

## *Treatment of Osteoarthritis of the Knee, 2<sup>nd</sup> edition*

### **SUMMARY OF RECOMMENDATIONS**

This summary of the AAOS clinical practice guideline, “*Treatment of Osteoarthritis of the Knee*” 2<sup>nd</sup> edition, contains a list of the evidence based treatment recommendations and includes only less invasive alternatives to knee replacement. Discussion of how each recommendation was developed and the complete evidence report are contained in the full guideline at [www.aaos.org/guidelines](http://www.aaos.org/guidelines). Readers are urged to consult the full guideline for the comprehensive evaluation of the available scientific studies. The recommendations were established using methods of evidence-based medicine that rigorously control for bias, enhance transparency, and promote reproducibility.

This summary of recommendations is not intended to stand alone. Medical care should be based on evidence, a physician’s expert judgment and the patient’s circumstances, values, preferences and rights. For treatment procedures to provide benefit, mutual collaboration with shared decision-making between patient and physician/allied healthcare provider is essential.

### **Conservative Treatments: Recommendations 1-6**

#### **RECOMMENDATION 1**

We recommend that patients with symptomatic osteoarthritis of the knee participate in self-management programs, strengthening, low-impact aerobic exercises, and neuromuscular education; and engage in physical activity consistent with national guidelines.

#### **Strength of Recommendation: Strong**

Description: Evidence is based on two or more “High” strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm and/or that the quality of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

#### **RATIONALE**

This recommendation is rated strong because of seven high-strength studies of which five showed beneficial outcomes. The exercise interventions were predominantly conducted under supervision, most often by a physical therapist. The self-management interventions were led by various healthcare providers including rheumatologists, nurses, physical and occupational therapists, and health educators. The evidence supports the use of self-management programs in primary care patients with knee osteoarthritis. One of the studies used an existing evidence-based program, the Arthritis Self-Management Program (ASMP), which was modified to include an exercise component.<sup>20</sup> In a high-strength study by Coleman et al.,<sup>21</sup> patients in a 6-week self-management program demonstrated statistically significant and possibly minimum clinically important improvements in WOMAC Pain, Stiffness, Function, and Total scores at eight weeks as compared to wait-listed controls. The program in that study was based on the same theoretical framework as the ASMP, but included content that was specifically tailored to patients with knee osteoarthritis.

Studies in this review reported improvements in 29 of 37 outcomes favoring strength training over a control (usual care, education, or no treatment). Statistically significant and clinically important improvements were reported for VAS Pain, WOMAC Pain, and WOMAC Function scores.

In addition, 7 of 23 outcomes indicated statistically significant improvements with strengthening exercises, when performed as part of a physical therapy treatment program, versus control.<sup>22-24</sup> Three of the seven outcomes were clinically significant and one was possibly clinically significant. One study reported statistically significant and possibly clinically significant improvement in WOMAC Total score following a combination of knee exercise and manual physical therapy as compared to subtherapeutic ultrasound (control).<sup>25</sup>

Studies also addressed the type and setting for strength training. Long-term outcomes did not vary among isometric, isotonic, or isokinetic exercises.<sup>26</sup> Both weight-bearing and nonweight-bearing exercises were superior to control in improving physical function, however, the results were conflicting when the exercises were compared to each other.<sup>27</sup> High-resistance strength training led to significantly faster walk times on spongy surfaces as compared to low-resistance training<sup>28</sup>. Ebnezar et al.<sup>29-31</sup> compared a combination of yoga and physical therapy to physical therapy alone. All eight outcomes were statistically and clinically significant favoring the combined treatment group measured by WOMAC Function and the SF-36 Physical Function and Bodily Pain subscales. Aquatic therapy was also deemed a suitable alternative to land-based strengthening exercises.<sup>32</sup> Of the three studies that investigated exercise in the home setting, the highest strength study favored home exercise versus no exercise in reducing patients' global pain rating; however, this finding did not meet the minimum clinically important improvement threshold.<sup>33</sup>

Three studies the effects of aerobic walking versus health education and one compared it to usual care in adults with osteoarthritis of the knee. There were statistically significant improvements with aerobic exercise in all but one of the performance-based functional tasks as compared to the education group. In the study by Kovar et al.,<sup>34</sup> favorable outcomes were reported by the supervised walking group rather than usual care with statistically significant improvements in 6-minute walking distance and the Arthritis Impact Measurement Scale (AIMS) Physical Activity and Pain subscales.

For neuromuscular education, three of four outcomes were statistically significant favoring combined kinesthesia, balance, and strength training exercises versus strength training alone. A high-strength study by Fitzgerald et al.<sup>35</sup> applied an effective treatment for anterior cruciate ligament injury to patients with osteoarthritis of the knee; they found that standard exercise combined with agility and perturbation therapy was not more effective than standard exercise therapy alone. Five of five outcomes were statistically significant for proprioception training. Lin et al.<sup>36</sup> randomized 108 patients to nonweight-bearing proprioception training, nonweight-bearing strength training, and non treatment groups. Both proprioception and strength training were significantly more effective in improving WOMAC Pain and Function scores than no treatment.

A number of fitness-related organizations have disseminated guidelines for physical activity. They generally emphasize the importance of aerobic conditioning and muscle- and bone-strengthening, regular activity, and balance exercises for older adults. In 2008, the federal government for the first time published national guidelines. Here is the link to the US Department of Health and Human Service's physical activity guidelines: <http://www.health.gov/paguidelines/guidelines/default.aspx>.

## **RECOMMENDATION 2**

We suggest weight loss for patients with symptomatic osteoarthritis of the knee and a BMI  $\geq$  25.  
**Strength of Recommendation: Moderate**

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

### **RATIONALE**

There was one moderate- and two low- strength studies included in this recommendation. Physical Function on the SF-36 showed minimum clinically important improvement in outcomes for this patient population. WOMAC function also showed statistical improvement which was possibly clinically significant. Diet and exercise combined revealed improved results. The workgroup considers that the public and patient health benefits of weight loss warranted an upgrade of the recommendation strength to moderate.<sup>53-55</sup>

## **RECOMMENDATION 3A**

We cannot recommend using acupuncture in patients with symptomatic osteoarthritis of the knee.

**Strength of Recommendation: Strong**

Description: Evidence is based on two or more "High" strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

### **RATIONALE**

There were five high- and five moderate- strength studies that compared acupuncture to comparison groups receiving non-intervention sham, usual care, or education. The five moderate-strength studies were included because they reported outcomes that were different than the high-strength evidence. High-strength studies included: Berman et al,<sup>61</sup> Suarez-Almazor et al.,<sup>62</sup> Weiner et al.,<sup>63</sup> Williamson et al.<sup>64</sup> and Taechaarpornkul et al.<sup>65</sup> Moderate-strength studies included: Sandgee et al.,<sup>66</sup> Vas et al.,<sup>67</sup> Witt et al.<sup>68</sup> and Berman et al.<sup>69</sup> The majority of studies were not statistically significant and an even larger proportion of the evidence was not clinically

significant. Some outcomes were associated with clinical- but not statistical- significance. The strength of this recommendation was based on lack of efficacy, not on potential harm.

### **RECOMMENDATION 3B**

We are unable to recommend for or against the use of physical agents (including electrotherapeutic modalities) in patients with symptomatic osteoarthritis of the knee.

#### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

### **RATIONALE**

The evidence was mixed regarding the efficacy of physical agents and electrotherapeutic modalities because of contradiction in findings, design flaws, or a low count of like studies. A single low-strength<sup>70</sup> and a single-moderate strength study<sup>71</sup> comparing pulsed electrical stimulation to placebo produced contradictory results. See the results of the Fary et al.<sup>70</sup> and Zizic et al.<sup>71</sup> articles in table 96. Trock et al.<sup>72</sup> conducted a moderate-strength study evaluating pulsed electromagnetic stimulation and found that it did not generate a statistically significant effect on pain during passive motion, but that tenderness and physician's overall assessment scores were superior in the experimental group. Atamaz et al.<sup>73</sup> conducted a moderate-strength study that compared transcutaneous electrical nerve stimulation (TENS), shortwave diathermy, and interferential current to a sham procedure. None of the treatments were associated with statistically significant effects on pain, physical mobility, or ambulation time at four, 12, or 26 weeks. Battisti et al.,<sup>74</sup> also in a moderate-strength study, found that therapeutic application of modulated electromagnetic field therapy (TAMMEF) did not produce statistically significant improvements in pain or Lequesne Index scores, compared to extremely low-frequency electromagnetic field therapy.

However, there was evidence that ultrasound was effective in patients with knee osteoarthritis. Huang et al.<sup>75</sup> and Yang et al.<sup>76</sup> conducted moderate-strength studies that compared ultrasound to a control group. Huang et al. found that patients who received isotonic exercise with ultrasound had significantly superior ambulation speed, Lequesne Index scores, and VAS pain scores. Yang et al. found VAS pain and Lequesne Index scores were significantly superior at 4 weeks in patients who received ultrasound over those who received a sham treatment.

Due to the overall inconsistent findings for various physical agents and electrotherapeutic modalities, we were unable to make a recommendation for or against their use in patients with symptomatic osteoarthritis of the knee.

## RECOMMENDATION 3C

We are unable to recommend for or against manual therapy in patients with symptomatic osteoarthritis of the knee.

### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

### **RATIONALE**

We were unable to recommend for or against manual therapy due to the lack of studies examining most manual therapy techniques. No studies evaluating joint mobilization, joint manipulation, chiropractic therapy, patellar mobilization, or myofascial release were found that met our inclusion criteria. Perlman et al.<sup>77</sup> examined Swedish massage therapy using a low-strength study design. The findings showed statistically significant results at 8 weeks, but not at 16 weeks. A conclusive recommendation regarding Swedish massage therapy could not be made based on this single low strength of evidence study.

## RECOMMENDATION 4

We are unable to recommend for or against the use of a valgus directing force brace (medial compartment unloader) for patients with symptomatic osteoarthritis of the knee.

### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

### **RATIONALE**

This recommendation is based on three separate studies; one high-strength study<sup>78</sup> compared a valgus producing brace plus usual care to a neoprene sleeve brace plus usual care and to usual care alone. A second high-strength study compared a valgus directing force brace to a lateral wedge foot orthotic.<sup>79</sup> The third study of moderate-strength compared a valgus directing force brace plus usual care to usual care alone.<sup>80</sup> Therapies were compared with respect to how much they improved pain, stiffness, self-reported functional capacity, and physical performance measures (observed walking distance and number of stairs climbed in 30 seconds). Improvement using the varus producing brace was not consistently significant across the four studies. For all statistically significant comparisons, the clinical significance of the improvements in pain and physical function were unclear.

Based on a lack of appropriate studies, the use of a varus directing force brace was not evaluated.

## RECOMMENDATION 5

We cannot suggest that lateral wedge insoles be used for patients with symptomatic medial compartment osteoarthritis of the knee.

### **Strength of Recommendation: Moderate**

Description: Evidence from two or more “Moderate” strength studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

### **RATIONALE**

This recommendation is based on five studies. Four studies, one of high-strength<sup>81</sup> and three of moderate-strength, compared outcomes using lateral wedge insoles to neutral insoles.<sup>82-84</sup> No significant changes in pain, self-reported physical function, or Patient Global Assessment scores were seen between the two types of insoles. A fifth low-strength study compared urethane lateral wedge insoles to rubber lateral insoles, and found a statistically significant improvement in Lequesne score for urethane insoles, but this outcome was of uncertain clinical significance.<sup>85</sup>

## RECOMMENDATION 6

We cannot recommend using glucosamine and chondroitin for patients with symptomatic osteoarthritis of the knee.

### **Strength of Recommendation: Strong**

Description: Evidence is based on two or more “High” strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

### **RATIONALE**

Twenty-one studies were included as evidence for this recommendation; all were prospective. Twelve focused on glucosamine alone, eight on chondroitin sulfate alone, and one (Clegg et al.<sup>86</sup>) assessed both. Sixteen were of moderate-strength and five were of high-strength.

Among the studies, eleven of 52 outcomes were statistically significant in favor of glucosamine when compared to placebo. WOMAC pain and function subscales scores and VAS pain were the critical outcomes and were not associated with statistical significance at any treatment duration period. When meta-analyses were run for WOMAC pain, function, stiffness and total subscale scores, all meta-analyses showed that the overall effect of glucosamine compared to placebo was not statistically significant.

Two studies compared glucosamine to active treatments. Glucosamine was compared to reparaGen<sup>87</sup> (a poly-herbal supplement), and enzymatic hydrolyzed collagen.<sup>88</sup> Glucosamine was found to have no significant effect on pain compared to these treatments.

**Figure 33. Chondroitin Sulfate Versus Placebo: VAS Pain** presents the meta-analysis results comparing chondroitin sulfate to placebo in pain scores on the VAS. The weighted mean difference revealed that scores were 11.89 points lower in the chondroitin group than in the placebo group. However, the difference was not clinically important.

At this time, both glucosamine and chondroitin sulfate have been extensively studied. Despite the availability of the literature, there is essentially no evidence that minimum clinically important outcomes have been achieved compared to placebo, whether evaluated alone or in combination. The strength of the recommendation is based on lack of efficacy, not on potential harm.

One of our search terms was nutraceuticals and we initially maintained a broad focus. However, the original guidance was to evaluate methylsulfonylmethane, omega-3, gelatin, vitamin D, dimethylsulfoxide, antioxidants, and coenzyme Q10. The general term was intended to guide the search of the specific terms. Additionally, the evidence for nutraceuticals was variable and could not be easily summarized. Two moderate-strength studies<sup>89;90</sup> comparing ginger extract to placebo arose in the included evidence. The only improvement in pain associated with both statistical significance and clinical importance was measured using WOMAC stiffness. Clinical importance could not be determined for four other pain measures, or they did not meet the minimum clinically important improvement threshold. The findings on outcomes of function were contradictory and low in count, which rendered them inconclusive. Glycosaminoglycan polysulfuric acid (GAGPS)<sup>91</sup> produced a true negative finding statistically and clinically, and gubitong was associated with higher WOMAC total scores than glucosamine in a non-control matched study where clinical importance could not be determined.

## **Pharmacologic Treatments: Recommendation 7**

### **RECOMMENDATION 7A**

We recommend nonsteroidal anti-inflammatory drugs (NSAIDs; oral or topical) or Tramadol for patients with symptomatic osteoarthritis of the knee.

#### **Strength of Recommendation: Strong**

Description: Evidence is based on two or more “High” strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

## RECOMMENDATION 7B

We are unable to recommend for or against the use of acetaminophen, opioids, or pain patches for patients with symptomatic osteoarthritis of the knee.

### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

## RATIONALE

This recommendation included studies of both selective (cyclo-oxygenase-2, COX-2 inhibitors) and non-selective NSAIDs. The endorsement for NSAIDs was based on 202 favorable outcomes from 19 studies comparing either the selective, non-selective or topical analgesics to placebo. Twelve studies were of selective NSAIDs, four were of non-selective oral NSAIDs, and six were of topical NSAIDs. (Three studies compared multiple types of analgesics to placebo.) Three were high-strength studies, 14 were moderate, and two were of low-strength. The moderate and low strength studies were included because they examined different outcomes than the high strength articles. Out of 202 total outcomes, 171 were statistically significant in favor of the experimental group. Fifteen outcomes were above the MCII threshold and 63 outcomes were possibly clinically significant. The remaining outcomes were neither statistically nor clinically significant.

Two high- and three moderate- strength studies examining the various outcome measures in this recommendation compared tramadol to placebo. They included outcome measurements with follow up periods that ranged from 8 to 13 weeks in duration. Ten of 14 outcomes were statistically significant in favor of the treatment group. Two statistically significant outcomes (WOMAC pain and stiffness subscale scores) were possibly clinically significant and the other eight outcomes could not be evaluated. Fishman et al.<sup>95</sup> did not find any statistically significant improvements in pain efficacy between tramadol contramid doses of 100mg, 200mg and 300mg. Beaulieu et al.<sup>96</sup> found similar treatment effects in tramadol and diclofenac in using WOMAC pain, stiffness and function subscale scales.

The recommendation on acetaminophen was downgraded from level B (i.e. Moderate) in the 2008 edition of the guideline to inconclusive in our current guideline. As opposed to the selection criteria previously used, our current systematic review examined acetaminophen separately and found only one relevant study that tested it against placebo (Miceli-Richard et al.<sup>97</sup>). Their study found no statistical significance or minimum clinically important improvement to patients compared to placebo. In addition, their findings and the previous clinical guideline were based on the usage of a maximum of 4000 mg of acetaminophen per day, and there has been a recent change to consider reducing the amount of the daily dosage to 3000 mg for over-the-counter patient use; for example, see this April 2012 reference from the Nevada Medicaid Services:

[Acetaminophen Dosage Announcement](#). The maximum prescription dose remains at 4000 mg per day.



The work group realizes that many practitioners prefer to start with acetaminophen prior to NSAIDs due to the side effect profile of NSAIDs. However, we found it unreasonable to recommend a treatment that does not show benefit over placebo.

Our literature review found no relevant studies meeting our inclusion criteria on opioids or pain patches for the treatment of knee osteoarthritis.

## **Procedural Treatments: Recommendation 8-11**

### **RECOMMENDATION 8**

We are unable to recommend for or against the use of intraarticular (IA) corticosteroids for patients with symptomatic osteoarthritis of the knee.

#### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

### **RATIONALE**

Our search found only four placebo comparison studies that met criteria and evaluated pain relief for a minimum treatment period of four weeks.<sup>102-105</sup> One study found IA corticosteroids to be superior to placebo on WOMAC total subscale scores at four weeks.<sup>102</sup> However, another study found IA corticosteroid injections inferior to hyaluronic acid injections<sup>106</sup> and a third study found IA corticosteroids inferior to needle lavage (tidal irrigation).<sup>107</sup> Since the evidence in the guideline did not support the use of hyaluronic acid or needle lavage, the work group interpreted the evidence to be inconclusive as to the benefit of IA corticosteroids.

### **RECOMMENDATION 9**

We cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee.

#### **Strength of Recommendation: Strong**

Description: Evidence is based on two or more “High” strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

### **RATIONALE**

Fourteen studies (three high-strength studies and 11 moderate-strength studies) assessed intraarticular hyaluronic acid (HA) injections. A comparison of the patients in these studies and the ones validating the MCII we used to judge clinical significance revealed that they were demographically comparable for WOMAC and VAS pain as well as WOMAC function on the basis of age, baseline pain scores, BMI, weight and gender. Meta-analysis in meaningfully important difference (MID) units showed that the over effect was less than 0.5 MID units,

indicating a low likelihood that an appreciable number of patients achieved clinically important benefits in the outcomes (Guyatt et al.). Although meta-analyses of WOMAC pain, function, and stiffness subscales scores all found statistically significant treatment effects, none of the improvements met the minimum clinically important improvement thresholds. When we differentiated high- versus low- molecular weight viscosupplementation, our analyses did show that most of the statistically significant outcomes were associated with high-molecular cross linked hyaluronic acid but when compared to mid-range molecular weight, statistical significance was not maintained. Treatment comparisons between any weights higher than 750 kDa were not significantly different. The strength of this recommendation was based on lack of efficacy, not on potential harm.

The 2008 edition of this guideline where the benefits of viscosupplementation were found to be inconclusive rather than non-affirming used a systematic review from AHRQ that compared Hylan G-F 20 to placebo. Although there was a statistically significant treatment effect associated with the high molecular weight, different pain measurement outcomes (WOMAC and VAS pain) were combined so clinical significance could not be determined. Also, the work group found evidence of publication bias (publicizing of primarily favorable studies). We excluded the AHRQ systematic review because the selection criteria did not match ours. The primary difference was that in the current edition of the guideline clinical efficacy beyond a 4-week treatment period was required for studies to be included. This 2<sup>nd</sup> edition was based on meta-analyses that combined like measurement instruments, which made it possible to determine that the overall effect of hyaluronic acid did not provide minimum clinically important improvement to patients. Additionally, the AHRQ review included trials of varying research-design quality due in part to variations in sample sizes. In AAOS clinical practice guidelines, evidence of lower strength is excluded when there are at least two higher strength studies evaluating an outcome, and we excluded many of the lower strength studies included in the AHRQ review since they did not meet our selection criterion of at least 30 patients in each treatment group. Noted in the AHRQ review was that “There is evidence consistent with potential publication bias. Pooled results from small trials (<100 patients) showed effects up to twice those of larger trials consistent with selective publication of underpowered positive trials” (page 64 of Full Guideline Document).” Future research using clinically relevant outcomes, sub-group analyses, and controls for bias are needed.

## **RECOMMENDATION 10**

We are unable to recommend for or against growth factor injections and/or platelet rich plasma for patients with symptomatic osteoarthritis of the knee.

### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

## **RATIONALE**

There was a paucity of articles on the use of platelet concentrates in the treatment of osteoarthritis. Sanchez et al.<sup>119;120</sup> used activated platelet aggregates in a fibrin matrix and Spakova et al.<sup>121</sup> used a platelet concentrate. None of the studies controlled for platelet volume. All studies used hyaluronic acid as the control group.

The studies showed decreased levels of pain in the post injection period but they were not constructed to allow for a comparative analysis of clinical effectiveness. The lack of controlled prospective blinded randomized clinical trials with a placebo control prevent the work group from making any recommendation on the use of platelets or platelet derived growth factor concentrates in the treatment of osteoarthritis of the knee.

## **RECOMMENDATION 11**

We cannot *suggest* that the practitioner use needle lavage for patients with symptomatic osteoarthritis of the knee.

### **Strength of Recommendation: Moderate**

Description: Evidence from two or more “Moderate” strength studies with consistent findings, or evidence from a single “High” quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the quality/applicability of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

## **RATIONALE**

This recommendation is based on one high strength study by Bradley et al.<sup>122</sup> and one moderate strength study by Vad et al.<sup>123</sup> The evidence showed little or no benefit from needle lavage in the treatment of osteoarthritis of the knee. Fourteen of 15 outcomes were not statistically significant, including three pain and three functional outcomes, indicating no measurable benefit to patients from needle lavage.

## Surgical Treatments: Recommendation 12-15

### RECOMMENDATION 12

We cannot recommend performing arthroscopy with lavage and/or debridement in patients with a primary diagnosis of symptomatic osteoarthritis of the knee.

#### Strength of Recommendation: Strong

Description: Evidence is based on two or more “High” strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the quality of the supporting evidence is high. A harms analysis on this recommendation was not performed.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

### RATIONALE

There were three studies that met the inclusion criteria for this recommendation. The Kirkley et al.<sup>124</sup> and Kalunian et al.<sup>125</sup> studies comparing arthroscopic lavage to placebo were rated as moderate strength and the Moseley et al.<sup>126</sup> study comparing arthroscopic lavage to sham arthroscopic surgery was rated as a high strength study.

Kirkley et al.<sup>124</sup> reported that a large number of patients were not eligible for participation in their study (38%) largely due to the exclusion criteria of substantial knee malalignment. In some cases, patients declined participation. Kirkley et al.<sup>124</sup> compared arthroscopic surgery to lavage and debridement combined with usual physical therapy and medical treatment, usual care. The authors used the pain, functional status and other symptoms subscales of the Arthritis Self-Efficacy Scale (ASES) and the McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) at multiple time points (ranging from three months to two years). Out of 20 outcomes, only two were statistically significant in favor of surgery with lavage. Differences in AIMS pain were statistically significant at three months and differences in AIMS-Other Arthritis Symptoms subscale scores remained significant after two years. In summary, this randomized controlled trial demonstrated no benefit of arthroscopic surgery compared to physical therapy and medical treatment for osteoarthritis of the knee.

Kalunian et al.<sup>125</sup> included a large number of enrolled patients from one institution with intraarticular crystals in their knee. They compared arthroscopic lavage with 3,000 ml saline to lavage with 250 ml saline. There were not any statistically significant differences in VAS and WOMAC pain scores between the two treatment groups.

The Moseley et al.<sup>126</sup> study raised questions regarding its limited sampling (mostly male veterans) as well as the number of potential study participants who declined randomization into a treatment group. In this RCT, the effects of arthroscopy with debridement or lavage were not statistically significant in the vast majority of patient oriented outcome measures for pain and function, at multiple time points from one week to two years following surgery.

Collectively all three included studies did not demonstrate clinical benefit of arthroscopic debridement or lavage. The work group also considered the potential risks to patients (anesthesia intolerance, infection, and venous thrombosis) associated with surgical intervention.

It was agreed that the lacking evidence for treatment benefit and increased risks from surgery were sufficient reasons to recommend against arthroscopic debridement and/or lavage in patients with a primary diagnosis of osteoarthritis of the knee.

None of the evidence we examined specifically included patients who had a primary diagnosis of meniscal tear, loose body, or other mechanical derangement, with concomitant diagnosis of osteoarthritis of the knee. The present recommendation does not apply to such patients.

### **RECOMMENDATION 13**

We are unable to recommend for or against arthroscopic partial meniscectomy in patients with osteoarthritis of the knee with a torn meniscus.

#### **Strength of Recommendation: Inconclusive**

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive**, exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

### **RATIONALE**

Currently, arthroscopic partial meniscectomy is routinely performed in patients with symptomatic osteoarthritis of the knee who also have primary signs and symptoms of a torn meniscus.

Herrlin et al.<sup>127</sup> compared arthroscopic partial meniscectomy followed by supervised exercise to supervised exercise alone and measured KOOS pain, symptoms, activities of daily life, sports/recreation, and quality of life subscales scores as outcomes. The study was downgraded from moderate- to low- strength because 40% of patients declined participation and the arthroscopic group had non-homogeneous preoperative KOOS scores. The authors reported no significant treatment benefits of meniscectomy using any of the outcomes at eight weeks and six months. Since there was only one low-strength study, the recommendation was graded inconclusive.

### **RECOMMENDATION 14**

The practitioner might perform a valgus producing proximal tibial osteotomy in patients with symptomatic medial compartment osteoarthritis of the knee.

#### **Strength of Recommendation: Limited**

Description: Evidence from two or more “Low” strength studies with consistent findings, or evidence from a single Moderate quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means that the quality of the supporting evidence is unconvincing, or that well-conducted studies show little clear advantage to one approach over another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might counter the current findings. Patient preference should have a substantial influencing role.

## **RATIONALE**

Nine low-strength case series studies found nine out of 10 outcomes significantly improved from baseline. A cross-sectional time series regression analysis was used to predict the placebo effect on VAS pain for comparison to that of the treatment group. Compared to the predicted placebo effect on VAS pain, the proximal tibial osteotomy group reported decreased pain on the VAS.

Based on a lack of appropriate studies, distal femoral (varus producing) osteotomy was not evaluated.

## **RECOMMENDATION 15**

In the absence of reliable evidence, it is the opinion of the work group not to use the free-floating (un-fixed) interpositional device in patients with symptomatic medial compartment osteoarthritis of the knee.

### **Strength of Recommendation: Consensus**

Description: The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria of the guideline's systematic review.

Implications: Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus**, although they may give it preference over alternatives. Patient preference should have a substantial influencing role.

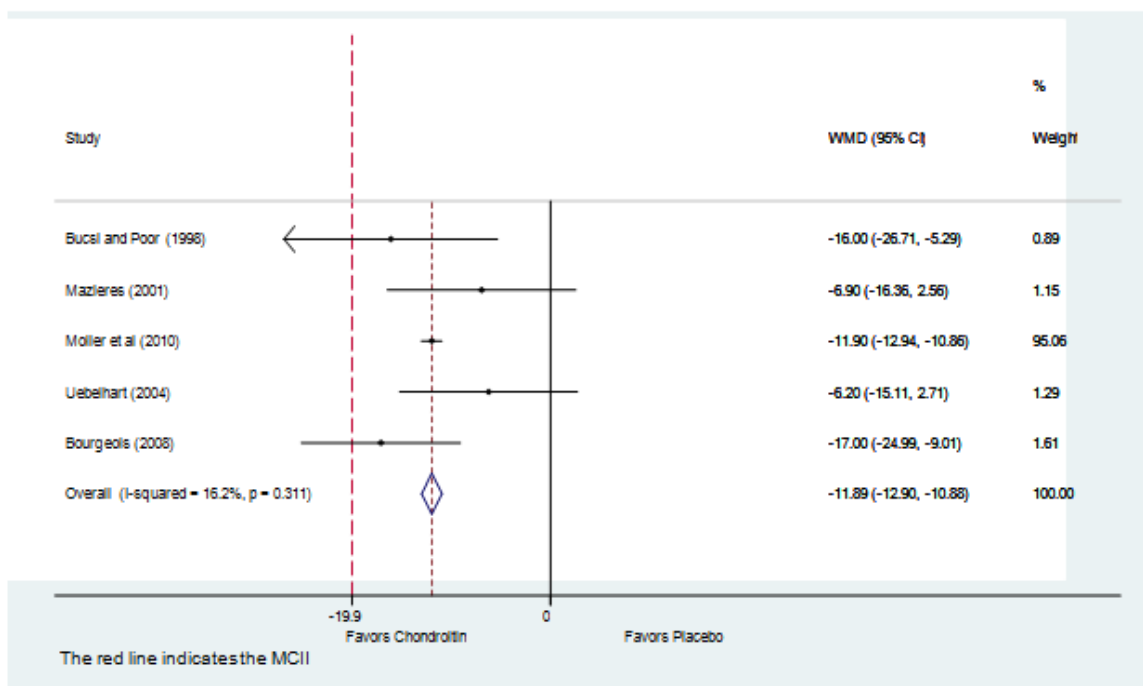
## **RATIONALE**

One published case series reported the results of free-floating (un-fixed) interpositional device surgery for treatment of medial unicompartmental OA of the knee.<sup>129</sup> We determined that the evidence was low-strength.

The evidence indicated high reoperation rates in the patients who were followed. Thirty-two percent of patients were revised to total knee arthroplasty. The evidence showed differences from baseline that were not clinically or statistically significant for increased pain measured with the VAS two years postoperatively. Knee Society Score function subscale scores were "poor" postoperatively.

The AAOS workgroup modified the grade of this recommendation to consensus, because of the high revision rates in this study, increased pain, and the potential harm associated with this intervention (anesthesia risks, VTE, infection, and reoperation).

**Figure 33. Chondroitin Sulfate Versus Placebo: VAS Pain**



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#### Additional Reference

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