12 wks	104/103	2.88%/0.97%	RR	2.97(0.31,28.1)	Not Sig.	na
Strand; 2017/High	9: NSAIDs (oral/IM)-SoluMatrix Diclofenac (TID)(35 mg three times daily for 12 weeks)	9: Placebo/Control-Placebo	Adverse events:Upper Abdominal Pain	12 wks	98/103	3.06%/0.97%	RR	3.15(0.33,29.8)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac bid(35 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Upper Abdominal Pain	12 wks	104/103	2.88%/0.97%	RR	2.97(0.31,28.1)	Not Sig.	na
Gibofsky; 2014/High	9: NSAIDs (oral/IM)-Submicron Diclofenac tid(35 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Upper Abdominal Pain	12 wks	98/103	3.06%/0.97%	RR	3.15(0.33,29.8)	Not Sig.	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	6 wks	410/208	8.78%/43.75%	RR	0.2(0.14,0.28)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-Diclofenac(50 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	6 wks	199/200	1.01%/1%	RR	1.01(0.14,7.06)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	13 wks	229/222	0.87%/1.8%	RR	0.48(0.09,2.62)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	13 wks	225/222	2.22%/1.8%	RR	1.23(0.34,4.53)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	13 wks	240/222	2.5%/1.8%	RR	1.39(0.4,4.85)	Not Sig.	na
Lohmander; 2005/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Upper abdominal pain	6 wks	417/116	3.12%/8.62%	RR	0.36(0.16,0.8)	Group 1	na
Bensen; 1999/High	9: NSAIDs (oral/IM)-Naproxen	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	12 wks	198/203	8.59%/5.42%	RR	1.58(0.76,3.3)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-Naproxen(500 mg/twice per day)	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection >5%	12 wks	183/178	4.92%/8.99%	RR	0.55(0.25,1.21)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	13 wks	240/222	0.42%/0.9%	RR	0.46(0.04,5.07)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	13 wks	229/222	1.75%/0.9%	RR	1.94(0.36,10.48)	Not Sig.	na
Schnitzer; 2010/High	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	13 wks	225/222	2.22%/0.9%	RR	2.47(0.48,12.58)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxen(500 mg)	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	6 wks	121/107	0%/4.67%	RD	-4.673(-8.741, 1.13)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 750 mg	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	6 wks	118/107	0.85%/4.67%	RR	0.18(0.02,1.53)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 375 mg	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	6 wks	111/107	0.9%/4.67%	RR	0.19(0.02,1.62)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-Naproxcinod 125 mg	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	6 wks	111/107	2.7%/4.67%	RR	0.58(0.14,2.36)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxen(500mg)	9: Placebo/Control-	Adverse events:Urinary tract infection	6 weeks	121/107	0%/4.67%	RD	-4.673(-8.741, 1.13)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (750 mg)	9: Placebo/Control-	Adverse events:Urinary tract infection	6 weeks	118/107	0.85%/4.67%	RR	0.18(0.02,1.53)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (375 mg)	9: Placebo/Control-	Adverse events:Urinary tract infection	6 weeks	111/107	0.9%/4.67%	RR	0.19(0.02,1.62)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-naproxcinod (125 mg)	9: Placebo/Control-	Adverse events:Urinary tract infection	6 weeks	111/107	2.7%/4.67%	RR	0.58(0.14,2.36)	Not Sig.	na
Singh; 2012/High	9: Other Systemic Tx-Diacerein(50 mg once twice per day)	9: Placebo/Control-Placebo	Adverse events:Urine Discoloration	4 mos	30/30	33.33%/3.33%	RR	10(1.36,73.33)	Group 2	na
Kivitz; 2004/High	9: NSAIDs (oral/IM)-Nabumetone(1000mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Vomiting	6 wks	410/208	0.24%/2.4%	RR	0.1(0.01,0.86)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pavelka; 2007/Moderate	9: Other Systemic Tx-Diacerein(50 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Withrawal Due to Adverse Events	6 mos	82/83	3.66%/4.82%	RR	0.76(0.18,3.29)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:any adverse event	13 weeks	222/222	77.93%/81.08%	RR	0.96(0.87,1.06)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:any adverse event	13 weeks	224/222	84.38%/81.08%	RR	1.04(0.96,1.13)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:any adverse event related to treatment	13 weeks	222/222	50.45%/45.5%	RR	1.11(0.91,1.35)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: Acetaminophen-paracetamol(500 mg twice daily)	Adverse events:any adverse event related to treatment	13 weeks	224/222	51.34%/45.5%	RR	1.13(0.93,1.37)	Not Sig.	na

PICO 9: Systemic Treatment

Cox2 vs. Control

Table 37: Cox2 vs Control

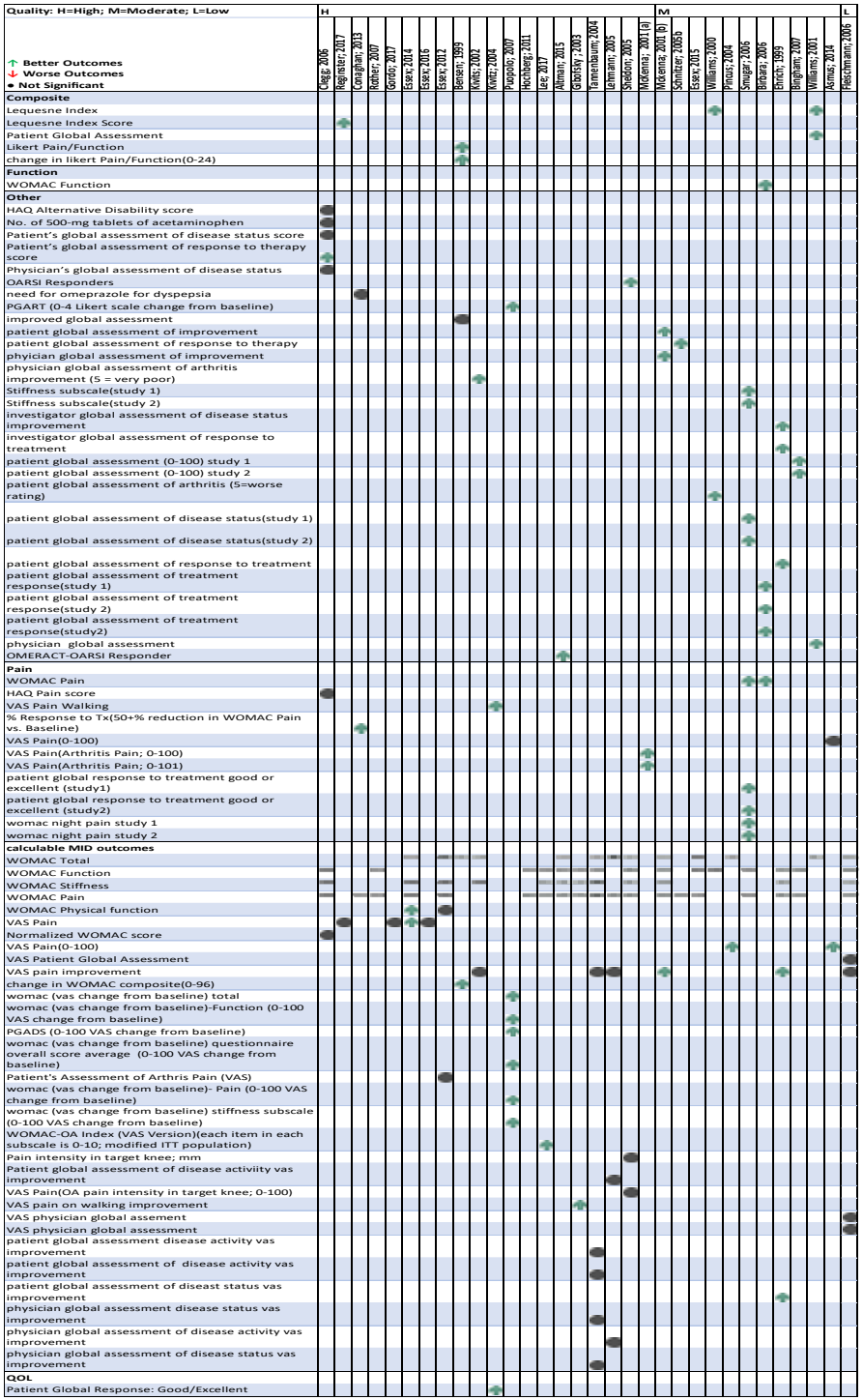

Quality: H=High; M=Moderate; L=Low
↑ Better Outcomes
↓ Worse Outcomes
• Not Significant
H
M
L
Clegg; 2006
Reginster; 2017
Conaghan; 2013
Richter; 2007
Gordo; 2017
Esser; 2014
Esser; 2016
Esser; 2012
Bensen; 1999
Kivitz; 2002
Kivitz; 2004
Puopolo; 2007
Hochberg; 2011
Lee; 2017
Altman; 2015
Ghoniem; 2003
Tannenbaum; 2004
Lehmann; 2005
Sheldon; 2005
McKenna; 2001(a)
McKenna; 2001(b)
Schnitzer; 2005b
Esser; 2015
Williams; 2000
Pincus; 2004
Smugar; 2006
Berkowa; 2006
Ehrich; 1999
Bingham; 2007
Williams; 2001
Asmus; 2014
Fleischmann; 2006
Composite
Lequesne Index
Lequesne Index Score
Patient Global Assessment
Likert Pain/Function
change in likert Pain/Function(0-24)
Function
WOMAC Function
Other
HAQ Alternative Disability score
No. of 500-mg tablets of acetaminophen
Patient's global assessment of disease status score
Patient's global assessment of response to therapy score
Physician's global assessment of disease status
OARSI Responders
need for omeprazole for dyspepsia
PGART (0-4 Likert scale change from baseline)
improved global assessment
patient global assessment of improvement
patient global assessment of response to therapy
phyician global assessment of improvement
physician global assessment of arthritis improvement (5 = very poor)
Stiffness subscale(study 1)
Stiffness subscale(study 2)
investigator global assessment of disease status improvement
investigator global assessment of response to treatment
patient global assessment (0-100) study 1
patient global assessment (0-100) study 2
patient global assessment of arthritis (5=worse rating)
patient global assessment of disease status(study 1)
patient global assessment of disease status(study 2)
patient global assessment of response to treatment
patient global assessment of treatment response(study 1)
patient global assessment of treatment response(study 2)
patient global assessment of treatment response(study2)
physician global assessment
OMERACT-OARSI Responder
Pain
WOMAC Pain
HAQ Pain score
VAS Pain Walking
% Response to Tx(50+% reduction in WOMAC Pain vs. Baseline)
VAS Pain(0-100)
VAS Pain(Arthritis Pain; 0-100)
VAS Pain(Arthritis Pain; 0-101)
patient global response to treatment good or excellent (study1)
patient global response to treatment good or excellent (study2)
womac night pain study 1
womac night pain study 2
calculable MID outcomes
WOMAC Total
WOMAC Function
WOMAC Stiffness
WOMAC Pain
WOMAC Physical function
VAS Pain
Normalized WOMAC score
VAS Pain(0-100)
VAS Patient Global Assessment
VAS pain improvement
change in WOMAC composite(0-96)
womac (vas change from baseline) total
womac (vas change from baseline)-Function (0-100 VAS change from baseline)
PGADS (0-100 VAS change from baseline)
womac (vas change from baseline) questionnaire overall score average (0-100 VAS change from baseline)
Patient's Assessment of Arthris Pain (VAS)
womac (vas change from baseline)- Pain (0-100 VAS change from baseline)
womac (vas change from baseline) stiffness subscale (0-100 VAS change from baseline)
WOMAC-OA Index (VAS Version)(each item in each subscale is 0-10; modified ITT population)
Pain intensity in target knee; mm
Patient global assessment of disease activiity vas improvement
VAS Pain(OA pain intensity in target knee; 0-100)
VAS pain on walking improvement
VAS physician global assement
VAS physician global assessment
patient global assessment disease activity vas improvement
patient global assessment of disease activity vas improvement
patient global assessment of diseast status vas improvement
physician global assessment disease status vas improvement
physician global assessment of disease activity vas improvement
physician global assessment of disease status vas improvement
QOL
Patient Global Response: Good/Excellent

Table 37 Continued: Cox2 vs Control

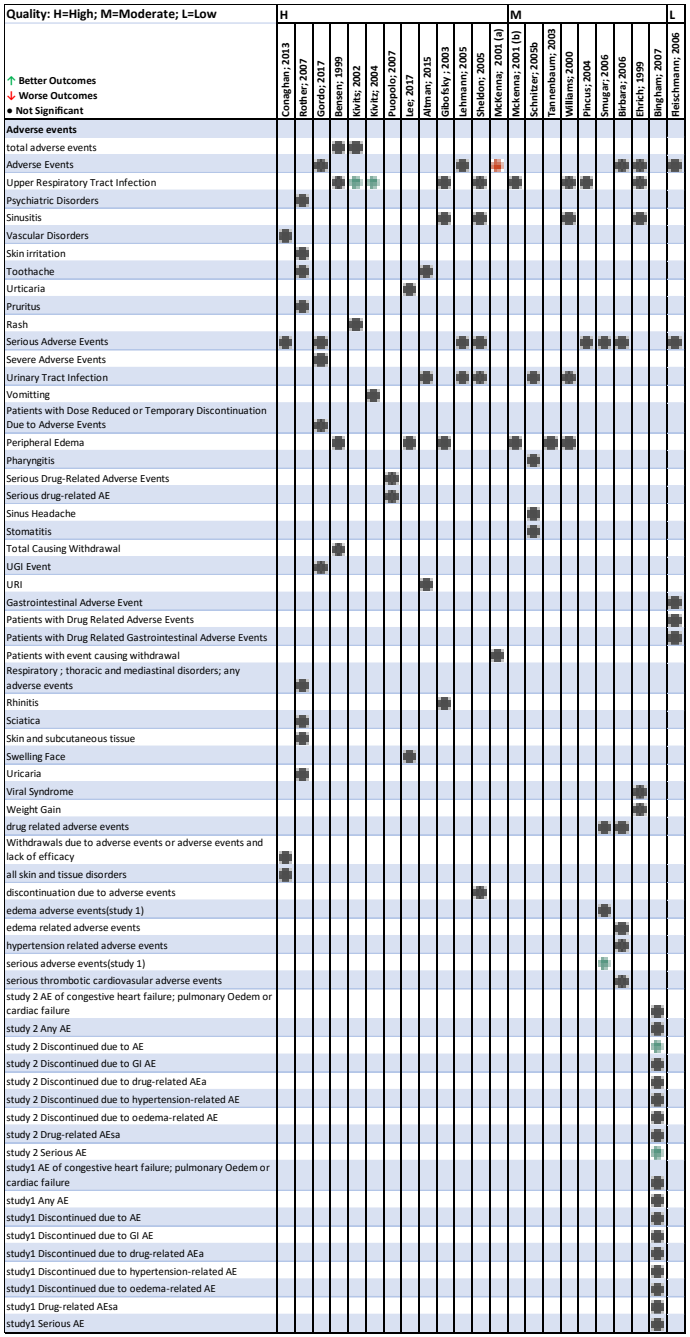


Table 37 Continued: Cox2 vs Control

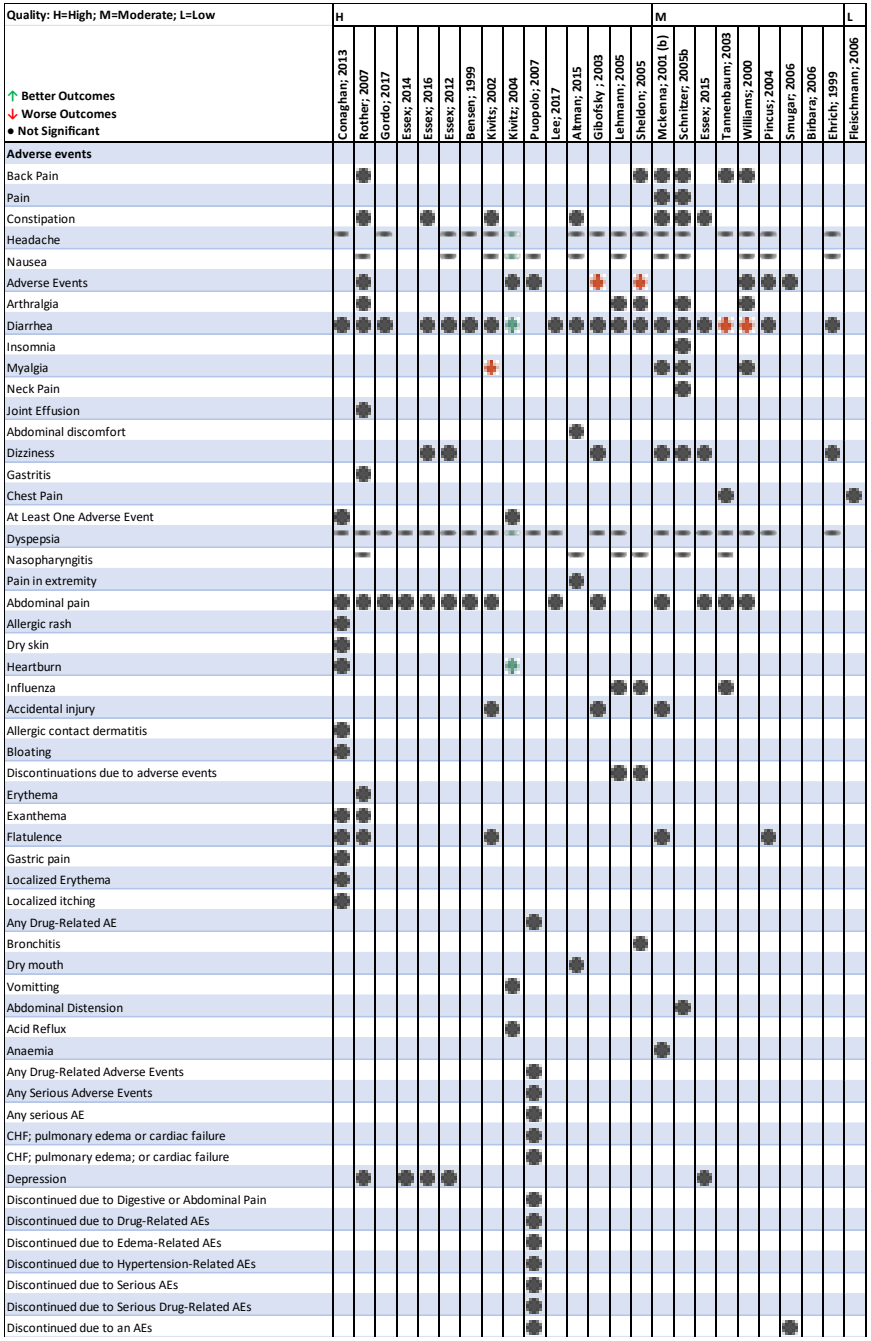
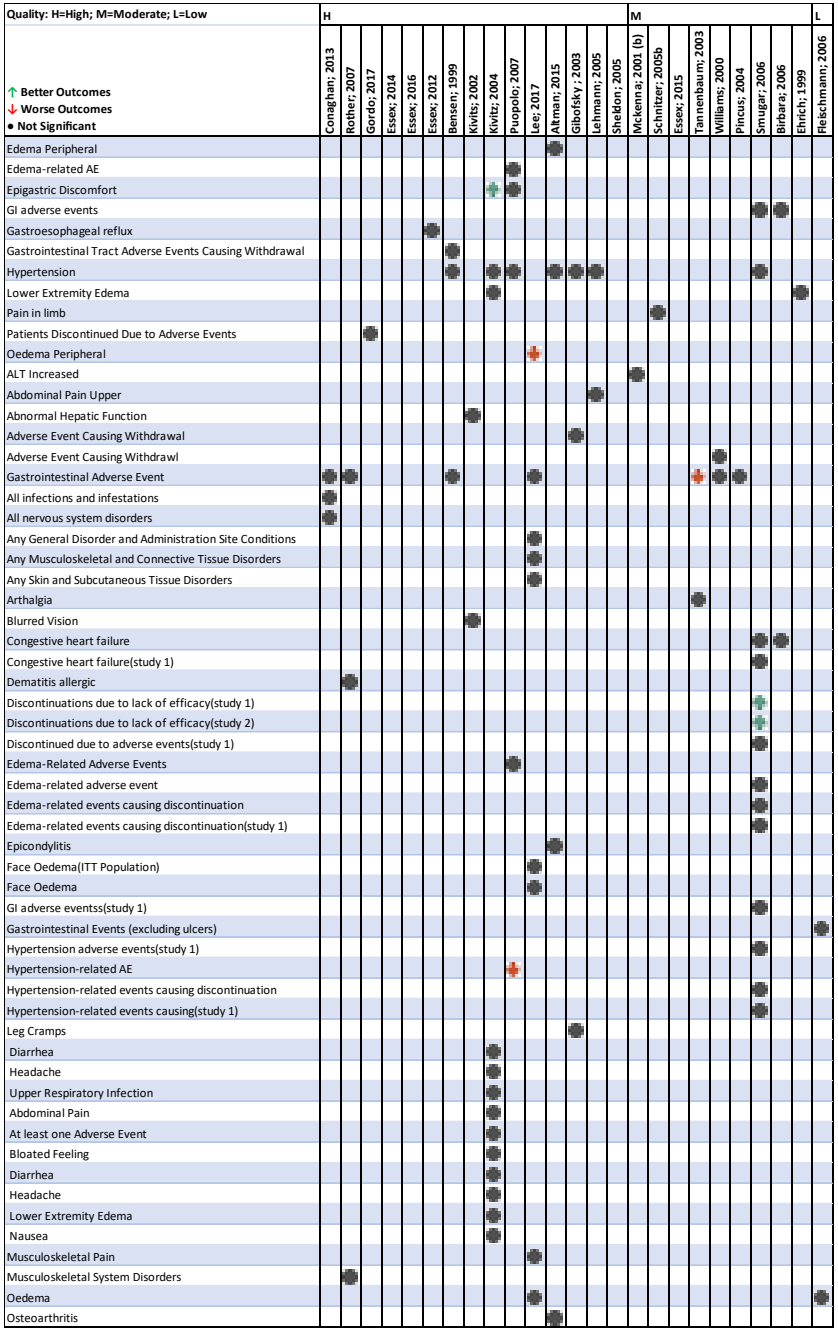
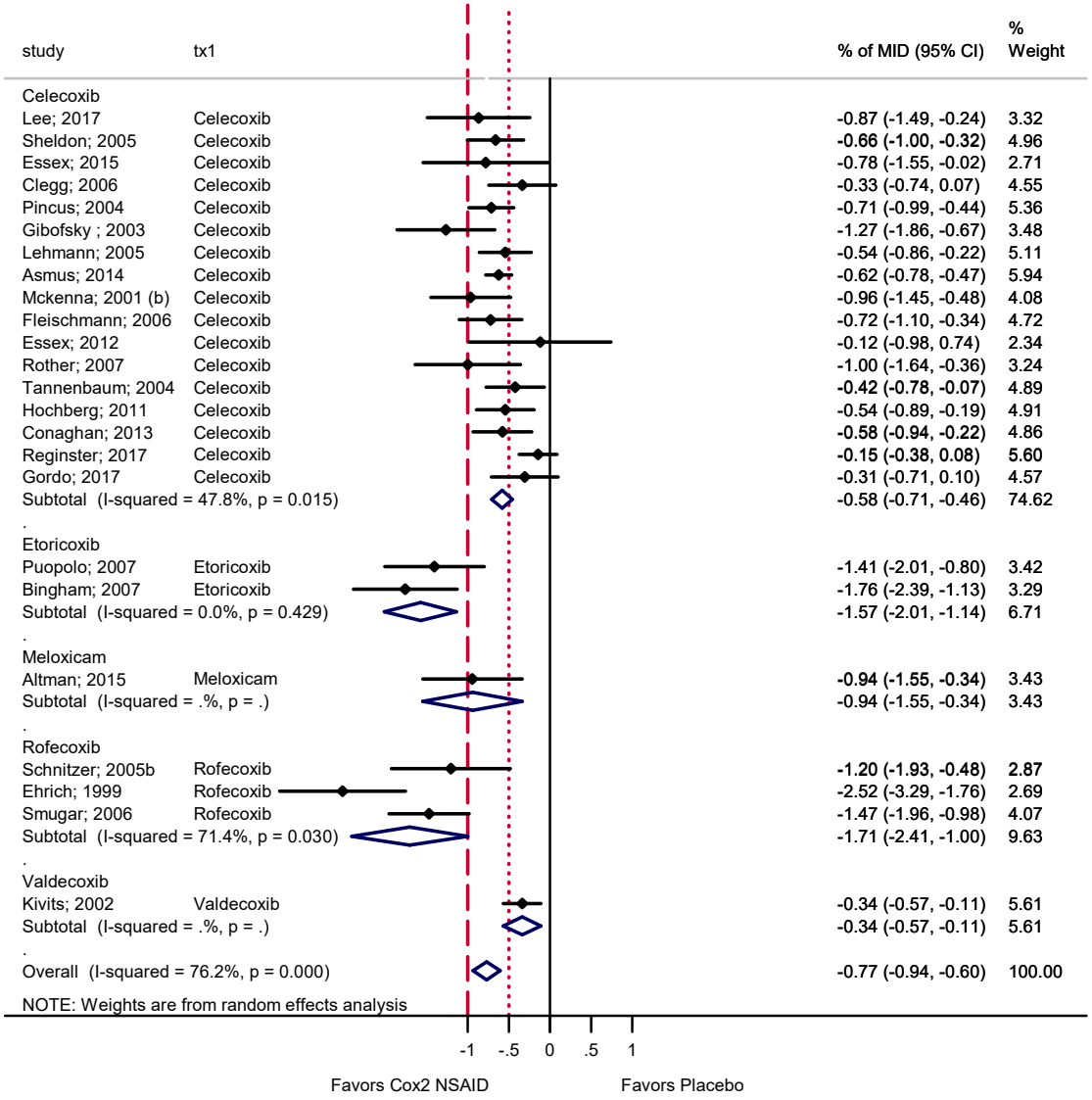


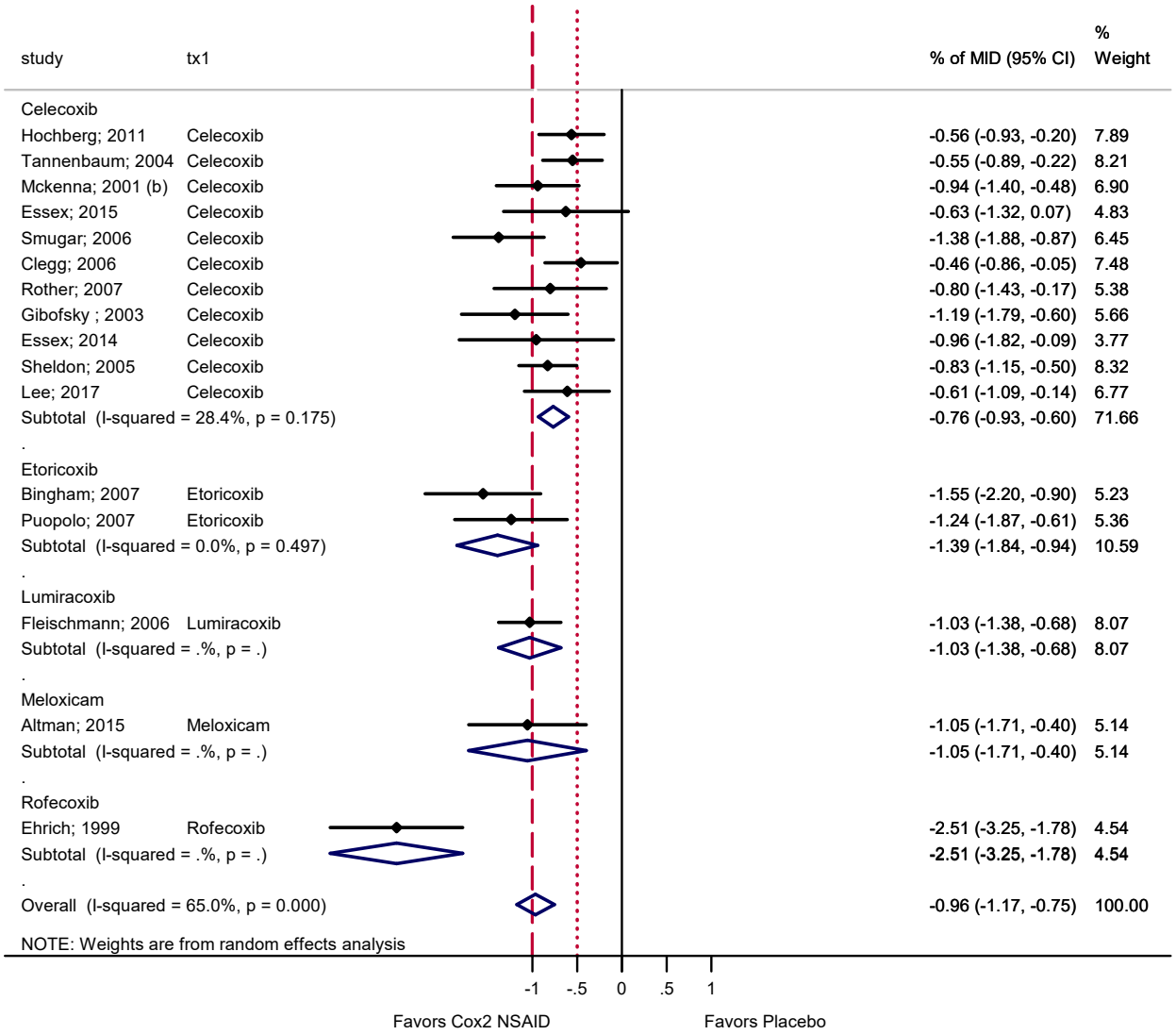
Table 37 Continued: Cox2 vs Control



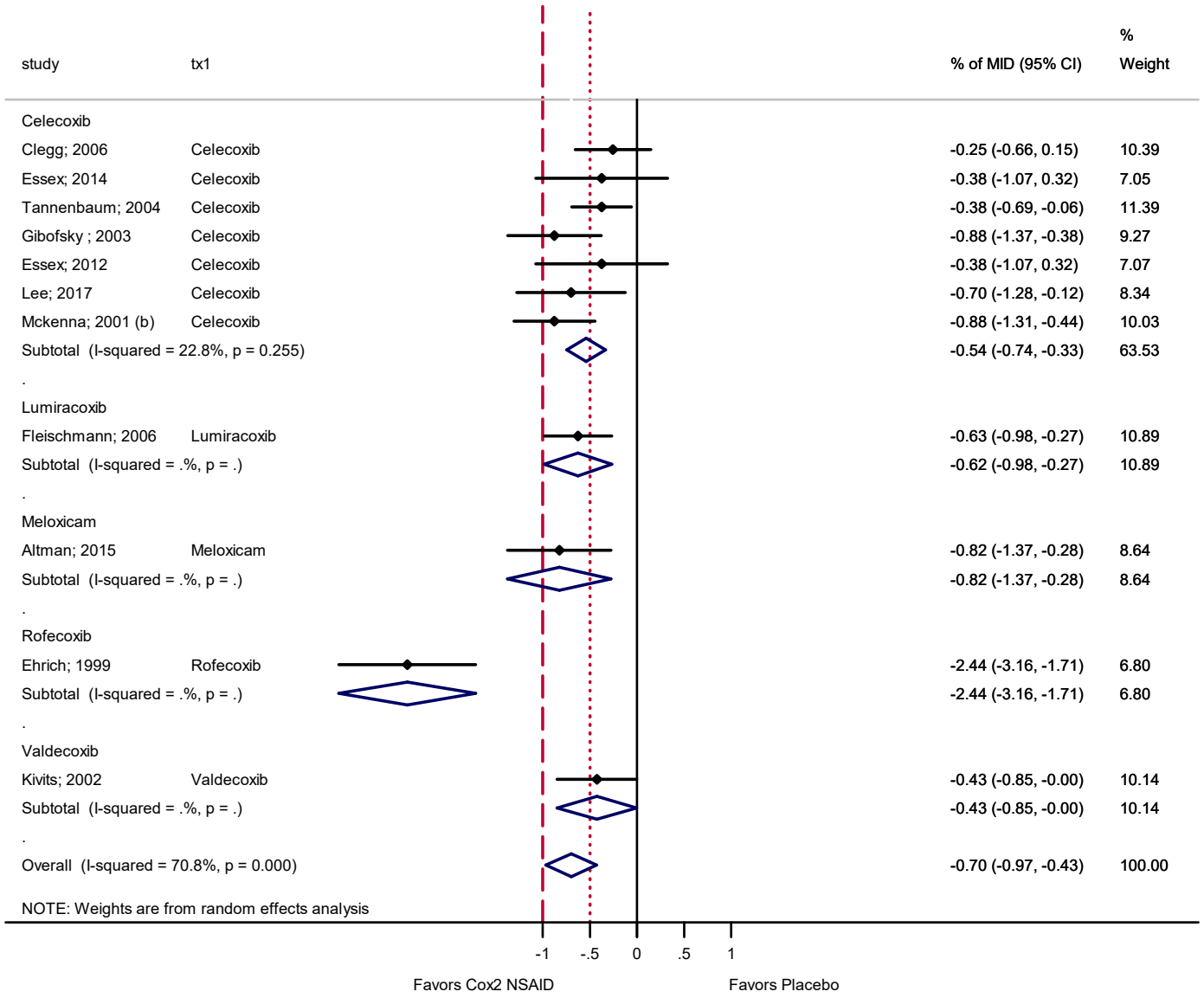
Meta-Analysis Figure 25: Cox2 vs Placebo- Pain



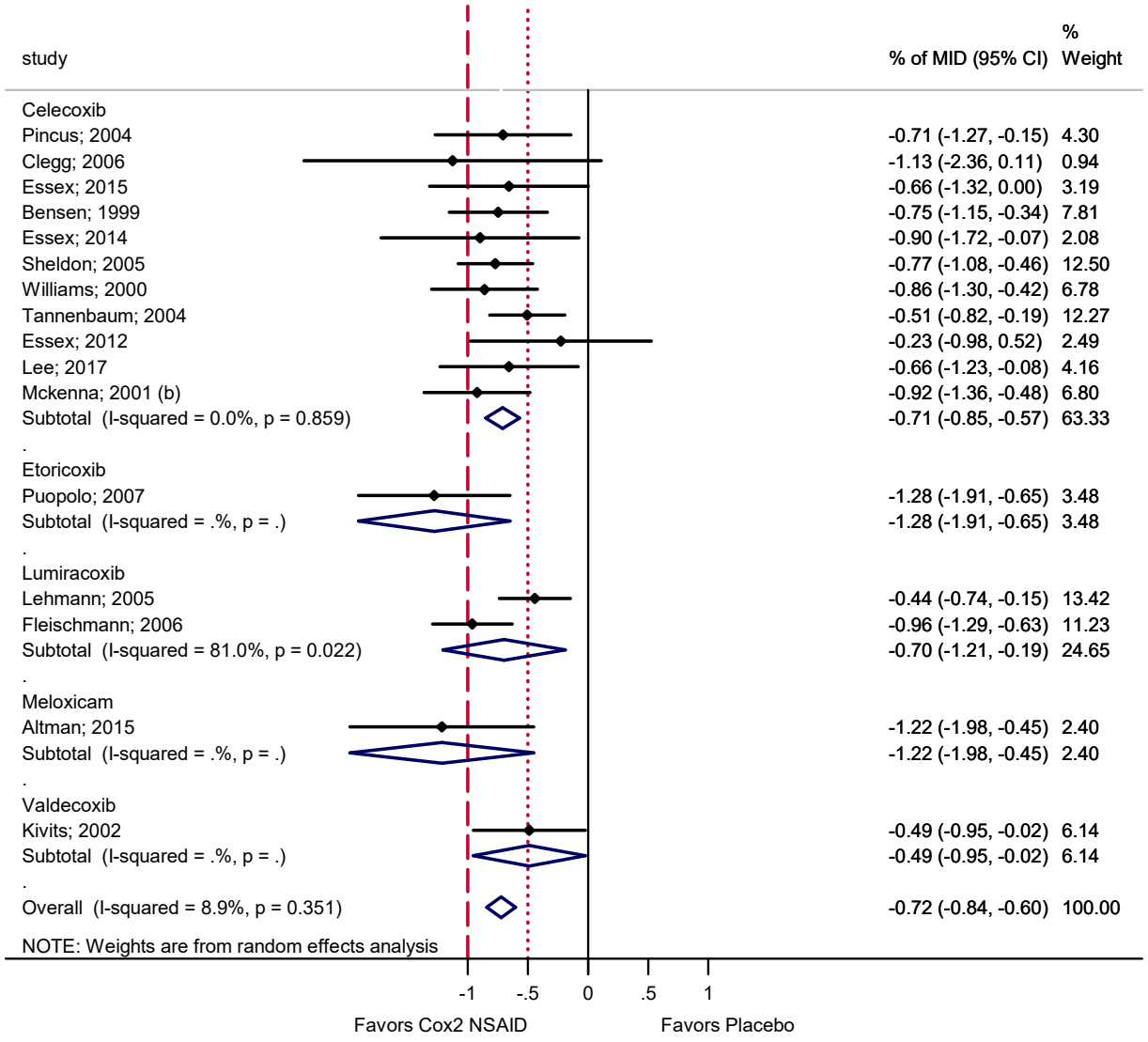
Meta-Analysis Figure 26: Cox2 vs Placebo- Function



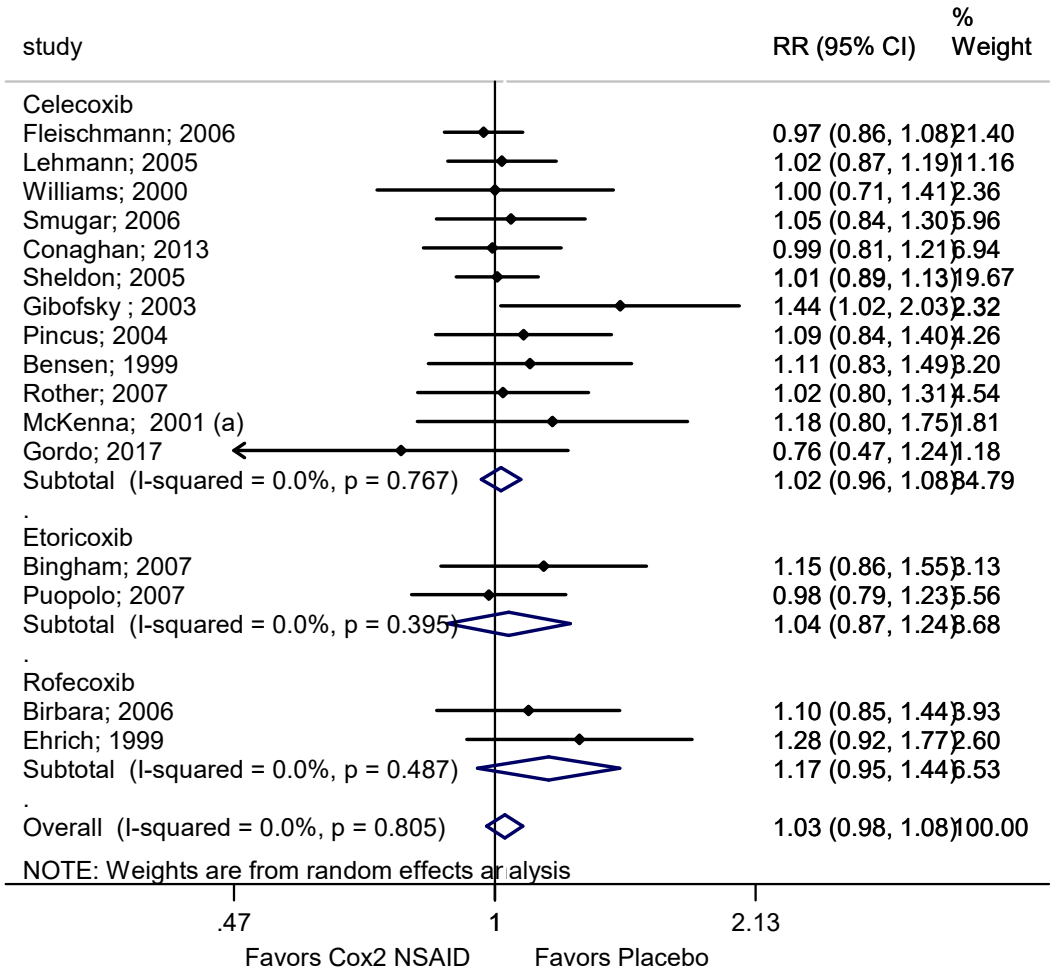
Meta-Analysis Figure 27: Cox2 vs Placebo- Stiffness



Meta-Analysis Figure 28: Cox2 vs Placebo- WOMAC Total



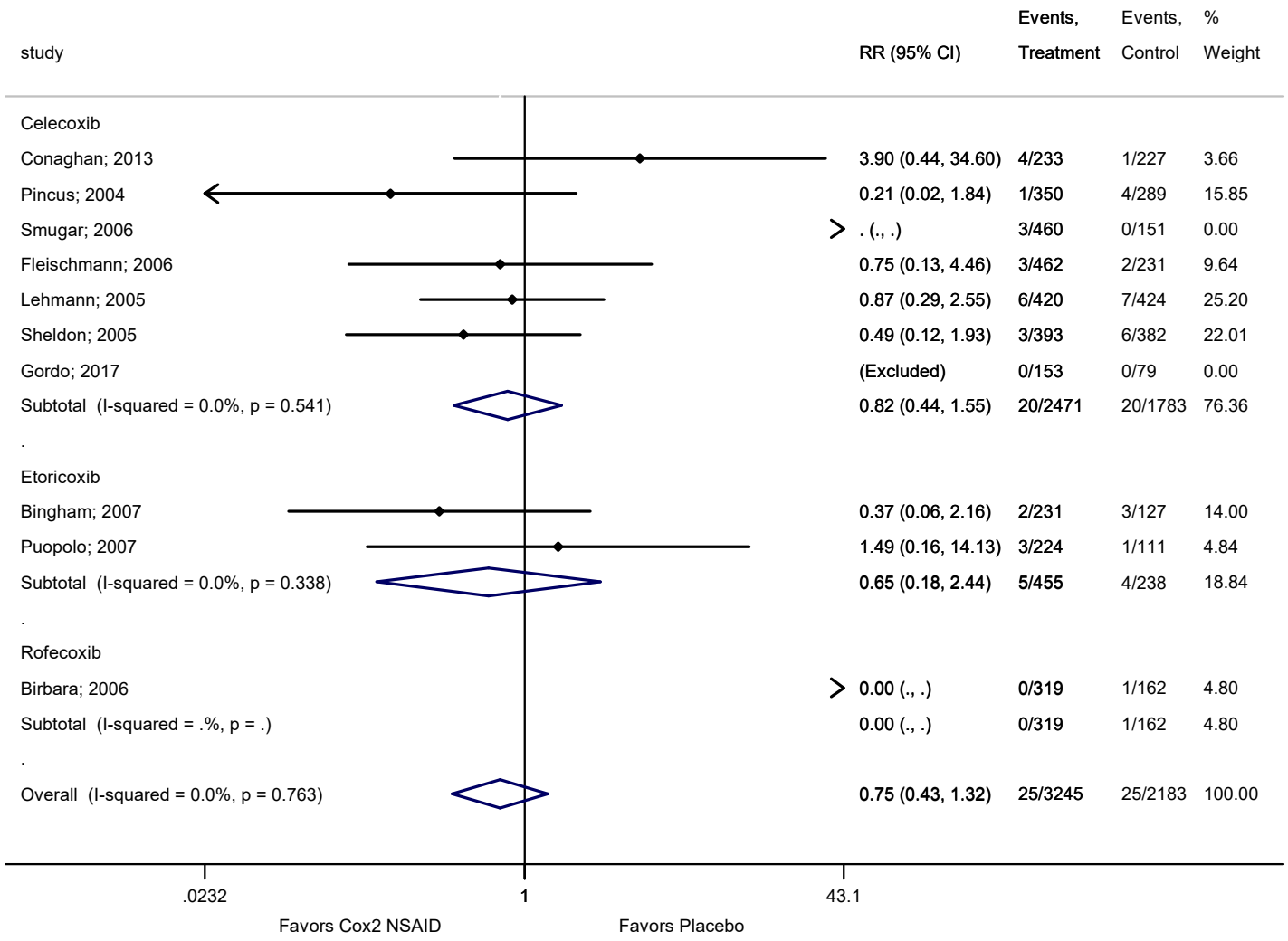
Meta-Analysis Figure 29: Cox2 vs Placebo- Overall Adverse Events



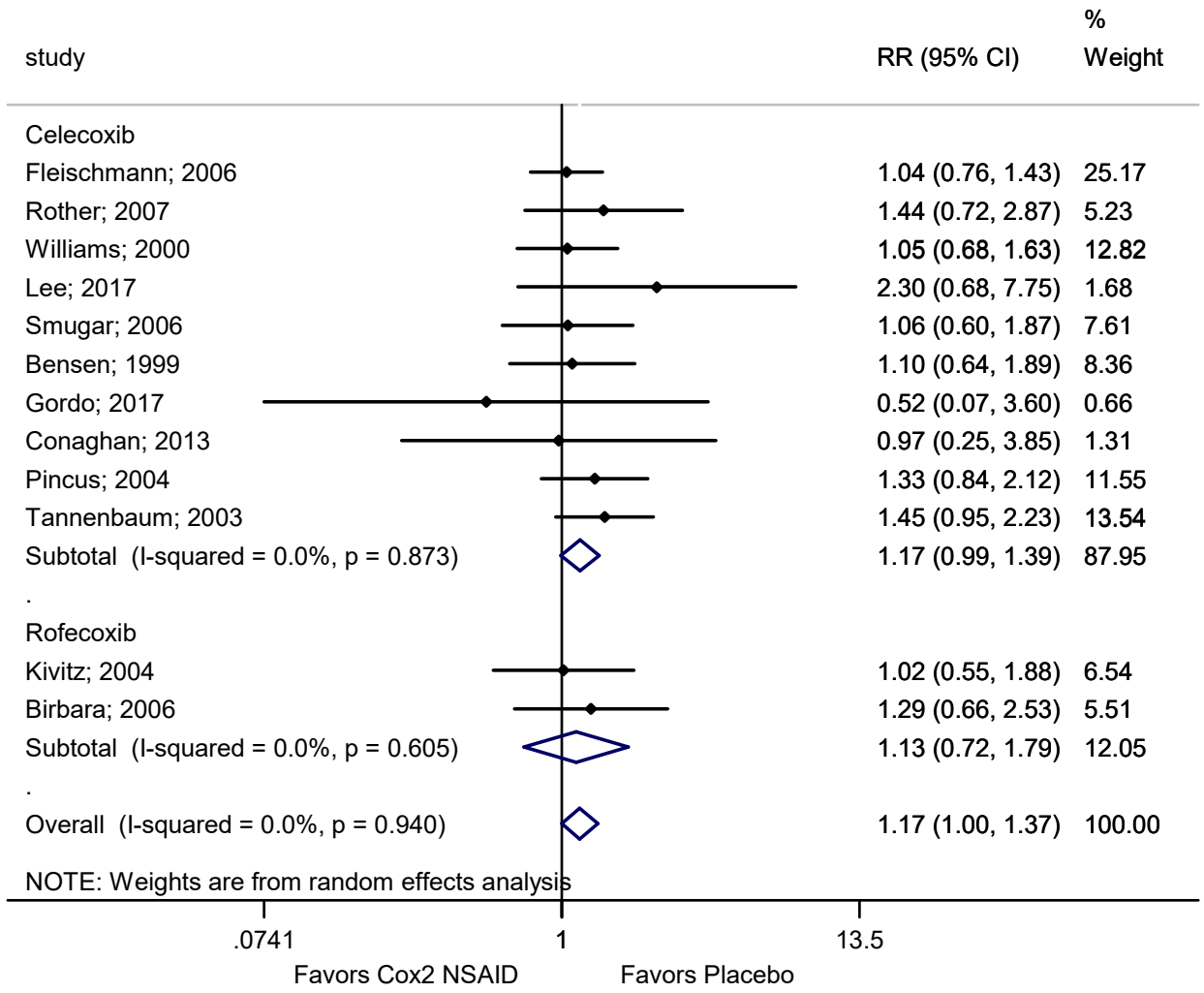
NNTH=83

number of excess AEs per 1000=13(-10,36)

Meta-Analysis Figure 30: Cox2 vs Placebo- Serious Adverse Events



Meta-Analysis Figure 31: Cox2 vs Placebo- GI Adverse Events



NNTH=65

number of excess AEs per 1000=16(-1,34)

Evidence Table 4336: Cox2 vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	#N/A:Oedema Peripheral(ITT Population)	6 wks	147/71	4.76%/0%	RD	4.762(0.021, 10.444)	Group 2	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	other:OMERACT-OARSI Responder	12 wks	131/129	0%/64.34%	RD	-64.341 (-73.373,-56.6)	Group 2	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	other:OMERACT-OARSI Responder	12 wks	137/129	75.91%/64.34%	RR	1.18(1.01,1.38)	Group 1	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib Oral(100mg 2x/day)	9: Placebo/Control-Oral Placebo(2x/day)	Pain:% Response to Tx(50+% reduction in WOMAC Pain vs. Baseline)	12 wks	233/227	42.92%/29.52%	RR	1.454(1.133, 1.867)	Group 1	na
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Pain:HAQ Pain score	24 weeks	313/318	-20.2(27.4)/-16.6(28)	Mean Diff	-3.6(-7.93,0.73)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Pain:Pain intensity in target knee; mm	13 wks	391/382	-25.1(25.87)/-18.1(25.51)	Mean Diff	-7(-10.63,-3.37)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg with loading dose; once daily	9: Placebo/Control-placebo	Pain:Pain intensity in target knee; mm	13 wks	385/382	-25.9(25.84)/-18.1(25.51)	Mean Diff	-7.8(-11.44,-4.16)	Group 1	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib (cox 2) with loading dose 100mg 1 times per day	9: Placebo/Control-placebo	Pain:Patient global assessment of disease activiity vas improvement	13 wks	420/424	21.9(25.5)/18.9(24.79)	Mean Diff	3(-0.4,6.4)	Not Sig.	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-celecoxib (cox 2) 200mg 1 times per day	9: Placebo/Control-placebo	Pain:Patient global assessment of disease activiity vas improvement	13 wks	420/424	22.9(24.64)/18.9(24.79)	Mean Diff	4(0.66,7.34)	Group 2	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib (cox 2) 100mg 1 times per day	9: Placebo/Control-placebo	Pain:Patient global assessment of disease activiity vas improvement	13 wks	420/424	25.1(23.97)/18.9(24.79)	Mean Diff	6.2(2.91,9.49)	Group 2	clinically insignificant
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Pain:Patient's Assessment of Arthris Pain (VAS)	6 wks	100/46	31.5(24)/36.5(28.49)	Mean Diff	-5(-14.64,4.64)	Not Sig.	clinically insignificant
Reginster; 2017/High	9: NSAIDs (oral/IM)-Celecoxib [Oral](200mg x1/day x6mo)	9: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	30 days	195/204	46.9(20.95)/49.7(20)	Mean Diff	-2.8(-6.83,1.23)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reginster; 2017/High	9: NSAIDs (oral/IM)-Celecoxib [Oral](200mg x1/day x6mo)	9: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	91 days	182/188	38.3(22.93)/41.2(21.94)	Mean Diff	-2.9(-7.49,1.69)	Not Sig.	clinically insignificant
Reginster; 2017/High	9: NSAIDs (oral/IM)-Celecoxib [Oral](200mg x1/day x6mo)	9: Placebo/Control-Placebo(x1/day x 6mo)	Pain:VAS Pain	182 days	173/172	30.5(22.36)/36.8(22.3)	Mean Diff	-6.3(-11.03,-1.57)	Group 1	clinically insignificant
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	122/56	-34.5(24.63)/-28.4(25.52)	Mean Diff	-6.1(-14.18, 1.98)	Not Sig.	clinically insignificant
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	96/47	24.3(23.52)/35.4(26.74)	Mean Diff	-11.1(-20.21,-1.99)	Group 1	possibly clinically significant
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Pain:VAS Pain	6 wks	121/58	21.7(20.9)/25.6(23.61)	Mean Diff	-3.9(-11.11, 3.31)	Not Sig.	clinically insignificant
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Pain:VAS Pain Walking	6 wks	672	none	Mean Difference	-15.1(-19.2,-11)	Group 1	na
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Pain:VAS Pain improvement	13 weeks	444/231	-27.4(27.72)/-21.3(26.33)	Mean Diff	-6.1(-10.37,-1.83)	Group 1	clinically insignificant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Pain:VAS Pain improvement	13 weeks	462/231	-28.7(28.36)/-21.3(26.33)	Mean Diff	-7.4(-11.68,-3.12)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Pain:VAS Pain improvement	13 weeks	463/231	-29.7(27.22)/-21.3(26.33)	Mean Diff	-8.4(-12.62,-4.18)	Group 1	clinically insignificant
Asmus; 2014/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg x1/day)	9: Placebo/Control-Placebo (Oral)	Pain:VAS Pain(0-100)	42 days	186/184	-27.3(16)/-14.9(14.53)	Mean Diff	-12.4(-15.52,-9.28)	Group 1	some may benefit
Asmus; 2014/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg x1/day)	9: Placebo/Control-Placebo (Oral)	Pain:VAS Pain(0-100)	42 days	194/186	-28(.)/-24.6(.)	Mean Diff(p value)	-3.4(p=.183)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:VAS Pain(0-100)	42 days	189/182	-21.8(26.53)/-7.6(26.85)	Mean Diff	-14.2(-19.65,-8.75)	Group 1	some may benefit
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:VAS Pain(0-100)	42 days	181/172	-19(25.7)/-10.5(25.18)	Mean Diff	-8.5(-13.83,-3.17)	Group 1	clinically insignificant
McKenna; 2001 (a)/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:VAS Pain(Arthritis Pain; 0-100)	42 days	63/60	none	pvalue	Sig (p < 0.05)	celecoxib p=.002	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Rofecoxib(25mg Q.D.)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:VAS Pain(Arthritis Pain; 0-101)	42 days	59/60	none	pvalue	Sig (p < 0.05)	rofecoxib p=.003	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:VAS Pain(OA pain intensity in target knee; 0-100)	91 days	393/382	-24.1(26.4)/-18.1(25.51)	Mean Diff	-6(-9.66,-2.34)	Group 1	clinically insignificant
Gibofsky ; 2003/High	9: Cox 2 agents-rofecoxib(25)	9: Placebo/Control-placebo	Pain:VAS pain on walking improvement	6 weeks	190/96	-29.2(27.57)/-19.2(37.12)	Mean Diff	-10(-18.47,-1.53)	Group 1	some may benefit
Gibofsky ; 2003/High	9: Cox 2 agents-celecoxib(200)	9: Placebo/Control-placebo	Pain:VAS pain on walking improvement	6 weeks	189/96	-31.5(27.5)/-19.2(37.12)	Mean Diff	-12.3(-20.77,-3.83)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-celecoxib (cox 2) 200mg 1 times per day	9: Placebo/Control-placebo	Pain:VAS physician global assement	13 weeks	444/231	24.5(24.25)/18.3(25.18)	Mean Diff	6.2(2.24,10.16)	Group 2	clinically insignificant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib (cox2) 400mg 1 times per day	9: Placebo/Control-placebo	Pain:VAS physician global assessment	13 weeks	463/231	-26.7(24.3)/-18.3(25.18)	Mean Diff	-8.4(-12.34,-4.46)	Group 1	clinically insignificant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib (cox2) 200mg 1 times per day	9: Placebo/Control-placebo	Pain:VAS physician global assessment	13 weeks	462/231	-27.2(24.61)/-18.3(25.18)	Mean Diff	-8.9(-12.86,-4.94)	Group 1	clinically insignificant
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	96/47	-5.2(3.92)/-4(4.11)	Mean Diff	-1.2(-2.63,0.23)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain	42 days	145/76	1.6%/0%	Mean Diff	-1.3(-2.56,-0.04)	Group 1	possibly clinically significant
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Pain:WOMAC Pain	6 wks	124/65	-4.9(4.45)/-4.7(4.84)	Mean Diff	-0.2(-1.63,1.23)	Not Sig.	clinically insignificant
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:WOMAC Pain	91 days	393/382	-3.4(4.21)/-2.3(3.84)	Mean Diff	-1.1(-1.67,-0.53)	Group 1	possibly clinically significant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Pain:WOMAC Pain	13 wks	481/243	-3.1(3.8)/-2.4(3.8)	Mean Diff	-0.7(-1.29,-0.11)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Pain:WOMAC Pain	13 wks	491/243	-3.2(3.8)/-2.4(3.8)	Mean Diff	-0.8(-1.39,-0.21)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Pain:WOMAC Pain	13 wks	487/243	-3.2(4.3)/-2.4(3.8)	Mean Diff	-0.8(-1.41,-0.19)	Group 1	clinically insignificant
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Pain:WOMAC Pain (0-10)	84 days	233/227	-1.9(1.62)/-1.42(1.62)	Mean Diff	-0.48(-0.78,-0.18)	Group 1	some may benefit
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Pain:WOMAC Pain (VAS Version)	12 wks	272	none	pvalue	Sig ($p < 0.05$)	Meloxicam Low Dose favored over Placebo	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Pain:WOMAC Pain (VAS Version)	12 wks	263	none	pvalue	Sig (p < 0.05)	Meloxicam High Dose favored over Placebo	possibly clinically significant
Hochberg; 2011/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Pain:WOMAC Pain (VAS Version)	84 days	244/122	-42.9(13.34)/-38.4(13.32)	Mean Diff	-4.5(-7.41,-1.59)	Group 1	some may benefit
Hochberg; 2011/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Pain:WOMAC Pain (VAS Version)	84 days	242/124	-41.8(12.68)/-35.6(12.94)	Mean Diff	-6.2(-9,-3.4)	Group 1	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain (VAS Version)	42 days	447/146	-33(21.14)/-22(21.75)	Mean Diff	-11(-15.06,-6.94)	Group 1	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain (VAS Version)	42 days	459/150	-30.8(21.42)/-16.7(22.05)	Mean Diff	-14.1(-18.16,-10.04)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Pain:WOMAC Pain (VAS Version)(each item in each subscale is 0-10; modified ITT population)	6 wks	126/66	-6(9.43)/-2.7(8.29)	Mean Diff	-3.3(-5.91,-0.69)	Group 1	possibly clinically significant
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Pain:WOMAC Pain (VAS Version)(each item in each subscale is 0-10; modified ITT population)	6 wks	132/66	-6.3(9.54)/-2.7(8.29)	Mean Diff	-3.6(-6.2,-1)	Group 1	possibly clinically significant
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain (VAS Version)(study 1)	14 days	160/81	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain (VAS Version)(study 1)	28 days	160/78	none	pvalue	Sig (p < 0.05)	rofecoxib	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain (VAS Version)(study 2)	42 days	158/78	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC Pain (VAS Version)(study2)	28 days	158/81	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Pain:WOMAC pain score	24 weeks	313/318	-100(102.9)/-86.1(114.2)	Mean Diff	-13.9(-30.89, 3.09)	Not Sig.	clinically insignificant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Pain:WOMAC pain subscale score	13 wks	391/382	-3.6(4.2)/-2.3(3.84)	Mean Diff	-1.3(-1.87,-0.73)	Group 1	possibly clinically significant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg with loading dose; once daily	9: Placebo/Control-placebo	Pain:WOMAC pain subscale score	13 wks	385/382	-3.7(4.16)/-2.3(3.84)	Mean Diff	-1.4(-1.97,-0.83)	Group 1	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC pain(night pain; 0-100)	28 days	447/146	-35.1(42.28)/-25.1(26.57)	Mean Diff	-10(-15.84,-4.16)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC pain(night pain; 0-100)	14 days	447/146	-33.2(14.78)/-22.6(25.4)	Mean Diff	-10.6(-14.97,-6.23)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC pain(night pain; 0-100)	42 days	447/146	-36.2(25.35)/-25.1(26.57)	Mean Diff	-11.1(-16.03,-6.17)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC pain(night pain; 0-100)	28 days	459/150	-32.5(25.69)/-20(29.37)	Mean Diff	-12.5(-17.78,-7.22)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC pain(night pain; 0-100)	42 days	459/150	-33(21.42)/-20.5(30.62)	Mean Diff	-12.5(-17.81,-7.19)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Pain:WOMAC pain(night pain; 0-100)	14 days	459/150	-32.1(23.61)/-18(20.81)	Mean Diff	-14.1(-18.09,-10.11)	Group 1	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib(25mg qd)	9: Placebo/Control-	Pain:change in WOMAC pain (VAS)	6 weeks	202	none	adusted mean difference	-10(-16,-4)	Group 1	possibly clinically significant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib 200mg (cox2)	9: Placebo/Control-placebo	Pain:patient global assessment disease activity vas improvement	13 wks	487/243	23.2(26.9)/15.7(26.1)	Mean Diff	7.5(3.43,11.57)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib 400mg (cox2)	9: Placebo/Control-placebo	Pain:patient global assessment disease activity vas improvement	13 wks	491/243	24.1(25)/15.7(26.1)	Mean Diff	8.4(4.43,12.37)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib 200mg (cox2)	9: Placebo/Control-placebo	Pain:patient global assessment of disease activity vas improvement	13 wks	481/243	22.4(25.7)/15.7(26.1)	Mean Diff	6.7(2.68,10.72)	Group 1	clinically insignificant
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 25 mg cox 5	9: Placebo/Control-placebo	Pain:patient global assessment of diseast status vas improvement	6 weeks	73/72	31.48(23.02)/9.58(18.77)	Mean Diff	21.9(15.01,28.79)	Group 2	possibly clinically significant
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 125 mg cox 5	9: Placebo/Control-placebo	Pain:patient global assessment of diseast status vas improvement	6 weeks	73/72	33.26(20.12)/9.58(18.77)	Mean Diff	23.68(17.29, 30.07)	Group 2	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib 200mg once daily	9: Placebo/Control-placebo	Pain:patient global response to treatment good or excellent (study1)	6 wks	447/146	49.89%/28.08%	RR	1.78(1.35,2.34)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Pain:patient global response to treatment good or excellent (study1)	6 wks	448/146	54.24%/28.08%	RR	1.93(1.47,2.54)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Pain:patient global response to treatment good or excellent (study1)	6 wks	452/146	57.3%/28.08%	RR	2.04(1.56,2.68)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib 200mg once daily	9: Placebo/Control-placebo	Pain:patient global response to treatment good or excellent (study2)	6 wks	459/148	49.89%/26.35%	RR	1.89(1.42,2.52)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Pain:patient global response to treatment good or excellent (study2)	6 wks	464/148	57.97%/26.35%	RR	2.2(1.66,2.91)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib 200mg (cox2)	9: Placebo/Control-placebo	Pain:physician global assessment disease status vas improvement	13 wks	487/243	23(22.4)/18(24.3)	Mean Diff	5(1.34, 8.66)	Group 2	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib 400mg (cox2)	9: Placebo/Control-placebo	Pain:physician global assessment disease status vas improvement	13 wks	491/243	23.6(21.4)/18(24.3)	Mean Diff	5.6(2,9.2)	Group 2	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib (cox 2) with loading dose 100mg 1 times per day	9: Placebo/Control-placebo	Pain:physician global assessment of disease activity vas improvement	13 wks	420/424	25(21.88)/20.4(22.28)	Mean Diff	4.6(1.62,7.58)	Group 2	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-celecoxib (cox 2) 200mg 1 times per day	9: Placebo/Control-placebo	Pain:physician global assessment of disease activity vas improvement	13 wks	420/424	25.4(21.64)/20.4(22.28)	Mean Diff	5(2.03, 7.97)	Group 2	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib (cox 2) 100mg 1 times per day	9: Placebo/Control-placebo	Pain:physician global assessment of disease activity vas improvement	13 wks	420/424	26.3(21.9)/20.4(22.28)	Mean Diff	5.9(2.92,8.88)	Group 2	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib 200mg (cox2)	9: Placebo/Control-placebo	Pain:physician global assessment of disease status vas improvement	13 wks	481/243	22.4(22)/18(24.3)	Mean Diff	4.4(0.76,8.04)	Group 2	clinically insignificant
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Pain:study 1 WOMAC pain	26 wks	228/126	39.6(22.9)/54.2(24.6)	Mean Diff	-14.6(-19.85,-9.35)	Group 1	clinically significant
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Pain:study 2 WOMAC pain	26 wks	243/112	41.6(23.7)/51.8(24.8)	Mean Diff	-10.2(-15.71,-4.69)	Group 1	possibly clinically significant
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib(25)	9: Placebo/Control-placebo	Pain:vas pain improvement	6 weeks	73/72	-36.03(21.66)/-15.4(21)	Mean Diff	-20.63(-27.63,-13.63)	Group 1	possibly clinically significant
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib(125)	9: Placebo/Control-placebo	Pain:vas pain improvement	6 weeks	73/72	-38(19.01)/-15.4(21)	Mean Diff	-22.6(-29.18,-16.02)	Group 1	possibly clinically significant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(10)	9: Placebo/Control-placebo	Pain:vas pain improvement	12 wks	205/205	-30.41(14.83)/-25.97(29.59)	Mean Diff	-4.44(-8.99,0.11)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(5)	9: Placebo/Control-placebo	Pain:vas pain improvement	12 wks	201/205	-31.33(29.58)/-25.97(29.59)	Mean Diff	-5.36(-11.13, 0.41)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(10)	9: Placebo/Control-placebo	Pain:vas pain improvement	6 wks	205/205	-29.85(27.87)/-23.92(27.76)	Mean Diff	-5.93(-11.33,-0.53)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(20)	9: Placebo/Control-placebo	Pain:vas pain improvement	12 wks	201/205	-32.7(14.86)/-25.97(29.59)	Mean Diff	-6.73(-11.29,-2.17)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(5)	9: Placebo/Control-placebo	Pain:vas pain improvement	6 wks	201/205	-30.81(27.78)/-23.92(27.76)	Mean Diff	-6.89(-12.31,-1.47)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(20)	9: Placebo/Control-placebo	Pain:vas pain improvement	6 wks	201/205	-32.28(27.88)/-23.92(27.76)	Mean Diff	-8.36(-13.79,-2.93)	Group 1	clinically insignificant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib(100)	9: Placebo/Control-placebo	Pain:vas pain improvement	6 wks	199/200	-34.9(28.1)/-23.1(28)	Mean Diff	-11.8(-17.32,-6.28)	Group 1	some may benefit
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Pain:vas pain improvement	13 wks	481/243	-25.2(24.7)/-19.8(26.1)	Mean Diff	-5.4(-9.37,-1.43)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Pain:vas pain improvement	13 wks	487/243	-26(36.3)/-19.8(26.1)	Mean Diff	-6.2(-10.81,-1.59)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Pain:vas pain improvement	13 wks	491/243	-27.4(24.5)/-19.8(26.1)	Mean Diff	-7.6(-11.54,-3.66)	Group 1	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib (cox 2) with loading dose(100)	9: Placebo/Control-placebo	Pain:vas pain improvement	13 wks	420/424	-26.2(24.08)/-21.4(23.97)	Mean Diff	-4.8(-8.05,-1.55)	Group 1	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Pain:vas pain improvement	13 wks	420/424	-26.6(23.65)/-21.4(23.97)	Mean Diff	-5.2(-8.42,-1.98)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib(100)	9: Placebo/Control-placebo	Pain:vas pain improvement	13 wks	420/424	-26.8(23.82)/-21.4(23.97)	Mean Diff	-5.4(-8.63,-2.17)	Group 1	clinically insignificant
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Pain:womac (vas change from baseline)-Pain (0-100 VAS change from baseline)	12 weeks	20/109	-28.14(6.61)/-16.47(21.46)	Mean Diff	-11.67(-16.69,-6.65)	Group 1	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Pain:womac night pain study 1	6 wks		none	pvalue	Sig (p < 0.05)	rofecoxib	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Pain:womac night pain study 1	6 wks		none	pvalue	Sig (p < 0.05)	rofecoxib	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Pain:womac night pain study 2	6 wks		none	pvalue	Sig (p < 0.05)	rofecoxib	na
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib(125)	9: Placebo/Control-placebo	Pain:womac pain	6 weeks	73/72	-5.6(3.63)/-1.41(4.09)	Mean Diff	-4.19(-5.46,-2.92)	Group 1	clinically significant
Gibofsky ; 2003/High	9: Cox 2 agents-rofecoxib(25)	9: Placebo/Control-placebo	Pain:womac pain	6 weeks	190/96	-4.6(4.14)/-2.6(3.92)	Mean Diff	-2(-2.99,-1.01)	Group 1	possibly clinically significant
Gibofsky ; 2003/High	9: Cox 2 agents-celecoxib(200)	9: Placebo/Control-placebo	Pain:womac pain	6 weeks	189/96	-4.7(4.12)/-2.6(3.92)	Mean Diff	-2.1(-3.09,-1.11)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib(100)	9: Placebo/Control-placebo	Pain:womac pain	6 wks	199/200	-4(4)/-2.4(4.2)	Mean Diff	-1.6(-2.41,-0.79)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Pain:womac pain	13 weeks	444/231	-3.5(4.11)/-2.3(3.9)	Mean Diff	-1.2(-1.83,-0.57)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Pain:womac pain	13 weeks	462/231	-3.7(4.14)/-2.3(3.9)	Mean Diff	-1.4(-2.03,-0.77)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Pain:womac pain	13 weeks	463/231	-3.7(4.14)/-2.3(3.9)	Mean Diff	-1.4(-2.03,-0.77)	Group 1	possibly clinically significant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib (cox 2) with loading dose(100)	9: Placebo/Control-placebo	Pain:womac pain	13 wks	420/424	-3.2(3.74)/-2.5(4.12)	Mean Diff	-0.7(-1.23,-0.17)	Group 1	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Pain:womac pain	13 wks	420/424	-3.4(3.67)/-2.5(4.12)	Mean Diff	-0.9(-1.43,-0.37)	Group 1	some may benefit
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib(100)	9: Placebo/Control-placebo	Pain:womac pain	13 wks	420/424	-3.4(3.93)/-2.5(4.12)	Mean Diff	-0.9(-1.44,-0.36)	Group 1	some may benefit
Rother; 2007/High	9: NSAIDs (oral/IM)-celecoxib	9: Placebo/Control-placebo	Pain:womac pain	6 wks	132/127	-20.7(22.7)/-12.4(20.8)	Mean Diff	-8.3(-13.62,-2.98)	Group 1	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Pain:womac pain(study 1)	6 wks	451/146	-34.2(21.24)/-22(21.75)	Mean Diff	-12.2(-16.26,-8.14)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Pain:womac pain(study 1)	6 wks	454/146	-35.5(21.31)/-22(21.75)	Mean Diff	-13.5(-17.56,-9.44)	Group 1	clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Pain:womac pain(study 2)	6 wks	465/150	-34.5(21.56)/-16.7(22.05)	Mean Diff	-17.8(-21.86,-13.74)	Group 1	clinically significant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Function:WOMAC DPDA subscale score	13 wks	391/382	-11.9(12.95)/-6.3(11.8)	Mean Diff	-5.6(-7.35,-3.85)	Group 1	possibly clinically significant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg with loading dose; once daily	9: Placebo/Control-placebo	Function:WOMAC DPDA subscale score	13 wks	385/382	-12(13.4)/-6.3(11.8)	Mean Diff	-5.7(-7.49,-3.91)	Group 1	possibly clinically significant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Function:WOMAC Function	13 wks	481/243	-9.2(11.6)/-6.2(11.8)	Mean Diff	-3(-4.81,-1.19)	Group 1	some may benefit
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Function:WOMAC Function	13 wks	491/243	-9.7(12.6)/-6.2(11.8)	Mean Diff	-3.5(-5.36,-1.64)	Group 1	some may benefit
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Function:WOMAC Function	13 wks	487/243	-9.8(12.1)/-6.2(11.8)	Mean Diff	-3.6(-5.44,-1.76)	Group 1	some may benefit
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Function:WOMAC Function (VAS Version)	12 wks	272	none	pvalue	Sig (p < 0.05)	Meloxicam Low Dose favored over Placebo	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Function:WOMAC Function (VAS Version)	12 wks	263	none	pvalue	Sig (p < 0.05)	Meloxicam High Dose favored over Placebo	possibly clinically significant
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Function:WOMAC Function (VAS Version)(each item in each subscale is 0-10; modified ITT population)	6 wks	132/66	-16.2(29.41)/-8.4(25.75)	Mean Diff	-8.3(-14.8-1.9)	Group 1	possibly clinically significant
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Function:WOMAC Function (VAS Version)(each item in each subscale is 0-10; modified ITT population)	6 wks	126/66	-16.7(29.07)/-8.4(25.75)	Mean Diff	-8.3(-16.39,-0.21)	Group 1	possibly clinically significant
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Function:WOMAC Physical Function	6 wks	96/47	-16.3(13.72)/-11.1(13.03)	Mean Diff	-5.2(-9.89,-0.51)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Function:WOMAC Physical Function	6 wks	124/65	-16(14.48)/-14.4(13.71)	Mean Diff	-1.6(-5.83,2.63)	Not Sig.	inconclusive
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Function:WOMAC Stiffness	6 wks	132/66	-1.9(4.25)/-0.5(3.66)	Mean Diff	-1.4(-2.55,-0.25)	Group 1	possibly clinically significant
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Function:WOMAC Stiffness	6 wks	126/66	-1.9(4.27)/-0.5(3.66)	Mean Diff	-1.4(-2.57,-0.23)	Group 1	possibly clinically significant
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	96/47	-1.9(1.96)/-1.6(1.37)	Mean Diff	-0.3(-0.86,0.26)	Not Sig.	inconclusive
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 wks	124/65	-1.8(2.23)/-1.5(1.61)	Mean Diff	-0.3(-0.86,0.26)	Not Sig.	inconclusive
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Function:WOMAC Stiffness	13 wks	481/243	-1.2(1.7)/-0.9(1.6)	Mean Diff	-0.3(-0.55,-0.05)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Function:WOMAC Stiffness	13 wks	487/243	-1.2(1.8)/-0.9(1.6)	Mean Diff	-0.3(-0.56,-0.04)	Group 1	clinically insignificant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Function:WOMAC Stiffness	13 wks	491/243	-0.9(1.2)/-0.9(1.6)	Mean Diff	0(-0.23,0.23)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Function:WOMAC Stiffness (VAS Version)	12 wks	272	none	pvalue	Sig (p < 0.05)	Meloxicam Low Dose favored over Placebo	possibly clinically significant
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Function:WOMAC Stiffness (VAS Version)	12 wks	263	none	pvalue	Sig (p < 0.05)	Meloxicam High Dose favored over Placebo	possibly clinically significant
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Function:WOMAC function score	24 weeks	313/318	-289.3(340.7)/-227.4(362.7)	Mean Diff	-61.9(-116.9,-6.9)	Group 1	clinically insignificant
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(0-100)	42 days	145/76	3.2%/4.92%	Mean Diff	-3.4(-7.19,0.39)	Not Sig.	inconclusive
Hochberg; 2011/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Function:WOMAC function(0-100)	84 days	244/122	-36.8(13.34)/-32.3(13.32)	Mean Diff	-4.5(-7.41,-1.59)	Group 1	some may benefit
Hochberg; 2011/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Function:WOMAC function(0-100)	84 days	242/124	-36.3(12.94)/-30.6(12.94)	Mean Diff	-5.7(-8.51,-2.89)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(0-100)	42 days	447/146	-27.4(21.14)/-16.4(21.75)	Mean Diff	-11(-15.06,-6.94)	Group 1	possibly clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(0-100)	42 days	459/150	-25.3(21.42)/-11.6(20.82)	Mean Diff	-13.7(-17.58,-9.82)	Group 1	clinically significant
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Function:WOMAC function(0-68)	91 days	393/382	-10.8(13.07)/-6.3(11.8)	Mean Diff	-4.5(-6.25,-2.75)	Group 1	possibly clinically significant
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(study 1)	42 days	160/78	none	pvalue	NS	Not Sig.	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(study 1)	28 days	160/78	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(study 2)	28 days	158/81	none	pvalue	Sig (p < 0.05)	rofecoxib	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Function:WOMAC function(study2)	42 days	158/81	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Function:WOMAC stiffness score	24 weeks	313/318	-41.5(50.3)/-36.4(52.3)	Mean Diff	-5.1(-13.12, 2.92)	Not Sig.	clinically insignificant
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Function:study 1 WOMAC function	26 wks	228/125	42.2(22.9)/54.6(23.9)	Mean Diff	-12.4(-17.56,-7.24)	Group 1	possibly clinically significant
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Function:study 2 WOMAC function	26 wks	243/112	44.2(24.1)/53.9(24.2)	Mean Diff	-9.7(-15.14,-4.26)	Group 1	possibly clinically significant
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Function:womac (vas change from baseline)-Function (0-100 VAS change from baseline)	12 weeks	219/109	-23.46(23.01)/-13.56(21.2)	Mean Diff	-9.9(-14.94,-4.86)	Group 1	possibly clinically significant
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib(125)	9: Placebo/Control-placebo	Function:womac function	6 weeks	73/72	-18.12(12.54)/-4.44(11.93)	Mean Diff	-13.68(-17.7,-9.66)	Group 1	clinically significant
Gibofsky ; 2003/High	9: Cox 2 agents-rofecoxib(25)	9: Placebo/Control-placebo	Function:womac function	6 weeks	190/96	-13.6(13.78)/-8.2(12.74)	Mean Diff	-5.4(-8.63,-2.17)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-celecoxib(200)	9: Placebo/Control-placebo	Function:womac function	6 weeks	189/96	-14.7(13.74)/-8.2(12.74)	Mean Diff	-6.5(-9.73,-3.27)	Group 1	possibly clinically significant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib(100)	9: Placebo/Control-placebo	Function:womac function	6 wks	199/200	-13.2(12.8)/-8.1(12.7)	Mean Diff	-5.1(-7.61,-2.59)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Function:womac function	13 weeks	463/231	-11.7(12.31)/-6.1(11.71)	Mean Diff	-5.6(-7.49,-3.71)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Function:womac function	13 weeks	462/231	-12.5(13.83)/-6.1(11.71)	Mean Diff	-6.4(-8.37,-4.43)	Group 1	possibly clinically significant
Rother; 2007/High	9: NSAIDs (oral/IM)-celecoxib	9: Placebo/Control-placebo	Function:womac function	6 wks	132/127	-11.29(14.06)/-6.94(13.79)	Mean Diff	-4.35(-7.76,-0.94)	Group 1	possibly clinically significant
Williams; 2000/Moderate	9: NSAIDs (oral/IM)-celecoxib 200MG QD	9: Placebo/Control-placebo	Function:womac function	6 wks	222/231	-36.7(17.88)/-43.5(1976)	Mean Diff	6.8(-249.38,262.98)	Not Sig.	inconclusive
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Function:womac function(study 1)	6 wks	451/146	-29(21.24)/-16.4(21.75)	Mean Diff	-12.6(-16.66,-8.54)	Group 1	clinically significant
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Function:womac function(study 1)	6 wks	454/146	-29.8(21.31)/-16.4(21.75)	Mean Diff	-13.4(-17.46,-9.34)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Function:womac function(study 2)	6 wks	465/150	-28.8(21.56)/-11.6(20.82)	Mean Diff	-17.2(-21.08,-13.32)	Group 1	clinically significant
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib(125)	9: Placebo/Control-placebo	Function:womac stiffness	6 weeks	73/72	-2.55(1.76)/-0.6(1.78)	Mean Diff	-1.95(-2.53,-1.37)	Group 1	clinically significant
Gibofsky ; 2003/High	9: Cox 2 agents-rofecoxib(25)	9: Placebo/Control-placebo	Function:womac stiffness	6 weeks	190/96	-1.7(0.1)/-1.1(0.2)	Mean Diff	-0.6(-0.64,-0.56)	Group 1	some may benefit
Gibofsky ; 2003/High	9: Cox 2 agents-celecoxib(200)	9: Placebo/Control-placebo	Function:womac stiffness	6 weeks	189/96	-1.8(0.1)/-1.1(0.2)	Mean Diff	-0.7(-0.74,-0.66)	Group 1	some may benefit
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(5)	9: Placebo/Control-placebo	Function:womac stiffness	6 wks	201/205	-1.25(1.66)/-1.04(1.64)	Mean Diff	-0.21(-0.53,0.11)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(5)	9: Placebo/Control-placebo	Function:womac stiffness	12 wks	201/205	-1.33(1.81)/-1.12(1.72)	Mean Diff	-0.21(-0.55,0.13)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(10)	9: Placebo/Control-placebo	Function:womac stiffness	12 wks	205/205	-1.41(1.75)/-1.12(1.72)	Mean Diff	-0.29(-0.63,0.05)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(20)	9: Placebo/Control-placebo	Function:womac stiffness	12 wks	201/205	-1.46(1.74)/-1.12(1.72)	Mean Diff	-0.34(-0.68,0)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(10)	9: Placebo/Control-placebo	Function:womac stiffness	6 wks	205/205	-1.42(1.64)/-1.04(1.64)	Mean Diff	-0.38(-0.7,-0.06)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(20)	9: Placebo/Control-placebo	Function:womac stiffness	6 wks	201/205	-1.43(1.66)/-1.04(1.64)	Mean Diff	-0.39(-0.71,-0.07)	Group 1	clinically insignificant
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib(100)	9: Placebo/Control-placebo	Function:womac stiffness	6 wks	199/200	-1.6(1.8)/-0.9(1.7)	Mean Diff	-0.7(-1.04,-0.36)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Function:womac stiffness	13 weeks	463/231	-1.4(1.88)/-0.9(1.78)	Mean Diff	-0.5(-0.79,-0.21)	Group 1	some may benefit
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Function:womac stiffness	13 weeks	462/231	-1.6(2)/-0.9(1.78)	Mean Diff	-0.7(-0.99,-0.41)	Group 1	possibly clinically significant
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Stiffness:womac (vas change from baseline) stiffness subscale (0-100 VAS change from baseline)	12 weeks	218/109	-24.6(24.87)/-16.26(22.91)	Mean Diff	-8.34(-13.79,-2.89)	Group 1	possibly clinically significant
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib(100)	9: Placebo/Control-placebo	Composite:Lequesne Index	6 wks	241/243	11.5(0.03)/12.8(0.03)	Mean Diff	-1.3(-1.31,-1.29)	Group 1	na
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Composite:Lequesne Index	6 wks	231/243	11.5(0.03)/44(1.2)	Mean Diff	-32.5(-32.65,-32.35)	Group 1	na
Williams; 2000/Moderate	9: NSAIDs (oral/IM)-celecoxib 100MG BID	9: Placebo/Control-placebo	Composite:Lequesne Index	6 wks	231/231	11.6(4.56)/13.1(4.56)	Mean Diff	-1.5(-2.33,-0.67)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williams; 2000/Moderate	9: NSAIDs (oral/IM)-celecoxib 200MG QD	9: Placebo/Control-placebo	Composite:Lequesne Index	6 wks	222/231	11.3(4.57)/13.1(4.56)	Mean Diff	-1.8(-2.64,-0.96)	Group 1	na
Reginster; 2017/High	9: NSAIDs (oral/IM)-Celecoxib [Oral](200mg x1/day x6mo)	9: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	30 days	195/204	9.1(4.19)/9.8(4.28)	Mean Diff	-0.7(-1.53,0.13)	Not Sig.	na
Reginster; 2017/High	9: NSAIDs (oral/IM)-Celecoxib [Oral](200mg x1/day x6mo)	9: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	91 days	182/188	8(4.05)/8.8(4.11)	Mean Diff	-0.8(-1.63,0.03)	Not Sig.	na
Reginster; 2017/High	9: NSAIDs (oral/IM)-Celecoxib [Oral](200mg x1/day x6mo)	9: Placebo/Control-Placebo(x1/day x 6mo)	Composite:Lequesne Index Score	182 days	173/172	7(3.95)/8(3.93)	Mean Diff	-1(-1.83,-0.17)	Group 1	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Low Dose)(50mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:Likert Pain/Function	84 days	203/203	-3.3(4.56)/-2(4.13)	Mean Diff	-1.3(-2.15,-0.45)	Group 1	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (High Dose)(200mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:Likert Pain/Function	84 days	202/203	-3.4(3.84)/-2(4.13)	Mean Diff	-1.4(-2.18,-0.62)	Group 1	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Middle Dose)(100mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:Likert Pain/Function	84 days	197/203	-3.8(4.07)/-2(4.13)	Mean Diff	-1.8(-2.61,-0.99)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Composite:Normalized WOMAC score	24 weeks	313/318	-57.7(59.8)/-48.8(65.1)	Mean Diff	-8.9(-18.67, 0.87)	Not Sig.	inconclusive
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	96/47	-23.1(19.6)/-16(17.82)	Mean Diff	-7.1(-13.61,-0.59)	Group 1	possibly clinically significant
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Composite:WOMAC Total	42 days	145/76	3.2%/1.64%	Mean Diff	-5.2(-10.41, 0.01)	Not Sig.	inconclusive
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Composite:WOMAC Total	6 wks	124/65	-22.6(20.04)/-20.8(19.35)	Mean Diff	-1.8(-7.73,4.13)	Not Sig.	clinically insignificant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Low Dose)(50mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:WOMAC Total	84 days	203/203	-9.5(15.82)/-6.1(15.53)	Mean Diff	-3.4(-6.46,-0.34)	Group 1	clinically insignificant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (High Dose)(200mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:WOMAC Total	84 days	202/203	-12(17.34)/-6.1(15.53)	Mean Diff	-5.9(-9.12,-2.68)	Group 1	possibly clinically significant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Middle Dose)(100mg bid)	9: Placebo/Control-Placebo (Oral)	Composite:WOMAC Total	84 days	197/203	-13.3(16.42)/-6.1(15.53)	Mean Diff	-7.2(-10.34,-4.06)	Group 1	possibly clinically significant
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-celecoxib(200)	9: Placebo/Control-placebo	Composite:WOMAC Total	13 wks	481/243	-13.4(15.8)/-9.4(16.1)	Mean Diff	-4(-6.47,-1.53)	Group 1	some may benefit
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Composite:WOMAC Total	13 wks	491/243	-14.1(16.9)/-9.4(16.1)	Mean Diff	-4.7(-7.22,-2.18)	Group 1	some may benefit

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2004/High	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Composite:WOMAC Total	13 wks	487/243	-14.1(16.8)/-9.4(16.1)	Mean Diff	-4.7(-7.22,-2.18)	Group 1	some may benefit
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Composite:WOMAC Total (VAS Version)	6 wks	263	none	pvalue	Sig (p < 0.05)	Meloxicam High Dose favored over Placebo	possibly clinically significant
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Composite:WOMAC Total (VAS Version)	12 wks	263	none	pvalue	Sig (p < 0.05)	Meloxicam High Dose favored over Placebo	possibly clinically significant
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Composite:WOMAC Total (VAS Version)	6 wks	272	none	pvalue	Sig (p < 0.05)	Meloxicam Low Dose favored over Placebo	possibly clinically significant
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Composite:WOMAC Total (VAS Version)	12 wks	272	none	pvalue	Sig (p < 0.05)	Meloxicam Low Dose favored over Placebo	possibly clinically significant
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total (VAS Version)	42 days	181/172	-10.4(20.72)/-4.8(21.77)	Mean Diff	-5.6(-10.05,-1.15)	Group 1	possibly clinically significant
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total (VAS Version)	42 days	189/182	-13.5(18.7)/-4.6(20.1)	Mean Diff	-8.9(-12.87,-4.93)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total(0-96)	91 days	393/382	-15.6(18.32)/-9.5(16.33)	Mean Diff	-6.1(-8.55,-3.65)	Group 1	possibly clinically significant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Composite:WOMAC total score	13 wks	391/382	-16.9(18.04)/-9.5(16.33)	Mean Diff	-7.4(-9.83,-4.97)	Group 1	possibly clinically significant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg with loading dose; once daily	9: Placebo/Control-placebo	Composite:WOMAC total score	13 wks	385/382	-17.2(18.56)/-9.5(16.33)	Mean Diff	-7.7(-10.18,-5.22)	Group 1	possibly clinically significant
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Composite:WOMAC-OA Index (VAS Version)(each item in each subscale is 0-10; modified ITT population)	6 wks	132/66	-24.5(41.48)/-11.5(36.23)	Mean Diff	-13(-24.34,-1.66)	Group 1	possibly clinically significant
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Composite:WOMAC-OA Index (VAS Version)(each item in each subscale is 0-10; modified ITT population)	6 wks	126/66	-24.7(41.08)/-11.5(36.23)	Mean Diff	-13.2(-24.6,-1.8)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(50mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in WOMAC composite(0-96)	12 weeks	203/203	-9.5(15.82)/-6.1(15.53)	Mean Diff	-3.4(-6.46,-0.34)	Group 1	clinically insignificant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(200mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in WOMAC composite(0-96)	12 weeks	202/203	-12(17.34)/-6.1(15.53)	Mean Diff	-5.9(-9.12,-2.68)	Group 1	possibly clinically significant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in WOMAC composite(0-96)	12 weeks	197/203	-13.3(16.42)/-6.1(15.53)	Mean Diff	-7.2(-10.34,-4.06)	Group 1	possibly clinically significant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(50mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in likert Pain/Function(0-24)	12 weeks	203/203	-3.3(4.56)/-2(4.13)	Mean Diff	-1.3(-2.15,-0.45)	Group 1	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(200mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in likert Pain/Function(0-24)	12 weeks	202/203	-3.4(3.84)/-2(4.13)	Mean Diff	-1.4(-2.18,-0.62)	Group 1	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Composite:change in likert Pain/Function(0-24)	12 weeks	197/203	-3.8(4.07)/-2(4.13)	Mean Diff	-1.8(-2.61,-0.99)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib (cox 2) 100mg 2 times per day	9: Placebo/Control-placebo	Composite:patient global assessment	6 wks	241/243	2.8(0.06)/3(1.09)	Mean Diff	-0.2(-0.34,-0.06)	Group 1	na
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib (cox 2) 200mg 4 times per day	9: Placebo/Control-placebo	Composite:patient global assessment	6 wks	231/243	2.6(0.06)/3(0.07)	Mean Diff	-0.4(-0.41,-0.39)	Group 1	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Composite:womac (vas change from baseline) total	12 weeks	218/109	-25.64(22.74)/-15.53(20.94)	Mean Diff	-10.11(-15.09,-5.13)	Group 1	possibly clinically significant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(5)	9: Placebo/Control-placebo	Composite:womac total	6 wks	201/205	-15.47(18.05)/-12.98(18.04)	Mean Diff	-2.49(-6.01,1.03)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(5)	9: Placebo/Control-placebo	Composite:womac total	12 wks	201/205	-16.84(18.92)/-13.48(18.92)	Mean Diff	-3.36(-7.05,0.33)	Not Sig.	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(20)	9: Placebo/Control-placebo	Composite:womac total	12 wks	201/205	-17.22(18.81)/-13.48(18.92)	Mean Diff	-3.74(-7.42,-0.06)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(10)	9: Placebo/Control-placebo	Composite:womac total	6 wks	205/205	-16.74(18.12)/-12.98(18.04)	Mean Diff	-3.76(-7.27,-0.25)	Group 1	clinically insignificant
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(10)	9: Placebo/Control-placebo	Composite:womac total	12 wks	205/205	-17.34(18.96)/-13.48(18.92)	Mean Diff	-3.86(-7.54,-0.18)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-valdecoxib(20)	9: Placebo/Control-placebo	Composite:womac total	6 wks	201/205	-17.33(17.97)/-12.98(18.04)	Mean Diff	-4.35(-7.86,-0.84)	Group 1	some may benefit
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib 100mg BID	9: Placebo/Control-placebo	Composite:womac total	6 wks	241/243	37.6(1.3)/44(1.2)	Mean Diff	-6.4(-6.62,-6.18)	Group 1	some may benefit
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib200mg QD	9: Placebo/Control-placebo	Composite:womac total	6 wks	231/243	37(1.3)/44(1.2)	Mean Diff	-7(-7.23,-6.77)	Group 1	some may benefit
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib(100)	9: Placebo/Control-placebo	Composite:womac total	6 wks	199/200	-18.8(17.5)/-11.5(17.8)	Mean Diff	-7.3(-10.77,-3.83)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(400)	9: Placebo/Control-placebo	Composite:womac total	13 weeks	463/231	-16.9(17.13)/-9.3(16.15)	Mean Diff	-7.6(-10.21,-4.99)	Group 1	possibly clinically significant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib(200)	9: Placebo/Control-placebo	Composite:womac total	13 weeks	462/231	-17.8(18.89)/-9.3(16.15)	Mean Diff	-8.5(-11.21,-5.79)	Group 1	possibly clinically significant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib(100)	9: Placebo/Control-placebo	Composite:womac total	13 wks	420/424	-14.8(16.35)/-11.3(18.27)	Mean Diff	-3.5(-5.84,-1.16)	Group 1	clinically insignificant
Lehmann; 2005/High	9: NSAIDs (oral/IM)-lumiracoxib(100)	9: Placebo/Control-placebo	Composite:womac total	13 wks	420/424	-15.2(16.97)/-11.3(18.27)	Mean Diff	-3.9(-6.28,-1.52)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	QOL:Patient Global Response: Good/Excellent	6 wks	672	none	Odds Ratio	3.39(2.35,4.89)	Group 1	na
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib (cox2) 200mg 1 times per day	9: Placebo/Control-placebo	QOL:vas patient global assessment	13 weeks	462/231	-25.3(28.57)/-16.1(27.45)	Mean Diff	-9.2(-13.61,-4.79)	Group 1	clinically insignificant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-lumiracoxib (cox2) 400mg 1 times per day	9: Placebo/Control-placebo	QOL:vas patient global assessment	13 weeks	463/231	-25.8(28.35)/-16.1(27.45)	Mean Diff	-9.7(-14.09,-5.31)	Group 1	clinically insignificant
Fleischmann; 2006/Low	9: NSAIDs (oral/IM)-celecoxib (cox 2) 200mg 1 times per day	9: Placebo/Control-placebo	QOL:vas patient global assessment	13 weeks	444/231	24.5(27.38)/16.1(27.45)	Mean Diff	8.4(4.03,12.77)	Group 2	clinically insignificant
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Other:HAQ Alternative Disability score	24 weeks	313/318	-0.2(0.35)/-0.16(0.36)	Mean Diff	-0.04(-0.1,0.02)	Not Sig.	na
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Other:No. of 500-mg tablets of acetaminophen	24 weeks	313/318	1.6(1.7)/1.8(1.8)	Mean Diff	-0.2(-0.47,0.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib 200mg once daily	9: Placebo/Control-placebo	Other:OARSI responders	13 wks	393/382	61.58%/49.21%	RR	1.25(1.1,1.42)	Group 1	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Other:OARSI responders	13 wks	391/382	64.71%/49.21%	RR	1.31(1.16,1.49)	Group 1	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Other:OARSI responders	13 wks	385/382	66.75%/49.21%	RR	1.36(1.2,1.54)	Group 1	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Other:PGADS (0-100 VAS change from baseline)	12 weeks	220/107	-29.5(25.63)/-17.85(23.79)	Mean Diff	-11.65(-17.32,-5.98)	Group 2	some may benefit
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Other:PGART (0-4 Likert scale change from baseline)	12 weeks	20/108	1.61(0.32)/2.29(1.05)	Mean Diff	-0.68(-0.93,-0.43)	Group 2	na
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Other:Patient's global assessment of disease status score	24 weeks	313/318	-14.9(27.1)/-13.6(27.5)	Mean Diff	-1.3(-5.57,2.97)	Not Sig.	na
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Other:Patient's global assessment of response to therapy score	24 weeks	313/318	41.7(31)/-45.2(30.5)	Mean Diff	86.9(82.09,91.71)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Clegg; 2006/High	9: Cox 2 agents-Celecoxib	9: Placebo/Control-placebo	Other:Physician's global assessment of disease status	24 weeks	313/318	-13.2(23)/-14.6(23.4)	Mean Diff	1.4(-2.23,5.03)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Other:Stiffness subscale(study 1)	6 wks	451/146	-32.9(23.36)/-17.6(22.96)	Mean Diff	-15.3(-19.62,-10.98)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Other:Stiffness subscale(study 1)	6 wks	454/146	-33.6(23.44)/-17.6(22.96)	Mean Diff	-16(-20.32,-11.68)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Other:Stiffness subscale(study 2)	6 wks	465/150	-32.5(21.56)/-13.9(23.27)	Mean Diff	-18.6(-22.83,-14.37)	Group 1	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg with loading dose; once daily	9: Placebo/Control-placebo	Other:WOMAC stiffness subscale score	13 wks	385/382	-1.5(1.87)/-0.9(1.68)	Mean Diff	-0.6(-0.85,-0.35)	Group 1	possibly clinically significant
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Other:WOMAC stiffness subscale score	13 wks	391/382	-1.5(1.85)/-0.9(1.68)	Mean Diff	-0.6(-0.85,-0.35)	Group 1	possibly clinically significant
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(50mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Other:improved global assessment	12 weeks	203/203	13.3%/11.82%	pvalue	1.13(.67, 1.88)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Other:improved global assessment	12 weeks	197/203	17.77%/11.82%	pvalue	1.50(.93, 2.431)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib (Oral)(200mg twice a day)	9: Placebo/Control-Placebo (Oral)(twice a day)	Other:improved global assessment	12 weeks	202/203	17.82%/11.82%	pvalue	1.51(.93, 2.43)	Not Sig.	na
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 25 mg cox 4	9: Placebo/Control-placebo	Other:investigator global assessment of disease status improvement	6 weeks	73/72	1.52(0.95)/0.53(0.94)	Mean Diff	0.99(0.68,1.3)	Group 2	na
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 125 mg cox 4	9: Placebo/Control-placebo	Other:investigator global assessment of disease status improvement	6 weeks	73/72	1.58(0.73)/0.53(0.94)	Mean Diff	1.05(0.77,1.33)	Group 2	na
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 125 mg cox 7	9: Placebo/Control-placebo	Other:investigator global assessment of disease status improvement	6 weeks	73/72	2.86(0.88)/1.56(1.24)	Mean Diff	1.3(0.95,1.65)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 25 mg cox 7	9: Placebo/Control-placebo	Other:investigator global assessment of response to treatment	6 weeks	73/72	2.81(1.02)/1.56(1.24)	Mean Diff	1.25(0.88,1.62)	Group 2	na
Conaghan; 2013/High	9: NSAIDs (oral/IM)-oral celecoxib 100mg bid	9: Placebo/Control-oral placebo	Other:need for omeprazole for dyspepsia	84 days	233/227	15.88%/13.22%	RR	1.2(0.77,1.88)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Other:patient global assessment (0-100) study 1	26 wks	228/126	41.3(22.7)/56.7(23.6)	Mean Diff	-15.4(-20.49,-10.31)	Group 1	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Other:patient global assessment (0-100) study 2	26 wks	243/111	43.8(22.9)/59.4(24.4)	Mean Diff	-15.6(-21.01,-10.19)	Group 1	na
Williams; 2000/Moderate	9: NSAIDs (oral/IM)-celecoxib 100mg (cox2)	9: Placebo/Control-placebo	Other:patient global assessment of arthritis (5=worse rating)	6 wks	231/231	2.6(1.52)/3.1(1.52)	Mean Diff	-0.5(-0.78,-0.22)	Group 1	na
Williams; 2000/Moderate	9: NSAIDs (oral/IM)-celecoxib 200mg (cox2)	9: Placebo/Control-placebo	Other:patient global assessment of arthritis (5=worse rating)	6 wks	222/231	2.6(1.52)/2.6(1.52)	Mean Diff	0(-0.28,0.28)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib 200mg once daily	9: Placebo/Control-placebo	Other:patient global assessment of disease status(study 1)	6 wks	447/146	-31.8(23.26)/-17.3(22.96)	Mean Diff	-14.5(-18.82,-10.18)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Other:patient global assessment of disease status(study 1)	6 wks	451/146	-32.8(23.36)/-17.3(22.96)	Mean Diff	-15.5(-19.82,-11.18)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Other:patient global assessment of disease status(study 1)	6 wks	454/146	-34.4(23.44)/-17.3(22.96)	Mean Diff	-17.1(-21.42,-12.78)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib 200mg once daily	9: Placebo/Control-placebo	Other:patient global assessment of disease status(study 2)	6 wks	459/150	-30.5(23.57)/-14.4(23.27)	Mean Diff	-16.1(-20.42,-11.78)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Other:patient global assessment of disease status(study 2)	6 wks	465/150	-33.7(23.72)/-14.4(23.27)	Mean Diff	-19.3(-23.62,-14.98)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib (cox2)	9: Placebo/Control-placebo	Other:patient global assessment of improvement	6 wks	199/200	1.4(1.1)/0.9(1.2)	Mean Diff	0.5(0.27,0.73)	Group 2	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-placebo	Other:patient global assessment of response to therapy	6 weeks	98/104	67.35%/31.73%	RR	2.12(1.55,2.9)	Group 1	na
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 25 mg cox 6	9: Placebo/Control-placebo	Other:patient global assessment of response to treatment	6 weeks	73/72	2.63(0.91)/1.33(1.2)	Mean Diff	1.3(0.95,1.65)	Group 2	na
Ehrich; 1999/Moderate	9: NSAIDs (oral/IM)-rofecoxib 125 mg cox 6	9: Placebo/Control-placebo	Other:patient global assessment of response to treatment	6 weeks	73/72	2.81(0.78)/1.33(1.2)	Mean Diff	1.48(1.15,1.81)	Group 2	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Other:patient global assessment of treatment response(study 1)	28 days	160/78	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Other:patient global assessment of treatment response(study 1)	42 days	160/78	none	pvalue	Sig (p < 0.05)	rofecoxib	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Other:patient global assessment of treatment response(study 2)	28 days	158/81	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Other:patient global assessment of treatment response(study2)	42 days	158/81	none	pvalue	Sig (p < 0.05)	rofecoxib	na
Mckenna; 2001 (b)/Moderate	9: NSAIDs (oral/IM)-celecoxib (cox2)	9: Placebo/Control-placebo	Other:phyician global assessment of improvement	6 wks	199/200	1.3(0.95)/0.9(1.1)	Mean Diff	0.4(0.2,0.6)	Group 2	na
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib (cox 2) 100mg 2 times per day	9: Placebo/Control-placebo	Other:physician global assessment	6 wks	241/243	2.7(0.06)/3(0.06)	Mean Diff	-0.3(-0.31,-0.29)	Group 1	na
Williams; 2001/Moderate	9: NSAIDs (oral/IM)-celecoxib (cox 2) 200mg 4 times per day	9: Placebo/Control-placebo	Other:physician global assessment	6 wks	231/243	2.6(0.06)/3(0.06)	Mean Diff	-0.4(-0.41,-0.39)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-20mg valdecoxib (cox2)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	6 wks	201/205	-1.41(0.98)/-1.22(0.99)	Mean Diff	-0.19(-0.38,0)	Not Sig.	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-5mg valdecoxib (cox-2)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	12 wks	201/205	-1.43(1.09)/-1.22(1.02)	Mean Diff	-0.21(-0.42,0)	Group 1	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-5mg valdecoxib (cox-2)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	6 wks	201/205	-1.44(0.98)/-1.22(0.99)	Mean Diff	-0.22(-0.41,-0.03)	Group 1	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-20mg valdecoxib (cox2)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	12 wks	201/205	-1.45(1.05)/-1.22(1.02)	Mean Diff	-0.23(-0.43,-0.03)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: NSAIDs (oral/IM)-10mg valdecoxib (cox2)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	6 wks	205/205	-1.5(0.99)/-1.22(0.99)	Mean Diff	-0.28(-0.47,-0.09)	Group 1	na
Kivits; 2002/High	9: NSAIDs (oral/IM)-10mg valdecoxib (cox2)	9: Placebo/Control-placebo	Other:physician global assessment of arthritis improvement (5 = very poor)	12 wks	205/205	-1.52(1.06)/-1.22(1.02)	Mean Diff	-0.3(-0.5,-0.1)	Group 1	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Other:womac (vas change from baseline) questionnaire overall score average (0-100 VAS change from baseline)	12 weeks	218/109	-24.9(22.66)/-14.43(20.83)	Mean Diff	-10.47(-15.43,-5.51)	Group 1	possibly clinically significant
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:ALT Increased	6 wks	199/200	0.5%/2.5%	RR	0.2(0.02,1.71)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Abdominal Discomfort	12 wks	138/133	0.72%/0%	RD	0.725(-2.541, 3.595)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Abdominal Discomfort	12 wks	131/133	1.53%/0%	RD	1.527(-2.342, 4.544)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal Distension	6 wks	104/107	1.92%/0%	RD	1.923(-2.896, 5.659)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	153/79	0.65%/1.27%	RR	0.52(0.03,8.15)	Not Sig.	na
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	125/61	1.6%/0%	RD	1.6(-2.446, 7.637)	Not Sig.	na
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	145/76	6.21%/3.95%	RR	1.57(0.44,5.64)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	125/66	0.8%/4.55%	RR	0.18(0.02,1.66)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	190/96	1.05%/2.08%	RR	0.51(0.07,3.53)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	189/96	1.59%/2.08%	RR	0.76(0.13,4.48)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	12 wks	203/203	1.97%/1.97%	RR	1(0.25,3.94)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	12 wks	197/203	2.03%/1.97%	RR	1.03(0.26,4.06)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	12 wks	202/203	3.47%/1.97%	RR	1.76(0.52,5.91)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	199/200	3.52%/7%	RR	0.5(0.21,1.22)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	13 wks	487/243	4.72%/2.47%	RR	1.91(0.79,4.64)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	13 wks	491/243	5.09%/2.47%	RR	2.06(0.86,4.96)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	13 wks	481/243	5.2%/2.47%	RR	2.1(0.88,5.06)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	132/127	3.03%/2.36%	RR	1.28(0.29,5.62)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	231/231	0.87%/1.3%	RR	0.67(0.11,3.95)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain	6 wks	222/231	1.35%/1.3%	RR	1.04(0.21,5.1)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Abdominal Pain - Upper(ITT Population)	6 wks	147/71	0.68%/1.41%	RR	0.48(0.03,7.61)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Abdominal Pain - Upper(ITT Population)	6 wks	144/71	2.78%/1.41%	RR	1.97(0.22,17.32)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >1%	12 wks	188/178	1.06%/2.25%	RR	0.47(0.09,2.55)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >1%	12 wks	185/178	1.08%/2.25%	RR	0.48(0.09,2.59)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >1%	12 wks	174/178	2.87%/2.25%	RR	1.28(0.35,4.68)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >5%	12 wks	185/178	6.49%/9.55%	RR	0.68(0.33,1.38)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >5%	12 wks	188/178	6.91%/9.55%	RR	0.72(0.36,1.45)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain >5%	12 wks	174/178	8.62%/9.55%	RR	0.9(0.47,1.75)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain Upper	13 wks	420/424	2.62%/1.42%	RR	1.85(0.69,4.96)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain Upper	13 wks	420/424	3.33%/1.42%	RR	2.36(0.91,6.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Abdominal Pain Upper	13 wks	420/424	3.57%/1.42%	RR	2.52(0.99,6.44)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Abdominal Pain(ITT Population)	6 wks	144/71	0%/1.41%	RD	-1.408(-4.254, 4.739)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Abdominal Pain(ITT Population)	6 wks	147/71	2.04%/1.41%	RR	1.45(0.15,13.68)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Abdominal distension	6 weeks	104/107	1.92%/0%	RD	1.923(-2.896, 5.659)	Not Sig.	na
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Abdominal pain	42 days	145/76	6.21%/3.95%	RR	1.57(0.44,5.64)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Abdominal pain	84 days	233/227	1.72%/1.32%	RR	1.3(0.29,5.74)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abnormal Hepatic Function >1%	12 wks	185/178	0%/0%	RD	0(-2.034, 2.113)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abnormal Hepatic Function >1%	12 wks	174/178	0%/0%	RD	0(-2.16,2.113)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Abnormal Hepatic Function >1%	12 wks	188/178	1.06%/0%	RD	1.064(-1.668, 3.313)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Accidental Injury >1%	12 wks	188/178	0%/1.12%	RD	-1.124(-3.285, 1.756)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Accidental Injury >1%	12 wks	174/178	0%/1.12%	RD	-1.124(-3.432, 1.756)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Accidental Injury >1%	12 wks	185/178	0.54%/1.12%	RR	0.48(0.04,5.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Accidential Injury	6 wks	189/96	1.06%/2.08%	RR	0.51(0.07,3.55)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Accidential Injury	6 wks	190/96	2.11%/2.08%	RR	1.01(0.19,5.42)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Accidential Injury >5%	12 wks	188/178	1.6%/5.62%	RR	0.28(0.08,1.02)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Accidential Injury >5%	12 wks	174/178	5.17%/5.62%	RR	0.92(0.38,2.21)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Accidential Injury >5%	12 wks	185/178	5.95%/5.62%	RR	1.06(0.46,2.43)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Acid Reflux	6 wks	424/208	0.24%/0.96%	RR	0.25(0.02,2.69)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Adverse Event Causing Withdrawal	6 wks	190/96	5.26%/5.21%	RR	1.01(0.36,2.87)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Adverse Event Causing Withdrawal	6 wks	189/96	5.82%/5.21%	RR	1.12(0.4,3.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Adverse Event Causing Withdrawl	6 wks	222/231	1.8%/3.9%	RR	0.46(0.14,1.48)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Adverse Event Causing Withdrawl	6 wks	231/231	2.16%/3.9%	RR	0.56(0.19,1.63)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Adverse Events	91 days	393/382	58.78%/58.38%	RR	1.01(0.89,1.13)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Adverse events	13 wks	391/382	64.71%/58.38%	RR	1.11(0.99,1.24)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Adverse events	13 wks	385/382	67.01%/58.38%	RR	1.15(1.03,1.28)	Group 2	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:All gastrointestinal disorders	84 days	233/227	15.88%/14.54%	RR	1.09(0.71,1.68)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:All infections and infestations	84 days	233/227	1.29%/0.44%	RR	2.92(0.31,27.89)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:All nervous system disorders	84 days	233/227	0.86%/2.2%	RR	0.39(0.08,1.99)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Allergic contact dermatitis	84 days	233/227	0%/0%	RD	0(-1.622, 1.664)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Allergic rash	84 days	233/227	0.43%/0%	RD	0.429(-1.532, 2.13)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Anaemia	6 wks	199/200	0.5%/3.5%	RR	0.14(0.02,1.16)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Any AE	12 weeks	224/111	50.45%/51.35%	RR	0.98(0.79,1.23)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	12 wks	224/111	50.45%/51.35%	RR	0.98(0.79,1.23)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	6 wks	190/96	42.11%/30.21%	RR	1.39(0.99,1.97)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	6 wks	189/96	43.39%/30.21%	RR	1.44(1.02,2.03)	Group 2	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Any Adverse Event	42 days	350/289	28.57%/26.3%	RR	1.09(0.84,1.4)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	6 wks	222/231	22.52%/22.51%	RR	1(0.71, 1.41)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	6 wks	231/231	22.94%/22.51%	RR	1.02(0.73,1.43)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Events	6 wks	132/127	50%/48.82%	RR	1.02(0.8,1.31)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Events		241/243	49.38%/47.74%	RR	1.03(0.86,1.24)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Events		231/243	53.68%/47.74%	RR	1.12(0.94,1.34)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Any Drug-Related Adverse Events	12 wks	224/111	28.57%/21.62%	RR	1.32(0.88,1.99)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any Gastrointestinal Disorder(ITT Population)	6 wks	144/71	9.72%/4.23%	RR	2.3(0.68,7.75)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any Gastrointestinal Disorder(ITT Population)	6 wks	147/71	10.2%/4.23%	RR	2.41(0.72,8.07)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Any Gastrointestinal Event	42 days	350/289	12%/9%	RR	1.33(0.84,2.12)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any General Disorder and Administration Site Conditions(ITT Population)	6 wks	144/71	5.56%/2.82%	RR	1.97(0.43,9.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any General Disorder and Administration Site Conditions(ITT Population)	6 wks	147/71	10.88%/2.82%	RR	3.86(0.91,16.35)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any Musculoskeletal and Connective Tissue Disorders(ITT Population)	6 wks	147/71	1.36%/4.23%	RR	0.32(0.06,1.88)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any Musculoskeletal and Connective Tissue Disorders(ITT Population)	6 wks	144/71	1.39%/4.23%	RR	0.33(0.06,1.92)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Any Serious Adverse Events	12 wks	224/111	1.34%/0.9%	RR	1.49(0.16,14.13)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any Skin and Subcutaneous Tissue Disorders(ITT Population)	6 wks	144/71	1.39%/2.82%	RR	0.49(0.07,3.43)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Any Skin and Subcutaneous Tissue Disorders(ITT Population)	6 wks	147/71	3.4%/2.82%	RR	1.21(0.24,6.07)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Any drug-related AE	12 weeks	224/111	28.57%/21.62%	RR	1.32(0.88,1.99)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Any serious AE	12 weeks	224/111	1.34%/0.9%	RR	1.49(0.16,14.13)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Arthalgia	13 wks	491/243	2.24%/4.53%	RR	0.49(0.22,1.13)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Arthalgia	13 wks	481/243	2.91%/4.53%	RR	0.64(0.3,1.39)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Arthalgia	13 wks	487/243	3.08%/4.53%	RR	0.68(0.32,1.46)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Arthralgia	13 wks	385/382	3.38%/4.71%	RR	0.72(0.36,1.44)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Arthralgia	91 days	393/382	3.82%/4.71%	RR	0.81(0.41,1.58)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Arthralgia	13 wks	391/382	4.6%/4.71%	RR	0.98(0.52,1.85)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	13 wks	420/424	1.19%/1.65%	RR	0.72(0.23,2.25)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	13 wks	420/424	1.67%/1.65%	RR	1.01(0.36,2.85)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	13 wks	420/424	2.14%/1.65%	RR	1.3(0.49,3.45)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	132/127	2.27%/3.15%	RR	0.72(0.16,3.16)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	104/107	8.65%/13.08%	RR	0.66(0.3,1.46)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Arthralgia	6 weeks	104/107	8.65%/13.08%	RR	0.66(0.3,1.46)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	222/231	0.45%/1.3%	RR	0.35(0.04,3.31)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Arthralgia	6 wks	231/231	0.87%/1.3%	RR	0.67(0.11,3.95)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:At least one adverse event	84 days	233/227	45.49%/45.81%	RR	0.99(0.81,1.21)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	199/200	2.51%/0.5%	RR	5.03(0.59,42.63)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Back Pain	13 wks	487/243	1.64%/3.29%	RR	0.5(0.19,1.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Back Pain	13 wks	491/243	2.85%/3.29%	RR	0.87(0.37,2.04)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Back Pain	13 wks	481/243	3.53%/3.29%	RR	1.07(0.47,2.45)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	132/127	4.55%/3.15%	RR	1.44(0.42,4.99)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	104/107	11.54%/10.28%	RR	1.12(0.52,2.43)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	222/231	0.9%/1.3%	RR	0.69(0.12,4.11)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Back Pain	6 wks	231/231	1.3%/1.3%	RR	1(0.2,4.9)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Back pain	13 wks	385/382	3.64%/4.71%	RR	0.77(0.39,1.53)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Back pain	91 days	393/382	3.82%/4.71%	RR	0.81(0.41,1.58)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Back pain	13 wks	391/382	4.35%/4.71%	RR	0.92(0.48,1.76)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Back pain	6 weeks	104/107	11.54%/10.28%	RR	1.12(0.52,2.43)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Bloating	84 days	233/227	0.86%/1.32%	RR	0.65(0.11,3.85)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Blurred Vision >1%	12 wks	188/178	0%/1.12%	RD	-1.124(-3.285, 1.756)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Blurred Vision >1%	12 wks	185/178	0%/1.12%	RD	-1.124(-3.315, 1.756)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Blurred Vision >1%	12 wks	174/178	0.57%/1.12%	RR	0.51(0.05,5.59)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Bronchitis	91 days	393/382	0.76%/1.83%	RR	0.42(0.11,1.6)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Bronchitis	13 wks	385/382	2.34%/1.83%	RR	1.28(0.48,3.39)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Bronchitis	13 wks	391/382	3.07%/1.83%	RR	1.67(0.67,4.21)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:CHF; pulmonary edema or cardiac failure	12 weeks	224/111	0.45%/0%	RD	0.446(-1.592, 3.812)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:CHF; pulmonary edema; or cardiac failure	12 wks	224/111	0.45%/0%	RD	0.446(-1.592, 3.812)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Chest Pain	13 wks	463/231	0.43%/0.43%	RR	1(0.09, 10.95)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Chest Pain	13 wks	462/231	0.43%/0.43%	RR	1(0.09, 10.97)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Chest Pain	13 wks	462/231	0.87%/0.43%	RR	2(0.22, 17.79)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Chest Pain	13 wks	481/243	0.42%/0.41%	RR	1.01(0.09,11.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Chest Pain	13 wks	487/243	0.62%/0.41%	RR	1.5(0.16,14.32)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Chest Pain	13 wks	491/243	0.81%/0.41%	RR	1.98(0.22,17.62)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Congestive heart failure	42 days	460/151	0%/0%	RD	0(-0.828, 2.481)	Not Sig.	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:Congestive heart failure	42 days	319/162	0%/0%	RD	0(-1.19,2.316)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:Congestive heart failure(study 1)	6 wks	456/150	0%/0%	RD	0(-0.835, 2.497)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Congestive heart failure(study 1)	6 wks	459/150	0.22%/0%	RD	0.218(-0.788, 2.721)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	145/76	0%/0%	RD	0(-2.581, 4.811)	Not Sig.	na
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Constipation	42 days	145/76	0%/0%	RD	0(-2.581, 4.811)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Constipation	12 wks	138/133	1.45%/1.5%	RR	0.96(0.14,6.74)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Constipation	12 wks	131/133	1.53%/1.5%	RR	1.02(0.15,7.1)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	199/200	1.01%/4%	RR	0.25(0.05,1.17)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	132/127	0%/0.79%	RD	-0.787(-3.689, 2.751)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Constipation	6 weeks	104/107	2.88%/1.87%	RR	1.54(0.26,9.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Constipation	6 wks	104/107	2.88%/1.87%	RR	1.54(0.26,9.05)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Constipation >5%	12 wks	174/178	0.57%/2.81%	RR	0.2(0.02,1.73)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Constipation >5%	12 wks	188/178	2.13%/2.81%	RR	0.76(0.21,2.78)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Constipation >5%	12 wks	185/178	2.16%/2.81%	RR	0.77(0.21,2.82)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Dematitis allergic	6 wks	132/127	0.76%/0%	RD	0.758(-2.651, 3.759)	Not Sig.	na
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Depression	6 wks	125/61	3.2%/4.92%	RR	0.65(0.15,2.82)	Not Sig.	na
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Depression	42 days	145/76	2.76%/2.63%	RR	1.05(0.2,5.59)	Not Sig.	na
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Depression	6 wks	145/76	2.76%/2.63%	RR	1.05(0.2,5.59)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Depression	6 wks	125/66	4%/4.55%	RR	0.88(0.22,3.57)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Depression	6 wks	132/127	2.27%/0%	RD	2.273(-1.923, 5.568)	Not Sig.	na
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Diarrhea	42 days	145/76	0%/0%	RD	0(-2.581, 4.811)	Not Sig.	na
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	145/76	0%/0%	RD	0(-2.581, 4.811)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Diarrhea	12 wks	131/133	2.29%/0.75%	RR	3.05(0.32,28.91)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Diarrhea	12 wks	138/133	2.9%/0.75%	RR	3.86(0.44,34.05)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	125/66	2.4%/1.52%	RR	1.58(0.17,14.93)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	424/208	4.48%/21.15%	RR	0.21(0.13,0.35)	Group 1	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	74/72	4.05%/2.78%	RR	1.46(0.25,8.48)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	73/72	4.11%/2.78%	RR	1.48(0.25,8.59)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	190/96	2.63%/1.04%	RR	2.53(0.3,21.32)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	189/96	4.23%/1.04%	RR	4.06(0.52,32.02)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	197/203	2.54%/2.46%	RR	1.03(0.3,3.5)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	203/203	2.96%/2.46%	RR	1.2(0.37,3.87)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	202/203	3.47%/2.46%	RR	1.41(0.45,4.36)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Diarrhea	91 days	393/382	3.82%/3.4%	RR	1.12(0.54,2.33)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Diarrhea	13 wks	385/382	3.9%/3.4%	RR	1.14(0.55,2.37)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Diarrhea	13 wks	391/382	5.12%/3.4%	RR	1.5(0.76,2.98)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	13 wks	481/243	2.29%/0.82%	RR	2.78(0.62,12.44)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	13 wks	487/243	2.67%/0.82%	RR	3.24(0.74,14.26)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	13 wks	491/243	3.67%/0.82%	RR	4.45(1.04,19.04)	Group 2	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	104/107	7.69%/4.67%	RR	1.65(0.56,4.87)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Diarrhea	6 weeks	104/107	7.69%/4.67%	RR	1.65(0.56,4.87)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	231/231	1.3%/1.3%	RR	1(0.2,4.9)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	6 wks	222/231	2.25%/1.3%	RR	1.73(0.42,7.17)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea		231/243	3.03%/1.23%	RR	2.45(0.64,9.38)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Diarrhea		241/243	4.98%/1.23%	RR	4.03(1.15,14.11)	Group 2	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >1%	12 wks	188/178	0%/0%	RD	0(-2.002, 2.113)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >1%	12 wks	185/178	0.54%/0%	RD	0.541(-1.917, 2.699)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >1%	12 wks	174/178	0.57%/0%	RD	0.575(-2.034, 2.74)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >5%	12 wks	188/178	3.72%/5.06%	RR	0.74(0.28,1.94)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >5%	12 wks	185/178	5.41%/5.06%	RR	1.07(0.44,2.57)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Diarrhea >5%	12 wks	174/178	6.9%/5.06%	RR	1.36(0.59,3.16)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea	6 wks	153/79	2.61%/1.27%	RR	2.07(0.23,18.17)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Diarrhoea	84 days	233/227	1.29%/1.32%	RR	0.97(0.2,4.78)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea	6 wks	199/200	4.52%/6.5%	RR	0.7(0.3,1.59)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea	6 wks	132/127	1.52%/0%	RD	1.515(-2.326, 4.65)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Diarrhoea	42 days	350/289	2.29%/1.38%	RR	1.65(0.5,5.43)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea NOS	13 wks	420/424	2.86%/3.54%	RR	0.81(0.38,1.7)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea NOS	13 wks	420/424	3.57%/3.54%	RR	1.01(0.5,2.04)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Diarrhoea NOS	13 wks	420/424	3.57%/3.54%	RR	1.01(0.5,2.04)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Diarrhoea(ITT Population)	6 wks	147/71	2.04%/0%	RD	2.041(-1.746, 7.347)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Diarrhoea(ITT Population)	6 wks	144/71	2.08%/0%	RD	2.083(-1.779, 7.396)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Discontinuations due to Adverse Events	91 days	393/382	4.07%/6.28%	RR	0.65(0.35,1.2)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Discontinuations due to any Adverse Events	13 wks	420/424	2.38%/4.01%	RR	0.59(0.28,1.28)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Discontinuations due to any Adverse Events	13 wks	420/424	3.33%/4.01%	RR	0.83(0.42,1.66)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Discontinuations due to any Adverse Events	13 wks	420/424	5.48%/4.01%	RR	1.37(0.74,2.52)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Discontinuations due to lack of efficacy(study 1)	6 wks	454/146	5.51%/26.03%	RR	0.21(0.13,0.34)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:Discontinuations due to lack of efficacy(study 1)	6 wks	451/146	8.2%/26.03%	RR	0.32(0.21,0.48)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Discontinuations due to lack of efficacy(study 2)	6 wks	465/150	6.24%/31.33%	RR	0.2(0.13,0.3)	Group 1	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Digestive or Abdominal Pain Adverse Events	12 wks	224/111	1.79%/3.6%	RR	0.5(0.13,1.94)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Drug-Related Adverse Events	12 wks	224/111	3.57%/4.5%	RR	0.79(0.27,2.37)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Edema-Related Adverse Events	12 wks	224/111	0.45%/0%	RD	0.446(-1.592, 3.812)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Hypertension-Related Adverse Events	12 wks	224/111	0.89%/0%	RD	0.893(-1.411, 4.3)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Serious Adverse Events	12 wks	224/111	0.45%/0%	RD	0.446(-1.592, 3.812)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to Serious Drug-Related Adverse Events	12 wks	224/111	0%/0%	RD	0(-1.686, 3.345)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:Discontinued due to adverse events(study 1)	6 wks	456/150	5.04%/5.33%	RR	0.95(0.43,2.07)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Discontinued due to adverse events(study 1)	6 wks	459/150	5.23%/5.33%	RR	0.98(0.45,2.14)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Discontinued due to an Adverse Events	12 wks	224/111	4.91%/4.5%	RR	1.09(0.39,3.06)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Discontinued due to the adverse events	42 days	460/151	2.83%/1.32%	RR	2.13(0.49,9.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	145/76	0%/0%	RD	0(-2.581, 4.811)	Not Sig.	na
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Dizziness	42 days	145/76	0%/0%	RD	0(-2.581, 4.811)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	125/66	2.4%/0%	RD	2.4(-2.019, 8.123)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	74/72	4.05%/2.78%	RR	1.46(0.25,8.48)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	73/72	4.11%/2.78%	RR	1.48(0.25,8.59)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	189/96	0.53%/1.04%	RR	0.51(0.03,8.03)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	190/96	2.63%/1.04%	RR	2.53(0.3,21.32)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	199/200	3.52%/2%	RR	1.76(0.52,5.91)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Dizziness	6 weeks	104/107	5.77%/0.93%	RR	6.17(0.76,50.4)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Dizziness	6 wks	104/107	5.77%/0.93%	RR	6.17(0.76,50.4)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Dry Mouth	12 wks	138/133	1.45%/0%	RD	1.449(-2.231, 4.447)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Dry Mouth	12 wks	131/133	1.53%/0%	RD	1.527(-2.342, 4.544)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Dry Skin	84 days	233/227	0%/0%	RD	0(-1.622, 1.664)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	153/79	2.61%/2.53%	RR	1.03(0.19,5.52)	Not Sig.	na
Essex; 2014/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	125/61	3.2%/1.64%	RR	1.95(0.22,17.09)	Not Sig.	na
Essex; 2016/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	145/76	1.38%/0%	RD	1.379(-2.131, 6.294)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Essex; 2015/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Dyspepsia	42 days	145/76	1.38%/0%	RD	1.379(-2.131, 6.294)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Dyspepsia	84 days	233/227	2.15%/1.32%	RR	1.62(0.39,6.72)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	125/66	0.8%/1.52%	RR	0.53(0.03,8.31)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	424/208	0.71%/4.33%	RR	0.16(0.04,0.6)	Group 1	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	73/72	1.37%/2.78%	RR	0.49(0.05,5.32)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	74/72	5.41%/2.78%	RR	1.95(0.37,10.3)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	224/111	3.13%/3.6%	RR	0.87(0.26,2.9)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Dyspepsia	12 weeks	224/111	3.13%/3.6%	RR	0.87(0.26,2.9)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	190/96	5.26%/3.13%	RR	1.68(0.47,5.98)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	189/96	5.82%/3.13%	RR	1.86(0.53,6.52)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	202/203	4.95%/3.94%	RR	1.26(0.51,3.12)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	197/203	5.08%/3.94%	RR	1.29(0.52,3.2)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	12 wks	203/203	5.42%/3.94%	RR	1.38(0.56,3.35)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	199/200	5.53%/7.5%	RR	0.74(0.35,1.56)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	481/243	3.53%/3.7%	RR	0.95(0.43,2.11)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	487/243	3.9%/3.7%	RR	1.05(0.48,2.29)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	491/243	4.28%/3.7%	RR	1.15(0.54,2.48)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	420/424	3.33%/2.59%	RR	1.28(0.59,2.8)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	420/424	3.81%/2.59%	RR	1.47(0.69,3.13)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	13 wks	420/424	4.05%/2.59%	RR	1.56(0.74,3.29)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	132/127	3.03%/0.79%	RR	3.85(0.44,33.97)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Dyspepsia	42 days	350/289	2.86%/1.04%	RR	2.75(0.76,9.91)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Dyspepsia	6 weeks	104/107	7.69%/5.61%	RR	1.37(0.49,3.82)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	104/107	7.69%/5.61%	RR	1.37(0.49,3.82)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia		231/243	3.9%/4.94%	RR	0.79(0.34,1.84)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia		241/243	6.22%/4.94%	RR	1.26(0.6,2.64)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	222/231	2.25%/1.73%	RR	1.3(0.35,4.78)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia	6 wks	231/231	3.46%/1.73%	RR	2(0.61, 6.55)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >1%	12 wks	185/178	0.54%/1.12%	RR	0.48(0.04,5.26)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >1%	12 wks	188/178	1.06%/1.12%	RR	0.95(0.13,6.65)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >1%	12 wks	174/178	1.72%/1.12%	RR	1.53(0.26,9.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >5%	12 wks	185/178	9.73%/7.3%	RR	1.33(0.67,2.64)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >5%	12 wks	188/178	10.64%/7.3%	RR	1.46(0.75,2.84)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Dyspepsia >5%	12 wks	174/178	10.92%/7.3%	RR	1.5(0.76,2.93)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Dyspepsia(ITT Population)	6 wks	144/71	3.47%/1.41%	RR	2.47(0.29,20.71)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Dyspepsia(ITT Population)	6 wks	147/71	4.76%/1.41%	RR	3.38(0.42,26.96)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Edema Peripheral	12 wks	138/133	0%/1.5%	RD	-1.504(-4.423, 2.309)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Edema Peripheral	12 wks	131/133	1.53%/1.5%	RR	1.02(0.15,7.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Edema-Related Adverse Events	12 wks	224/111	3.57%/1.8%	RR	1.98(0.43,9.18)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Edema-related AE	12 weeks	224/111	3.57%/1.8%	RR	1.98(0.43,9.18)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Edema-related adverse event	42 days	460/151	0%/0%	RD	0(-0.828, 2.481)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Edema-related events causing discontinuation	42 days	460/151	0.22%/0%	RD	0.217(-0.786, 2.705)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:Edema-related events causing discontinuation(study 1)	6 wks	456/150	0.66%/0%	RD	0.658(-0.6,3.192)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Edema-related events causing discontinuation(study 1)	6 wks	459/150	0.87%/0%	RD	0.871(-0.476, 3.425)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Epicondylitis	12 wks	138/133	0%/1.5%	RD	-1.504(-4.423, 2.309)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Epicondylitis	12 wks	131/133	0%/1.5%	RD	-1.504(-4.554, 2.309)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Epigastric Discomfort	6 wks	424/208	2.12%/6.25%	RR	0.34(0.15,0.78)	Group 1	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Epigastric Discomfort	12 wks	224/111	2.68%/1.8%	RR	1.49(0.3,7.25)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Epigastric discomfort	12 weeks	224/111	2.68%/1.8%	RR	1.49(0.3,7.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Erythema	6 wks	132/127	13.64%/16.54%	RR	0.82(0.46,1.47)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Exanthema	84 days	233/227	0%/0%	RD	0(-1.622, 1.664)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Exanthema	6 wks	132/127	1.52%/0.79%	RR	1.92(0.18,20.96)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Face Oedema(ITT Population)	6 wks	144/71	1.39%/1.41%	RR	0.99(0.09,10.69)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Face Oedema(ITT Population)	6 wks	147/71	2.04%/1.41%	RR	1.45(0.15,13.68)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Flatulence	84 days	233/227	0%/2.2%	RD	-2.203(-4.255, 0.646)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Flatulence	6 wks	199/200	2.51%/1.5%	RR	1.68(0.41,6.91)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Flatulence	6 wks	132/127	1.52%/0%	RD	1.515(-2.326, 4.65)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Flatulence	42 days	350/289	2.29%/0.35%	RR	6.61(0.83,52.51)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Flatulence >5%	12 wks	174/178	2.3%/6.18%	RR	0.37(0.12,1.15)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Flatulence >5%	12 wks	188/178	3.72%/6.18%	RR	0.6(0.24,1.52)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Flatulence >5%	12 wks	185/178	4.32%/6.18%	RR	0.7(0.29,1.7)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:GI adverse events	42 days	460/151	9.78%/9.27%	RR	1.06(0.6,1.87)	Not Sig.	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:GI adverse events	42 days	319/162	8.78%/6.79%	RR	1.29(0.66,2.53)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:GI adverse eventss(study 1)	6 wks	456/150	10.09%/8.67%	RR	1.16(0.65,2.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:GI adverse eventss(study 1)	6 wks	459/150	13.94%/8.67%	RR	1.61(0.91,2.84)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Gastric pain	84 days	233/227	3.86%/2.2%	RR	1.75(0.6,5.15)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Gastritis	6 wks	132/127	0%/2.36%	RD	-2.362(-5.59,1.991)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Gastrooesophageal reflux	6 wks	125/66	2.4%/1.52%	RR	1.58(0.17,14.93)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event	13 wks	481/243	14.97%/10.29%	RR	1.45(0.95,2.23)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event	13 wks	487/243	17.45%/10.29%	RR	1.7(1.12,2.58)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event	13 wks	491/243	19.55%/10.29%	RR	1.9(1.26,2.87)	Group 2	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event		231/243	14.72%/13.99%	RR	1.05(0.68,1.63)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event	6 wks	231/231	7.36%/6.06%	RR	1.21(0.61,2.41)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event	6 wks	222/231	7.66%/6.06%	RR	1.26(0.64,2.5)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Adverse Event		241/243	20.33%/13.99%	RR	1.45(0.97,2.17)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Disorders	6 wks	132/127	13.64%/9.45%	RR	1.44(0.72,2.87)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Events (excluding ulcers)	13 wks	462/231	15.58%/17.75%	RR	0.88(0.62,1.25)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Events (excluding ulcers)	13 wks	463/231	20.52%/17.75%	RR	1.16(0.83,1.61)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Events (excluding ulcers)	13 wks	462/231	20.78%/17.75%	RR	1.17(0.84,1.63)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Acid Reflux	6 wks	424/208	0.24%/0%	RD	0.236(-0.852, 2.06)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: At least one Adverse Event	6 wks	424/208	6.84%/6.73%	RR	1.02(0.55,1.88)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Dyspepsia	6 wks	424/208	0.71%/0.48%	RR	1.47(0.15,14.06)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Epigastric Discomfort	6 wks	424/208	2.12%/0.96%	RR	2.21(0.48,10.13)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Heartburn	6 wks	424/208	1.42%/0.96%	RR	1.47(0.3,7.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Nausea	6 wks	424/208	2.36%/4.33%	RR	0.55(0.22,1.32)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Nuisance Adverse Event: Vomitting	6 wks	424/208	0.71%/0.48%	RR	1.47(0.15,14.06)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Causing Withdrawal	12 wks	203/203	0.49%/0.49%	RR	1(0.06, 15.88)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Causing Withdrawal	12 wks	202/203	1.49%/0.49%	RR	3.01(0.32,28.74)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Causing Withdrawal	12 wks	197/203	1.52%/0.49%	RR	3.09(0.32,29.47)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Total	12 wks	202/203	11.88%/10.84%	RR	1.1(0.64,1.89)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Total	12 wks	197/203	13.71%/10.84%	RR	1.26(0.75,2.14)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal Tract Adverse Events Total	12 wks	203/203	13.79%/10.84%	RR	1.27(0.75,2.15)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Gastrointestinal disorder	84 days	233/227	1.72%/1.76%	RR	0.97(0.25,3.85)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	153/79	0%/2.53%	RD	-2.532(-5.592, 3.705)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Headache	12 wks	138/133	1.45%/3.01%	RR	0.48(0.09,2.59)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Headache	12 wks	131/133	3.82%/3.01%	RR	1.27(0.35,4.62)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Headache	84 days	233/227	0%/2.2%	RD	-2.203(-4.255, 0.646)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Headache	6 wks	125/66	2.4%/3.03%	RR	0.79(0.14,4.62)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	424/208	10.38%/51.92%	RR	0.2(0.15,0.27)	Group 1	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	73/72	5.48%/6.94%	RR	0.79(0.22,2.82)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	74/72	12.16%/6.94%	RR	1.75(0.62,4.97)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	190/96	4.74%/4.17%	RR	1.14(0.36,3.6)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	189/96	7.94%/4.17%	RR	1.9(0.65,5.58)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	202/203	7.43%/10.84%	RR	0.69(0.37,1.28)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	197/203	9.14%/10.84%	RR	0.84(0.47,1.52)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	203/203	9.36%/10.84%	RR	0.86(0.48,1.55)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	199/200	7.04%/8%	RR	0.88(0.44,1.75)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Headache	13 wks	391/382	9.21%/12.04%	RR	0.76(0.51,1.16)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Headache	91 days	393/382	11.96%/12.04%	RR	0.99(0.68,1.45)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Headache	13 wks	385/382	12.99%/12.04%	RR	1.08(0.74,1.57)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Headache	13 wks	487/243	3.9%/3.7%	RR	1.05(0.48,2.29)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Headache	13 wks	481/243	5.61%/3.7%	RR	1.52(0.72,3.17)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Headache	13 wks	491/243	5.91%/3.7%	RR	1.59(0.77,3.32)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Headache	42 days	350/289	1.14%/1.73%	RR	0.66(0.18,2.44)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	104/107	26.92%/30.84%	RR	0.87(0.57,1.34)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Headache	6 weeks	104/107	26.92%/30.84%	RR	0.87(0.57,1.34)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	231/231	7.36%/7.79%	RR	0.94(0.5,1.79)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Headache		241/243	16.18%/17.28%	RR	0.94(0.63,1.39)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Headache		231/243	16.88%/17.28%	RR	0.98(0.66,1.45)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Headache	6 wks	222/231	8.11%/7.79%	RR	1.04(0.56,1.95)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Headache >5%	12 wks	174/178	3.45%/5.62%	RR	0.61(0.23,1.65)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Headache >5%	12 wks	188/178	5.85%/5.62%	RR	1.04(0.45,2.39)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Headache >5%	12 wks	185/178	7.03%/5.62%	RR	1.25(0.56,2.78)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Headache NOS	13 wks	420/424	6.43%/6.6%	RR	0.97(0.58,1.62)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Headache NOS	13 wks	420/424	6.9%/6.6%	RR	1.05(0.63,1.73)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Headache NOS	13 wks	420/424	6.9%/6.6%	RR	1.05(0.63,1.73)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Heartburn	84 days	233/227	3%/1.76%	RR	1.7(0.51,5.74)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Heartburn	6 wks	424/208	1.42%/8.65%	RR	0.16(0.07,0.41)	Group 1	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Hypertension	12 wks	138/133	0%/0.75%	RD	-0.752(-3.53,2.632)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Hypertension	12 wks	131/133	0%/0.75%	RD	-0.752(-3.667,2.632)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Hypertension	6 wks	424/208	0.71%/0.96%	RR	0.74(0.12,4.37)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	224/111	4.02%/0.9%	RR	4.46(0.57,34.76)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Hypertension	12 weeks	224/111	4.02%/0.9%	RR	4.46(0.57,34.76)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension	6 wks	189/96	0.53%/0%	RD	0.529(-1.877, 4.401)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension	6 wks	190/96	3.16%/0%	RD	3.158(-0.401, 7.365)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	203/203	0.49%/0.49%	RR	1(0.06, 15.88)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	202/203	0.5%/0.49%	RR	1(0.06, 15.96)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	197/203	0.51%/0.49%	RR	1.03(0.06,16.36)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension NOS	13 wks	420/424	1.9%/3.3%	RR	0.58(0.24,1.36)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Hypertension NOS	13 wks	420/424	2.14%/3.3%	RR	0.65(0.28,1.48)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Hypertension NOS	13 wks	420/424	2.86%/3.3%	RR	0.87(0.41,1.85)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Hypertension adverse event	42 days	460/151	0.43%/0%	RD	0.435(-0.702, 2.936)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:Hypertension adverse events(study 1)	6 wks	456/150	0.66%/1.33%	RR	0.49(0.08,2.92)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Hypertension adverse events(study 1)	6 wks	459/150	0.87%/1.33%	RR	0.65(0.12,3.53)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Hypertension-Related Adverse Events	12 wks	224/111	6.25%/0.9%	RR	p<.05	Placebo favored over Etoricoxib	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Hypertension-related AE	12 weeks	224/111	6.25%/0.9%	RR	6.94(0.92,52.09)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Hypertension-related events causing discontinuation	42 days	460/151	0%/0%	RD	0(-0.828, 2.481)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:Hypertension-related events causing(study 1)	6 wks	456/150	0%/0%	RD	0(-0.835, 2.497)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:Hypertension-related events causing(study 1)	6 wks	459/150	0.87%/0%	RD	0.871(-0.476, 3.425)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Influenza	91 days	393/382	4.07%/4.19%	RR	0.97(0.49,1.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Influenza	13 wks	385/382	4.16%/4.19%	RR	0.99(0.5,1.96)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Influenza	13 wks	391/382	5.63%/4.19%	RR	1.34(0.72,2.52)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Influenza	13 wks	487/243	2.26%/2.88%	RR	0.78(0.31,2)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Influenza	13 wks	481/243	2.29%/2.88%	RR	0.79(0.31,2.02)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Influenza	13 wks	491/243	3.26%/2.88%	RR	1.13(0.47,2.71)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Influenza	13 wks	420/424	1.67%/2.12%	RR	0.79(0.3,2.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Influenza	13 wks	420/424	2.14%/2.12%	RR	1.01(0.4,2.52)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Influenza	13 wks	420/424	3.81%/2.12%	RR	1.79(0.8,4.02)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Injury - Accidental	6 wks	199/200	1.51%/1.5%	RR	1.01(0.21,4.92)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Insomnia	6 wks	104/107	1.92%/0%	RD	1.923(-2.896, 5.659)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Insomnia	6 weeks	104/107	1.92%/0%	RD	1.923(-2.896, 5.659)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Joint Effusion	6 wks	132/127	1.52%/0.79%	RR	1.92(0.18,20.96)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Leg Cramps	6 wks	189/96	0%/0%	RD	0(-1.992, 3.848)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Leg Cramps	6 wks	190/96	2.11%/0%	RD	2.105(-1.077, 6.161)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Localized erythema	84 days	233/227	0%/0%	RD	0(-1.622, 1.664)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Localized itching	84 days	233/227	0%/0.44%	RD	-0.441(-2.103, 1.572)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Lower Extremity Edema	6 wks	424/208	2.36%/0.96%	RR	2.45(0.54,11.09)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Lower Extremity Edema	6 wks	73/72	2.74%/0%	RD	2.74(-3.971, 8.18)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Lower Extremity Edema	6 wks	74/72	6.76%/0%	RD	6.757(-1.348, 13.111)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: At least one Adverse Event	6 wks	424/208	50%/50%	RR	1(0.85, 1.18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: Diarrhea	6 wks	424/208	4.48%/5.29%	RR	0.85(0.41,1.75)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: Headache	6 wks	424/208	10.38%/13.46%	RR	0.77(0.49,1.2)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Clinical Adverse Events: Upper Respiratory Infection	6 wks	424/208	8.96%/8.17%	RR	1.1(0.63,1.9)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Abdominal Pain	6 wks	424/208	0.47%/0%	RD	0.472(-0.76,2.317)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: At least one Adverse Event	6 wks	424/208	5.66%/3.85%	RR	1.47(0.67,3.22)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Bloated Feeling	6 wks	424/208	0.47%/0%	RD	0.472(-0.76,2.317)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Diarrhea	6 wks	424/208	0.71%/0%	RD	0.708(-0.644, 2.58)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Headache	6 wks	424/208	0.47%/0%	RD	0.472(-0.76,2.317)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Lower Extremity Edema	6 wks	424/208	0.24%/0.48%	RR	0.49(0.03,7.8)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg)	9: Placebo/Control-Placebo	Adverse events:Most Common Withdrawal Adverse Events: Nausea	6 wks	424/208	0.47%/0%	RD	0.472(-0.76,2.317)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Musculoskeletal Pain(ITT Population)	6 wks	147/71	0%/2.82%	RD	-2.817(-6.081, 4.068)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Musculoskeletal Pain(ITT Population)	6 wks	144/71	0%/2.82%	RD	-2.817(-6.121, 4.068)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Musculoskeletal System Disorders	6 wks	132/127	14.39%/15.75%	RR	0.91(0.51,1.63)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	199/200	1.51%/2.5%	RR	0.6(0.15,2.49)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	104/107	3.85%/2.8%	RR	1.37(0.31,5.98)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Myalgia	6 weeks	104/107	3.85%/2.8%	RR	1.37(0.31,5.98)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	222/231	0.45%/1.3%	RR	0.35(0.04,3.31)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Myalgia	6 wks	231/231	1.3%/1.3%	RR	1(0.2,4.9)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Myalgia >5%	12 wks	185/178	1.08%/0%	RD	1.081(-1.693, 3.334)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Myalgia >5%	12 wks	174/178	1.72%/0%	RD	1.724(-1.497, 4.123)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Myalgia >5%	12 wks	188/178	6.38%/0%	RD	6.383(1.942, 9.807)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Nasopharyngitis	12 wks	138/133	0.72%/0%	RD	0.725(-2.541, 3.595)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Nasopharyngitis	12 wks	131/133	2.29%/0%	RD	2.29(-1.937, 5.477)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Nasopharyngitis	91 days	393/382	7.12%/9.42%	RR	0.76(0.47,1.21)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Nasopharyngitis	13 wks	391/382	9.21%/9.42%	RR	0.98(0.63,1.52)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Nasopharyngitis	13 wks	385/382	9.35%/9.42%	RR	0.99(0.64,1.54)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	13 wks	481/243	4.78%/4.94%	RR	0.97(0.49,1.91)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	13 wks	491/243	5.7%/4.94%	RR	1.15(0.6,2.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	13 wks	487/243	6.98%/4.94%	RR	1.41(0.75,2.68)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	13 wks	420/424	5.48%/8.25%	RR	0.66(0.4,1.1)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	13 wks	420/424	6.43%/8.25%	RR	0.78(0.48,1.26)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	13 wks	420/424	6.67%/8.25%	RR	0.81(0.5,1.3)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	6 wks	132/127	8.33%/4.72%	RR	1.76(0.67,4.63)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Nasopharyngitis	6 weeks	104/107	3.85%/4.67%	RR	0.82(0.23,2.98)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	6 wks	104/107	3.85%/4.67%	RR	0.82(0.23,2.98)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Nausea	12 wks	138/133	2.17%/0%	RD	2.174(-1.848, 5.325)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Nausea	12 wks	131/133	2.29%/0%	RD	2.29(-1.937, 5.477)	Not Sig.	na
Essex; 2012/High	9: Cox 2 agents-Celecoxib(200 mg per day)	1: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	125/66	2.4%/3.03%	RR	0.79(0.14,4.62)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	424/208	2.36%/11.54%	RR	0.2(0.1,0.42)	Group 1	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	74/72	1.35%/0%	RD	1.351(-4.563, 6.537)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	73/72	5.48%/0%	RD	5.479(-2.3,11.54)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	224/111	1.79%/2.7%	RR	0.66(0.15,2.9)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Nausea	12 weeks	224/111	1.79%/2.7%	RR	0.66(0.15,2.9)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	199/200	2.01%/3.5%	RR	0.57(0.17,1.93)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Nausea	13 wks	420/424	1.9%/1.65%	RR	1.15(0.42,3.15)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Nausea	13 wks	420/424	1.9%/1.65%	RR	1.15(0.42,3.15)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Nausea	13 wks	420/424	2.14%/1.65%	RR	1.3(0.49,3.45)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	132/127	2.27%/1.57%	RR	1.44(0.25,8.49)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Nausea	42 days	350/289	2%/1.73%	RR	1.16(0.37,3.6)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	104/107	0.96%/0.93%	RR	1.03(0.07,16.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Nausea	6 weeks	104/107	0.96%/0.93%	RR	1.03(0.07,16.23)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	231/231	0.87%/2.16%	RR	0.4(0.08,2.04)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Nausea	6 wks	222/231	0.9%/2.16%	RR	0.42(0.08,2.12)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Nausea >5%	12 wks	185/178	4.32%/5.06%	RR	0.86(0.34,2.17)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Nausea >5%	12 wks	174/178	8.05%/5.06%	RR	1.59(0.71,3.58)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Nausea >5%	12 wks	188/178	9.04%/5.06%	RR	1.79(0.82,3.91)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Nausea >1%	12 wks	188/178	0.53%/1.12%	RR	0.47(0.04,5.18)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Nausea >1%	12 wks	185/178	0.54%/1.12%	RR	0.48(0.04,5.26)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Nausea >1%	12 wks	174/178	1.15%/1.12%	RR	1.02(0.15,7.18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Neck Pain	6 wks	104/107	2.88%/1.87%	RR	1.54(0.26,9.05)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Neck pain	6 weeks	104/107	2.88%/1.87%	RR	1.54(0.26,9.05)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Oedema	13 wks	463/231	2.16%/1.73%	RR	1.25(0.4,3.93)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Oedema	13 wks	462/231	2.38%/1.73%	RR	1.38(0.44,4.27)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Oedema	13 wks	462/231	2.6%/1.73%	RR	1.5(0.49,4.6)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Oedema(ITT Population)	6 wks	144/71	0%/0%	RD	0(-2.598, 5.133)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Oedema(ITT Population)	6 wks	147/71	2.72%/0%	RD	2.721(-1.345, 8.115)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:One or more Clinical Adverse Events	42 days	460/151	43.7%/41.72%	RR	1.05(0.84,1.3)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Osteoarthritis	12 wks	131/133	0.76%/2.26%	RR	0.34(0.04,3.21)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Osteoarthritis	12 wks	138/133	2.9%/2.26%	RR	1.29(0.29,5.63)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Pain	6 wks	199/200	0.5%/0%	RD	0.503(-1.786, 2.432)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Pain NOS	6 wks	104/107	5.77%/3.74%	RR	1.54(0.45,5.31)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Pain NOS	6 weeks	104/107	5.77%/3.74%	RR	1.54(0.45,5.31)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Pain in Extremity	12 wks	138/133	0.72%/1.5%	RR	0.48(0.04,5.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Pain in Extremity	12 wks	131/133	0.76%/1.5%	RR	0.51(0.05,5.53)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Pain in limb	6 weeks	104/107	5.77%/9.35%	RR	0.62(0.23,1.64)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Pain in limb	6 wks	104/107	5.77%/9.35%	RR	0.62(0.23,1.64)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients Discontinued Due to Adverse Events	6 wks	153/79	3.27%/6.33%	RR	0.52(0.15,1.73)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Patients with > 1 Adverse Experience	6 wks	73/72	52.05%/44.44%	RR	1.17(0.83,1.64)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Patients with > 1 Adverse Experience	6 wks	74/72	56.76%/44.44%	RR	1.28(0.92,1.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	6 wks	153/79	20.26%/26.58%	RR	0.76(0.47,1.24)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	13 wks	463/231	63.5%/66.67%	RR	0.95(0.85,1.07)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	13 wks	462/231	64.5%/66.67%	RR	0.97(0.86,1.08)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	13 wks	462/231	66.23%/66.67%	RR	0.99(0.89,1.11)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	13 wks	420/424	42.86%/41.98%	RR	1.02(0.87,1.19)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	13 wks	420/424	47.62%/41.98%	RR	1.13(0.98,1.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Patients with Adverse Events	13 wks	420/424	48.57%/41.98%	RR	1.16(1, 1.34)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Any Adverse Events	13 wks	462/231	18.18%/18.61%	RR	0.98(0.7,1.36)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Any Adverse Events	13 wks	463/231	22.89%/18.61%	RR	1.23(0.9,1.69)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Any Adverse Events	13 wks	462/231	23.16%/18.61%	RR	1.24(0.91,1.71)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Dose Reduced or Temporary Discontinuation Due to Adverse Events	6 wks	153/79	0%/1.27%	RD	-1.266(-3.928, 4.296)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Drug Related Adverse Events	13 wks	462/231	20.56%/20.78%	RR	0.99(0.73,1.35)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Drug Related Adverse Events	13 wks	462/231	20.56%/20.78%	RR	0.99(0.73,1.35)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Drug Related Adverse Events	13 wks	463/231	20.73%/20.78%	RR	1(0.73, 1.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Drug Related Gastrointestinal Adverse Events	13 wks	462/231	12.12%/10.82%	RR	1.12(0.72,1.75)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Drug Related Gastrointestinal Adverse Events	13 wks	462/231	12.12%/10.82%	RR	1.12(0.72,1.75)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Drug Related Gastrointestinal Adverse Events	13 wks	463/231	12.96%/10.82%	RR	1.2(0.77,1.86)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Gastrointestinal Adverse Events	13 wks	462/231	20.78%/19.91%	RR	1.04(0.76,1.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Gastrointestinal Adverse Events	13 wks	462/231	25.32%/19.91%	RR	1.27(0.94,1.72)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Gastrointestinal Adverse Events	13 wks	463/231	25.49%/19.91%	RR	1.28(0.95,1.73)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	6 wks	153/79	0%/0%	RD	0(-2.449, 4.637)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Celecoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	13 wks	462/231	0.65%/0.87%	RR	0.75(0.13,4.46)	Not Sig.	na
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 400 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	13 wks	463/231	0.86%/0.87%	RR	1(0.18, 5.41)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Fleischmann; 2006/Low	9: Cox 2 agents-Lumiracoxib 200 mg(Once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	13 wks	462/231	1.52%/0.87%	RR	1.75(0.37,8.36)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	13 wks	420/424	1.43%/1.65%	RR	0.87(0.29,2.55)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	13 wks	420/424	1.43%/1.65%	RR	0.87(0.29,2.55)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Patients with Serious Adverse Events	13 wks	420/424	1.67%/1.65%	RR	1.01(0.36,2.85)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Patients with Severe Adverse Events	6 wks	153/79	0.65%/3.8%	RR	0.17(0.02,1.63)	Not Sig.	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Patients with event causing withdrawal	42 days	63/60	6.35%/1.67%	RR	3.81(0.44,33.12)	Not Sig.	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Celecoxib(200 mg)	9: Placebo/Control-Placebo	Adverse events:Patients with event causing withdrawal	6 wks	63/60	6.35%/1.67%	RR	3.81(0.44,33.12)	Not Sig.	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Patients with event causing withdrawal	6 wks	59/60	6.78%/1.67%	RR	4.07(0.47,35.33)	Not Sig.	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Rofecoxib(25mg Q.D.)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Patients with one or more adverse event	42 days	59/60	61.02%/41.67%	RR	1.46(1.02,2.1)	Group 2	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Celecoxib(200 mg)	9: Placebo/Control-Placebo	Adverse events:Patients with one or more event	6 wks	63/60	49.21%/41.67%	RR	1.18(0.8,1.75)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McKenna; 2001 (a)/High	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Patients with one or more event	42 days	63/60	49.21%/41.67%	RR	1.18(0.8,1.75)	Not Sig.	na
McKenna; 2001 (a)/High	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Patients with one or more event	6 wks	59/60	61.02%/41.67%	RR	1.46(1.02,2.1)	Group 2	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Pedema Peripheral(ITT Population)	6 wks	144/71	2.08%/0%	RD	2.083(-1.779, 7.396)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	6 wks	189/96	2.12%/2.08%	RR	1.02(0.19,5.45)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	6 wks	190/96	4.21%/2.08%	RR	2.02(0.44,9.33)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	12 wks	203/203	0.99%/0.49%	RR	2(0.18, 21.88)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	12 wks	197/203	1.02%/0.49%	RR	2.06(0.19,22.55)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	12 wks	202/203	1.98%/0.49%	RR	4.02(0.45,35.65)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (High Dose) [oral](400mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	13 wks	491/243	0.81%/1.65%	RR	0.49(0.12,1.96)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Lumiracoxib (Low Dose) [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	13 wks	487/243	1.23%/1.65%	RR	0.75(0.21,2.63)	Not Sig.	na
Tannenbaum; 2003/Moderate	9: Cox 2 agents-Celecoxib [oral](200mg x1/day x13 wks)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	13 wks	481/243	1.25%/1.65%	RR	0.76(0.22,2.66)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	6 wks	231/231	0.43%/0.87%	RR	0.5(0.05,5.48)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Peripheral Edema	6 wks	222/231	1.35%/0.87%	RR	1.56(0.26,9.25)	Not Sig.	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Peripheral Oedema	6 wks	199/200	5.03%/2.5%	RR	2.01(0.7,5.78)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Pharyngitis	6 weeks	104/107	0.96%/2.8%	RR	0.34(0.04,3.24)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Pharyngitis	6 wks	104/107	0.96%/2.8%	RR	0.34(0.04,3.24)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Pruritus	6 wks	132/127	3.79%/3.15%	RR	1.2(0.33,4.38)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Psychiatric Disorders	6 wks	132/127	4.55%/0.79%	RR	5.77(0.7,47.28)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Rash >1%	12 wks	185/178	0%/0%	RD	0(-2.034, 2.113)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Rash >1%	12 wks	174/178	0.57%/0%	RD	0.575(-2.034, 2.74)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Rash >1%	12 wks	188/178	1.06%/0%	RD	1.064(-1.668, 3.313)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Respiratory ; thoracic and mediastinal disorders; any adverse events	6 wks	132/127	10.61%/7.87%	RR	1.35(0.62,2.92)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Rhinitis	6 wks	190/96	1.05%/1.04%	RR	1.01(0.09,11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Rhinitis	6 wks	189/96	2.12%/1.04%	RR	2.03(0.23,17.93)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Sciatica	6 wks	132/127	3.03%/0.79%	RR	3.85(0.44,33.97)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Serious Adverse Events	91 days	393/382	0.76%/1.57%	RR	0.49(0.12,1.93)	Not Sig.	na
Puopolo; 2007/High	9: Cox 2 agents-Etoricoxib(30 mg)	9: Placebo/Control-Placebo	Adverse events:Serious Drug-Related Adverse Events	12 wks	224/111	0%/0%	RD	0(-1.686, 3.345)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Serious Events	42 days	350/289	0.29%/1.38%	RR	0.21(0.02,1.84)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Serious adverse events	84 days	233/227	1.72%/0.44%	RR	3.9(0.44,34.6)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:Serious adverse events	42 days	460/151	0.65%/0%	RD	0.652(-0.595, 3.17)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:Serious adverse events	42 days	319/162	0%/0.62%	RD	-0.617(-1.911, 2.179)	Not Sig.	na
Puopolo; 2007/High	9: NSAIDs (oral/IM)-etoricoxib 30mg	9: Placebo/Control-placebo	Adverse events:Serious drug-related AE	12 weeks	224/111	0%/0%	RD	0(-1.686, 3.345)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Sinus Headache	6 wks	104/107	0.96%/1.87%	RR	0.51(0.05,5.59)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Sinus headache	6 weeks	104/107	0.96%/1.87%	RR	0.51(0.05,5.59)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Sinusitis	6 wks	74/72	4.05%/2.78%	RR	1.46(0.25,8.48)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Sinusitis	6 wks	73/72	4.11%/2.78%	RR	1.48(0.25,8.59)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	6 wks	189/96	1.59%/0%	RD	1.587(-1.388, 5.575)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Sinusitis	6 wks	190/96	3.16%/0%	RD	3.158(-0.401, 7.365)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Sinusitis	91 days	393/382	2.54%/2.36%	RR	1.08(0.44,2.63)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Sinusitis	13 wks	391/382	3.32%/2.36%	RR	1.41(0.61,3.26)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Sinusitis	13 wks	385/382	4.16%/2.36%	RR	1.76(0.79,3.94)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Sinusitis		231/243	3.46%/2.47%	RR	1.4(0.49,3.98)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Sinusitis		241/243	5.39%/2.47%	RR	2.18(0.84,5.65)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Skin and subcutaneous tissue	6 wks	132/127	20.45%/22.05%	RR	0.93(0.58,1.48)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Skin irritation	6 wks	132/127	0%/0%	RD	0(-2.828, 2.936)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Stomatitis	6 weeks	104/107	1.92%/0.93%	RR	2.06(0.19,22.35)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Stomatitis	6 wks	104/107	1.92%/0.93%	RR	2.06(0.19,22.35)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Swelling Face(ITT Population)	6 wks	144/71	0%/0%	RD	0(-2.598, 5.133)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Swelling Face(ITT Population)	6 wks	147/71	2.04%/0%	RD	2.041(-1.746, 7.347)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Toothache	12 wks	138/133	0%/0.75%	RD	-0.752(-3.53,2.632)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Toothache	12 wks	131/133	1.53%/0.75%	RR	2.03(0.19,22.12)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Toothache	6 wks	132/127	2.27%/0.79%	RR	2.89(0.3,27.39)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	6 wks	153/79	28.1%/34.18%	RR	0.82(0.55,1.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	12 wks	202/203	32.18%/29.06%	RR	1.11(0.83,1.49)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	12 wks	203/203	33.99%/29.06%	RR	1.17(0.88,1.56)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events	12 wks	197/203	35.03%/29.06%	RR	1.21(0.9,1.61)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >1%	12 wks	185/178	5.41%/8.43%	RR	0.64(0.3,1.39)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >1%	12 wks	188/178	5.85%/8.43%	RR	0.69(0.33,1.47)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >1%	12 wks	174/178	8.62%/8.43%	RR	1.02(0.52,2.03)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >5%	12 wks	174/178	55.17%/53.37%	RR	1.03(0.85,1.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >5%	12 wks	188/178	55.85%/53.37%	RR	1.05(0.87,1.26)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Total Adverse Events >5%	12 wks	185/178	60%/53.37%	RR	1.12(0.94,1.35)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Total Causing Withdrawal	12 wks	203/203	4.43%/3.94%	RR	1.13(0.44,2.86)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Total Causing Withdrawal	12 wks	202/203	4.95%/3.94%	RR	1.26(0.51,3.12)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Total Causing Withdrawal	12 wks	197/203	8.12%/3.94%	RR	2.06(0.9,4.71)	Not Sig.	na
Gordo; 2017/High	9: Cox 2 agents-Celecoxib(200 mg once daily)	9: Placebo/Control-Placebo	Adverse events:UGI Event	6 wks	153/79	1.31%/2.53%	RR	0.52(0.07,3.6)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:URI	12 wks	138/133	1.45%/1.5%	RR	0.96(0.14,6.74)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:URI	12 wks	131/133	1.53%/1.5%	RR	1.02(0.15,7.1)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Uniary Tract Infection	6 wks	231/231	0.43%/0.87%	RR	0.5(0.05,5.48)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Uniary Tract Infection	6 wks	222/231	1.35%/0.87%	RR	1.56(0.26,9.25)	Not Sig.	na
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	6 wks	424/208	8.96%/43.75%	RR	0.2(0.15,0.29)	Group 1	na
Mckenna; 2001 (b)/Moderate	9: Cox 2 agents-Celecoxib(100 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	6 wks	199/200	3.02%/1%	RR	3.02(0.62,14.76)	Not Sig.	na
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (Low Dose x2)(100mg x2/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection		241/243	7.05%/4.94%	RR	1.43(0.7,2.93)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Williams; 2000/Moderate	9: Cox 2 agents-Celecoxib (High Dose x1)(200mg x1/day x6wks)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection		231/243	7.36%/4.94%	RR	1.49(0.73,3.05)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	6 wks	73/72	9.59%/5.56%	RR	1.73(0.53,5.64)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	6 wks	74/72	13.51%/5.56%	RR	2.43(0.8,7.4)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Rofecoxib(25 mg per day)	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	6 wks	190/96	0.53%/2.08%	RR	0.25(0.02,2.75)	Not Sig.	na
Gibofsky ; 2003/High	9: Cox 2 agents-Celecoxib(200 mg per day)	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	6 wks	189/96	1.06%/2.08%	RR	0.51(0.07,3.55)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 50 mg	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	12 wks	203/203	5.42%/5.42%	RR	1(0.44, 2.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 200 mg	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	12 wks	202/203	6.44%/5.42%	RR	1.19(0.55,2.59)	Not Sig.	na
Bensen; 1999/High	9: Cox 2 agents-Celecoxib 100 mg	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection	12 wks	197/203	6.6%/5.42%	RR	1.22(0.56,2.65)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Upper respiratory tract infection	13 wks	385/382	4.94%/6.02%	RR	0.82(0.45,1.48)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Upper respiratory tract infection	91 days	393/382	5.6%/6.02%	RR	0.93(0.53,1.64)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Upper respiratory tract infection	13 wks	391/382	5.88%/6.02%	RR	0.98(0.56,1.71)	Not Sig.	na
Pincus; 2004/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Upper respiratory tract infection	42 days	350/289	4.57%/3.11%	RR	1.47(0.66,3.27)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 20 mg(20 mg/day)	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection >5%	12 wks	185/178	3.24%/8.99%	RR	0.36(0.14,0.9)	Group 1	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 5 mg(5 mg/day)	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection >5%	12 wks	188/178	4.26%/8.99%	RR	0.47(0.21,1.08)	Not Sig.	na
Kivits; 2002/High	9: Cox 2 agents-Valdecoxib 10 mg(10 mg/day)	9: Placebo/Control-Placebo	Adverse events:Upper respiratory tract infection >5%	12 wks	174/178	5.17%/8.99%	RR	0.58(0.26,1.27)	Not Sig.	na
Rother; 2007/High	9: Cox 2 agents-Celecoxib(100 mg)	9: Placebo/Control-Placebo	Adverse events:Uricaria	6 wks	132/127	0.76%/0.79%	RR	0.96(0.06,15.22)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam High Dose (SoluMatrix meloxicam)(10mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Urinary Tract Infection	12 wks	131/133	1.53%/2.26%	RR	0.68(0.11,3.99)	Not Sig.	na
Altman; 2015/High	9: Cox 2 agents-Meloxicam Low Dose (SoluMatrix meloxicam)(5mg daily)	9: Placebo/Control-Placebo(daily)	Adverse events:Urinary Tract Infection	12 wks	138/133	2.17%/2.26%	RR	0.96(0.2,4.69)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Celecoxib (Oral)(200mg 1x/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Urinary Tract Infection	91 days	393/382	2.54%/2.88%	RR	0.88(0.38,2.06)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: Cox 2 agents-Rofecoxib(25 mg)	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection	6 wks	104/107	1.92%/4.67%	RR	0.41(0.08,2.07)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Celecoxib(200 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection NOS	13 wks	420/424	1.43%/2.12%	RR	0.67(0.24,1.87)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib(100 mg once per day)	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection NOS	13 wks	420/424	1.67%/2.12%	RR	0.79(0.3,2.09)	Not Sig.	na
Lehmann; 2005/High	9: Cox 2 agents-Lumiracoxib with loading dose(100 mg once per day with initial loading dose of 200 mg once per day for the first two weeks)	9: Placebo/Control-Placebo	Adverse events:Urinary Tract Infection NOS	13 wks	420/424	1.9%/2.12%	RR	0.9(0.35,2.3)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:Urinary tract infection	13 wks	385/382	2.34%/2.88%	RR	0.81(0.34,1.94)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:Urinary tract infection	13 wks	391/382	3.58%/2.88%	RR	1.24(0.57,2.7)	Not Sig.	na
Schnitzer; 2005b/Moderate	9: NSAIDs (oral/IM)-rofecoxib (25mg qd)	9: Placebo/Control-	Adverse events:Urinary tract infection	6 weeks	104/107	1.92%/4.67%	RR	0.41(0.08,2.07)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Celecoxib(Once daily for 6 weeks; 200 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Urticaria(ITT Population)	6 wks	144/71	0%/2.82%	RD	-2.817(-6.121, 4.068)	Not Sig.	na
Lee; 2017/High	9: Cox 2 agents-Polmacoxib(Once daily for 6 weeks; 2 mg)	9: Placebo/Control-Placebo(Once daily for 6 weeks;)	Adverse events:Urticaria(ITT Population)	6 wks	147/71	0.68%/2.82%	RR	0.24(0.02,2.62)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Vascular disorders	84 days	233/227	1.72%/0.44%	RR	3.9(0.44,34.6)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Viral Syndrome	6 wks	74/72	4.05%/1.39%	RR	2.92(0.31,27.41)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Viral Syndrome	6 wks	73/72	6.85%/1.39%	RR	4.93(0.59,41.18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kivitz; 2004/High	9: Cox 2 agents-Rofecoxib(12.5 mg/day x 6wks)	9: Placebo/Control-Placebo	Adverse events:Vomiting	6 wks	424/208	0.71%/2.4%	RR	0.29(0.07,1.22)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 25 mg	9: Placebo/Control-Placebo	Adverse events:Weight Gain	6 wks	73/72	0%/4.17%	RD	-4.167(-9.867, 3.216)	Not Sig.	na
Ehrich; 1999/Moderate	9: Cox 2 agents-Rofecoxib 125 mg	9: Placebo/Control-Placebo	Adverse events:Weight Gain	6 wks	74/72	5.41%/4.17%	RR	1.3(0.3,5.59)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Celecoxib (Oral)(200mg once daily)	9: Placebo/Control-Placebo (Oral)(placebo once daily)	Adverse events:With drug-related adverse events	42 days	460/151	13.04%/11.26%	RR	1.16(0.7,1.92)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:Withdrawals due to adverse events or adverse events and lack of efficacy	84 days	233/227	5.58%/6.61%	RR	0.84(0.41,1.73)	Not Sig.	na
Conaghan; 2013/High	9: Cox 2 agents-Celecoxib (Oral)(100mg twice daily)	9: Placebo/Control-Placebo (Oral)(placebo twice daily)	Adverse events:all skin and tissue disorders	84 days	233/227	2.15%/0.88%	RR	2.44(0.48,12.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:discontinuation due to adverse events	13 wks	385/382	3.9%/6.28%	RR	0.62(0.33,1.16)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:discontinuation due to adverse events	13 wks	391/382	5.37%/6.28%	RR	0.85(0.48,1.51)	Not Sig.	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:drug related adverse events	42 days	319/162	10.66%/10.49%	RR	1.02(0.59,1.76)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:edema adverse events(study 1)	6 wks	456/150	0.66%/0%	RD	0.658(-0.6,3.192)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:edema adverse events(study 1)	6 wks	459/150	1.09%/0%	RD	1.089(-0.346, 3.663)	Not Sig.	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:edema related adverse events	42 days	319/162	0.63%/0.62%	RR	1.02(0.09,11.12)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:hypertension related adverse events	42 days	319/162	0.31%/0.62%	RR	0.51(0.03,8.07)	Not Sig.	na
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:overall adverse events	42 days	319/162	36.05%/32.72%	RR	1.1(0.85,1.44)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-lumiracoxib 100mg once daily with loading dose	9: Placebo/Control-placebo	Adverse events:serious adverse events	13 wks	385/382	1.3%/1.57%	RR	0.83(0.25,2.69)	Not Sig.	na
Sheldon; 2005/High	9: Cox 2 agents-Lumiracoxib 100mg once daily	9: Placebo/Control-placebo	Adverse events:serious adverse events	13 wks	391/382	1.53%/1.57%	RR	0.98(0.32,3)	Not Sig.	na
Smugar; 2006/Moderate	9: Cox 2 agents-Rofecoxib 12.5mg once daily	9: Placebo/Control-placebo	Adverse events:serious adverse events(study 1)	6 wks	456/150	0.66%/3.33%	RR	0.2(0.05,0.82)	Group 1	na
Smugar; 2006/Moderate	9: Cox 2 agents-rofecoxib 25mg once daily	9: Placebo/Control-placebo	Adverse events:serious adverse events(study 1)	6 wks	459/150	1.09%/3.33%	RR	0.33(0.1,1.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Birbara; 2006/Moderate	9: Cox 2 agents-Rofecoxib(12.5mg once daily)	9: Placebo/Control-Placebo (Oral)	Adverse events:serious thrombotic cardiovasular adverse events	42 days	319/162	0%/0.62%	RD	-0.617(-1.911, 2.179)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 AE of congestive heart failure; pulmonary Oedem or cardiac failure	26 wks	243/117	0%/0.85%	RD	-0.855(-2.563, 2.974)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Any AE	26 wks	243/117	52.26%/52.14%	RR	1(0.81, 1.24)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Discontinued due to AE	26 wks	243/117	3.7%/10.26%	RR	0.36(0.16,0.83)	Group 1	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Discontinued due to GI AE	26 wks	243/117	1.23%/4.27%	RR	0.29(0.07,1.19)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Discontinued due to drug-related AEa	26 wks	243/117	2.47%/5.98%	RR	0.41(0.14,1.2)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Discontinued due to hypertension-related AE	26 wks	243/117	0%/0%	RD	0(-1.556, 3.179)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Discontinued due to oedema-related AE	26 wks	243/117	0.41%/0%	RD	0.412(-1.471, 3.608)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Drug-related AEsa	26 wks	243/117	18.93%/17.09%	RR	1.11(0.69,1.78)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 2 Serious AE	26 wks	243/117	0.41%/4.27%	RR	0.1(0.01,0.81)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 AE of congestive heart failure; pulmonary Oedem or cardiac failure	26 wks	231/127	0%/0%	RD	0(-1.636, 2.936)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Any AE	26 wks	231/127	38.1%/33.07%	RR	1.15(0.86,1.55)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Discontinued due to AE	26 wks	231/127	4.33%/4.72%	RR	0.92(0.34,2.46)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Discontinued due to GI AE	26 wks	231/127	1.3%/0%	RD	1.299(-1.151, 4.357)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Discontinued due to drug-related AEa	26 wks	231/127	2.6%/0.79%	RR	3.3(0.4,27.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Discontinued due to hypertension-related AE	26 wks	231/127	0.87%/0%	RD	0.866(-1.37,3.868)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Discontinued due to oedema-related AE	26 wks	231/127	0.43%/0%	RD	0.433(-1.545, 3.39)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Drug-related AEsa	26 wks	231/127	12.12%/5.51%	RR	2.2(0.99,4.89)	Not Sig.	na
Bingham; 2007/Moderate	9: Cox 2 agents-etoricoxib 30mg 1/day	9: Placebo/Control-Placebo	Adverse events:study 1 Serious AE	26 wks	231/127	0.87%/2.36%	RR	0.37(0.06,2.16)	Not Sig.	na

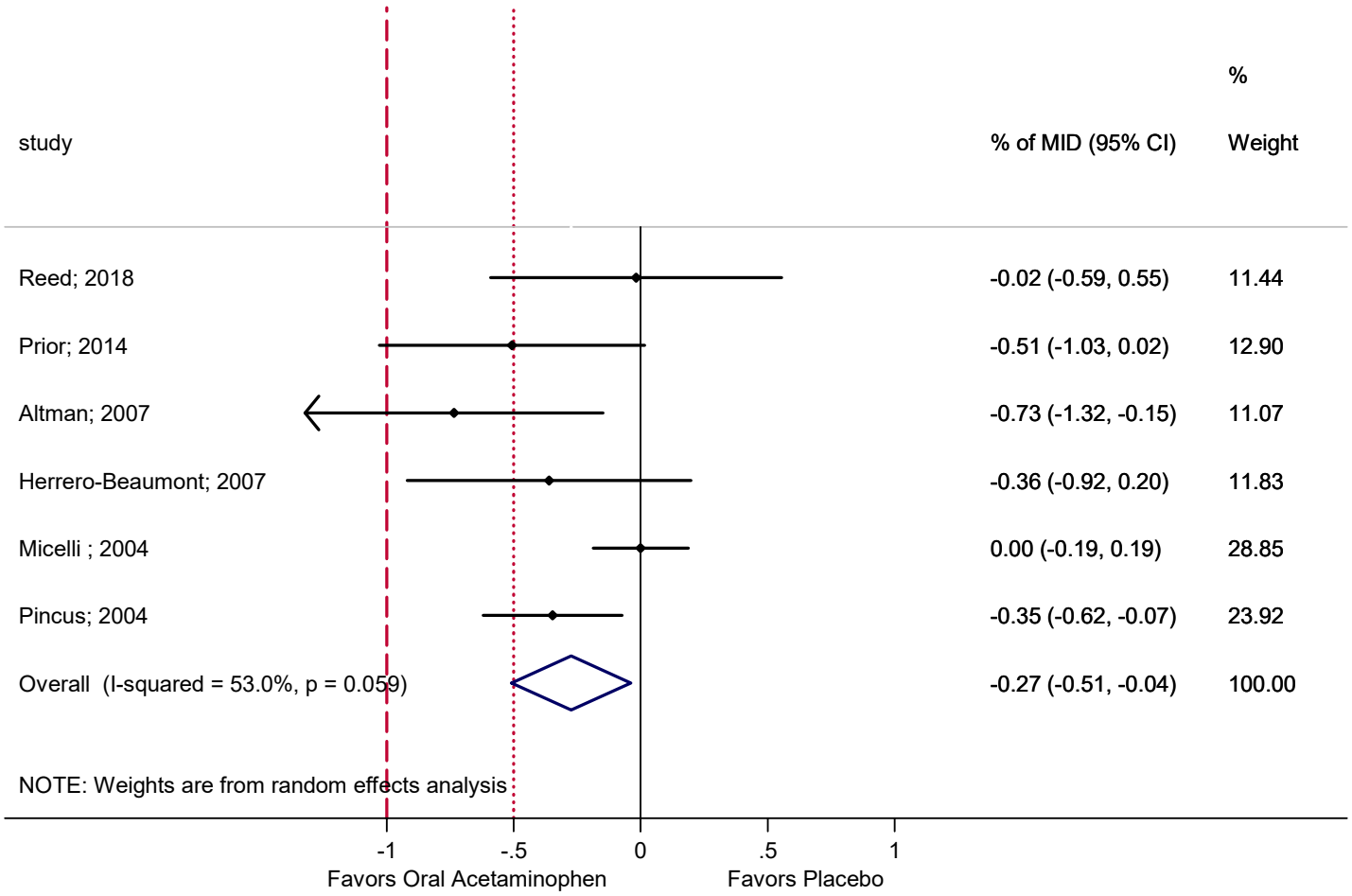
PICO 9: Systemic Treatment

Acetaminophen vs. Control

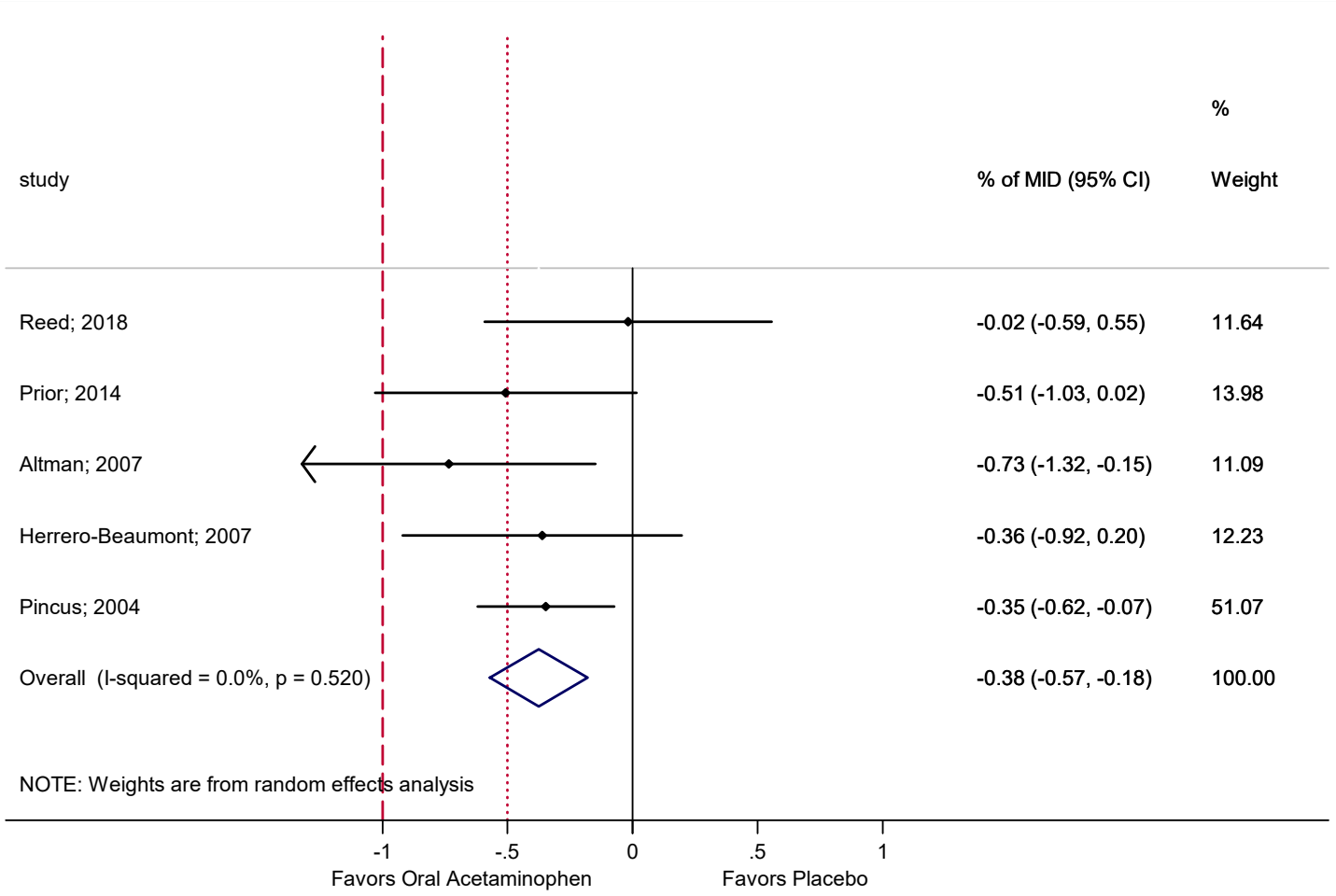
Table 38: Acetaminophen vs Control

Quality: H=High; M=Moderate; L=Low	H				M		
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Herrero-Beaumont; 2007	Doherty; 2011	Reed; 2018	Prior; 2014	Micelli ; 2004	Pincus; 2004	Altman; 2007
Composite							
Lequesne Index	●						
OARSI-A responder criteria	↑						
OARSI-B responder criteria	↑						
Global Patient Assessment of Osteoarthritis (VAS)			●				
Function							
WOMAC Function	↑						
Sit-to-stand test; seconds; mean;SD (n)		●					
Other							
Patient global assessment†; patients rating treatment as excellent or good; n/N (%)		↑					
patient global assessment of response to therapy			●				
Pain							
WOMAC Pain MCII(unclear threshold)	●						
Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)		●					
Adverse events							
Back Pain	●						
Any Adverse Event		●		●		●	
Headache	●		●	●		●	
Nausea		●	●	↓		●	
Diarrhea	●		●	●			
Neck Pain	●						
Upper Respiratory Tract Infection			●			●	
Dizziness	●						
Dyspepsia	●	↓				●	
Abdominal pain	●						
Diarrhoea		↓				↓	
Flatulence						●	
Respiratory System Disorders					●		
Hypertension			●				
Injury	●						
any adverse event related to treatment		↓					
Musculoskeletal System Disorders					●		
Alanine Aminotransferase Increase			●				
Alanine Aminotransferase Increase Occuring in Less than 2% of Any Treatment Group			●				
Any Gastrointestinal Event						●	
Any Treatment-Related Treatment Emergent Adverse Events			●				
Body as a whole - General Disorders					●		
Central and Peripheral Nervous System Disorders					●		
Coughing and associated symptoms	●						
Definite Relationship with Study Drug					●		
Drug-Related Adverse Events				●			
Fall	●						
Gastroenteritis	●		●				
Gastrointestinal System Disorders					●		
Improbable Relationship with Study Drug					●		
Mild Adverse Events					●		
Missing Data					●		
Moderate Adverse Events					●		
Patients with at least 1 serious adverse events					●		
Patients with at least 1 treatment emergent adverse events					●		
Patients withdrawn for safety reasons					●		
Possible Relationship with Study Drug					●		
Probable Relationship with Study Drug					●		
Respiratory tract infections	●						
Serious Adverse Event				●			
Serious Events						●	
Serious Treatment Emergent Adverse Events			●				
Severe Treatment Emergent Adverse Events			●				
Skin and Appendages Disorders					●		
Total Number of Reported Adverse Events					●		
Treatment Emergent Adverse Events			●				
calculable MID outcomes							
WOMAC Total	↑	●		↑		●	↑
WOMAC Function	↑	●					↑
WOMAC Stiffness		●	●	↑			
WOMAC Pain	●	●	●	●			↑
WOMAC Physical function			●	↑			
VAS Pain(0-100)						●	
QOL							
Nottingham Health Profile Energy Subscale Score				●			
Patient's Global Assessment of Response to Therapy				↑			

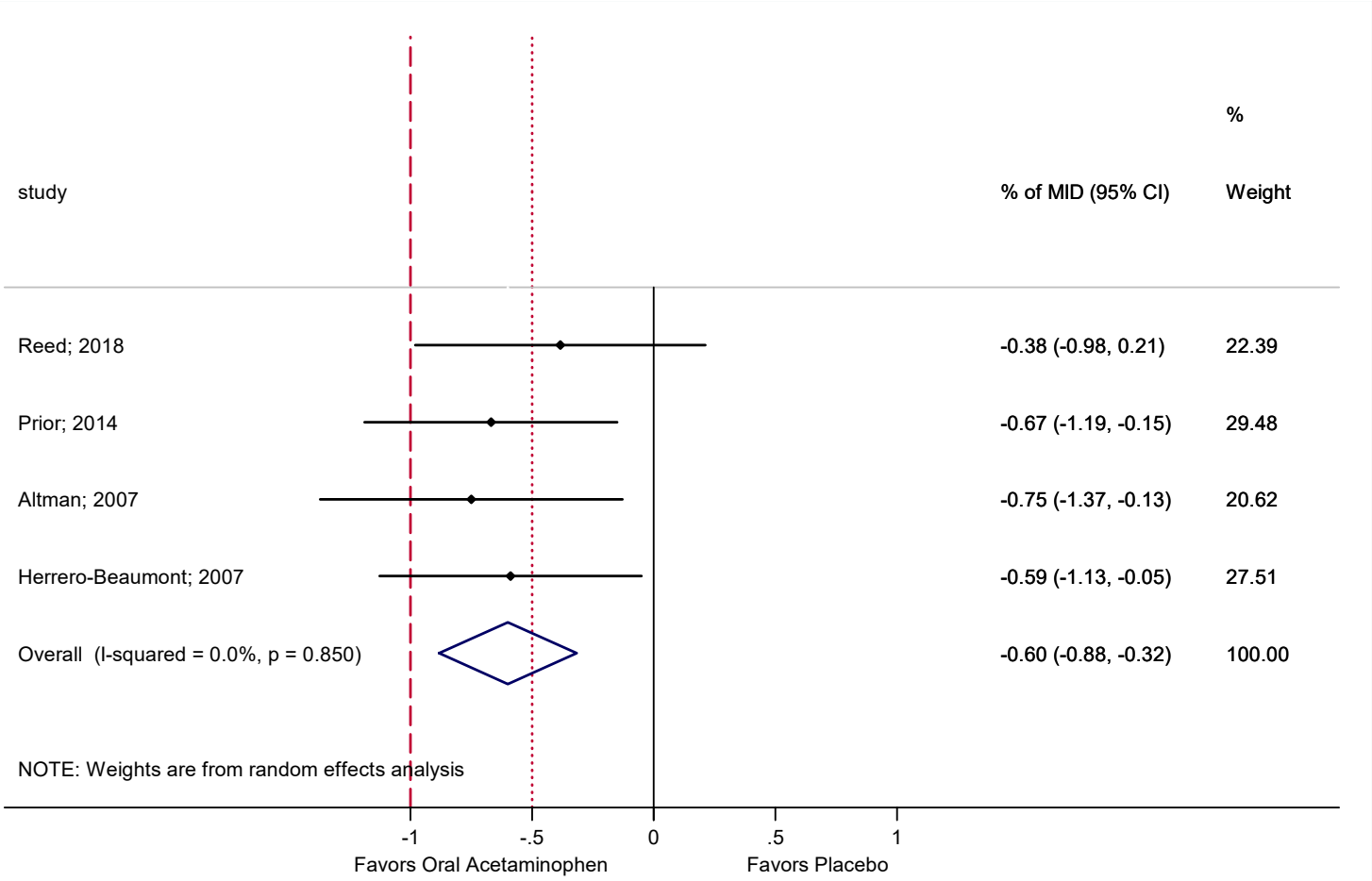
Meta-Analysis Figure 32: Acetaminophen vs Placebo- Pain All Studies



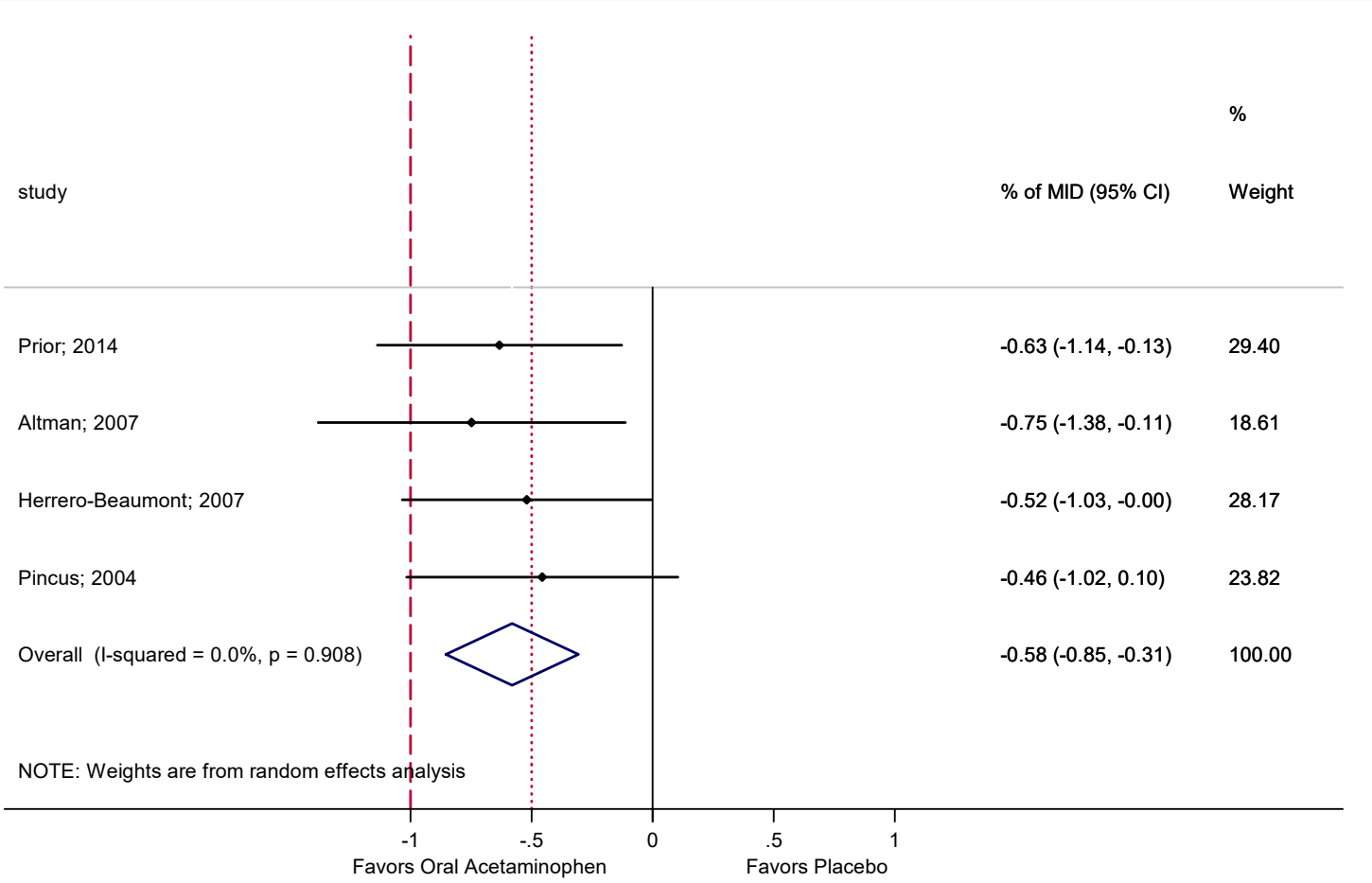
Meta-Analysis Figure 33: Acetaminophen vs Placebo- Pain Excluding Micelli Study



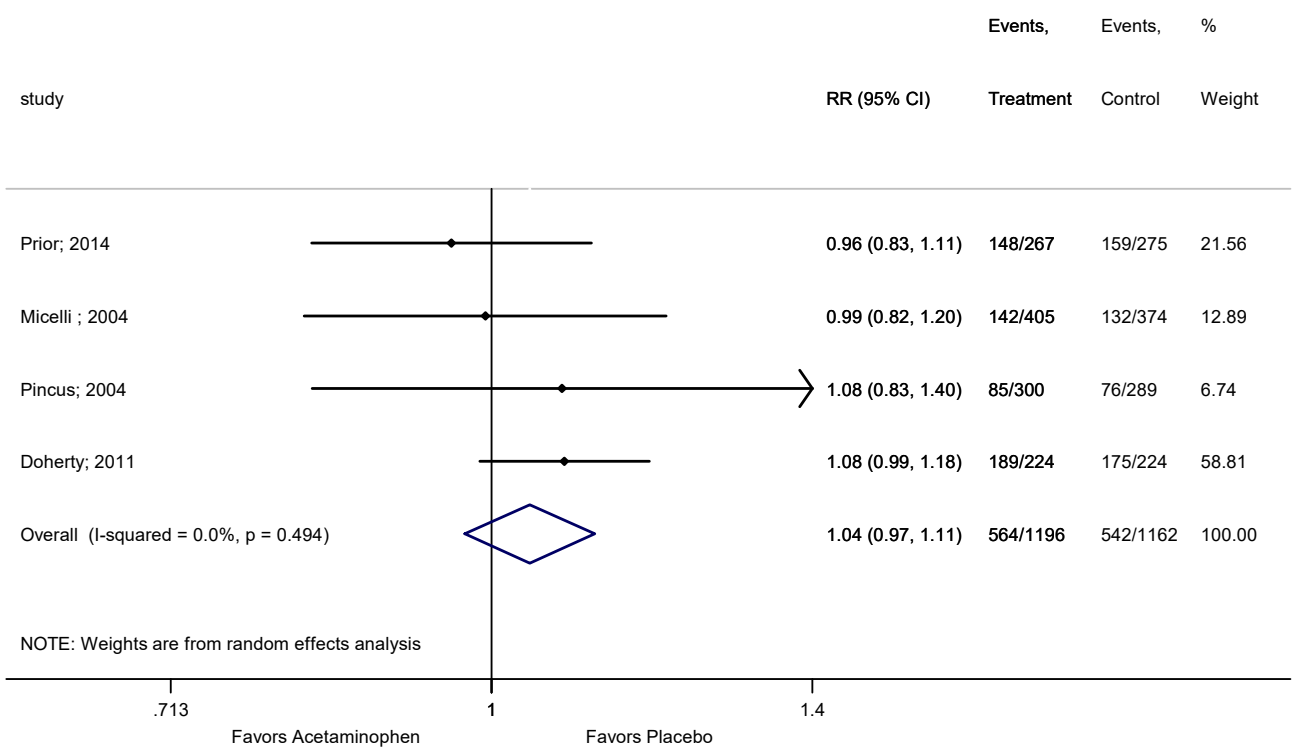
Meta-Analysis Figure 34: Acetaminophen vs Placebo- Function



Meta-Analysis Figure 35: Acetaminophen vs Placebo- WOMAC Total Score



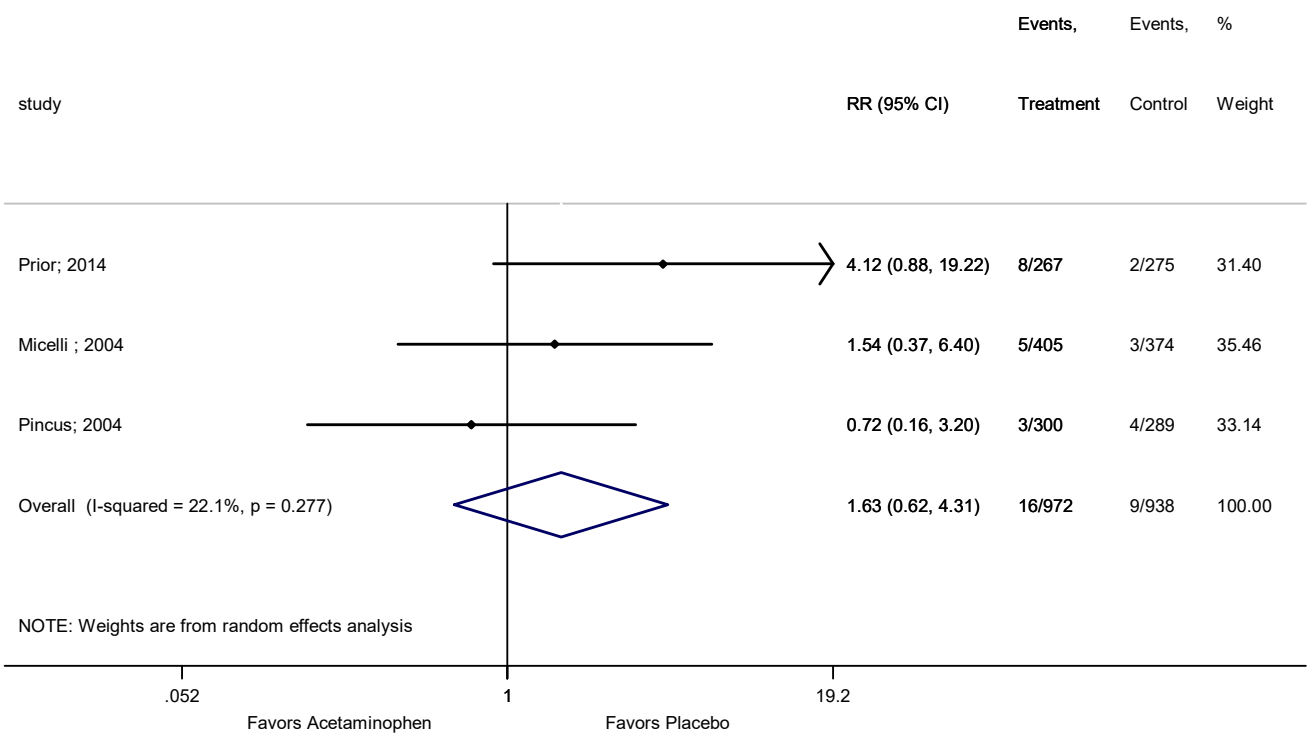
Meta-Analysis Figure 36: Acetaminophen vs Placebo- Overall Adverse Events



NNTH=53

number of excess AEs per 1000=20(-13,54)

Meta-Analysis Figure 37: Acetaminophen vs Placebo- Serious Adverse Events



NNTH=198

number of excess AEs per 1000=6(-4,27)

Evidence Table 4437: Acetaminophen vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	13 weeks	220/217	64.09%/64.06%	RR	1(0.87, 1.15)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	7 weeks	158/174	68.99%/67.82%	RR	1.02(0.88,1.18)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	13 weeks	220/217	65.45%/64.06%	RR	1.02(0.89,1.17)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Pain:Acceptability of knee pain in last 48 h; number reporting yes to acceptability question (n)	7 weeks	177/174	75.14%/67.82%	RR	1.11(0.97,1.27)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:VAS Pain(0-100)	42 days	185/182	-13.8(23.67)/-7.6(26.85)	Mean Diff	-6.2(-11.4,-1)	Group 1	clinically insignificant
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Pain:VAS Pain(0-100)	42 days	171/172	-17.4(26.02)/-10.5(25.18)	Mean Diff	-6.9(-12.34,-1.46)	Group 1	clinically insignificant
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	12 wks	225/227	-25.89(25.65)/-25.74(25.76)	Mean Diff	-0.15(-4.9,4.6)	Not Sig.	clinically insignificant
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	12 wks	224/227	-28.25(25.44)/-25.74(25.76)	Mean Diff	-2.51(-7.25,2.23)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Pain:WOMAC Pain	12 wks	267/275	-29.96(25.69)/-25.75(25.69)	Mean Diff	-4.21(-8.55,0.13)	Not Sig.	inconclusive
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Pain:WOMAC Pain	180 days	108/104	-2.4(3.18)/-1.8(3.64)	Mean Diff	-0.6(-1.53,0.33)	Not Sig.	clinically insignificant
Altman; 2007/Moderate	9: Acetaminophen-Acetaminophen ER Low Dose [Oral](1950mg/day)	9: Placebo/Control-Placebo (Oral)(Placebo 3x/day)	Pain:WOMAC Pain (VAS Version)(Normalized to scale of 0-100)	84 days	158/165	-22.5(22.25)/-19.8(22.35)	Mean Diff	-2.7(-7.58,2.18)	Not Sig.	clinically insignificant
Altman; 2007/Moderate	9: Acetaminophen-Acetaminophen ER High Dose [Oral](3900mg/day)	9: Placebo/Control-Placebo (Oral)(Placebo 3x/day)	Pain:WOMAC Pain (VAS Version)(Normalized to scale of 0-100)	84 days	160/165	-25.9(22.26)/-19.8(22.35)	Mean Diff	-6.1(-10.97,-1.23)	Group 1	possibly clinically significant
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Pain:WOMAC Pain MCII(unclear threshold)	180 days	108/104	43.52%/32.69%	RR	1.33(0.94,1.89)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Pain:womac pain	13 weeks	220/217	-14.7(18.7)/-13.3(20.7)	Mean Diff	-1.4(-5.11,2.31)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Pain:womac pain	7 weeks	161/174	-17.1(18.8)/-15(19.7)	Mean Diff	-2.1(-6.24,2.04)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Pain:womac pain	13 weeks	218/217	-15.5(20.7)/-13.3(20.7)	Mean Diff	-2.2(-6.1,1.7)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Pain:womac pain	7 weeks	173/174	-18(20.3)/-15(19.7)	Mean Diff	-3(-7.22,1.22)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	13 weeks	207/208	14.5(6)/15.7(6.5)	Mean Diff	-1.2(-2.41,0.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	7 weeks	171/168	14.1(6.2)/15.3(5.9)	Mean Diff	-1.2(-2.49,0.09)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	7 weeks	152/168	15.3(6)/15.3(5.9)	Mean Diff	0(-1.31,1.31)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Function:Sit-to-stand test; seconds; mean;SD (n)	13 weeks	204/208	16(7.1)/15.7(6.5)	Mean Diff	0.3(-1.02,1.62)	Not Sig.	na
Altman; 2007/Moderate	9: Acetaminophen-Acetaminophen ER Low Dose [Oral](1950mg/day)	9: Placebo/Control-Placebo (Oral)(Placebo 3x/day)	Function:WOMAC Function (VAS Version)(Normalized to scale of 0-100)	84 days	158/164	-19(22.63)/-18.2(22.67)	Mean Diff	-0.8(-5.77,4.17)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2007/Moderate	9: Acetaminophen-Acetaminophen ER High Dose [Oral](3900mg/day)	9: Placebo/Control-Placebo (Oral)(Placebo 3x/day)	Function:WOMAC Function (VAS Version)(Normalized to scale of 0-100)	84 days	160/164	-24.2(22.77)/-18.2(22.67)	Mean Diff	-6(-10.97,-1.03)	Group 1	possibly clinically significant
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Function:WOMAC Function MCII(unclear threshold)	180 days	108/104	52.78%/37.5%	RR	1.41(1.04,1.91)	Group 1	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Function:WOMAC Physical Function	12 wks	225/227	-24.13(25.95)/-23.36(25.91)	Mean Diff	-0.77(-5.56,4.02)	Not Sig.	clinically insignificant
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Function:WOMAC Physical Function	12 wks	224/227	-26.43(25.59)/-23.36(25.91)	Mean Diff	-3.07(-7.84,1.7)	Not Sig.	clinically insignificant
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Function:WOMAC Physical Function	12 wks	267/275	-26.64(24.59)/-21.29(24.63)	Mean Diff	-5.35(-9.5,-1.2)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	12 wks	225/227	-23.47(25.8)/-22.69(25.91)	Mean Diff	-0.78(-5.56,4)	Not Sig.	clinically insignificant
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	12 wks	224/227	-26.16(25.44)/-22.69(25.91)	Mean Diff	-3.47(-8.22,1.28)	Not Sig.	clinically insignificant
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Function:WOMAC Stiffness	12 wks	267/275	-26.91(25.39)/-20.73(25.41)	Mean Diff	-6.18(-10.47,-1.89)	Group 1	possibly clinically significant
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Function:WOMAC function	180 days	108/104	-8.7(10.07)/-5.5(11.45)	Mean Diff	-3.2(-6.12,-0.28)	Group 1	possibly clinically significant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Function:womac function	13 weeks	216/213	-10.9(17.4)/-10.5(17.8)	Mean Diff	-0.4(-3.74,2.94)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Function:womac function	7 weeks	154/170	-14.1(16.2)/-13.1(17)	Mean Diff	-1(-4.63,2.63)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Function:womac function	13 weeks	217/213	-12.5(18.8)/-10.5(17.8)	Mean Diff	-2(-5.47,1.47)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Function:womac function	7 weeks	171/170	-16(19.1)/-13.1(17)	Mean Diff	-2.9(-6.75,0.95)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Function:womac stiffness	7 weeks	160/174	-21.7(24.1)/-20.8(21.9)	Mean Diff	-0.9(-5.87,4.07)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Function:womac stiffness	13 weeks	219/217	-18.2(25.1)/-17.2(24)	Mean Diff	-1(-5.62,3.62)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Function:womac stiffness	13 weeks	217/217	-19.4(25.8)/-17.2(24)	Mean Diff	-2.2(-6.9,2.5)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Function:womac stiffness	7 weeks	173/174	-23.1(23.6)/-20.8(21.9)	Mean Diff	-2.3(-7.11,2.51)	Not Sig.	clinically insignificant
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Composite:Global Patient Assessment of Osteoarthritis (VAS)	12 wks	225/227	-33.1(34.95)/-32.1(34.2)	Mean Diff	-1(-7.39,5.39)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Composite:Global Patient Assessment of Osteoarthritis (VAS)	4 wks	225/227	-26.3(31.8)/-24.4(30.89)	Mean Diff	-1.9(-7.7,3.9)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Composite:Global Patient Assessment of Osteoarthritis (VAS)	8 wks	225/227	-32.1(34.95)/-29.8(33.9)	Mean Diff	-2.3(-8.67,4.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Composite:Global Patient Assessment of Osteoarthritis (VAS)	8 wks	224/227	-33.3(32.93)/-29.8(33.9)	Mean Diff	-3.5(-9.68,2.68)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Composite:Global Patient Assessment of Osteoarthritis (VAS)	4 wks	224/227	-28.5(30.68)/-24.4(30.89)	Mean Diff	-4.1(-9.8,1.6)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Composite:Global Patient Assessment of Osteoarthritis (VAS)	12 wks	224/227	-36.7(33.23)/-32.1(34.2)	Mean Diff	-4.6(-10.84, 1.64)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:Lequesne Index	180 days	108/104	-2.7(3.18)/-1.9(3.64)	Mean Diff	-0.8(-1.73,0.13)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:OARSI-A responder criteria	180 days	108/104	33.33%/21.15%	RR	1.58(1, 2.49)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:OARSI-B responder criteria	180 days	108/104	32.41%/19.23%	RR	1.69(1.04,2.72)	Group 1	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Composite:WOMAC Total	12 wks	267/275	-27.34(24.49)/-22.16(24.53)	Mean Diff	-5.18(-9.32,-1.04)	Group 1	possibly clinically significant
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Composite:WOMAC Total	180 days	108/104	-12.3(13.79)/-8.2(16.13)	Mean Diff	-4.1(-8.17,-0.03)	Group 1	possibly clinically significant
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total (VAS Version)	42 days	171/172	-8.4(19.88)/-4.8(21.77)	Mean Diff	-3.6(-8.03,0.83)	Not Sig.	inconclusive
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Composite:WOMAC Total (VAS Version)	42 days	185/182	-8.4(17.82)/-4.6(20.1)	Mean Diff	-3.8(-7.7,0.1)	Not Sig.	clinically insignificant
Altman; 2007/Moderate	9: Acetaminophen-Acetaminophen ER Low Dose [Oral](1950mg/day)	9: Placebo/Control-Placebo (Oral)(Placebo 3x/day)	Composite:WOMAC Total (VAS Version)(Normalized to scale of 0-100)	84 days	158/164	-19.8(22.63)/-18.6(23.05)	Mean Diff	-1.2(-6.21,3.81)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 2007/Moderate	9: Acetaminophen-Acetaminophen ER High Dose [Oral](3900mg/day)	9: Placebo/Control-Placebo (Oral)(Placebo 3x/day)	Composite:WOMAC Total (VAS Version)(Normalized to scale of 0-100)	84 days	160/164	-24.5(22.77)/-18.6(23.05)	Mean Diff	-5.9(-10.91,-0.89)	Group 1	possibly clinically significant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Composite:womac total	13 weeks	220/215	-12.2(16.8)/-11.9(17.8)	Mean Diff	-0.3(-3.56,2.96)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Composite:womac total	7 weeks	160/172	-15(16)/-14.3(16.8)	Mean Diff	-0.7(-4.24,2.84)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Composite:womac total	13 weeks	218/215	-13.7(18.7)/-11.9(17.8)	Mean Diff	-1.8(-5.25,1.65)	Not Sig.	clinically insignificant
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Composite:womac total	7 weeks	173/172	-17(18.6)/-14.3(16.8)	Mean Diff	-2.7(-6.45,1.05)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	QOL:Nottingham Health Profile Energy Subscale Score	12 wks	267/275	-20.2(26.14)/-15.95(26.18)	Mean Diff	-4.25(-8.67,0.17)	Not Sig.	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	QOL:Patient's Global Assessment of Response to Therapy	12 wks	267/275	2(1.27)/1.72(1.28)	Mean Diff	0.28(0.06,0.5)	Group 1	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Other:Patient Global Assessment of Response to Therapy	8 wks	225/227	2.45(1.46)/2.41(1.42)	Mean Diff	0.04(-0.23,0.31)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Other:Patient Global Assessment of Response to Therapy	4 wks	225/227	2.34(1.32)/2.25(1.28)	Mean Diff	0.09(-0.15,0.33)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Other:Patient Global Assessment of Response to Therapy	12 wks	225/227	2.51(1.55)/2.37(1.52)	Mean Diff	0.14(-0.14,0.42)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Other:Patient Global Assessment of Response to Therapy	4 wks	224/227	2.41(1.26)/2.25(1.28)	Mean Diff	0.16(-0.08,0.4)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Other:Patient Global Assessment of Response to Therapy	8 wks	224/227	2.6(1.38)/2.41(1.42)	Mean Diff	0.19(-0.07,0.45)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Other:Patient Global Assessment of Response to Therapy	12 wks	224/227	2.62(1.47)/2.37(1.52)	Mean Diff	0.25(-0.03,0.53)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	7 weeks	161/176	59.63%/56.82%	RR	1.05(0.88,1.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen(200mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	13 weeks	220/219	54.09%/50.68%	RR	1.07(0.89,1.28)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	7 weeks	178/176	66.85%/56.82%	RR	1.18(1, 1.39)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Other:Patient global assessment†; patients rating treatment as excellent or good; n/N (%)	13 weeks	221/219	60.18%/50.68%	RR	1.19(1, 1.41)	Group 1	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Abdominal pain	180 days	108/104	3.7%/3.85%	RR	0.96(0.25,3.75)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase Increase	12 wks	236/237	1.69%/0%	RD	1.695(-0.886, 3.596)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase Increase	12 wks	234/237	2.99%/0%	RD	2.991(-0.062, 5.205)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase Increase Occuring in Less than 2% of Any Treatment Group	12 wks	236/237	1.69%/0%	RD	1.695(-0.886, 3.596)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Alanine Aminotransferase Increase Occuring in Less than 2% of Any Treatment Group	12 wks	234/237	2.56%/0%	RD	2.564(-0.352, 4.676)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Any Adverse Event	12 wks	267/275	55.43%/57.82%	RR	0.96(0.83,1.11)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Any Adverse Event	42 days	300/289	28.33%/26.3%	RR	1.08(0.83,1.4)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Any Gastrointestinal Event	42 days	300/289	9.33%/9%	RR	1.04(0.62,1.73)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Any Treatment-Related Treatment Emergent Adverse Events	12 wks	236/237	6.78%/4.22%	RR	1.61(0.74,3.47)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Any Treatment-Related Treatment Emergent Adverse Events	12 wks	234/237	8.12%/4.22%	RR	1.92(0.91,4.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Back Pain	180 days	108/104	3.7%/4.81%	RR	0.77(0.21,2.79)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Body as a whole - General Disorders	6 wks	405/374	1.98%/3.21%	RR	0.62(0.25,1.49)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Central and Peripheral Nervous System Disorders	6 wks	405/374	1.73%/1.6%	RR	1.08(0.37,3.18)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Coughing and associated symptoms	180 days	108/104	3.7%/0%	RD	3.704(-1.731, 7.919)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Definite Relationship with Study Drug	6 wks	405/374	3.21%/2.14%	RR	1.5(0.63,3.58)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	234/237	2.56%/0.84%	RR	3.04(0.62,14.9)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	236/237	2.97%/0.84%	RR	3.51(0.74,16.74)	Not Sig.	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Diarrhea	12 wks	267/275	5.24%/2.55%	RR	2.06(0.84,5.02)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Diarrhea	180 days	108/104	3.7%/3.85%	RR	0.96(0.25,3.75)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Diarrhoea	42 days	300/289	4.67%/1.38%	RR	3.37(1.12,10.12)	Group 2	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:Diarrhoea	13 weeks	222/224	4.95%/4.02%	RR	1.23(0.52,2.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:Diarrhoea	13 weeks	224/224	9.38%/4.02%	RR	2.33(1.09,4.98)	Group 2	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Dizziness	180 days	108/104	3.7%/0.96%	RR	3.85(0.44,33.89)	Not Sig.	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Drug-Related Adverse Events	12 wks	267/275	16.1%/14.18%	RR	1.14(0.76,1.69)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Dyspepsia	180 days	108/104	1.85%/3.85%	RR	0.48(0.09,2.57)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Dyspepsia	42 days	300/289	2.33%/1.04%	RR	2.25(0.59,8.61)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:Dyspepsia	13 weeks	224/224	11.16%/9.82%	RR	1.14(0.66,1.95)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:Dyspepsia	13 weeks	222/224	17.12%/9.82%	RR	1.74(1.07,2.85)	Group 2	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Fall	180 days	108/104	2.78%/1.92%	RR	1.44(0.25,8.47)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Flatulence	42 days	300/289	1.33%/0.35%	RR	3.85(0.43,34.27)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Gastroenteritis	12 wks	236/237	0.42%/0.42%	RR	1(0.06,15.96)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Gastroenteritis	12 wks	234/237	2.56%/0.42%	RR	6.08(0.74,50.09)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Gastroenteritis	180 days	108/104	0%/1.92%	RD	-1.923(-5.63,2.896)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Gastrointestinal System Disorders	6 wks	405/374	11.36%/11.23%	RR	1.01(0.68,1.5)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	236/237	2.12%/2.11%	RR	1(0.29,3.42)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	234/237	2.14%/2.11%	RR	1.01(0.3,3.45)	Not Sig.	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Headache	12 wks	267/275	16.1%/20.73%	RR	0.78(0.54,1.11)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Headache	180 days	108/104	5.56%/3.85%	RR	1.44(0.42,4.97)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Headache	42 days	300/289	3.67%/1.73%	RR	2.12(0.75,6.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	236/237	0.85%/0.42%	RR	2.01(0.18,22)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Hypertension	12 wks	234/237	2.56%/0.42%	RR	6.08(0.74,50.09)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Improbable Relationship with Study Drug	6 wks	405/374	15.56%/17.38%	RR	0.9(0.65,1.23)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Injury	180 days	108/104	3.7%/0%	RD	3.704(-1.731, 7.919)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Mild Adverse Events	6 wks	405/374	10.37%/8.02%	RR	1.29(0.83,2.02)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Missing Data	6 wks	405/374	1.23%/0.53%	RR	2.31(0.45,11.83)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Moderate Adverse Events	6 wks	405/374	19.01%/18.45%	RR	1.03(0.77,1.38)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Musculoskeletal System Disorders	6 wks	405/374	2.47%/4.28%	RR	0.58(0.27,1.26)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	236/237	2.12%/1.69%	RR	1.26(0.34,4.62)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	234/237	3.42%/1.69%	RR	2.03(0.62,6.64)	Not Sig.	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Nausea	12 wks	267/275	7.12%/3.27%	RR	2.17(1, 4.72)	Group 2	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Nausea	42 days	300/289	2.33%/1.73%	RR	1.35(0.43,4.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:Nausea	13 weeks	224/224	5.36%/5.36%	RR	1(0.46, 2.18)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:Nausea	13 weeks	222/224	6.76%/5.36%	RR	1.26(0.6,2.63)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Neck Pain	180 days	108/104	1.85%/0%	RD	1.852(-2.798, 5.659)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Patients with at least 1 serious adverse events	6 wks	405/374	1.23%/0.8%	RR	1.54(0.37,6.4)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Patients with at least 1 treatment emergent adverse events	6 wks	405/374	20.99%/22.99%	RR	0.91(0.7,1.19)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Patients withdrawn for safety reasons	6 wks	405/374	8.89%/7.75%	RR	1.15(0.72,1.83)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Possible Relationship with Study Drug	6 wks	405/374	6.91%/6.15%	RR	1.12(0.66,1.92)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Probable Relationship with Study Drug	6 wks	405/374	9.38%/9.63%	RR	0.97(0.63,1.5)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Respiratory System Disorders	6 wks	405/374	2.96%/3.48%	RR	0.85(0.39,1.84)	Not Sig.	na
Herrero-Beaumont; 2007/High	9: Acetaminophen-Acetaminophen (Oral)(1 gm tablets 3x/day)	9: Placebo/Control-Placebo (Oral)(placebo tablet 3x/day)	Adverse events:Respiratory tract infections	180 days	108/104	3.7%/8.65%	RR	0.43(0.14,1.35)	Not Sig.	na
Prior; 2014/High	9: Acetaminophen-Acetaminophen ER(650 mg two times daily)	9: Placebo/Control-Placebo	Adverse events:Serious Adverse Event	12 wks	267/275	3%/0.73%	RR	4.12(0.88,19.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Serious Events	42 days	300/289	1%/1.38%	RR	0.72(0.16,3.2)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Serious Treatment Emergent Adverse Events	12 wks	234/237	1.71%/0%	RD	1.709(-0.893, 3.615)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Serious Treatment Emergent Adverse Events	12 wks	236/237	2.12%/0%	RD	2.119(-0.626, 4.121)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Severe Treatment Emergent Adverse Events	12 wks	234/237	1.71%/1.69%	RR	1.01(0.26,4)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Severe Treatment Emergent Adverse Events	12 wks	236/237	2.97%/1.69%	RR	1.76(0.52,5.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Skin and Appendages Disorders	6 wks	405/374	1.48%/1.07%	RR	1.39(0.39,4.87)	Not Sig.	na
Micelli ; 2004/Moderate	9: Acetaminophen-Paracetamol(4 g per day)	9: Placebo/Control-Placebo	Adverse events:Total Number of Reported Adverse Events	6 wks	405/374	35.06%/35.29%	RR	0.99(0.82,1.2)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Treatment Emergent Adverse Events	12 wks	234/237	28.63%/21.52%	RR	1.33(0.97,1.83)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Treatment Emergent Adverse Events	12 wks	236/237	29.24%/21.52%	RR	1.36(0.99,1.86)	Not Sig.	na
Reed; 2018/High	9: Acetaminophen-Paracetamol Extended Release(665 mg three times daily)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	12 wks	236/237	1.27%/0.84%	RR	1.51(0.25,8.93)	Not Sig.	na

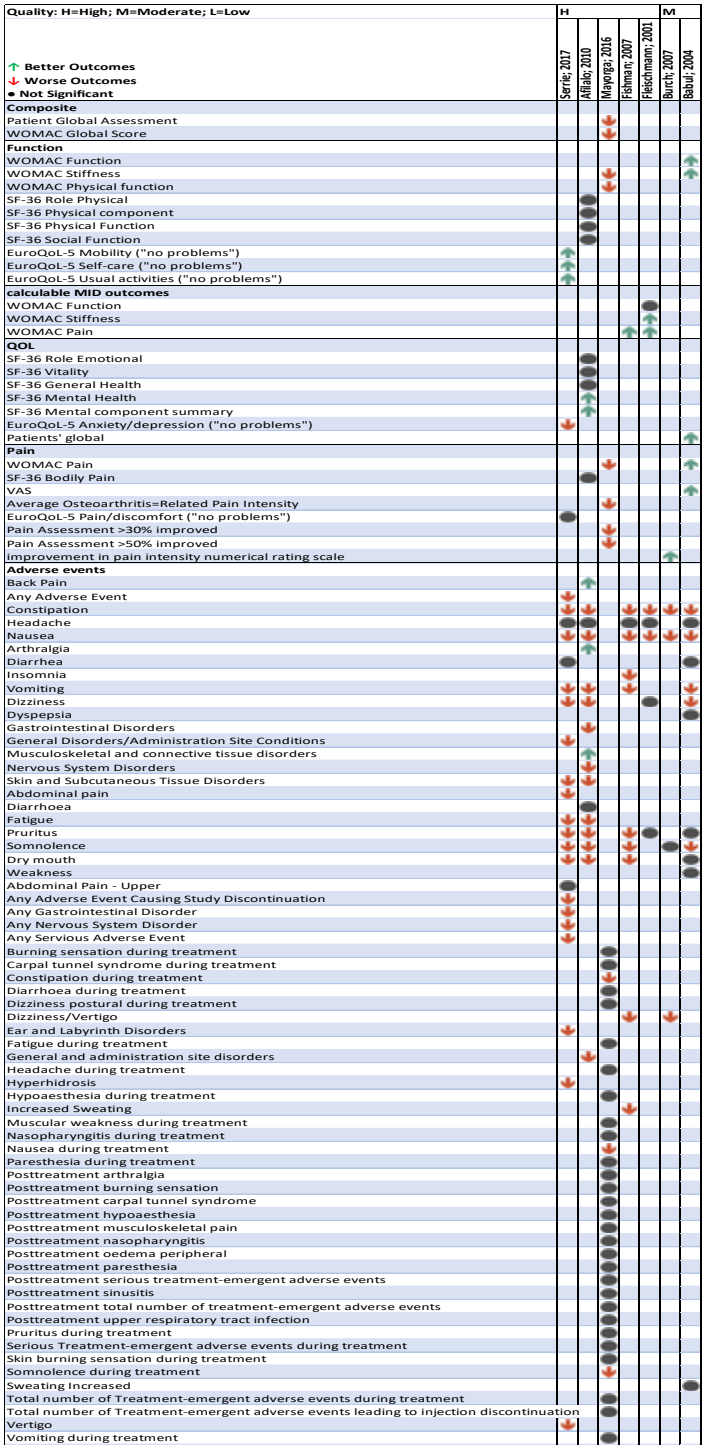
study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Reed; 2018/High	9: Acetaminophen-Paracetamol Slow Release(1;000 mg twice daily)	9: Placebo/Control-Placebo	Adverse events:Upper Respiratory Tract Infection	12 wks	234/237	2.14%/0.84%	RR	2.53(0.5,12.92)	Not Sig.	na
Pincus; 2004/Moderate	9: Acetaminophen-Acetaminophen (Oral)(1000mg x4/day)	9: Placebo/Control-Placebo (Oral)(placebo)	Adverse events:Upper respiratory tract infection	42 days	300/289	5.67%/3.11%	RR	1.82(0.82,4.02)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:any adverse event	13 weeks	222/224	77.93%/78.13%	RR	1(0.9,1.1)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:any adverse event	13 weeks	224/224	84.38%/78.13%	RR	1.08(0.99,1.18)	Not Sig.	na
Doherty; 2011/High	9: NSAIDs (oral/IM)-1 dose of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:any adverse event related to treatment	13 weeks	222/224	50.45%/41.52%	RR	1.22(0.99,1.49)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Doherty; 2011/High	9: NSAIDs (oral/IM)-2 doses of combined ibprofen (200mg) and paracetamol (500mg)	9: NSAIDs (oral/IM)-Ibuprofen (200mg twice daily)	Adverse events:any adverse event related to treatment	13 weeks	224/224	51.34%/41.52%	RR	1.24(1.01,1.51)	Group 2	na

PICO 9: Systemic Treatment

Oral Narcotics vs. Control

Table 39: Oral Narcotics vs Control


Quality: H=High; M=Moderate; L=Low
H
M
↑ Better Outcomes
↓ Worse Outcomes
● Not Significant
Serrie; 2017
Affaitic; 2010
Mayorga; 2016
Fishman; 2007
Fleischmann; 2001
Burch; 2007
Babul; 2004
Composite
Patient Global Assessment
WOMAC Global Score
Function
WOMAC Function
WOMAC Stiffness
WOMAC Physical function
SF-36 Role Physical
SF-36 Physical component
SF-36 Physical Function
SF-36 Social Function
EuroQoL-5 Mobility ("no problems")
EuroQoL-5 Self-care ("no problems")
EuroQoL-5 Usual activities ("no problems")
calculable MID outcomes
WOMAC Function
WOMAC Stiffness
WOMAC Pain
QOL
SF-36 Role Emotional
SF-36 Vitality
SF-36 General Health
SF-36 Mental Health
SF-36 Mental component summary
EuroQoL-5 Anxiety/depression ("no problems")
Patients' global
Pain
WOMAC Pain
SF-36 Bodily Pain
VAS
Average Osteoarthritis=Related Pain Intensity
EuroQoL-5 Pain/discomfort ("no problems")
Pain Assessment >30% improved
Pain Assessment >50% improved
improvement in pain intensity numerical rating scale
Adverse events
Back Pain
Any Adverse Event
Constipation
Headache
Nausea
Arthralgia
Diarrhea
Insomnia
Vomiting
Dizziness
Dyspepsia
Gastrointestinal Disorders
General Disorders/Administration Site Conditions
Musculoskeletal and connective tissue disorders
Nervous System Disorders
Skin and Subcutaneous Tissue Disorders
Abdominal pain
Diarrhoea
Fatigue
Pruritus
Somnolence
Dry mouth
Weakness
Abdominal Pain - Upper
Any Adverse Event Causing Study Discontinuation
Any Gastrointestinal Disorder
Any Nervous System Disorder
Any Servious Adverse Event
Burning sensation during treatment
Carpal tunnel syndrome during treatment
Constipation during treatment
Diarrhoea during treatment
Dizziness postural during treatment
Dizziness/Vertigo
Ear and Labyrinth Disorders
Fatigue during treatment
General and administration site disorders
Headache during treatment
Hyperhidrosis
Hypoaesthesia during treatment
Increased Sweating
Muscular weakness during treatment
Nasopharyngitis during treatment
Nausea during treatment
Paresthesia during treatment
Posttreatment arthralgia
Posttreatment burning sensation
Posttreatment carpal tunnel syndrome
Posttreatment hypoaesthesia
Posttreatment musculoskeletal pain
Posttreatment nasopharyngitis
Posttreatment oedema peripheral
Posttreatment paresthesia
Posttreatment serious treatment-emergent adverse events
Posttreatment sinusitis
Posttreatment total number of treatment-emergent adverse events
Posttreatment upper respiratory tract infection
Pruritus during treatment
Serious Treatment-emergent adverse events during treatment
Skin burning sensation during treatment
Somnolence during treatment
Sweating Increased
Total number of Treatment-emergent adverse events during treatment
Total number of Treatment-emergent adverse events leading to injection discontinuation
Vertigo
Vomiting during treatment

Evidence Table 4538: Oral Narcotics vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Pain:EuroQoL-5 Pain/discomfort ("no problems")		331/319	9.97%/16.93%	RR	0.59(0.39,0.88)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Function:EuroQoL-5 Mobility ("no problems")		330/319	25.76%/39.18%	RR	0.66(0.52,0.83)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Function:EuroQoL-5 Self-care ("no problems")		331/319	63.75%/70.85%	RR	0.9(0.81,1)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Function:EuroQoL-5 Usual activities ("no problems")		331/319	32.02%/43.89%	RR	0.73(0.6,0.89)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	QOL:EuroQoL-5 Anxiety/depression ("no problems")		331/319	47.43%/57.05%	RR	0.83(0.72,0.96)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Abdominal Pain		331/319	5.44%/1.25%	RR	4.34(1.48,12.67)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Abdominal Pain - Upper		331/319	4.53%/4.08%	RR	1.11(0.54,2.3)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Any Adverse Event		331/319	84.89%/67.08%	RR	1.27(1.16,1.38)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Any Adverse Event Causing Study Discontinuation		331/319	42.3%/18.81%	RR	2.25(1.73,2.92)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Any Gastrointestinal Disorder		331/319	67.67%/41.69%	RR	1.62(1.4,1.89)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Any Nervous System Disorder		331/319	45.92%/40.75%	RR	1.13(0.94,1.34)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Any Servious Adverse Event		331/319	3.93%/0.63%	RR	6.26(1.42,27.54)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Constipation		331/319	35.05%/17.87%	RR	1.96(1.49,2.59)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Diarrhea		331/319	7.85%/5.02%	RR	1.57(0.86,2.86)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Dizziness		331/319	26.89%/21.94%	RR	1.23(0.93,1.61)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Dry Mouth		331/319	3.93%/5.96%	RR	0.66(0.33,1.31)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Ear and Labyrinth Disorders		331/319	6.95%/6.58%	RR	1.06(0.6,1.87)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Fatigue		331/319	9.97%/7.84%	RR	1.27(0.77,2.09)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:General Disorders/Administration Site Conditions		331/319	20.85%/17.24%	RR	1.21(0.88,1.66)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Headache		331/319	8.16%/10.34%	RR	0.79(0.49,1.28)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Hyperhidrosis		331/319	8.16%/9.09%	RR	0.9(0.54,1.48)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Nausea		331/319	37.46%/20.38%	RR	1.84(1.42,2.38)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Pruritus		331/319	10.88%/1.25%	RR	8.67(3.12,24.09)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Skin and Subcutaneous Tissue Disorders		331/319	22.96%/11.91%	RR	1.93(1.35,2.76)	Group 2	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Somnolence		331/319	14.5%/10.66%	RR	1.36(0.9,2.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Vertigo		331/319	6.34%/5.96%	RR	1.07(0.58,1.94)	Not Sig.	na
Serrie; 2017/High	9: Narcotics/opioids-Oxycodone(Twice a day for 12 weeks; >20 mg)	9: Narcotics/opioids-Tapentadol PR(Twice a day for 12 weeks; >100 mg)	Adverse events:Vomiting		331/319	25.98%/10.34%	RR	2.51(1.73,3.64)	Group 2	na

PICO 10: Locally Invasive Treatment

Hyaluronic Acid vs. Control

Table 40: Hyaluronic Acid vs Control

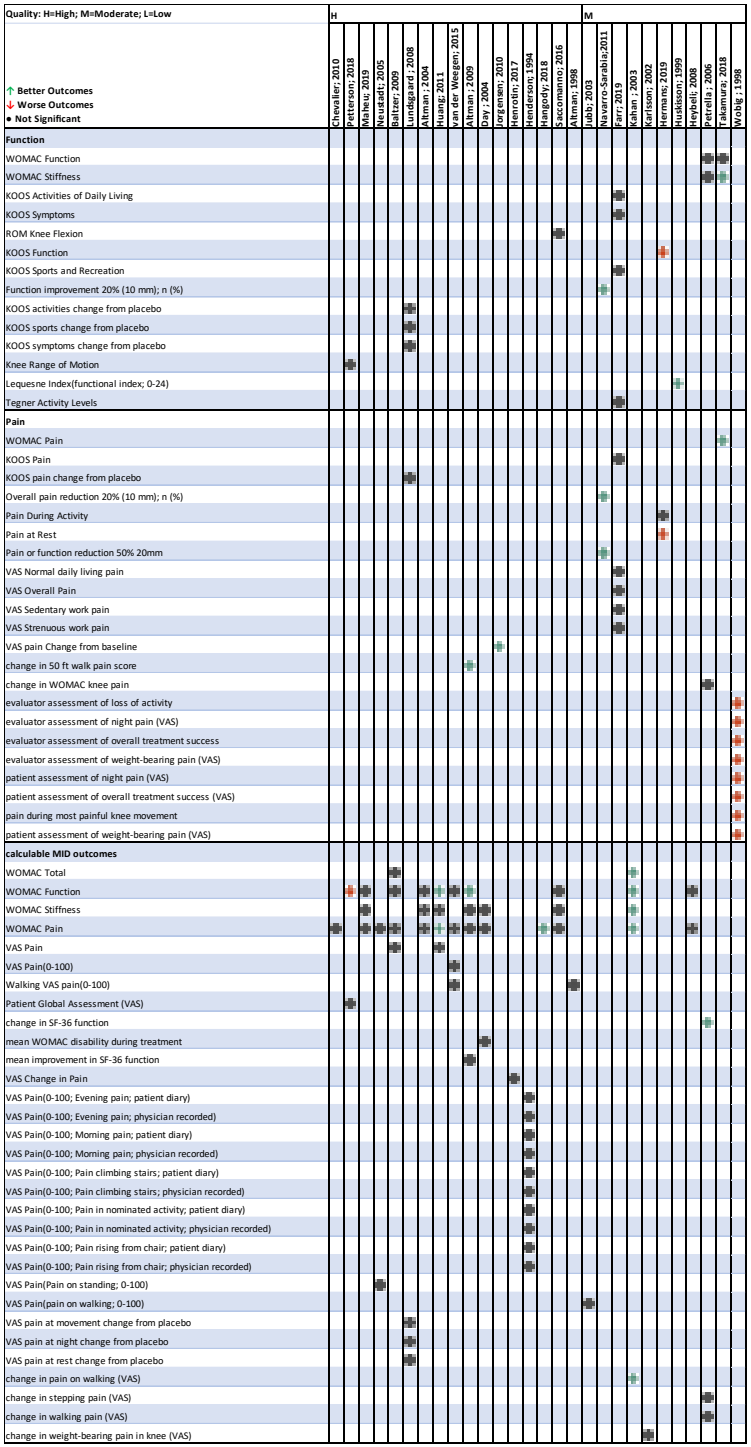
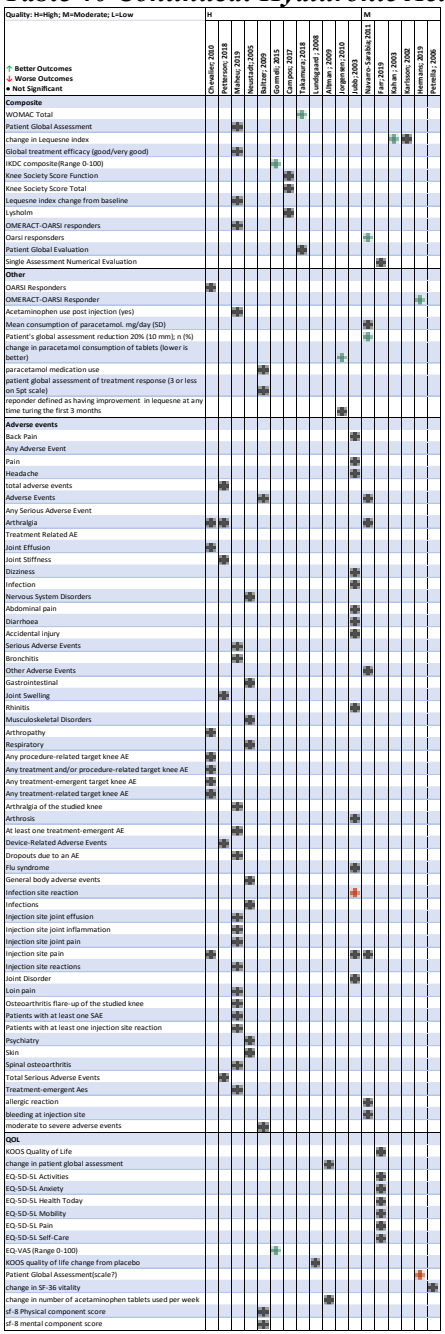
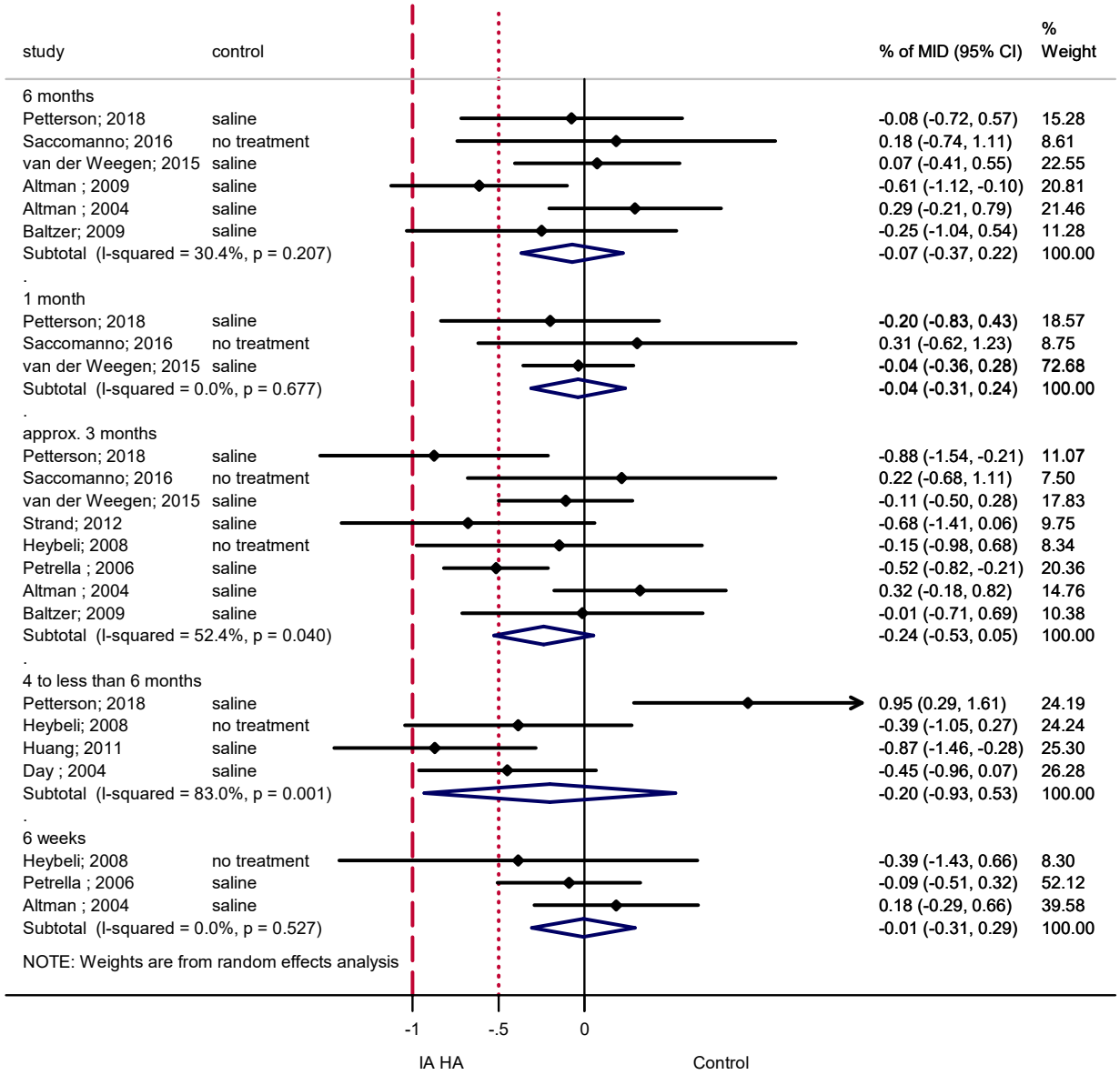

Quality: H=High; M=Moderate; L=Low
H
M
↑ Better Outcomes
↓ Worse Outcomes
• Not Significant
Chevalier; 2010
Petterson; 2018
Maheu; 2019
Neustadt; 2005
Baltzer; 2009
Lundgaard ; 2008
Altman; 2004
Huang; 2011
van der Weegen; 2015
Altman ; 2009
Day ; 2004
Jorgensen; 2010
Henrotin; 2017
Henderson; 1994
Mangoldy; 2018
Saccomanno; 2016
Altman; 1998
Juni; 2003
Navarro-Sarabia;2011
Farr; 2019
Kahan ; 2003
Karlsson; 2002
Hermens; 2019
Huskisson; 1999
Heydel; 2008
Petrella ; 2006
Takamura; 2018
Wobig ; 1998
Function
WOMAC Function
WOMAC Stiffness
KOOS Activities of Daily Living
KOOS Symptoms
ROM Knee Flexion
KOOS Function
KOOS Sports and Recreation
Function improvement 20% (10 mm); n (%)
KOOS activities change from placebo
KOOS sports change from placebo
KOOS symptoms change from placebo
Knee Range of Motion
Lequesne Index(functional index; 0-24)
Tegner Activity Levels
Pain
WOMAC Pain
KOOS Pain
KOOS pain change from placebo
Overall pain reduction 20% (10 mm); n (%)
Pain During Activity
Pain at Rest
Pain or function reduction 50% 20mm
VAS Normal daily living pain
VAS Overall Pain
VAS Sedentary work pain
VAS Strenuous work pain
VAS pain Change from baseline
change in 50 ft walk pain score
change in WOMAC knee pain
evaluator assessment of loss of activity
evaluator assessment of night pain (VAS)
evaluator assessment of overall treatment success
evaluator assessment of weight-bearing pain (VAS)
patient assessment of night pain (VAS)
patient assessment of overall treatment success (VAS)
pain during most painful knee movement
patient assessment of weight-bearing pain (VAS)
calculable MID outcomes
WOMAC Total
WOMAC Function
WOMAC Stiffness
WOMAC Pain
VAS Pain
VAS Pain(0-100)
Walking VAS pain(0-100)
Patient Global Assessment (VAS)
change in SF-36 function
mean WOMAC disability during treatment
mean improvement in SF-36 function
VAS Change in Pain
VAS Pain(0-100; Evening pain; patient diary)
VAS Pain(0-100; Evening pain; physician recorded)
VAS Pain(0-100; Morning pain; patient diary)
VAS Pain(0-100; Morning pain; physician recorded)
VAS Pain(0-100; Pain climbing stairs; patient diary)
VAS Pain(0-100; Pain climbing stairs; physician recorded)
VAS Pain(0-100; Pain in nominated activity; patient diary)
VAS Pain(0-100; Pain in nominated activity; physician recorded)
VAS Pain(0-100; Pain rising from chair; patient diary)
VAS Pain(0-100; Pain rising from chair; physician recorded)
VAS Pain(Pain on standing; 0-100)
VAS Pain(pain on walking; 0-100)
VAS pain at movement change from placebo
VAS pain at night change from placebo
VAS pain at rest change from placebo
change in pain on walking (VAS)
change in stepping pain (VAS)
change in walking pain (VAS)
change in weight-bearing pain in knee (VAS)

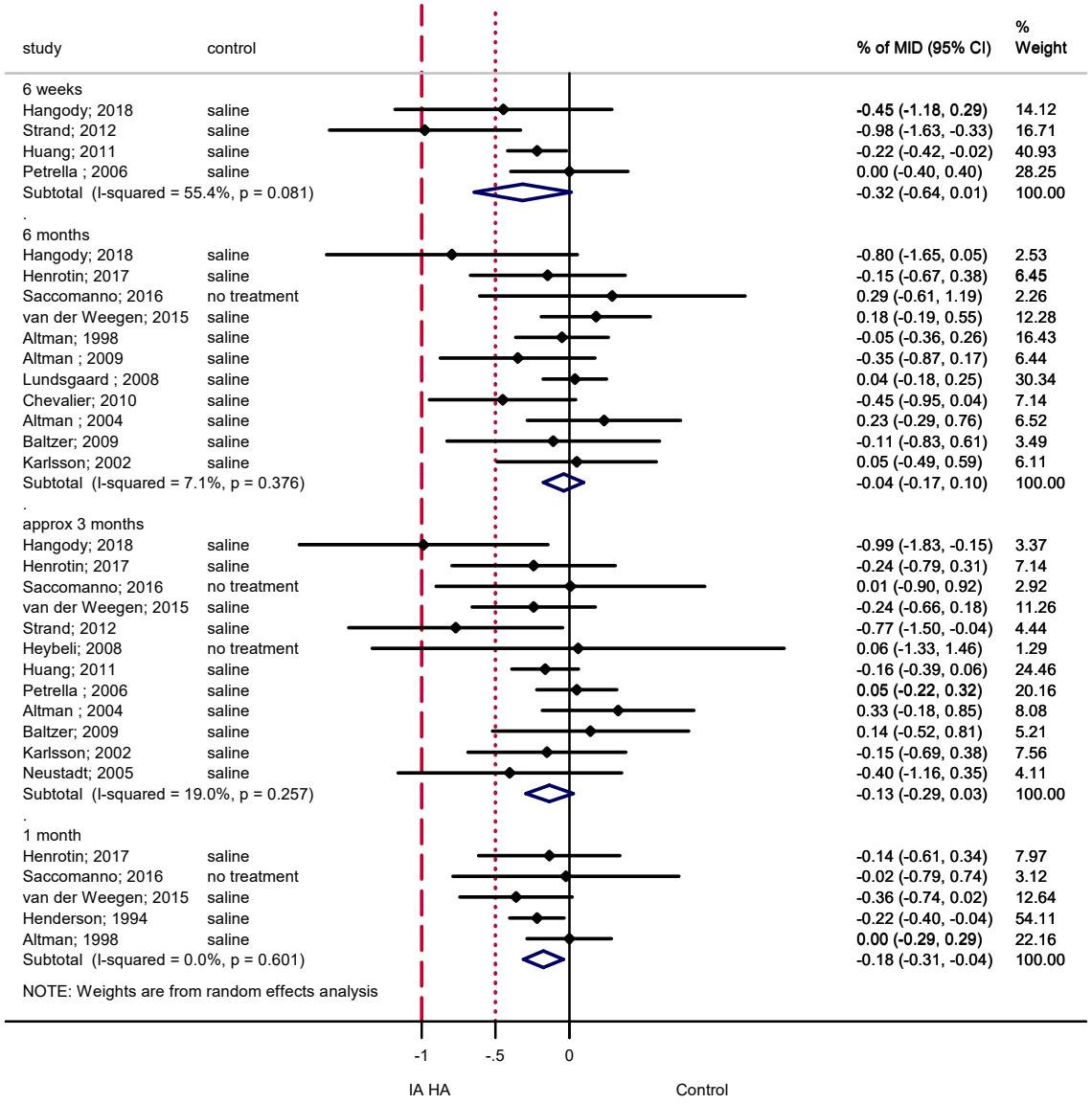
Table 40 Continued: Hyaluronic Acid vs Control



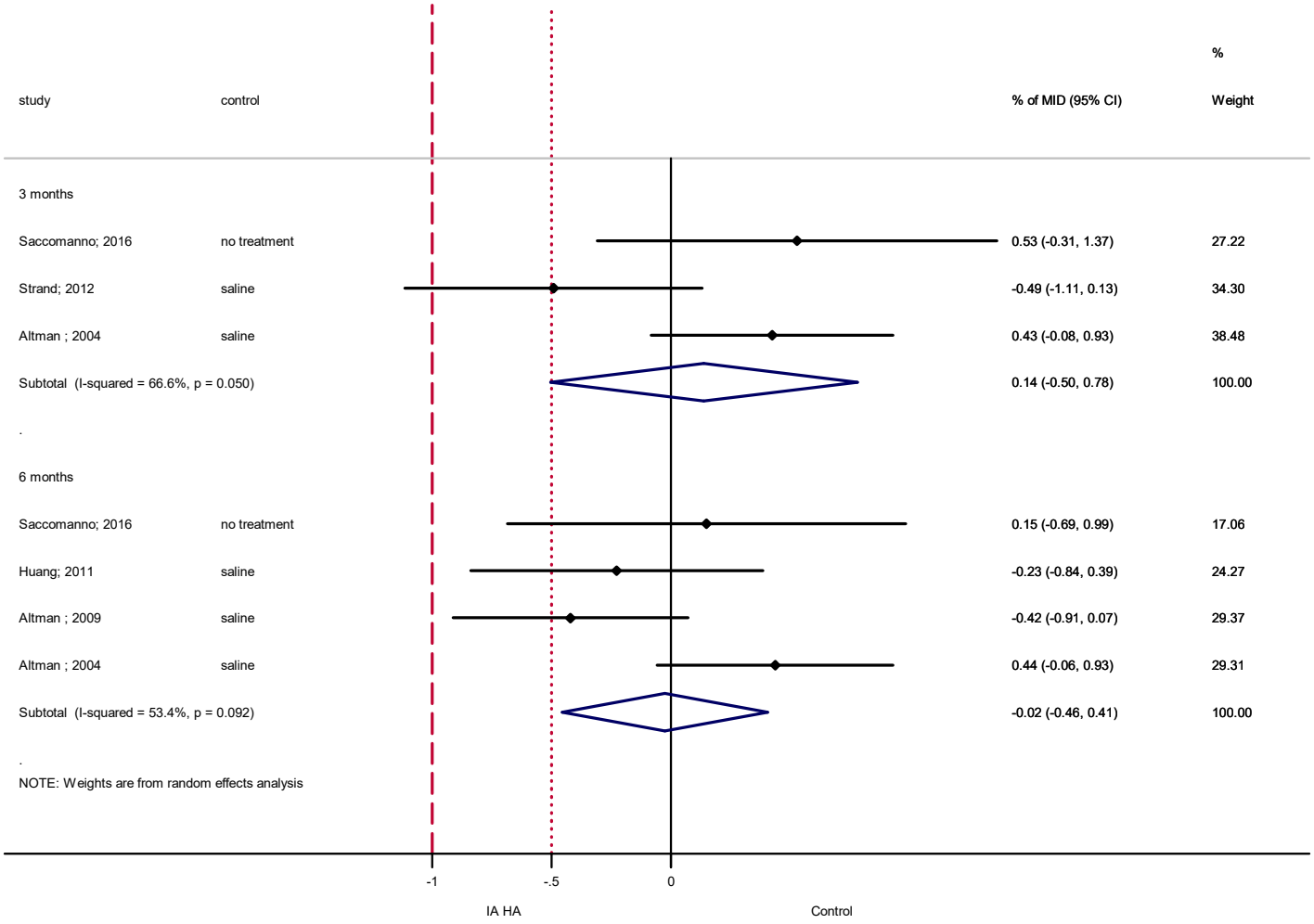
Meta-Analysis Figure 38: Hyaluronic Acid vs Control- WOMAC Function Using All Control Group Types



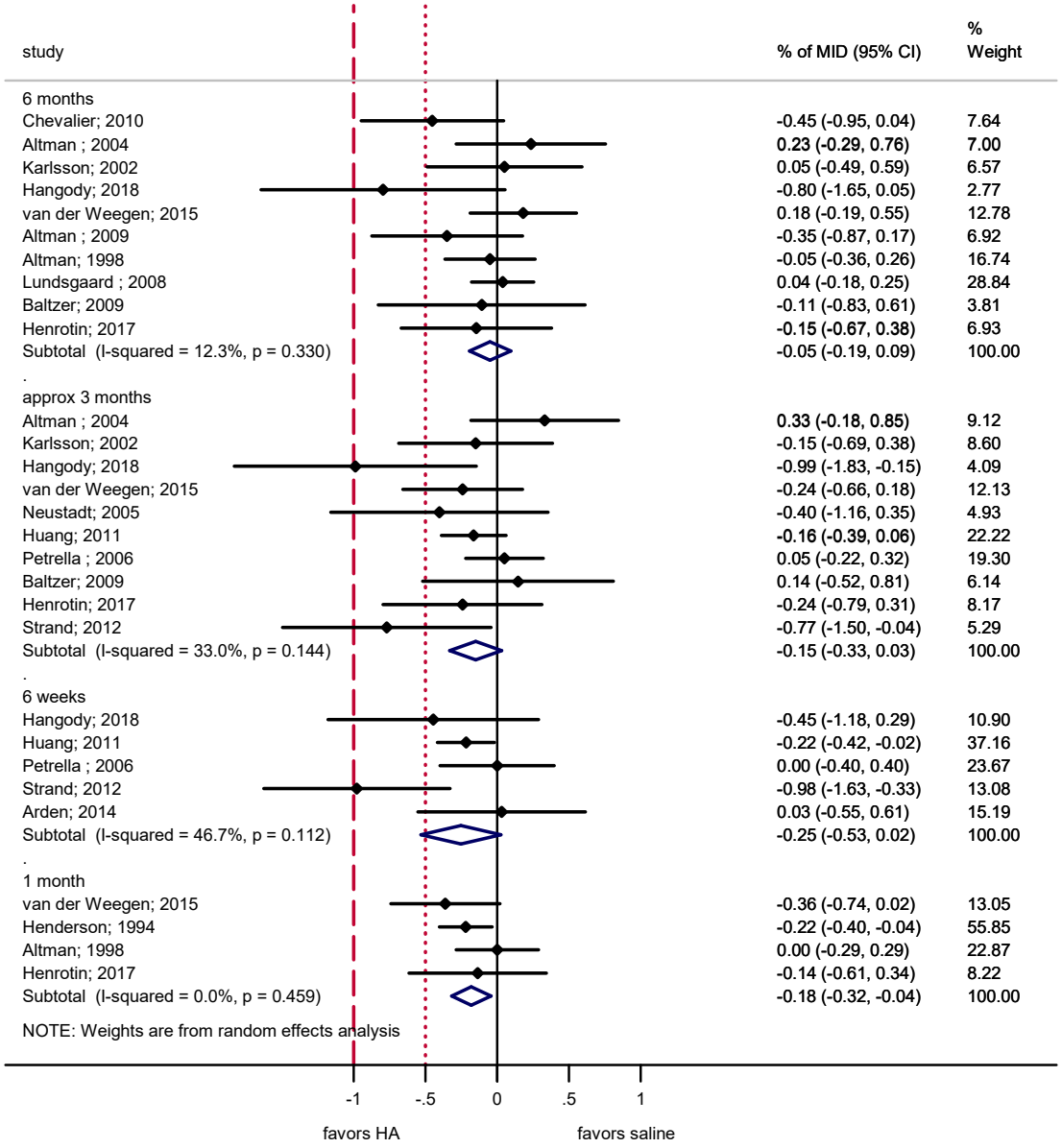
Meta-Analysis Figure 39: Hyaluronic Acid vs Control- Pain Using All Control Group Types



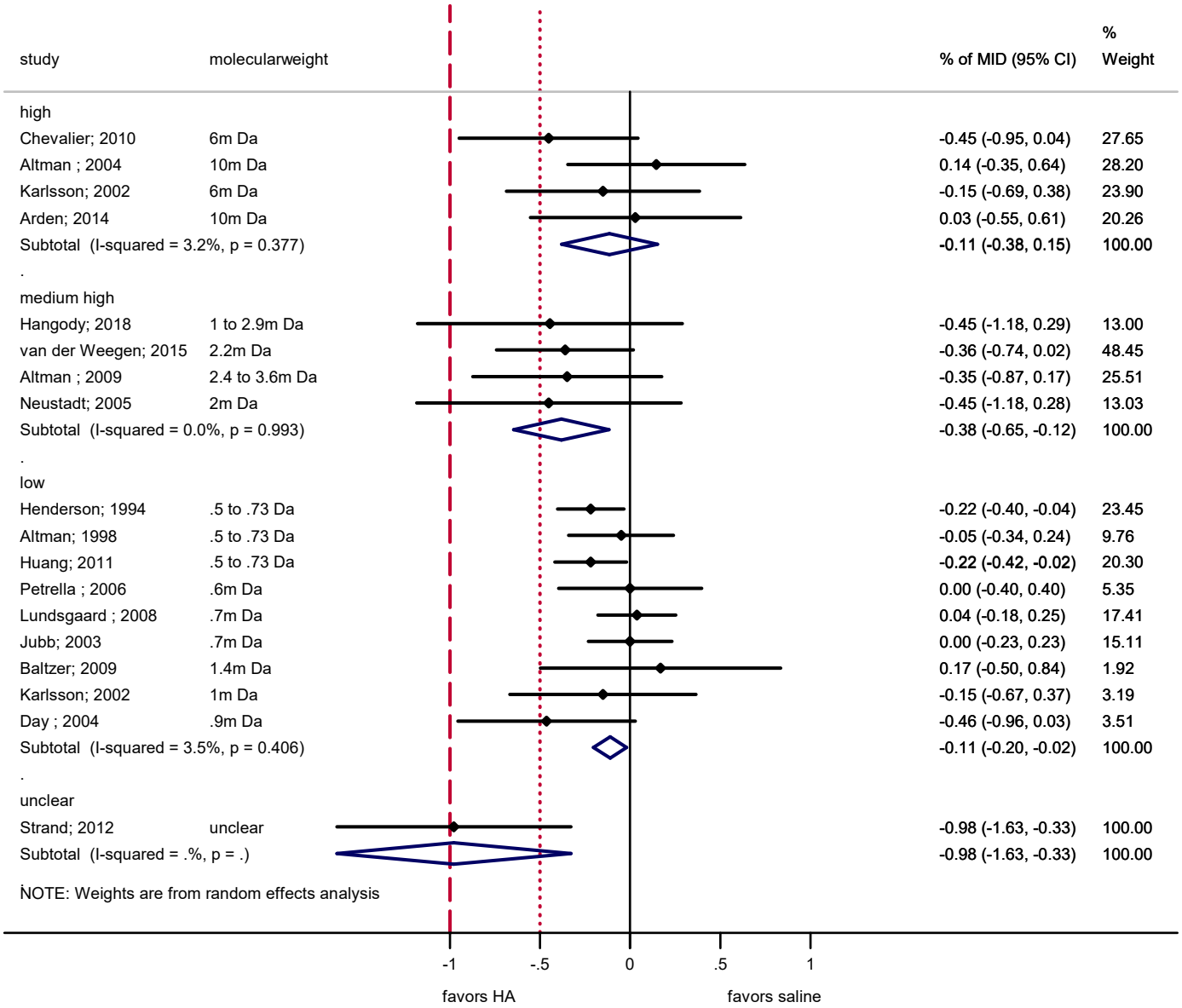
Meta-Analysis Figure 40: Hyaluronic Acid vs Control- Stiffness Using All Control Group Types



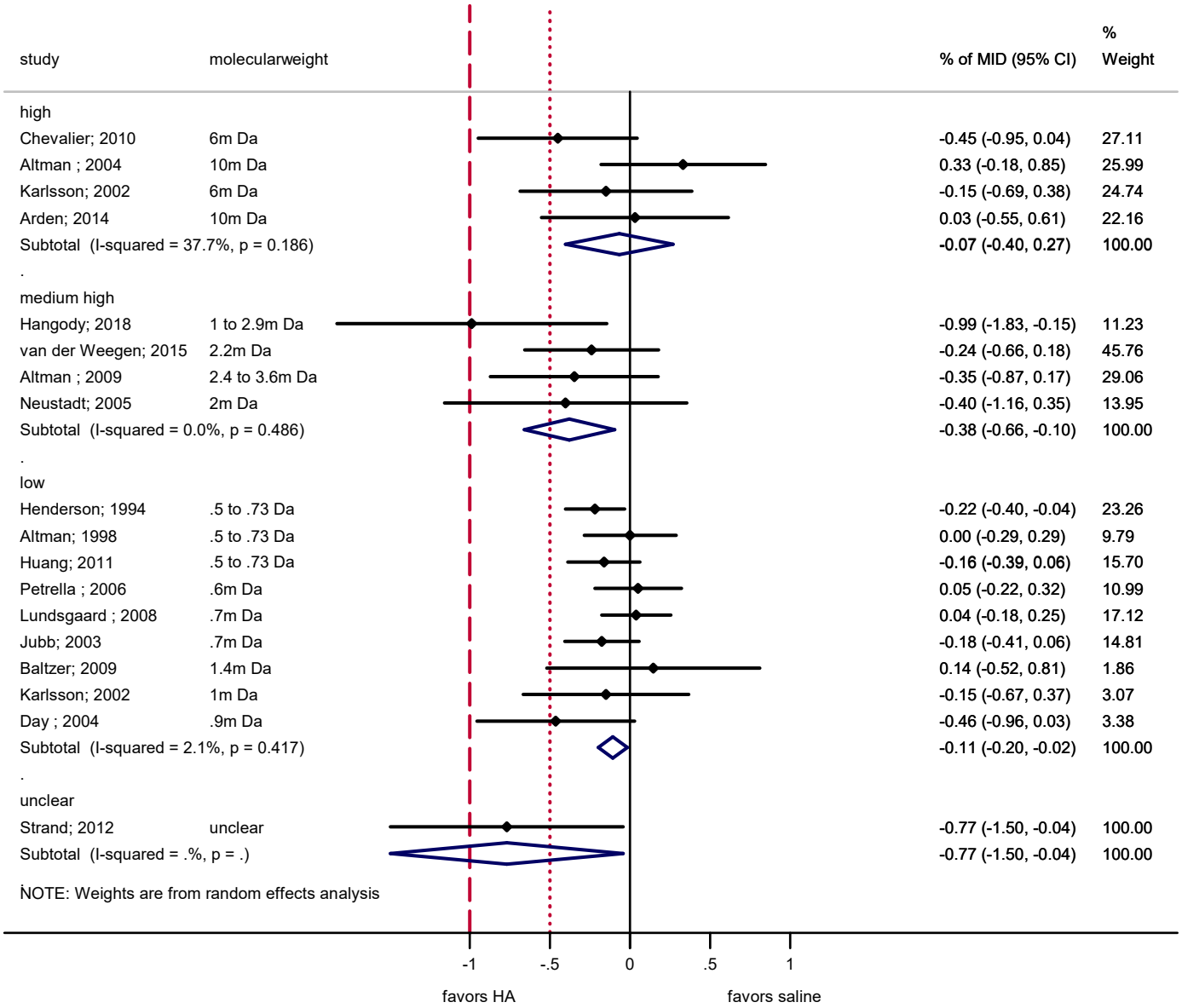
Meta-Analysis Figure 41: Hyaluronic Acid vs Saline- Pain by Follow Up



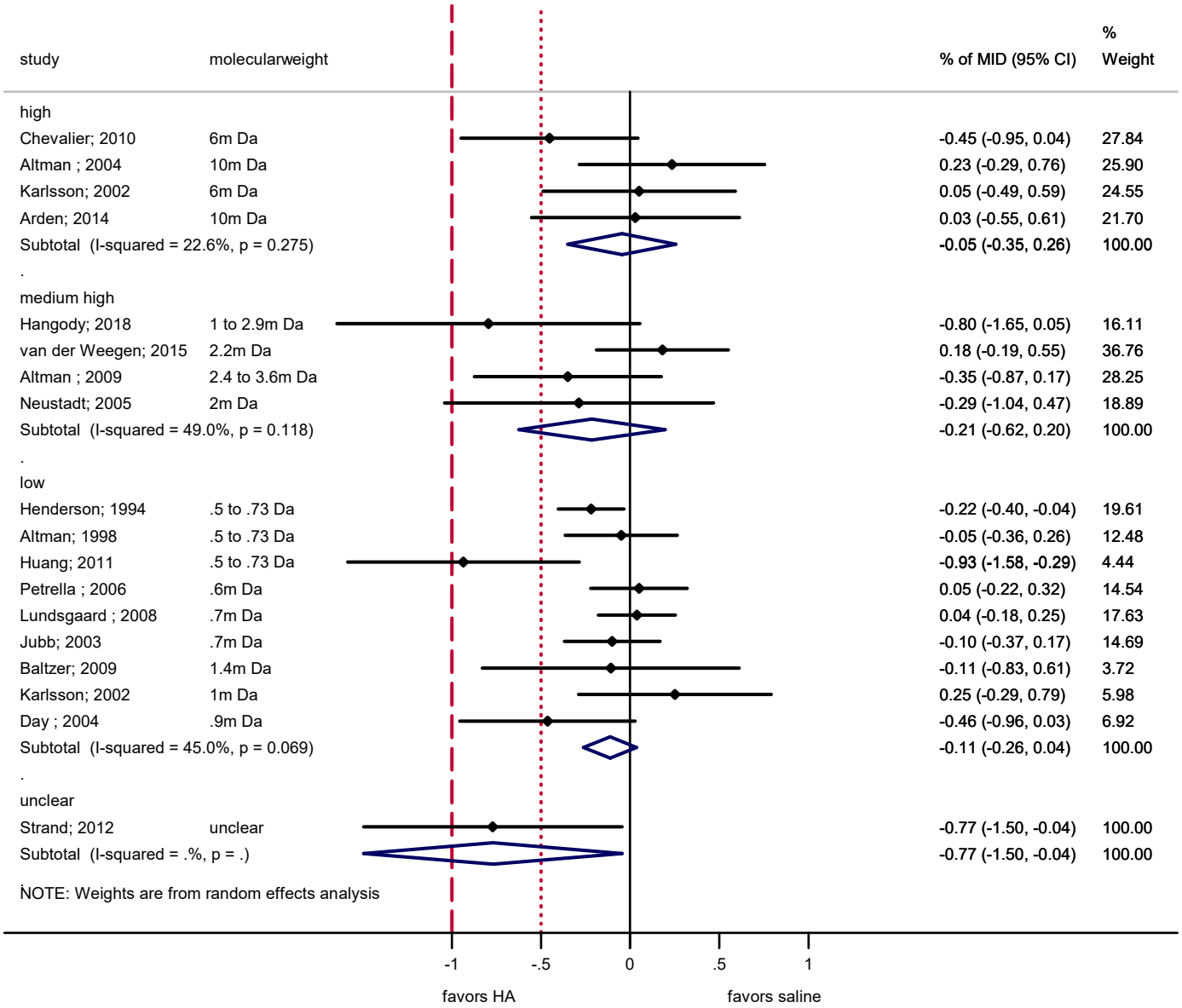
Meta-Analysis Figure 42: Hyaluronic Acid vs Saline- Pain by Molecular Weight Earliest Follow Up Time



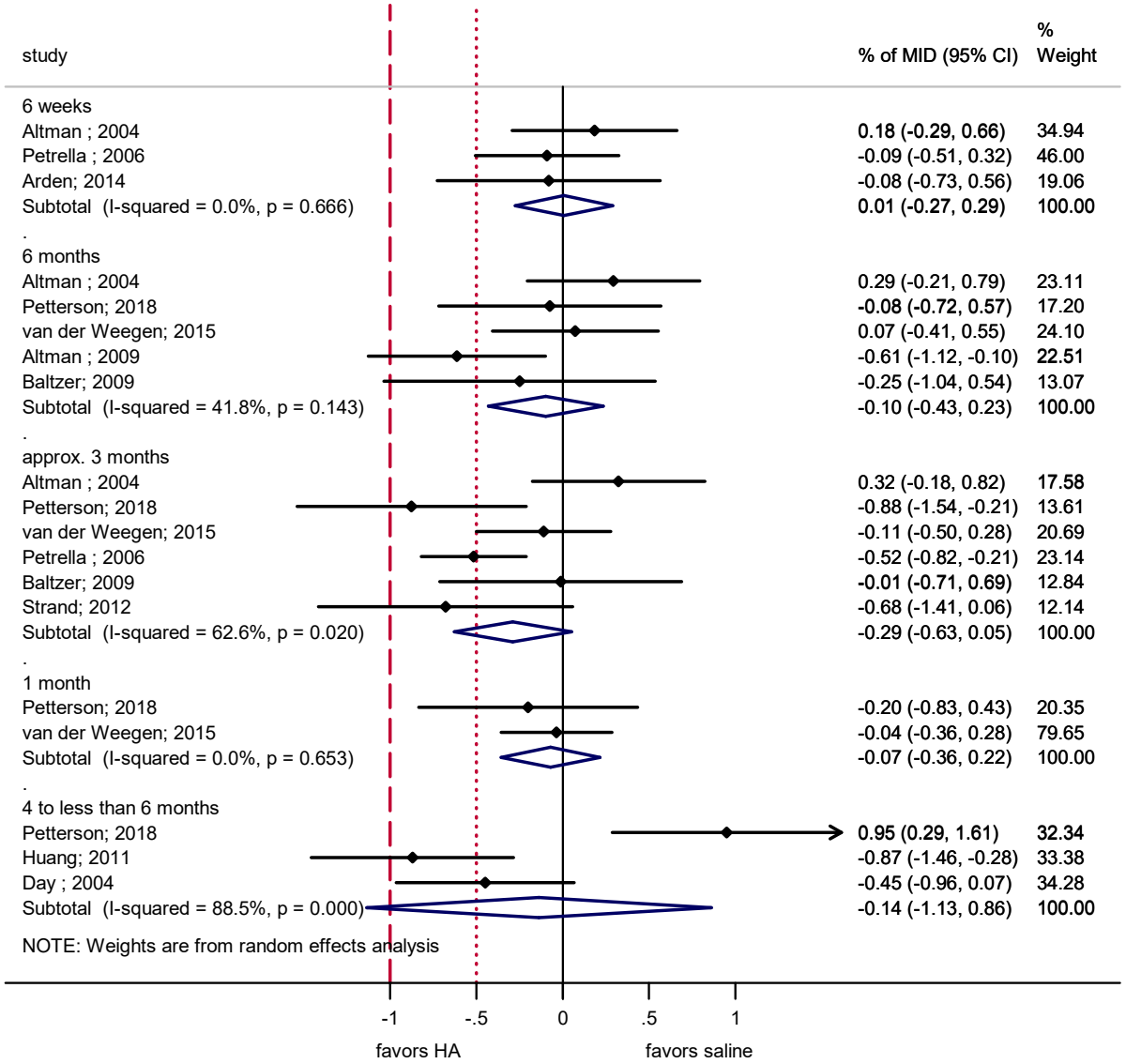
Meta-Analysis Figure 43: Hyaluronic Acid vs Saline- Pain by Molecular Weight Closest to 3-Month Follow Up



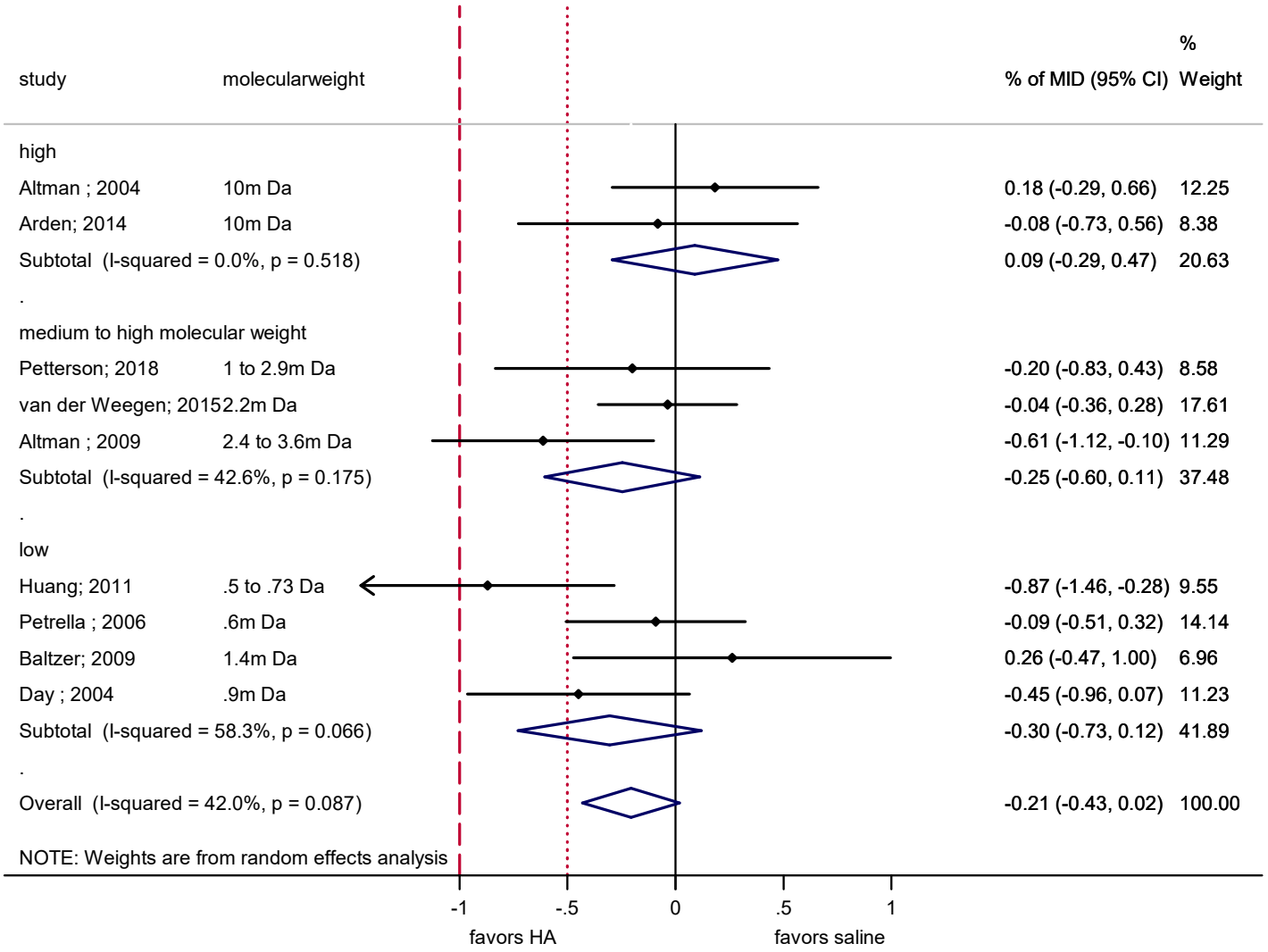
Meta-Analysis Figure 44: Hyaluronic Acid vs Saline- Pain by Molecular Weight Closest to 6-Month Follow Up



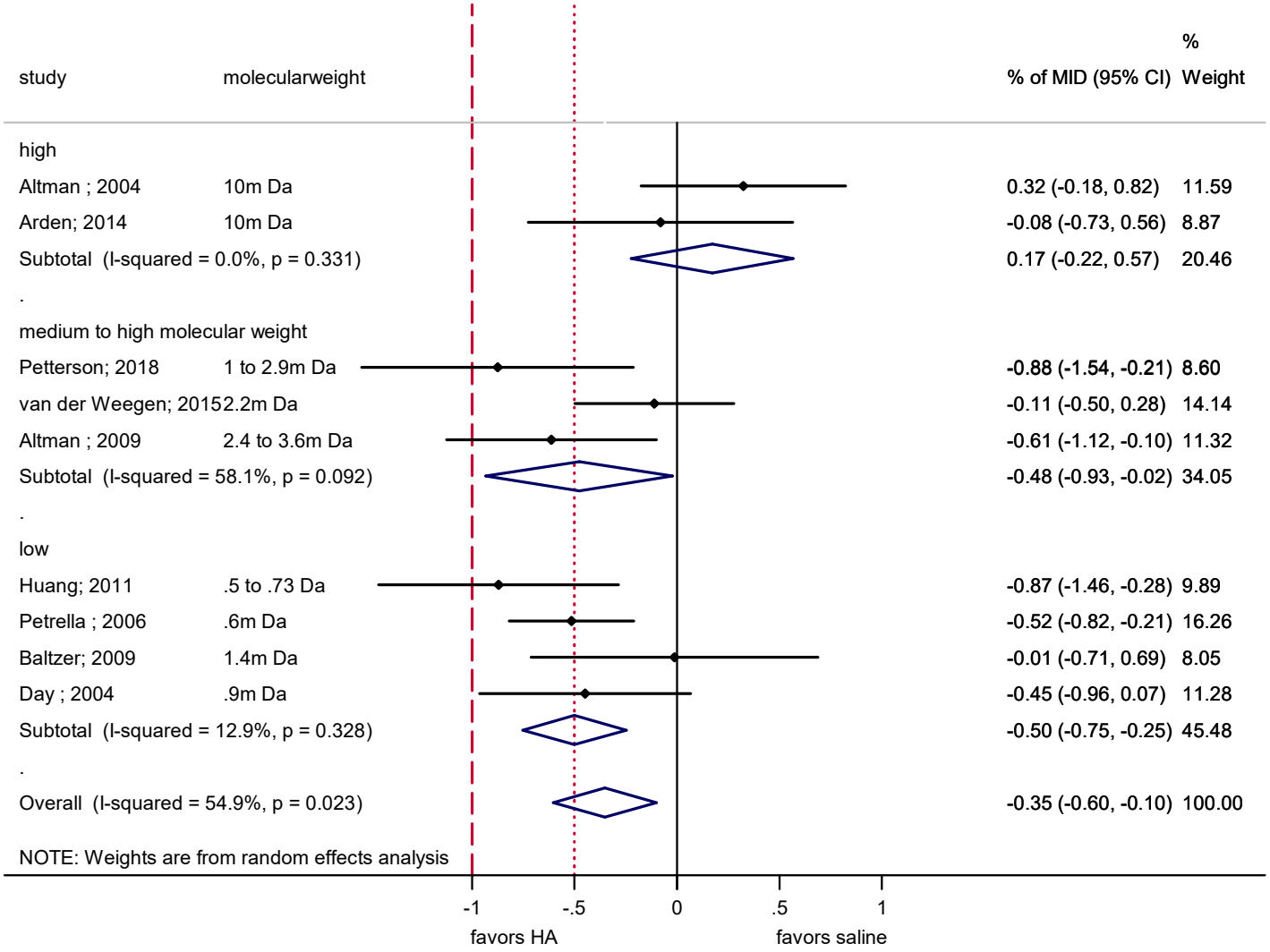
Meta-Analysis Figure 45: Hyaluronic Acid vs Saline- Function by Follow Up Time



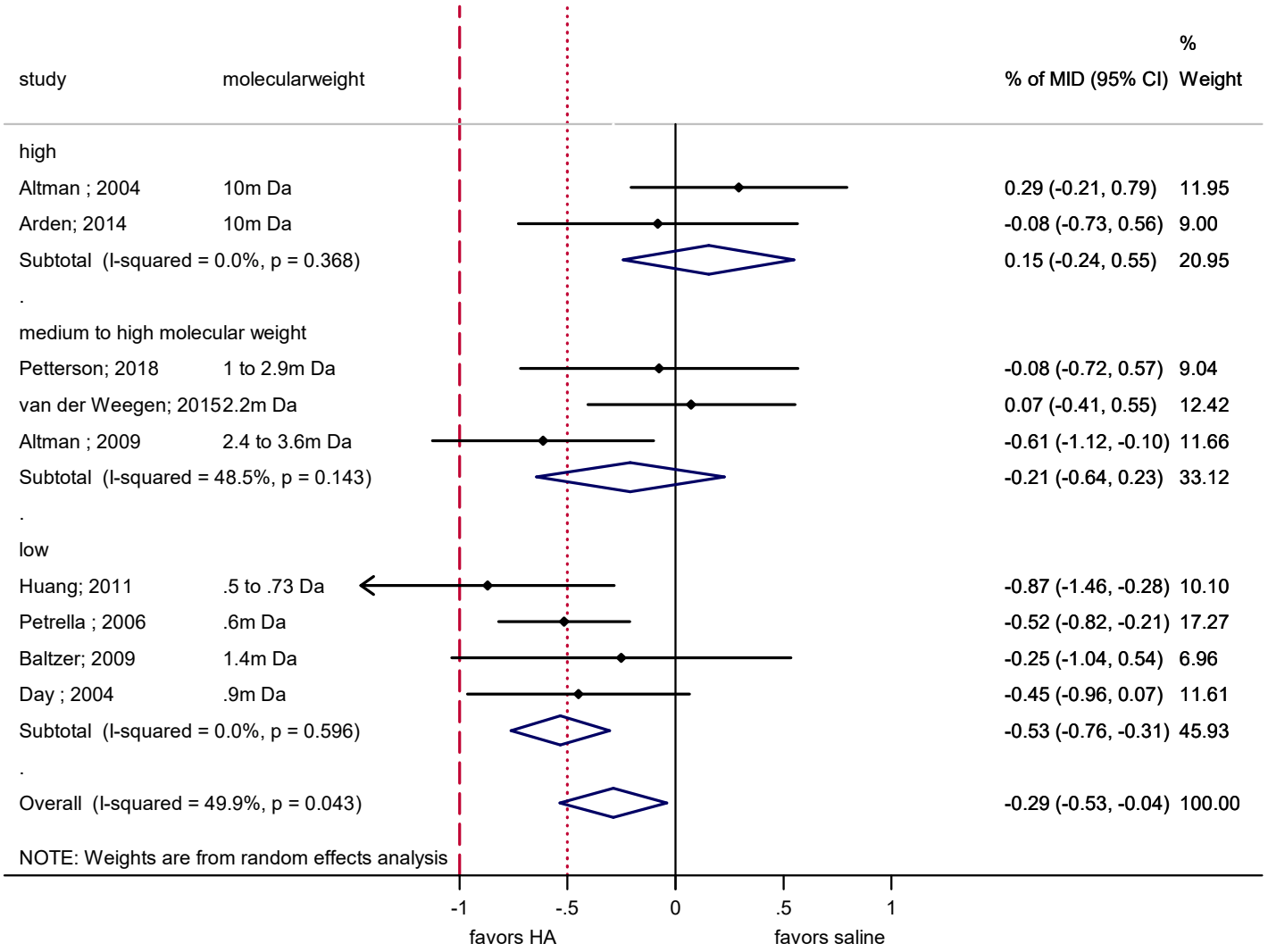
Meta-Analysis Figure 46: Hyaluronic Acid vs Saline- Function by Molecular Weight Earliest Follow Up



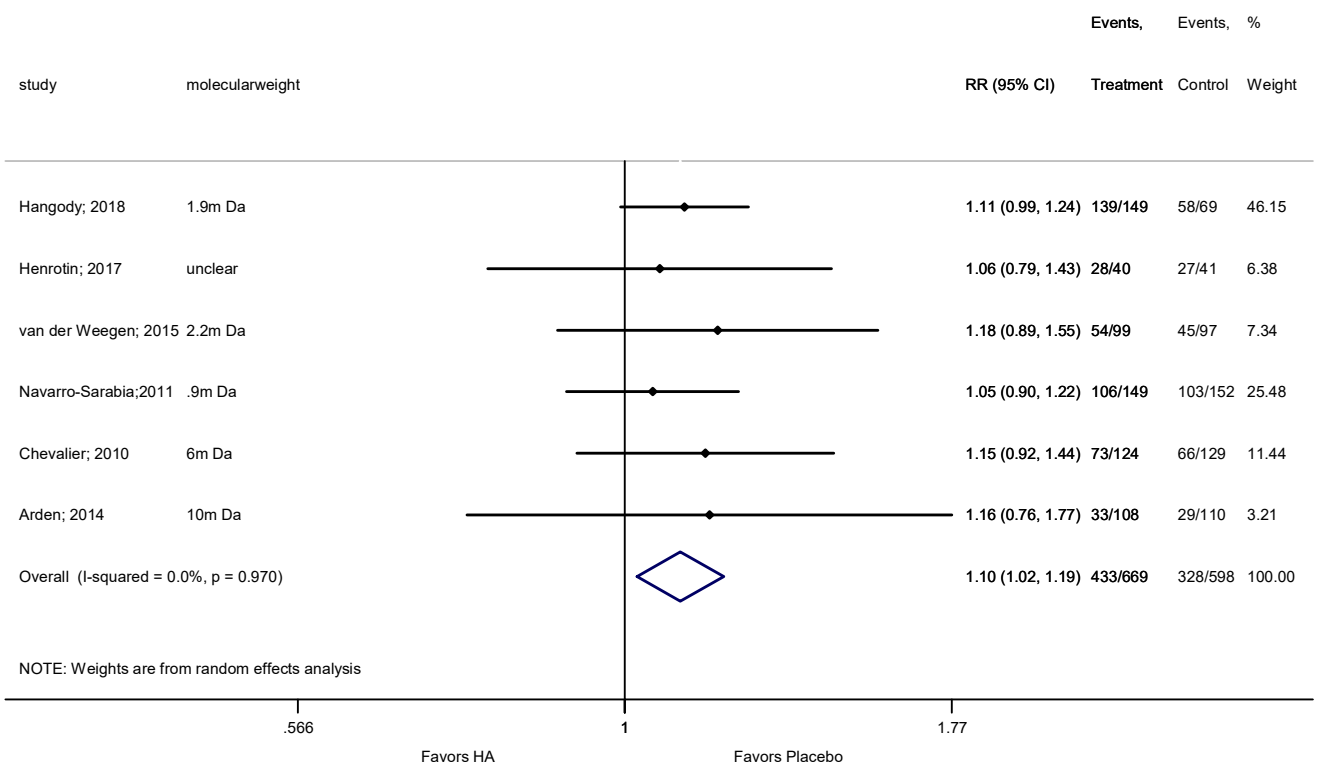
Meta-Analysis Figure 47: Hyaluronic Acid vs Saline- Function by Molecular Weight Closest to 3-Month Follow Up



Meta-Analysis Figure 48: Hyaluronic Acid vs Saline- Function by Molecular Weight Closest to 6-Month Follow Up



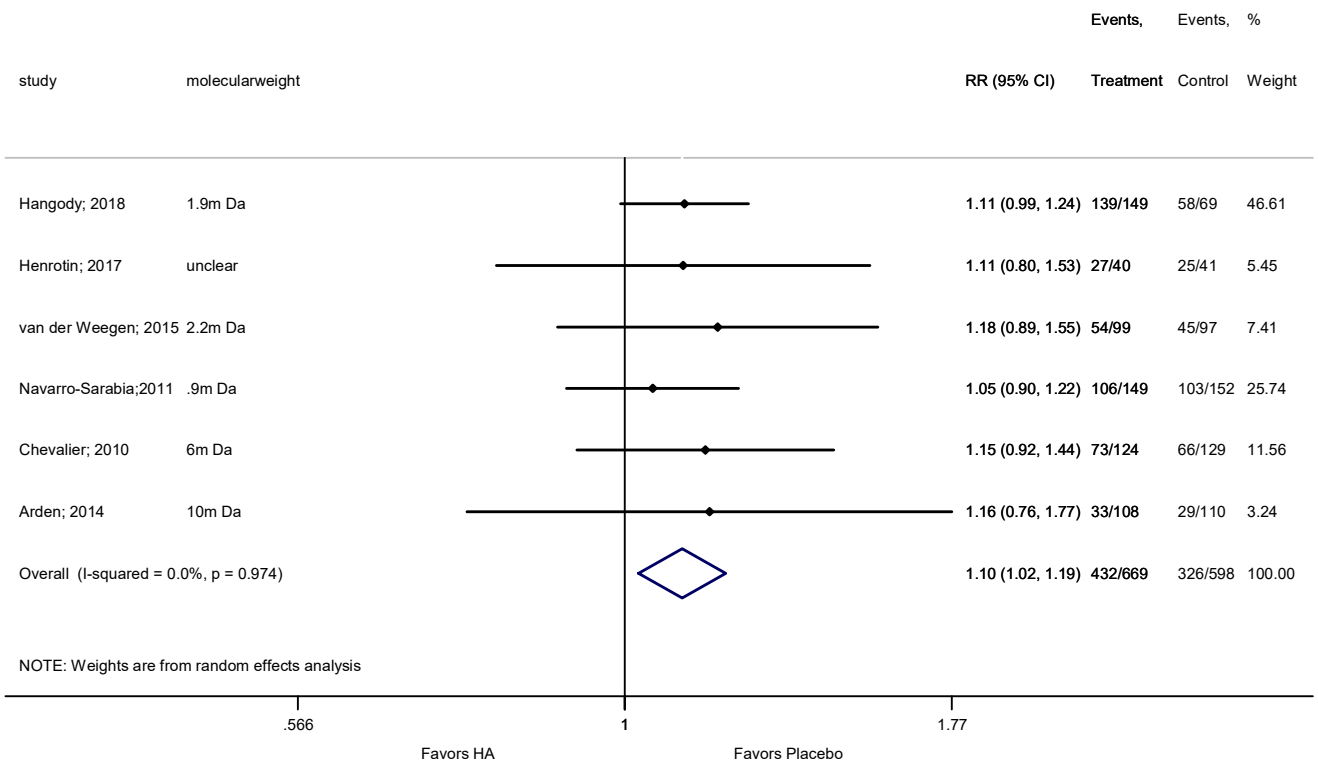
Meta-Analysis Figure 49: Hyaluronic Acid vs Saline- Oarsi Responders Closest to 3-Month Follow Up



NNTB=17

number of excess responsders with HA per 1000=60(13,111)

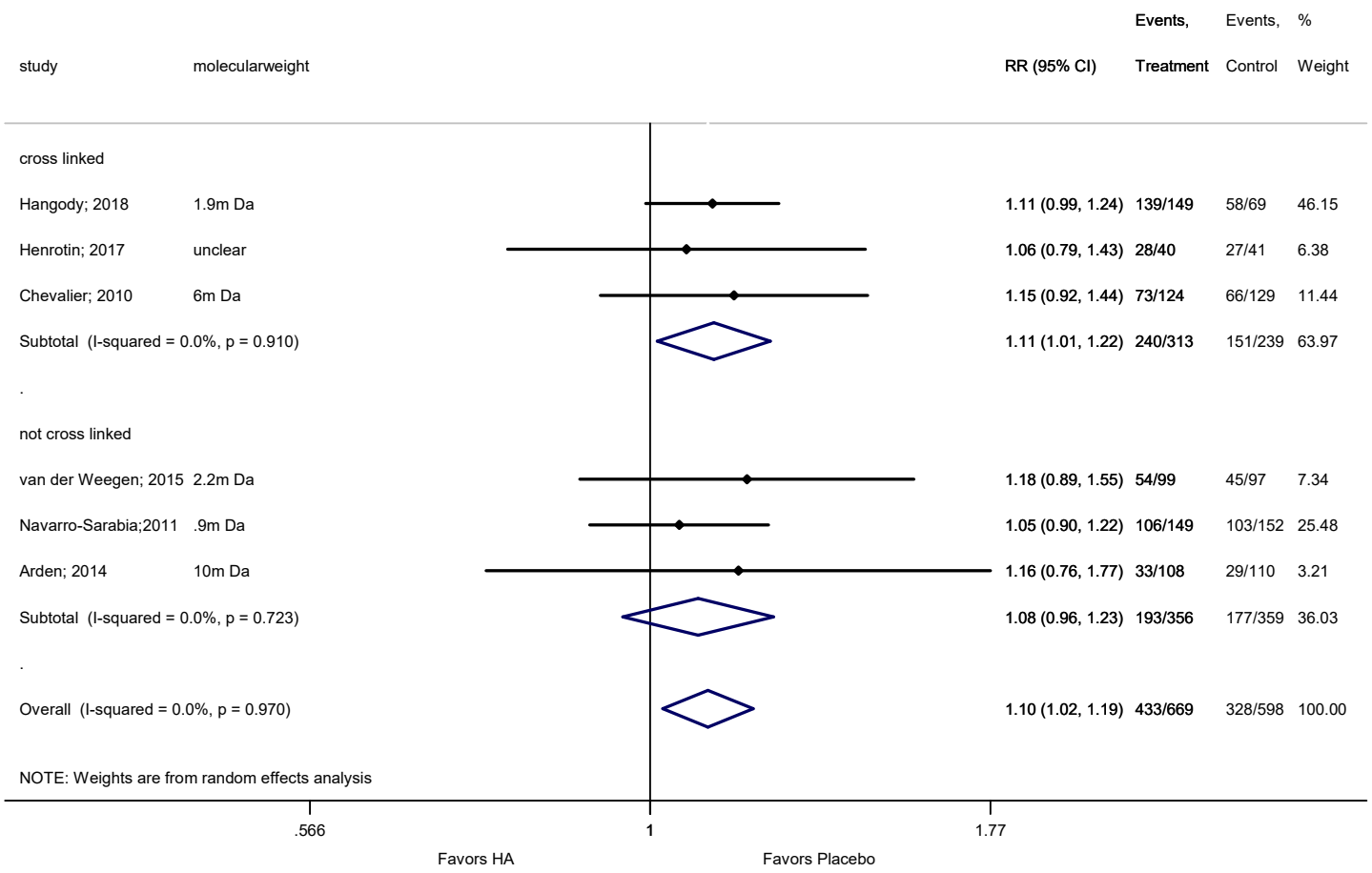
Meta-Analysis Figure 50: Hyaluronic Acid vs Saline- Oarsi Responders Closest to 6-Month Follow Up



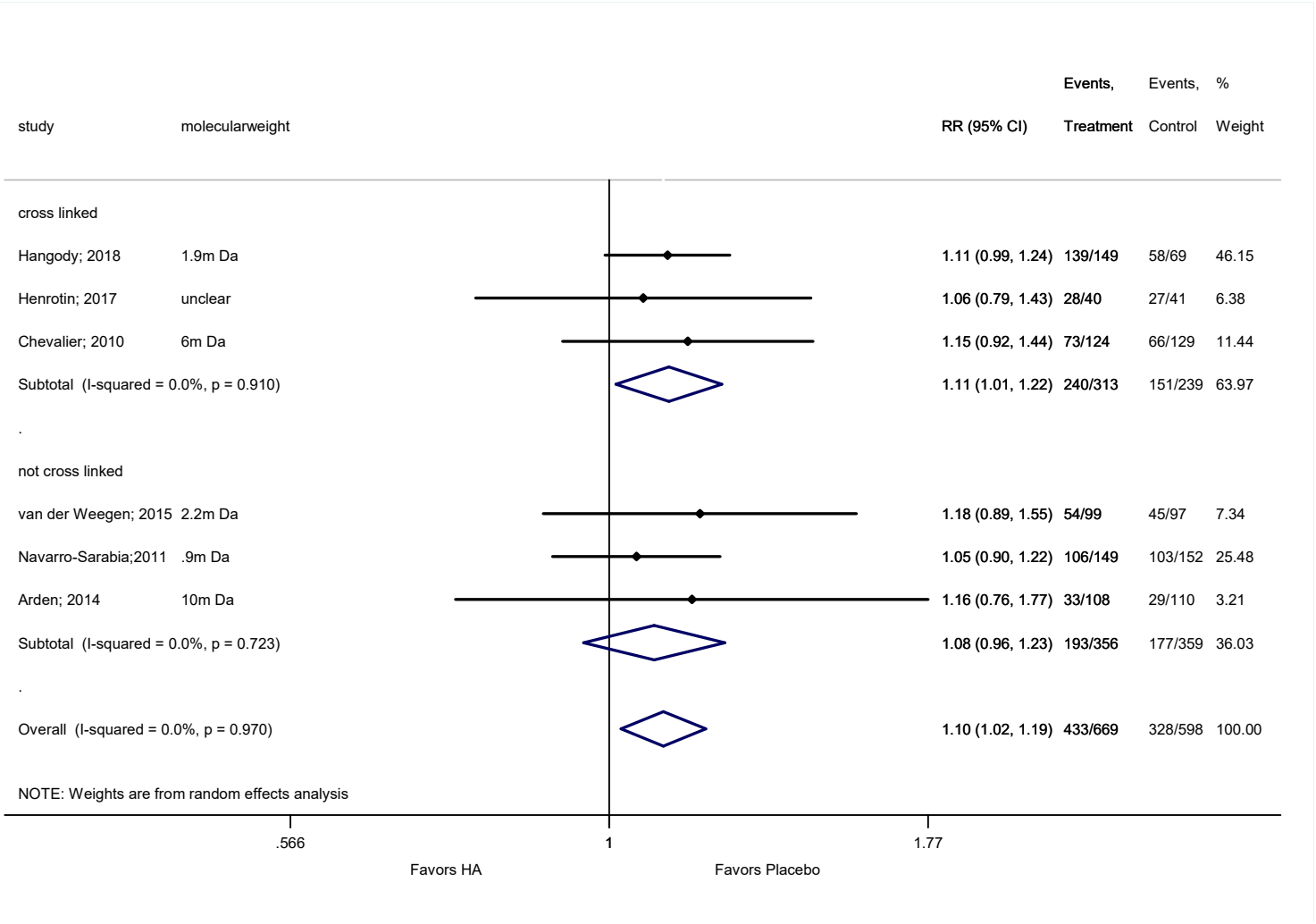
NNTB=17

number of excess responsders with HA per 1000=59(14,108)

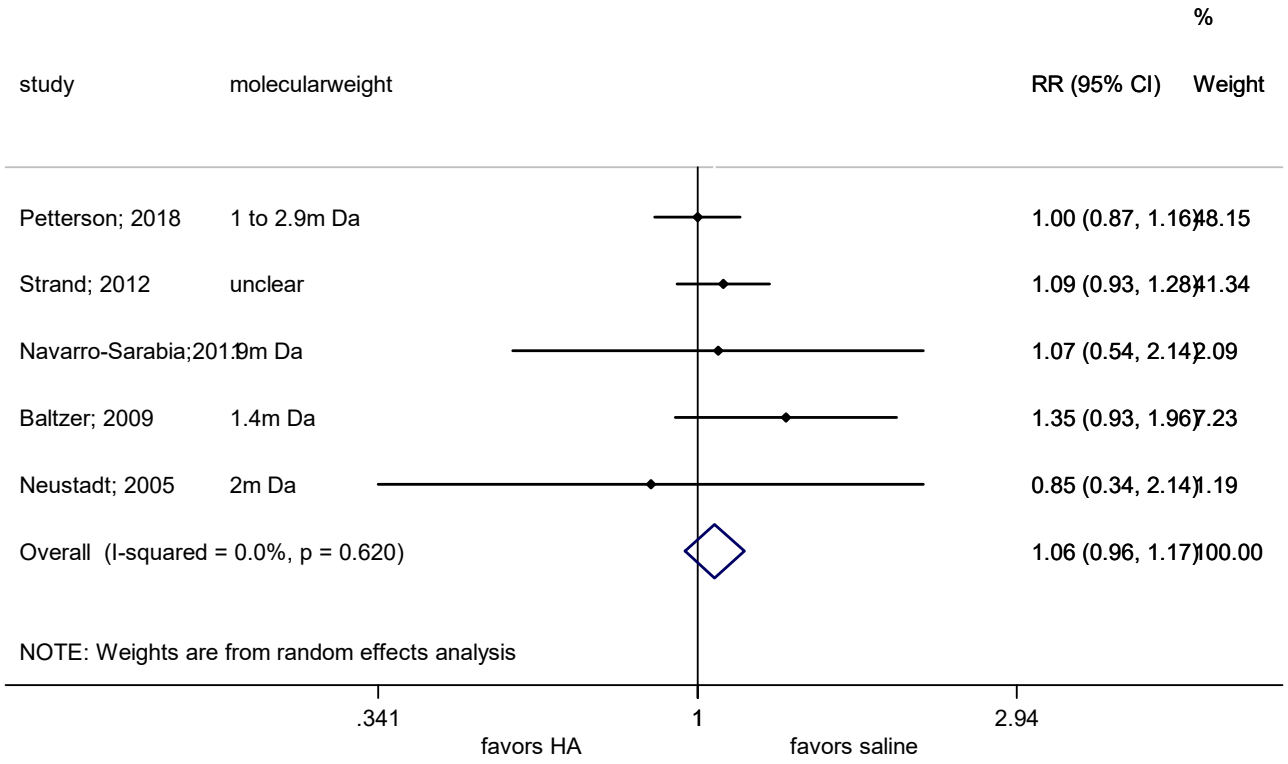
Meta-Analysis Figure 51: Hyaluronic Acid vs Saline- Oarsi Responders by Cross Linking Closest to 3-Month Follow Up



Meta-Analysis Figure 52: Hyaluronic Acid vs Saline- Oarsi Responders by Cross Linking Closest to 6-Month Follow Up



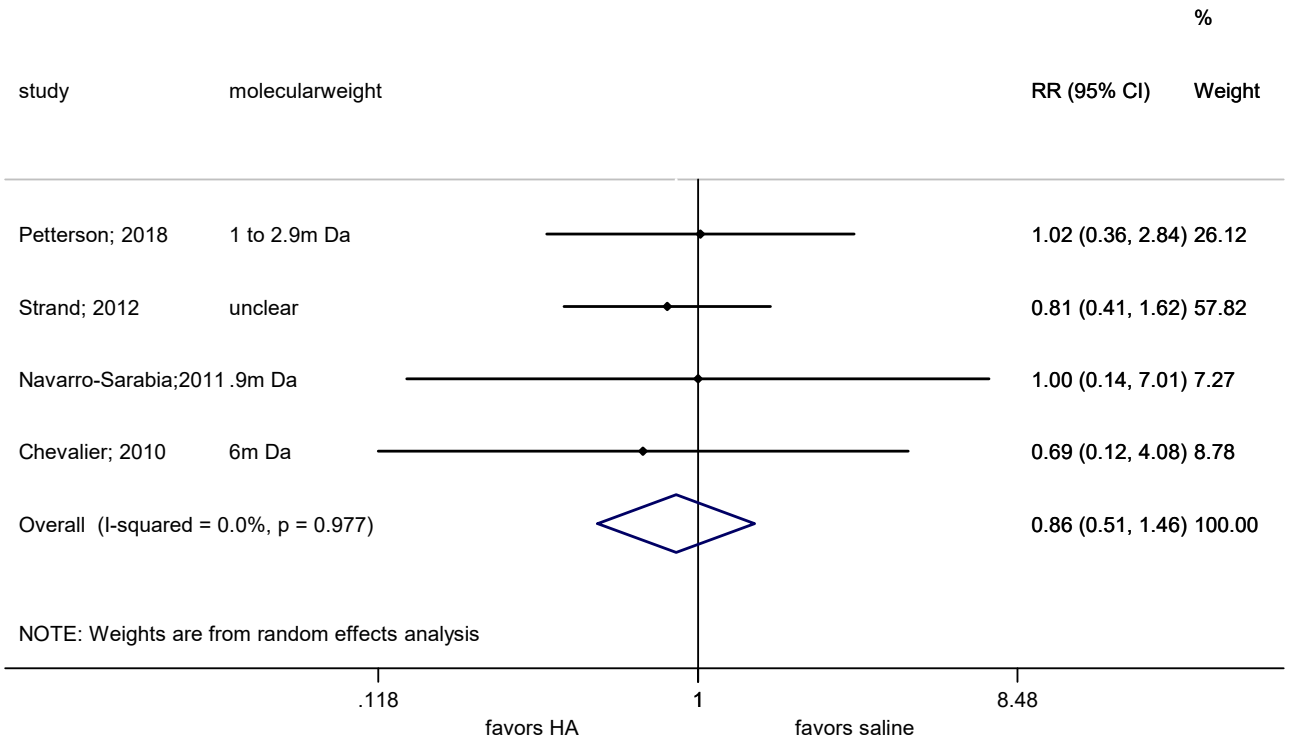
Meta-Analysis Figure 53: Hyaluronic Acid vs Saline- Overall Adverse Events



nnt=61

# of additional responders per 1000=17(-12,48)

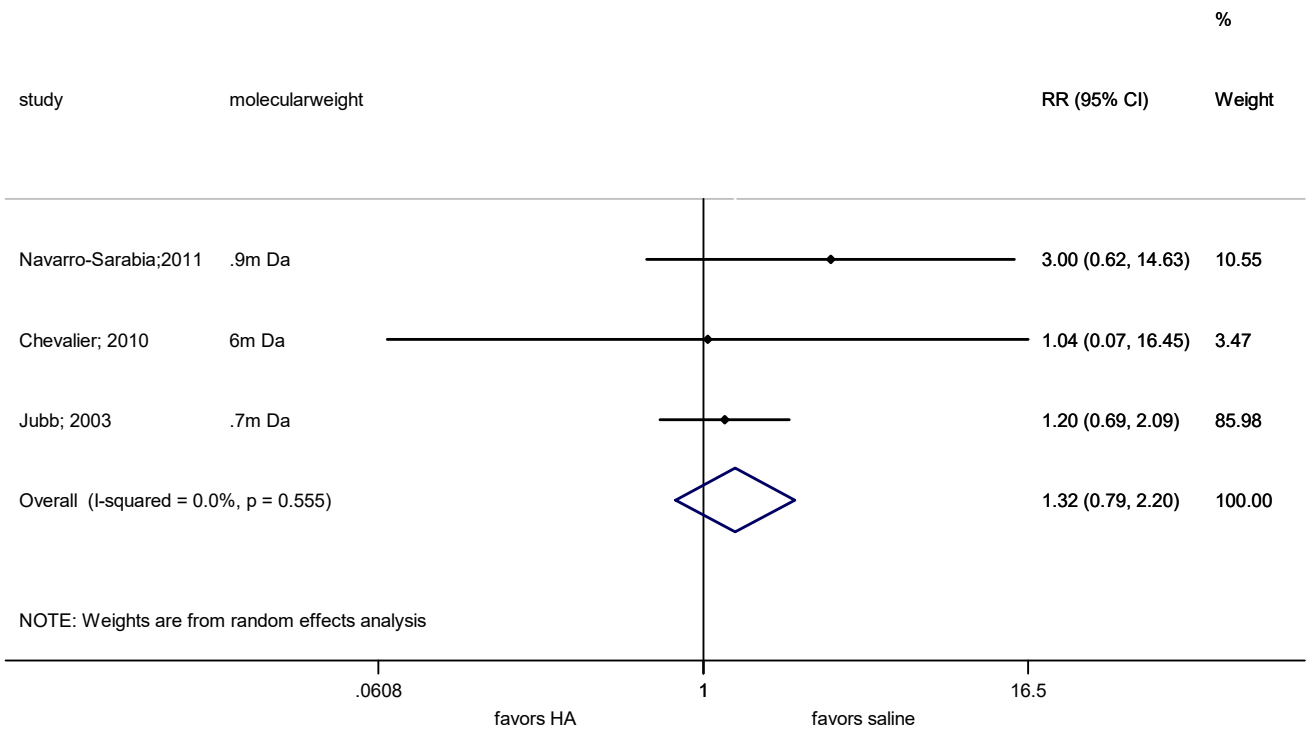
Meta-Analysis Figure 54: Hyaluronic Acid vs Saline- Adverse Events Arthralgia



NNTB=239

number of events avoided per 1000=4.2(-14.1,15)

Meta-Analysis Figure 55: Hyaluronic Acid vs Saline- Adverse Events Injection Site Pain



NNTH=242

number of excess events per 1000=4.1(-2.8,15.7)

Evidence Table 4639: Hyaluronic Acid vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hermans; 2019/Moderate	10: IA HA-Hyaluronic Acid (High Molecular Weight Hylan G-F 20)(6000 kDa)	10: Placebo/Control-Control (Usual Care)	other:OMERACT-OARSI Responder	52 wks	77/79	57.14%/34.18%	RR	1.67(1.16,2.4)	Group 1	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Pain:KOOS Pain	3 mos	60/66	61.95(.)/62.21(.)	Mean Diff	-0.26	Not Sig.	na
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Pain:KOOS pain change from placebo	26 wks	84/83	none	Mean Diff	-1.41(-5.79,2.97)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Pain:Overall pain reduction 20% (10 mm); n (%)	40 months	149/152	79.19%/67.76%	RR	1.17(1.02,1.34)	Group 1	na
Hermans; 2019/Moderate	10: IA HA-Hyaluronic Acid (High Molecular Weight Hylan G-F 20)(6000 kDa)	10: Placebo/Control-Control (Usual Care)	Pain:Pain During Activity	52 wks	156	none	Mean Difference	0.6(0,1.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hermans; 2019/Moderate	10: IA HA-Hyaluronic Acid (High Molecular Weight Hylan G-F 20)(6000 kDa)	10: Placebo/Control-Control (Usual Care)	Pain:Pain at Rest	52 wks	156	none	Mean Difference	0.8(0.2,1.4)	Group 2	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Pain:Pain or function reduction 50% 20mm	40 months	149/152	65.1%/51.97%	RR	1.25(1.03,1.52)	Group 1	na
Henrotin; 2017/High	10: IA HA-Hyaluronic Acid(KARTILAGE CROSS)	10: Placebo/Control-Placebo	Pain:VAS Change in Pain	30 days	40/41	35.9(21.5)/38.6(21.6)	Mean Diff	-2.7(-12.23, 6.83)	Not Sig.	clinically insignificant
Henrotin; 2017/High	10: IA HA-Hyaluronic Acid(KARTILAGE CROSS)	10: Placebo/Control-Placebo	Pain:VAS Change in Pain	180 days	40/41	27.9(23.2)/30.8(23.9)	Mean Diff	-2.9(-13.32, 7.52)	Not Sig.	clinically insignificant
Henrotin; 2017/High	10: IA HA-Hyaluronic Acid(KARTILAGE CROSS)	10: Placebo/Control-Placebo	Pain:VAS Change in Pain	90 days	40/41	31.4(24.2)/36.2(25.6)	Mean Diff	-4.8(-15.82, 6.22)	Not Sig.	clinically insignificant
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Pain:VAS Normal daily living pain	3 mos	60/66	53.14(.)/50.07(.)	Mean Diff	3.07	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Pain:VAS Overall Pain	3 mos	60/66	61.08(.)/58.31(.)	Mean Diff	2.77	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Pain:VAS Pain	182 days	135/107	49.3(25.9)/48.2(25.59)	Mean Diff	1.1(-5.46,7.66)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Pain:VAS Pain	91 days	135/107	52.1(22.97)/48.8(22.51)	Mean Diff	3.3(-2.49,9.09)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Pain:VAS Pain	49 days	135/107	52.6(23.15)/46.7(23.52)	Mean Diff	5.9(-0.06,11.86)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:VAS Pain(0-100)	30 days	99/97	21.7(10.44)/21.4(10.44)	Mean Diff	0.3(-2.64,3.24)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:VAS Pain(0-100)	180 days	99/97	23.1(13.56)/21.5(13.56)	Mean Diff	1.6(-2.22,5.42)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:VAS Pain(0-100)	90 days	99/97	18.4(11.63)/14.8(11.63)	Mean Diff	3.6(0.32,6.88)	Group 2	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Evening pain; patient diary)	35 days	40/44	53.59(9.82)/57.95(6.45)	Mean Diff	-4.36(-8.02,-0.7)	Group 1	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Evening pain; physician recorded)	35 days	40/44	34.54(9.41)/34.54(7.25)	Mean Diff	0(-3.68,3.68)	Not Sig.	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Morning pain; patient diary)	35 days	40/44	47.2(7.72)/55.56(7.42)	Mean Diff	-8.36(-11.65,-5.07)	Group 1	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Morning pain; physician recorded)	35 days	40/44	21.88(7.15)/27.15(7.43)	Mean Diff	-5.27(-8.44,-2.1)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Pain climbing stairs; patient diary)	35 days	40/44	60.75(7.6)/65.28(10.37)	Mean Diff	-4.53(-8.46,-0.6)	Group 1	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Pain climbing stairs; physician recorded)	35 days	40/44	33.02(9.07)/34.43(6.02)	Mean Diff	-1.41(-4.8,1.98)	Not Sig.	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Pain in nominated activity; patient diary)	35 days	40/44	55.37(8.95)/59.07(6.96)	Mean Diff	-3.7(-7.21,-0.19)	Group 1	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Pain in nominated activity; physician recorded)	35 days	40/44	28.27(8.29)/33.23(8.34)	Mean Diff	-4.96(-8.57,-1.35)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Pain rising from chair; patient diary)	35 days	40/44	56.37(9.59)/60.67(7.6)	Mean Diff	-4.3(-8.09,-0.51)	Group 1	clinically insignificant
Henderson; 1994/High	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(phosphate buffered saline; 5 weekly injections)	Pain:VAS Pain(0-100; Pain rising from chair; physician recorded)	35 days	40/44	30.59(8.1)/31.63(7.17)	Mean Diff	-1.04(-4.38,2.3)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	56 days	90/100	-28.7(28.8)/-27.8(29.7)	Mean Diff	-0.9(-9.28,7.48)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	154 days	90/100	-25.5(30.2)/-24.6(29.9)	Mean Diff	-0.9(-9.52,7.72)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	154 days	104/100	-29.5(31.4)/-24.6(29.9)	Mean Diff	-4.9(-13.36, 3.56)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	112 days	104/100	-32.9(30.6)/-26.4(28.1)	Mean Diff	-6.5(-14.61, 1.61)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	56 days	104/100	-34.6(28.3)/-27.8(29.7)	Mean Diff	-6.8(-14.82, 1.22)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	84 days	104/100	-34.9(30)/-26.2(27.9)	Mean Diff	-8.7(-16.69,-0.71)	Group 1	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	112 days	90/100	-25.4(29.6)/-26.4(28.1)	Mean Diff	1(-7.28,9.28)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:VAS Pain(Pain on standing; 0-100)	84 days	90/100	-25(29.1)/-26.2(27.9)	Mean Diff	1.2(-6.98,9.38)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	196 days	208/200	48(29.43)/50(25.25)	Mean Diff	-2(-7.33,3.33)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	315 days	208/200	48(29.43)/50(28.86)	Mean Diff	-2(-7.67,3.67)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	364 days	208/200	48(29.43)/51(28.86)	Mean Diff	-3(-8.67,2.67)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	77 days	208/200	47(25.75)/50.5(21.65)	Mean Diff	-3.5(-8.12,1.12)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	245 days	208/200	48(29.43)/52.5(28.86)	Mean Diff	-4.5(-10.17, 1.17)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	28 days	208/200	44.5(25.75)/44.5(21.65)	Mean Diff	0(-4.62,4.62)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	126 days	208/200	50.5(25.75)/50.5(21.65)	Mean Diff	0(-4.62,4.62)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	266 days	208/200	46.5(29.43)/46.5(28.86)	Mean Diff	0(-5.67,5.67)	Not Sig.	clinically insignificant
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Pain:VAS Pain(pain on walking; 0-100)	147 days	208/200	48(25.75)/45.5(25.25)	Mean Diff	2.5(-2.46,7.46)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Pain:VAS Sedentary work pain	3 mos	60/66	32.75(.)/34.28(.)	Mean Diff	-1.53	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Pain:VAS Strenuous work pain	3 mos	60/66	80.42(.)/77.12(.)	Mean Diff	3.3	Not Sig.	na
Huang; 2011/High	10: IA HA-hyalgan(5 injections 500-730kda)	10: Placebo/Control-Placebo	Pain:VAS pain	13 weeks	100/98	-27.27(14.97)/-24.01(16.95)	Mean Diff	-3.26(-7.75,1.23)	Not Sig.	clinically insignificant
Huang; 2011/High	10: IA HA-hyalgan(5 injections 500-730kda)	10: Placebo/Control-Placebo	Pain:VAS pain	5 weeks	100/98	-24.75(12.66)/-20.41(15.38)	Mean Diff	-4.34(-8.29,-0.39)	Group 1	clinically insignificant
Huang; 2011/High	10: IA HA-hyalgan(5 injections 500-730kda)	10: Placebo/Control-Placebo	Pain:VAS pain	25 weeks	100/98	-30.85(14.16)/-23.62(16.38)	Mean Diff	-7.23(-11.53,-2.93)	Group 1	clinically insignificant
Jorgensen; 2010/High	10: IA HA-Hyalgan(5 Injections 500-730kda)	10: Placebo/Control-placebo(5 Injections)	Pain:VAS pain Change from baseline (negative numbers are better; converted to 100mm VAS)	13 wks		none	pvalue	Sig (p<0.05)	Hyalgan favored over Placebo	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Pain:VAS pain at movement change from placebo	26 wks	84/83	none	Mean Diff	5.46(-0.08,11)	Not Sig.	clinically insignificant
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Pain:VAS pain at night change from placebo	26 wks	84/83	none	Mean Diff	-1.8(-7.36,3.76)	Not Sig.	clinically insignificant
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Pain:VAS pain at rest change from placebo	26 wks	84/83	none	Mean Diff	0.75(-3.54,5.04)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:WOMAC Pain	90 days	99/97	4.7(2.46)/5.1(2.46)	Mean Diff	-0.4(-1.09,0.29)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:WOMAC Pain	30 days	99/97	6(2.24)/6.6(2.24)	Mean Diff	-0.6(-1.23,0.03)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:WOMAC Pain	180 days	99/97	6.4(2.18)/6.1(2.18)	Mean Diff	0.3(-0.31,0.91)	Not Sig.	clinically insignificant
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Pain:WOMAC Pain	6 weeks	172/174	-3.15(3.9)/-3.39(3.81)	Mean Diff	0.24(-0.58,1.06)	Not Sig.	clinically insignificant
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Pain:WOMAC Pain	26 weeks	172/174	-2.5(4)/-2.89(4.17)	Mean Diff	0.39(-0.47,1.25)	Not Sig.	clinically insignificant
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Pain:WOMAC Pain	13 weeks	172/174	-2.87(3.97)/-3.42(4.1)	Mean Diff	0.55(-0.3,1.4)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Pain:WOMAC Pain (0-10)	182 days	135/107	3.59(2.47)/3.68(2.24)	Mean Diff	-0.09(-0.69,0.51)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Pain:WOMAC Pain (0-10)	91 days	135/107	3.73(2.22)/3.61(2.11)	Mean Diff	0.12(-0.43,0.67)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Pain:WOMAC Pain (0-10)	49 days	135/107	3.63(2.09)/3.49(2.23)	Mean Diff	0.14(-0.41,0.69)	Not Sig.	clinically insignificant
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Pain:WOMAC Pain (0-500)	1 mos	53/51	134.8(77.6)/135.8(85.3)	Mean Diff	-1(-32.76, 30.76)	Not Sig.	clinically insignificant
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Pain:WOMAC Pain (0-500)	3 mos	53/51	154.9(102.1)/154.6(92)	Mean Diff	0.3(-37.47, 38.07)	Not Sig.	clinically insignificant
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Pain:WOMAC Pain (0-500)	6 mos	53/51	173.7(101.6)/161.6(90.2)	Mean Diff	12.1(-25.24, 49.44)	Not Sig.	inconclusive
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	154 days	115/114	-123.7(123.4)/-111.8(117)	Mean Diff	-11.9(-43.21, 19.41)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	84 days	115/114	-146.2(119.3)/-129.5(121.7)	Mean Diff	-16.7(-48.08, 14.68)	Not Sig.	inconclusive
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	56 days	115/114	-144.7(113.3)/-126(120.2)	Mean Diff	-18.7(-49.12, 11.72)	Not Sig.	inconclusive
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	112 days	115/114	-145.5(119.1)/-125.8(117.6)	Mean Diff	-19.7(-50.52, 11.12)	Not Sig.	inconclusive
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	56 days	107/114	-113.1(121.9)/-126(120.2)	Mean Diff	12.9(-19.22, 45.02)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	154 days	107/114	-108.4(124.6)/-111.8(117)	Mean Diff	3.4(-28.7,35.5)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	112 days	107/114	-121.1(123.2)/-125.8(117.6)	Mean Diff	4.7(-27.27, 36.67)	Not Sig.	clinically insignificant
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Pain:WOMAC Pain (0-500)	84 days	107/114	-121(120.5)/-129.5(121.7)	Mean Diff	8.5(-23.62, 40.62)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Pain:WOMAC Pain (VAS Version)	9 wks	375	none	Mean Difference	5.77(0.26,11.29)	Group 1	possibly clinically significant
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Pain:WOMAC Pain (VAS Version)	13 wks	375	none	Mean Difference	6.39(0.37,12.41)	Group 1	possibly clinically significant
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Pain:WOMAC Pain (VAS Version)	6 wks	375	none	Mean Difference	8.12(2.73,13.5)	Group 1	possibly clinically significant
Hangody; 2018/High	10: IA HA-Cingal	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	12 wks	137/63	-41.1(20.5)/-30.8(23.7)	Mean Diff	-10.3(-17.16,-3.44)	Group 1	possibly clinically significant
Hangody; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	6 wks	135/63	-39.2(20.1)/-35.5(20.2)	Mean Diff	-3.7(-9.79,2.39)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Hangody; 2018/High	10: IA HA-Cingal	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	6 wks	137/63	-40.5(20.7)/-35.5(20.2)	Mean Diff	-5(-11.13, 1.13)	Not Sig.	inconclusive
Hangody; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	26 wks	135/63	-39.5(22.8)/-32.9(23.6)	Mean Diff	-6.6(-13.66, 0.46)	Not Sig.	inconclusive
Hangody; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	18 wks	135/63	-38.5(23.8)/-31.4(24.2)	Mean Diff	-7.1(-14.37, 0.17)	Not Sig.	inconclusive
Hangody; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	12 wks	135/63	-39(21.9)/-30.8(23.7)	Mean Diff	-8.2(-15.2,-1.2)	Group 1	possibly clinically significant
Hangody; 2018/High	10: IA HA-Cingal	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	18 wks	137/63	-40.5(20.4)/-31.4(24.2)	Mean Diff	-9.1(-16.06,-2.14)	Group 1	possibly clinically significant
Hangody; 2018/High	10: IA HA-Cingal	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain (VAS)	26 wks	137/63	-42.4(18.7)/-32.9(23.6)	Mean Diff	-9.5(-16.2,-2.8)	Group 1	possibly clinically significant
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Pain:WOMAC Pain Subscores	6 wks	152/159	-20.3(.)/-16.3(.)	Mean Diff	-4	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Pain:WOMAC Pain Subscores	12 wks	152/159	-22.1(.)/-16.5(.)	Mean Diff	-5.6	Gel-200 favored over Phosphate Buffered Sali	na
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Pain:WOMAC Pain Subscores	26 wks	152/159	-21(.)/-14.8(.)	Mean Diff	-6.2	Gel-200 favored over Phosphate Buffered Sali	na
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Pain:WOMAC Pain Subscores	18 wks	152/159	-23.9(.)/-16.4(.)	Mean Diff	-7.5	Gel-200 favored over Phosphate Buffered Sali	na
Heybeli; 2008/Moderate	10: IA HA-Atrhroscopic debridement+ orthovisc(3 injections 1-2.9 million Da)	10: Placebo/Control-Atrhroscopic debridement+ no treatment	Pain:WOMAC pain	24 weeks	33/34	5(2.2)/5.45(2.3)	Mean Diff	-0.45(-1.55,0.65)	wrong sig extracted	clinically insignificant
Heybeli; 2008/Moderate	10: IA HA-Atrhroscopic debridement+ orthovisc(3 injections 1-2.9 million Da)	10: Placebo/Control-Atrhroscopic debridement+ no treatment	Pain:WOMAC pain	12 weeks	33/34	6.1(6)/6(2.8)	Mean Diff	0.1(-2.22,2.42)	wrong sig extracted	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heybeli; 2008/Moderate	10: IA HA-Atrhroscopic debridement+ orthovisc(3 injections 1-2.9 million Da)	10: Placebo/Control-Atrhroscopic debridement+ no treatment	Pain:WOMAC pain	6 weeks	33/34	6.7(3.5)/6.5(3.1)	Mean Diff	0.2(-1.42,1.82)	Not Sig.	inconclusive
Huang; 2011/High	10: IA HA-hyalgan(5 injections 500-730kda)	10: Placebo/Control-Placebo	Pain:WOMAC pain	25 weeks	100/98	-29.28(19.2)/-21.52(19.21)	Mean Diff	-7.76(-13.14,-2.38)	Group 1	possibly clinically significant
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Pain:WOMAC pain	26 weeks	124/129	-0.84(0.67)/-0.69(0.66)	Mean Diff	-0.15(-0.31,0.01)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:Walking VAS pain(0-100)	180 days	99/97	38.1(15.19)/39.6(15.19)	Mean Diff	-1.5(-5.78,2.78)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:Walking VAS pain(0-100)	30 days	99/97	38.8(14.3)/40.6(14.3)	Mean Diff	-1.8(-5.83,2.23)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Pain:Walking VAS pain(0-100)	90 days	99/97	30.4(15.58)/29.5(15.58)	Mean Diff	0.9(-3.49,5.29)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman; 1998/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan ; 20mg/2mL in 5 weekly injections and placebo pill twice daily)	10: Placebo/Control-Placebo (Intra-articular)(Placebo pill twice daily and saline injections 5 times weekly)	Pain:Walking VAS pain(0-100)	28 days	143/156	27(24)/28(27)	Mean Diff	-1(-6.81,4.81)	Not Sig.	clinically insignificant
Altman; 1998/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan ; 20mg/2mL in 5 weekly injections and placebo pill twice daily)	10: Placebo/Control-Placebo (Intra-articular)(Placebo pill twice daily and saline injections 5 times weekly)	Pain:Walking VAS pain(0-100)	182 days	160/163	27(27)/28(30)	Mean Diff	-1(-7.25,5.25)	Not Sig.	clinically insignificant
Altman; 1998/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan ; 20mg/2mL in 5 weekly injections and placebo pill twice daily)	10: Placebo/Control-Placebo (Intra-articular)(Placebo pill twice daily and saline injections 5 times weekly)	Pain:Walking VAS pain(0-100)	35 days	136/149	25(24)/25(25)	Mean Diff	0(-5.72,5.72)	Not Sig.	clinically insignificant
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	Pain:change in 50 ft walk pain score	26 weeks	291/295	-25.7(28.9)/-18.5(32.5)	Mean Diff	-7.2(-12.19,-2.21)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Pain:change in WOMAC knee pain	6 wks	53/53	-8(11.6)/-8.1(10)	Mean Diff	0.1(-4.07,4.27)	Not Sig.	na
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Pain:change in WOMAC knee pain	12 wks	53/53	-2.2(4.8)/-2.5(5.4)	Mean Diff	0.3(-1.67,2.27)	Not Sig.	na
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	Pain:change in WOMAC pain	26 weeks	291/295	-19.2(26.8)/-16.3(26.8)	Mean Diff	-2.9(-7.25,1.45)	Not Sig.	clinically insignificant
Kahan ; 2003/Moderate	10: IA HA-Synvisc (Hylan G-F 20)(3 injections(1 per week) 6 million Daltons)	10: Non-arthro Tx-conventional treatments	Pain:change in WOMAC pain	36 wks	251/246	-24.6(20)/-12.2(21.6)	Mean Diff	-12.4(-16.07,-8.73)	Group 1	clinically significant
Kahan ; 2003/Moderate	10: IA HA-Synvisc (Hylan G-F 20)(3 injections(1 per week) 6 million Daltons)	10: Non-arthro Tx-conventional treatments	Pain:change in pain on walking (VAS)	36 wks	253/253	-37.4(22.3)/-24.4(24)	Mean Diff	-13(-17.05,-8.95)	Group 1	some may benefit
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Pain:change in stepping pain (VAS)	6 wks	53/53	-1.6(2.4)/-1.5(2.6)	Mean Diff	-0.1(-1.06,0.86)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Pain:change in stepping pain (VAS)	12 wks	53/53	-0.2(1.2)/-0.3(1.8)	Mean Diff	0.1(-0.49,0.69)	Not Sig.	clinically insignificant
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Pain:change in walking pain (VAS)	6 wks	53/53	-36(20)/-36(21)	Mean Diff	0(-7.9,7.9)	Not Sig.	clinically insignificant
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Pain:change in walking pain (VAS)	12 wks	53/53	-2(10)/-3(17)	Mean Diff	1(-4.39,6.39)	Not Sig.	clinically insignificant
Karlsson; 2002/Moderate	10: IA HA-Artzal(3 injections(1 per week) ~10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Pain:change in weight-bearing pain in knee (VAS)	20 wks	76/57	-21(26)/-19(29)	Mean Diff	-2(-11.63, 7.63)	Not Sig.	clinically insignificant
Karlsson; 2002/Moderate	10: IA HA-Artzal(3 injections(1 per week) ~10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Pain:change in weight-bearing pain in knee (VAS)	12 wks	76/57	-22(26)/-19(32)	Mean Diff	-3(-13.28, 7.28)	Not Sig.	clinically insignificant
Karlsson; 2002/Moderate	10: IA HA-Synvisc (3 injections(1 per week) ~7 x 10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Pain:change in weight-bearing pain in knee (VAS)	12 wks	77/57	-22(29)/-19(32)	Mean Diff	-3(-13.65, 7.65)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Karlsson; 2002/Moderate	10: IA HA-Synvisc (3 injections(1 per week) ~7 x 10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Pain:change in weight-bearing pain in knee (VAS)	20 wks	77/57	-27(29)/-19(29)	Mean Diff	-8(-18.03, 2.03)	Not Sig.	clinically insignificant
Karlsson; 2002/Moderate	10: IA HA-Synvisc (3 injections(1 per week) ~7 x 10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Pain:change in weight-bearing pain in knee (VAS)	26 wks	77/57	-20(31)/-21(31)	Mean Diff	1(-9.72,11.72)	Not Sig.	clinically insignificant
Karlsson; 2002/Moderate	10: IA HA-Artzal(3 injections(1 per week) ~10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Pain:change in weight-bearing pain in knee (VAS)	26 wks	76/57	-16(31)/-21(31)	Mean Diff	5(-5.75,15.75)	Not Sig.	clinically insignificant
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of loss of activity (VAS); # symptom free	26 wks	57/60	59.65%/26.67%	RR	2.24(1.4,3.58)	Group 2	na
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of loss of activity (VAS); # symptom free	12 wks	57/60	59.65%/16.67%	RR	3.58(1.95,6.55)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of night pain (VAS); # symptom free	26 wks	57/60	70.18%/45%	RR	1.56(1.12,2.16)	Group 2	na
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of night pain (VAS); # symptom free	12 wks	57/60	77.19%/41.67%	RR	1.85(1.33,2.58)	Group 2	na
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of overall treatment success (VAS); # symptom free	12 wks	57/60	50.88%/15%	RR	3.39(1.76,6.52)	Group 2	na
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of weight-bearing pain (VAS); # symptom free	26 wks	57/60	38.6%/13.33%	RR	2.89(1.4,5.97)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:evaluator assessment of weight-bearing pain (VAS); # symptom free	12 wks	57/60	47.37%/8.33%	RR	5.68(2.35,13.74)	Group 2	na
Day ; 2004/High	10: IA HA-sodium HA(5 injections(1 per week) 6.2-11.7 x 10^5 Da)	10: Placebo/Control-placebo(5 injections(1 per week))	Pain:mean WOMAC pain during treatment	18 wks	116/124	19.2(16.35)/23.05(15.7)	Mean Diff	-3.85(-7.93,0.23)	Not Sig.	clinically insignificant
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:patient assessment of night pain (VAS); # symptom free	12 wks	57/60	82.46%/53.33%	RR	1.55(1.19,2.02)	Group 2	na
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:patient assessment of overall treatment success (VAS); # symtom free	12 wks	57/60	70.18%/18.33%	RR	3.83(2.19,6.7)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:patient assessment of pain during most painful knee movement (VAS); # symptom free	12 wks	57/60	59.65%/13.33%	RR	4.47(2.27,8.83)	Group 2	na
Wobig ; 1998/Moderate	10: IA HA-Hylan G-F 20(3 injections(1 per week) 6 million Da)	10: Placebo/Control-saline(3 injections(1 per week))	Pain:patient assessment of weight-bearing pain (VAS); # symptom free	12 wks	57/60	56.14%/11.67%	RR	4.81(2.31,10.02)	Group 2	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Function:Function improvement 20% (10 mm); n (%)	40 months	149/152	70.47%/57.89%	RR	1.22(1.03,1.44)	Group 1	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Function:KOOS Activities of daily living	3 mos	60/66	69.84(.)/70.82(.)	Mean Diff	-0.98	Not Sig.	na
Hermans; 2019/Moderate	10: IA HA-Hyaluronic Acid (High Molecular Weight Hylan G-F 20)(6000 kDa)	10: Placebo/Control-Control (Usual Care)	Function:KOOS Function	52 wks	156	none	Mean Difference	-6.8(-11.9,-1.7)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Function:KOOS Sports and Recreation	3 mos	60/66	42.02(.)/40.86(.)	Mean Diff	1.16	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Function:KOOS Symptoms	3 mos	60/66	50.65(.)/51.27(.)	Mean Diff	-0.62	Not Sig.	na
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Function:KOOS activities change from placebo	26 wks	84/83	none	Mean Diff	-3.67(-8.54,1.2)	Not Sig.	na
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Function:KOOS sports change from placebo	26 wks	84/83	none	Mean Diff	-1.31(-7.13,4.5)	Not Sig.	na
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	Function:KOOS symptoms change from placebo	26 wks	84/83	none	Mean Diff	-3.12(-6.14,1.79)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:Knee Range of Motion	8 wks	181/184	117.3(14.7)/118.7(14.5)	Mean Diff	-1.4(-4.41,1.61)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:Knee Range of Motion	12 wks	181/184	117.8(14.4)/119.3(15.2)	Mean Diff	-1.5(-4.55,1.55)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:Knee Range of Motion	26 wks	181/184	117.2(13.9)/118.8(14.2)	Mean Diff	-1.6(-4.49,1.29)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:Knee Range of Motion	20 wks	181/184	118.4(14.7)/118.3(14.7)	Mean Diff	0.1(-2.93,3.13)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:Knee Range of Motion	4 wks	181/184	119(16.2)/117.8(13.1)	Mean Diff	1.2(-1.84,4.24)	Not Sig.	na
Huskisson; 1999/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 20mg/2mL; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline; 5 weekly injections)	Function:Lequesne Index(functional index; 0-24)	168 days	40/41	11.2(4.4)/12.6(4.8)	Mean Diff	-1.4(-3.44,0.64)	Not Sig.	na
Huskisson; 1999/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 20mg/2mL; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline; 5 weekly injections)	Function:Lequesne Index(functional index; 0-24)	35 days	40/41	10(4.6)/12.1(3.8)	Mean Diff	-2.1(-3.97,-0.23)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huskisson; 1999/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 20mg/2mL; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline; 5 weekly injections)	Function:Lequesne Index(functional index; 0-24)	56 days	40/41	9.9(4.8)/12(4)	Mean Diff	-2.1(-4.06,-0.14)	Group 1	na
Huskisson; 1999/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(Hyalgan; 20mg/2mL; 5 weekly injections)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline; 5 weekly injections)	Function:Lequesne Index(functional index; 0-24)	112 days	40/41	10.2(4.8)/12.4(4.2)	Mean Diff	-2.2(-4.2,-0.2)	Group 1	na
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:ROM Knee Flexion	1 mos	53/51	122.1(10)/123.1(9.3)	Mean Diff	-1(-4.75,2.75)	Not Sig.	na
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:ROM Knee Flexion	3 mos	53/51	120.7(11.6)/122.8(9.9)	Mean Diff	-2.1(-6.29,2.09)	Not Sig.	na
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:ROM Knee Flexion	6 mos	53/51	119.5(13.6)/122.3(11.1)	Mean Diff	-2.8(-7.62,2.02)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Function:Tegner Activity Levels	3 mos	60/66	4.1(.)/3.7(.)	Mean Diff	0.4	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function	26 wks	181/184	32.5(24.8)/33.1(25.2)	Mean Diff	-0.6(-5.75,4.55)	Not Sig.	clinically insignificant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function	4 wks	181/184	34.7(24.4)/36.3(24.9)	Mean Diff	-1.6(-6.67,3.47)	Not Sig.	clinically insignificant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function	8 wks	181/184	33.1(25.5)/31.9(24.1)	Mean Diff	1.2(-3.91,6.31)	Not Sig.	clinically insignificant
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Function:WOMAC Function	26 wks	152/159	none	pvalue	NS	Not Sig.	na
Heybeli; 2008/Moderate	10: IA HA-Atrhroscopic debridement+ orthovisc(3 injections 1-2.9 million Da)	10: Placebo/Control-Atrhroscopic debridement+ no treatment	Function:WOMAC Function	12 weeks	33/34	21.2(9)/22(9.5)	Mean Diff	-0.8(-5.31,3.71)	wrong sig extracted	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Heybeli; 2008/Moderate	10: IA HA-Atrhroscopic debridement+ orthovisc(3 injections 1-2.9 million Da)	10: Placebo/Control-Atrhroscopic debridement+ no treatment	Function:WOMAC Function	24 weeks	33/34	16.5(7.2)/18.6(7.5)	Mean Diff	-2.1(-5.69,1.49)	wrong sig extracted	inconclusive
Heybeli; 2008/Moderate	10: IA HA-Atrhroscopic debridement+ orthovisc(3 injections 1-2.9 million Da)	10: Placebo/Control-Atrhroscopic debridement+ no treatment	Function:WOMAC Function	6 weeks	33/34	22.2(11.9)/24.3(11.3)	Mean Diff	-2.1(-7.77,3.57)	wrong sig extracted	inconclusive
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Function:WOMAC Function	6 weeks	172/174	-7.52(12.12)/-8.52(12.41)	Mean Diff	1(-1.59,3.59)	Not Sig.	clinically insignificant
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Function:WOMAC Function	26 weeks	172/174	-5.82(12.16)/-7.42(13.52)	Mean Diff	1.6(-1.12,4.32)	Not Sig.	clinically insignificant
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Function:WOMAC Function	13 weeks	172/174	-6.96(12.27)/-8.72(13.39)	Mean Diff	1.76(-0.96,4.48)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D) 1.4m Daltons	10: Placebo/Control-Placebo	Function:WOMAC Function (0-10)	91 days	135/107	4(2.19)/4.01(2.2)	Mean Diff	-0.01(-0.57,0.55)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D) 1.4m Daltons	10: Placebo/Control-Placebo	Function:WOMAC Function (0-10)	182 days	135/107	3.74(2.44)/3.94(2.48)	Mean Diff	-0.2(-0.83,0.43)	Not Sig.	inconclusive
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Function:WOMAC Function (0-10)	49 days	135/107	4.04(2.14)/3.83(2.42)	Mean Diff	0.21(-0.38,0.8)	Not Sig.	clinically insignificant
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks) + exercise 5x/week)	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:WOMAC Function (VAS Version)	6 mos	53/51	643.5(336.4)/618.5(310.4)	Mean Diff	25(-100.83,150.83)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:WOMAC Function (VAS Version)	3 mos	53/51	625.8(327)/596.5(298.9)	Mean Diff	29.3(-92.48, 151.08)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:WOMAC Function (VAS Version)	1 mos	53/51	589.8(320.1)/548.3(325.8)	Mean Diff	41.5(-84.18, 167.18)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Function:WOMAC Function (VAS Version)	13 wks	375	none	Mean Difference	5.42(-0.47,11.31)	Not Sig.	inconclusive
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function 12 wk	12 wks	181/184	24.7(26.2)/31.7(25.3)	Mean Diff	-7(-12.3,-1.7)	Group 1	possibly clinically significant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function 20 wk	20 wks	181/184	30.3(25.5)/22.7(26)	Mean Diff	7.6(2.3,12.9)	Group 2	possibly clinically significant
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Function:WOMAC Stiffness	26 wks	152/159	none	pvalue	Sig ($p < 0.05$)	Gel-200 favored over Phosphate Buffered Sali	na
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 weeks	172/174	-0.87(1.96)/-1.03(1.39)	Mean Diff	0.16(-0.2,0.52)	Not Sig.	clinically insignificant
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Function:WOMAC Stiffness	13 weeks	172/174	-0.71(1.87)/-1.05(1.96)	Mean Diff	0.34(-0.07,0.75)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman ; 2004/High	10: IA HA-Hyaluronic Acid (Durolane)(single injection) 10000kDa	10: Placebo/Control-Placebo	Function:WOMAC Stiffness	26 weeks	172/174	-0.47(1.77)/-0.82(1.96)	Mean Diff	0.35(-0.04,0.74)	Not Sig.	clinically insignificant
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:WOMAC Stiffness (VAS Version)	3 mos	53/51	72.2(44.3)/61.6(41.8)	Mean Diff	10.6(-6.15,27.35)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:WOMAC Stiffness (VAS Version)	1 mos	53/51	67.2(42.2)/54.4(39)	Mean Diff	12.8(-3,28.6)	Not Sig.	inconclusive
Saccomanno; 2016/Moderate	10: IA HA-IA HA + Exercise(Orthovisc 2 ml; 15mg/ml; 3 injections (one every other week over 6 weeks))	10: Placebo/Control-Control (Exercise Alone)(5x/week)	Function:WOMAC Stiffness (VAS Version)	6 mos	53/51	68.9(45.5)/65.9(40.3)	Mean Diff	3(-13.7,19.7)	Not Sig.	clinically insignificant
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Function:WOMAC Stiffness (VAS Version)	13 wks	375	none	Mean Difference	4.91(-1.31,11.14)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2011/High	10: IA HA-hyalgan(5 injections 500-730kda)	10: Placebo/Control-Placebo	Function:WOMAC function	25 weeks	100/98	-25.16(16.7)/-18.2(16.73)	Mean Diff	-6.96(-11.65,-2.27)	Group 1	possibly clinically significant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections) sodium hyaluronate 2.2Md	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Function:WOMAC function(0-68)	30 days	99/97	20.4(6.19)/20.6(6.19)	Mean Diff	-0.2(-1.94,1.54)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections) sodium hyaluronate 2.2Md	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Function:WOMAC function(0-68)	90 days	99/97	15.6(7.5)/16.2(7.5)	Mean Diff	-0.6(-2.71,1.51)	Not Sig.	clinically insignificant
van der Weegen; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(15mg/2 mL HA; 3 weekly injections) sodium hyaluronate 2.2Md	10: Placebo/Control-Placebo (Intra-articular)(2mL buffered saline)	Function:WOMAC function(0-68)	180 days	99/97	20.3(9.26)/19.9(9.26)	Mean Diff	0.4(-2.21,3.01)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2011/High	10: IA HA-hyalgan(5 injections 500-730kda)	10: Placebo/Control-Placebo	Function:WOMAC stiffness	25 weeks	100/98	-24.85(21.8)/-22.58(21.88)	Mean Diff	-2.27(-8.39,3.85)	Not Sig.	clinically insignificant
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Function:change in SF-36 function	6 wks	53/53	1.3(3.8)/1(3.3)	Mean Diff	0.3(-1.07,1.67)	Not Sig.	clinically insignificant
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Function:change in SF-36 function	12 wks	53/53	3.2(2.5)/1.5(2.7)	Mean Diff	1.7(0.7,2.7)	Group 1	some may benefit
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	Function:change in WOMAC function	26 weeks	291/295	-19.5(24.7)/-14.6(25.8)	Mean Diff	-4.9(-9,-0.8)	Group 1	possibly clinically significant
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Function:change in WOMAC function	12 wks	53/53	-4.8(14.9)/-5.1(15.9)	Mean Diff	0.3(-5.64,6.24)	Not Sig.	na
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Function:change in WOMAC function	6 wks	53/53	-22.9(28)/-27(27.8)	Mean Diff	4.1(-6.65,14.85)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kahan ; 2003/Moderate	10: IA HA-Synvisc (Hylan G-F 20)(3 injections(1 per week) 6 million Daltons)	10: Non-arthro Tx-conventional treatments	Function:change in WOMAC function	36 wks	251/247	-18.4(19.6)/-7(20.6)	Mean Diff	-11.4(-14.94,-7.86)	Group 1	possibly clinically significant
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Function:change in WOMAC stiffness	6 wks	53/53	-5.2(4.8)/-4.2(4.3)	Mean Diff	-1(-2.76,0.76)	Not Sig.	na
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	Function:change in WOMAC stiffness	12 wks	53/53	-0.7(2.7)/-1(2.5)	Mean Diff	0.3(-0.7,1.3)	Not Sig.	na
Kahan ; 2003/Moderate	10: IA HA-Synvisc (Hylan G-F 20)(3 injections(1 per week) 6 million Daltons)	10: Non-arthro Tx-conventional treatments	Function:change in WOMAC stiffness	36 wks	252/246	-20.7(25.9)/-7.7(26.1)	Mean Diff	-13(-17.58,-8.42)	Group 1	possibly clinically significant
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	Function:change in WOMAC stiffness (VAS)	26 weeks	291/295	-19.6(31.27)/-15.4(29.33)	Mean Diff	-4.2(-9.12,0.72)	Not Sig.	clinically insignificant
Day ; 2004/High	10: IA HA-sodium HA(5 injections(1 per week) 6.2-11.7 x 10^5 Da)	10: Placebo/Control-placebo(5 injections(1 per week))	Function:mean WOMAC disability during treatment	18 wks	116/124	15.37(11.41)/17.81(10.53)	Mean Diff	-2.44(-5.24,0.36)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Day ; 2004/High	10: IA HA-sodium HA(5 injections(1 per week) 6.2-11.7 x 10^5 Da)	10: Placebo/Control-placebo(5 injections(1 per week))	Function:mean WOMAC stiffness during treatment	18 wks	116/124	26.38(17.75)/30.75(18)	Mean Diff	-4.37(-8.92,0.18)	Not Sig.	clinically insignificant
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	Function:mean improvement in SF-36 function	26 weeks	291/295	4.77(9.65)/3.18(9.05)	Mean Diff	1.59(0.07,3.11)	Group 1	clinically insignificant
Gormeli; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 injections 30mg/2mL orthovisc)	10: Placebo/Control-Placebo (Intra-articular)(3 saline injections)	Composite:IKDC composite(Range 0-100)	180 days	39/40	48.4(6.2)/36.5(4.8)	Mean Diff	11.9(9.41,14.39)	Group 1	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Knee Society Score Function	3 mos	36/40	53.1(16.9)/54(18.7)	Mean Diff	-0.9(-9.04,7.24)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Knee Society Score Function	6 mos	30/38	42.4(23.7)/47.9(22.8)	Mean Diff	-5.5(-16.88,5.88)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Knee Society Score Function	1 mos	46/51	61(22.3)/53.2(21.9)	Mean Diff	7.8(-1.13,16.73)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Knee Society Score Total	6 mos	30/38	43.7(21.6)/40.4(23.8)	Mean Diff	3.3(-7.72,14.32)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Knee Society Score Total	3 mos	36/40	55(24.7)/50.9(23.4)	Mean Diff	4.1(-6.93,15.13)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Knee Society Score Total	1 mos	46/51	69.9(12.7)/65(19.1)	Mean Diff	4.9(-1.59,11.39)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Lysholm	3 mos	36/40	44.7(19.4)/45.5(19)	Mean Diff	-0.8(-9.6,8)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Lysholm	1 mos	46/51	47.5(15.6)/49.2(15.9)	Mean Diff	-1.7(-8.06,4.66)	Not Sig.	na
Campos; 2017/High	10: Other IA Tx-Corticosteroids and HA-hylan gf 20 comination	10: IA corticosteroids-Corticosteroids	Composite:Lysholm	6 mos	30/38	33.2(21.1)/39.1(19.6)	Mean Diff	-5.9(-15.89, 4.09)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Composite:Oarsi responsders	7 months	149/152	71.14%/67.76%	RR	1.05(0.9,1.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Composite:Oarsi responsders	21 months	149/152	77.85%/67.76%	RR	1.15(1, 1.32)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Composite:Oarsi responsders	27 months	149/152	77.85%/67.76%	RR	1.15(1, 1.32)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Composite:Oarsi responsders	14 months	149/152	76.51%/65.13%	RR	1.17(1.01,1.36)	Group 1	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Composite:Oarsi responsders	40 months	149/152	80.54%/65.79%	RR	1.22(1.07,1.41)	Group 1	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Composite:Oarsi responsders	34 months	149/152	81.21%/65.13%	RR	1.25(1.08,1.43)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Composite:Patient Global Assessment	13 wks	375	none	Mean Difference	0.92(-4.63,6.47)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Composite:Patient Global Assessment (VAS)	8 wks	181/184	33.4(26.3)/34.6(26.2)	Mean Diff	-1.2(-6.6,4.2)	Not Sig.	clinically insignificant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Composite:Patient Global Assessment (VAS)	20 wks	181/184	31.1(26.2)/32.4(27.1)	Mean Diff	-1.3(-6.79,4.19)	Not Sig.	clinically insignificant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Composite:Patient Global Assessment (VAS)	4 wks	181/184	36.1(25.9)/38.1(26.8)	Mean Diff	-2(-7.42,3.42)	Not Sig.	clinically insignificant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Composite:Patient Global Assessment (VAS)	26 wks	181/184	33.7(26)/33.4(26.2)	Mean Diff	0.3(-5.07,5.67)	Not Sig.	clinically insignificant
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Composite:Patient Global Assessment (VAS)	12 wks	181/184	33.7(27.5)/33.2(26.9)	Mean Diff	0.5(-5.1,6.1)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Composite:Patient Global Evaluation	26 wks	152/159	none	pvalue	NS	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	Composite:Single Assessment Numerical Evaluation	3 mos	60/66	64.78(.)/63.76(.)	Mean Diff	1.02	Not Sig.	na
Takamura; 2018/Moderate	10: IA HA-Hyaluronic Acid (Gel-200)(single dose)	10: Placebo/Control-Phosphate Buffered Saline(single dose)	Composite:WOMAC Total	26 wks	152/159	none	pvalue	Sig (p < 0.05)	Gel-200 favored over Phosphate Buffered Sali	na
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Composite:WOMAC Total (0-10)	182 days	135/107	3.75(2.42)/3.93(2.38)	Mean Diff	-0.18(-0.79,0.43)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Composite:WOMAC Total (0-10)	91 days	135/107	4(2.17)/3.99(2.13)	Mean Diff	0.01(-0.54,0.56)	Not Sig.	clinically insignificant
Baltzer; 2009/High	10: IA HA-Hyaluronic Acid(2mL x1/wk; 1.4x10^6 D)	10: Placebo/Control-Placebo	Composite:WOMAC Total (0-10)	49 days	135/107	4.02(2.09)/3.81(2.33)	Mean Diff	0.21(-0.36,0.78)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Composite:WOMAC Total (VAS Version)	13 wks	375	none	Mean Difference	5.64(-0.2,11.47)	Not Sig.	inconclusive
Kahan ; 2003/Moderate	10: IA HA-Synvisc (Hylan G-F 20)(3 injections(1 per week) 6 million Daltons)	10: Non-arthro Tx-conventional treatments	Composite:change in Lequesne Index	36 wks	253/253	-3.6(4.1)/-1.6(4)	Mean Diff	-2(-2.71,-1.29)	Group 1	na
Karlsson; 2002/Moderate	10: IA HA-Synvisc (3 injections(1 per week) ~7 x 10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Composite:change in Lequesne Index	20 wks	77/57	-4.9(3.6)/-5.1(4.4)	Mean Diff	0.2(-1.21,1.61)	Not Sig.	na
Karlsson; 2002/Moderate	10: IA HA-Synvisc (3 injections(1 per week) ~7 x 10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Composite:change in Lequesne Index	26 wks	77/57	-4.4(4.1)/-4.7(4.4)	Mean Diff	0.3(-1.18,1.78)	Not Sig.	na
Karlsson; 2002/Moderate	10: IA HA-Artzal(3 injections(1 per week) ~10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Composite:change in Lequesne Index	26 wks	76/57	-3.9(4.6)/-4.7(4.4)	Mean Diff	0.8(-0.76,2.36)	Not Sig.	na
Karlsson; 2002/Moderate	10: IA HA-Artzal(3 injections(1 per week) ~10^6 Da)	10: Placebo/Control-placebo(3 injections(1 per week))	Composite:change in Lequesne Index	20 wks	76/57	-4.2(3.7)/-5.1(4.4)	Mean Diff	0.9(-0.53,2.33)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kahan ; 2003/Moderate	10: IA HA-Synvisc (Hylan G-F 20)(3 injections(1 per week) 6 million Daltons)	10: Non-arthro Tx-conventional treatments	Composite:change in WOMAC total	36 wks	250/245	-19.8(18.9)/-8.1(20)	Mean Diff	-11.7(-15.14,-8.26)	Group 1	clinically significant
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:EQ-5D-5L Activities	3 mos	60/66	2.1(.)/2(.)	Mean Diff	0.1	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:EQ-5D-5L Anxiety	3 mos	60/66	1.5(.)/1.4(.)	Mean Diff	0.1	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:EQ-5D-5L Health Today	3 mos	60/66	82.38(.)/78.17(.)	Mean Diff	4.21	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:EQ-5D-5L Mobility	3 mos	60/66	2.1(.)/2(.)	Mean Diff	0.1	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:EQ-5D-5L Pain	3 mos	60/66	2.6(.)/2.5(.)	Mean Diff	0.1	Not Sig.	na
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:EQ-5D-5L Self-Care	3 mos	60/66	1.3(.)/1.3(.)	Mean Diff	0	Not Sig.	na
Gormeli; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 injections 30mg/2mL orthovisc)	10: Placebo/Control-Placebo (Intra-articular)(3 saline injections)	QOL:EQ-VAS (Range 0-100)	180 days	39/40	60.8(7.2)/48(5.1)	Mean Diff	12.8(9.99,15.61)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Farr; 2019/Moderate	10: IA HA-Hylauronic acid(4 mL) Monovisc	10: Placebo/Control-	QOL:KOOS Quality of Life	3 mos	60/66	43.26(.)/40.37(.)	Mean Diff	2.89	Not Sig.	na
Lundsgaard ; 2008/High	10: IA HA-hyaluronate 2 mL(4x weekly injections 10.3 mg/mL)	10: Placebo/Control-physiological saline 20 mL(4x weekly injections)	QOL:KOOS quality of life change from placebo	26 wks	84/83	none	Mean Diff	-2.72(-7.31,1.87)	Not Sig.	na
Hermans; 2019/Moderate	10: IA HA-Hyaluronic Acid (High Molecular Weight Hylan G-F 20)(6000 kDa)	10: Placebo/Control-Control (Usual Care)	QOL:Patient Global Assessment(scale?)	52 wks	156	none	Mean Difference	-0.7(-0.9,-0.4)	Group 2	na
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	QOL:change in SF-36 vitality	6 wks	53/53	0.8(2.4)/1(3.3)	Mean Diff	-0.2(-1.31,0.91)	Not Sig.	na
Petrella ; 2006/Moderate	10: IA HA-HA sodium salt(6 injections(1 per week) 20 mg/mL)	10: Placebo/Control-saline(6 injections(1 per week))	QOL:change in SF-36 vitality	12 wks	53/53	2.6(1.4)/2.1(2.1)	Mean Diff	0.5(-0.19,1.19)	Not Sig.	na
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	QOL:change in number of acetaminophen tablets used per week	26 weeks	291/295	12.7(14.56)/12.9(15.23)	Mean Diff	-0.2(-2.62,2.22)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Altman ; 2009/High	10: IA HA-IA-BioHA(3 weekly injections 2.4-3.6 million d)	10: Placebo/Control-IA-SA(3 weekly injections)	QOL:change in patient global assessment	26 weeks	291/295	-22(30.4)/-17.8(28.8)	Mean Diff	-4.2(-9.01,0.61)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	QOL:sf-8 Physical component score	7 wks	135/107	34.57(9.07)/35.6(9.12)	Mean Diff	-1.03(-3.35,1.29)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	QOL:sf-8 Physical component score	13 wks	135/107	34.66(9.42)/34.52(8.59)	Mean Diff	0.14(-2.15,2.43)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	QOL:sf-8 Physical component score	26 wks	135/107	35.62(10.1)/34.99(8.96)	Mean Diff	0.63(-1.79,3.05)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	QOL:sf-8 mental component score	7 wks	135/107	46.5(12.46)/47.26(11.08)	Mean Diff	-0.76(-3.75,2.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	QOL:sf-8 mental component score	26 wks	135/107	46.51(11.48)/46.22(11.07)	Mean Diff	0.29(-2.58,3.16)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	QOL:sf-8 mental component score	13 wks	135/107	46.43(11.19)/45.69(10.61)	Mean Diff	0.74(-2.03,3.51)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Other:Mean consumption of paracetamol. mg/day (SD)	40 months	149/152	408.8(644.2)/451.4(925.8)	Mean Diff	-42.6(-223.3, 138.1)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Other:OARSI responders	26 weeks	124/129	34.68%/40.31%	RR	0.86(0.62,1.18)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Other:Patient's global assessment reduction 20% (10 mm); n (%)	40 months	149/152	74.5%/57.89%	RR	1.29(1.09,1.52)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jorgensen; 2010/High	10: IA HA-Hyalgan(5 Injections 500-730kda)	10: Placebo/Control-placebo(5 Injections)	Other:change in paracetamol consumption of tablets (lower is better)	13 wks		none	pvalue	Sig (p<0.05)	Hyalgan favored over Placebo	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	Other:paracetamol medication use	26 wks	135/107	25.93%/30.84%	RR	0.84(0.56,1.26)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	Other:patient global assessment of treatment response (3 or less on 5pt scale)	26 wks	135/107	40%/42.06%	RR	0.95(0.7,1.29)	Not Sig.	na
Jorgensen; 2010/High	10: IA HA-Hyalgan(5 Injections 500-730kda)	10: Placebo/Control-placebo(5 Injections)	Other:responder defined as having improvement in lequesne at any time turing the first 3 months	13 wks	165/170	67.88%/72.35%	RR	0.94(0.82,1.08)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Abdominal pain	364 days	208/200	5.29%/6%	RR	0.88(0.4,1.95)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Accidental Injury	364 days	208/200	13.46%/10.5%	RR	1.28(0.75,2.18)	Not Sig.	na
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Adverse events:Any Adverse Event	13 wks	249/128	69.08%/63.28%	RR	1.09(0.93,1.28)	Not Sig.	na
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Adverse events:Any Serious Adverse Event	13 wks	249/128	3.21%/0%	RD	3.213(0.215, 6.525)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Any procedure-related target knee AE	26 weeks	124/129	4.84%/3.1%	RR	1.56(0.45,5.4)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Any treatment and/or procedure-related target knee AE	26 weeks	124/129	5.65%/3.1%	RR	1.82(0.55,6.07)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Any treatment-emergent target knee AE	26 weeks	124/129	35.48%/34.11%	RR	1.04(0.74,1.46)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Any treatment-related target knee AE	26 weeks	124/129	3.23%/0.78%	RR	4.16(0.47,36.72)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Adverse events:Arthralgia	26 wks	181/184	3.87%/3.8%	RR	1.02(0.36,2.84)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Adverse events:Arthralgia	13 wks	249/128	7.63%/9.38%	RR	0.81(0.41,1.62)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Arthralgia	26 weeks	124/129	1.61%/2.33%	RR	0.69(0.12,4.08)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Arthropathy	26 weeks	124/129	0.81%/0%	RD	0.806(-2.814, 3.773)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Arthrosis	364 days	208/200	9.13%/8%	RR	1.14(0.6,2.16)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Back Pain	364 days	208/200	10.58%/9.5%	RR	1.11(0.62,1.99)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Adverse events:Device-Related Adverse Events	26 wks	181/184	7.18%/5.43%	RR	1.32(0.59,2.94)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Diarrhoea	364 days	208/200	5.29%/5%	RR	1.06(0.46,2.44)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Dizziness	364 days	208/200	6.25%/4%	RR	1.56(0.66,3.69)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Flu syndrome	364 days	208/200	20.67%/17.5%	RR	1.18(0.79,1.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Gastrointestinal	154 days	128/123	7.81%/8.13%	RR	0.96(0.41,2.23)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Gastrointestinal	154 days	119/123	9.24%/8.13%	RR	1.14(0.5,2.58)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:General body adverse events	154 days	128/123	6.25%/7.32%	RR	0.85(0.34,2.14)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:General body adverse events	154 days	119/123	10.92%/7.32%	RR	1.49(0.66,3.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Headache	364 days	208/200	12.5%/7.5%	RR	1.67(0.91,3.05)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Infection	364 days	208/200	10.58%/13.5%	RR	0.78(0.46,1.33)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Infection site reaction	364 days	208/200	24.04%/12.5%	RR	1.92(1.24,2.98)	Group 2	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Infections	154 days	119/123	18.49%/18.7%	RR	0.99(0.58,1.68)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Infections	154 days	128/123	21.09%/18.7%	RR	1.13(0.69,1.86)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Injection site pain	26 weeks	124/129	0.81%/0.78%	RR	1.04(0.07,16.45)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Injection site pain	364 days	208/200	12.02%/10%	RR	1.2(0.69,2.09)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Joint Disorder	364 days	208/200	9.13%/6.5%	RR	1.41(0.71,2.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Adverse events:Joint Effusion	13 wks	249/128	11.24%/10.16%	RR	1.11(0.59,2.06)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Adverse events:Joint Stiffness	26 wks	181/184	0.55%/1.09%	RR	0.51(0.05,5.56)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Adverse events:Joint Swelling	26 wks	181/184	1.1%/0.54%	RR	2.03(0.19,22.23)	Not Sig.	na
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Adverse events:Joint Swelling	13 wks	249/128	14.06%/11.72%	RR	1.2(0.68,2.11)	Not Sig.	na
Chevalier; 2010/High	10: IA HA-Hylan G-F 20(1 injection 6 million Da)	10: Placebo/Control-Placebo	Adverse events:Joint effusion	26 weeks	124/129	1.61%/0%	RD	1.613(-2.464, 4.732)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Musculoskeletal disorders	154 days	119/123	19.33%/17.07%	RR	1.13(0.66,1.93)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Musculoskeletal disorders	154 days	128/123	27.34%/17.07%	RR	1.6(0.99,2.59)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Nervous system disorders	154 days	119/123	15.13%/21.14%	RR	0.72(0.41,1.23)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Nervous system disorders	154 days	128/123	15.63%/21.14%	RR	0.74(0.44,1.25)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Pain	364 days	208/200	33.65%/30.5%	RR	1.1(0.83,1.46)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Psychiatry	154 days	128/123	0.78%/1.63%	RR	0.48(0.04,5.23)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Psychiatry	154 days	119/123	0.84%/1.63%	RR	0.52(0.05,5.62)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Respiratory	154 days	119/123	3.36%/4.07%	RR	0.83(0.23,3.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Respiratory	154 days	128/123	3.91%/4.07%	RR	0.96(0.29,3.24)	Not Sig.	na
Jubb; 2003/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(20mg/2 mL HA weekly for 3 wks; repeated twice more at 4mos intervals)	10: Placebo/Control-Placebo (Intra-articular)(2mL saline weekly for 3 wks; repeated twice more at 4mos intervals)	Adverse events:Rhinitis	364 days	208/200	8.65%/9%	RR	0.96(0.52,1.79)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3x HMW hyaluronan injections plus 1x control arthrocentesis only procedure)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Skin	154 days	119/123	0.84%/3.25%	RR	0.26(0.03,2.28)	Not Sig.	na
Neustadt; 2005/High	10: IA HA-Hyaluronic Acid (Intra-articular)(4x HMW hyaluronan injection)	10: Placebo/Control-Placebo (Intra-articular)(4x control arthrocentesis only procedures)	Adverse events:Skin	154 days	128/123	2.34%/3.25%	RR	0.72(0.16,3.15)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Adverse events:Total Adverse Events	26 wks	181/184	66.85%/66.85%	RR	1(0.87, 1.16)	Not Sig.	na
Petterson; 2018/High	10: IA HA-Monovisc	10: Placebo/Control-Placebo(Saline Solution)	Adverse events:Total Serious Adverse Events	26 wks	181/184	4.42%/2.72%	RR	1.63(0.54,4.88)	Not Sig.	na
Strand; 2012/High	10: IA HA-Hyaluronic Acid (Gel-200) [IA](30mg cross-linked HA in 3.0mL single dose)	10: Placebo/Control-Placebo(Saline)	Adverse events:Treatment Related AE	13 wks	249/128	26.91%/25.78%	RR	1.04(0.73,1.49)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Adverse events:adverse events	40 months	153/153	9.8%/9.15%	RR	1.07(0.54,2.14)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	Adverse events:adverse events	26 wks	135/107	37.78%/28.04%	RR	1.35(0.93,1.96)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Adverse events:allergic reaction	40 months	153/153	1.96%/1.96%	RR	1(0.21, 4.88)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Adverse events:arthralgia	40 months	153/153	1.31%/1.31%	RR	1(0.14, 7.01)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Adverse events:bleeding at injection site	40 months	153/153	1.31%/3.92%	RR	0.33(0.07,1.63)	Not Sig.	na
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Adverse events:injection site pain	40 months	153/153	3.92%/1.31%	RR	3(0.62, 14.63)	Not Sig.	na
Baltzer; 2009/High	10: IA HA-hyaject 1.4*10^6 Daltons; 3 injections over 3 weeks (2mL x1/wk)	10: Placebo/Control-placebo(saline)	Adverse events:moderate to severe adverse events	26 wks	135/107	10.37%/3.74%	RR	2.77(0.94,8.18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Navarro-Sarabia;2011/Moderate	10: IA HA-2.5 ml 1 % sodium hyaluronate with a mean molecular weight of 900 000 daltons	10: Placebo/Control-saline	Adverse events:other adverse events	40 months	153/153	1.31%/0.65%	RR	2(0.18, 21.83)	Not Sig.	na

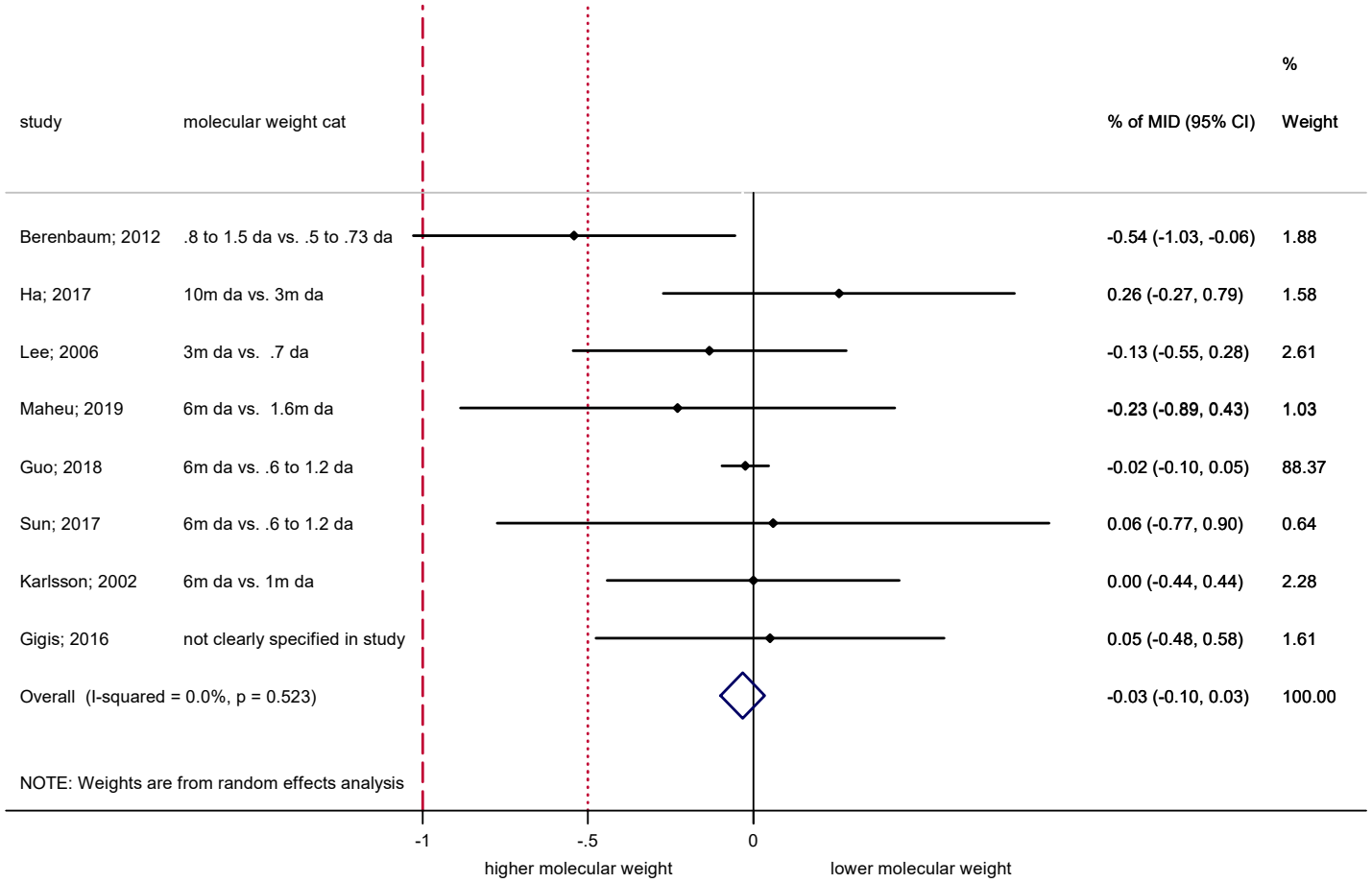
PICO 10: Locally Invasive Treatment

High Molecular Weight Hyaluronic Acid vs. Low Molecular Weight Hyaluronic Acid

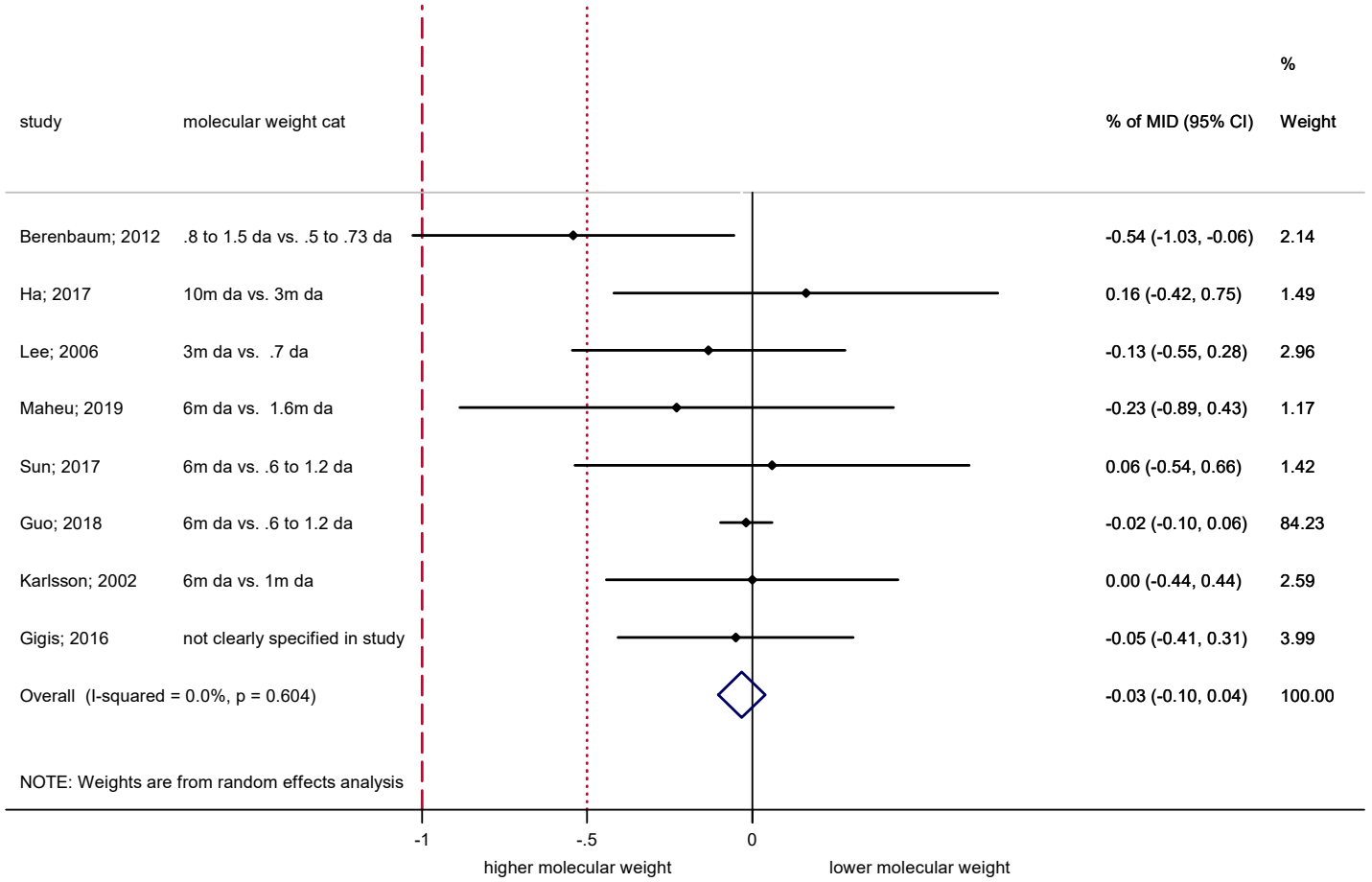
Table 40: High Molecular Weight Hyaluronic Acid vs Low Molecular Weight Hyaluronic Acid

Quality: H=High; M=Moderate; L=Low	H			M		L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Gigis; 2016	Strand;2012	Al-Omran; 2014	Raman; 2008	Wobig; 1999	Lee; 2006	Shewale; 2017
Composite							
lequesne index		●					
WOMAC Total		●	↑				
Omerac OARSI responders		●					
Patient Global Assessment			●			●	
Function							
WOMAC Function		●		↑		●	
WOMAC Stiffness		●				●	
Other							
evaluator assessment of response to treatment (percent symptom free)					↑		
number of patients who used paracetamol as rescue medication						●	
patient response to treatment (percent symptom free)					●		
use of rescue medicine						●	
Pain							
WOMAC Pain	●			↑		●	
Evaluator VAS overall condition improvement (higher is better)					↑		
Patient VAS improvement in most painful knee (higher is better)					↑		
VAS Pain improvement (higher is better)					↑		
evaluator assessment of weight bearing pain improvement (higher is better)					↑		
patient assessment of weight bearing pain improvement (higher is better)					↑		
vas pain vas weight bearing pain						●	
Adverse events							
Serious Adverse Events		●					
Bronchitis		●					
Arthralgia of the studied knee		●					
At least one treatment-emergent AE		●					
Dropouts due to an AE		●					
Injection site joint effusion		●					
Injection site joint inflammation		●					
Injection site joint pain		●					
Injection site reactions		●					
Loin pain		●					
Osteoarthritis flare-up of the studied knee		●					
Patients with at least one SAE		●					
Patients with at least one injection site reaction		●					
Spinal osteoarthritis		●					
Treatment-emergent Aes		●					
Adverse Events				●			
Injection site pain						●	
local adverse events					●		
overall complications						●	
calculable MID outcomes							
change in weight-bearing pain in knee (VAS)						●	
VAS Score Mean	●						
WOMAC Score Mean (VAS)	●						
OA progression							
need for any surgical intervention							●
need for any surgical intervention(accounting for other surgical interventions as a competing risk)							↑
need for any surgical intervention(starting from last injection until 6 months after)(accounts for varying number of injections between groups)							↑
Time to arthroplasty							
TKA							●
TKA(accounting for other surgical interventions as a competing risk)							↑
TKA(starting from last injection until 6 months after)(accounts for varying number of injections between groups)							●
UKA or TKA							●
UKA or TKA(accounting for other surgical interventions as a competing risk)							↑
UKA or TKA(starting from last injection until 6 months after)(accounts for varying number of injections between groups)							●

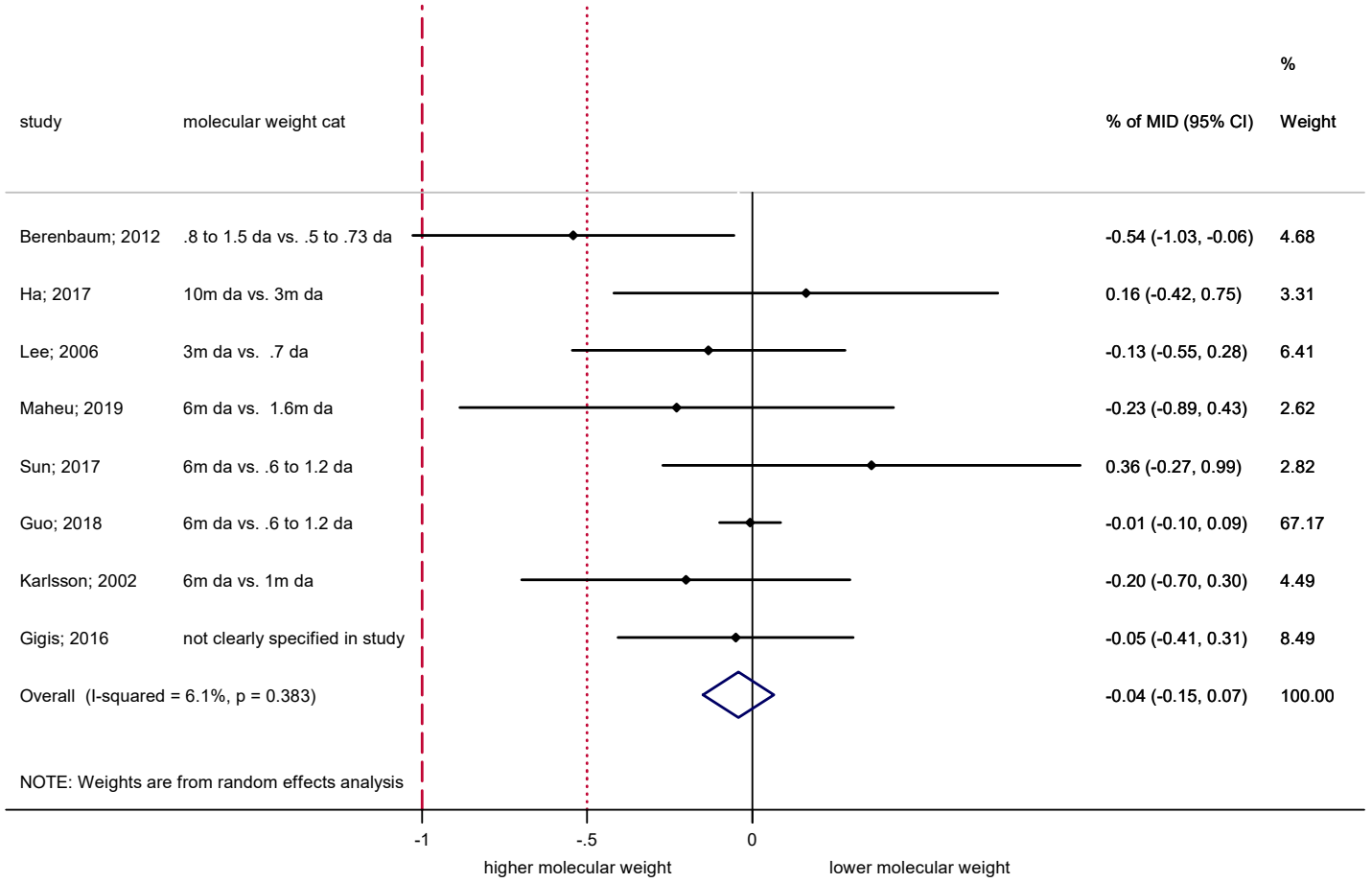
Meta-Analysis Figure 56: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid - Pain Earliest Follow Up



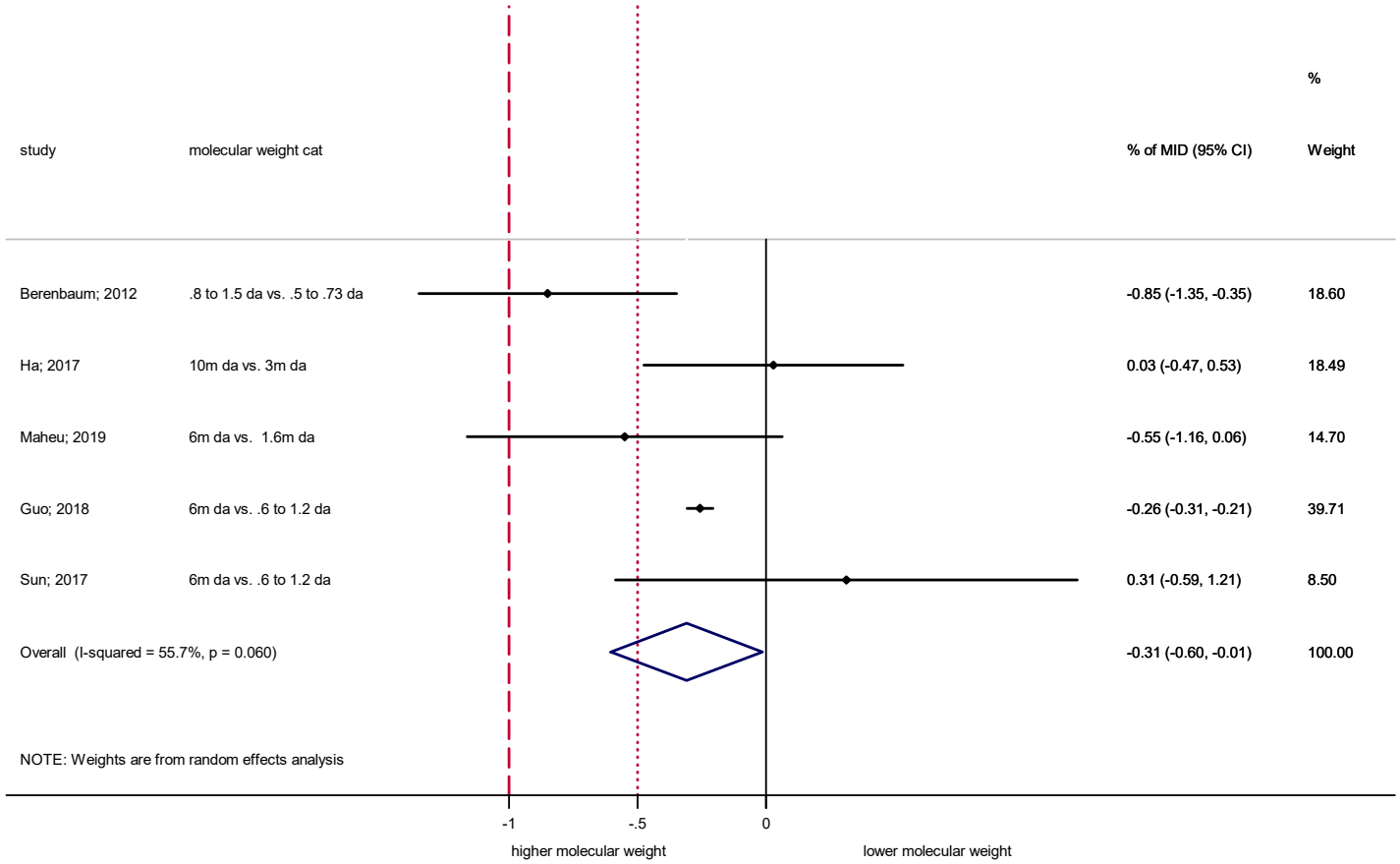
Meta-Analysis Figure 57: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid - Pain Closest to 3-Month Follow Up



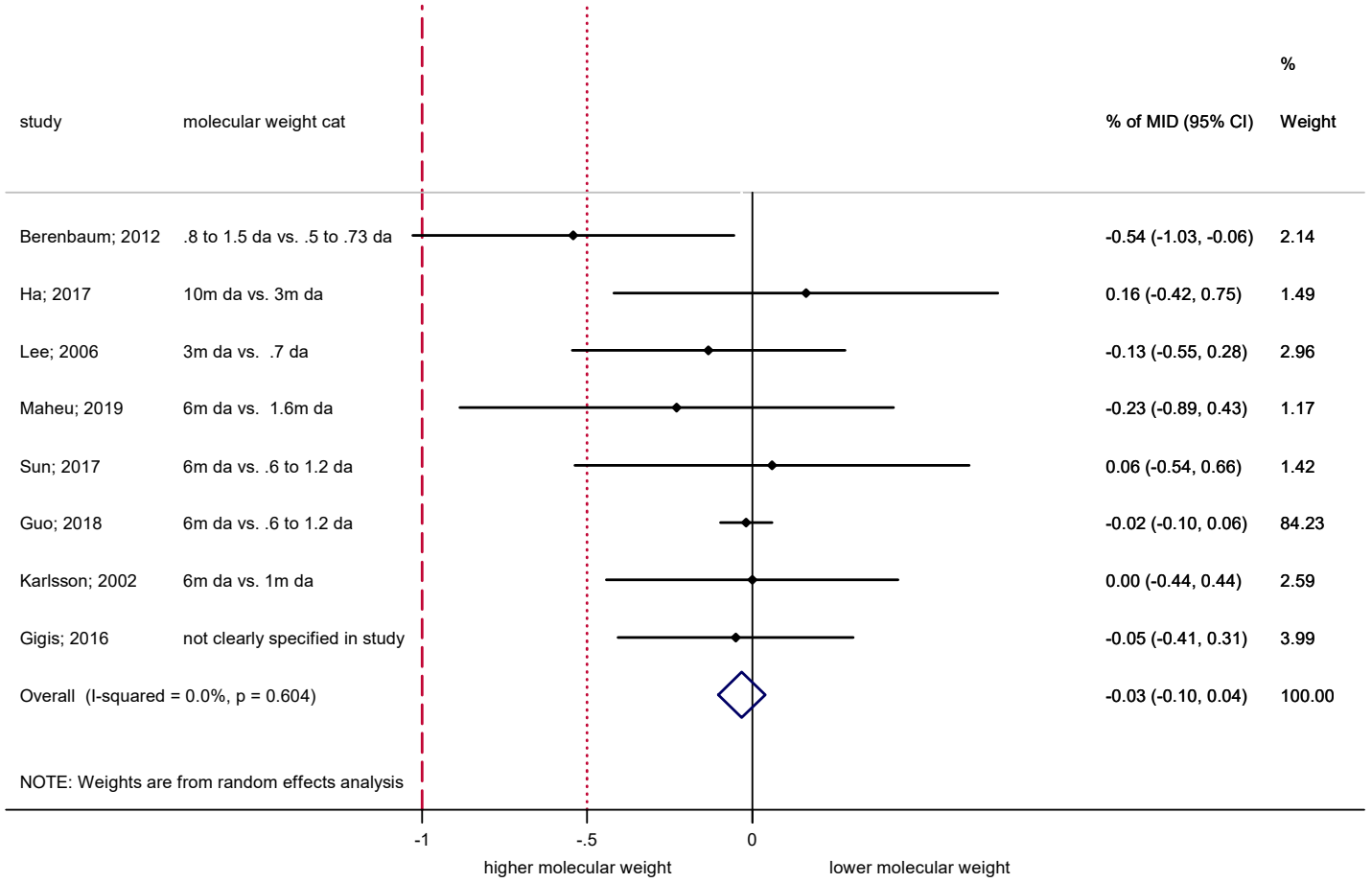
Meta-Analysis Figure 58: High Molecular Weight vs Low Molecular Weigh Hyaluronic Acid t- Pain Closest to 6-Month Follow Up



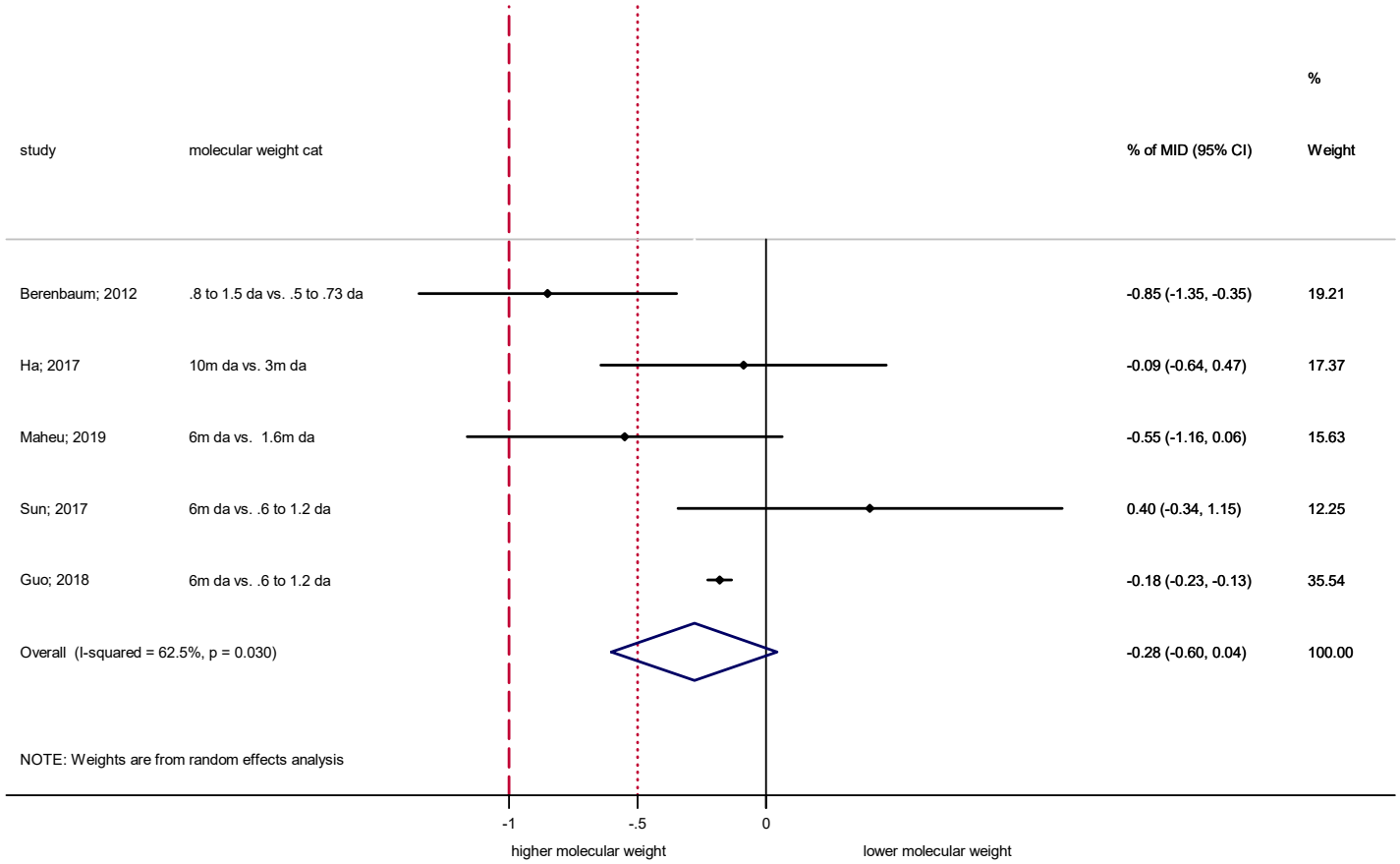
Meta-Analysis Figure 59: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid - Function Earliest Follow Up



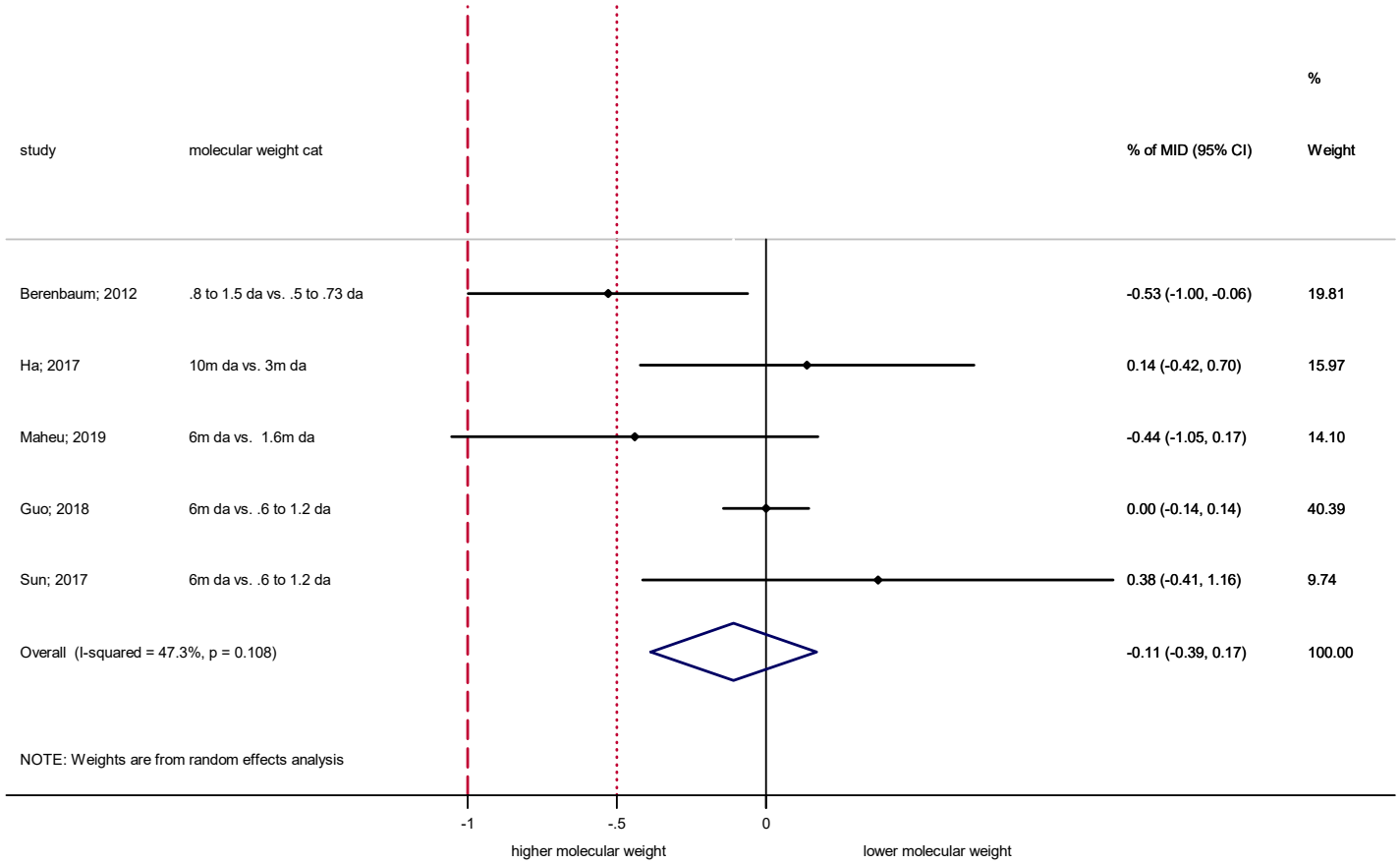
Meta-Analysis Figure 60: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid - Function Closest to 3-Month Follow Up



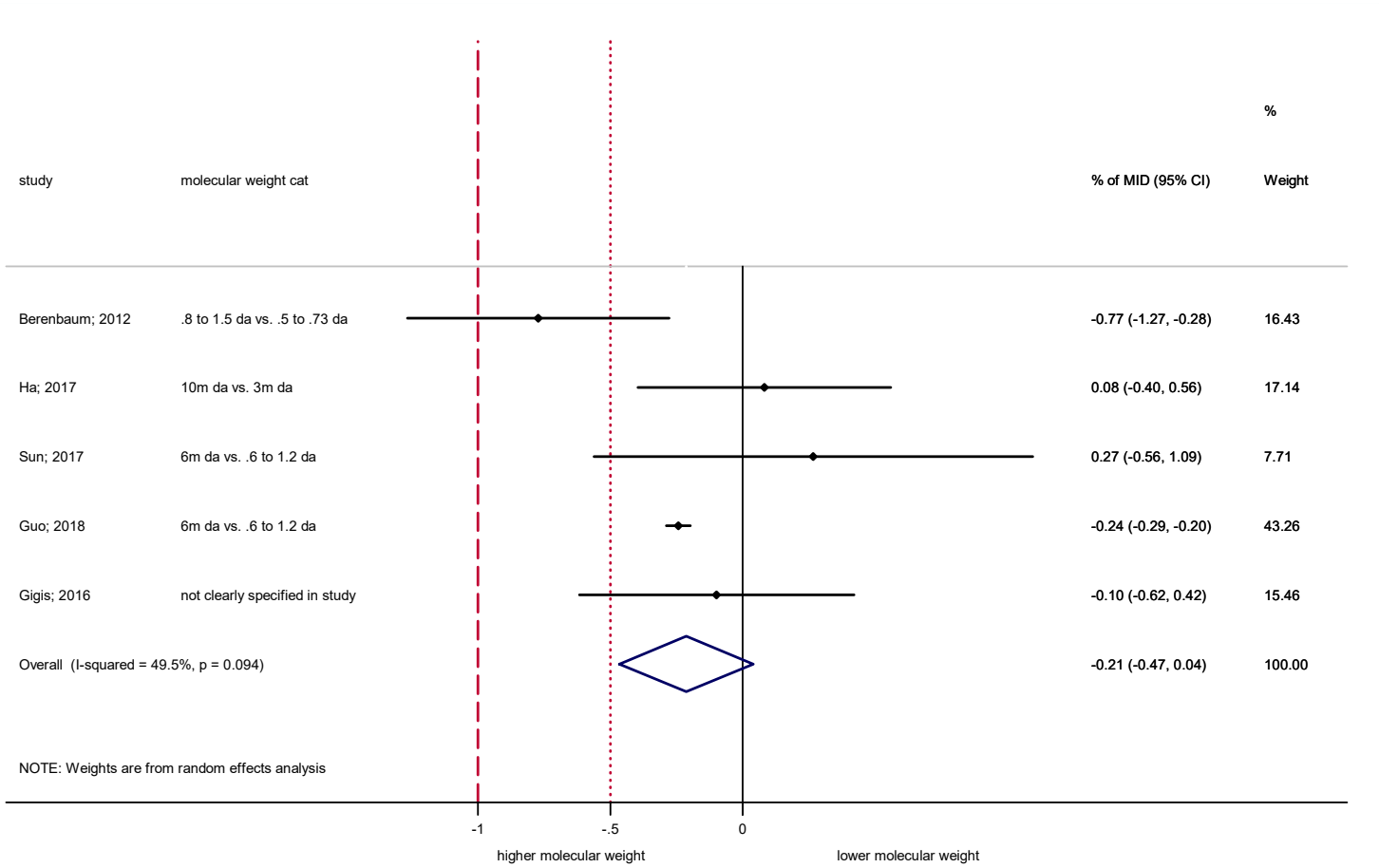
Meta-Analysis Figure 61: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid - Function Closest to 6-Month Follow Up



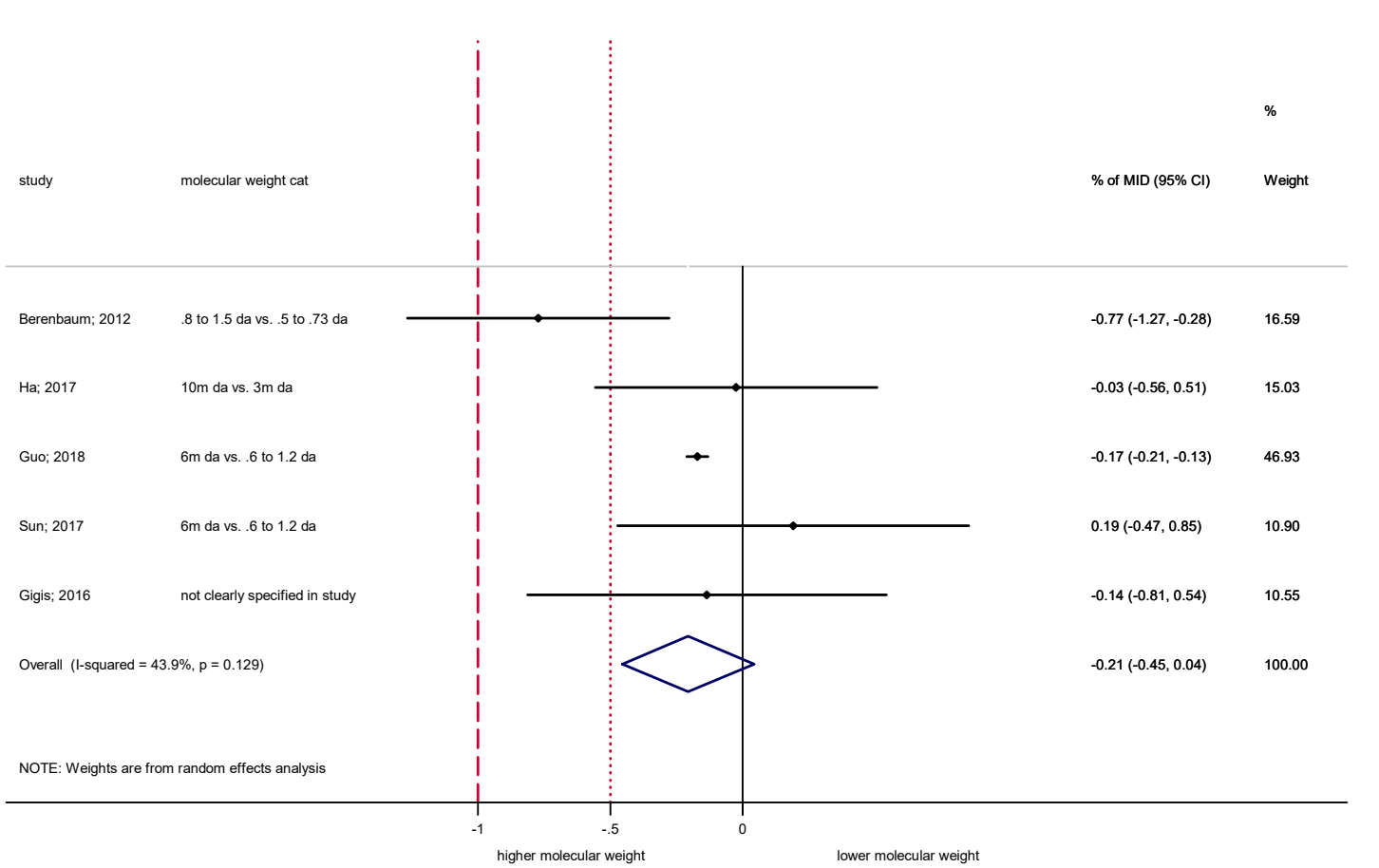
Meta-Analysis Figure 62: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid - Stiffness Earliest Follow Up



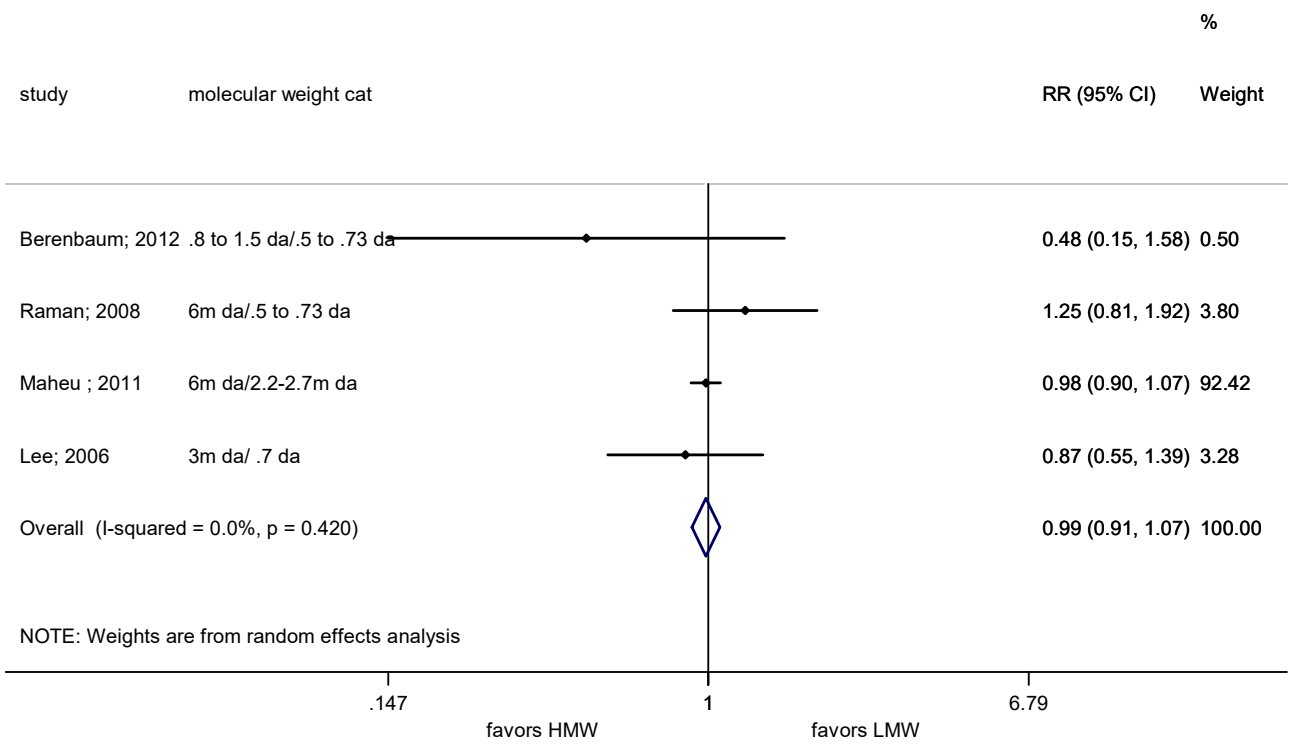
Meta-Analysis Figure 63: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid – WOMAC Total Earliest Follow Up



Meta-Analysis Figure 64: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid – WOMAC Total Closest to 3-Month Follow Up



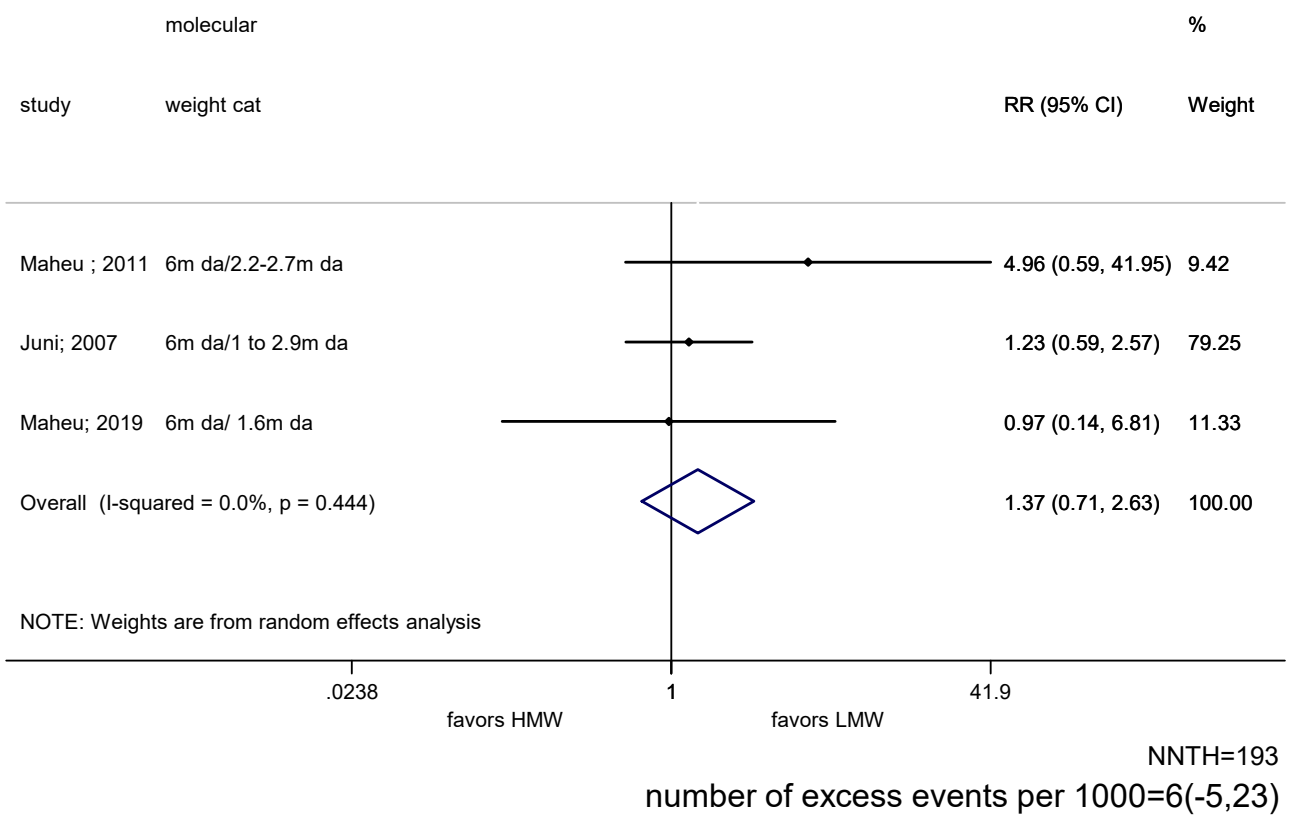
Meta-Analysis Figure 65: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid – Overall Adverse Events



NNTB=280

number of avoided events per 1000=3.6(-19,24)

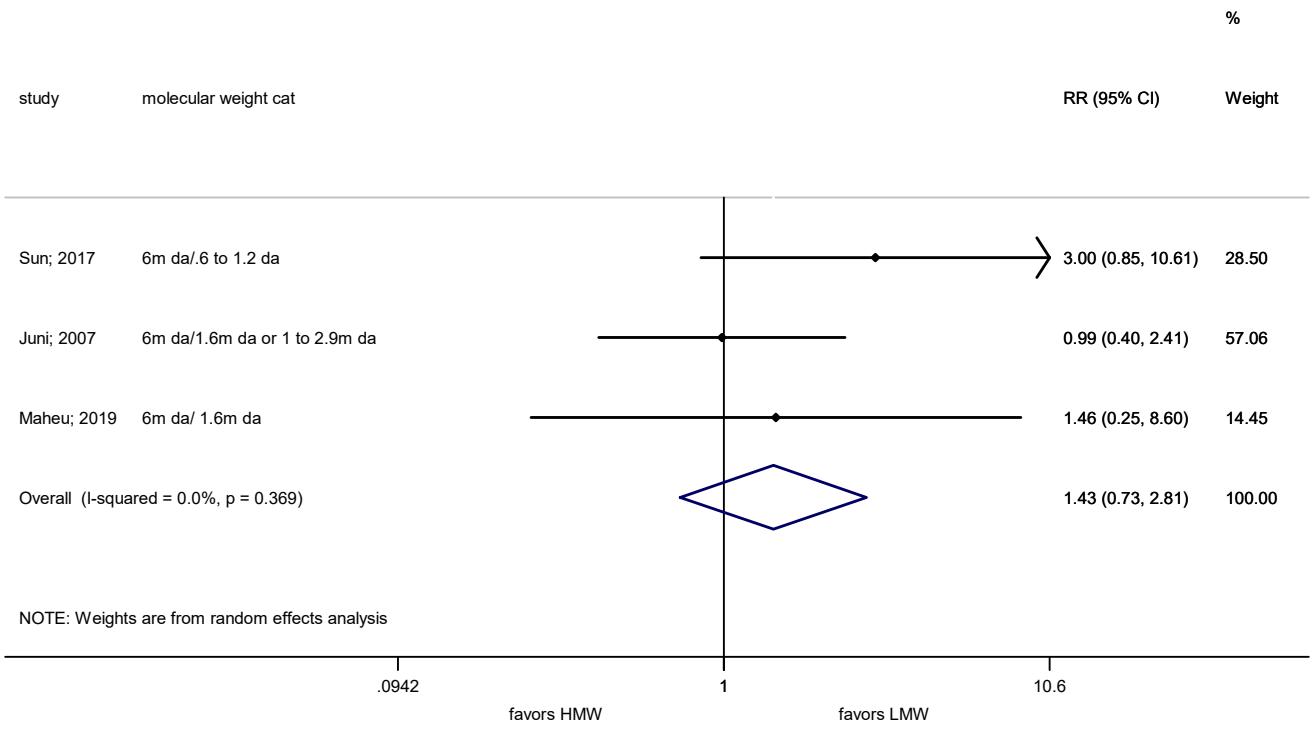
Meta-Analysis Figure 66: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid – Serious Adverse Events



NNTH=193

number of excess events per 1000=6(-5,23)

Meta-Analysis Figure 67: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid –Adverse Events Effusions



NNTH=73

number of excess events per 1000=14(-9,58)

Evidence Table 4740: High Molecular Weight vs Low Molecular Weight Hyaluronic Acid

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Pain:Evaluator VAS overall condition improvement (higher is better)	12 wks		none	pvalue	Sig (p<0.05)	Hylan G-F 20 favored over Low MW HA Injectio	na
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Pain:Patient VAS improvement in most painful knee (higher is better)	12 wks		none	pvalue	Sig (p<0.05)	Hylan G-F 20 favored over Low MW HA Injectio	na
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Pain:VAS Pain improvement (higher is better)	12 wks		none	pvalue	Sig (p<0.05)	Hylan G-F 20 favored over Low MW HA Injectio	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Pain:WOMAC Pain	6 mos	113/112	-34.3(19.13)/-36.2(22.22)	Mean Diff	-1.9(-7.35,3.55)	Not Sig.	clinically insignificant
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Pain:Womac pain Likert	26 wks	194/186	none	pvalue	Sig (p<0.05)	Hylan G-F 20	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Pain:Womac pain Likert	13 wks	194/186	none	pvalue	Sig (p<0.05)	Hylan G-F 20	na
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Pain:Womac pain Likert	52 wks	194/186	none	pvalue	Sig (p<0.05)	Hylan G-F 20	na
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Pain:Womac pain Likert	6 wks	194/186	none	pvalue	NS	Sodium Hyaluronate (5 Injections .5 wks (Hyl	na
Lee; 2006/Low	10: IA HA-HMW hyaluronates(3 injections(1 per week) 3000 kD)	10: IA HA-LMW hyaluronates(3 injections(1 per week) 750 kD)	Pain:change in weight-bearing pain in knee (VAS)	12 wks	36/32	33(22)/38(23)	Mean Diff	-5(-15.94, 5.94)	Not Sig.	clinically insignificant
Lee; 2006/Low	10: IA HA-HMW hyaluronates(3 injections(1 per week) 3000 kD)	10: IA HA-LMW hyaluronates(3 injections(1 per week) 750 kD)	Pain:change in weight-bearing pain in knee (VAS)	12 wks	39/39	20(22)/19(26)	Mean Diff	1(-9.87,11.87)	Not Sig.	clinically insignificant
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Pain:evaluator assessment of weight bearing pain improvement (higher is better)	12 wks		none	pvalue	Sig (p<0.05)	Hylan G-F 20 favored over Low MW HA Injectio	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Pain:patient assessment of weight bearing pain improvement (higher is better)	12 wks		none	pvalue	Sig (p<0.05)	Hylan G-F 20 favored over Low MW HA Injectio	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Pain:vas pain vas weight bearing pain	12 weeks	75/71	26(.)/27(.)	Mean Diff	-1	Not Sig.	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Pain:womac pain	12 weeks	75/71	none	pvalue	NS	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Function:WOMAC Function	6 mos	113/112	-21.3(17.01)/-25.7(20.11)	Mean Diff	-4.4(-9.3,0.5)	Not Sig.	inconclusive
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Function:WOMAC Stiffness	6 mos	113/112	-22.5(24.45)/-26.9(22.22)	Mean Diff	-4.4(-10.54, 1.74)	Not Sig.	inconclusive
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Function:WOMAC function Likert	13 wks	194/186	17.7(.)/18.4(.)	Mean Diff	-0.7	Sodium Hyaluronate (5 Injections .5 wks (Hyl	na
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Function:WOMAC function Likert	26 wks	194/186	14.3(.)/27.9(.)	Mean Diff	-13.6	Hylan G-F 20	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Function:WOMAC function Likert	52 wks	194/186	15(.)/33.3(.)	Mean Diff	-18.3	Hylan G-F 20	na
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Function:WOMAC function Likert	6 wks	194/186	29.3(.)/28.6(.)	Mean Diff	0.7	Sodium Hyaluronate (5 Injections .5 wks (Hyl	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Function:womac function	12 weeks	75/71	none	pvalue	NS	Not Sig.	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Function:womac stiffness	12 weeks	75/71	none	pvalue	NS	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Composite:Global treatment efficacy (good/very good)	6 mos	113/112	66.37%/66.96%	RR	0.99(1.19,0.82)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Composite:Lequesne index change from baseline	6 mos	113/112	-4.3(3.19)/-4.7(4.23)	Mean Diff	-0.4(-1.39,0.59)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Composite:OMERACT-OARSI responders	6 mos	113/112	82.3%/85.71%	RR	0.96(1.08,0.86)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Composite:Patient global assessment	6 mos	113/112	-25.4(23.39)/-27(21.17)	Mean Diff	-1.6(-7.46,4.26)	Not Sig.	na
Gigis; 2016/High	10: IA HA-Hyaluronic Acid (High Molecular Weight)(5 mg once a week for three weeks)	10: IA HA-Hyaluronic Acid (Low Molecular Weight)(5 mg once a week for five weeks)	Composite:VAS Score Mean	1 yrs	40/40	4.25(1.02)/4.35(1.54)	Mean Diff	-0.1(-0.68,0.48)	Not Sig.	clinically insignificant
Gigis; 2016/High	10: IA HA-Hyaluronic Acid (High Molecular Weight)(5 mg once a week for three weeks)	10: IA HA-Hyaluronic Acid (Low Molecular Weight)(5 mg once a week for five weeks)	Composite:VAS Score Mean	3 mos	40/40	3.1(1.35)/3.2(1.8)	Mean Diff	-0.1(-0.81,0.61)	Not Sig.	clinically insignificant
Gigis; 2016/High	10: IA HA-Hyaluronic Acid (High Molecular Weight)(5 mg once a week for three weeks)	10: IA HA-Hyaluronic Acid (Low Molecular Weight)(5 mg once a week for five weeks)	Composite:VAS Score Mean	5 wks	40/40	4.1(2.39)/4(2.32)	Mean Diff	0.1(-0.95,1.15)	Not Sig.	clinically insignificant
Gigis; 2016/High	10: IA HA-Hyaluronic Acid (High Molecular Weight)(5 mg once a week for three weeks)	10: IA HA-Hyaluronic Acid (Low Molecular Weight)(5 mg once a week for five weeks)	Composite:WOMAC Score Mean (VAS)	1 yrs	40/40	21.93(14.79)/22.48(13.43)	Mean Diff	-0.55(-6.84,5.74)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Gigis; 2016/High	10: IA HA-Hyaluronic Acid (High Molecular Weight)(5 mg once a week for three weeks)	10: IA HA-Hyaluronic Acid (Low Molecular Weight)(5 mg once a week for five weeks)	Composite:WOMAC Score Mean (VAS)	5 wks	40/40	23.02(8.98)/23.8(9.4)	Mean Diff	-0.78(-4.87,3.31)	Not Sig.	clinically insignificant
Gigis; 2016/High	10: IA HA-Hyaluronic Acid (High Molecular Weight)(5 mg once a week for three weeks)	10: IA HA-Hyaluronic Acid (Low Molecular Weight)(5 mg once a week for five weeks)	Composite:WOMAC Score Mean (VAS)	3 mos	40/40	20.75(12.76)/21.82(11.2)	Mean Diff	-1.07(-6.42,4.28)	Not Sig.	clinically insignificant
Al-Omran; 2014/High	10: IA HA-Hylan G-F 20 (Synvisc)	10: Other IA Tx-Sodium hyaluronate (Durolane)	Composite:WOMAC Total	6 mos	70/69	46.8(4.6)/53.1(7.4)	Mean Diff	-6.3(-8.37,-4.23)	Group 1	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Composite:patient global assessment	12 weeks	75/71	none	pvalue	NS	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Other:Acetaminophen use post injection (yes)	6 mos	113/112	72.57%/66.07%	RR	1.1(1.31,0.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Other:evaluator assessment of response to treatment (percent symptom free)	12 wks		none	pvalue	Sig (p<0.05)	Hylan G-F 20 favored over Low MW HA Injectio	na
Lee; 2006/Low	10: IA HA-HMW hyaluronates(3 injections(1 per week) 3000 kD)	10: IA HA-LMW hyaluronates(3 injections(1 per week) 750 kD)	Other:number of patients who used paracetamol as rescue medication	12 wks	75/71	52%/54.93%	RR	0.95(0.7,1.28)	Not Sig.	na
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Other:patient response to treatment (percent symptom free)	12 wks		none	pvalue	NS	.75 – million)(3 injections (percentpainject	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Other:use of rescue medicine	12 weeks	75/71	65.33%/78.87%	RR	0.83(0.68,1.02)	Not Sig.	na
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	Time to arthroplasty: TKA	Not Reported	20936	none	Hazard Ratio	0.97(0.88,1.06)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	Time to arthroplasty: TKA(accounting for other surgical interventions as a competing risk)	Not Reported	20936	none	Hazard Ratio	0.89(0.83,0.94)	Group 1	na
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	Time to arthroplasty: TKA(starting from last injection until 6 months after)(accounts for varying number of injections between groups)	6 mos	20936	none	Hazard Ratio	0.9(0.81,1.01)	Not Sig.	na
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	Time to arthroplasty: UKA or TKA	Not Reported	20936	none	Hazard Ratio	0.94(0.86,1.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	Time to arthroplasty: UKA or TKA(accounting for other surgical interventions as a competing risk)	Not Reported	20936	none	Hazard Ratio	0.87(0.82,0.93)	Group 1	na
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	Time to arthroplasty: UKA or TKA(starting from last injection until 6 months after)(accounts for varying number of injections between groups)	6 mos	20936	none	Hazard Ratio	0.9(0.8,1)	Not Sig.	na
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	OA progression:need for any surgical intervention	Not Reported	20936	none	Hazard Ratio	0.94(0.87,1.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	OA progression:need for any surgical intervention(accounting for other surgical interventions as a competing risk)	Not Reported	20936	none	Hazard Ratio	0.88(0.84,0.93)	Group 1	na
Shewale; 2017/Low	10: IA HA-High Molecular Weight (Synvisc or Synvisc One)	10: IA HA-Low Molecular Weight(Hyalgan; Supartz)	OA progression:need for any surgical intervention(starting from last injection until 6 months after)(accounts for varying number of injections between groups)	6 mos	20936	none	Hazard Ratio	0.9(0.82,0.98)	Group 1	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Arthralgia of the studied knee	6 mos	142/146	7.75%/6.16%	RR	1.26(2.94,0.54)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:At least one treatment-emergent AE	6 mos	142/146	27.46%/34.93%	RR	0.79(1.11,0.56)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Bronchitis	6 mos	142/146	2.11%/2.05%	RR	1.03(5.01,0.21)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Dropouts due to an AE	6 mos	142/146	0%/2.05%	RD	2.055(-1.757, 5.016)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Injection site joint effusion	6 mos	142/146	1.41%/2.05%	RR	0.69(4.04,0.12)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Injection site joint inflammation	6 mos	142/146	2.82%/4.11%	RR	0.69(2.38,0.2)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Injection site joint pain	6 mos	142/146	7.75%/10.96%	RR	0.71(1.47,0.34)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Injection site reactions	6 mos	142/146	11.97%/17.12%	RR	0.7(1.24,0.39)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Loin pain	6 mos	142/146	2.82%/4.11%	RR	0.69(2.38,0.2)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Osteoarthritis flare-up of the studied knee	6 mos	142/146	0.7%/3.42%	RR	0.21(1.74,0.02)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Patients with at least one SAE	6 mos	142/146	0.7%/1.37%	RR	0.51(5.61,0.05)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Patients with at least one injection site reaction	6 mos	142/146	8.45%/13.01%	RR	0.65(1.29,0.33)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Serious Adverse Events	6 mos	142/146	1.41%/1.37%	RR	1.03(7.2,0.15)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Spinal osteoarthritis	6 mos	142/146	0.7%/2.05%	RR	0.34(3.26,0.04)	Not Sig.	na
Maheu; 2019/High	10: IA HA(Hylan G-F 20)	10: IA HA-Sodium hyaluronate	Adverse events:Treatment-emergent Aes	6 mos	142/146	42.25%/50.68%	RR	0.83(1.07,0.65)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Raman; 2008/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Sodium Hyaluronate (5 injections .5 to .73 million Daltons)	Adverse events:adverse events	52 wks	194/186	20.1%/16.13%	RR	1.25(0.81,1.92)	Not Sig.	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Adverse events:injection site pain	12 weeks	75/71	30.67%/33.8%	RR	0.91(0.57,1.45)	Not Sig.	na
Wobig; 1999/Moderate	10: IA HA-Hylan G-F 20(3 injections 6 million Daltons)	10: IA HA-Low MW Hyaluronic Acid (.75 – million)(3 injections .75 – million)	Adverse events:local adverse events	12 wks		none	pvalue	NS	.75 – million)(3 injections (Hylanloinjection	na
Lee; 2006/Low	10: IA HA-hmw hyruan 3 injections(3000kd)	10: IA HA-LMW Hyal 5 injections (750kd)	Adverse events:overall complications	12 weeks	75/71	30.67%/35.21%	RR	0.87(0.55,1.39)	Not Sig.	na

PICO 10: Locally Invasive Treatment

Intraarticular vs. Control

Table 41: Intraarticular Corticosteroid vs Control

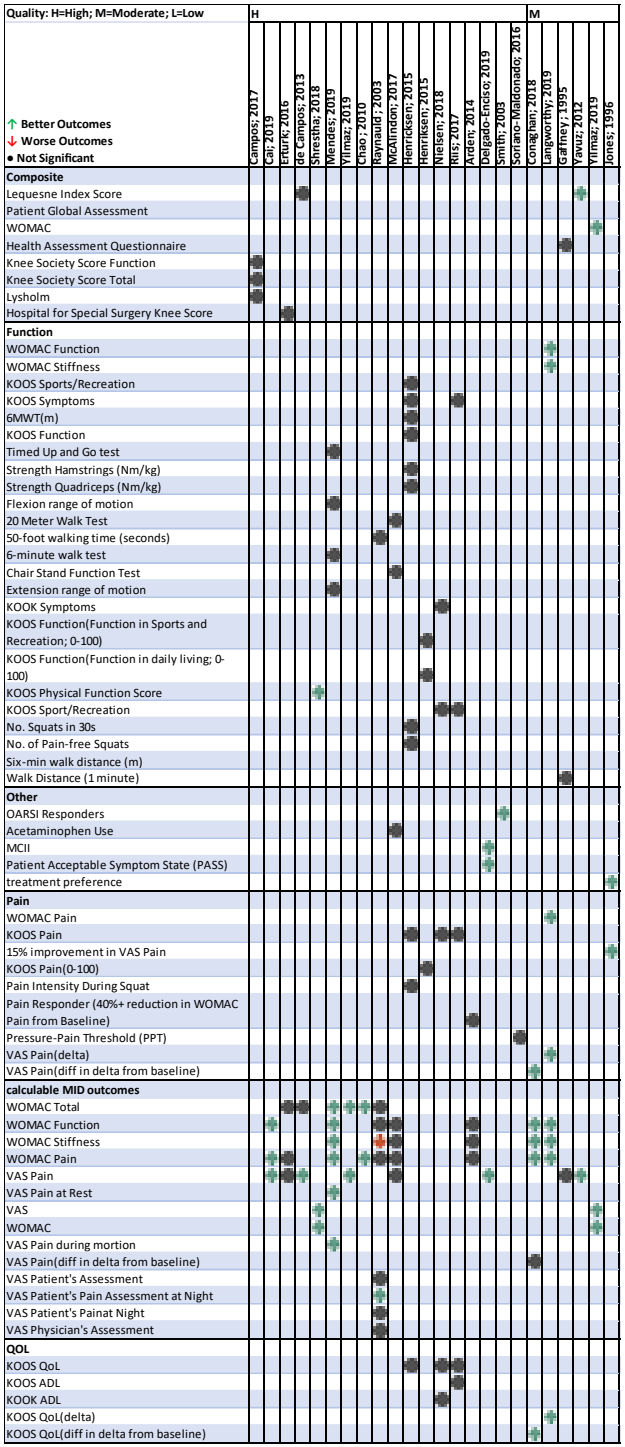
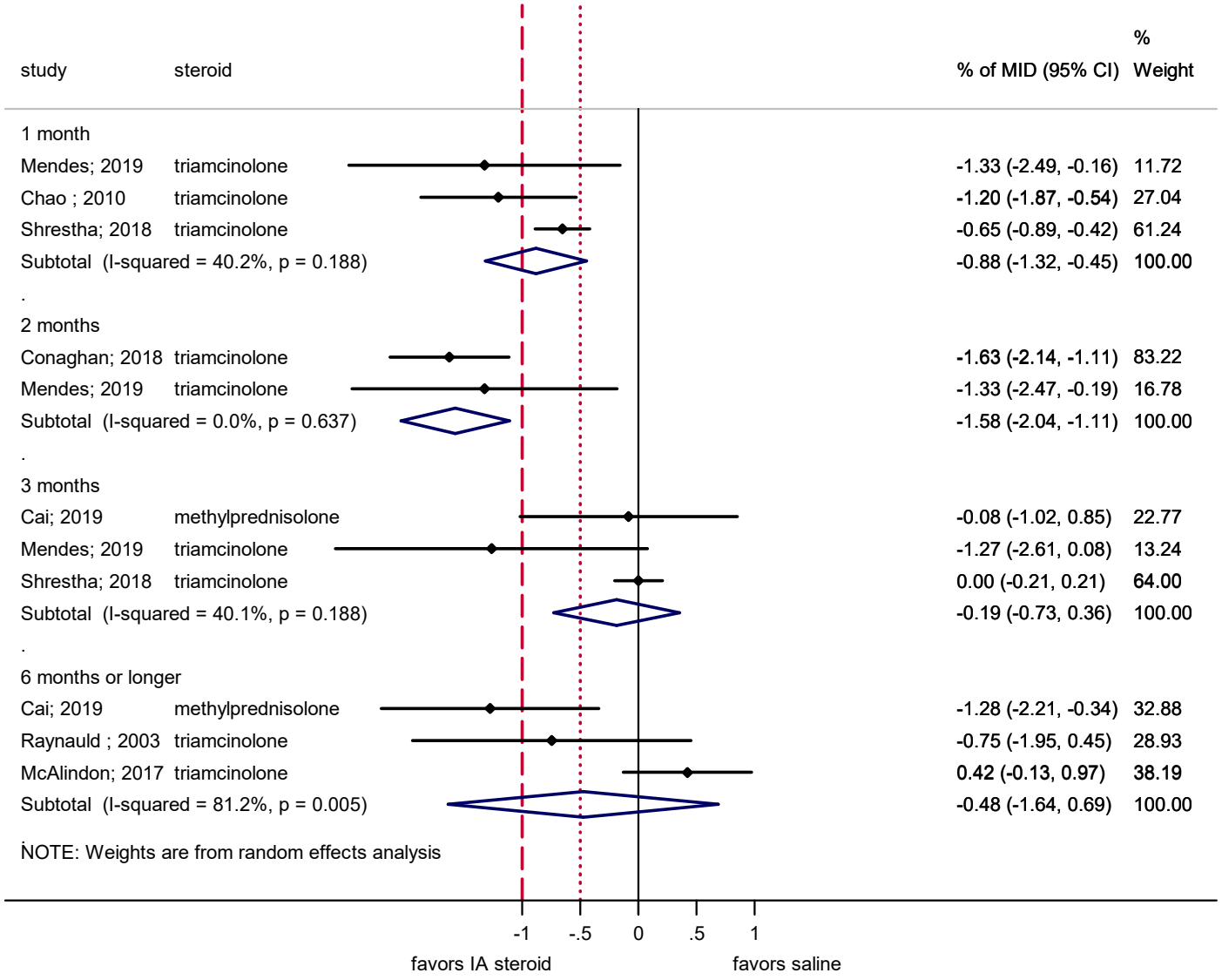

Quality: H=High; M=Moderate; L=Low
H
M
↑ Better Outcomes
↓ Worse Outcomes
● Not Significant
Campos; 2017
Cai; 2019
Erturk; 2016
de Campos; 2013
Shrestha; 2018
Mendes; 2019
Yilmaz; 2019
Chao; 2010
Raynauld; 2003
McAlindon; 2017
Henriksen; 2015
Henriksen; 2015
Nielsen; 2018
Kiis; 2017
Arden; 2014
Delgado-Enciso; 2019
Smith; 2003
Soriano-Maldonado; 2016
Conaghan; 2018
Langworthy; 2019
Gaffney; 1995
Yavuz; 2012
Yilmaz; 2019
Jones; 1996
Composite
Lequesne Index Score
Patient Global Assessment
WOMAC
Health Assessment Questionnaire
Knee Society Score Function
Knee Society Score Total
Lysholm
Hospital for Special Surgery Knee Score
Function
WOMAC Function
WOMAC Stiffness
KOOS Sports/Recreation
KOOS Symptoms
6MWT(m)
KOOS Function
Timed Up and Go test
Strength Hamstrings (Nm/kg)
Strength Quadriceps (Nm/kg)
Flexion range of motion
20 Meter Walk Test
50-foot walking time (seconds)
6-minute walk test
Chair Stand Function Test
Extension range of motion
KOOK Symptoms
KOOS Function(Function in Sports and Recreation; 0-100)
KOOS Function(Function in daily living; 0-100)
KOOS Physical Function Score
KOOS Sport/Recreation
No. Squats in 30s
No. of Pain-free Squats
Six-min walk distance (m)
Walk Distance (1 minute)
Other
OARSI Responders
Acetaminophen Use
MCII
Patient Acceptable Symptom State (PASS)
treatment preference
Pain
WOMAC Pain
KOOS Pain
15% improvement in VAS Pain
KOOS Pain(0-100)
Pain Intensity During Squat
Pain Responder (40%+ reduction in WOMAC Pain from Baseline)
Pressure-Pain Threshold (PPT)
VAS Pain(delta)
VAS Pain(diff in delta from baseline)
calculable MID outcomes
WOMAC Total
WOMAC Function
WOMAC Stiffness
WOMAC Pain
VAS Pain
VAS Pain at Rest
VAS
WOMAC
VAS Pain during mortion
VAS Pain(diff in delta from baseline)
VAS Patient's Assessment
VAS Patient's Pain Assessment at Night
VAS Patient's Painat Night
VAS Physician's Assessment
QOL
KOOS QoL
KOOS ADL
KOOK ADL
KOOS QoL(delta)
KOOS QoL(diff in delta from baseline)

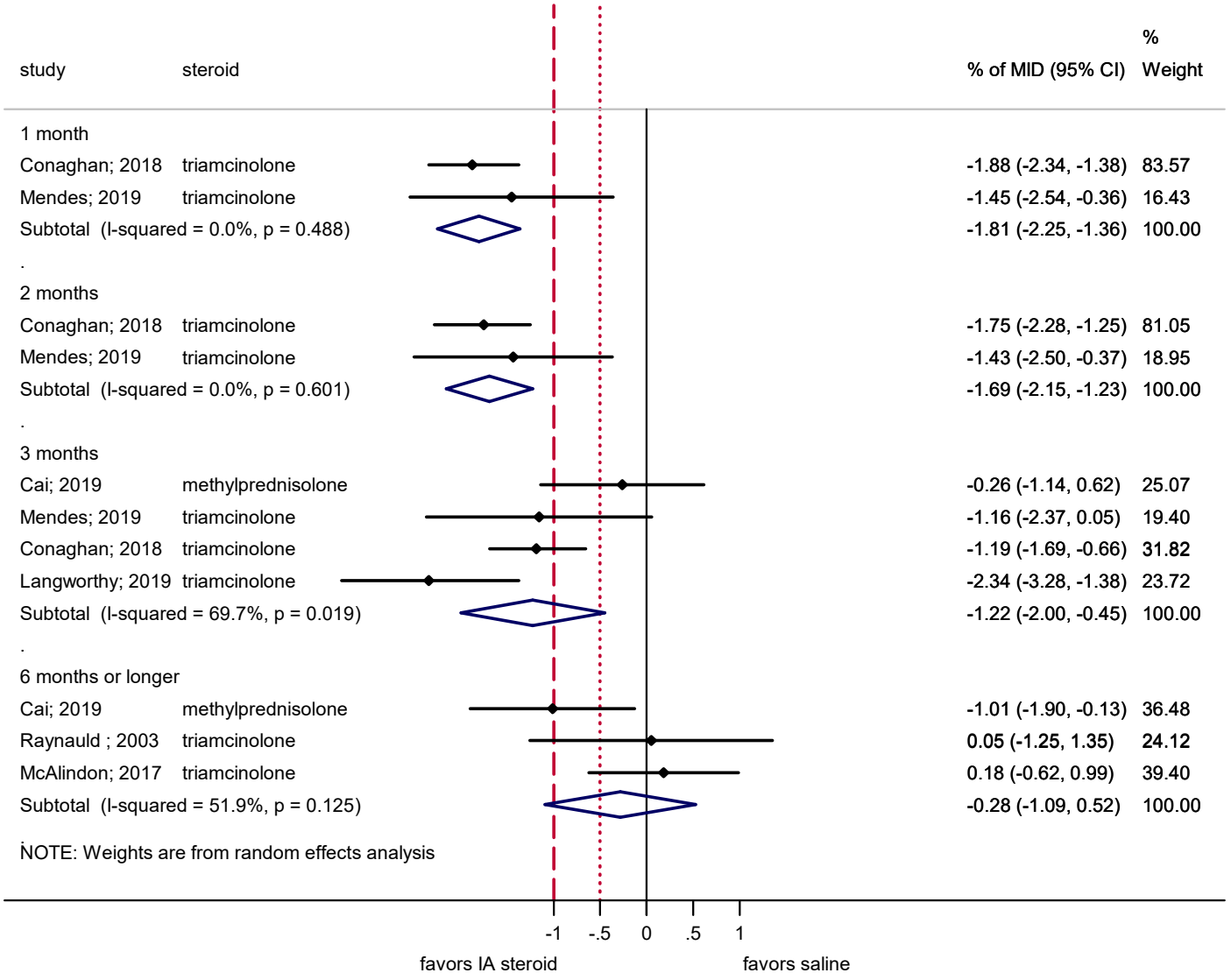
Table 41 Continued: Intraarticular Corticosteroid vs Control

Quality: H=High; M=Moderate; L=Low	H	M		
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Cai; 2019	Conaghan; 2018	Conaghan; 2018	Langworthy; 2019
Adverse events				
Back Pain			●	
Any Adverse Event			●	●
Headache			●	●
Any Serious Adverse Event			●	●
Arthralgia				●
Diarrhea				
Upper Respiratory Tract Infection				●
Joint Effusion				●
Gastritis				
Nasopharyngitis				●
Rash				
Serious Adverse Events	●			
Gastroesophageal reflux				●
Hypertension				
Peripheral Edema				
Arthalgia			●	
Sciatica				●
Weight Gain				
>2% of patients Arthralgia		●		
>2% of patients Back pain		●		
>2% of patients Bronchitis		●		
>2% of patients Headache		●		
>2% of patients Joint swelling		●		
>2% of patients Ligament sprain		●		
>2% of patients Nasopharyngitis		●		
>2% of patients Neck pain		●		
>2% of patients Sinusitis		●		
>2% of patients Toothache		●		
Any AE Leading to Discontinuation			●	
Cancer	●			
Cardiovascular problems	●			
Discontinuation due to drug		●		
Discontinuation due to seroius AE		●		
Discontinued Due to AE				●
Elective hospital admissions other than knee surgery	●			
Gastrointestinal problems	●			
Hyperglycemia				
Index knee-related Aes occuring in >2% of patients in any treatment group Arthralgia		●		
Index knee-related Aes occuring in >2% of patients in any treatment group joint swelling		●		
Index knee-related Aes occuring in >2% of patients in any treatment group ligament sprain		●		
Injuries	●			
Knee replacement	●			
Musculoskeletal pain and stiffness	●			
Neuropathy	●			
Other problems	●			
Patients with >1 AE		●		
Patients with >1 AE leading to study discontinuation		●		
Patients with >1 index knee-related AE		●		
Patients with >1 index knee-related AE leading to study discontinuation		●		
Patients with >1 index knee-related AE leading to study discontinuation Drug-related		●		
Patients with >1 index knee-related AE leading to study discontinuation Due to serious AE		●		
Patients with >1 index knee-related serious AE		●		
Patients with >1 serious AE		●		
Patients with at least one other adverse event	●			
Pneumonia	●			
Skin diseases	●			

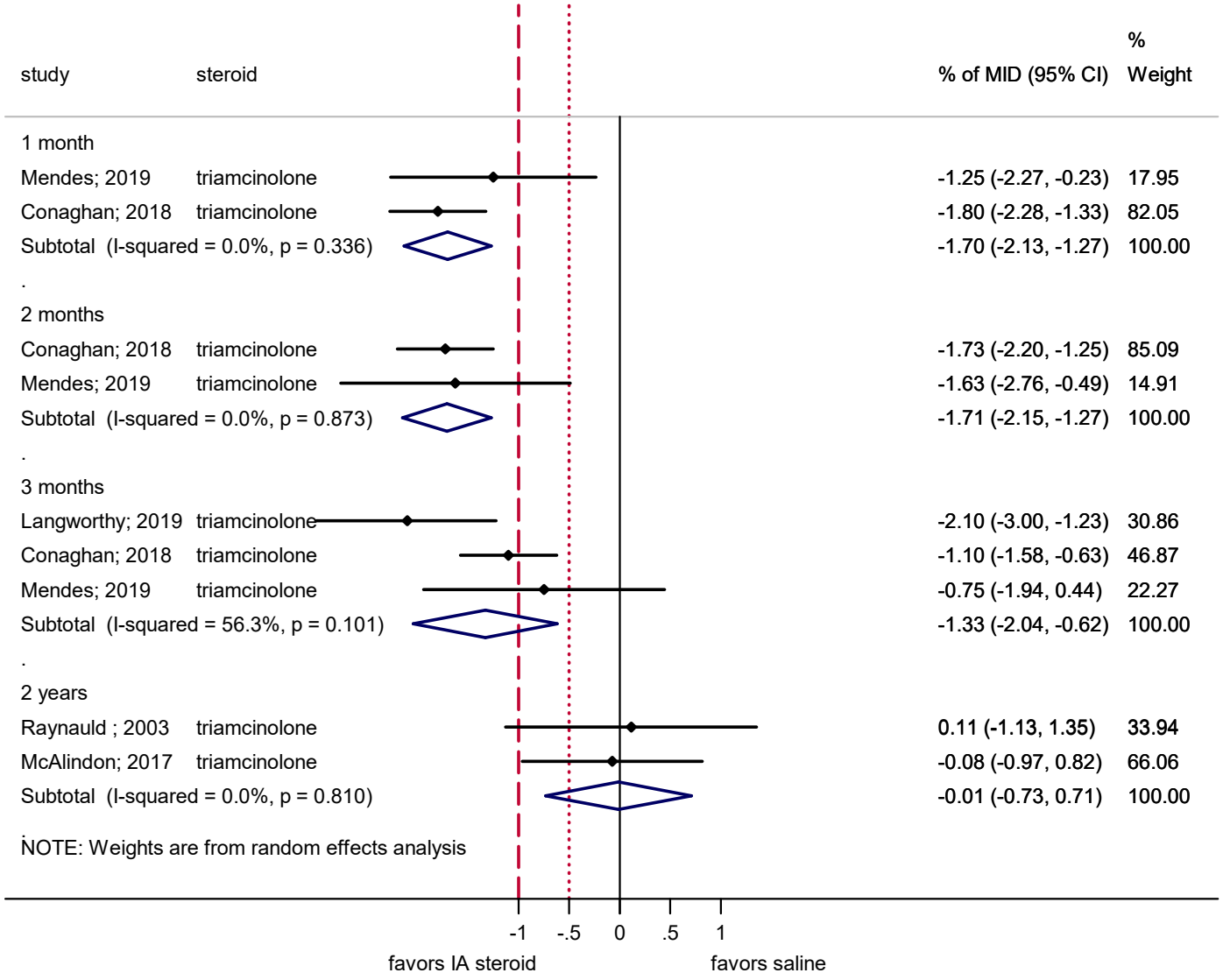
Meta-Analysis Figure 68: Intraarticular Corticosteroids vs Saline–Pain by Follow Up



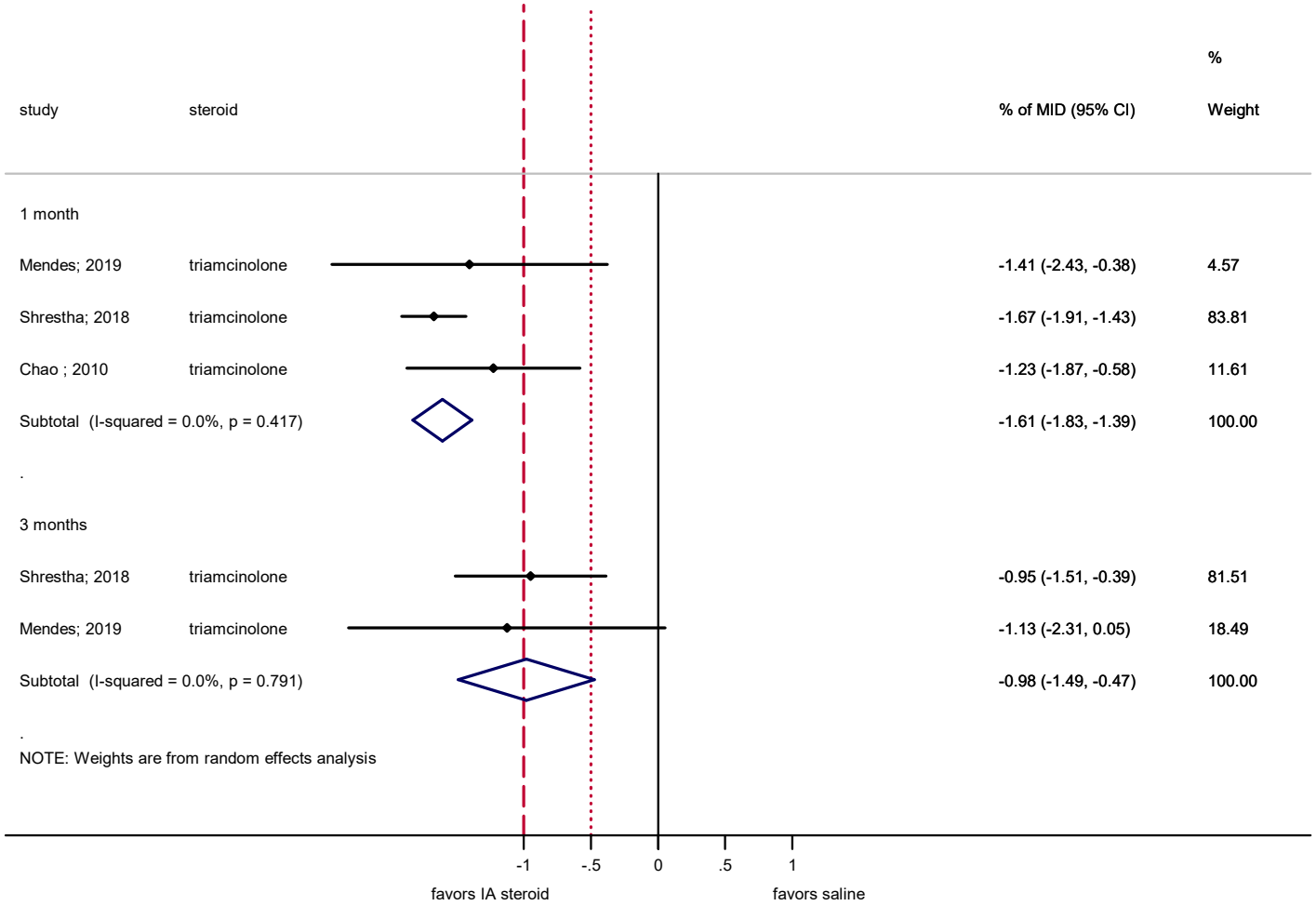
Meta-Analysis Figure 69: Intraarticular Corticosteroids vs Saline–Function by Follow Up



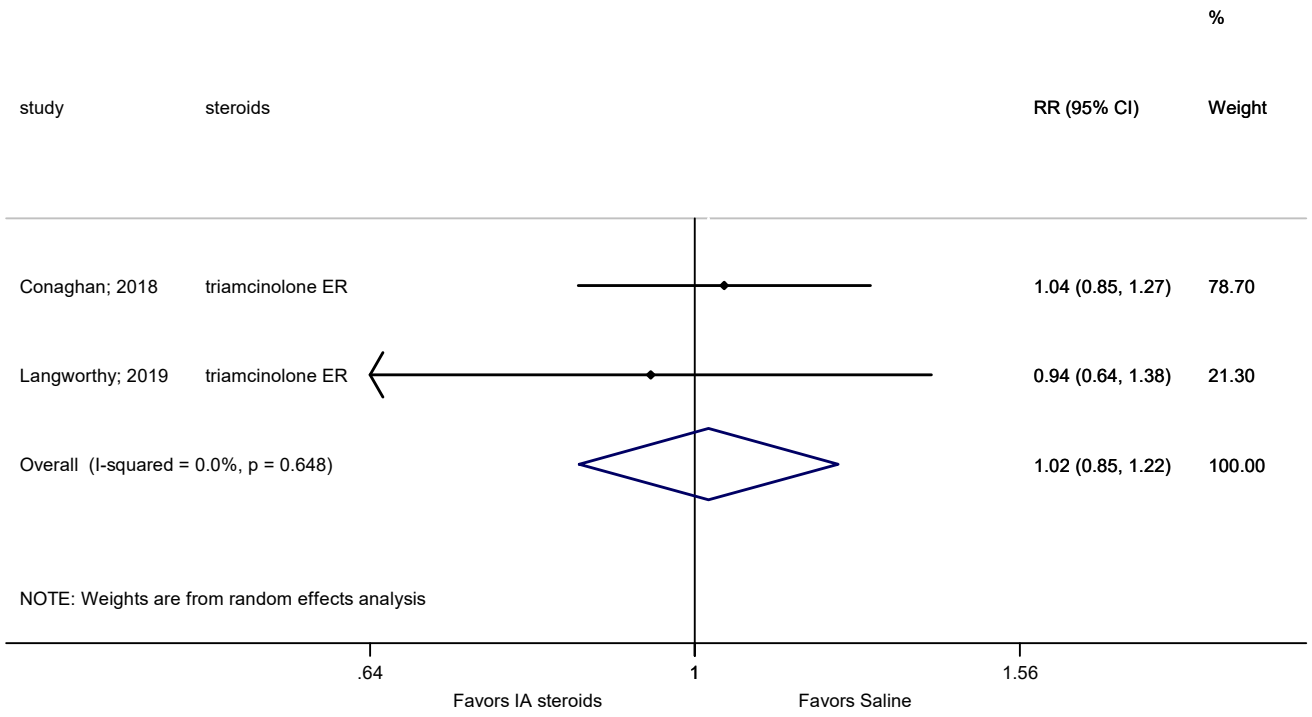
Meta-Analysis Figure 70: Intraarticular Corticosteroids vs Saline–Stiffness by Follow Up Time



Meta-Analysis Figure 71: Intraarticular Corticosteroids vs Saline–WOMAC Total by Follow Up Time



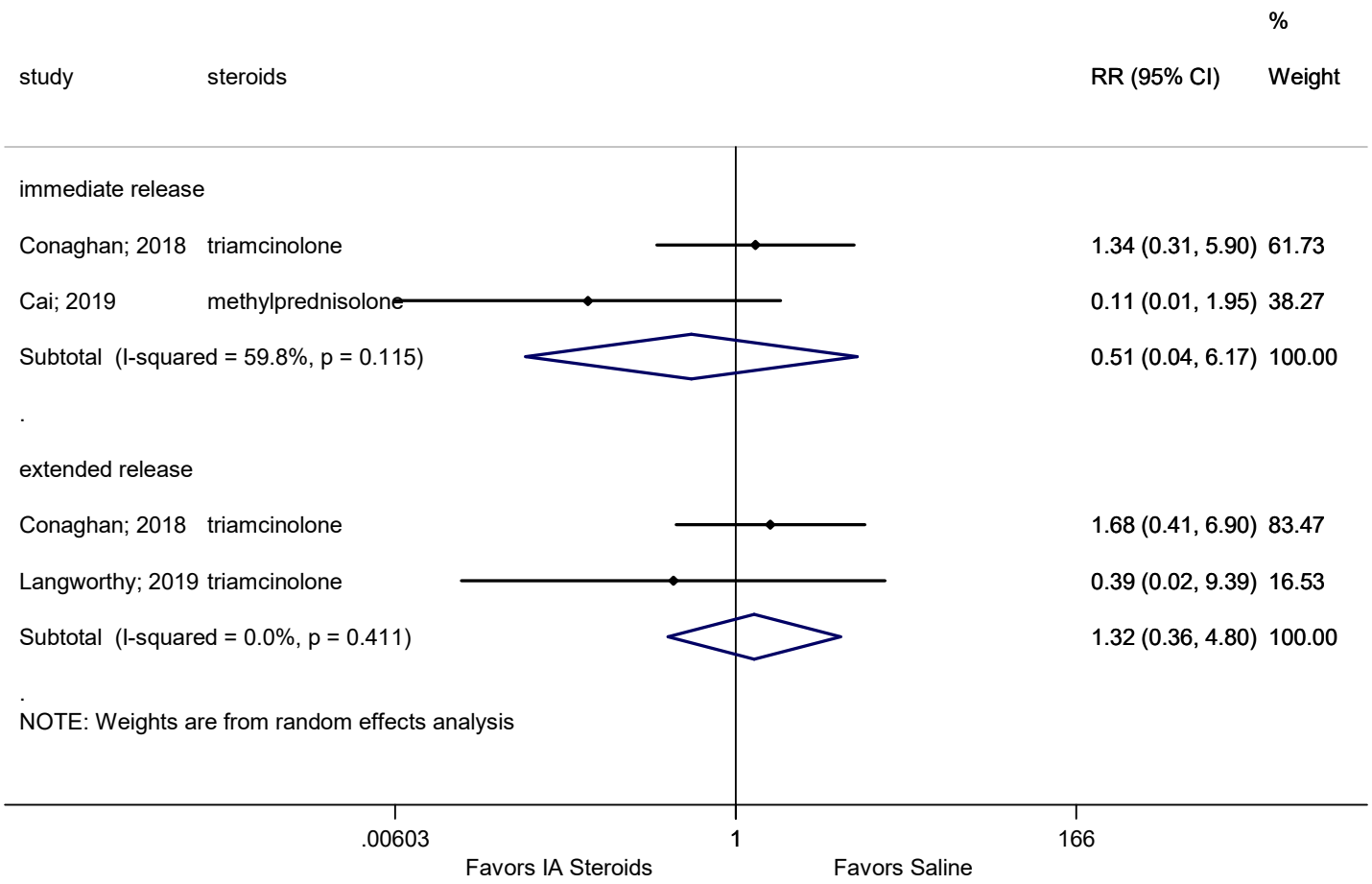
Meta-Analysis Figure 72: Intraarticular Corticosteroids vs Saline–Overall Adverse Events



NNTH=102

number of excess events per 1000=10(-76,113)

Meta-Analysis Figure 73: Intraarticular Corticosteroids vs Saline–Serious Adverse Events



Evidence Table 4841: Intraarticular Corticosteroid vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Evcik; 2003/Low	9: NSAIDs (oral/IM)-IATenoxicam	9: Placebo/Control-Placebo	Pain:VAS Ascending stairs	26 weeks	39/37	3.4(1.5)/5.6(0.7)	Mean Diff	-2.2(-2.73,-1.67)	Group 1	possibly clinically significant
Evcik; 2003/Low	9: NSAIDs (oral/IM)-IATenoxicam	9: Placebo/Control-Placebo	Pain:VAS At rest	26 weeks	39/37	3.5(1.1)/5.3(2.4)	Mean Diff	-1.8(-2.67,-0.93)	Group 1	possibly clinically significant
Evcik; 2003/Low	9: NSAIDs (oral/IM)-IATenoxicam	9: Placebo/Control-Placebo	Pain:VAS Descending stairs	26 weeks	39/37	3.3(0.7)/6.1(2.2)	Mean Diff	-2.8(-3.56,-2.04)	Group 1	clinically significant
Yilmaz; 2019/High	10: Other IA Tx-IA Tenoxicam + Corticosteroid Injection	10: IA corticosteroids-Corticosteroid Injection	Pain:VAS Pain	1 mos	30/30	0.33(0.47)/1.37(1.21)	Mean Diff	-1.04(-1.52,-0.56)	Group 1	some may benefit
Yilmaz; 2019/High	10: Other IA Tx-IA Tenoxicam + Corticosteroid Injection	10: IA corticosteroids-Corticosteroid Injection	Pain:VAS Pain	6 mos	30/30	1.97(1.12)/7.27(0.86)	Mean Diff	-5.3(-5.82,-4.78)	Group 1	clinically significant
Yilmaz; 2019/High	10: Other IA Tx-IA Tenoxicam + Corticosteroid Injection	10: IA corticosteroids-Corticosteroid Injection	Pain:VAS Pain	3 mos	30/30	0.93(0.98)/6.87(1.35)	Mean Diff	-5.94(-6.55,-5.33)	Group 1	clinically significant
Evcik; 2003/Low	9: NSAIDs (oral/IM)-IATenoxicam	9: Placebo/Control-Placebo	Pain:VAS Walking	26 weeks	39/37	4.1(1.2)/6.3(1.9)	Mean Diff	-2.2(-2.93,-1.47)	Group 1	possibly clinically significant
Evcik; 2003/Low	9: NSAIDs (oral/IM)-IATenoxicam	9: Placebo/Control-Placebo	Composite:Lequesne Index	26 weeks	39/37	5.6(2.7)/10.3(2.7)	Mean Diff	-4.7(-5.93,-3.47)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yilmaz; 2019/High	10: Other IA Tx-IA Tenoxicam + Corticosteroid Injection	10: IA corticosteroids-Corticosteroid Injection	Composite:WOMAC Total	1 mos	30/30	6.67(0.95)/8.83(2.7)	Mean Diff	-2.16(-3.22,-1.1)	Group 1	clinically insignificant
Yilmaz; 2019/High	10: Other IA Tx-IA Tenoxicam + Corticosteroid Injection	10: IA corticosteroids-Corticosteroid Injection	Composite:WOMAC Total	6 mos	30/30	10.43(3.7)/32.83(4.87)	Mean Diff	-22.4(-24.64,-20.16)	Group 1	clinically significant
Yilmaz; 2019/High	10: Other IA Tx-IA Tenoxicam + Corticosteroid Injection	10: IA corticosteroids-Corticosteroid Injection	Composite:WOMAC Total	3 mos	30/30	7.87(1.96)/30.8(7.7)	Mean Diff	-22.93(-25.88,-19.98)	Group 1	clinically significant
Evcik; 2003/Low	9: NSAIDs (oral/IM)-IATenoxicam	9: Placebo/Control-Placebo	Other:Health assessment questionaire	26 weeks	39/37	14.7(4.8)/23.5(3.9)	Mean Diff	-8.8(-10.8,-6.8)	Group 1	na

PICO 10: Locally Invasive Treatment

Intraarticular Steroid High Dose vs. Low Dose

Table 42: Intraarticular Steroid High Dose vs Low Dose

Quality: H=High; M=Moderate; L=Low	H	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Bodick; 2015	Conaghan; 2018
Other		
OMERACT-OARSI Responder	●	
Pain		
WOMAC Moving Pain (Likert Version)	●	
Adverse events		
Any Adverse Event	●	
Headache	●	
Any Mild Adverse Event	●	
Any Moderate Adverse Event	●	
Any Severe Adverse Event	●	
Arthralgia	●	
Upper Respiratory Tract Infection	●	
Joint Stiffness	●	
Nasopharyngitis	●	
>2% of patients Arthralgia		●
>2% of patients Back pain		●
>2% of patients Bronchitis		●
>2% of patients Headache		●
>2% of patients Joint swelling		●
>2% of patients Ligament sprain		●
>2% of patients Nasopharyngitis		●
>2% of patients Neck pain		●
>2% of patients Sinusitis		●
>2% of patients Toothache		●
Discontinuation due to drug		●
Discontinuation due to seroius AE		●
Index knee-related Aes occuring in >2% of patients in any treatment group Arthralgia		●
Index knee-related Aes occuring in >2% of patients in any treatment group joint swelling		●
Index knee-related Aes occuring in >2% of patients in any treatment group ligament sprain		●
Patients with >1 AE		●
Patients with >1 AE leading to study discontinuation		●
Patients with >1 index knee-related AE		●
Patients with >1 index knee-related AE leading to study discontinuation		●
Patients with >1 index knee-related AE leading to study discontinuation Drug-related		●
Patients with >1 index knee-related AE leading to study discontinuation Due to serious AE		●
Patients with >1 index knee-related serious AE		●
Patients with >1 serious AE		●
calculable MID outcomes		
WOMAC Function	●	
WOMAC Stiffness	●	
WOMAC Pain	●	
VAS Pain	●	
VAS Pain(diff in deltas)	●	
QOL		
Patient Global Impression of Change	↑	

Evidence Table 4942: Intraarticular Steriod High Dose vs Low Dose

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	QoL:Patient Global Impression of Change	8 wks	59/58	1.8(1.23)/1.9(1.22)	Mean Diff	-0.1(-0.55,0.35)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	QoL:Patient Global Impression of Change	8 wks	60/58	2.4(1.24)/1.9(1.22)	Mean Diff	0.5(0.05,0.95)	Group 1	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	QoL:Patient Global Impression of Change	8 wks	60/59	2.4(1.24)/1.8(1.23)	Mean Diff	0.6(0.15,1.05)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	other:OMERACT-OARSI Responder	8 wks	60/59	78.33%/89.83%	RR	0.87(0.74,1.02)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	other:OMERACT-OARSI Responder	8 wks	60/58	78.33%/89.66%	RR	0.87(0.75,1.02)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	other:OMERACT-OARSI Responder	8 wks	59/58	89.83%/89.66%	RR	1(0.89, 1.13)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Pain:VAS Pain	8 wks	60/59	-3.9(2.17)/-4.3(2.15)	Mean Diff	0.4(-0.38,1.18)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Pain:VAS Pain	10 wks	60/59	-3.6(2.17)/-4.1(2.23)	Mean Diff	0.5(-0.3,1.3)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Pain:VAS Pain	12 wks	60/59	-3.2(2.32)/-3.7(2.3)	Mean Diff	0.5(-0.34,1.34)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:VAS Pain(diff in deltas)	12 wks	59/58	-3.7(2.3)/-3.6(2.28)	Mean Diff	-0.1(-0.94,0.74)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:VAS Pain(diff in deltas)	10 wks	59/58	-4.1(2.23)/-3.8(2.21)	Mean Diff	-0.3(-1.11,0.51)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:VAS Pain(diff in deltas)	8 wks	59/58	-4.3(2.15)/-3.9(2.13)	Mean Diff	-0.4(-1.18,0.38)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:VAS Pain(diff in deltas)	8 wks	60/58	-3.9(2.17)/-3.9(2.13)	Mean Diff	0(-0.78,0.78)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:VAS Pain(diff in deltas)	10 wks	60/58	-3.6(2.17)/-3.8(2.21)	Mean Diff	0.2(-0.6,1)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:VAS Pain(diff in deltas)	12 wks	60/58	-3.2(2.32)/-3.6(2.28)	Mean Diff	0.4(-0.44,1.24)	Not Sig.	clinically insignificant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:WOMAC Moving Pain (Likert Version)	8 wks	59/58	-1.2(0.92)/-1.2(0.91)	Mean Diff	0(-0.34,0.34)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Pain:WOMAC Moving Pain (Likert Version)	8 wks	60/59	-1.1(0.85)/-1.2(0.92)	Mean Diff	0.1(-0.22,0.42)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:WOMAC Moving Pain (Likert Version)	8 wks	60/58	-1.1(0.85)/-1.2(0.91)	Mean Diff	0.1(-0.22,0.42)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:WOMAC Pain (Likert Version)	8 wks	59/58	-1.33(0.75)/-1.23(0.75)	Mean Diff	-0.1(-0.37,0.17)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Pain:WOMAC Pain (Likert Version)	8 wks	60/58	-1.16(0.75)/-1.23(0.75)	Mean Diff	0.07(-0.2,0.34)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Pain:WOMAC Pain (Likert Version)	8 wks	60/59	-1.16(0.75)/-1.33(0.75)	Mean Diff	0.17(-0.1,0.44)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Function:WOMAC Function (Likert Version)	8 wks	59/58	-1.32(0.74)/-1.22(0.73)	Mean Diff	-0.1(-0.37,0.17)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Function:WOMAC Function (Likert Version)	8 wks	60/58	-1.13(0.74)/-1.22(0.73)	Mean Diff	0.09(-0.18,0.36)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Function:WOMAC Function (Likert Version)	8 wks	60/59	-1.13(0.74)/-1.32(0.74)	Mean Diff	0.19(-0.08,0.46)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Function:WOMAC Stiffness (Likert Version)	8 wks	59/58	-1.49(0.86)/-1.37(0.86)	Mean Diff	-0.12(-0.43,0.19)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Function:WOMAC Stiffness (Likert Version)	8 wks	60/58	-1.24(0.86)/-1.37(0.86)	Mean Diff	0.13(-0.18,0.44)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Function:WOMAC Stiffness (Likert Version)	8 wks	60/59	-1.24(0.86)/-1.49(0.86)	Mean Diff	0.25(-0.06,0.56)	Not Sig.	inconclusive
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Arthralgia	24 wks	104/102	7.69%/9.8%	RR	0.78(0.32,1.91)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Back pain	24 wks	104/102	1.92%/2.94%	RR	0.65(0.11,3.83)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Bronchitis	24 wks	104/102	1.92%/2.94%	RR	0.65(0.11,3.83)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Headache	24 wks	104/102	3.85%/2.94%	RR	1.31(0.3,5.7)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Joint swelling	24 wks	104/102	4.81%/3.92%	RR	1.23(0.34,4.44)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Ligament sprain	24 wks	104/102	3.85%/3.92%	RR	0.98(0.25,3.82)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Nasopharyngitis	24 wks	104/102	1.92%/1.96%	RR	0.98(0.14,6.83)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Neck pain	24 wks	104/102	2.88%/0%	RD	2.885(-2.371, 6.981)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Sinusitis	24 wks	104/102	1.92%/2.94%	RR	0.65(0.11,3.83)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:>2% of patients Toothache	24 wks	104/102	2.88%/0%	RD	2.885(-2.371, 6.981)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Any Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Mild Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Any Mild Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Mild Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Any Moderate Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Moderate Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Moderate Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Severe Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Any Severe Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Any Severe Adverse Event	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Arthralgia	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Arthralgia	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Arthralgia	12 wks		none	pvalue	NS	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Discontinuation due to drug	24 wks	104/102	0%/0.98%	RD	-0.98(-4.633, 3.385)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Discontinuation due to seroius AE	24 wks	104/102	0.96%/0%	RD	0.962(-3.324, 4.676)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Headache	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Headache	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Headache	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Index knee-related Aes occuring in >2% of patients in any treatment group Arthralgia	24 wks	104/102	6.73%/7.84%	RR	0.86(0.32,2.28)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Index knee-related Aes occuring in >2% of patients in any treatment group joint swelling	24 wks	104/102	3.85%/3.92%	RR	0.98(0.25,3.82)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Index knee-related Aes occuring in >2% of patients in any treatment group ligament sprain	24 wks	104/102	0.96%/2.94%	RR	0.33(0.03,3.09)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Joint Stiffness	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Joint Stiffness	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Joint Stiffness	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Nasopharyngitis	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Nasopharyngitis	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Nasopharyngitis	12 wks		none	pvalue	NS	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 AE	24 wks	104/102	44.23%/42.16%	RR	1.05(0.77,1.44)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 AE leading to study discontinuation	24 wks	104/102	3.85%/3.92%	RR	0.98(0.25,3.82)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 index knee-related AE	24 wks	104/102	13.46%/14.71%	RR	0.92(0.47,1.8)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 index knee-related AE leading to study discontinuation	24 wks	104/102	2.88%/3.92%	RR	0.74(0.17,3.21)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 index knee-related AE leading to study discontinuation Drug-related	24 wks	104/102	0%/0.98%	RD	-0.98(-4.633, 3.385)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 index knee-related AE leading to study discontinuation Due to serious AE	24 wks	104/102	0%/0%	RD	0(-3.562, 3.629)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 index knee-related serious AE	24 wks	104/102	0.96%/0.98%	RR	0.98(0.06,15.47)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone acetonide(32 mg)	10: IA corticosteroids-Triamcinolone acetonide(16 mg)	Adverse events:Patients with >1 serious AE	24 wks	104/102	2.88%/0.98%	RR	2.94(0.31,27.82)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Upper Respiratory Tract Infection	12 wks		none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	Adverse events:Upper Respiratory Tract Infection	12 wks		none	pvalue	NS	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	Adverse events:Upper Respiratory Tract Infection	12 wks		none	pvalue	NS	Not Sig.	na

PICO 10: Locally Invasive Treatment

Intraarticular Steroid Extended vs. Immediate Release

Table 43: Intraarticular Steroid Extended vs Immediate Release

Quality: H=High; M=Moderate; L=Low	H	M	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Bodick; 2015	Conaghan; 2018	Langworthy; 2019
Function			
WOMAC Function			↑
WOMAC Stiffness			↑
Other			
OMERACT-OARSI Responder	↑		
Pain			
WOMAC Pain			↑
VAS Pain(delta)			↑
VAS Pain(diff in delta from baseline)		●	
WOMAC Moving Pain (Likert Version)	↑		
VAS Pain(diff in deltas)	↑		
Adverse events			
Back Pain		●	
Any Adverse Event	●	●	●
Headache	●	●	●
Any Mild Adverse Event	●		
Any Moderate Adverse Event	●		
Any Serious Adverse Event		●	●
Any Severe Adverse Event	●		
Arthralgia	●		●
Upper Respiratory Tract Infection	↓		●
Joint Effusion			●
Joint Stiffness	●		
Nasopharyngitis	●		●
Gastroesophageal reflux			●
Arthalgia		●	
Sciatica			●
Any AE Leading to Discontinuation		●	
Discontinued Due to AE			●
calculable MID outcomes			
WOMAC Function	↑	↑	↑
WOMAC Stiffness	↑	↑	↑
WOMAC Pain	↑	↑	↑
QOL			
KOOS QoL(delta)			↑
KOOS QoL(diff in delta from baseline)		↑	
Patient Global Impression of Change	↓		

Evidence Table 5043: Intraarticular Steroid Extended vs Immediate Release

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	QoL:KOOS QoL(delta)	24 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	QoL:KOOS QoL(delta)	8 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	QoL:KOOS QoL(delta)	4 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	QoL:KOOS QoL(delta)	12 wks	110	none	Mean Difference	8.18(0.56,15.8)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	QoL:KOOS QoL(diff in delta from baseline)	8 wks	484	none	LSM Difference	5.28(0.65,9.91)	Group 1	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	QoL:KOOS QoL(diff in delta from baseline)	12 wks	484	none	LSM Difference	5.42(0.78,10.06)	Group 1	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	QoL:KOOS QoL(diff in delta from baseline)	4 wks	484	none	LSM Difference	7.9(3.29,12.52)	Group 1	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	QoL:Patient Global Impression of Change	8 wks	60/51	2.4(1.24)/2.5(1.21)	Mean Diff	-0.1(-0.56,0.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	QoL:Patient Global Impression of Change	8 wks	58/51	1.9(1.22)/2.5(1.21)	Mean Diff	-0.6(-1.06,-0.14)	Group 2	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	QoL:Patient Global Impression of Change	8 wks	59/51	1.8(1.23)/2.5(1.21)	Mean Diff	-0.7(-1.16,-0.24)	Group 2	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	other:OMERACT-OARSI Responder	8 wks	60/51	78.33%/62.75%	RR	1.25(0.97,1.6)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	other:OMERACT-OARSI Responder	8 wks	59/51	89.83%/62.75%	RR	1.43(1.14,1.8)	Group 1	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	other:OMERACT-OARSI Responder	8 wks	58/51	89.66%/62.75%	RR	1.43(1.14,1.8)	Group 1	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	22 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	23 wks	110	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	24 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	9 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	8 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	19 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	13 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	14 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	4 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	16 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	20 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	17 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	18 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	21 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	5 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	6 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	7 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	11 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	10 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	15 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:VAS Pain(delta)	12 wks	110	none	Mean Difference	-1.14(-2,-0.28)	Group 1	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Pain:VAS Pain(diff in delta from baseline)	12 wks	484	none	LSM Difference	-0.26(-0.74,0.23)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	12 wks	109	none	Mean Difference	-0.3(-1,0.5)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	10 wks	111	none	Mean Difference	-0.4(-1.1,0.3)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	12 wks	110	none	Mean Difference	-0.4(-1.1,0.4)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	8 wks	109	none	Mean Difference	-0.5(-1.2,0.1)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	10 wks	109	none	Mean Difference	-0.5(-1.2,0.2)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	8 wks	111	none	Mean Difference	-0.5(-1.2,0.2)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	10 wks	110	none	Mean Difference	-0.9(-1.5,-0.2)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	8 wks	110	none	Mean Difference	-0.9(-1.6,-0.3)	Group 1	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:VAS Pain(diff in deltas)	12 wks	111	none	Mean Difference	0.1(-0.7,0.8)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:WOMAC Moving Pain (Likert Version)	8 wks	60/51	-1.1(0.85)/-0.8(0.93)	Mean Diff	-0.3(-0.64,0.04)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:WOMAC Moving Pain (Likert Version)	8 wks	58/51	-1.2(0.91)/-0.8(0.93)	Mean Diff	-0.4(-0.75,-0.05)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:WOMAC Moving Pain (Likert Version)	8 wks	59/51	-1.2(0.92)/-0.8(0.93)	Mean Diff	-0.4(-0.75,-0.05)	Group 1	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:WOMAC Pain (Likert Version)	8 wks	60/51	-1.16(0.75)/-0.96(0.77)	Mean Diff	-0.2(-0.49,0.09)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:WOMAC Pain (Likert Version)	8 wks	58/51	-1.23(0.75)/-0.96(0.77)	Mean Diff	-0.27(-0.56,0.02)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Pain:WOMAC Pain (Likert Version)	8 wks	59/51	-1.33(0.75)/-0.96(0.77)	Mean Diff	-0.37(-0.66,-0.08)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Pain:WOMAC Pain (Likert Version)(diff in delta from baseline)	12 wks	484	none	LSM Difference	-0.17(-0.34,-.00)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Pain:WOMAC Pain (Likert Version)(diff in delta from baseline)	8 wks	484	none	LSM Difference	-0.21(-0.38,-0.04)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Pain:WOMAC Pain (Likert Version)(diff in delta from baseline)	4 wks	484	none	LSM Difference	-0.23(-0.39,-0.07)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs)[IA](40mg (5mL))	Pain:WOMAC Pain(delta)	16 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs)[IA](40mg (5mL))	Pain:WOMAC Pain(delta)	20 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs)[IA](40mg (5mL))	Pain:WOMAC Pain(delta)	8 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs)[IA](40mg (5mL))	Pain:WOMAC Pain(delta)	4 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:WOMAC Pain(delta)	24 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Pain:WOMAC Pain(delta)	12 wks	110	none	Mean Difference	-0.39(-0.7,-0.09)	Group 1	possibly clinically significant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Function:WOMAC Function (Likert Version)	8 wks	60/51	-1.13(0.74)/-0.94(0.76)	Mean Diff	-0.19(-0.47,0.09)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Function:WOMAC Function (Likert Version)	8 wks	58/51	-1.22(0.73)/-0.94(0.76)	Mean Diff	-0.28(-0.56,0)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Function:WOMAC Function (Likert Version)	8 wks	59/51	-1.32(0.74)/-0.94(0.76)	Mean Diff	-0.38(-0.66,-0.1)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Function:WOMAC Function (Likert Version)(diff in delta from baseline)	12 wks	484	none	LSM Difference	-0.22(-0.38,-0.05)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Function:WOMAC Function (Likert Version)(diff in delta from baseline)	4 wks	484	none	LSM Difference	-0.24(-0.4,-0.08)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Function:WOMAC Function (Likert Version)(diff in delta from baseline)	8 wks	484	none	LSM Difference	-0.29(-0.45,-0.12)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Function(delta)	16 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Function(delta)	20 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Function(delta)	24 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Function(delta)	8 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Function(delta)	4 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Function(delta)	12 wks	110	none	Mean Difference	-0.35(-0.65,-0.05)	Group 1	possibly clinically significant
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Function:WOMAC Stiffness (Likert Version)	8 wks	60/51	-1.24(0.86)/-0.99(0.89)	Mean Diff	-0.25(-0.58,0.08)	Not Sig.	inconclusive
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Function:WOMAC Stiffness (Likert Version)	8 wks	58/51	-1.37(0.86)/-0.99(0.89)	Mean Diff	-0.38(-0.71,-0.05)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Function:WOMAC Stiffness (Likert Version)	8 wks	59/51	-1.49(0.86)/-0.99(0.89)	Mean Diff	-0.5(-0.83,-0.17)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Function:WOMAC Stiffness (Likert Version)(diff in delta from baseline)	12 wks	484	none	LSM Difference	-0.23(-0.42,-0.04)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Function:WOMAC Stiffness (Likert Version)(diff in delta from baseline)	4 wks	484	none	LSM Difference	-0.23(-0.42,-0.04)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Function:WOMAC Stiffness (Likert Version)(diff in delta from baseline)	8 wks	484	none	LSM Difference	-0.32(-0.51,-0.13)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Stiffness(delta)	24 wks	110	none	pvalue	NS	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Stiffness(delta)	4 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Stiffness(delta)	8 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Stiffness(delta)	20 wks	110	none	pvalue	Sig ($p < 0.05$)	TA-ER	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Stiffness(delta)	16 wks	110	none	pvalue	Sig (p < 0.05)	TA-ER	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Function:WOMAC Stiffness(delta)	12 wks	110	none	Mean Difference	-0.36(-0.71,-0.01)	Group 1	possibly clinically significant
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Adverse events:Any AE Leading to Discontinuation	12 wks	161/161	0%/0.62%	RD	-0.621(-3.007, 2.192)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Adverse events:Any Adverse Event	12 wks	161/161	55.28%/56.52%	RR	0.98(0.81,1.19)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Adverse Event	12 wks	58/51	46.55%/54.9%	RR	0.85(0.58,1.23)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Adverse Event	12 wks	59/51	55.93%/54.9%	RR	1.02(0.73,1.43)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Adverse Event	12 wks	60/51	56.67%/54.9%	RR	1.03(0.74,1.44)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Any Adverse Event	24 wks	51/59	47.06%/50.85%	RR	0.93(0.63,1.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Mild Adverse Event	12 wks	58/51	29.31%/27.45%	RR	1.07(0.59,1.94)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Mild Adverse Event	12 wks	60/51	31.67%/27.45%	RR	1.15(0.65,2.06)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Mild Adverse Event	12 wks	59/51	33.9%/27.45%	RR	1.23(0.7,2.19)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Moderate Adverse Event	12 wks	58/51	15.52%/23.53%	RR	0.66(0.3,1.44)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Moderate Adverse Event	12 wks	59/51	22.03%/23.53%	RR	0.94(0.47,1.87)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Moderate Adverse Event	12 wks	60/51	25%/23.53%	RR	1.06(0.55,2.06)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Adverse events:Any Serious Adverse Event	12 wks	161/161	3.11%/2.48%	RR	1.25(0.34,4.57)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Any Serious Adverse Event	24 wks	51/59	0%/0%	RD	0(-7.005, 6.113)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Severe Adverse Event	12 wks	60/51	0%/3.92%	RD	-3.922(-10.575,5.373)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Severe Adverse Event	12 wks	59/51	0%/3.92%	RD	-3.922(-10.662,5.373)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Any Severe Adverse Event	12 wks	58/51	1.72%/3.92%	RR	0.44(0.04,4.71)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Adverse events:Arthalgia	12 wks	161/161	14.29%/7.45%	RR	1.92(0.99,3.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Arthralgia	12 wks	60/51	6.67%/3.92%	RR	1.7(0.32,8.9)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Arthralgia	12 wks	58/51	8.62%/3.92%	RR	2.2(0.45,10.85)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Arthralgia	12 wks	59/51	13.56%/3.92%	RR	3.46(0.77,15.55)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Arthralgia	24 wks	51/59	7.84%/8.47%	RR	0.93(0.26,3.26)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Adverse events:Back Pain	12 wks	161/161	5.59%/7.45%	RR	0.75(0.33,1.73)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Discontinued Due to AE	24 wks	51/59	0%/0%	RD	0(-7.005, 6.113)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Gastroesophageal Reflux	24 wks	51/59	0%/0%	RD	0(-7.005, 6.113)	Not Sig.	na
Conaghan; 2018/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA](32mg/5mL; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg/1mL; single dose;)	Adverse events:Headache	12 wks	161/161	8.7%/9.32%	RR	0.93(0.47,1.87)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Headache	12 wks	58/51	1.72%/9.8%	RR	0.18(0.02,1.46)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Headache	12 wks	60/51	3.33%/9.8%	RR	0.34(0.07,1.68)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Headache	12 wks	59/51	8.47%/9.8%	RR	0.86(0.27,2.82)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Headache	24 wks	51/59	9.8%/8.47%	RR	1.16(0.35,3.77)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Joint Effusion	24 wks	51/59	0%/5.08%	RD	-5.085(-12.845,3.747)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Joint Stiffness	12 wks	59/51	0%/5.88%	RD	-5.882(-13.113,4.16)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Joint Stiffness	12 wks	60/51	3.33%/5.88%	RR	0.57(0.1,3.26)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Joint Stiffness	12 wks	58/51	3.45%/5.88%	RR	0.59(0.1,3.37)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Nasopharyngitis	12 wks	60/51	0%/5.88%	RD	-5.882(-13.032,4.16)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Nasopharyngitis	12 wks	59/51	3.39%/5.88%	RR	0.58(0.1,3.31)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Nasopharyngitis	12 wks	58/51	3.45%/5.88%	RR	0.59(0.1,3.37)	Not Sig.	na
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Nasopharyngitis	24 wks	51/59	1.96%/8.47%	RR	0.23(0.03,1.92)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Sciatica	24 wks	51/59	1.96%/5.08%	RR	0.39(0.04,3.59)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Middle Dose(40mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Upper Respiratory Tract Infection	12 wks	59/51	0%/0%	RD	0(-6.113, 7.005)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] Low Dose(10mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Upper Respiratory Tract Infection	12 wks	58/51	1.72%/0%	RD	1.724(-5.693, 8.871)	Not Sig.	na
Bodick; 2015/High	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (FX006) [IA] High Dose(60mg; single dose;)	10: IA corticosteroids-Triamcinolone Acetonide Immediate Release [IA](40mg; single dose;)	Adverse events:Upper Respiratory Tract Infection	12 wks	60/51	11.67%/0%	RD	11.667 (1.155, 20.824)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Langworthy; 2019/Moderate	10: IA corticosteroids-Triamcinolone Acetonide Extended Release (TA-ER)[IA](32mg (5mL))	10: IA corticosteroids-Triamcinolone Acetonide Crystalline Suspension (Tacs) [IA](40mg (5mL))	Adverse events:Upper Respiratory Tract Infection	24 wks	51/59	0%/3.39%	RD	-3.39(-10.812,4.764)	Not Sig.	na

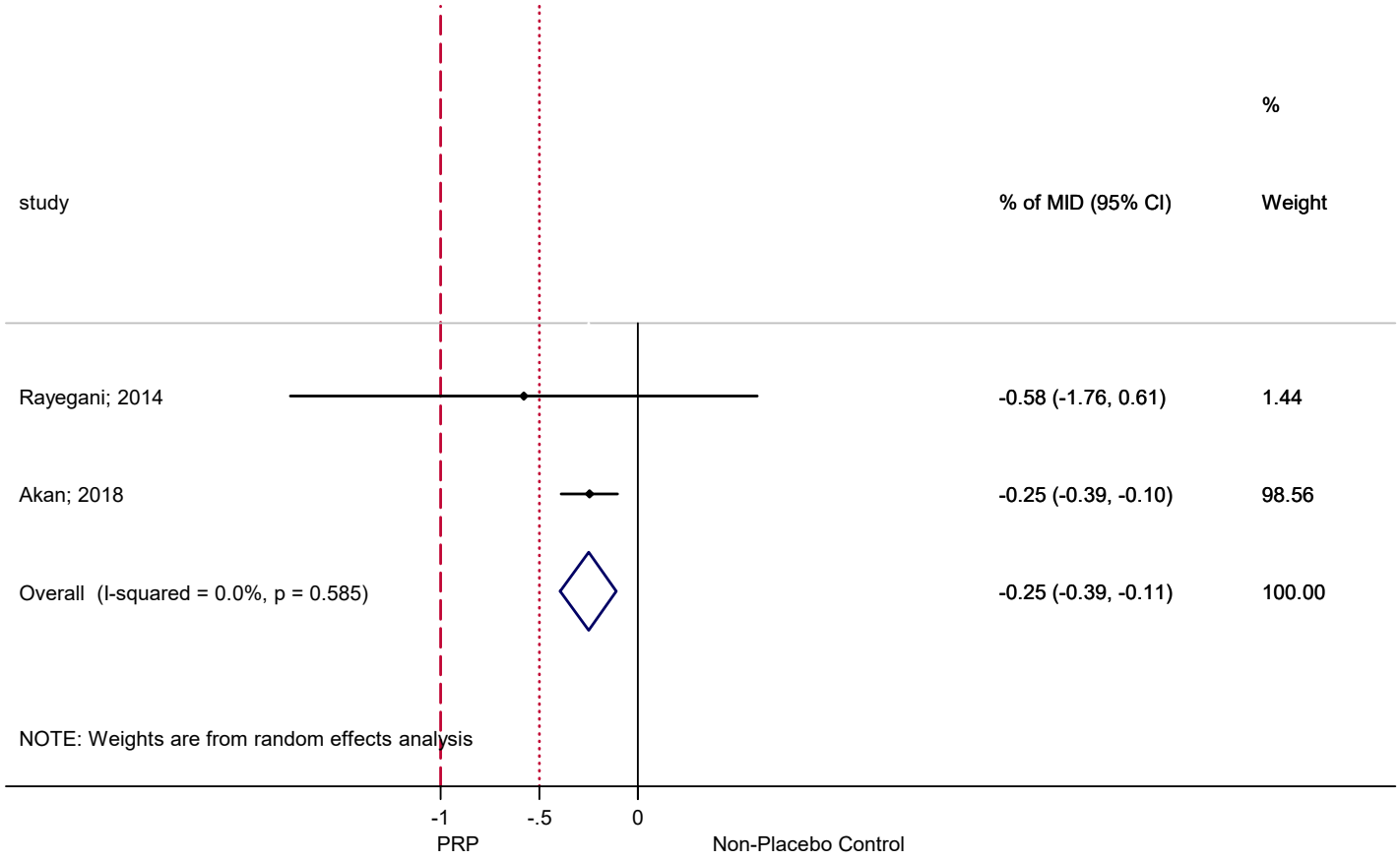
PICO 10: Locally Invasive Treatment

Platelet-Rich Plasma vs Control

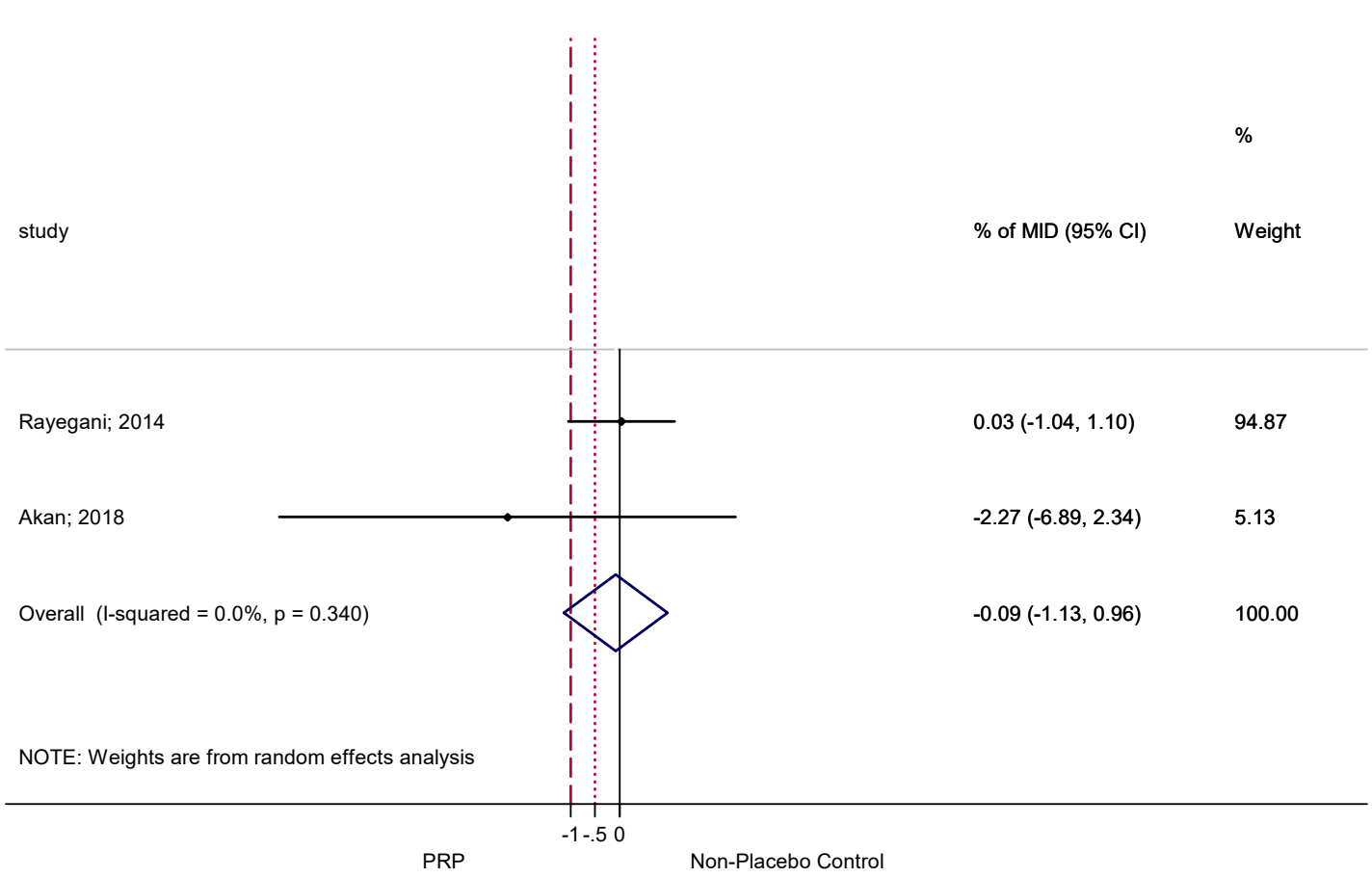
Table 44: Platelet-Rich Plasma vs Control

Quality: H=High; M=Moderate; L=Low	H			M	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Gormeli; 2015	Rayegani; 2014	Joshi Juber; 2017	Huang; 2018	Akan; 2018
Composite					
IKDC composite(Range 0-100)	↑				
SF-36 General Health(scale not provided; numbers don't match with PROMS sheet)					↑
Function					
SF-36 Physical role					↑
SF-36 Social Function					↑
SF-36 Social Function(scale not provided; numbers don't match with PROMS sheet)					↑
Adverse events					
Constipation				●	
Diarrhea				●	
Vomiting				●	
Fatigue				●	
Rash				●	
Edema Peripheral				●	
Hypertension				↓	
Decreased Appetite				●	
Proteinuria				↓	
Epistaxis				●	
Hypertriglyceridemia				●	
Lethargy				●	
Weight decreased				●	
calculable MID outcomes					
WOMAC Function		●			
WOMAC Stiffness		●			
WOMAC Pain		●			
VAS Pain			●		
SF-36 Physical Function					●
SF-36 Pain					●
SF-36 Pain(scale not provided; numbers don't match with PROMS sheet)					●
QOL					
SF-36 Vitality					●
SF-36 General Health					↑
SF-36 Mental Health					●
SF-36 Emotional role					↑
EQ-VAS (Range 0-100)	↑				

Meta-Analysis Figure 74: Platelet-Rich Plasma vs Non-Placebo Control–Pain



Meta-Analysis Figure 75: Platelet-Rich Plasma vs Non-Placebo Control–Function



Evidence Table 5144: Platelet-Rich Plasma vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	QoL:SF-36 General Health	6 mos	30/30	16.98(3.54)/14.87(3.22)	Mean Diff	2.11(0.36,3.86)	Group 1	na
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	QoL:SF-36 Mental health	6 mos	30/30	22(33.48)/17(9.37)	Mean Diff	5(-7.91,17.91)	Not Sig.	na
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	Pain:SF-36 Pain	6 mos	30/30	7.28(2.35)/5.36(1.95)	Mean Diff	1.92(0.8,3.04)	Group 1	clinically insignificant
Akan; 2018/Moderate	10: Blood derived-Platelet-Rich Plasma + Exercise(PRP: 3x/3wks; Exercise: 3x/wk)	10: Placebo/Control-Control (Exercise)(3x/wk)	Pain:SF-36 Pain(scale not provided; numbers don't match with PROMS sheet)	6 mos	30/30	7.28(2.35)/5.36(1.95)	Mean Diff	1.92(0.8,3.04)	Group 1	clinically insignificant
Rayegani; 2014/High	10: Blood derived-Platelet Rich Plasma(4 week interval injections)	10: Placebo/Control-Placebo	Pain:WOMAC Pain	6 mos	31/31	4.2(3.08)/5.16(4.5)	Mean Diff	-0.96(-2.92,1)	Not Sig.	inconclusive
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	Function:SF-36 Physical Function	6 mos	30/30	22(29.46)/14.5(29.46)	Mean Diff	7.5(-7.73,22.73)	Not Sig.	inconclusive
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	Function:SF-36 Physical Role	6 mos	30/30	8(5.36)/4(5.36)	Mean Diff	4(1.23,6.77)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Akan; 2018/Moderate	10: Blood derived-Platelet-Rich Plasma + Exercise(PRP: 3x/3wks; Exercise: 3x/wk)	10: Placebo/Control-Control (Exercise)(3x/wk)	Function:SF-36 Social Function(scale not provided; numbers don't match with PROMS sheet)	6 mos	30/30	7.1(2.04)/5.37(1.92)	Mean Diff	1.73(0.71,2.75)	Group 1	na
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	Function:SF-36 Social function	6 mos	30/30	7.1(2.04)/5.37(1.92)	Mean Diff	1.73(0.71,2.75)	Group 1	na
Rayegani; 2014/High	10: Blood derived-Platelet Rich Plasma(4 week interval injections)	10: Placebo/Control-Placebo	Function:WOMAC Function	6 mos	31/31	14.1(9.12)/13.93(13.4)	Mean Diff	0.17(-5.67,6.01)	Not Sig.	inconclusive
Rayegani; 2014/High	10: Blood derived-Platelet Rich Plasma(4 week interval injections)	10: Placebo/Control-Placebo	Function:WOMAC Stiffness	6 mos	31/31	0.83(1.28)/0.83(1.31)	Mean Diff	0(-0.66,0.66)	Not Sig.	clinically insignificant
Gormeli; 2015/High	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 injections)	10: Placebo/Control-Placebo (Intra-articular)(3 saline injections)	Composite:IKDC composite(Range 0-100)	180 days	39/40	60.8(9.8)/36.5(4.8)	Mean Diff	24.3(20.81,27.79)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Akan; 2018/Moderate	10: Blood derived-Platelet-Rich Plasma + Exercise(PRP: 3x/3wks; Exercise: 3x/wk)	10: Placebo/Control-Control (Exercise)(3x/wk)	Composite:SF-36 General Health(scale not provided; numbers don't match with PROMS sheet)	6 mos	30/30	16.98(3.54)/14.87(3.22)	Mean Diff	2.11(0.36,3.86)	Group 1	na
Gormeli; 2015/High	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 injections)	10: Placebo/Control-Placebo (Intra-articular)(3 saline injections)	QOL:EQ-VAS (Range 0-100)	180 days	39/40	71.4(10.8)/48(5.1)	Mean Diff	23.4(19.57,27.23)	Group 1	na
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	QOL:SF-36 Emotional Role	6 mos	30/30	6(4.02)/3(4.02)	Mean Diff	3(0.92, 5.08)	Group 1	na
Akan; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Control	QOL:SF-36 Vitality	6 mos	30/30	18(26.78)/13.5(22.76)	Mean Diff	4.5(-8.35,17.35)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Constipation	8 wks	310/56	0.97%/0%	RD	0.968(-0.871, 7.419)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Decreased appetite	8 wks	310/56	0.32%/0%	RD	0.323(-1.159, 6.747)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Diarrhea	8 wks	310/56	1.29%/0%	RD	1.29(-0.69,7.758)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Edema peripheral	8 wks	310/56	0.97%/0%	RD	0.968(-0.871, 7.419)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Epistaxis	8 wks	310/56	1.29%/0%	RD	1.29(-0.69,7.758)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Fatigue	8 wks	310/56	0.97%/0%	RD	0.968(-0.871, 7.419)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Hypertension	8 wks	310/56	3.55%/0%	RD	3.548(0.856, 10.154)	Group 2	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Hypertriglyceridemia	8 wks	310/56	0.65%/0%	RD	0.645(-1.031, 7.082)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Lethargy	8 wks	310/56	0.97%/0%	RD	0.968(-0.871, 7.419)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Proteinuria	8 wks	310/56	3.23%/0%	RD	3.226(0.616, 9.81)	Group 2	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Rash	8 wks	310/56	2.26%/0%	RD	2.258(-0.071, 8.781)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Vomiting	8 wks	310/56	0.32%/0%	RD	0.323(-1.159, 6.747)	Not Sig.	na
Huang; 2018/Moderate	10: Blood derived-Platelet Rich Plasma	10: Placebo/Control-Placebo	Adverse events:Weight decreased	8 wks	310/56	0.65%/0%	RD	0.645(-1.031, 7.082)	Not Sig.	na

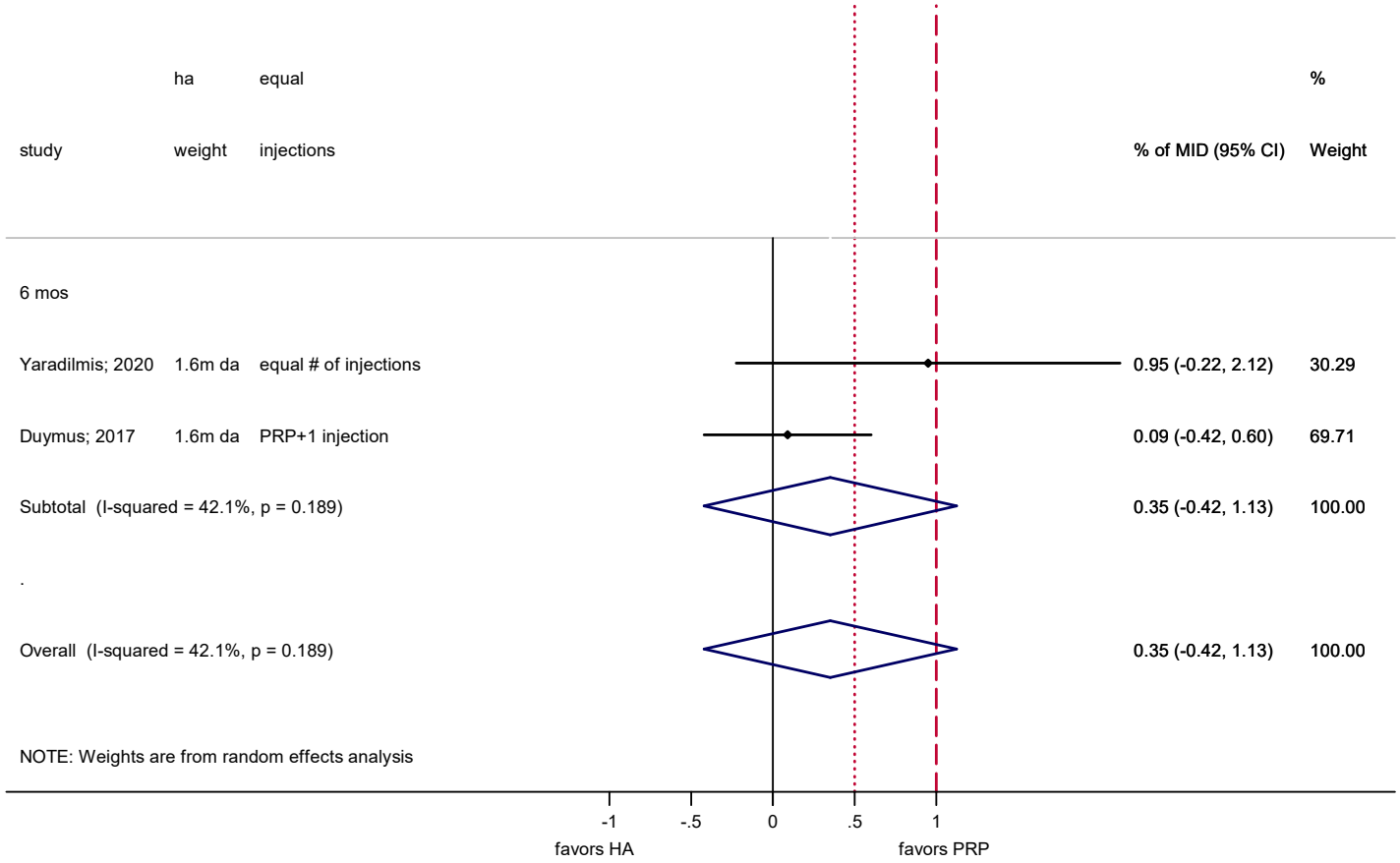
PICO 10: Locally Invasive Treatment

Intraarticular Hyaluronic Acid vs Platelet-Rich Plasma

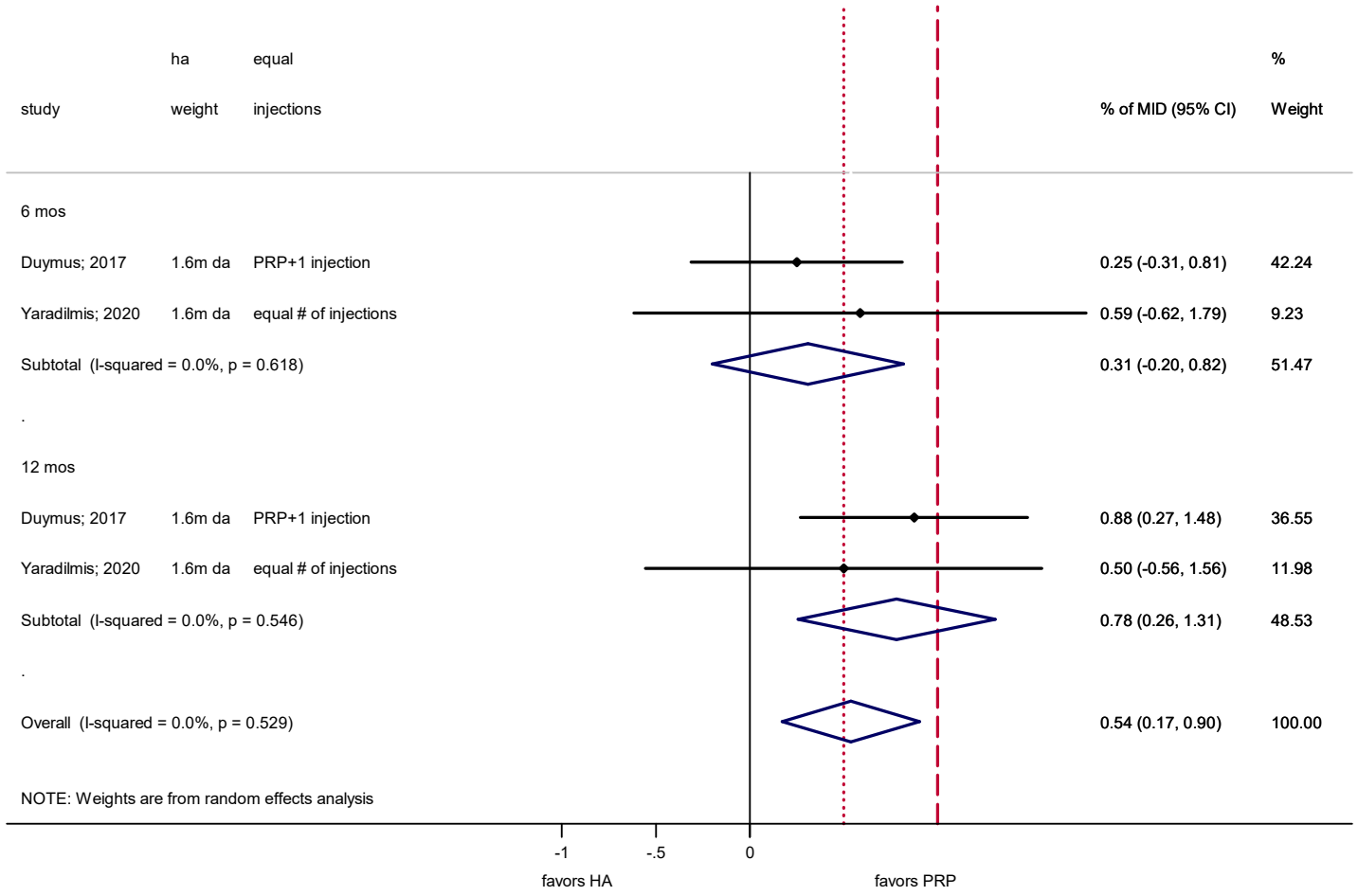
Table 45: Intraarticular Hyaluronic Acid vs Platelet- Rich Plasma

Quality: H=High; M=Moderate; L=Low	H									M								L	
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Gormeli; 2015	Vaquerizo; 2013	Yaradilmis; 2020	Filardo; 2015	Filardo; 2012	Sanchez ; 2012	Buendia-Lopez; 2018	Cole; 2017	Di Martino; 2019	Huang; 2019	Raeissadat; 2017	Spakova; 2012	Ahmad; 2018	Zhang; 2018	Duymus; 2017	Raeissadat; 2015	Lana; 2016	Sanchez ; 2008	Annaniemi; 2018
Composite																			
WOMAC Total																		↓	
Lequesne Index						●													
Lequesne Index Score		↓																	
WOMAC												↓							
International Knee Documentation Committee Score													↓						
IKDC composite(Range 0-100)	↓																		
IKDC composite(0-100)				●	●														
Lysholm score(patient with concommittant infection)														↓					
Function																			
WOMAC Function																		↓	
WOMAC Stiffness																	●		
WOMAC Physical Activity																	●		
KOOS Function(Function in daily living; 0-100)				●															
20% Decrease WOMAC Physical Function							↓												
20% Decrease WOMAC Stiffness							↓												
KOOS Function(0-100; ADL)					●														
KOOS Function(0-100; Sport)					●														
KOOS Function(sport and rec function; 0-100)				●															
Likert Scale function(Tegner Scale; 0-10)				●	●														
Other																			
OARSI Responders						●													
OMERACT-OARSI Responder		↓																	
Acetaminophen use (g/day)						●													
CRP(patient with concommittant infection)(mg/L)														↓					
WBC count(patient with concommittant infection)(*10^9/L)														↓					
patient stisfaction			↓																
Pain																			
WOMAC Pain								●									●		
VAS Pain																	↓		
20% decrease in WOMAC pain						●													
50% decrease in WOMAC pain						↓													
NRS Pain												↓							
KOOS Pain(0-100)				●	●														
20% Decrease VAS Pain							●												
20% Decrease WOMAC Pain							↓												
40% WOMAC pain reduction subscale																		↓	
Adverse events																			
Any Adverse Event		●																	
Pain										●									
DVT										●									
Infections										●									
local adverse events			↑																
Low-Grade Fever										●									
Minor Complications Due to Injection											●								
temporary mild worsening of knee pain after application												↑							
calculable MID outcomes																			
WOMAC Total		↓	↓			●					●	↓			↓	↓			
WOMAC Function		↓	●			●					●					↓			
WOMAC Stiffness		↓	●			●					●				↓				
WOMAC Pain		↓	↓			●					●				↓	●			
WOMAC Physical function															↓				
VAS Pain			↓					●			●		↓		↓				
WOMAC Score Mean (VAS)										↓									
VAS Scores										●									
VAS function(SF-36; 0-100)																↓			
VAS Pain(SF-36; 0-100)																↓			
VAS Pain(patient with concommittant infection)														↓					
QOL																			
EQ-VAS (Range 0-100)	↓																		
EuroQol (VAS)									●										
Time to arthroplasty																			
need for TKA(propensity score matched)																			●
need for any arthroplasty hazard ratio(propensity score matched groups-PRP vs HA)																			●
need for unicompartmental arthroplasty(propensity score matched)																			↓

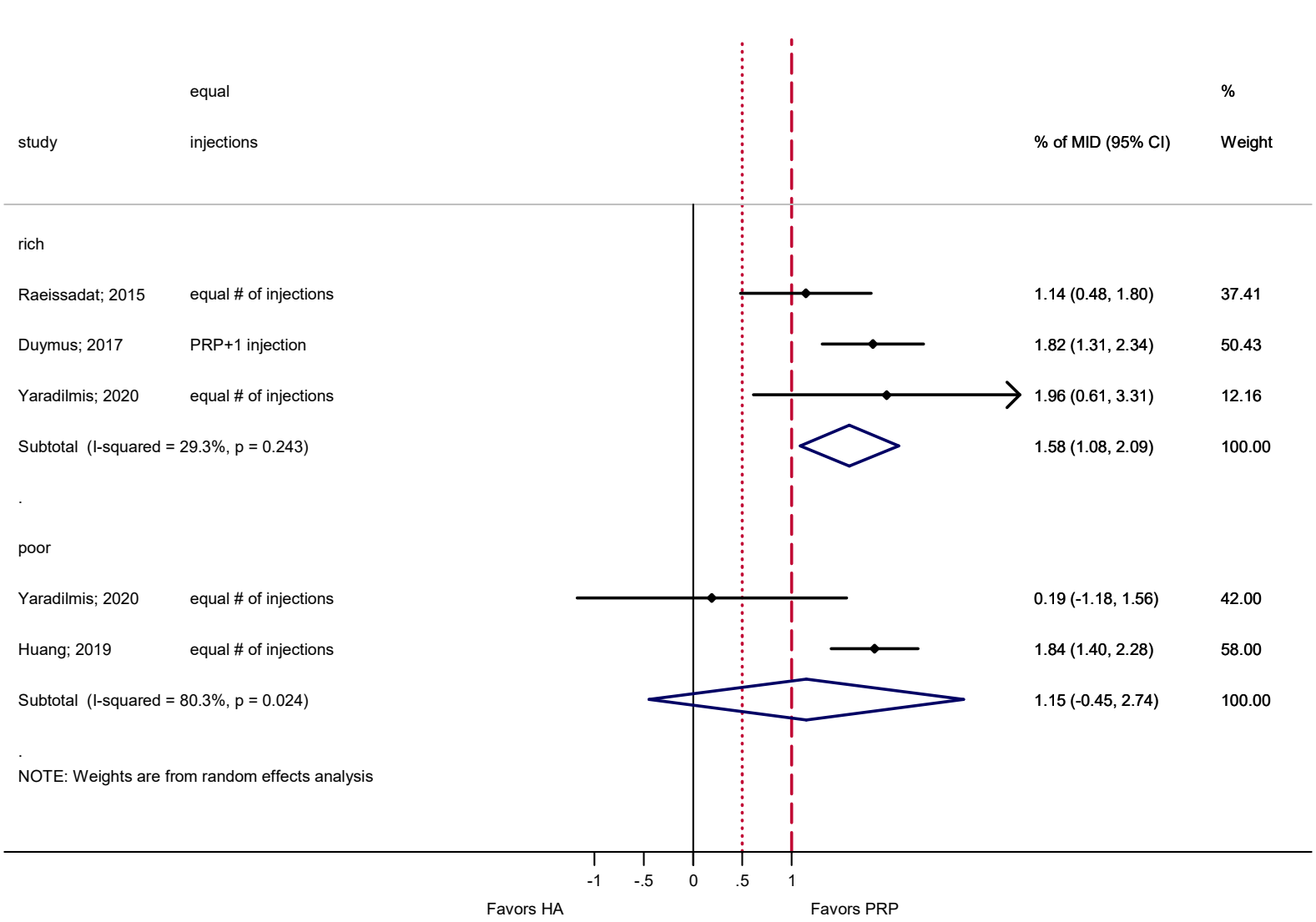
Meta-Analysis Figure 77: Hyaluronic Acid vs Leukocyte Rich Platelet-Rich Plasma–Function at 6-Months



Meta-Analysis Figure 78: Hyaluronic Acid vs Leukocyte Rich Platelet-Rich Plasma–Stiffness by Follow Up Time



Meta-Analysis Figure 79: Hyaluronic Acid vs Platelet-Rich Plasma by Leukocyte Status–WOMAC Function at 1 Year



Evidence Table 5245: Platelet-Rich Plasma vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	other:OMERACT-OARSI Responder	48 wks	42/48	21.43%/68.75%	RR	0.31(0.17,0.57)	Group 2	na
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	other:OMERACT-OARSI Responder	24 wks	48/48	27.08%/83.33%	RR	0.33(0.2,0.53)	Group 2	na
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Pain:20% Decrease VAS Pain	52 wks	32/33	0%/15.15%	RD	-15.152 (-28.831,0.617)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Pain:20% Decrease VAS Pain	26 wks	32/33	25%/48.48%	RR	0.52(0.26,1.03)	Not Sig.	na
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Pain:20% Decrease WOMAC Pain	52 wks	32/33	0%/30.3%	RD	-30.303 (-47.096,-13.268)	Group 2	na
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Pain:20% Decrease WOMAC Pain	26 wks	32/33	21.88%/48.48%	RR	0.45(0.21,0.95)	Group 2	na
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Pain:20% decrease in WOMAC pain	24 wks	87/89	52.87%/57.3%	RR	0.92(0.71,1.21)	Not Sig.	na
Sanchez ; 2008/Low	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Pain:40% WOMAC pain reduction subscale	4 wks	30/30	10%/33.33%	RR	0.3(0.09,0.98)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Pain:50% decrease in WOMAC pain	24 wks	87/89	24.14%/38.2%	RR	0.63(0.4,1)	Group 2	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Pain:KOOS Pain(0-100)	60 days	89/94	72.6(17.9)/73.8(19.9)	Mean Diff	-1.2(-6.72,4.32)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Pain:KOOS Pain(0-100)	180 days	89/94	74.8(17.6)/74.7(19.3)	Mean Diff	0.1(-5.28,5.48)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Pain:KOOS Pain(0-100)	360 days	89/94	75.4(19)/74.9(19.3)	Mean Diff	0.5(-5.09,6.09)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Pain:KOOS Pain(0-100)	180 days	55/54	73.2(18.1)/74.2(19.6)	Mean Diff	-1(-8.17,6.17)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Pain:KOOS Pain(0-100)	60 days	55/54	71.1(18.6)/73.1(21.5)	Mean Diff	-2(-9.64,5.64)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Pain:KOOS Pain(0-100)	360 days	55/54	74(19.4)/74(19.4)	Mean Diff	0(-7.37,7.37)	Not Sig.	na
Spakova; 2012/Moderate	10: IA HA-Erectus 1.2%-3 weekly injections	10: Blood derived-PRP-3 weekly injections	Pain:NRS Pain	6 mos	30/30	4.3(2.07)/2.69(1.86)	Mean Diff	1.61(0.59,2.63)	Group 2	na
Spakova; 2012/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:NRS Pain	26 wks	60/60	4.3(2.07)/2.69(1.86)	Mean Diff	1.61(0.9,2.32)	Group 2	na
Spakova; 2012/Moderate	10: IA HA-Erectus 1.2%-3 weekly injections	10: Blood derived-PRP-3 weekly injections	Pain:NRS Pain	3 mos	30/30	3.98(2.27)/2.06(2.02)	Mean Diff	1.92(0.81,3.03)	Group 2	na
Spakova; 2012/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:NRS Pain	13 wks	60/60	3.98(2.27)/2.06(2.02)	Mean Diff	1.92(1.14,2.7)	Group 2	na
Raeissadat; 2017/Moderate	10: IA HA-Hyaluronic Acid(20 mg of active ingredient sodium hyaluronate in 2 mL of liquid)	10: Blood derived-Plasma Rich in Growth Factor	Pain:VAS Pain	6 mos	33/36	4.8(2.39)/4.6(2.78)	Mean Diff	0.2(-1.04,1.44)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ahmad; 2018/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:VAS Pain	3 mos	44/45	5.3(1.6)/4.6(1.6)	Mean Diff	0.7(0.03,1.37)	Group 2	clinically insignificant
Ahmad; 2018/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:VAS Pain	6 mos	44/45	5.95(1.52)/4.14(1.44)	Mean Diff	1.81(1.19,2.43)	Group 2	possibly clinically significant
Cole; 2017/High	10: IA HA-Hyaluronic Acid(3 treatments for 3 weeks)	10: Blood derived-Platelet-Rich Plasma(3 treatments for 3 weeks)	Pain:VAS Pain	52 wks	50/49	57.3(26.87005769)/44(32.2)	Mean Diff	0.09(-1.24,1.42)	Not Sig.	clinically insignificant
Cole; 2017/High	10: IA HA-Hyaluronic Acid(3 treatments for 3 weeks)	10: Blood derived-Platelet-Rich Plasma(3 treatments for 3 weeks)	Pain:VAS Pain	24 wks	50/49	48.6(26.1629509)/34.6(22.68)	Mean Diff	0.09(-1.24,1.42)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:VAS Pain	3 mos	34/33	3.1(0.9)/2.9(0.7)	Mean Diff	0.2(-0.19,0.59)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:VAS Pain	6 mos	34/33	4.3(1.3)/4(1.3)	Mean Diff	0.3(-0.33,0.93)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:VAS Pain	1 mos	34/33	3.1(0.9)/2.5(0.7)	Mean Diff	0.6(0.21,0.99)	Group 2	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:VAS Pain	12 mos	34/33	6.8(0.1)/5.1(1.3)	Mean Diff	1.7(1.24,2.16)	Group 2	possibly clinically significant
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:VAS Pain	30 days	36/36	-3(.)/-4.5(.)	median difference	1.5	Group 2	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:VAS Pain	180 days	36/36	-3(.)/-5(.)	median difference	2	Group 2	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:VAS Pain	90 days	36/36	-3(.)/-6(.)	median difference	3	Group 2	na
Raeissadat; 2015/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(2mL 20mg HA; 17mg NaCl; 0.1mg monobasic sodium phosphate; 1.2mg dibasic sodium phosphate; up to 2cc water; x3 in 1wk intervals)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(4-6mL PRP x3 in 1wk intervals)	Pain:VAS Pain(SF-36; 0-100)	364 days	62/77	53.56(27.89)/77.11(19.56)	Mean Diff	-23.55(-31.85,-15.25)	Group 2	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Pain:VAS Pain(patient with concommittant infection)	1 mos	30/30	5.62(0.44)/4.25(0.57)	Mean Diff	1.37(1.11,1.63)	Group 2	some may benefit
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Pain:VAS Pain(patient with concommittant infection)	3 mos	30/30	6.83(0.45)/3.39(0.4)	Mean Diff	3.44(3.22,3.66)	Group 2	clinically significant
Raeissadat; 2017/Moderate	10: IA HA-Hyaluronic Acid(20 mg of active ingredient sodium hyaluronate in 2 mL of liquid)	10: Blood derived-Plasma Rich in Growth Factor	Pain:WOMAC Pain	6 mos	33/36	5.9(2.79)/5.3(3.6)	Mean Diff	0.6(-0.94,2.14)	Not Sig.	inconclusive
Cole; 2017/High	10: IA HA-Hyaluronic Acid(3 treatments for 3 weeks)	10: Blood derived-Platelet-Rich Plasma(3 treatments for 3 weeks)	Pain:WOMAC Pain	6 wks	50/49	4.66(3.32)/4.57(3.36)	Mean Diff	0.09(-1.24,1.42)	Not Sig.	na
Cole; 2017/High	10: IA HA-Hyaluronic Acid(3 treatments for 3 weeks)	10: Blood derived-Platelet-Rich Plasma(3 treatments for 3 weeks)	Pain:WOMAC Pain	24 wks	50/49	5(3.54)/4.11(3.92)	Mean Diff	0.89(-0.6,2.38)	Not Sig.	na
Cole; 2017/High	10: IA HA-Hyaluronic Acid(3 treatments for 3 weeks)	10: Blood derived-Platelet-Rich Plasma(3 treatments for 3 weeks)	Pain:WOMAC Pain	52 wks	50/49	4(4.24)/3.02(3.36)	Mean Diff	0.98(-0.55,2.51)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Cole; 2017/High	10: IA HA-Hyaluronic Acid(3 treatments for 3 weeks)	10: Blood derived-Platelet-Rich Plasma(3 treatments for 3 weeks)	Pain:WOMAC Pain	12 wks	50/49	5(4.24)/3.98(4.41)	Mean Diff	1.02(-0.71,2.75)	Not Sig.	na
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:WOMAC Pain	3 mos	34/33	7(1.74)/7.24(2.37)	Mean Diff	-0.24(-1.26,0.78)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:WOMAC Pain	1 mos	34/33	6.1(2.4)/6.8(1.8)	Mean Diff	-0.7(-1.73,0.33)	Not Sig.	inconclusive
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:WOMAC Pain	6 mos	34/33	9.7(1.6)/9.4(1.7)	Mean Diff	0.3(-0.51,1.11)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Pain:WOMAC Pain	12 mos	34/33	14.2(1.1)/11.4(2.4)	Mean Diff	2.8(1.88,3.72)	Group 2	clinically significant
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:WOMAC Pain	30 days	36/36	-200(.)/-175(.)	median difference	-25	Not Sig.	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:WOMAC Pain	90 days	36/36	-187.5(.)/-225(.)	median difference	37.5	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Pain:WOMAC Pain	180 days	36/36	-162.5(.)/-225(.)	median difference	62.5	Not Sig.	na
Raeissadat; 2015/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(2mL 20mg HA; 17mg NaCl; 0.1mg monobasic sodium phosphate; 1.2mg dibasic sodium phosphate; up to 2cc water; x3 in 1wk intervals)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(4-6mL PRP x3 in 1wk intervals)	Pain:WOMAC Pain	364 days	62/77	5.08(3.71)/4.03(3.36)	Mean Diff	1.05(-0.15,2.25)	Not Sig.	inconclusive
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Pain:WOMAC Pain	48 wks	42/48	10.7(3.7)/6.3(2.6)	Mean Diff	4.4(3.04,5.76)	Group 2	clinically significant
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Pain:WOMAC Pain	24 wks	48/48	10.3(4.8)/5(3.1)	Mean Diff	5.3(3.66,6.94)	Group 2	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Pain:Womac Pain	24 wks	87/89	26.9(15.8)/24.1(15.5)	Mean Diff	2.8(-1.86,7.46)	Not Sig.	clinically insignificant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Pain:vas pain	2 mos	30/30	3.57(2.49)/2.87(1.94)	Mean Diff	0.7(-0.46,1.86)	Not Sig.	clinically insignificant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Pain:vas pain	6 mos	30/30	3.7(2.51)/2.97(1.48)	Mean Diff	0.73(-0.34,1.8)	Not Sig.	clinically insignificant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Pain:vas pain	12 mos	30/30	4.97(2.67)/4.17(2.34)	Mean Diff	0.8(-0.5,2.1)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Pain:vas pain	2 mos	30/30	3.57(2.49)/2.6(2.25)	Mean Diff	0.97(-0.26,2.2)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Pain:vas pain	6 mos	30/30	3.7(2.51)/1.83(2)	Mean Diff	1.87(0.7,3.04)	Group 2	possibly clinically significant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Pain:vas pain	12 mos	30/30	4.97(2.67)/2.23(2.33)	Mean Diff	2.74(1.44,4.04)	Group 2	possibly clinically significant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Pain:womac Pain	6 mos	30/30	9.17(2.01)/9.73(5.35)	Mean Diff	-0.56(-2.67,1.55)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Pain:womac Pain	2 mos	30/30	10.8(5.9)/10.2(6.26)	Mean Diff	0.6(-2.54,3.74)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Pain:womac Pain	12 mos	30/30	12.23(4.89)/9.83(5.83)	Mean Diff	2.4(-0.38,5.18)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Pain:womac Pain	6 mos	30/30	9.17(2.01)/3.5(1.7)	Mean Diff	5.67(4.71,6.63)	Group 2	clinically significant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Pain:womac Pain	2 mos	30/30	10.8(5.9)/4.5(2.44)	Mean Diff	6.3(3.94,8.66)	Group 2	clinically significant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Pain:womac Pain	12 mos	30/30	12.23(4.89)/4.13(2.35)	Mean Diff	8.1(6.1,10.1)	Group 2	clinically significant
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Function:20% Decrease WOMAC Physical Function	52 wks	32/33	0%/24.24%	RD	-24.242 (-39.897,-7.46)	Group 2	na
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Function:20% Decrease WOMAC Physical Function	26 wks	32/33	15.63%/45.45%	RR	0.34(0.14,0.84)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Function:20% Decrease WOMAC Stiffness	52 wks	32/33	0%/27.27%	RD	-27.273 (-43.516,-10.328)	Group 2	na
Buendia-Lopez; 2018/High	10: IA HA-Hyaluronic Acid (Durolane; high molecular weight preparation)(60 mg/2 mL for 52 weeks)	10: Blood derived-Platelet Rich Plasma(5 mL injection)	Function:20% Decrease WOMAC Stiffness	26 wks	32/33	15.63%/45.45%	RR	0.34(0.14,0.84)	Group 2	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:KOOS Function(0-100; ADL)	360 days	55/54	77.3(19.8)/77.9(20.6)	Mean Diff	-0.6(-8.27,7.07)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:KOOS Function(0-100; ADL)	180 days	55/54	77.3(18.6)/79.1(19)	Mean Diff	-1.8(-8.94,5.34)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:KOOS Function(0-100; ADL)	60 days	55/54	78.2(17.4)/81.2(17.9)	Mean Diff	-3(-9.7,3.7)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:KOOS Function(0-100; Sport)	360 days	55/54	46.6(27.9)/47.4(28.2)	Mean Diff	-0.8(-11.45, 9.85)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:KOOS Function(0-100; Sport)	60 days	55/54	45(24.1)/48.8(25.9)	Mean Diff	-3.8(-13.3,5.7)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:KOOS Function(0-100; Sport)	180 days	55/54	44.7(27.8)/48.7(29.5)	Mean Diff	-4(-14.89, 6.89)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:KOOS Function(function in daily living; 0-100)	180 days	89/94	78.4(18.6)/79.1(19.6)	Mean Diff	-0.7(-6.27,4.87)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:KOOS Function(function in daily living; 0-100)	60 days	89/94	78(17.9)/79(19.8)	Mean Diff	-1(-6.5,4.5)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:KOOS Function(function in daily living; 0-100)	360 days	89/94	78.4(19.3)/78.4(20.7)	Mean Diff	0(-5.83,5.83)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:KOOS Function(sport and rec function; 0-100)	360 days	89/94	46.3(28.1)/49.3(28.6)	Mean Diff	-3(-11.27, 5.27)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:KOOS Function(sport and rec function; 0-100)	60 days	89/94	44(25.5)/48(26.1)	Mean Diff	-4(-11.53, 3.53)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:KOOS Function(sport and rec function; 0-100)	180 days	89/94	45.1(27)/49.6(28.6)	Mean Diff	-4.5(-12.61, 3.61)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:Likert Scale function(Tegner Scale; 0-10)	180 days	89/94	3.5(1.5)/3.7(1.5)	Mean Diff	-0.2(-0.64,0.24)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:Likert Scale function(Tegner Scale; 0-10)	360 days	89/94	3.4(1.5)/3.7(1.3)	Mean Diff	-0.3(-0.71,0.11)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Function:Likert Scale function(Tegner Scale; 0-10)	60 days	89/94	3.3(1.5)/3.6(1.4)	Mean Diff	-0.3(-0.72,0.12)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Function:Likert Scale function(Tegner Scale; 0-10)	360 days	55/54	3.4(1.6)/3.8(1.3)	Mean Diff	-0.4(-0.95,0.15)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Raeissadat; 2015/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(2mL 20mg HA; 17mg NaCl; 0.1mg monobasic sodium phosphate; 1.2mg dibasic sodium phosphate; up to 2cc water; x3 in 1wk intervals)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(4-6mL PRP x3 in 1wk intervals)	Function:VAS function(SF-36; 0-100)	364 days	62/77	44.29(28.14)/56.82(25.68)	Mean Diff	-12.53(-21.67,-3.39)	Group 2	clinically significant
Raeissadat; 2017/Moderate	10: IA HA-Hyaluronic Acid(20 mg of active ingredient sodium hyaluronate in 2 mL of liquid)	10: Blood derived-Plasma Rich in Growth Factor	Function:WOMAC Function	6 mos	33/36	20.1(7.77)/17.6(11.7)	Mean Diff	2.5(-2.25,7.25)	Not Sig.	inconclusive
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Function:WOMAC Function	24 wks	48/48	36.2(16.8)/19.7(11.1)	Mean Diff	16.5(10.72,22.28)	Group 2	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Function:WOMAC Function	48 wks	42/48	38.9(14.2)/21.9(11.3)	Mean Diff	17(11.56,22.44)	Group 2	clinically significant
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Function:WOMAC Physical Activity	30 days	36/36	-362.5(.)/-375(.)	median difference	12.5	Not Sig.	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Function:WOMAC Physical Activity	180 days	36/36	-462.5(.)/-625(.)	median difference	162.5	Not Sig.	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Function:WOMAC Physical Activity	90 days	36/36	-512.5(.)/-550(.)	median difference	37.5	Not Sig.	na
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Physical Function	6 mos	34/33	30.1(5.7)/29.6(5.7)	Mean Diff	0.5(-2.28,3.28)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Physical Function	12 mos	34/33	49.6(3.3)/38.6(7.7)	Mean Diff	11(8.07,13.93)	Group 2	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Physical Function	3 mos	34/33	25.1(8.9)/22(5.4)	Mean Diff	3.1(-0.49,6.69)	Not Sig.	inconclusive
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Physical Function	1 mos	34/33	24.3(9.5)/19.7(7.1)	Mean Diff	4.6(0.51,8.69)	Group 2	possibly clinically significant
Raeissadat; 2017/Moderate	10: IA HA-Hyaluronic Acid(20 mg of active ingredient sodium hyaluronate in 2 mL of liquid)	10: Blood derived-Plasma Rich in Growth Factor	Function:WOMAC Stiffness	6 mos	33/36	1.3(1.48)/1.5(1.84)	Mean Diff	-0.2(-1,0.6)	Not Sig.	inconclusive
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Stiffness	1 mos	34/33	2.7(1.1)/2.8(0.8)	Mean Diff	-0.1(-0.57,0.37)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Stiffness	6 mos	34/33	3.8(1.1)/3.6(0.7)	Mean Diff	0.2(-0.25,0.65)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Stiffness	3 mos	34/33	3.2(1)/3(1.1)	Mean Diff	0.2(-0.31,0.71)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Function:WOMAC Stiffness	12 mos	34/33	5.4(0.7)/4.7(1.2)	Mean Diff	0.7(0.22,1.18)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Function:WOMAC Stiffness	30 days	36/36	-50(.)/-50(.)	median difference	0	Not Sig.	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Function:WOMAC Stiffness	180 days	36/36	-62.5(.)/-62.5(.)	median difference	0	Not Sig.	na
Lana; 2016/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Function:WOMAC Stiffness	90 days	36/36	-50(.)/-100(.)	median difference	50	Not Sig.	na
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Function:WOMAC Stiffness	24 wks	48/48	4(2.3)/2.5(1.7)	Mean Diff	1.5(0.68,2.32)	Group 2	possibly clinically significant
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Function:WOMAC Stiffness	48 wks	42/48	4.7(2)/2.6(1.4)	Mean Diff	2.1(1.36,2.84)	Group 2	clinically significant
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Function:WOMAC function	24 wks	87/89	25.9(17.2)/24.8(15.9)	Mean Diff	1.1(-3.83,6.03)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez ; 2008/Low	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Function:WOMAC function	4 wks		none	pvalue	Sig (p<0.05)	Platelet Rich Plasma favored over Hyaluronic	na
Raeissadat; 2015/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(2mL 20mg HA; 17mg NaCl; 0.1mg monobasic sodium phosphate; 1.2mg dibasic sodium phosphate; up to 2cc water; x3 in 1wk intervals)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(4-6mL PRP x3 in 1wk intervals)	Function:WOMAC function(0-68)	364 days	62/77	19.51(11.9)/13.19(10.39)	Mean Diff	6.32(2.52,10.12)	Group 2	possibly clinically significant
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Function:WOMAC stiffness	24 wks	87/89	25.5(17.9)/25.2(15.4)	Mean Diff	0.3(-4.67,5.27)	Not Sig.	clinically insignificant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Function:womac function	6 mos	30/30	30.17(2.01)/30.33(15.55)	Mean Diff	-0.16(-6.01,5.69)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Function:wo mac function	2 mos	30/30	33.5(17.9)/33.9(14.36)	Mean Diff	-0.4(-8.8,8)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Function:wo mac function	12 mos	30/30	35.33(21.89)/34.83(19.83)	Mean Diff	0.5(-10.3,11.3)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Function:wo mac function	2 mos	30/30	33.5(17.9)/30.5(13.54)	Mean Diff	3(-5.22,11.22)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Function:wo mac function	6 mos	30/30	30.17(2.01)/25(17)	Mean Diff	5.17(-1.21,11.55)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Function:wo mac function	12 mos	30/30	35.33(21.89)/29.83(19.35)	Mean Diff	5.5(-5.18,16.18)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Function:womac stiffness	12 mos	30/30	4.23(1.89)/4.13(1.84)	Mean Diff	0.1(-0.86,1.06)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Function:womac stiffness	2 mos	30/30	3.9(1.9)/3.7(1.86)	Mean Diff	0.2(-0.77,1.17)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Function:womac stiffness	6 mos	30/30	4.17(2.01)/3.9(1.55)	Mean Diff	0.27(-0.66,1.2)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Function:womac stiffness	2 mos	30/30	3.9(1.9)/3.6(2.14)	Mean Diff	0.3(-0.75,1.35)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Function:womac stiffness	12 mos	30/30	4.23(1.89)/3.83(1.32)	Mean Diff	0.4(-0.44,1.24)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Function:womac stiffness	6 mos	30/30	4.17(2.01)/3.7(1.7)	Mean Diff	0.47(-0.49,1.43)	Not Sig.	inconclusive
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Composite:IKDC composite(0-100)	180 days	89/94	63.5(17.1)/65(16.1)	Mean Diff	-1.5(-6.35,3.35)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Composite:IKDC composite(0-100)	360 days	89/94	64.2(18)/66.2(16.7)	Mean Diff	-2(-7.07,3.07)	Not Sig.	na
Filardo; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(30mg/2 mL x3 weekly; high molecular weight)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(5mL injection x3 weekly)	Composite:IKDC composite(0-100)	60 days	89/94	63.5(15.2)/63.2(16.6)	Mean Diff	0.3(-4.34,4.94)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Composite:IKDC composite(0-100)	60 days	55/54	61.4(16.2)/62.8(17.6)	Mean Diff	-1.4(-7.83,5.03)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Composite:IKDC composite(0-100)	360 days	55/54	61.7(19)/64.9(16.8)	Mean Diff	-3.2(-10.01, 3.61)	Not Sig.	na
Filardo; 2012/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 weekly injections)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 weekly injections)	Composite:IKDC composite(0-100)	180 days	55/54	61(18.2)/64.3(16.4)	Mean Diff	-3.3(-9.88,3.28)	Not Sig.	na
Gormeli; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 injections 30mg/2mL orthovisc)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 injections)	Composite:IKDC composite(Range 0-100)	180 days	39/39	48.4(6.2)/60.8(9.8)	Mean Diff	-12.4(-16.11,-8.69)	Group 2	na
Ahmad; 2018/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Composite:International Knee Documentation Committee Score	6 mos	44/45	65.6(16.9)/75.7(15.1)	Mean Diff	-10.1(-16.86,-3.34)	Group 2	na
Ahmad; 2018/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Composite:International Knee Documentation Committee Score	3 mos	44/45	59.6(15.4)/67.9(13.7)	Mean Diff	-8.3(-14.45,-2.15)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Composite:Lequesne Index Score	48 wks	42/48	14.4(3.8)/8.9(3.7)	Mean Diff	5.5(3.92,7.08)	Group 2	na
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Composite:Lequesne index	24 wks	87/89	5.4(3.3)/5.2(3.4)	Mean Diff	0.2(-0.8,1.2)	Not Sig.	na
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Composite:Lysholm score(patient with concommittant infection)	3 mos	30/30	47.67(5.42)/76.8(5.94)	Mean Diff	-29.13(-32.07,-26.19)	Group 2	na
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Composite:Lysholm score(patient with concommittant infection)	1 mos	30/30	57(6.04)/65.33(5.98)	Mean Diff	-8.33(-11.44,-5.22)	Group 2	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Composite:VAS Scores	12 mos	40/40	2.14(1.52)/2.26(1.71)	Mean Diff	-0.12(-0.84,0.6)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Composite:VAS Scores	12 mos	40/40	2.14(1.52)/1.98(1.44)	Mean Diff	0.16(-0.5,0.82)	Not Sig.	clinically insignificant
Spakova; 2012/Moderate	10: IA HA-Erectus 1.2%-3 weekly injections	10: Blood derived-PRP-3 weekly injections	Composite:WOMAC	3 mos	30/30	26.17(17.47)/14.35(14.18)	Mean Diff	11.82(3.59,20.05)	Group 2	na
Spakova; 2012/Moderate	10: IA HA-Erectus 1.2%-3 weekly injections	10: Blood derived-PRP-3 weekly injections	Composite:WOMAC	6 mos	30/30	30.9(16.57)/18.85(14.09)	Mean Diff	12.05(4.1,20)	Group 2	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	3 mos	40/40	25.02(4.98)/25.15(5.24)	Mean Diff	-0.13(-2.41,2.15)	Not Sig.	clinically insignificant
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	9 mos	40/40	27.86(4.34)/28.16(5.12)	Mean Diff	-0.3(-2.41,1.81)	Not Sig.	clinically insignificant
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	12 mos	40/40	30.64(8.36)/32.18(6.88)	Mean Diff	-1.54(-4.95,1.87)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	3 mos	40/40	25.02(4.98)/24.78(4.55)	Mean Diff	0.24(-1.88,2.36)	Not Sig.	clinically insignificant
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	6 mos	40/40	26.38(5.2)/25(4.65)	Mean Diff	1.38(-0.82,3.58)	Not Sig.	clinically insignificant
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	12 mos	40/40	30.64(8.36)/16.1(7.22)	Mean Diff	14.54(11.06, 18.02)	Group 2	clinically significant
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	6 mos	40/40	26.38(5.2)/21.14(5.17)	Mean Diff	5.24(2.93,7.55)	Group 2	some may benefit
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Composite:WOMAC Score Mean (VAS)	9 mos	40/40	27.86(4.34)/20.12(4.66)	Mean Diff	7.74(5.74,9.74)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Raeissadat; 2017/Moderate	10: IA HA-Hyaluronic Acid(20 mg of active ingredient sodium hyaluronate in 2 mL of liquid)	10: Blood derived-Plasma Rich in Growth Factor	Composite:WOMAC Total	6 mos	33/36	27.4(11.38)/24.4(16.54)	Mean Diff	3(-3.79,9.79)	Not Sig.	inconclusive
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Composite:WOMAC Total	6 mos	34/33	44.5(6.6)/42.8(7.1)	Mean Diff	1.7(-1.65,5.05)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Composite:WOMAC Total	12 mos	34/33	69.3(4.3)/54.9(10.8)	Mean Diff	14.4(10.32,18.48)	Group 2	clinically significant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Composite:WOMAC Total	3 mos	34/33	35.3(10.5)/32.2(7.8)	Mean Diff	3.1(-1.41,7.61)	Not Sig.	clinically insignificant
Duymus; 2017/Moderate	10: IA HA-Hyaluronic Acid(1 injection)	10: Blood derived-Platelet Rich Plasma(2 injections)	Composite:WOMAC Total	1 mos	34/33	33.2(12.2)/26.4(9.5)	Mean Diff	6.8(1.47,12.13)	Group 2	possibly clinically significant
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Composite:WOMAC Total	24 wks	48/48	50.4(23.2)/27.2(15.1)	Mean Diff	23.2(15.25,31.15)	Group 2	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Composite:WOMAC Total	48 wks	42/48	54.2(19.2)/30.8(15.5)	Mean Diff	23.4(16.01,30.79)	Group 2	clinically significant
Raeissadat; 2015/Moderate	10: IA HA-Hyaluronic Acid (Intra-articular)(2mL 20mg HA; 17mg NaCl; 0.1mg monobasic sodium phosphate; 1.2mg dibasic sodium phosphate; up to 2cc water; x3 in 1wk intervals)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(4-6mL PRP x3 in 1wk intervals)	Composite:WOMAC Total(0-96)	364 days	62/77	27.46(16.36)/18.44(14.35)	Mean Diff	9.02(3.79,14.25)	Group 2	possibly clinically significant
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Composite:WOMAC total	24 wks	87/89	78.3(48.1)/74(42.7)	Mean Diff	4.3(-9.24,17.84)	Not Sig.	inconclusive
Spakova; 2012/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Composite:WOMAC total	13 wks	60/60	26.17(17.47)/14.35(14.18)	Mean Diff	11.82(6.07,17.57)	Group 2	possibly clinically significant
Spakova; 2012/Moderate	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	Composite:WOMAC total	26 wks	60/60	30.9(16.57)/18.85(14.09)	Mean Diff	12.05(6.49,17.61)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Sanchez ; 2008/Low	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Composite:WOMAC total	4 wks		none	pvalue	Sig (p<0.05)	Platelet Rich Plasma favored over Hyaluronic	na
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Composite:womac total	2 mos	30/30	46.5(21.9)/46.9(18.36)	Mean Diff	-0.4(-10.85, 10.05)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Composite:womac total	6 mos	30/30	44.17(12.01)/43.33(15.55)	Mean Diff	0.84(-6.35,8.03)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Composite:womac total	12 mos	30/30	51.33(21.89)/49.83(19.83)	Mean Diff	1.5(-9.3,12.3)	Not Sig.	inconclusive
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Composite:womac total	6 mos	30/30	44.17(12.01)/32(17)	Mean Diff	12.17(4.54,19.8)	Group 2	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Composite:womac total	12 mos	30/30	51.33(21.89)/35.83(19.35)	Mean Diff	15.5(4.82,26.18)	Group 2	possibly clinically significant
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Composite:womac total	2 mos	30/30	46.5(21.9)/39.5(17.54)	Mean Diff	7(-3.26,17.26)	Not Sig.	inconclusive
Gormeli; 2015/High	10: IA HA-Hyaluronic Acid (Intra-articular)(3 injections 30mg/2mL orthovisc)	10: Blood derived-Platelet Rich Plasma (Intra-articular)(3 injections)	QOL:EQ-VAS (Range 0-100)	180 days	39/39	60.8(7.2)/71.4(10.8)	Mean Diff	-10.6(-14.75,-6.45)	Group 2	na
Di Martino; 2019/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	QOL:EuroQol (VAS)	2 mos	82/85	74.6(12.8)/76.5(12.7)	Mean Diff	-1.9(-5.8,2)	Not Sig.	na
Di Martino; 2019/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	QOL:EuroQol (VAS)	6 mos	82/85	73.8(15.6)/76.9(12.2)	Mean Diff	-3.1(-7.39,1.19)	Not Sig.	na
Di Martino; 2019/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	QOL:EuroQol (VAS)	12 mos	82/85	72.5(15.3)/77.6(10.5)	Mean Diff(adjusted p value)	-5.1(p>.05)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Di Martino; 2019/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelet Rich Plasma	QOL:EuroQol (VAS)	24 mos	82/85	74.3(17.3)/79.4(13.4)	Mean Diff(adjusted p value)	-5.1(p>.05)	Not Sig.	na
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Other:Acetaminophen use (g/day)	24 wks		none	pvalue	NS	Platelets rich in growth factors vs. wkscHy	na
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Other:CRP(patient with concommittant infection)(mg/L)	3 mos	30/30	27.18(1.84)/10.78(2.15)	Mean Diff	16.4(15.37,17.43)	Group 2	na
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Other:CRP(patient with concommittant infection)(mg/L)	1 mos	30/30	21.8(4.12)/16.98(3.63)	Mean Diff	4.82(2.81,6.83)	Group 2	na
Sanchez ; 2012/High	10: IA HA-Hyaluronic Acid	10: Blood derived-Platelets rich in growth factors	Other:OARSI responders	24 wks	87/89	49.43%/52.81%	RR	0.94(0.7,1.25)	Not Sig.	na
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Other:WBC count(patient with concommittant infection)(*10^9/L)	1 mos	30/30	4.93(0.66)/3.42(0.57)	Mean Diff	1.51(1.19,1.83)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Zhang; 2018/Moderate	10: IA HA-sodium hyaluronate + gentamicin(4ml)	10: Blood derived-PRP+ gentamicin(4ml)	Other:WBC count(patient with concommittant infection)(*10^9/L)	3 mos	30/30	6.13(0.81)/1.45(0.57)	Mean Diff	4.68(4.32,5.04)	Group 2	na
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Other:patient stisfaction	12 mos	30/30	2.9(1.1)/3.4(0.9)	Mean Diff	-0.5(-1.02,0.02)	Not Sig.	na
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Other:patient stisfaction	12 mos	30/30	2.9(1.1)/4.5(0.4)	Mean Diff	-1.6(-2.03,-1.17)	Group 2	na
Annaniemi; 2018/Low	10: IA HA-Hylan GF2 20 (synvisc-one) or socium hyaluronate or hyalgan- 1 to 3 injections	10: Blood derived-PRP-3 injections at 10-14 day intervals	Time to arthroplasty: need for TKA(propensity score matched)	Not Reported	39/39	17.95%/7.69%	RR	2.33(0.65,8.37)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Annaniemi; 2018/Low	10: IA HA-Hylan GF2 20 (synvisc-one) or socium hyaluronate or hyalgan- 1 to 3 injections	10: Blood derived-PRP-3 injections at 10-14 day intervals	Time to arthroplasty: need for any arthroplasty hazard ratio(propensity score matched groups-PRP vs HA)	Not Reported	78	none	Hazard Ratio	4.35(0.95,20)	Not Sig.	na
Annaniemi; 2018/Low	10: IA HA-Hylan GF2 20 (synvisc-one) or socium hyaluronate or hyalgan- 1 to 3 injections	10: Blood derived-PRP-3 injections at 10-14 day intervals	Time to arthroplasty: need for unicompartmental arthroplasty(propensity score matched)	Not Reported	39/39	23.08%/5.13%	RR	4.5(1.04,19.5)	Group 2	na
Vaquerizo; 2013/High	10: IA HA-Hyaluronic Acid (Durolane)(60mg/3mL)	10: Blood derived-Platelet Rich Plasma (Plasma Rich in Growth Factors; PRGF)(8mL 1 injection/2weeks x3 injections)	Adverse events:Any Adverse Event	48 wks	48/48	18.75%/14.58%	RR	1.29(0.52,3.17)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Adverse events:Deep Venous Thrombosis	12 mos	40/40	0%/0%	RD	0(-8.762, 8.762)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Adverse events:Deep Venous Thrombosis	12 mos	40/40	0%/0%	RD	0(-8.762, 8.762)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Adverse events:Infections	12 mos	40/40	0%/0%	RD	0(-8.762, 8.762)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Adverse events:Infections	12 mos	40/40	0%/0%	RD	0(-8.762, 8.762)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Adverse events:Low-Grade Fever	12 mos	40/40	0%/0%	RD	0(-8.762, 8.762)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Adverse events:Low-Grade Fever	12 mos	40/40	0%/0%	RD	0(-8.762, 8.762)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Raeissadat; 2017/Moderate	10: IA HA-Hyaluronic Acid(20 mg of active ingredient sodium hyaluronate in 2 mL of liquid)	10: Blood derived-Plasma Rich in Growth Factor	Adverse events:Minor Complications Due to Injection	6 mos	33/36	21.21%/5.56%	RR	3.82(0.85,17.09)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: Blood derived-Platelet-Rich Plasma(4 ml three times every three weeks)	Adverse events:Pain	12 mos	40/40	5%/12.5%	RR	0.4(0.08,1.94)	Not Sig.	na
Huang; 2019/Moderate	10: IA HA-Hyaluronic Acid(2 ml per week for three weeks)	10: IA corticosteroids-Corticosteroids(1 ml three times every three weeks)	Adverse events:Pain	12 mos	40/40	5%/7.5%	RR	0.67(0.12,3.78)	Not Sig.	na
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte rich platelet rich plasma (3 injections at 1 week intervals)	Adverse events:local adverse events	12 mos	30/30	6.67%/40%	RR	0.17(0.04,0.68)	Group 1	na
Yaradilmis; 2020/High	10: IA HA-Hyaluronic acid (ostenil 1-2 million daltons; 3 injections at 1 week intervals)	10: Blood derived-leukocyte poor platelet rich plasma(3 injections at 1 week intervals)	Adverse events:local adverse events	12 mos	30/30	6.67%/10%	RR	0.67(0.12,3.71)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Spakova; 2012/Moderate	10: IA HA-Erectus 1.2%-3 weekly injections	10: Blood derived-PRP-3 weekly injections	Adverse events:temporary mild worsening of knee pain after application	6 mos	30/30	0%/20%	RD	-20(-35.459,-2.694)	Group 1	na

PICO 10: Locally Invasive Treatment

Denervation Therapy vs Control

Table 46: Cryoablation vs Control

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Radnovich; 2017**
Adverse events	
Knee Pain	●
Any Adverse Event	●
Bruising	●
Itching	●
Redness	●
Swelling	●
Numbness	↓
Altered Sensation	●
Local Pain	●
Pain Aggrivated	●
Tenderness Upon Palpation	●
Tingling	●
Vasovagal Reaction	●
calculable MID outcomes	
WOMAC Total	↑
WOMAC Stiffness	↑
WOMAC Pain	↑
WOMAC Physical function	↑
VAS Pain	↑

Evidence Table 5346: Cyroablation vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:VAS Pain	30 days	121/59	-40.09(31.57)/-27.83(28.27)	Mean Diff	-12.26(-21.5,-3.02)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:VAS Pain	150 days	93/48	-48.88(27.58)/-34.28(24.94)	Mean Diff	-14.6(-23.72,-5.48)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:VAS Pain	120 days	121/59	-35.49(32.23)/-30.59(28.88)	Mean Diff	-4.9(-14.33, 4.53)	Not Sig.	clinically insignificant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:VAS Pain	60 days	121/59	-38.53(32.01)/-32.44(28.65)	Mean Diff	-6.09(-15.45, 3.27)	Not Sig.	clinically insignificant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:VAS Pain	90 days	121/59	-37.9(33.11)/-31.58(29.65)	Mean Diff	-6.32(-16.01, 3.37)	Not Sig.	clinically insignificant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:VAS Pain	180 days	87/40	-45.4(30.03)/-37.41(26.25)	Mean Diff	-7.99(-18.43, 2.45)	Not Sig.	clinically insignificant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:WOMAC Pain	120 days	121/59	-15.27(14.08)/-12.45(12.67)	Mean Diff	-2.82(-6.95,1.31)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:WOMAC Pain	180 days	87/40	-20.75(11.94)/-17.61(10.44)	Mean Diff	-3.14(-7.29,1.01)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:WOMAC Pain	60 days	121/59	-16.64(13.64)/-11.98(12.29)	Mean Diff	-4.66(-8.67,-0.65)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:WOMAC Pain	90 days	121/59	-17.03(14.3)/-11.37(12.9)	Mean Diff	-5.66(-9.86,-1.46)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:WOMAC Pain	150 days	93/48	-20.58(12.54)/-14.19(11.43)	Mean Diff	-6.39(-10.56,-2.22)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Pain:WOMAC Pain	30 days	121/59	-16.65(13.86)/-9.54(12.52)	Mean Diff	-7.11(-11.19,-3.03)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Physical Function	60 days	121/59	-52.64(46.31)/-39.23(41.71)	Mean Diff	-13.41(-27.01, 0.19)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Physical Function	90 days	121/59	-56(46.31)/-40.11(41.79)	Mean Diff	-15.89(-29.5,-2.28)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Physical Function	150 days	93/48	-66.32(41.95)/-46.41(38.45)	Mean Diff	-19.91(-33.9,-5.92)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Physical Function	30 days	121/59	-55.48(45.21)/-34.18(40.79)	Mean Diff	-21.3(-34.59,-8.01)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Physical Function	180 days	87/40	-66.72(40.67)/-58.1(35.73)	Mean Diff	-8.62(-22.81, 5.57)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Physical Function	120 days	121/59	-51.82(45.76)/-42.66(41.25)	Mean Diff	-9.16(-22.6,4.28)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Stiffness	120 days	121/59	-6.28(6.16)/-5.01(5.53)	Mean Diff	-1.27(-3.07,0.53)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Stiffness	180 days	121/40	-8.51(6.6)/-7.22(5.06)	Mean Diff	-1.29(-3.28,0.7)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Stiffness	60 days	121/59	-6.51(6.05)/-4.87(5.53)	Mean Diff	-1.64(-3.43,0.15)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Stiffness	90 days	121/59	-6.79(5.94)/-4.97(5.38)	Mean Diff	-1.82(-3.57,-0.07)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Stiffness	30 days	121/59	-6.7(5.83)/-4.38(5.3)	Mean Diff	-2.32(-4.04,-0.6)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Function:WOMAC Stiffness	150 days	121/48	-8.42(5.94)/-5.7(4.85)	Mean Diff	-2.72(-4.47,-0.97)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Composite:WOMAC Total	180 days	87/40	-94.75(58.11)/-83.74(51.17)	Mean Diff	-11.01(-31.31, 9.29)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Composite:WOMAC Total	120 days	121/59	-73.33(65.01)/-60.32(58.68)	Mean Diff	-13.01(-32.12, 6.1)	Not Sig.	inconclusive
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Composite:WOMAC Total	60 days	121/59	-75.75(64.57)/-56.28(58.22)	Mean Diff	-19.47(-38.44,-0.5)	Group 1	possibly clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Composite:WOMAC Total	90 days	121/59	-80.31(64.79)/-56.51(58.38)	Mean Diff	-23.8(-42.83,-4.77)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Composite:WOMAC Total	150 days	93/48	-95.08(59.12)/-66.5(54.25)	Mean Diff	-28.58(-48.3,-8.86)	Group 1	clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Composite:WOMAC Total	30 days	121/59	-78.78(63.91)/-48.26(57.69)	Mean Diff	-30.52(-49.31,-11.73)	Group 1	clinically significant
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Altered Sensation	180 days	121/59	2.48%/3.39%	RR	0.73(0.13,4.26)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Any Adverse Event	180 days	121/59	47.11%/45.76%	RR	1.03(0.74,1.44)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Bruising	180 days	121/59	3.31%/3.39%	RR	0.98(0.18,5.17)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Itching	180 days	121/59	1.65%/0%	RD	1.653(-2.521, 7.882)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Knee Pain	182 days	121/59	0%/5.08%	RD	-5.085(-9.626, 3.747)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Local Pain	180 days	121/59	7.44%/6.78%	RR	1.1(0.35,3.42)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Numbness	180 days	121/59	14.88%/1.69%	RR	8.78(1.2,64.17)	Group 2	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Pain Aggrivated	186 days	121/59	0%/1.69%	RD	-1.695(-5.073, 5.606)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Redness	180 days	121/59	0%/3.39%	RD	-3.39(-7.326, 4.764)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Swelling	180 days	121/59	2.48%/5.08%	RR	0.49(0.1,2.34)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Tenderness Upon Palpation	180 days	121/59	11.57%/13.56%	RR	0.85(0.38,1.92)	Not Sig.	na
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Tingling	180 days	121/59	2.48%/1.69%	RR	1.46(0.16,13.76)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Radnovich; 2017/High	10: Cryoablation-Cryoneurolysis	10: Placebo/Control-Placebo(Sham Treatment)	Adverse events:Vasovagal Reaction	190 days	121/59	0.83%/0%	RD	0.826(-2.88,6.977)	Not Sig.	na

PICO 10: Locally Invasive Treatment

Denervation Therapy vs Control

Table 47: Chemical Ablation vs Control

Quality: H=High; M=Moderate; L=Low	H	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Mendes; 2019	McAlindon; 2018
Function		
Timed Up and Go test	↑	
Flexion range of motion	●	
6-minute walk test	↑	
Extension range of motion	●	
Pain		
VAS Pain(delta)		●
Worst Pain in Last 7 Days		●
Adverse events		
Headache		●
Any Serious Adverse Event		●
Arthralgia		●
Joint Effusion		●
Nasopharyngitis		●
Joint Swelling		●
Hypertension		●
Osteoarthritis		●
Sciatica		●
Fall		●
Gastroenteritis		●
Discontinued Due to AE		●
Any Treatment-Related Serious AE		●
Nasal Congestion		●
Treatment Emergent AE		●
Treatment-Related AE		●
calculable MID outcomes		
WOMAC Total	●	
WOMAC Function	●	
WOMAC Stiffness	●	
WOMAC Pain	↑	●
VAS Pain at Rest	●	
VAS Pain during mortion	●	
QOL		
Patient Global Impression of Change		●

Evidence Table 5447: Chemical Ablation vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (Onabotulinumtoxin A) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	QoL:Patient Global Impression of Change	8 wks	132	none	Mean Difference	-0.2(-0.58,0.28)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (Onabotulinumtoxin A) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	QoL:Patient Global Impression of Change	8 wks	173	none	Mean Difference	0(-0.38,0.31)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (Onabotulinumtoxin A) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	QoL:Patient Global Impression of Change	8 wks	133	none	Mean Difference	0.1(-0.35,0.5)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:VAS Pain at rest	8 wks	35/35	1.7(2.5)/2.4(2.7)	Mean Diff	-0.7(-1.94,0.54)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:VAS Pain at rest	12 wks	35/35	1.3(2.2)/2.2(2.7)	Mean Diff	-0.9(-2.08,0.28)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:VAS Pain at rest	4 wks	35/35	2.2(2.8)/1.8(2.6)	Mean Diff	0.4(-0.89,1.69)	Not Sig.	clinically insignificant
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:VAS Pain during mortion	4 wks	35/35	3.8(2.4)/4(3.2)	Mean Diff	-0.2(-1.55,1.15)	Not Sig.	clinically insignificant
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:VAS Pain during mortion	8 wks	35/35	3.3(2.5)/3.7(3)	Mean Diff	-0.4(-1.72,0.92)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:VAS Pain during mortion	12 wks	35/35	2.5(2.7)/3.2(3)	Mean Diff	-0.7(-2.06,0.66)	Not Sig.	inconclusive
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Pain:VAS Pain(delta)	8 wks	132	none	Mean Difference	-0.03(-0.7,0.64)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Pain:VAS Pain(delta)	8 wks	173	none	Mean Difference	0.22(-0.33,0.76)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Pain:VAS Pain(delta)	8 wks	133	none	Mean Difference	0.42(-0.26,1.1)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain	4 wks	35/35	6.1(2.9)/6.9(4.4)	Mean Diff	-0.8(-2.58,0.98)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain	8 wks	35/35	5(3.2)/7(4.3)	Mean Diff	-2(-3.81,-0.19)	Group 1	possibly clinically significant
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Pain:WOMAC Pain	12 wks	35/35	5.3(3.6)/7.4(5.1)	Mean Diff	-2.1(-4.21,0.01)	Not Sig.	inconclusive
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Pain:WOMAC Pain	8 wks	133	none	Mean Difference	-0.3(-0.99,0.48)	Not Sig.	inconclusive
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Pain:WOMAC Pain	8 wks	173	none	Mean Difference	0(-0.61,0.59)	Not Sig.	clinically insignificant
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Pain:WOMAC Pain	8 wks	132	none	Mean Difference	0.2(-0.5,0.99)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Pain:Worst Pain in Last 7 Days	8 wks	132	none	Mean Difference	0.14(-0.58,0.86)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Pain:Worst Pain in Last 7 Days	8 wks	173	none	Mean Difference	0.28(-0.3,0.86)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Pain:Worst Pain in Last 7 Days	8 wks	133	none	Mean Difference	0.39(-0.35,1.12)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:6-minute walk test	4 wks	35/35	294.6(41.5)/268.2(69.2)	Mean Diff	26.4(-0.93,53.73)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:6-minute walk test	12 wks	35/35	304.1(49.7)/270.4(54.1)	Mean Diff	33.7(8.92,58.48)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:6-minute walk test	8 wks	35/35	307.4(42.6)/267.9(46.5)	Mean Diff	39.5(18.23,60.77)	Group 1	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Extension range of motion	4 wks	35/35	10.4(2.9)/10.6(2.7)	Mean Diff	-0.2(-1.54,1.14)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Extension range of motion	8 wks	35/35	10(3)/10.4(2.5)	Mean Diff	-0.4(-1.72,0.92)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Extension range of motion	12 wks	35/35	10.1(2.3)/10.8(3.5)	Mean Diff	-0.7(-2.12,0.72)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Flexion range of motion	8 wks	35/35	122.2(10.6)/121(8.9)	Mean Diff	1.2(-3.47,5.87)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Flexion range of motion	12 wks	35/35	124.3(11.2)/122(8.8)	Mean Diff	2.3(-2.51,7.11)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Flexion range of motion	4 wks	35/35	123.9(10.3)/120.1(9.2)	Mean Diff	3.8(-0.86,8.46)	Not Sig.	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Timed Up and Go Test	12 wks	35/35	9.8(2.1)/10.9(2.5)	Mean Diff	-1.1(-2.2,0)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Timed Up and Go Test	4 wks	35/35	10(1.9)/11.4(2.9)	Mean Diff	-1.4(-2.57,-0.23)	Group 1	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:Timed Up and Go Test	8 wks	35/35	9.5(1.7)/11.3(2.3)	Mean Diff	-1.8(-2.77,-0.83)	Group 1	na
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function	4 wks	35/35	21.6(12.2)/24.8(12)	Mean Diff	-3.2(-8.97,2.57)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function	8 wks	35/35	18.9(12.7)/24.1(12.6)	Mean Diff	-5.2(-11.23, 0.83)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Function	12 wks	35/35	18.1(11.4)/23.3(15.1)	Mean Diff	-5.2(-11.59, 1.19)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Stiffness	4 wks	35/35	2.6(1.7)/2.7(1.8)	Mean Diff	-0.1(-0.94,0.74)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Stiffness	12 wks	35/35	2.1(1.6)/2.7(2)	Mean Diff	-0.6(-1.46,0.26)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Function:WOMAC Stiffness	8 wks	35/35	2.4(1.9)/3(2)	Mean Diff	-0.6(-1.53,0.33)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Composite:WOMAC Total	4 wks	35/35	30.3(15.2)/34.4(16.3)	Mean Diff	-4.1(-11.62, 3.42)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Composite:WOMAC Total	8 wks	35/35	26.3(16.6)/34.1(17.3)	Mean Diff	-7.8(-15.89, 0.29)	Not Sig.	inconclusive
Mendes; 2019/High	10: Chemical ablation-Botulinum Toxin type A(100 IU of Botulinum toxin type A in 2 mL of saline solution 0.9%)	10: Placebo/Control-Placebo(Saline Solution)	Composite:WOMAC Total	12 wks	35/35	25.4(15.6)/33.3(21.3)	Mean Diff	-7.9(-16.82, 1.02)	Not Sig.	inconclusive
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Any Serious Adverse Event	8 wks	43/89	9.3%/6.74%	RR	1.38(0.41,4.63)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Any Serious Adverse Event	8 wks	87/89	10.34%/6.74%	RR	1.53(0.57,4.13)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Any Serious Adverse Event	8 wks	44/89	11.36%/6.74%	RR	1.69(0.54,5.22)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Any Treatment-Related Serious AE	8 wks	87/89	0%/0%	RD	0(-4.229, 4.138)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Any Treatment-Related Serious AE	8 wks	44/89	0%/0%	RD	0(-8.03,4.138)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Any Treatment-Related Serious AE	8 wks	43/89	0%/0%	RD	0(-8.201, 4.138)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Arthralgia	8 wks	44/89	9.09%/10.11%	RR	0.9(0.29,2.76)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Arthralgia	8 wks	87/89	14.94%/10.11%	RR	1.48(0.67,3.28)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Arthralgia	8 wks	43/89	20.93%/10.11%	RR	2.07(0.89,4.84)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Discontinued Due to AE	8 wks	44/89	2.27%/0%	RD	2.273(-7.262, 6.813)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Discontinued Due to AE	8 wks	87/89	2.3%/0%	RD	2.299(-3.402, 6.759)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Discontinued Due to AE	8 wks	43/89	2.33%/0%	RD	2.326(-7.408, 6.884)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Fall	8 wks	43/89	2.33%/1.12%	RR	2.07(0.13,32.31)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Fall	8 wks	87/89	3.45%/1.12%	RR	3.07(0.33,28.94)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Fall	8 wks	44/89	4.55%/1.12%	RR	4.05(0.38,43.41)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Gastroenteritis	8 wks	43/89	0%/0%	RD	0(-8.201, 4.138)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Gastroenteritis	8 wks	87/89	2.3%/0%	RD	2.299(-3.402, 6.759)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Gastroenteritis	8 wks	44/89	4.55%/0%	RD	4.545(-6.044, 9.832)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Headache	8 wks	43/89	0%/1.12%	RD	-1.124(-9.377, 3.846)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Headache	8 wks	87/89	2.3%/1.12%	RR	2.05(0.19,22.16)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Headache	8 wks	44/89	4.55%/1.12%	RR	4.05(0.38,43.41)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Hypertension	8 wks	44/89	2.27%/2.25%	RR	1.01(0.09,10.85)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Hypertension	8 wks	87/89	4.6%/2.25%	RR	2.05(0.38,10.88)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Hypertension	8 wks	43/89	6.98%/2.25%	RR	3.1(0.54,17.9)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Joint Effusion	8 wks	43/89	0%/0%	RD	0(-8.201, 4.138)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Joint Effusion	8 wks	87/89	2.3%/0%	RD	2.299(-3.402, 6.759)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Joint Effusion	8 wks	44/89	4.55%/0%	RD	4.545(-6.044, 9.832)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Joint Swelling	8 wks	44/89	0%/4.49%	RD	-4.494(-12.976 ,2.004)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Joint Swelling	8 wks	87/89	4.6%/4.49%	RR	1.02(0.26,3.96)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Joint Swelling	8 wks	43/89	9.3%/4.49%	RR	2.07(0.54,7.88)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Nasal Congestion	8 wks	44/89	0%/0%	RD	0(-8.03,4.138)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Nasal Congestion	8 wks	87/89	2.3%/0%	RD	2.299(-3.402, 6.759)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Nasal Congestion	8 wks	43/89	4.65%/0%	RD	4.651(-6.153, 9.985)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	8 wks	44/89	2.27%/7.87%	RR	0.29(0.04,2.28)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	8 wks	87/89	3.45%/7.87%	RR	0.44(0.12,1.64)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Nasopharyngitis	8 wks	43/89	4.65%/7.87%	RR	0.59(0.13,2.73)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Osteoarthritis	8 wks	44/89	2.27%/7.87%	RR	0.29(0.04,2.28)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Osteoarthritis	8 wks	87/89	3.45%/7.87%	RR	0.44(0.12,1.64)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Osteoarthritis	8 wks	43/89	4.65%/7.87%	RR	0.59(0.13,2.73)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Sciatica	8 wks	43/89	0%/0%	RD	0(-8.201, 4.138)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Sciatica	8 wks	87/89	2.3%/0%	RD	2.299(-3.402, 6.759)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Sciatica	8 wks	44/89	4.55%/0%	RD	4.545(-6.044, 9.832)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Treatment Emergent AE	8 wks	44/89	54.55%/57.3%	RR	0.95(0.69,1.32)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Treatment Emergent AE	8 wks	87/89	62.07%/57.3%	RR	1.08(0.85,1.38)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Treatment Emergent AE	8 wks	43/89	69.77%/57.3%	RR	1.22(0.93,1.59)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Treatment-Related AE	8 wks	43/89	2.33%/3.37%	RR	0.69(0.07,6.44)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](200/400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Treatment-Related AE	8 wks	87/89	3.45%/3.37%	RR	1.02(0.21,4.93)	Not Sig.	na
McAlindon; 2018/Moderate	10: Chemical ablation-Botox (OnabotulinumtoxinA) [IA](400 U IA 2mL)	10: Placebo/Control-Placebo	Adverse events:Treatment-Related AE	8 wks	44/89	4.55%/3.37%	RR	1.35(0.23,7.78)	Not Sig.	na

PICO 10: Locally Invasive Treatment

Denervation Therapy vs Control

Table 48: Thermal Ablation vs Control

Quality: H=High; M=Moderate; L=Low	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	El-Hakeim; 2018
calculable MID outcomes	
WOMAC Total	↑
WOMAC Function	↑
WOMAC Stiffness	●
WOMAC Pain	●
VAS	↑

Evidence Table 5548: Thermal Ablation vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: IA corticosteroids-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Pain:VAS	90 days	30/30	2.83(2.74)/4.93(1.1)	Mean Diff	-2.1(-3.19,-1.01)	Group 1	possibly clinically significant
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Pain:VAS	180 days	30/30	3.13(1.64)/5.73(1.42)	Mean Diff	-2.6(-3.39,-1.81)	Group 1	possibly clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Pain:WOMAC Pain	180 days	30/30	6.57(4.93)/7.9(2.85)	Mean Diff	-1.33(-3.42,0.76)	Not Sig.	inconclusive
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Pain:WOMAC Pain	90 days	30/30	4.63(4.98)/4.5(1.64)	Mean Diff	0.13(-1.81,2.07)	Not Sig.	inconclusive
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Function:WOMAC Function	90 days	30/30	15.9(17.53)/29.43(8.76)	Mean Diff	-13.53(-20.75,-6.31)	Group 1	clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Function:WOMAC Function	180 days	30/30	22.93(16.43)/32.4(10.41)	Mean Diff	-9.47(-16.61,-2.33)	Group 1	possibly clinically significant
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Function:WOMAC Stiffness	180 days	30/30	3.63(2.08)/3.2(1.1)	Mean Diff	0.43(-0.44,1.3)	Not Sig.	inconclusive
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Function:WOMAC Stiffness	90 days	30/30	3.7(2.03)/3.13(1.04)	Mean Diff	0.57(-0.27,1.41)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Composite:WOMAC Total	180 days	30/30	33.13(22.46)/43.5(10.95)	Mean Diff	-10.37(-19.58,-1.16)	Group 1	possibly clinically significant
El-Hakeim; 2018/Moderate	10: Thermal Ablation-RFA (Rescue paracetamol supplement and 24hr ice)	10: Placebo/Control-usual care analgesics-Oral paracetamol (max 1g/6hrs); Diclofenac (75mg; twice per day); rescue physiotherapy	Composite:WOMAC Total	90 days	30/30	24.23(23.55)/37.1(10.41)	Mean Diff	-12.87(-22.37,-3.37)	Group 1	possibly clinically significant

PICO 11: Arthroscopic Debridement

Arthroscopic Debridement and Lavage vs Control

Table 49: Arthroscopic Debridement and Lavage vs Control

Quality: H=High; M=Moderate; L=Low	H	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Moseley ; 2002*	Kirkley ; 2008#
Composite		
MACTAR		●
womac total 3 months- KL grade 2 subgroup		●
womac total 6,12,18, 24 months- KL grade 2 subgroup		●
womac total 3 months- KL grade 3 and 4 subgroup		↑
womac total 6,12,18, 24 months- KL grade 3 and 4 subgroup		●
ASES other symptoms (3, 6, 12, 18 months)		●
ASES other symptoms (24 months)		↑
Standard-gamble utility score		●
Function		
AIMS walking and bending	●	
ASES Function		●
Pain		
AIMS pain	●	
ASES Pain 3 months		↑
ASES Pain(6 12 18 and 24 months)		●
calculable MID outcomes		
WOMAC Total		●
WOMAC Function		●
WOMAC Stiffness		●
WOMAC Pain		●
SF-36 pain	●	
SF-36 physical function	●	
SF-36 Physical component		●

Evidence Table 5649: Arthroscopic Debridement and Lavage vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:ASES pain	13 wks	90/80	73.9(15.8)/68.6(17)	Mean Diff	5.3(0.35,10.25)	Group 1	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:ASES pain	26 wks	90/73	71.5(16.9)/67.9(17)	Mean Diff	3.6(-1.63,8.83)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:ASES pain	52 wks	80/77	70.5(20)/69.5(16.8)	Mean Diff	1(-4.77,6.77)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:ASES pain	78 wks	78/70	69.8(18.9)/66.6(19)	Mean Diff	3.2(-2.92,9.32)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:ASES pain	104 wks	88/80	68.8(18.5)/63.8(19.8)	Mean Diff	5(-0.81,10.81)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:WOMAC pain	26 wks	90/73	5.72(4.52)/6.2(4.72)	Mean Diff	-0.48(-1.92,0.96)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:WOMAC pain	104 wks	88/80	6.72(5.36)/7.4(5.28)	Mean Diff	-0.68(-2.3,0.94)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:WOMAC pain	13 wks	90/80	5.64(4.36)/6.88(4.96)	Mean Diff	-1.24(-2.66,0.18)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:WOMAC pain	52 wks	80/77	6.2(5)/5.88(4.64)	Mean Diff	0.32(-1.2,1.84)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Pain:WOMAC pain	78 wks	78/70	7.16(5.6)/6.32(4.6)	Mean Diff	0.84(-0.82,2.5)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement + physical and medical therapy	11: Placebo/Control-physical and medical therapy alone	Function:ASES function	13 wks	90/80	80.7(18.2)/81.9(19.6)	Mean Diff	-1.2(-6.95,4.55)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:ASES function	78 wks	78/70	82(18.5)/83.2(18.5)	Mean Diff	-1.2(-7.22,4.82)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:ASES function	52 wks	80/77	81.4(19.1)/84.4(15.8)	Mean Diff	-3(-8.52,2.52)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:ASES function	26 wks	90/73	83.8(14.7)/83.2(16.1)	Mean Diff	0.6(-4.22,5.42)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:ASES function	104 wks	88/80	83.5(17)/81.9(18.4)	Mean Diff	1.6(-3.81,7.01)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:SF-36 Physical Component Summary	104 wks	88/80	37(11.4)/37.2(10.6)	Mean Diff	-0.2(-3.55,3.15)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:SF-36 Physical Component Summary	78 wks	78/70	37.7(11.9)/38.4(10.4)	Mean Diff	-0.7(-4.32,2.92)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:SF-36 Physical Component Summary	26 wks	90/73	38.7(9.3)/38.1(10.2)	Mean Diff	0.6(-2.45,3.65)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:SF-36 Physical Component Summary	52 wks	80/77	38.3(10.7)/37.7(10)	Mean Diff	0.6(-2.66,3.86)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:SF-36 Physical Component Summary	13 wks	90/80	38.7(9)/37.7(10.2)	Mean Diff	1(-1.93,3.93)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC function	104 wks	88/80	24.48(17.92)/24.92(17.56)	Mean Diff	-0.44(-5.85,4.97)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC function	13 wks	90/80	20.88(13.64)/22.72(14.76)	Mean Diff	-1.84(-6.16,2.48)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC function	26 wks	90/73	22.04(15.28)/20.8(14.72)	Mean Diff	1.24(-3.42,5.9)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC function	78 wks	78/70	23.12(17.08)/21.48(15.4)	Mean Diff	1.64(-3.64,6.92)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC function	52 wks	80/77	22.8(16.68)/20.52(14.8)	Mean Diff	2.28(-2.69,7.25)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC stiffness	13 wks	90/80	3.2(2.16)/3.36(2.12)	Mean Diff	-0.16(-0.81,0.49)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC stiffness	26 wks	90/73	3.44(2.12)/3.28(1.88)	Mean Diff	0.16(-0.46,0.78)	Not Sig.	clinically insignificant
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC stiffness	52 wks	80/77	3.4(2.24)/3.24(2.04)	Mean Diff	0.16(-0.52,0.84)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC stiffness	104 wks	88/80	3.72(2.4)/3.52(2.04)	Mean Diff	0.2(-0.48,0.88)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Function:WOMAC stiffness	78 wks	78/70	3.76(2.36)/3.2(1.96)	Mean Diff	0.56(-0.14,1.26)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:ASES other symptoms	52 wks	80/77	78.4(18.4)/76.1(16.5)	Mean Diff	2.3(-3.21,7.81)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:ASES other symptoms	13 wks	90/80	77.4(17)/74.7(15.8)	Mean Diff	2.7(-2.27,7.67)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:ASES other symptoms	78 wks	78/70	76.3(16.3)/73.1(18.8)	Mean Diff	3.2(-2.55,8.95)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:ASES other symptoms	26 wks	90/73	78.3(15.8)/74.3(15.2)	Mean Diff	4(-0.81,8.81)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:ASES other symptoms	104 wks	88/80	78.8(16.3)/73.4(18.2)	Mean Diff	5.4(0.12,10.68)	Group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:MACTAR	26 wks	90/73	234(118)/246(115)	Mean Diff	-12(-48.2,24.2)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:MACTAR	104 wks	88/80	238(146)/244(133)	Mean Diff	-6(-48.5,36.5)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:MACTAR	78 wks	78/70	251(141)/221(115)	Mean Diff	30(-11.64, 71.64)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:MACTAR	52 wks	80/77	232(128)/225(117)	Mean Diff	7(-31.64, 45.64)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:MACTAR	13 wks	90/80	257(108)/249(109)	Mean Diff	8(-24.93, 40.93)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:Standard-gamble utility score	52 wks	80/77	0.82(0.21)/0.86(0.16)	Mean Diff	-0.04(-0.1,0.02)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:Standard-gamble utility score	104 wks	88/80	0.87(0.18)/0.86(0.16)	Mean Diff	0.01(-0.04,0.06)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:Standard-gamble utility score	13 wks	90/80	0.81(0.21)/0.8(0.22)	Mean Diff	0.01(-0.06,0.08)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:Standard-gamble utility score	26 wks	90/73	0.84(0.2)/0.81(0.22)	Mean Diff	0.03(-0.04,0.1)	Not Sig.	na
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:WOMAC total	104 wks	88/80	34.96(24.96)/35.88(23.32)	Mean Diff	-0.92(-8.27,6.43)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:WOMAC total	13 wks	90/80	29.72(20.8)/32.96(20.8)	Mean Diff	-3.24(-9.55,3.07)	Not Sig.	inconclusive
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:WOMAC total	26 wks	90/73	31.2(20.72)/30.28(20.4)	Mean Diff	0.92(-5.47,7.31)	Not Sig.	clinically insignificant
Kirkley ; 2008/Moderate	11: Arthroscopic debridement-Arthroscopic Surgery with lavage and debridement	11: Placebo/Control-physical and medical therapy alone	Composite:WOMAC total	52 wks	80/77	32.44(23.04)/29.64(20.56)	Mean Diff	2.8(-4.08,9.68)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	13 wks	58/56	49.9(21.7)/50.1(21.3)	Mean Diff	-0.2(-8.18,7.78)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	52 wks	51/54	53.3(25.4)/53.6(22.1)	Mean Diff	-0.3(-9.54,8.94)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	6 wks	59/57	49.9(23.3)/50.8(23.2)	Mean Diff	-0.9(-9.45,7.65)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	78 wks	51/52	50.7(24.4)/55.6(23.6)	Mean Diff	-4.9(-14.29, 4.49)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	104 wks	53/55	54(23.3)/52.5(25.1)	Mean Diff	1.5(-7.74,10.74)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	26 wks	55/57	52(20.8)/50(20.7)	Mean Diff	2(-5.77,9.77)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	13 wks	58/56	46.8(21.9)/46.9(24.9)	Mean Diff	-0.1(-8.82,8.62)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	26 wks	55/57	45.1(20.6)/46.3(26.4)	Mean Diff	-1.2(-10.05, 7.65)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	6 wks	59/57	46.6(21)/49.8(23.3)	Mean Diff	-3.2(-11.37, 4.97)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	52 wks	51/54	44.5(24.3)/43.6(24.8)	Mean Diff	0.9(-8.6,10.4)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	104 wks	52/55	45(23)/42.3(24.2)	Mean Diff	2.7(-6.35,11.75)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	78 wks	51/52	46.8(22.8)/40.8(24.9)	Mean Diff	6(-3.33,15.33)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	78 wks	51/52	53.1(29.3)/55.6(26.6)	Mean Diff	-2.5(-13.45, 8.45)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	6 wks	59/57	49.9(30.8)/47.3(22.3)	Mean Diff	2.6(-7.27,12.47)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	104 wks	53/55	56.4(29.4)/53.8(27.5)	Mean Diff	2.6(-8.27,13.47)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	26 wks	55/57	52.5(28.7)/49.1(25.8)	Mean Diff	3.4(-6.83,13.63)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	13 wks	58/56	53.5(28.6)/49.9(21.6)	Mean Diff	3.6(-5.79,12.99)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	52 wks	51/54	56.4(28.4)/49.4(25.5)	Mean Diff	7(-3.47,17.47)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	104 wks	52/54	47.9(26.6)/49(27.2)	Mean Diff	-1.1(-11.46, 9.26)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	6 wks	59/57	49.2(26.5)/51(24.2)	Mean Diff	-1.8(-11.13, 7.53)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	52 wks	50/54	47.3(27.1)/49.3(24.5)	Mean Diff	-2(-12.08, 8.08)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	13 wks	58/56	49.6(24.2)/52.4(23.5)	Mean Diff	-2.8(-11.65, 6.05)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	78 wks	51/52	50.9(26.1)/49.1(25)	Mean Diff	1.8(-8.19,11.79)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic debridement	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	26 wks	55/57	51(25.9)/48.4(25.9)	Mean Diff	2.6(-7.1,12.3)	Not Sig.	inconclusive

PICO 11: Arthroscopic Debridement

Arthroscopic Lavage vs Control

Table 50: Arthroscopic Lavage vs Control

Quality: H=High; M=Moderate; L=Low	H	M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Moseley ; 2002	Kalunian ; 2000
Function		
Arthritis Impact Measurement Scale Walking-Bending	●	
Pain		
Arthritis Impact Measurement Scale Pain	●	
calculable MID outcomes		
WOMAC Total		●
WOMAC Function		●
WOMAC Stiffness		●
WOMAC Pain		●
sf-36 physical Function	●	
sf-36 physical pain	●	
patient pain VAS		●

Evidence Table 5750: Arthroscopic Lavage vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	78 wks	57/52	55.4(24.6)/55.6(23.6)	Mean Diff	-0.2(-9.36,8.96)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	6 wks	57/57	52.4(22.1)/50.8(23.2)	Mean Diff	1.6(-6.81,10.01)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	13 wks	59/56	53.7(23.1)/50.1(21.3)	Mean Diff	3.6(-4.6,11.8)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	52 wks	57/54	57.8(23.5)/53.6(22.1)	Mean Diff	4.2(-4.38,12.78)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	104 wks	56/55	56.7(24.1)/52.5(25.1)	Mean Diff	4.2(-5.06,13.46)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:Arthritis Impact Measurement Scale Pain	26 wks	59/57	54.8(21.6)/50(20.7)	Mean Diff	4.8(-2.98,12.58)	Not Sig.	na
Kalunian ; 2000/Moderate	11: Arthroscopic debridement-full arthroscopic Irrigation (3000ml saline)	11: Placebo/Control-Minimal Irrigation (250ml saline)	Pain:WOMAC pain likert	52 wks	41/49	-4.2(16.82)/-2.3(8.57)	Mean Diff	-1.9(-7.7,3.9)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kalunian ; 2000/Moderate	11: Arthroscopic debridement-full arthroscopic Irrigation (3000ml saline)	11: Placebo/Control-Minimal Irrigation (250ml saline)	Pain:patient pain VAS	52 wks	41/49	-1.47(8.65)/-0.12(0.54)	Mean Diff	-1.35(-4.08,1.38)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	26 wks	59/57	46(22)/46.3(26.4)	Mean Diff	-0.3(-9.26,8.66)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	52 wks	57/54	42.8(21.2)/43.6(24.8)	Mean Diff	-0.8(-9.51,7.91)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	6 wks	57/57	45.2(21.1)/49.8(23.3)	Mean Diff	-4.6(-12.85, 3.65)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	13 wks	59/56	47.1(21.1)/46.9(24.9)	Mean Diff	0.2(-8.35,8.75)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	104 wks	57/55	44.4(22.4)/42.3(24.2)	Mean Diff	2.1(-6.64,10.84)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Pain:sf-36 physical pain	78 wks	57/52	44.4(24.9)/40.8(24.9)	Mean Diff	3.6(-5.87,13.07)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	6 wks	57/57	47.2(28.8)/47.3(22.3)	Mean Diff	-0.1(-9.67,9.47)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	26 wks	59/57	48.7(31.6)/49.1(25.8)	Mean Diff	-0.4(-11,10.2)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	13 wks	59/56	47.9(30.1)/49.9(21.6)	Mean Diff	-2(-11.65, 7.65)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	104 wks	56/55	51.1(28.3)/53.8(27.5)	Mean Diff	-2.7(-13.2,7.8)	Not Sig.	na
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	78 wks	57/52	50.5(28.5)/55.6(26.6)	Mean Diff	-5.1(-15.56, 5.36)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:Arthritis Impact Measurement Scale Walking-Bending	52 wks	57/54	49.6(29.1)/49.4(25.5)	Mean Diff	0.2(-10.08, 10.48)	Not Sig.	na
Kalunian ; 2000/Moderate	11: Arthroscopic debridement-full arthroscopic Irrigation (3000ml saline)	11: Placebo/Control-Minimal Irrigation (250ml saline)	Function:WOMAC function likert	52 wks	41/49	-9.9(13.22)/-6.1(11.7)	Mean Diff	-3.8(-9.09,1.49)	Not Sig.	inconclusive
Kalunian ; 2000/Moderate	11: Arthroscopic debridement-full arthroscopic Irrigation (3000ml saline)	11: Placebo/Control-Minimal Irrigation (250ml saline)	Function:WOMAC stiffness likert	52 wks	41/49	-1.2(9.14)/-0.7(4.29)	Mean Diff	-0.5(-3.61,2.61)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	78 wks	57/52	47(28.8)/49.1(25)	Mean Diff	-2.1(-12.32, 8.12)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	6 wks	57/57	51.2(26.3)/51(24.2)	Mean Diff	0.2(-9.18,9.58)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	13 wks	59/56	52.9(26.7)/52.4(23.5)	Mean Diff	0.5(-8.78,9.78)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	52 wks	57/54	50(28)/49.3(24.5)	Mean Diff	0.7(-9.18,10.58)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	104 wks	57/54	50.9(27.3)/49(27.2)	Mean Diff	1.9(-8.36,12.16)	Not Sig.	inconclusive
Moseley ; 2002/High	11: Arthroscopic debridement-arthroscopic lavage	11: Placebo/Control-placebo surgery	Function:sf-36 physical Function	26 wks	59/57	53.4(27.6)/48.4(25.9)	Mean Diff	5(-4.84,14.84)	Not Sig.	inconclusive
Kalunian ; 2000/Moderate	11: Arthroscopic debridement-full arthroscopic Irrigation (3000ml saline)	11: Placebo/Control-Minimal Irrigation (250ml saline)	Composite:WOMAC total	52 wks	41/49	-15.5(25.63)/-8.9(14.49)	Mean Diff	-6.6(-15.61, 2.41)	Not Sig.	inconclusive

PICO 11: Arthroscopic Debridement

Arthroscopic Lavage vs Debridement

Table 51: Arthroscopic Lavage vs Debridement

Quality: H=High; M=Moderate; L=Low	**H**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Moseley ; 2002**
Function	
Arthritis Impact Measurement Scale Walking-Bending	●
Pain	
Arthritis Impact Measurement Scale Pain	●
calculable MID outcomes	
sf-36 physical Function	●
sf-36 physical pain	●

Evidence Table 5851: Arthroscopic Lavage vs Debridement

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:Arthritis Impact Measurement Scale Pain	6 wks	57/59	52.4(22.1)/49.9(23.3)	Mean Diff	2.5(-5.85,10.85)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:Arthritis Impact Measurement Scale Pain	104 wks	56/53	56.7(24.1)/54(23.3)	Mean Diff	2.7(-6.3,11.7)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:Arthritis Impact Measurement Scale Pain	26 wks	59/55	54.8(21.6)/52(20.8)	Mean Diff	2.8(-5.07,10.67)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:Arthritis Impact Measurement Scale Pain	13 wks	59/58	53.7(23.1)/49.9(21.7)	Mean Diff	3.8(-4.41,12.01)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:Arthritis Impact Measurement Scale Pain	52 wks	57/51	57.8(23.5)/53.3(25.4)	Mean Diff	4.5(-4.87,13.87)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:Arthritis Impact Measurement Scale Pain	78 wks	57/51	55.4(24.6)/50.7(24.4)	Mean Diff	4.7(-4.66,14.06)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:sf-36 physical pain	104 wks	57/52	44.4(22.4)/45(23)	Mean Diff	-0.6(-9.24,8.04)	Not Sig.	inconclusive

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:sf-36 physical pain	6 wks	57/59	45.2(21.1)/46.6(21)	Mean Diff	-1.4(-9.15,6.35)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:sf-36 physical pain	52 wks	57/51	42.8(21.2)/44.5(24.3)	Mean Diff	-1.7(-10.45, 7.05)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:sf-36 physical pain	78 wks	57/51	44.4(24.9)/46.8(22.8)	Mean Diff	-2.4(-11.5,6.7)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:sf-36 physical pain	13 wks	59/58	47.1(21.1)/46.8(21.9)	Mean Diff	0.3(-7.58,8.18)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Pain:sf-36 physical pain	26 wks	59/55	46(22)/45.1(20.6)	Mean Diff	0.9(-7.01,8.81)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:Arthritis Impact Measurement Scale Walking-Bending	78 wks	57/51	50.5(28.5)/53.1(29.3)	Mean Diff	-2.6(-13.66, 8.46)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:Arthritis Impact Measurement Scale Walking-Bending	6 wks	57/59	47.2(28.8)/49.9(30.8)	Mean Diff	-2.7(-13.66, 8.26)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:Arthritis Impact Measurement Scale Walking-Bending	26 wks	59/55	48.7(31.6)/52.5(28.7)	Mean Diff	-3.8(-14.99, 7.39)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:Arthritis Impact Measurement Scale Walking-Bending	104 wks	56/53	51.1(28.3)/56.4(29.4)	Mean Diff	-5.3(-16.27, 5.67)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:Arthritis Impact Measurement Scale Walking-Bending	13 wks	59/58	47.9(30.1)/53.5(28.6)	Mean Diff	-5.6(-16.35, 5.15)	Not Sig.	na
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:Arthritis Impact Measurement Scale Walking-Bending	52 wks	57/51	49.6(29.1)/56.4(28.4)	Mean Diff	-6.8(-17.78, 4.18)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:sf-36 physical Function	78 wks	57/51	47(28.8)/50.9(26.1)	Mean Diff	-3.9(-14.37, 6.57)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:sf-36 physical Function	6 wks	57/59	51.2(26.3)/49.2(26.5)	Mean Diff	2(-7.71,11.71)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:sf-36 physical Function	26 wks	59/55	53.4(27.6)/51(25.9)	Mean Diff	2.4(-7.53,12.33)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:sf-36 physical Function	52 wks	57/50	50(28)/47.3(27.1)	Mean Diff	2.7(-7.88,13.28)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:sf-36 physical Function	104 wks	57/52	50.9(27.3)/47.9(26.6)	Mean Diff	3(-7.24,13.24)	Not Sig.	inconclusive
Moseley ; 2002/High	10: Needle lavage-arthroscopic lavage	10: Non-arthro Tx-arthroscopic debridement	Function:sf-36 physical Function	13 wks	59/58	52.9(26.7)/49.6(24.2)	Mean Diff	3.3(-6.03,12.63)	Not Sig.	inconclusive

PICO 11: Arthroscopic Debridement

Intraarticular Hyaluronic Acid vs Arthroscopic Debridement

Table 52: Intraarticular Hyaluronic Acid vs Arthroscopic Debridement

Quality: H=High; M=Moderate; L=Low	L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Saeed; 2015
Pain	
kss pain score 40 or greater	↓

Evidence Table 5952: Intraarticular Hyaluronic Acid vs Arthroscopic Debridement

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Saeed; 2015/Low	11: Arthroscopic debridement-Arthroscopic deribement	10: IA HA-Hyaluronic acid	Pain:kss pain score 40 or greater	1 mos	60/60	36.67%/60%	pvalue	.61(.413, .904)	Group 2	na
Saeed; 2015/Low	11: Arthroscopic debridement-Arthroscopic deribement	10: IA HA-Hyaluronic acid	Pain:kss pain score 40 or greater	3 mos	60/60	36.67%/60%	pvalue	.61(.413, .904)	Group 2	na
Saeed; 2015/Low	11: Arthroscopic debridement-Arthroscopic deribement	10: IA HA-Hyaluronic acid	Pain:kss pain score 40 or greater	6 mos	60/60	36.67%/60%	pvalue	.61(.413, .904)	Group 2	na

PICO 12: Partial Meniscectomy

Partial Meniscectomy vs Control

Table 53: Partial Meniscectomy vs Control

Quality: H=High; M=Moderate; L=Low	M		
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Herrlin; 2007*	Katz; 2013/2019#	van de Graaf; 2018##
calculable MID outcomes			
VAS weight bearing pain			●
WOMAC function		●	
Function			
KOOS Activities of Daily Living	●		
KOOS Symptoms	●		
koos sports/rec	●		
IKDC score			↑
sf-36 physical activity		●	
Pain			
KOOS pain 3 months		↑	
KOOS pain (6 and 12 months)		●	
KOOS Pain (8 weeks and 6 months)	●	●	
QOL			
KOOS QoL	●		
subgroup analysis of IKDC improvement			
mechanical complaints-yes vs. no			●
tear location: medial vs. lateral			●
tear location: both medial and lateral vs. lateral only			●
OA severity: moderate/severe vs low			●
sex: female vs male			●
age: older vs younger			●
BMI: overweight vs. obese**			↓
BMI: normal vs. obese**			↓
Adverse Events			
Acute myocardial infarction			●
Sudden death			●
Venous Thromboembolism			●
Neurological			●
Alcoholic pancreatitis			●
Lymph node malignancy			●
Rectal polyp			●
Arthroscopy needed			●
need for arthroplasty		●	●
serious adverse events			●
Reactive arthritis			●
Knee pain resulting in extra consultation			●
Pain in back			●
Surgical site infection			●
non serious adverse events			●

Evidence Table 6053: Partial Meniscectomy vs Control

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	WOMAC functional improvement	6 months	161/169	None	MeanDiff	2.4 (−1.8 to 6.5)	Not sig.	Not clinically significant
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	KOOS Pain improvement	6 months	161/169	None	MeanDiff	2.9 (−1.2 to 7.0)	Not sig.	na
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	SF-36 physical activity score	6 months	161/169	None	MeanDiff	1.1 (−4.4 to 6.6)	Not sig.	na
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	WOMAC functional improvement	12 months	161/169	None	MeanDiff	0.7 (−3.5 to 4.9)	Not sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	KOOS Pain improvement	12 months	161/169	None	MeanDiff	−0.4 (−4.8 to 4.0)	Not sig.	na
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	SF-36 physical activity score	12 months	161/169	None	MeanDiff	−3.0 (−8.8 to 2.7)	Not sig.	na
Katz; 2013/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	KOOS Pain raw score at 3 months	3 months	161/169	None	P value	P<.05	Immediate partial meniscectomy	na
Katz; 2019/Moderate	Immediate arthroscopic partial meniscectomy for menical tear and OA	Immediate physical therapy with optional delayed partial meniscectomy if PT is ineffective	Need for TKA	5 years	161/169	None	HR	2(.84, 4.9)	Not sig.	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Pain:Koos pain	26 weeks	47/43	none	pvalue	NS	None	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Pain:Koos pain	8 weeks	47/43	none	pvalue	NS	None	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Function:koos activities of daily living	8 weeks	47/43	none	pvalue	NS	None	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Function:koos activities of daily living	26 weeks	47/43	none	pvalue	NS	None	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Function:koos sports/rec	8 weeks	47/43	none	pvalue	NS	None	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Function:koos sports/rec	26 weeks	47/43	none	pvalue	NS	None	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Function:koos symptoms	8 weeks	47/43	none	pvalue	NS	None	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	Function:koos symptoms	26 weeks	47/43	none	pvalue	NS	None	na
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	QOL:koos QOL	8 weeks	47/43	none	pvalue	NS	None	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Herrlin; 2007/Moderate	12: Partial meniscectomy-arthroscopic partial meniscectiony followed by exercise	12: Placebo/Control-exercise only	QOL:koos QOL	26 weeks	47/43	none	pvalue	NS	None	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC score	all follow-ups	159/162	none	MeanDiff	4.4(1.3,7.5)	group 1	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC score	3 months	159/162	none	MeanDiff	1.1(-2.8,5)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC score	6 months	159/162	none	MeanDiff	4.2(0.3,8.1)	group 1	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC score	12 months	159/162	none	MeanDiff	7.1(3.1,11.1)	group 1	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC score	24 months	159/162	none	MeanDiff	5.3(1.3,9.3)	group 1	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	VAS Weight Bearing Pain	all follow-ups	159/162	none	MeanDiff	-6.7(-11.3,-2.2)	group 1	not clinically significant
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	VAS Weight Bearing Pain	3 months	159/162	none	MeanDiff	-3.3(-9.3,-2.7)	group 1	not clinically significant
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	VAS Weight Bearing Pain	6 months	159/162	none	MeanDiff	-9.1(-15.2,-3)	group 1	not clinically significant
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	VAS Weight Bearing Pain	12 months	159/162	none	MeanDiff	-7(-13.3,-0.67)	group 1	not clinically significant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	VAS Weight Bearing Pain	24 months	159/162	none	MeanDiff	-8.3(-14.9,-1.7)	group 1	not clinically significant
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-mechanical complaints-yes vs. no	24 months	159/162	none	MeanDiff	-.73(-6.63,5.17)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-tear location: medial vs. lateral	24 months	159/162	none	MeanDiff	-6.4(-14.5 – 1.7)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-tear location: both medial and lateral vs. lateral only	24 months	159/162	none	MeanDiff	-7(-22.7 – 8.8)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-OA severity: moderate/severe vs low	24 months	159/162	none	MeanDiff	1.01(-5.07 – 7.10)	not sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-sex: female vs male	24 months	159/162	none	MeanDiff	-1.5(-7.2 – 4.2)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-age: older vs younger	24 months	159/162	none	MeanDiff	.14(-0.29 – 0.57)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-BMI: overweight vs. obese	24 months	159/162	none	MeanDiff	-9.6(-17.0, -2.2)	effect stronger in obese subgroup	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	IKDC interaction effect-BMI: normal vs. obese	24 months	159/162	none	MeanDiff	-9.4(-17.1, -1.6)	effect stronger in obese subgroup	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Acute myocardial infarction	24 months	159/162	0%\0.62%	RD	-.62(-3.03,2.18)	not sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Sudden death	24 months	159/162	0%\0.62%	RD	-.62(-3.03,2.18)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Venous Thromboembolism	24 months	159/162	0%\0%	RD	0(-2.36,2.32)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Neurological	24 months	159/162	0.63%\0.62%	RR	1.02(.06,16.15)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Alcoholic pancreatitis	24 months	159/162	0%\0.62%	RD	-.62(-3.03,2.18)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Lymph node malignancy	24 months	159/162	0.63%\0%	RD	.63(-2.22,3)	not sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Rectal polyp	24 months	159/162	0.63%\0%	RD	.63(-2.22,3)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Arthroscopy needed	24 months	159/162	1.89%\0.62%	RR	3.06(.32,29.07)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	needed tka	24 months	159/162	1.26%\1.85%	RR	.68(.12,4.01)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	serious adverse events	24 months	159/162	5.66%\4.94%	RR	1.15(.45,2.9)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Reactive arthritis	24 months	159/162	0.63%\0%	RD	.63(-2.22,3)	not sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Knee pain resulting in extra consultation	24 months	159/162	3.77%\1.23%	RR	3.06(.63,14.92)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Pain in back	24 months	159/162	1.26%\0%	RD	1.26(-1.95,3.75)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	Surgical site infection	24 months	159/162	0%\0%	RD	0(-2.36,2.32)	not sig.	na
van de Graaf; 2018/ Moderate	12: Partial Meniscectomy-Partial meniscectomy	12: Physical therapy Only-with option to have meniscectomy at a later data	non serious adverse events	24 months	159/162	5.66%\2.47%	RR	2.29(.72,7.29	not sig.	na

PICO 13: Osteotomy

High Tibial Osteotomy vs Conservative Treatment (Valgus Knee Brace)

Table 54: High Tibial Osteotomy vs Conservative Treatment

Quality: H=High; M=Moderate; L=Low	L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	van Outeren;2017
Calculable MID outcomes	
VAS Pain	
function	
Hospital for Special Surgery Function score	

Evidence Table 6154: High Tibial Osteotomy vs Conservative Treatment

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
van Outeren/Low	13: High Tibial Osteotomy	13: conservative knee brace treatment	VAS Pain(cm)	1 year	83/30	none	Mean Diff.	-1.1(-2.2,-.1)	Osteotomy	Possibly clinically significant
van Outeren/Low	13: High Tibial Osteotomy	13: conservative knee brace treatment	Hospital For Special Surgery Score	1 year	83/30	none	Mean Diff	2.1(-3.1,.73)	Not Sig.	na

PICO 13: Osteotomy

Open Wedge Osteotomy vs Closed Wedge Osteotomy

Table 55: Open Wedge vs Closed Wedge Osteotomy

Quality: H=High; M=Moderate; L=Low	H			M
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Nerhus; 2017	Kim; 2016	Brouwer; 2006 (a)	Duivenvoorden; 2014
Composite				
KSS Score		●		
Lysholm Knee Score	●			
Oxford Knee Score	●			
Function				
KOOS Activities of Daily Living	●			●
KOOS Sports/Recreation				●
KOOS Symptoms	●			●
KSS Function		●		
Walking Distance (m)				●
Flexion Contracture (deg)(scale direction?)		↑		
HSS Score		●		●
Passive ROM	●			
ROM (deg)(scale direction?)		●		
Tegner Activity Scale	●			
UCLA Activity Scale	●			
Walk distance(km)			●	
Pain				
KOOS Pain	●			●
Adverse events				
Any Adverse Event	●			
Infection	●			
Pneumonia	●			
Discomfort Due to Lower Limb Length Discrepancy		↓		
Fracture of the tibial plateau			●	
Iliac-crest morbidity			↓	
Neurological AE	●			
Nonunion			●	
Nonunion of tibia/fibia	●			
Pain in proximal tibiofibular joint			●	
Palsy of the common peroneal nerve			●	
Re-operation (further valgus correction)			●	
Re-operation (reduction of valgus correction			●	
Re-operations (metal removal)	●			
Re-operations due to AE	●			
Removal of osteosynthesis material			↓	
Revision to joint replacement			●	
TKA During Follow-Up	●			↑
Thromboemobolic AE	●			
Wound infection			●	
calculable MID outcomes				
VAS Pain		●	●	●
QOL				
KOOS QoL	●			●
OA progression				
Progression of Lateral Compartment OA (KL Scale)				●
Progression of Medial Compartment OA (KL Scale)				●

Evidence Table 6255: Open Wedge Osteotomy vs Closed Wedge Osteotomy

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:KOOS Pain	3 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:KOOS Pain	24 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:KOOS Pain	12 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:KOOS Pain	6 mos	70	none	pvalue	NS	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:KOOS Pain	6 yrs	36/45	67.7(24.7)/67.3(26.2)	Mean Diff	0.4(-10.9,11.7)	Not Sig.	na
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:VAS Pain	1 yrs	30/30	1.5(0.5)/1.1(1.4)	Mean Diff	0.4(-0.15,0.95)	Not Sig.	clinically insignificant
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:VAS Pain	6 yrs	36/45	3.4(3.2)/4(3.2)	Mean Diff	-0.6(-2.03,0.83)	Not Sig.	inconclusive
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Pain:VAS Pain	1 yrs	36/45	3.6(2.9)/3.6(2.2)	Mean Diff	0(-1.17,1.17)	Not Sig.	clinically insignificant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Pain:VAS Pain	52 weeks	45/47	3.6(2.9)/3.6(2.2)	Mean Diff	0(-1.07,1.07)	Not Sig.	clinically insignificant
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Flexion Contracture (deg)(scale direction?)	1 yrs	30/30	0.3(1.2)/1(1.4)	Mean Diff	-0.7(-1.37,-0.03)	Group 1	na
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:HSS Score	1 yrs	30/30	92.2(3.1)/93.7(3.1)	Mean Diff	-1.5(-3.1,0.1)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:HSS Score	6 yrs	36/45	80.8(13.8)/81.8(13)	Mean Diff	-1(-6.99,4.99)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:HSS Score	1 yrs	36/45	80.9(13.5)/79.4(12)	Mean Diff	1.5(-4.23,7.23)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Activities of Daily Living	24 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Activities of Daily Living	12 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Activities of Daily Living	3 mos	70	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Activities of Daily Living	6 mos	70	none	pvalue	NS	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Activities of Daily Living	6 yrs	36/45	67.7(26.8)/68.2(27.2)	Mean Diff	-0.5(-12.52, 11.52)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Sports/Recreation	6 yrs	36/45	36.2(32.1)/40.4(30.7)	Mean Diff	-4.2(-18.23, 9.83)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Symptoms	12 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Symptoms	3 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Symptoms	6 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Symptoms	24 mos	70	none	pvalue	NS	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KOOS Symptoms	6 yrs	36/45	70(22.8)/68.7(21)	Mean Diff	1.3(-8.51,11.11)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:KSS Function	1 yrs	30/30	88.4(5)/90.1(6.3)	Mean Diff	-1.7(-4.64,1.24)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Passive ROM	3 mos	35/35	127(8.73)/128(8.73)	Mean Diff	-1(-5.16,3.16)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Passive ROM	12 mos	35/35	132(8.73)/133(8.73)	Mean Diff	-1(-5.16,3.16)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Passive ROM	6 mos	35/35	131(8.73)/133(8.73)	Mean Diff	-2(-6.16,2.16)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Passive ROM	24 mos	35/35	130(8.73)/134(8.73)	Mean Diff	-4(-8.16,0.16)	Not Sig.	na
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:ROM (deg)(scale direction?)	1 yrs	30/30	135.3(5.7)/134(9.6)	Mean Diff	1.3(-2.8,5.4)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Tegner Activity Scale	24 mos	35/35	2.9(1.31)/3.1(1.6)	Mean Diff	-0.2(-0.9,0.5)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Tegner Activity Scale	3 mos	35/35	1.6(1.46)/1.8(1.46)	Mean Diff	-0.2(-0.9,0.5)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Tegner Activity Scale	12 mos	35/35	3(1.46)/3.4(1.46)	Mean Diff	-0.4(-1.1,0.3)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Tegner Activity Scale	6 mos	35/35	2.1(1.31)/2.5(1.6)	Mean Diff	-0.4(-1.1,0.3)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:UCLA Activity Scale	24 mos	35/35	6(1.89)/6.4(1.89)	Mean Diff	-0.4(-1.3,0.5)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:UCLA Activity Scale	6 mos	35/35	4.9(1.89)/5.4(1.89)	Mean Diff	-0.5(-1.4,0.4)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:UCLA Activity Scale	3 mos	35/35	3.9(1.89)/4.5(1.89)	Mean Diff	-0.6(-1.5,0.3)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:UCLA Activity Scale	12 mos	35/35	6.2(1.89)/6(1.89)	Mean Diff	0.2(-0.7,1.1)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Function:Walk distance(km)	52 weeks	45/47	5.3(4.4)/4.6(3.6)	Mean Diff	0.7(-0.97,2.37)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Walking Distance (m)	1 yrs	36/45	5.3(4.4)/4.6(3.6)	Mean Diff	0.7(-1.11,2.51)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Function:Walking Distance (m)	6 yrs	36/45	8.2(4.7)/6.7(4.2)	Mean Diff	1.5(-0.5,3.5)	Not Sig.	na
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:KSS Score	1 yrs	30/30	91.4(5.1)/93.1(2.7)	Mean Diff	-1.7(-3.82,0.42)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Lysholm Knee Score	6 mos	35/35	69(15.72)/69.1(15.87)	Mean Diff	-0.1(-7.63,7.43)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Lysholm Knee Score	24 mos	35/35	70.6(15.72)/73.8(16.59)	Mean Diff	-3.2(-10.91, 4.51)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Lysholm Knee Score	12 mos	35/35	73.5(15.87)/70.3(16.16)	Mean Diff	3.2(-4.44,10.84)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Lysholm Knee Score	3 mos	35/35	54.1(15.72)/50.5(15.87)	Mean Diff	3.6(-3.93,11.13)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Oxford Knee Score	24 mos	35/35	36.7(6.55)/37.4(6.84)	Mean Diff	-0.7(-3.89,2.49)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Oxford Knee Score	3 mos	35/35	28.3(6.55)/27(6.55)	Mean Diff	1.3(-1.82,4.42)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Oxford Knee Score	6 mos	35/35	34.3(6.7)/33(6.55)	Mean Diff	1.3(-1.86,4.46)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Composite:Oxford Knee Score	12 mos	35/35	37.8(6.7)/35(6.55)	Mean Diff	2.8(-0.36,5.96)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	QOL:KOOS QoL	6 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	QOL:KOOS QoL	24 mos	70	none	pvalue	NS	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	QOL:KOOS QoL	12 mos	70	none	pvalue	NS	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	QOL:KOOS QoL	3 mos	70	none	pvalue	NS	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	QOL:KOOS QoL	6 yrs	36/45	44.6(25.8)/47.2(27.9)	Mean Diff	-2.6(-14.51, 9.31)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	OA progression:Progression of Lateral Compartment OA (KL Scale)	6 yrs	33/36	96.97%/91.67%	RR	1.06(0.94,1.19)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	OA progression:Progression of Medial Compartment OA (KL Scale)	6 yrs	33/36	63.64%/77.78%	RR	0.82(0.6,1.12)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Any Adverse Event	24 mos	35/35	28.57%/37.14%	RR	0.77(0.39,1.52)	Not Sig.	na
Kim; 2016/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Discomfort Due to Lower Limb Length Discrepancy	1 yrs	30/30	36.67%/6.67%	RR	5.5(1.33,22.73)	Group 2	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Fracture of the tibial plateau	52 weeks	45/47	4.44%/2.13%	RR	2.09(0.2,22.24)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Iliac-crest morbidity	52 weeks	45/47	20%/0%	RD	20(6.177,31.831)	Group 2	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Infection	24 mos	35/35	14.29%/2.86%	RR	5(0.62,40.64)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Neurological AE	24 mos	35/35	5.71%/5.71%	RR	1(0.15,6.71)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Nonunion	52 weeks	45/47	4.44%/0%	RD	4.444(-5.939,12.657)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Nonunion of tibia/fibia	24 mos	35/35	2.86%/17.14%	RR	0.17(0.02,1.31)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Pain in proximal tibiofibular joint	52 weeks	45/47	0%/2.13%	RD	-2.128(-10.185,6.858)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Palsy of the common peroneal nerve	52 weeks	45/47	0%/2.13%	RD	-2.128(-10.185,6.858)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Pneumonia	24 mos	35/35	2.86%/0%	RD	2.857(-8.819, 13.023)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Re-operation (further valgus correction)	52 weeks	45/47	6.67%/0%	RD	6.667(-4.523, 15.397)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Re-operation (reduction of valgus correction	52 weeks	45/47	6.67%/0%	RD	6.667(-4.523, 15.397)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Re-operations (metal removal)	24 mos	37/35	21.62%/11.43%	RR	1.89(0.62,5.73)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Re-operations due to AE	24 mos	36/35	5.56%/22.86%	RR	0.24(0.06,1.07)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Removal of osteosynthesis material	52 weeks	45/47	60%/23.4%	RR	2.56(1.45,4.53)	Group 2	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Revision to joint replacement	52 weeks	45/47	0%/2.13%	RD	-2.128(-10.185,6.858)	Not Sig.	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:TKA During Follow-Up	24 mos	35/35	0%/2.86%	RD	-2.857(-13.023,8.819)	Not Sig.	na
Duivenvoorden; 2014/Moderate	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:TKA During Follow-Up	6 yrs	36/45	8.33%/22.22%	percent difference in hazard rates	-14(-21.7, -.2)	Group 1	na
Nerhus; 2017/High	13: Osteotomy-Osteotomy (Opening-Wedge)	13: Osteotomy-Osteotomy (Closing-Wedge)	Adverse events:Thromboemobolic AE	24 mos	35/35	5.71%/11.43%	RR	0.5(0.1,2.56)	Not Sig.	na
Brouwer; 2006 (a)/High	13: Osteotomy-Open wedge osteotomy	13: Non-arthro Tx-closed wedge osteotomy	Adverse events:Wound infection	52 weeks	45/47	2.22%/0%	RD	2.222(-7.122, 9.996)	Not Sig.	na

PICO 13: Osteotomy

Distal Tibial Tubercle Osteotomy vs Proximal Tibial Tubercle Osteotomy

Table 56: Distal Tibial Tubercle Osteotomy vs Proximal Tibial Tubercle Osteotomy

Quality: H=High; M=Moderate; L=Low	**L**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Ogawa; 2019**
Composite	
KSS Subtotal knee score	●
Function	
KSS Range of motion	●
KSS Stability	●
KSS Stairs	●
KSS Subtotal functional score	●
KSS Walking	●
Pain	
KSS Pain Subscale	●

Evidence Table 6356: Distal Tibial Tubercle Osteotomy vs Proximal Tibial Tubercle Osteotomy

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Pain:KSS Pain Subscale	1 yrs	43/41	47.6(16.25)/45(31.68)	Mean Diff	2.6(-8.47,13.67)	Not Sig.	na
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Function:KSS Range of motion	1 yrs	43/41	24.9(3.25)/24.7(7.92)	Mean Diff	0.2(-2.47,2.87)	Not Sig.	na
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Function:KSS Stability	1 yrs	43/41	25(8.12)/24.9(7.92)	Mean Diff	0.1(-3.38,3.58)	Not Sig.	na
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Function:KSS Stairs	1 yrs	43/41	45.1(32.49)/42.1(31.68)	Mean Diff	3(-10.93, 16.93)	Not Sig.	na
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Function:KSS Subtotal functional score	1 yrs	43/41	94.4(64.99)/88.6(71.28)	Mean Diff	5.8(-23.86, 35.46)	Not Sig.	na
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Function:KSS Walking	1 yrs	43/41	49(32.49)/48.5(31.68)	Mean Diff	0.5(-13.43, 14.43)	Not Sig.	na
Ogawa; 2019/Low	13: Osteotomy-Distal Tibial Tubercle Osteotomy	13: Osteotomy-Proximal Tibial Tubercle Osteotomy	Composite:KSS Subtotal knee score	1 yrs	43/41	97.6(24.37)/94.2(31.68)	Mean Diff	3.4(-8.93,15.73)	Not Sig.	na

PICO 13: Osteotomy

Fibular Shaft Osteotomy vs Tibiofibular Osteotomy

Table 57: Fibular Shaft Osteotomy vs Tibiofibular Osteotomy

Quality: H=High; M=Moderate; L=Low	**L**
↑ Better Outcomes **↓ Worse Outcomes** **● Not Significant**	**Park; 2019**
Composite	
AKSKS(scale not provided; follow-up not specified beyond ">2 years")	●
HSS(scale not provided; follow-up not specified beyond ">2 years")	●
IKDC(scale not provided; follow-up not specified beyond ">2 years")	●
LKS(scale not provided; follow-up not specified beyond ">2 years")	↑
Function	
KSFS(scale not provided; follow-up not specified beyond ">2 years")	●
calculable MID outcomes	
WOMAC(scale not provided; follow-up not specified beyond ">2 years")	↑

Evidence Table 6457: Fibular Shaft Osteotomy vs Tibiofibular Osteotomy

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Park; 2019/Low	13: Osteotomy-Fibular Shaft Osteotomy(1x)	13: Osteotomy-Tibiofibular Division(1x)	Function:KSFS(scale not provided; follow-up not specified beyond ">2 years")	Postop	51/45	79.9(17.3)/84.4(21.2)	Mean Diff	-4.5(-12.42, 3.42)	Not Sig.	na
Park; 2019/Low	13: Osteotomy-Fibular Shaft Osteotomy(1x)	13: Osteotomy-Tibiofibular Division(1x)	Composite:AKSKS(scale not provided; follow-up not specified beyond ">2 years")	Postop	51/45	92(10.8)/90.6(14.1)	Mean Diff	1.4(-3.75,6.55)	Not Sig.	na
Park; 2019/Low	13: Osteotomy-Fibular Shaft Osteotomy(1x)	13: Osteotomy-Tibiofibular Division(1x)	Composite:HSS(scale not provided; follow-up not specified beyond ">2 years")	Postop	51/45	90.6(10.1)/88.5(11.9)	Mean Diff	2.1(-2.41,6.61)	Not Sig.	na
Park; 2019/Low	13: Osteotomy-Fibular Shaft Osteotomy(1x)	13: Osteotomy-Tibiofibular Division(1x)	Composite:IKDC(scale not provided; follow-up not specified beyond ">2 years")	Postop	51/45	58.1(17.2)/51.7(19.2)	Mean Diff	6.4(-1.03,13.83)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Park; 2019/Low	13: Osteotomy-Fibular Shaft Osteotomy(1x)	13: Osteotomy-Tibiofibular Division(1x)	Composite:LKS(scale not provided; follow-up not specified beyond ">2 years")	Postop	51/45	84.6(11.2)/71.4(13.3)	Mean Diff	13.2(8.18,18.22)	Group 1	na
Park; 2019/Low	13: Osteotomy-Fibular Shaft Osteotomy(1x)	13: Osteotomy-Tibiofibular Division(1x)	Composite:WOMAC(scale not provided; follow-up not specified beyond ">2 years")	Postop	51/45	10.1(9.8)/16.5(10.1)	Mean Diff	-6.4(-10.45,-2.35)	Group 1	possibly clinically significant

PICO 13: Osteotomy

I-Balance Medial Opening Wedge High Tibial Osteotomy vs High Tibial Osteotomy with Other Implant

Table 58: I-Balance Medial Opening Wedge High Tibial Osteotomy vs High Tibial Osteotomy with Other Implant

Quality: H=High; M=Moderate; L=Low	L
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant	Getgood ; 2013
Function	
SF-36 Physical health	●
KOOS Sports and Recreation	●
KOOS Functions of Daily Life	●
Other	
Altered sensation around wound	●
Impaired osteotomy healing	●
Impaired wound healing	●
KOOS Other Symptoms	●
Ligament laxity	●
Pain	
KOOS Pain	●
Persistent joint line pain	●
Adverse events	
Joint Stiffness	●
Infection	●
DVT	●
Fasciitis	●
Fracture	●
Medical device complication	●
Persistent joint swelling	↓
QOL	
SF-36 Mental Health	●
KOOS Quality of Life	●

Evidence Table 6558: I-Balance Medial Opening Wedge High Tibial Osteotomy vs High Tibial Osteotomy with Other Implant

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	QoL:SF-36 Mental Health	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	QoL:SF-36 Mental Health	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Pain:KOOS Pain	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Pain:KOOS Pain	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Pain:Persistent joint line pain	12 mos	32/32	50%/31.25%	RR	1.6(0.86,2.97)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Function:KOOS Functions of Daily Life	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Function:KOOS Functions of Daily Life	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Function:KOOS Sports and Recreation	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Function:KOOS Sports and Recreation	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Function:SF-36 Physical Health	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Function:SF-36 Physical Health	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	QOL:KOOS Quality of Life	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	QOL:KOOS Quality of Life	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Other:Altered sensation around wound	12 mos	32/32	12.5%/9.38%	RR	1.33(0.32,5.49)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Other:Impaired osteotomy healing	12 mos	32/32	6.25%/12.5%	RR	0.5(0.1,2.54)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Other:Impaired wound healing	12 mos	32/32	28.13%/25%	RR	1.13(0.5,2.55)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Other:KOOS Other Symptoms	6 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Other:KOOS Other Symptoms	12 mos		none	pvalue	NS	iBalance Medial Opening Wedge High Tibial Os	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Other:Ligament laxity	12 mos	32/32	3.13%/0%	RD	3.125 (-9.494, 14.147)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Deep vein thrombosis	12 mos	32/32	3.13%/0%	RD	3.125 (-9.494, 14.147)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Fasciitis	12 mos	32/32	0%/3.13%	RD	-3.125 (-14.147,9.494)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Fracture	12 mos	32/32	12.5%/6.25%	RR	2(0.39,10.16)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Infection	12 mos	32/32	3.13%/0%	RD	3.125 (-9.494, 14.147)	Not Sig.	na

study/quality	Group1	Group2	Outcome	time	Ns	data grp1/grp2	result type	Result (95% CI)	Favored Group	Clinical Sig.
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Joint stiffness	12 mos	32/32	3.13%/3.13%	RR	1(0.07,15.3)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Medical device complication	12 mos	32/32	0%/3.13%	RD	-3.125 (-14.147,9.494)	Not Sig.	na
Getgood ; 2013/Low	13: Osteotomy-iBalance Medial Opening Wedge High Tibial Osteotomy	13: Non-arthro Tx-High tibial osteotomy with either a puddu plate or tomofix plate	Adverse events:Persistent joint swelling	12 mos	32/32	28.13%/6.25%	RR	4.5(1.05,19.22)	Group 2	na