

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

Review Period Report

Table of Contents

Overview of the Review Period	4
Reviewer Key	5
Table 1. Reviewer Key.....	5
Reviewer Demographics.....	8
Table 2: Reviewer Demographics	8
Reviewers' Disclosure Information.....	10
Table 3. Disclosure Question Key.....	10
Table 4. Reviewer's Disclosure Information	11
Reviewer Responses to Structured Review Form Questions.....	13
Table 5. Reviewer Responses to Structured Review Questions 1-4	13
Table 6. Reviewer Responses to Structured Review Questions 5-8	16
Table 7. Reviewer Responses to Structured Review Questions 9-12.....	19
Table 8. Reviewer Responses to Structured Review Questions 13-16	22
Reviewer Detailed Responses and Editorial Suggestions.....	28
Reviewer #1, Paul Castello, M.D.....	28
<i>Workgroup Response to Reviewer #1</i>	29
Reviewer #2, Marc Levine, M.D.	30
<i>Workgroup Response to Reviewer #2</i>	31
Reviewer #3, John Chef, M.D., MPH, FAAOS.....	32
<i>Workgroup Response to Reviewer #3</i>	33
Reviewer #4, Conjeevaram Maheshwer, FRCS, FAAOS	34
<i>Workgroup Response to Reviewer #4</i>	35
Reviewer #5, Michael O'Malley, M.D., MS, FAAOS	36
<i>Workgroup Response to Reviewer #5</i>	37
Reviewer #6, Adam Bruggeman, M.D.	38
<i>Workgroup Response to Reviewer #6</i>	39
Reviewer #7, Miriam Hakim-Zargar, M.D., MPH, FAAOS	40
<i>Workgroup Response to Reviewer #7</i>	41
Reviewer #8, F. Scott Gray, M.D.	42
<i>Workgroup Response to Reviewer #8</i>	43
Reviewer #9, Nicholas Bedard, M.D.....	44
<i>Workgroup Response to Reviewer #9</i>	47
Reviewer #10, David Scalzitti, PT, PhD	48

<i>Workgroup Response to Reviewer #10</i>	49
Reviewer #11, Laura Tosi, M.D.	50
<i>Workgroup Response to Reviewer #11</i>	51
Reviewer #12, Johnathan Bernard, M.D., MPH.....	52
<i>Workgroup Response to Reviewer #12</i>	53
Reviewer #13, Julie Dodds, M.D.....	54
<i>Workgroup Response to Reviewer #13</i>	55
Reviewer #14, Anita Bemis-Dougherty, PT, DPT, MAS.....	56
<i>Workgroup Response to Reviewer #14</i>	59
Reviewer #15, F. Suzette Song, M.D.....	61
<i>Workgroup Response to Reviewer #15</i>	63
Reviewer #16, Adolph Yates, M.D.....	64
<i>Workgroup Response to Reviewer #16</i>	82
Reviewer #17, Vinod Dasa, M.D.....	91
<i>Workgroup Response to Reviewer #17</i>	92
Reviewer #18, Luis Pulido, M.D.	93
<i>Workgroup Response to Reviewer #18</i>	94
Reviewer #19, Fred Nelson, M.D.....	95
<i>Workgroup Response to Reviewer #19</i>	97
Reviewer #20, Charles Hummer, M.D.	98
<i>Workgroup Response to Reviewer #20</i>	99
Reviewer #21, Barry Kraushaar, M.D.	100
<i>Workgroup Response to Reviewer #21</i>	101
Reviewer #22, Bernard Roehr, M.D., MHCDS	102
<i>Workgroup Response to Reviewer #22</i>	103
Reviewer #23, Kenneth Jaffe, M.D.....	104
<i>Workgroup Response to Reviewer #23</i>	105
Reviewer #24, Douglas Naudie, M.D., FRCSC.....	106
<i>Workgroup Response to Reviewer #24</i>	108
Reviewer #25, Alexandra Page, M.D.....	109
<i>Workgroup Response to Reviewer #25</i>	110
Reviewer #26, Matthew Abdel, M.D.	111
<i>Workgroup Response to Reviewer #26</i>	112

Reviewer #27, Alison Chang, PT, DPT, MS 113
Workgroup Response to Reviewer #27 115
Reviewer #28, Ajay Srivastava, M.D..... 116
Workgroup Response to Reviewer #28 117
Reviewer #29, Laura Bruse, M.D..... 118
Workgroup Response to Reviewer #29 120
Reviewer #30, Stephen Weber, M.D. and Louis McIntyre, M.D. 122
Workgroup Response to Reviewer #30 124
Reviewer #31, Rafael Sierra, M.D. 125
Workgroup Response to Reviewer #31 126
Reviewer #32, Alexander Sah, M.D., FAAOS 127
Workgroup Response to Reviewer #32 128
Reviewer #33, Benjamin Miller, M.D. 129
Workgroup Response to Reviewer #33 130
Reviewer #34, Matthew Landfried, M.D. 131
Workgroup Response to Reviewer #34 132
Reviewer #35, Matthew Austin, M.D. 133
Workgroup Response to Reviewer #35 135
Appendix A – Structured Review Form 136

Management of Osteoarthritis of the Knee (Non-Arthroplasty)

Overview of the Review Period

The reviews and comments related to this clinical practice guideline are reprinted in this document and posted on the AAOS website. All reviewers are required to disclose their conflict of interests.

Review Process:

AAOS contacted 6 organizations with content expertise to review a draft of the clinical practice guideline during the three-week peer review period in March 2021.

Additionally, the draft was also provided to members of the AAOS Board of Directors (BOD), members of the Council on Research and Quality (CORQ), members of the Board of Councilors (BOC), members of the Board of Specialty Societies (BOS) and members of the Committee on Evidence-Based Quality and Value (EBQV) for review and comment.

- Thirty-five (35) individuals provided comments via the electronic structured peer review form. No reviewers asked to remain anonymous.
- All thirty-five reviews were on behalf of a society and/or committee.
- The work group considered all comments and made some modifications when they were consistent with the evidence.

Reviewer Key

Each reviewer was assigned a number (see below). All responses in this document are listed by the assigned peer reviewer's number.

Table 1. Reviewer Key

Reviewer Number	Name of Reviewer	Society/ Committee Being Represented
1	Paul Castello	Board of Councilors, American Academy of Orthopaedic Surgeons
2	Marc Levine	Board of Councilors, American Academy of Orthopaedic Surgeons
3	John Cherf	Committee on Evidence-Based Quality and Value, American Academy of Orthopaedic Surgeons
4	Conjeevaram Maheshwer	American Academy of Orthopaedic Surgeons
5	Michael O'Malley	Board of Councilors, American Academy of Orthopaedic Surgeons
6	Adam Bruggeman	Board of Councilors, American Academy of Orthopaedic Surgeons
7	Mariam Hakim-Zargar	Board of Councilors, American Academy of Orthopaedic Surgeons
8	F. Scott Gray	Board of Councilors, American Academy of Orthopaedic Surgeons
9	Nicholas Bedard	American Academy of Hip and Knee Surgeons
10	David Scalzitti	Key Informant Panelist, American Academy of Orthopaedic Surgeons
11	Laura Tosi	Committee on Research and Quality/ Board of Councilors, American Academy of Orthopaedic Surgeons
12	Johnathan Bernard	Key Informant Panelist, American Academy of Orthopaedic Surgeons
13	Julie Dodds	Board of Specialty Societies, American Academy of Orthopaedic Surgeons
14	Anita Bemis-Dougherty	American Physical Therapy Association

15	Suzette Song	Board of Councilors, American Academy of Orthopaedic Surgeons
16	Adolph Yates	Board of Councilors, American Academy of Orthopaedic Surgeons
17	Vinod Dasa	Key Informant Panelist, American Academy of Orthopaedic Surgeons
18	Luis Pulido	American Academy of Orthopaedic Surgeons
19	Fred Nelson	American Academy of Orthopaedic Surgeons
20	Charles Hummer	Key Informant Panelist, American Academy of Orthopaedic Surgeons
21	Barry Kraushaar	Board of Councilors, American Academy of Orthopaedic Surgeons
22	Bernard Roehr	American Academy of Orthopaedic Surgeons
23	Kenneth Jaffe	American Academy of Orthopaedic Surgeons
24	Douglas Naudie	The Knee Society
25	Alexandra Page	Board of Directors, American Academy of Orthopaedic Surgeons
26	Matthew Abdel	Board of Directors, American Academy of Orthopaedic Surgeons
27	Alison Chang	Key Informant Panelist, American Academy of Orthopaedic Surgeons
28	Ajay Srivastava	Committee on Evidence-Based Quality and Value, American Academy of Orthopaedic Surgeons
29	Laura Bruse	American Academy of Orthopaedic Surgeons
30	Stephen Weber	Arthroscopy Association of North America (with Louis McIntyre)
31	Rafael Sierra	The Knee Society
32	Alexander Sah	Key Informant Panelist, American Academy of Orthopaedic Surgeons
33	Benjamin Miller	Committee on Evidence-Based Quality and Value, American Academy of Orthopaedic Surgeons
34	Matthew Landfried	American Academy of Orthopaedic Surgeons

Reviewer Demographics

Table 2: Reviewer Demographics

Reviewer Number	Name of Reviewer	Primary Specialty	Work Setting
1	Paul Castello	Sports Medicine	Private Group or Practice
2	Marc Levine	Adult Spine	Clinical Hospital
3	John Cherf	Sports Medicine	Private Group or Practice
4	Conjeevaram Maheshwer	Total Joint	Private Group or Practice
5	Michael O'Malley	Sports Medicine	Academic Practice
6	Adam Bruggeman	Adult Spine	Private Group or Practice
7	Mariam Hakim-Zargar	Foot and Ankle	Private Group or Practice
8	F. Scott Gray	Foot and Ankle	Private Group or Practice
9	Nicholas Bedard	Total Joint	Academic Practice
10	David Scalzitti	Rehab/Prosthetics and Orthotics	Academic Practice
11	Laura Tosi	Pediatric Orthopaedics	Clinical Hospital
12	Johnathan Bernard	Sports Medicine	Private Group or Practice
13	Julie Dodds	Sports Medicine	Private Group or Practice
14	Anita Bemis-Dougherty	Other	Other
15	Suzette Song	Foot and Ankle	Private Group or Practice

16	Adolph Yates	Total Joint	Academic Practice
17	Vinod Dasa	Adult Knee	Academic Practice
18	Luis Pulido	Adult Knee	Academic Practice
19	Fred Nelson	Adult Knee	Academic Practice
20	Charles Hummer	Sports Medicine	Private Group or Practice
21	Barry Kraushaar	Sports Medicine	Private Group or Practice
22	Bernard Roehr	Total Joint	Clinical Hospital
23	Kenneth Jaffe	Ortho/Oncology	Private Group or Practice
24	Douglas Naudie	Adult Knee	Academic Practice
25	Alexandra Page	Foot and Ankle	Private Group or Practice
26	Matthew Abdel	Adult Hip	Academic Practice
27	Alison Chang	Adult Knee	Academic Practice
28	Ajay Srivastava	Adult Knee	Private Group or Practice
29	Laura Bruse	Other	Other
30	Stephen Weber	Sports Medicine	Academic Practice
31	Rafael Sierra	Adult Hip	Academic Practice
32	Alexander Sah	Total Joint	Private Group or Practice
33	Benjamin Miller	Ortho/Oncology	Academic Practice
34	Matthew Landfried	Adult Knee	Clinical Hospital
35	Matthew Austin	Total Joint	Academic Practice

Reviewers' Disclosure Information

All reviewers are required to disclose any possible conflicts that would bias their review via a series of 10 questions (see Table 3). For any positive responses to the questions (i.e. "Yes"), the reviewer was asked to provide details on their possible conflict.

Table 3. Disclosure Question Key

Disclosure Question	Disclosure Question Details
A	A) Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device?
B	B) Within the past twelve months, have you or a member of your immediate family served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company?
C	C) Are you or a member of your immediate family a PAID EMPLOYEE for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
D	D) Are you or a member of your immediate family a PAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
E	E) Are you or a member of your immediate family an UNPAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
F	F) Do you or a member of your immediate family own stock or stock options in any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds)
G	G) Do you or a member of your immediate family receive research or institutional support as a principal investigator from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
H	H) Do you or a member of your immediate family receive any other financial or material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier?
I	I) Do you or a member of your immediate family receive any royalties, financial or material support from any medical and/or orthopaedic publishers?
J	J) Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication?

Table 4. Reviewer's Disclosure Information

Reviewer Number	Name of Reviewer	Disclosure Available via AAOS Disclosure System	A	B	C	D	E	F	G	H	I	J
1	Paul Castello	No	No	No	No	No	No	No	No	No	No	No
2	Marc Levine	Yes										
3	John Cherf	Yes										
4	Conjeevaram Maheshwer	Yes										
5	Michael O'Malley	Yes										
6	Adam Bruggeman	Yes										
7	Mariam Hakim-Zargar	Yes										
8	F. Scott Gray	No	No	No	No	No	No	No	No	No	No	No
9	Nicholas Bedard	Yes										
10	David Scalzitti	No	No	No	No	No	No	No	No	No	Yes	No
11	Laura Tosi	Yes										
12	Johnathan Bernard	Yes										
13	Julie Dodds	Yes										
14	Anita Bemis-Dougherty	No	No	No	No	No	No	No	No	No	No	No
15	Suzette Song	No	No	No	No	No	No	No	No	No	No	No
16	Adolph Yates	Yes										

17	Vinod Dasa	Yes										
18	Luis Pulido	No	No	No	No	No	No	No	No	No	No	No
19	Fred Nelson	No	No	No	No	No	No	No	No	No	Yes	No
20	Charles Hummer	Yes										
21	Barry Kraushaar	Yes	No	No	No	Yes	No	No	No	No	No	No
22	Bernard Roehr	Yes										
23	Kenneth Jaffe	Yes										
24	Douglas Naudie	No	Yes	Yes	No	Yes	No	No	No	Yes	No	No
25	Alexandra Page	Yes										
26	Matthew Abdel	Yes										
27	Alison Chang	Yes										
28	Ajay Srivastava	Yes										
29	Laura Bruse	Yes										
30	Stephen Weber	Yes										
31	Rafael Sierra	Yes										
32	Alexander Sah	Yes										
33	Benjamin Miller	Yes										
34	Matthew Landfried	No	No	No	No	No	No	No	No	No	No	No
35	Matthew Austin	Yes										

Reviewer Responses to Structured Review Form Questions

All reviewers are asked 16 structured review questions which have been adapted from the Appraisal of Guidelines for Research and Evaluation (AGREE) II Criteria*. Their responses to these questions are listed on the next few pages.

Table 5. Reviewer Responses to Structured Review Questions 1-4

Reviewer Number	Name of Reviewer	1. The overall objective(s) of the guideline is (are) specifically described.	2. The health question(s) covered by the guideline is (are) specifically described.	3. The guideline's target audience is clearly described.	4. There is an explicit link between the recommendations and the supporting evidence.
1	Paul Castello	Agree	Agree	Strongly Agree	Strongly Agree
2	Marc Levine	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
3	John Cherf	Agree	Agree	Agree	Agree
4	Conjeevaram Maheshwer	Strongly Agree	Strongly Agree	Agree	Agree
5	Michael O'Malley	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Adam Bruggeman	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
7	Mariam Hakim-Zargar	Strongly Agree	Strongly Agree	Strongly Agree	Agree
8	F. Scott Gray	Strongly Agree	Agree	Strongly Agree	Agree
9	Nicholas Bedard	Strongly Agree	Strongly Agree	Strongly Agree	Agree
10	David Scalzitti	Strongly Agree	Strongly Agree	Agree	Agree
11	Laura Tosi	Agree	Strongly Agree	Strongly Agree	Disagree
12	Johnathan Bernard	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

13	Julie Dodds	Agree	Strongly Agree	Strongly Agree	Strongly Disagree
14	Anita Bemis-Dougherty	Agree	Agree	Agree	Agree
15	Suzette Song	Agree	Neutral	Neutral	Neutral
16	Adolph Yates	Neutral	Neutral	Agree	Disagree
17	Vinod Dasa	Agree	Agree	Agree	Agree
18	Luis Pulido	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
19	Fred Nelson	Agree	Strongly Agree	Strongly Agree	Strongly Agree
20	Charles Hummer	Strongly Agree	Strongly Agree	Strongly Agree	Agree
21	Barry Kraushaar	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
22	Bernard Roehr	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
23	Kenneth Jaffe	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
24	Douglas Naudie	Strongly Agree	Strongly Agree	Strongly Agree	Agree
25	Alexandra Page	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
26	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
27	Alison Chang	Strongly Agree	Strongly Agree	Strongly Agree	Agree
28	Ajay Srivastava	Strongly Agree	Strongly Agree	Strongly Agree	Agree
29	Laura Bruse	Strongly Agree	Strongly Agree	Agree	Strongly Agree
30	Stephen Weber	Strongly Agree	Neutral	Neutral	Agree
31	Rafael Sierra	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
32	Alexander Sah	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

33	Benjamin Miller	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
34	Matthew Landfried	Agree	Agree	Strongly Agree	Agree
35	Matthew Austin	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

Table 6. Reviewer Responses to Structured Review Questions 5-8

Reviewer Number	Name of Reviewer	5. Given the nature of the topic and the data, all clinically important outcomes are considered.	6. The patients to whom this guideline is meant to apply are specifically described.	7. The criteria used to select articles for inclusion are appropriate.	8. The reasons why some studies were excluded are clearly described.
1	Paul Castello	Strongly Agree	Strongly Agree	Strongly Agree	Agree
2	Marc Levine	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
3	John Cherf	Agree	Agree	Agree	Agree
4	Conjeevaram Maheshwer	Strongly Agree	Agree	Agree	Neutral
5	Michael O'Malley	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Adam Bruggeman	Agree	Strongly Agree	Strongly Agree	Strongly Agree
7	Mariam Hakim-Zargar	Agree	Agree	Agree	Agree
8	F. Scott Gray	Agree	Strongly Agree	Agree	Neutral
9	Nicholas Bedard	Agree	Agree	Strongly Agree	Agree
10	David Scalzitti	Strongly Agree	Strongly Agree	Strongly Agree	Agree
11	Laura Tosi	Agree	Agree	Agree	Agree
12	Johnathan Bernard	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
13	Julie Dodds	Strongly Disagree	Strongly Agree	Strongly Disagree	Agree
14	Anita Bemis-Dougherty	Agree	Agree	Neutral	Neutral

15	Suzette Song	Agree	Neutral	Agree	Neutral
16	Adolph Yates	Disagree	Agree	Disagree	Disagree
17	Vinod Dasa	Agree	Agree	Agree	Agree
18	Luis Pulido	Strongly Agree	Strongly Agree	Strongly Agree	Agree
19	Fred Nelson	Agree	Agree	Agree	Agree
20	Charles Hummer	Neutral	Strongly Agree	Agree	Neutral
21	Barry Kraushaar	Strongly Agree	Strongly Agree	Strongly Agree	Agree
22	Bernard Roehr	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
23	Kenneth Jaffe	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
24	Douglas Naudie	Agree	Agree	Agree	Neutral
25	Alexandra Page	Agree	Agree	Strongly Agree	Agree
26	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
27	Alison Chang	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
28	Ajay Srivastava	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
29	Laura Bruse	Agree	Agree	Agree	Agree
30	Stephen Weber	Neutral	Agree	Neutral	Agree
31	Rafael Sierra	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
32	Alexander Sah	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
33	Benjamin Miller	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
34	Matthew Landfried	Agree	Agree	Neutral	Neutral

35	Matthew Austin	Strongly Disagree	Disagree	Strongly Agree	Strongly Agree
----	----------------	-------------------	----------	----------------	----------------

Table 7. Reviewer Responses to Structured Review Questions 9-12

Reviewer Number	Name of Reviewer	9. All important studies that met the article inclusion criteria are included	10. The validity of the studies is appropriately appraised.	11. The methods are described in such a way as to be reproducible	12. The statistical methods are appropriate to the material and the objectives of this guideline
1	Paul Castello	Agree	Agree	Agree	Agree
2	Marc Levine	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
3	John Cherf	Agree	Strongly Agree	Agree	Agree
4	Conjeevaram Maheshwer	Agree	Agree	Strongly Agree	Strongly Agree
5	Michael O'Malley	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Adam Bruggeman	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
7	Mariam Hakim-Zargar	Agree	Agree	Agree	Agree
8	F. Scott Gray	Neutral	Agree	Agree	Neutral
9	Nicholas Bedard	Agree	Agree	Agree	Agree
10	David Scalzitti	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
11	Laura Tosi	Agree	Agree	Disagree	Neutral
12	Johnathan Bernard	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
13	Julie Dodds	Agree	Strongly Disagree	Agree	Agree
14	Anita Bemis-Dougherty	Neutral	Agree	Agree	Agree

15	Suzette Song	Agree	Agree	Agree	Agree
16	Adolph Yates	Strongly Disagree	Disagree	Strongly Disagree	Strongly Disagree
17	Vinod Dasa	Agree	Agree	Agree	Agree
18	Luis Pulido	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
19	Fred Nelson	Agree	Strongly Agree	Strongly Agree	Agree
20	Charles Hummer	Neutral	Agree	Neutral	Agree
21	Barry Kraushaar	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
22	Bernard Roehr	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
23	Kenneth Jaffe	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
24	Douglas Naudie	Neutral	Agree	Agree	Agree
25	Alexandra Page	Agree	Strongly Agree	Strongly Agree	Strongly Agree
26	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
27	Alison Chang	Strongly Agree	Agree	Strongly Agree	Strongly Agree
28	Ajay Srivastava	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
29	Laura Bruse	Agree	Agree	Agree	Agree
30	Stephen Weber	Neutral	Strongly Disagree	Strongly Disagree	Strongly Disagree
31	Rafael Sierra	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
32	Alexander Sah	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
33	Benjamin Miller	Agree	Strongly Agree	Strongly Agree	Strongly Agree
34	Matthew Landfried	Agree	Agree	Agree	Agree

35	Matthew Austin	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
----	----------------	----------------	----------------	----------------	----------------

Table 8. Reviewer Responses to Structured Review Questions 13-16

Reviewer Number	Name of Reviewer	13. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed.	14. Health benefits, side effects, and risks are adequately addressed.	15. The writing style is appropriate for health care professionals.	16. The grades assigned to each recommendation are appropriate.
1	Paul Castello	Agree	Agree	Agree	Agree
2	Marc Levine	Strongly Agree	Agree	Strongly Agree	Strongly Agree
3	John Cherf	Agree	Agree	Agree	Agree
4	Conjeevaram Maheshwer	Agree	Neutral	Agree	Agree
5	Michael O'Malley	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Adam Bruggeman	Strongly Agree	Strongly Agree	Strongly Agree	Agree
7	Mariam Hakim-Zargar	Agree	Agree	Agree	Agree
8	F. Scott Gray	Neutral	Agree	Strongly Agree	Neutral
9	Nicholas Bedard	Agree	Agree	Strongly Agree	Neutral
10	David Scalzitti	Strongly Agree	Strongly Agree	Agree	Strongly Agree
11	Laura Tosi	Neutral	Neutral	Strongly Agree	Disagree
12	Johnathan Bernard	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
13	Julie Dodds	Strongly Disagree	Strongly Disagree	Strongly Agree	Strongly Disagree

14	Anita Bemis-Dougherty	Agree	Agree	Agree	Agree
15	Suzette Song	Agree	Neutral	Agree	Neutral
16	Adolph Yates	Strongly Disagree	Disagree	Agree	Strongly Disagree
17	Vinod Dasa	Agree	Agree	Agree	Neutral
18	Luis Pulido	Strongly Agree	Agree	Strongly Agree	Strongly Agree
19	Fred Nelson	Strongly Agree	Strongly Agree	Strongly Agree	Agree
20	Charles Hummer	Agree	Neutral	Strongly Agree	Agree
21	Barry Kraushaar	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
22	Bernard Roehr	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
23	Kenneth Jaffe	Neutral	Strongly Agree	Strongly Agree	Neutral
24	Douglas Naudie	Agree	Agree	Strongly Agree	Disagree
25	Alexandra Page	Neutral	Disagree	Strongly Agree	Strongly Agree
26	Matthew Abdel	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
27	Alison Chang	Strongly Agree	Agree	Strongly Agree	Agree
28	Ajay Srivastava	Strongly Agree	Strongly Agree	Agree	Strongly Agree
29	Laura Bruse	Agree	Neutral	Agree	Agree
30	Stephen Weber	Agree	Agree	Agree	Agree
31	Rafael Sierra	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
32	Alexander Sah	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
33	Benjamin Miller	Strongly Agree	Strongly Agree	Strongly Agree	Agree

34	Matthew Landfried	Agree	Strongly Agree	Agree	Strongly Agree
35	Matthew Austin	Strongly Disagree	Strongly Agree	Strongly Agree	Strongly Agree

Reviewers' Recommendation for Use of this Guideline in Clinical Practice

Would you recommend these guidelines for use in clinical practice?

Reviewer Number	Name of Reviewer	Would you recommend these guidelines for use in clinical practice?
1	Paul Castello	Strongly Recommend
2	Marc Levine	Strongly Recommend
3	John Cherf	Strongly Recommend
4	Conjeevaram Maheshwer	Strongly Recommend
5	Michael O'Malley	Strongly Recommend
6	Adam Bruggeman	Strongly Recommend
7	Mariam Hakim-Zargar	Recommend
8	F. Scott Gray	Recommend
9	Nicholas Bedard	Recommend
10	David Scalzitti	Strongly Recommend
11	Laura Tosi	Would Not Recommend
12	Johnathan Bernard	Strongly Recommend
13	Julie Dodds	Would Not Recommend
14	Anita Bemis-Dougherty	Recommend

15	Suzette Song	Would Not Recommend
16	Adolph Yates	Unsure
17	Vinod Dasa	Strongly Recommend
18	Luis Pulido	Strongly Recommend
19	Fred Nelson	Recommend
20	Charles Hummer	Recommend
21	Barry Kraushaar	Strongly Recommend
22	Bernard Roehr	Strongly Recommend
23	Kenneth Jaffe	Recommend
24	Douglas Naudie	Recommend
25	Alexandra Page	Strongly Recommend
26	Matthew Abdel	Strongly Recommend
27	Alison Chang	Strongly Recommend
28	Ajay Srivastava	Strongly Recommend
29	Laura Bruse	Recommend
30	Stephen Weber	Would Not Recommend
31	Rafael Sierra	Strongly Recommend
32	Alexander Sah	Strongly Recommend
33	Benjamin Miller	Strongly Recommend
34	Matthew Landfried	

35

Matthew Austin

Would Not Recommend

Reviewer Detailed Responses and Editorial Suggestions

Reviewer #1, Paul Castello, M.D

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
1	Paul Castello, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons)	<p>A. No problem with the structure and content. Couple of questions: The molecular weight of the of HA viscoelastic supplement was not addressed. HA injections were just linked together as one treatment modality.</p> <p>B. Similar to above concerns, PRP recommendation did not address specifically any difference with neutrophil deficient preparation.</p> <p>C. Partial meniscectomy was supported to treat mild-moderate OA but there was no definition of what mild-moderate OA represents. Is it the relative joint space on a weightbearing PA x-ray Is it the absence of subchondral cysts/sclerosis, peripheral osteophytes or malalignment?</p>

Workgroup Response to Reviewer #1

Dear Paul Castello, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Details regarding high- versus low- molecular weight viscosupplementation, as supported by the applicable evidence, can be found in the full rationale for this recommendation. The supporting evidence was not sufficient to make a directional recommendation in support of a specific molecular weight.
- B. The available evidence did not provide the direct comparisons necessary to make a directional statement, as noted in the future research section “Specifically, to platelet rich plasma it will be of outmost importance to include comprehensive platelet rich plasma characterization and description of platelet rich plasma preparation protocol.” The available evidence comparing leukocyte-rich PRP (LR-PRP) and leukocyte-poor PRP (LP-PRP) was limited and insufficient to make a preparation-specific recommendation.
- C. Supporting evidence used the criteria of: knee osteoarthritis grade 0 or 1 on weight-bearing knee radiographs according to Ahlbäcks classification as well as mild-to-moderate OA as seen on imaging.

Reviewer #2, Marc Levine, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
2	Marc Levine, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	A. The material presented represents a thoughtful multi-disciplinary evaluation of non-operative treatment modalities. The participants are to be commended for the time and effort put forth.

Workgroup Response to Reviewer #2

Dear Marc Levine, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for the positive feedback.

Reviewer #3, John Chef, M.D., MPH, FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
3	John Chef, M.D., MPH, FAAOS	Committee on Evidence-Based Quality and Value, American Academy of Orthopaedic Surgeons	A. Please look at line 378. There should only be 3 stars for this moderate recommendation (currently has 4 stars)

Workgroup Response to Reviewer #3

Dear John Cheff, M.D., MPH, FAAOS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for your comment.

Reviewer #4, Conjeevaram Maheshwer, FRCS, FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
4	Conjeevaram Maheshwer, FRCS, FAAOS	American Academy of Orthopaedic Surgeons	A. I may be late in submission, but the guidelines were extremely important and were well analyzed and covered.

Workgroup Response to Reviewer #4

Dear Conjeevaram Maheshwer, FRCS, FAAOS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for the positive feedback.

Reviewer #5, Michael O'Malley, M.D., MS, FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
5	Michael O'Malley, M.D., MS, FAAOS	Board of Councilors, American Academy of Orthopaedic Surgeons	A. I think the guidelines appear comprehensive and in accordance with the current literature. They appear clear and concise, for any orthopedic surgeon, within any subspeciality, to be able to follow.

Workgroup Response to Reviewer #5

Dear Michael O'Malley, M.D., MS, FAAOS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for the positive feedback.

Reviewer #6, Adam Bruggeman, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
6	Adam Bruggeman, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	A. This is well written and accurately reflects the current state of the literature. I would have liked to see the inclusion of stem cell injections in this list.

Workgroup Response to Reviewer #6

Dear Adam Bruggeman, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your positive feedback. Stem cell injections were not included in the scope of this guideline as defined by the work group.

Reviewer #7, Miriam Hakim-Zargar, M.D., MPH, FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
7	Miriam Hakim-Zargar, M.D., MPH, FAAOS	Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. I am happy to see that the recommendations regarding viscosupplementation are updated. The recommendations reflect the many modalities we have at our disposal to help alleviate the symptoms of knee OA, given that there is currently no actual treatment. Most of us use a variety of these symptom modifiers and customize their use to the specific patient's age, degree of arthrosis, activity level etc. Accuracy in determining degree of osteoarthritis is difficult, which in turn limits interpretation of the study results. The limiting factor here is that most studies have a variety of patients. Inter-reliability (k) of different reviewers estimating degree of osteoarthritis on x-ray is quite variable.</p> <p>B. I'm happy to see the data and recommendation on use of Viscosupplementation. We have very few options for the treatment of symptoms in young patients with severe osteoarthritis. Inter-observer reliability in reading xrays for OA is very poor and patient variability in the study can dilute the results. Power analysis can be quite tricky and studies are often under powered. Thank you for this comprehensive look at the issue!</p>

Workgroup Response to Reviewer #7

Dear Miriam Hakim-Zargar, M.D., MPH, FAAOS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for the positive feedback.

B. Thank you for the positive feedback.

Reviewer #8, F. Scott Gray, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
8	F. Scott Gray, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. Self Management lines 198-204 is not defined so that I can easily understand what clinical / patient care information is being considered.</p> <p>B. Hyaluronic Acid lines 314-320 with a "no" recommendation is controversial, and I continue not to support this decision. In my opinion there is enough level II and III literature evidence supporting its use to reverse the AAOS stance on this management. This means I feel there is enough evidence based non pharmaceutical industry published material to support and reverse this decision.</p> <p>C. I can not support the recommend guidelines as it pertains to Hyaluronic Acid</p>

Workgroup Response to Reviewer #8

Dear F. Scott Gray, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Self Management is fully defined within the full recommendation rationale on page 100.
- B. Following the Review Period, the work group reconsidered this recommendation. The recommendation was both reworded to provide additional clarity and downgraded to Moderate strength.
- C. No response.

Reviewer #9, Nicholas Bedard, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
9	Nicholas Bedard, M.D.	American Academy of Hip and Knee Surgeons	<p>A. The objectives of the guidelines are articulated well in lines 467-481 as is the guidelines target audience in lines 481-467. The patient population for which these guidelines are meant to apply is clearly stated in lines 500-501, 506-507 and the scope of non-arthroplasty treatments covered in this guideline are appropriate.</p> <p>B. The Patient Education recommendation (lines 1189-1201) would benefit from a more extensive rationale section that is similar to the other recommendations. This would provide the reader with more context regarding what specific types of education programs the recommendation is referring too. Additionally, this recommendation does not have the sections regarding benefit/harms, outcome importance, cost effectiveness/resource utilization, feasibility, or future research like the other recommendations in the CPG.</p> <p>C. Overall, the grades assigned to each recommendation are appropriate for the evidence available. However, there is some concern regarding the wording or strength of the recommendation for three of the recommendations.</p> <p>D. Arthroscopic partial meniscectomy in appropriately indicated patients may improve pain and function for the treatment of meniscal tears with concomitant mild to moderate knee osteoarthritis: Consideration should be given to downgrading the strength of this recommendation from Moderate to Limited. The rationale for this recommendation does cite three randomized, controlled trials that demonstrate that partial meniscectomy is as effective as physical therapy. However, these studies do not support the true recommendation from this clinical practice guideline found in lines 2124-2127: “This procedure should be considered in patients with mild-to-moderate knee OA and an MRI confirmed meniscal tear who have previously failed appropriate conservative treatment such as physical therapy, corticosteroid injections, and a course of non-steroidal anti-inflammatory medications.” As stated in lines 2120-2121, there are no studies that support this proposed treatment recommendation (consider meniscectomy in patients who have failed appropriate conservative treatment) and thus, the strength of this recommendation would be more accurately categorized as limited.</p> <p>E. Hyaluronic acid is not recommended for the vast majority of patients with symptomatic osteoarthritis of the knee: Consideration should be given to removing “the vast majority of” (line</p>

1714) from the recommendation regarding hyaluronic acid. The rationale provided clearly articulates that the data does not support a clinically meaningful improvement in patient outcomes scores when compared to controls. It is important to comment on the few studies that demonstrate a statistical benefit with use of hyaluronic acid which has been done in the rationale, as it does provide context to those reading the recommendations. However, there is limited evidence to indicate which subset of patients may benefit from HA use and thus the recommendation as written does not provide much clarity to the healthcare provider utilizing the recommendation despite being a “strong” recommendation.

- F. Brace treatment could be used to improve function, pain and quality of life in patients with knee osteoarthritis: It would be important to note in either the recommendation itself or the rationale section that “in select patients” brace treatment could be used as the strongest evidence provided for this recommendation comes from studies evaluating the effects of unloader bracing for unicompartmental knee osteoarthritis and varus deformity. Additionally, the rationale cites one study evaluating bracing for patella-femoral osteoarthritis. Thus, the recommendation best applies to patients with unicompartmental knee osteoarthritis or patella-femoral osteoarthritis.
- G. It would be important to address within the clinical practice guideline that there is a spectrum of severity of osteoarthritis. As such, the efficacy of the interventions and treatments addressed within this clinical practice guideline like depend upon the severity of osteoarthritis a patient is presenting with. It would be important to note that despite the strength of a recommendation or level of evidence supporting a given intervention, a patient with mild osteoarthritis (Kellgren and Lawrence (KL) grade I or II) and neutral alignment would likely respond differently to the intervention than a patient presenting with KL grade IV osteoarthritis and significant deformity. Just as a total knee replacement is less effective in a patient with KL grade I osteoarthritis than in a patient with KL grade IV osteoarthritis; so too can the severity of osteoarthritis impact the efficacy of injections, therapy, NSAIDs, etc. This limitation should be made clear to the readers of the clinical practice guideline and ultimately the decision to utilize a given intervention for knee osteoarthritis should depend not only on the evidence supporting its use, but also on the patient presentation and shared decision making between the patient and the provider.
- H. Furthermore, osteoarthritis is a very heterogeneous condition. The progression of the disease and the symptomatology is affected by numerous factors that may not have been considered when conducting studies to evaluate the efficacy of an intervention. Factors such as patient engagement with a conservative management program, the presence of adjacent/remote joint disease, pre-existing comorbidities, in particular metabolic syndrome, genetic predisposition, the phenotype of osteoarthritis (ie. osteoarthritis with an inflammatory component), deformity and range of motion of the affected joint, as well as many other parameters influence the course of the disease and the efficacy of interventions that are implemented. Taking the latter into account together with the fact that the medical community has limited non-operative strategies available to treat patients with

			osteoarthritis (of the knee), the guidelines should not be prescriptive and should give latitude to clinicians to exercise their acumen in selecting the best therapy for their patients.
--	--	--	---

Workgroup Response to Reviewer #9

Dear Nicholas Bedard, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. The workgroup has edited the rationale to the Patient Education recommendation.
- C. Thank you for your comment.
- D. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.
- E. Following the Review Period, the work group reconsidered this recommendation and removed the term 'the vast majority of.'
- F. The supporting evidence for this recommendation included unicompartmental knee osteoarthritis and patella-femoral osteoarthritis. The inclusion criteria for this PICO was patients with osteoarthritis of the knee receiving a brace/orthotic device.
- G. The majority of the supporting evidence covered KL1-3 but some articles included KL4. The work group highlighted the need for future research with more detailed sub-group stratification of osteoarthritis severity.
- H. The following verbiage has been included in the introduction "This guideline should not be construed as including all possible methods of care or excluding acceptable interventions similarly directed at obtaining favorable outcomes. The final decision to use a specific procedure must be made after assessing all concerns presented by the patient and consideration of locality-specific resources.

Reviewer #10, David Scalzitti, PT, PhD

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
10	David Scalzitti, PT, PhD	Key Informant Panelist, American Academy of Orthopaedic Surgeons	<p>A. Overall, the methods are transparent, and the literature included is relevant for the PICO questions.</p> <p>B. The ordering of the recommendations is not clear. For example, why was lateral wedge insoles discussed first as this may be one of the less frequently used interventions.</p>

Workgroup Response to Reviewer #10

Dear David Scalzitti, PT, PhD,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. The recommendations are presented in the order by which the PICO questions were created.

Reviewer #11, Laura Tosi, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
11	Laura Tosi, M.D.	Committee on Research and Quality/ Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. Overall, I am excited that the AAOS has updated its methodology for performing CPGs. In the past we seemed to throw the baby out with the bathwater when there were no prospective reviews or metaanalyses available.</p> <p>B. However, I think this CPG may have gone a bit too far. Almost all recommendations are the result of a structured review. That's OK , but the authors do not specifically say that..... which is a disingenuous given the AAOS's history. Please spell it out topic by topic.</p> <p>C. The questionnaire above is a problem because I really only have one "grade upset", namely support for arthroscopic partial meniscectomy. My interpretation of the write up is that outcomes are no worse than with PT. If I am reading the write up correctly, we are recommending a major procedure when PT would have been just fine.</p>

Workgroup Response to Reviewer #11

Dear Laura Tosi, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. The structured review methodology applied to all recommendations is detailed in the Methods section.
- C. The recommendation is for knee arthroscopy/partial meniscectomy to be available as an option for patients with mild-to-moderate knee osteoarthritis and an MRI confirmed meniscal tear who have previously failed appropriate conservative treatment such as physical therapy, corticosteroid injections, and a course of non-steroidal anti-inflammatory medications. These patient indications are detailed within the recommendation's rationale.

Reviewer #12, Johnathan Bernard, M.D., MPH

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
12	Johnathan Bernard, M.D., MPH	Key Informant Panelist, American Academy of Orthopaedic Surgeons	<p>A. Very well done updated guidelines for the non-arthroplasty treatment of osteoarthritis. Very few comments below:</p> <p>B. In both the benefits/harms of implementation and acceptability sections of Oral NSAIDs and Oral Acetaminophen, both are grouped together in the rationale of treatment, although each are a separate clinical guideline in the treatment of OA: Oral NSAIDs: draft page 51 line 1581-'Although oral NSAIDs and acetaminophen are widely used to treat osteoarthritis of the knee...' Oral Acetaminophen, draft page 53 line 1650, 'Currently oral NSAIDs and acetaminophen are commonly utilized approach in treating symptomatic knee osteoarthritis,...' You could consider only discussing NSAIDs or acetaminophen in their respective sections.</p> <p>C. Oral Narcotics: The recommendations, wording, and conclusion for the role of oral narcotics is well stated and very appropriate.</p> <p>D. Hyaluronic Acid: Updating these recommendations to include the statistically significant improvements associated with high molecular cross-linked hyaluronic acid as well as its limitations is a solid addition to these recommendations</p> <p>E. Partial Meniscectomy: Page 68 It might be worth at least mentioning the inclusion/exclusion criteria for the patients that underwent a partial meniscectomy and whether they had degenerative meniscal pathology or mechanical symptoms in the setting of osteoarthritis for the Katz study LINE 2081 and the Van de Graaf LINE 2095. LINE 2124-7 is very important to describing who would benefit from these specific recommendations.</p>

Workgroup Response to Reviewer #12

Dear Johnathan Bernard, M.D., MPH,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. Thank you for your comment. The draft has been modified.
- C. Thank you for the positive feedback.
- D. Thank you for the positive feedback.
- E. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.

Reviewer #13, Julie Dodds, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
13	Julie Dodds, M.D.	Board of Specialty Societies, American Academy of Orthopaedic Surgeons	<p>A. As repeatedly expressed by multiple representatives of AANA and other specialty societies, the studies used to evaluate viscosupplementation are inaccurate, poorly done and should not serve as "evidence" to recommend against viscosupplementation. By discouraging viscosupplementation, we are doing an egregious omission of a potential minimally invasive treatment which can greatly improve quality of life in our patients, with little or no potential harmful effects.</p>

Workgroup Response to Reviewer #13

Dear Julie Dodds, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Following the Review Period, the work group reconsidered this recommendation. The recommendation was both reworded to provide additional clarity and downgraded to Moderate strength.

Reviewer #14, Anita Bemis-Dougherty, PT, DPT, MAS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
14	Anita Bemis-Dougherty, PT, DPT, MAS	American Physical Therapy Association	<p>Line #</p> <p>A. 492- "in making clinical decisions with their patients..."Change to: "in making shared clinical decisions with their patients..."</p> <p>B. 511- "including trauma, overuse, and genetic predisposition" Suggest change to: "...including trauma, overuse, obesity, and genetic predisposition"</p> <p>C. 936-946- "showed either improvement or no change..." Suggest: list the number of studies showing improvement separate from those where no change is demonstrated. Comment: This statement lists a number of articles and then the statement listed in column B, it would be more clear if the number of studies that showed improvement were listed separately from those where no change was demonstrated.</p> <p>D. In addition, in other sections of this CPG, detail from specific studies are listed. Minimal detail is listed here. This is a commonly asked question by patients "Will it help my knee to take glucosamine or chondroitin"? The lack of detail in this section makes it difficult for a provider to answer this question.</p> <p>E. 936-958- Comment: If there is one or more high quality studies recommending this intervention, why is the strength of evidence 2 stars?</p> <p>F. 1152-1153- States: Two moderate quality study are mentioned but only one is listed. Suggestion: What is the additional study? List reference, change to "studies". Comment: Are these the 2 studies listed on line 1156? I would move them up to where "two moderate quality study" are listed</p> <p>G. 1218 (in Arthritis Care and Research)- Comment: Why do you list the publication with this reference and not others? Suggest you delete this.</p> <p>H. 1224- "in JAMA" Comment: Suggest deleting publication and only reference name and year to keep this consistent throughout the manuscript. Be consistent throughout the publication</p>

- | | | | |
|--|--|--|--|
| | | | <p>I. 1281-1283- "increase in knee pain or muscle soreness when engaging in manual therapy and exercise..." Suggestion: substantiate the claim or remove this statement. Comment: Are there a references to substantiate this claim?</p> <p>J. 1584- Comment: Should a statement be included that the benefits from oral NSAIDS are short term?</p> <p>K. 1636- Comment: Should a statement be included that the benefits from oral Acetaminophen are short term?</p> <p>L. 1801- Comment: Should a statement be included that the benefits from corticosteroid injections are short term or is there evidence of long-term benefit? If so, this should be included. Any studies substantiating the long-term benefits of intra-articular corticosteroids?</p> <p>M. 1908-1909, 1879-1881- Current Text: "Adverse events were higher in the PRP group than IA HA, both local soreness and injection pain (two 1880 studies (Spakova; 2012, Yaradilmis; 2020)) and one study (Huang; 2018)) systemic events (proteinuria 1881 and hypertension). " Suggestion: Adverse events are listed in lines 1879-1881, should these be listed as harms?</p> <p>N. 1949-1984- Comment: Mention is made of "improved WOMAC total..." (line 1961) or "improve patient pain" (line 1974) "denervation therapy may reduce pain and improve function..." (line 1980). Suggestion: It would be helpful for the reader to know at what point these changes were made, 3 months? 6 months? a year? What was the follow up period? This is just one example but there are other sections of the manuscript where outcomes are reported but no mention of the length of follow up.</p> <p>O. 2086, 2105, 2159, 2172- Comment: Good! Follow up is mentioned</p> <p>P. 2234, 2252- Comment: It would be helpful for the reader to be aware of what the conversion rates to TKA are when patients undergo a HTO. Is this data available?</p> <p>Q. 2276- Comment: line 1399 in the acupuncture section states "The treatment should be administered by a certified acupuncture practitioner" Suggest stating: "The treatment should be administered by a physical therapist or other practitioner certified in Dry Needling"</p> <p>R. Comment: The majority of dry needling (and published literature on the subject) is performed by physical therapists. State Physical Therapy practice acts require physical therapists to be certified to perform dry needling. A statement should be added similar to the statement used in the acupuncture section.</p> |
|--|--|--|--|

- | | | | |
|--|--|--|---|
| | | | <p>S. Line# 305- Comment: Recommendation on oral narcotics isn't written in recommendation format as an action statement.</p> <p>T. 975- Comment: replace "much" with "must"</p> <p>U. 1037- Comment: Would have liked more information on who/profession was doing the supervising of the exercise including who developed the exercise programs- are we to assume it was PT, personal trainers, etc.?</p> <p>V. 1153- Comment: replace "study" with "studies" and reference second study</p> <p>W. 1201- Comment: recommendation is missing EtD framework</p> <p>X. 1282- Comment: provide a reference to "patients may experience a temporary increase in knee pain or muscle soreness..." was that a finding in one of the included studies or is it the opinion of the workgroup?</p> <p>Y. 1335- Comment: It is not clear to me why the recommendation was downgraded. 2 high quality and 1 moderate with positive results. Maybe it was related to feasibility?</p> <p>Z. 1383- Comment: this line states they selected a moderate strength yet the recommendation on line 1367 says limited</p> <p>AA. 1389- Comment: this line states they selected a moderate strength yet the recommendation on line 1367 says limited</p> <p>BB.1587- Comment: talks about narcotics when the recommendation is about NSAIDS</p> <p>CC.1639- Comment: talks about narcotics when recommendation is about oral acetaminophen</p> <p>DD. 1665- Comment: same comment as line 305- its not written as an action statement but more of a fact</p> |
|--|--|--|---|

Workgroup Response to Reviewer #14

Dear Anita Bemis-Dougherty, PT, DPT, MAS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your comment. The draft has been modified.
- B. The etiology of obesity and osteoarthritis is the result of increased forces across the joint. It has the similar affect as other overuse means of leading to osteoarthritis. Therefore, the work group believes obesity falls within the umbrella of overuse.
- C. . Unfortunately, each study cannot be reported as a dichotomous outcome of either showing improvement or no improvement. Within each study, multiple outcomes are reported and not each outcome showed completely agreement within a single study (i.e. all reported outcomes for a study showing improvement for each outcome). Therefore, the work group was not able to simply list the studies as showing improvement or no improvement.
- D. This recommendation was downgraded due to inconsistency in findings. Supporting evidence found both improvement and no significant change in patient outcomes; future research in this area is needed to make a directional recommendation.
- E. This recommendation was downgraded from Moderate to Limited by the work group due to inconsistency of findings and unclear efficacy.
- F. Thank you for your comment. The draft has been modified.
- G. Thank you for your comment. The draft has been modified.
- H. Thank you for your comment. The draft has been modified.
- I. The work group feels that the temporary increase in knee pain or muscle soreness is to be expected in patients with osteoarthritis of the knee.
- J. When taken intermittently for osteoarthritis and pain in patient without a medical contraindication, it can be taken for relatively long periods as many patients use it for years before seeking more invasive procedures.
- K. When taken intermittently for osteoarthritis and pain in patient without a medical contraindication, it can be taken for relatively long periods as many patients use it for years before seeking more invasive procedures.
- L. The recommendation language (i.e. short-term relief) represents the results of the supporting evidence; there are no supporting studies that demonstrate a long-term effect.
- M. Thank you for your comment. The draft has been modified.
- N. The supporting evidence for this recommendation included studies with follow-up date from 30 to 190 days.

- O. Thank you for the positive feedback.
- P. This analysis was not included in the a priori scope as determined by the work group members.
- Q. There are a number of healthcare professionals besides physical therapists who are trained to administer acupuncture. The key is they should be certified as an acupuncture practitioner. The work group feels it is unnecessary to add physical therapist to the statement.
- R. The work group did not elect to make a Benefits/Harms statement because the consensus recommendation is not directional in nature.
- S. Given the safety concerns and negative outcomes found in the supporting evidence, the workgroup elected to write the recommendation in a way that encourages providers to reconsider use of oral narcotics.
- T. Thank you for your comment. The draft has been modified.
- U. The supporting evidence did not specifically compare the effects of different professions providing the supervision on the outcomes of exercise.
- V. Thank you for your comment. The draft has been modified.
- W. The workgroup has edited the rationale to the Patient Education recommendation.
- X. The work group felt that temporary increase in knee pain and muscle soreness was to be expected in patients with osteoarthritis of the knee following exercise and did not feel that specific mention was necessary.
- Y. This recommendation was downgraded due to inconsistency in findings. Supporting evidence found both improvement and no significant change in patient outcomes.
- Z. Thank you for your comment. The draft has been modified.
- AA. Thank you for your comment. The draft has been modified.
- BB. Thank you for your comment. The draft has been modified.
- CC. Thank you for your comment. The draft has been modified.
- DD. Given the safety concerns and negative outcomes found in the supporting evidence, the workgroup elected to write the recommendation in a way that encourages providers to reconsider use of oral narcotics.

Reviewer #15, F. Suzette Song, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
16	Suzette Song, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. There are contradictory statements with regards to the Hyaluronic acid section.</p> <p>B. Also, the "self-management" part is full of supervised programs “taught by healthcare professionals and trained layperson instructors.” That kind of goes against the whole “self” thing. Meet several times over several weeks. Who pays for this? We’re supposed to set this up for free? This whole section is vague as I don’t know precisely what they are talking about. It also mentions cognitive behavioral therapy, which is really not available. It’s impossible to get adequate access to psychology and psychiatry services as it is.</p> <p>C. Hyaluronic acid is not recommended for the vast majority of patients with symptomatic osteoarthritis of the knee. The 2013 edition of this guideline strongly recommended against the use of viscosupplementation. In 1746 contrast to this updated version, the 2021 version found that statistically significant improvements were associated with high-molecular cross-linked hyaluronic acid but when compared to mid-range molecular weight, statistical significance was not maintained. This newer analysis did not demonstrate clinically relevant differences when compared to controls. However, as previous research reported benefits in their use, the group felt that a specific subset of patients might benefit from its use." This is contradictory – they state that it was statistically significant and then that it wasn’t. Some research reported benefits, some didn’t. This does not seem to be language supportive of a very strong recommendation against. The insurance companies will key on the fact that it is not recommended for the vast majority of patients. The detail states some patients may benefit, but doesn’t state who those might be or how we might go about deciding that. Then they state there will be no effect on current practice. I would disagree. They also say there won’t be any difference in cost – that also doesn’t make sense, because there absolutely will be if insurance companies stop covering it.</p> <p>D. In contrast to this updated version, the 2021 version found that statistically significant improvements were associated with high-molecular cross-linked hyaluronic acid but when compared to mid-range molecular weight, statistical significance was not maintained." This is the sentence I find most confusing. Why are we comparing high molecular weight hyaluronic acid to mid-range molecular weight? Should be compared to controls. I feel that statements for CPG’s should be much less ambiguous. Same goes for the actual statement – what does “vast majority” mean? 70% 80%. 90%? What about those for whom it does help? Based on</p>

what I can tell from the research they should be differentiating between high and mid-range molecular weight. They also should recommend against use in patients with severe OA KL-stage IV.

- E. Some studies demonstrated a statistical benefit with the use of HA but could not reach the significance for a minimally clinically meaningful difference, leading to the conclusion that viscosupplementation can represent a viable option for some patients that failed other treatments when appropriately indicated." So how can the actual statement say that HA is not recommended for the vast majority if in the detail says that it is a viable option for some patients that failed other treatments. To me, those don't sound compatible.

- F. Self-Management: Self-management programs are recommended to improve pain and function for patients with knee osteoarthritis. Self-management programs refer to formalized training and education programs that are taught by both 1146healthcare professionals and trained layperson instructors. They typically include several sessions over 1147several weeks. These programs train people in several elements of self-management for osteoarthritis 1148including medication compliance, pain management and pain coping strategies, joint protection strategies 1149during physical activity, exercise advice, problem solving approaches and stress management techniques." Are these really self-management programs? By the sound of things, these are really supervised programs "taught by healthcare professionals and trained layperson instructors." That kind of goes against the whole "self" thing. Meet several times over several weeks. Who pays for this? We're supposed to set this up for free? More uncompensated time? This whole section is vague as I don't know precisely what they are talking about. It also mentions cognitive behavioral therapy, which is really not available. It's impossible to get adequate access to psychology and psychiatry services as it is.

Workgroup Response to Reviewer #15

Dear Suzettee Song, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your comment. Please see response for Hyaluronic Acid comment below.
- B. The supporting studies defined self-management programs as having been taught by professionals. As stated in the rationale "Self-management programs refer to formalized training and education programs that are taught by both healthcare professionals and trained layperson instructors." Cognitive behavioral therapy (CBT) was investigated by the workgroup; however, the available evidence did not warrant a directional statement in favor of CBT for osteoarthritis of the knee patients.
- C. Following the Review Period, the work group reconsidered this recommendation. The term "the vast majority" has been removed and the strength has been downgraded to Moderate.
- D. Following the Review Period, the work group reconsidered this recommendation. The term "the vast majority" has been removed and the strength has been downgraded to Moderate.
- E. Following the Review Period, the work group reconsidered this recommendation and removed the term "the vast majority of." The work group also clarified in the recommendation that the recommendation pertains to first line treatment.
- F. The supporting studies defined self-management programs as having been taught by professionals. As stated in the rationale "Self-management programs refer to formalized training and education programs that are taught by both healthcare professionals and trained layperson instructors." Cognitive behavioral therapy (CBT) was investigated by the workgroup; however, the available evidence did not warrant a directional statement in favor of CDT for osteoarthritis of the knee patients.

Reviewer #16, Adolph Yates, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
16	Adolph Yates, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. Overall Comments: Review Process:</p> <ul style="list-style-type: none"> • This process is not conducive to full review. • The CPG and its e-appendices are not transparent regarding underlying methodology and various underlying sourcing of anchors for MID. These had to be requested. This is was more transparent in the last CPG on OAK. • The time period for review is too short for practicing surgeons. • The time period for the BOC Research and Quality Committee to review and discuss was especially too short. • The time period for review and comment should be extended. <p>B. Preamble/Introduction: The following language is a welcome return: “This guideline is not intended for use as a benefits determination document. It does not cover allocation of resources, business and ethical considerations, and other factors needed to determine the material value of orthopaedic care”.</p> <p>C. Methodology: It is understood that AAOS was in a transition phase from its own methodological structure to hopefully relying on GRADE methodology. This has been pronounced as a goal.</p> <p>D. The rationales for almost all recommendations are written as structured reviews without mention of the documented attempts to perform meta-analysis.</p> <p>E. The AAOS 2013 OAK CPG emphasized use of MID, and mention it again for a few topics in this CPG, but, with a few exceptions, the rationales consistently do not mention the prepared Forest plots in the second e-appendix that refute most of their recommendations if the intervention needs to reach the full MID. Most of the presented rationales are structured reviews, not attempts at meta-analysis. Comment on this within the rationales is advised.</p> <p>F. The CPG claims utilization of GRADE methodology, but complete adherence is not apparent in the CPG or its supporting appendices.</p> <p>G. It is not clear that a patient centered ordering of the importance of outcomes was performed either through a Delphi approach or otherwise.</p>

- H. Involvement of the expert panel to assess the pulled literature before data extraction and creation of evidence tables is not evident. This requires additional considerable work by the panels, but oversight by those with clinical expertise is critical in avoiding misinterpretations.
- I. There are no Evidence to Decision Tables (ETDs) presented in the CPG or e-appendices. It is not clear that this valuable GRADE tool was used.
- J. In particular, number needed to treat (NNT) analyses are not offered in the CPG or the appendices. These are useful in terms of weighing benefits against harms of interventions.

MID/MCII

- K. It was communicated, only after inquiry, that the same anchors for MID were used across the evaluated interventions. Given the disparate literature for the various interventions, it is not clear if this was possible. Ideally, the use of anchor versus distribution derivation of MID would have been made clear in each section.
- L. The stated papers from which anchors were derived, had patient populations and interventions that are very different and necessarily applicable to the interventions reviewed in this CPG.
- The Angst papers used (1,2) used for MID anchors involved before and three months after PROs in patients with OA admitted to a Swiss rehabilitation hospital undergoing multiple modes of intervention. The anchor was based on a Likert scale without a minimal or “fair” response, which defines the MID; MCID was originally described as “the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management’ (3).
 - Expectations from these multiple simultaneous interventions were potentially much higher than that of patients undergoing isolated outpatient interventions.
 - The Tubach (4) paper used for a pain MID anchor looked at both first time and/or new drug, prescription of NSAIDs. Over 50% of the patients were on some other form of non-NSAID analgesia not defined, which could have included narcotics, thus raising expectations of results. The paper did not use the “fair” response for its MID, instead using the two top box responses to define MCII. This raises the bar higher than expected in terms of meeting MID.
- M. Neither of the three papers from Angst and Tubach utilized placebos; no placebo effect could be subtracted. This is contrary to the methodology used by this CPG which subtracted the effect of the placebo arm of the studies from the intervention improvements in PROs. This is only one way of comparing effects (5). Other studies using OMERACT criteria before after treatment within each arm of the study including Petterson (6) and several of the studies used

in this CPG show efficacy of HA (7). A meta-analysis of overlapping meta-analyses found benefit for IHA as well (8). A The PRO being used should be measured for each cohort of a study and can be compared, but in formulating the effect of the intervention, its impact and confidence levels, should not be done with the placebo subtracted. There are multiple methodologists that recommend using more than one analysis.

- N. The point above is especially salient in that it has been recognized that saline injections have significant therapeutic effect and cannot be rationally used as controls (9,10,11).
- O. Network meta-analysis has shown benefit from HA (12) and in particular HMW HA in a paper that directly challenges the 2013 OAK CPG whose methodology was revisited in this current product (13).
- P. Proportional MID was used in some Forest Plots and, although not clearly stated, in some rationales and not in others. This should have been more consistent. Methodologists in the literature emphasize the need to consider that the collective partial MID improvement of a PRO for an intervention be given credit for a proportion of the population improving that is significant. “We suggest the following guide for interpretation given a 0.5 MID: if the pooled estimate is greater than 0.5, and one accepts that the estimate of effect is accurate, many patients may gain important benefits from treatment. If the estimate of effect lies between 0.25 and 0.5, the treatment may benefit an appreciable number of patients. As the pooled estimate falls below 0.25 (i.e. 50% of the MID), it becomes progressively less likely that an appreciable number of patients will achieve important benefits from treatment.” (14). If this was used is not clearly stated or utilized. The importance of this is emphasized by Angst in 2017 (15).
- Q. It appears that key meta-analyses from other authors and the Cochrane group were not utilized. Meta-analysis using level one data is level one data and should be made known to the group; at minimum it allows relative benchmarking.
- R. Harmonization with other external guidelines: It is not clear that the most recent recommendations from the ACR (16) or OMERACT (17) were made available to the work group and used for benchmarking and feedback.

Specific Comments Regarding Recommendation Sections (this review is at this time more cursory than desired due to time limitations).

Insoles:

- S. The most recent Cochrane review for this intervention is not referenced, which would have been confirmatory.

T. A Forest plot was created and presented in the e-appendix, but the results are not discussed in the rationale. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

U. In keeping with the overall comments, it is not transparent whether or not the MID was derived by distribution or anchor techniques

V. It is not clear that there was a reasonable placebo to subtract for the quoted studies. If not subtracted for this intervention, why is it subtracted in other parts of the CPG?

Canes:

W. Moderate recommendation for use.

X. Recommendation without Forest plot or discussion of MID

Y. No real placebo to subtract from MID if used.

Z. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised. If a moderate strength recommendation can be generated without the above, why the inconsistency with other recommendations in the CPG?

Braces:

AA. The Forest plot presented would argue for a less than moderate level response, especially given the limited literature. This introduces inconsistency with other recommendations within the CPG that relied on MID. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

BB. It is not clear what the MID was based on or whether placebo was subtracted.

CC. The rationale introduces the “walking pain” outcome, which is used in many studies on OA. It is not uniformly used in other recommendations in the CPG

DD. The most recent Cochrane review on this intervention would have added validity to the recommendation and perspective if discussed in the rationale.

Oral/Dietary Supplements:

EE. A limited recommendation was given despite not reaching MID on the given Forest plots.

FF. It is not clear what the MID was based on or whether placebo was subtracted.

GG. It is not clear if proportional MID results drove the recommendations. The above are not discussed in the rationale. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

Topical NSAIDs:

HH. Given a “strong” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

II. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

JJ. The strong recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

Supervised Exercise:

KK. Given a “strong” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

LL. The strong recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. The evidence table presented using AAOS methodology is not impressive in terms of justifying a “strong” response. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Neuromuscular Training:

MM. Given a “moderate” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

NN. The “moderate” recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

OO. The evidence table presented using AAOS methodology is not impressive in terms of justifying a “moderate” response. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Self-Management:

PP. Given a “strong” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

QQ. The strong recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

RR. The evidence table presented using AAOS methodology is not impressive in terms of justifying a “strong” response. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Education:

SS. Given a “strong” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

TT. The strong recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

UU. The evidence table presented using AAOS methodology is not impressive in terms of justifying a “strong” response, especially given the limited literature. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Weight Loss:

VV. Given a “moderate” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

WW. The “moderate” recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

XX. The evidence table presented using AAOS methodology is not impressive in terms of justifying a “moderate” response. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Manual Therapy/Massage:

YY. Given a “limited” recommendation without consideration of MID in the rationale and without presentation of a Forest plot.

ZZ. The “limited” recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation.

AAA. The evidence table presented using AAOS methodology is not impressive in terms of justifying a “limited” response. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Laser

BBB. A limited recommendation was given; despite not reaching MID on the given Forest plots, a proportional MID analysis would have raised the level.

CCC. It is not clear what the MID was based on or whether placebo was subtracted.

DDD. The above are not discussed in the rationale. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Acupuncture:

EEE. A limited recommendation was given; despite not reaching MID on the given Forest plots, a proportional MID analysis would have raised the level.

FFF. It is not clear what the MID was based on or whether placebo was subtracted.

GGG. The above are not discussed in the rationale. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

TENS/PENS:

HHH. A limited recommendation was given; despite not reaching MID on the given Forest plots, a proportional MID analysis would have raised the level.

III. It is not clear what the MID was based on or whether placebo was subtracted.

JJJ. The above are not discussed in the rationale. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Shock Wave:

KKK. A limited recommendation was given; despite not reaching MID on the given Forest plots, a proportional MID analysis would have raised the level.

LLL. It is not clear what the MID was based on or whether placebo was subtracted. The above are not discussed in the rationale.

MMM. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

NSAIDS:

NNN. Given a “strong” recommendation without consideration of MID in the rational and despite not reaching MID on the given Forest plots; a proportional MID analysis would have justified the level.

OOO. It is not clear what the MID was based on or whether placebo was subtracted.

PPP. The strong recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Acetaminophen:

QQQ. Given a “strong” recommendation without consideration of MID in the rational and despite not reaching MID on the given Forest plots; a proportional MID analysis would have justified the level.

RRR. It is not clear what the MID was based on or whether placebo was subtracted.

SSS. The strong recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Oral Narcotics:

TTT. No evidence presented in the e-appendices.

UUU. There is no discussion about the use of low-grade narcotics for patients with terminal illness or far advanced age and contra-indications to NSAIDS and surgery.

VVV. 3.) As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

Hyaluronic Acid

WWW. The use of the word “vast” in the recommendation is not the norm in guidelines and EBM; it belies an underlying bias. The “strong recommendation against” status is paradoxical and internally inconsistent with the other “limited for” and “moderate for” recommendations within this CPG with equally challenging literature and which did not meet the artificially high MID criteria as well.

XXX. The “strong” recommendation against should be changed to, at minimum, a “limited recommendation” for patients that have exhausted other options and when HMW IHA is used. The authors of the rationale recognize this in an oblique fashion.

YYY. A subset of HMW HA and patient populations showed improvement.

ZZZ. The stated papers from which anchors were derived, had patient populations and interventions that are very different and not necessarily applicable to the interventions reviewed in this CPG.

MID/MCII

AAAA. It was communicated, only after inquiry, that the same anchors for MID were used across the evaluated interventions. Given the disparate literature for the various interventions, it is not clear if this was possible. Ideally, the use of anchor versus distribution derivation of MID would have been made clear in each section.

BBBB. The stated papers from which anchors were derived, had patient populations and interventions that are very different and necessarily applicable to the interventions reviewed in this CPG.

CCCC. View bulleted comments:

- The Angst papers used (1,2) used for MID anchors involved before and three months after PROs in patients with OA admitted to a Swiss rehabilitation hospital undergoing multiple modes of intervention. The anchor was based on a Likert scale without a minimal or “fair” response, which defines the MID; MCID was originally described as “the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management’ (3).
- Expectations from these multiple simultaneous interventions were potentially much higher than that of patients undergoing isolated outpatient interventions.
- The Tubach (4) paper used for a pain MID anchor looked at both first time and/or new drug, prescription of NSAIDs. Over 50% of the patients were on some other form of non-NSAID analgesia not defined, which could have included narcotics, thus raising

expectations of results. The paper did not use the “fair” response for its MID, instead using the two top box responses to define MCII. This raises the bar higher than expected in terms of meeting MID.

- Neither of the three papers from Angst and Tubach utilized placebos; no placebo effect could be subtracted. This is contrary to the methodology used by this CPG which subtracted the effect of the placebo arm of the studies from the intervention improvements in PROs. This is only one way of comparing effects (5). Other studies using OMERACT criteria before after treatment within each arm of the study including Petterson (6) and several of the studies used in this CPG that show efficacy of HA (7). A meta-analysis of overlapping meta-analyses found benefit for IHA as well (8). The PRO being used should be measured for each cohort of a study and improvements within the cohorts can be compared, but in formulating the effect of the intervention, its impact and confidence levels should not be performed with the placebo subtracted. There are multiple methodologists that recommend using more than one analysis.
- The point above is especially salient in that it has been recognized that saline injections have significant therapeutic effect and cannot be rationally used as controls (9,10,11).
- Network meta-analysis has shown benefit from HA (12) and in particular HMW HA in a paper that directly challenges the 2013 OAK CPG whose methodology was revisited in this current product (13).
- Proportional MID was used in some Forest Plots and, although not clearly stated, in rationales and not in others. This should have been more consistent. Methodologists in the literature emphasize the need to consider that the collective partial MID improvement of a PRO for an intervention be given credit for a proportion of the population improving that is significant. “We suggest the following guide for interpretation given a 0.5 MID: if the pooled estimate is greater than 0.5, and one accepts that the estimate of effect is accurate, many patients may gain important benefits from treatment. If the estimate of effect lies between 0.25 and 0.5, the treatment may benefit an appreciable number of patients. As the pooled estimate falls below 0.25 (i.e. 50% of the MID), it becomes progressively less likely that an appreciable number of patients will achieve important benefits from treatment.” (14). If this was used is not clearly stated or utilized. The importance of this is emphasized by Angst in 2017 (15).

DDDD. It appears that key meta-analyses from other authors and the Cochrane group were not utilized. Meta-analysis using level one data is level one data and should be made known to the group; at minimum it allows relative benchmarking.

EEEE. Harmonization with other external guidelines: It is not clear that the most recent recommendations from the ACR (16) or OMERACT (17) were made available to the work-group and used for benchmarking and feedback.

FFFF. Multiple recommendations, if not the majority, within this CPG receive “limited”, “moderate”, and/or “strong” recommendations despite not reaching the MID or showing evidence of subtracting placebo effect. Even given that bias, the panel found reason to recommend HA in some circumstances. A “strong” recommendation against use is inconsistent with the methods used in the rest of the CPG. At minimum, the recommendation should be “limited” for use with comment on it being within a limited population that has failed other treatments.

GGGG. Given the flawed anchors used for MID, SMD would have been preferable. Within the papers reviewed with high evidence, there is one that shows adequate SMD over placebo and another within an internal Likert scale.

HHHH. The flawed anchors might be confounding the HMW to LMW comparison. A recent meta-analysis demonstrated the efficacy of HMW but is not cited.

III. External guidelines offer an opportunity for benchmarking and normalization, especially if bias high. The 2019 ACR guideline (16) is conditionally against use of HA, meaning it recognizes its utility for patients that have failed other modalities. In comparison, the 2019 OMERACT guideline (17) gives a level 1B recommendation to use HA in knee OA.

JJJJ. At the level of a structured review, there are missing papers. The paper referenced in the rationale as “Baltzer” is not in the given citations nor is it retrievable through PubMed. Two papers that compare HA with PRP favorably are not included for this section (18, 19). Given that PRP was given a positive recommendation, this seems paradoxical.

IACS:

KKKK. Given a “moderate” recommendation without consideration of MID in the rationale and despite not reaching MID on the given Forest plots; a proportional MID analysis would have justified the level.

LLLL. It is not clear what the MID was based on or whether placebo was subtracted.

MMMM. The “moderate” recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised

PRP:

NNNN. Given a “limited” recommendation without consideration of MID in the rationale and despite not reaching MID on the given Forest plots; a proportional MID analysis would have justified the level.

OOOO. It is not clear what the MID was based on or whether placebo was subtracted.

PPPP. The “limited” recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

QQQQ. Given that the control in many of the papers was HA and in many of the papers it performed equally as well (18, 19), it would seem logical that HA would have an equal “limited” recommendation for use. That this is not the case is internally contradictory.

RRRR. This would have been an excellent PICO question for a GRADE quality evidence to decision table (ETD). It was recognized in the rationale that there were more adverse events with PRP than HA, which led some authors to recommend HA over PRP. An appropriate number needed to treat analysis within an ETD would have changed this recommendation.

SSSS. Were the group’s participants asked to declare COI over having an investment in delivering PRP services and were they asked to recuse themselves? The centrifuge is reported to cost up to \$36,000.

Denervation

TTTT. A limited recommendation was given; despite not having a MID analysis or Forest plots.

UUUU. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

VVVV. The very few available papers and the limitations above would have warranted moving this to the consensus section. This raises the question of why this CPG and AAOS CPGs overall have not returned to routinely allowing indeterminant findings of being unable to advise for or against even when some evidence exists. Losing that option remains a major deficit.

Arthroscopic Debridement:

WWWW. It is surprising that this CPG crossed from non-operative to operative interventions. This PICO question and the ones to follow should have remained possible options when revisiting the SMOAK CPG.

XXXX. There is no MID analysis or Forest plot offered.

YYYY. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

ZZZZ. Given the quoted literature, this recommendation could have been upgraded to strong if approached through a GRADE ETD with a NNT analysis.

Arthroscopic Partial Meniscectomy:

AAAAA. This recommendation will be one of two that elicits the most internal and external criticism, along with the HA recommendation. These PICO question generates a moderate recommendation for the intervention which is internally contradictory to the Arthroscopic Debridement question and given methodology.

BBBBB. No MID or Forest plot offered.

CCCCC. The rationale quotes three Level One studies that demonstrate that there is no added benefit to arthroscopy. There is no logical reason to support the recommendation as given.

DDDDD. The rationale uses the absence of studies involving patients that have failed therapy as the supposed reason for a “moderate for” recommendation. They then, without evidence, suggest that such patients should undergo arthroscopic PMM/PLM. This special population should have been part of the language of the actual man recommendation.

EEEEE. It is to be expected that most patients with moderate or worse OA of the knee will have meniscal tears. One cannot reach bone on bone disease if the meniscus is in the way. This recommendation opens the door to justifying unnecessary MRI’s and subsequent unnecessary surgery.

FFFFF. This recommendation, made in the face of evidence against it, would have better been left to the consensus section if in fact internal consensus within the workgroup was the reason for overriding the evidence as given.

GGGGG. If the CPG group can make a “moderate for” recommendation for this intervention for a specific population failing other modalities shy of TKA, it could have even more readily found an equally “moderate for” recommendation for HA in similar populations given that evidence actually exists for HA. The internal contradictions in this CPG need to be reconciled.

HHHHH. The best case scenario for justifying this recommendation would be in middle aged patients with MRI proven meniscus tears and low grade to no radiographic OA. Degenerative meniscus tears represent the earliest and lowest grade of OA. This makes the deliberate exclusion of the several papers from the Fidelity group (20,21, 22) disconcerting in that they elegantly demonstrate the lack of success of the procedure. They should be incorporated.

IIII. As an editorial aside, and to avoid claims of hypocrisy, this reviewer was one of the authors of a letter to the editor (NEJM) disputing the first major Fidelity group paper (21) and arguing for justification of PMM/PLM in the case of mechanical symptoms, which was consistent with the last OA AUC. After further review and a number of communications with the senior author of the Fidelity group publications, and after further review of the literature, I have conceded that argument. This recommendation needs significant modification and the argument for PMM/PLM in the given scenario needs to be demonstrated before being recommended unless it is through a consensus route.

Osteotomy

JJJJ. A limited recommendation was given; despite not having a MID analysis or Forest plots.

KKKKK. The limited recommendation given for this intervention is not consistent with other interventions in the CPG where the MID was used to determine a negative recommendation. As presented, it is a structured review of the literature, not an attempt at meta-analysis. Comment on this within the rationale is advised.

LLLLL. The very few available papers and the limitations above would have warranted moving this to the consensus section. This raises the question of why this CPG and AAOS CPGs overall have not returned to routinely allowing indeterminant findings of being unable to advise for or against even when evidence exists. Losing that option remains a major deficit.

MMMMM. This PICO question is illustrative of the significant barriers that have existed in terms of prospective randomized trials in all of surgery, let alone within orthopaedics.

Dry Needling:

NNNNN. The return to consensus recognition of inability to advise for or against is to be congratulated.

Spacer:

OOOOO. The return to consensus recognition to advise against an intervention due to a dearth of proof is to be congratulated.

- Angst F, Aeschlimann A, Michel BA, Stucki G. Minimal clinically important rehabilitation effects in patients with osteoarthritis of the lower extremities. *J Rheumatol* 2002 January;29(1):131-8.
- Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. *Arthritis Rheum* 2001 August;45(4):384-91.
- Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials*. 1989 Dec;10(4):407-15. doi: 10.1016/0197-2456(89)90005-6. PMID: 2691207.
- Tubach F, Wells GA, Ravaud P, Dougados M. Minimal clinically important difference, low disease activity state, and patient acceptable symptom state: methodological issues. *J Rheumatol* 2005 October;32(10):2025-9.
- Mouelhi Y, Jouve E, Castelli C, Gentile S. How is the minimal clinically important difference established in health-related quality of life instruments? Review of anchors and methods. *Health Qual Life Outcomes*. 2020 May 12;18(1):136. doi: 10.1186/s12955-020-01344-w. PMID: 32398083; PMCID: PMC7218583.
- Petterson SC, Plancher KD. Single intra-articular injection of lightly cross-linked hyaluronic acid reduces knee pain in symptomatic knee osteoarthritis: a multicenter, double-blind, randomized, placebo-controlled trial. *Knee Surg Sports Traumatol Arthrosc*. 2019 Jun;27(6):1992-2002. doi: 10.1007/s00167-018-5114-0. Epub 2018 Aug 29. PMID: 30159738.
- Strand V, McIntyre LF, Beach WR, Miller LE, Block JE. Safety and efficacy of US-approved viscosupplements for knee osteoarthritis: a systematic review and meta-analysis of randomized, saline-controlled trials. *J Pain Res*. 2015 May 7;8:217-28. doi: 10.2147/JPR.S83076. PMID: 26005358; PMCID: PMC4428363.
- Campbell KA, Erickson BJ, Saltzman BM, Mascarenhas R, Bach BR Jr, Cole BJ, Verma NN. Is Local Viscosupplementation Injection Clinically Superior to Other Therapies in the Treatment of Osteoarthritis of the Knee: A Systematic Review of Overlapping Meta-analyses. *Arthroscopy*. 2015 Oct;31(10):2036-45.e14. doi: 10.1016/j.arthro.2015.03.030. Epub 2015 May 19. PMID: 25998016.
- Mendes JG, Natour J, Nunes-Tamashiro JC, Toffolo SR, Rosenfeld A, Furtado RNV. Comparison between intra-articular Botulinum toxin type A, corticosteroid, and saline in knee osteoarthritis: a randomized controlled trial. *Clinical Rehabilitation*. 2019;33(6):1015-1026. doi:10.1177/0269215519827996
- Altman RD, Devji T, Bhandari M, Fierlinger A, Niazi F, Christensen R. Clinical benefit of intra-articular saline as a comparator in clinical trials of knee osteoarthritis treatments: A systematic review and meta-analysis of randomized trials. *Semin*

Arthritis Rheum. 2016 Oct;46(2):151-159. doi: 10.1016/j.semarthrit.2016.04.003. Epub 2016 Apr 27. PMID: 27238876.

- Saltzman BM, Leroux T, Meyer MA, Basques BA, Chahal J, Bach BR Jr, Yanke AB, Cole BJ. The Therapeutic Effect of Intra-articular Normal Saline Injections for Knee Osteoarthritis: A Meta-analysis of Evidence Level 1 Studies. *Am J Sports Med.* 2017 Sep;45(11):2647-2653. doi: 10.1177/0363546516680607. Epub 2016 Dec 27. PMID: 28027657.
- Han SB, Seo IW, Shin YS. Intra-Articular Injections of Hyaluronic Acid or Steroids Associated With Better Outcomes Than Platelet-Rich Plasma, Adipose Mesenchymal Stromal Cells, or Placebo in Knee Osteoarthritis: A Network Meta-analysis. *Arthroscopy.* 2021 Jan;37(1):292-306. doi: 10.1016/j.arthro.2020.03.041. Epub 2020 Apr 17. PMID: 32305424.
- Hummer CD, Angst F, Ngai W, Whittington C, Yoon SS, Duarte L, Manitt C, Schemitsch E. High molecular weight Intraarticular hyaluronic acid for the treatment of knee osteoarthritis: a network meta-analysis. *BMC Musculoskelet Disord.* 2020 Oct 23;21(1):702. doi: 10.1186/s12891-020-03729-w. PMID: 33097031; PMCID: PMC7585216.
- Johnston BC, Patrick DL, Thorlund K, Busse JW, da Costa BR, Schünemann HJ, Guyatt GH. Patient-reported outcomes in meta-analyses-part 2: methods for improving interpretability for decision-makers. *Health Qual Life Outcomes.* 2013 Dec 21;11:211. doi: 10.1186/1477-7525-11-211. PMID: 24359184; PMCID: PMC3984637.
- Angst F, Aeschlimann A, Angst J. The minimal clinically important difference raised the significance of outcome effects above the statistical level, with methodological implications for future studies. *J Clin Epidemiol.* 2017;82:128–36.
- Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, Felson D, Gellar K, Harvey WF, Hawker G, Herzig E, Kwoh CK, Nelson AE, Samuels J, Scanzello C, White D, Wise B, Altman RD, DiRenzo D, Fontanarosa J, Giradi G, Ishimori M, Misra D, Shah AA, Shmagel AK, Thoma LM, Turgunbaev M, Turner AS, Reston J. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Rheumatol.* 2020 Feb;72(2):220-233. doi: 10.1002/art.41142. Epub 2020 Jan 6. PMID: 31908163.
- Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, Kraus VB, Lohmander LS, Abbott JH, Bhandari M, Blanco FJ, Espinosa R, Haugen IK, Lin J, Mandl LA, Moilanen E, Nakamura N, Snyder-Mackler L, Trojian T, Underwood M, McAlindon TE. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage.* 2019 Nov;27(11):1578-1589. doi: 10.1016/j.joca.2019.06.011. Epub 2019 Jul 3. PMID: 31278997.

- Filardo G, Di Matteo B, Di Martino A, Merli ML, Cenacchi A, Fornasari P, Marcacci M, Kon E. Platelet-Rich Plasma Intra-articular Knee Injections Show No Superiority Versus Viscosupplementation: A Randomized Controlled Trial. *Am J Sports Med.* 2015 Jul;43(7):1575-82. doi: 10.1177/0363546515582027. Epub 2015 May 7. PMID: 25952818.
- Di Martino A, Di Matteo B, Papio T, Tentoni F, Selleri F, Cenacchi A, Kon E, Filardo G. Platelet-Rich Plasma Versus Hyaluronic Acid Injections for the Treatment of Knee Osteoarthritis: Results at 5 Years of a Double-Blind, Randomized Controlled Trial. *Am J Sports Med.* 2019 Feb;47(2):347-354. doi: 10.1177/0363546518814532. Epub 2018 Dec 13. PMID: 30545242.
- Sihvonen R, Paavola M, Malmivaara A, Itälä A, Joukainen A, Nurmi H, Kalske J, Järvinen TL; Finnish Degenerative Meniscal Lesion Study (FIDELITY) Group. Arthroscopic partial meniscectomy versus sham surgery for a degenerative meniscal tear. *N Engl J Med.* 2013 Dec 26;369(26):2515-24. doi: 10.1056/NEJMoA1305189. PMID: 24369076.
- Sihvonen R, Paavola M, Malmivaara A, Itälä A, Joukainen A, Kalske J, Nurmi H, Kumm J, Sillanpää N, Kiekara T, Turkiewicz A, Toivonen P, Englund M, Taimela S, Järvinen TLN; FIDELITY (Finnish Degenerative Meniscus Lesion Study) Investigators. Arthroscopic partial meniscectomy for a degenerative meniscus tear: a 5 year follow-up of the placebo-surgery controlled FIDELITY (Finnish Degenerative Meniscus Lesion Study) trial. *Br J Sports Med.* 2020 Nov;54(22):1332-1339. doi: 10.1136/bjsports-2020-102813. Epub 2020 Aug 27. PMID: 32855201; PMCID: PMC7606577.
- Sihvonen R, Englund M, Turkiewicz A, Järvinen TL; Finnish Degenerative Meniscal Lesion Study Group. Mechanical Symptoms and Arthroscopic Partial Meniscectomy in Patients With Degenerative Meniscus Tear: A Secondary Analysis of a Randomized Trial. *Ann Intern Med.* 2016 Apr 5;164(7):449-55. doi: 10.7326/M15-0899. Epub 2016 Feb 9. PMID: 26856620.

PPPPP. I am specifically concerned about a few of the more irregular treatments receiving some form of positive recommendation. On the other hand, the negative HA recommendation appears to have been reached in a way inconsistent with the academic largesse given many of the other interventions. This is especially true regarding the arthroscopic meniscectomy recommendation for which the rationale clearly quotes nothing but strong level one literature arguing against its utilization. It may have a role yet to be better defined but making that argument would have been better handled as a consensus statement recognizing that such a role lacks current scientific support.

QQQQQ. From a methods perspective, the use of the attempts at meta-analysis were rarely applied within the rationales and not consistent. The rationales review the papers collected for the CPG, but the accumulated data and analysis is not shared for most of the questions. This

			<p>gives the rationales the appearance of structured reviews, not true meta-analyses. The anchor method used for the MID's possibly creates overly restrictive targets that could have been mitigated with acceptance of proportional MID criteria or could have been mitigated by switching to distribution based MIDs/SMD. In terms of evolving to GRADE methodology: 1.) Ideally the PICO questions would have been driven by some form of Delphi process; 2.) If the expert panel was involved in the process assigning levels of evidence and supervising the data extraction, it is not clear, and if not involved, should be; they have the clinical expertise to interpret outcomes, and;3.) Presentation of data to the workgroup and within the appendix through Evidence to Decision Tables (ETDs), utilizing number needed to treat (NNT) analysis, would have helped to define the harm/benefit ratios of interventions. It is understood that this CPG started before and/or during a shift to a new commitment by AAOS to use GRADE methods; for both internal and external use, recognizing that a transition was occurring would aid transparency.</p>
--	--	--	---

Workgroup Response to Reviewer #16

Dear Adolph Yates, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. The 3-week Review Period enables AAOS to adhere to project deadlines and ensure there are no lengthy delays to publication. To encourage AAOS BOC and BOS participation, future guideline drafts will be sent directly to all members at the start of the Review Period.
- B. No response.
- C. No response.
- D. . When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.
- E. No response.
- F. The AAOS utilizes a modified GRADE methodology.
- G. The ordering of the importance of outcomes was determined by the workgroup
- H. The guideline work group reviews and assesses the literature prior to the final meeting.
- I. The work group utilized the GRADE Evidence-to-Decision framework during their deliberations and when formulating the final recommendations.
- J. No response.

Statistical methods

When possible, we recalculate the results reported in individual studies and compile them to answer the recommendations. Study data was extracted into a standardized Excel data abstraction spreadsheet. For data reported as group means and standard deviations, the mean difference between groups and the 95% confidence interval was calculated, and a two-tailed t-test of independent groups was used to determine statistical significance. In studies that report standard errors or confidence intervals, the standard deviation was back-calculated. In the absence of measures of dispersion, the results of the statistical analyses conducted by the authors are used. For proportions, we report the percentage of patients that experienced an outcome in each group. Relative risk ratios were computed when possible, and the risk difference was calculated when there were zero events in any treatment arm of a study. P-values < 0.05 were considered statistically significant. SAS 9.4 was used to calculate these results.

When possible, we performed meta-analyses using the random effects method of DerSimonian and Laird. In meta-analyses of proportions where one or more studies had zero events in a treatment arm, fixed effects Mantel-Haenszel models were run without a continuity correction. Heterogeneity

was assessed with the I-squared statistic. Meta-analyses with I-squared values less than 50% were considered as evidence. Those with I-squared larger than 50% were not considered as evidence for this guideline. All meta-analyses were performed using STATA 12.1.

Meta-Analyses using the Minimal Important Difference (MID)

In following the methodology from the previous edition of this guideline, we used published Minimal Important Differences (MIDs) to aid in the interpretation of treatment effects. We used MID estimates for these outcomes: VAS pain (Tubach 2005), WOMAC total/subscales (Angst 2002), SF-36 physical function, SF-36 physical component, and SF-36 bodily pain(Angst 2001). The MIDs used for all the different versions of the WOMAC are found in table III, and the MIDs for other outcomes are found in table IV.

To pool outcomes with different MIDs together in a meta-analysis, each study outcome was standardized by converting it to MID units (Johnston 2010). This method divides each study mean difference and its standard error by the MID for that outcome instrument. MID effect sizes between .5 and 1 (50 %to 100% of the MID) indicate that an appreciable number of patients may benefit from the intervention. It is unlikely that an appreciable number of patients will benefit with MID effect sizes less than .5, or less than half of the MID (Johnston 2010).

Table III. WOMAC MIDs

WOMAC subscale	WOMAC (0-96)	WOMAC-VAS (0-100)	WOMAC SUM(0-2400)
pain	1.66	8.3	41.5
function	5.44	8	136
stiffness	.8	10	20
total	7.9	8.2	197.5

Table IV. MIDs for Other Outcomes

instrument	MID
SF-36 Bodily pain	7.8
SF-36 Physical Function	3.3
SF-36 Physical component	2
VAS Pain	19.9mm

Supplemental OMERACT-OARSI analysis

The MID analysis described above was supplemented with an analysis of the OMERACT-OARSI responder criteria (Pham 2004) for the Hyaluronic Acid meta-analysis. The OARSI criteria takes a more global perspective of how a patient might benefit from a treatment than just evaluating and meta-analyzing pain and functional outcomes individually.

For the OARSI responder analysis, we computed the relative risk of meeting the response criteria for Hyaluronic Acid (HA) vs Saline/Placebo injections. To aid in interpretability, we computed the number needed to treat (NNT) with HA to find 1 additional responder over placebo injections. These were computed using the relative risk, and the median placebo group response rate among the studies included in the meta-analysis. That NNT was used to estimate the expected number of additional responders over placebo per 1000 patients treated. This statistic, along with the NNT, can be found in the lower right-hand side of the forest plots.

References added to the draft

Tubach F, Wells GA, Ravaud P, Dougados M. Minimal clinically important difference, low disease activity state, and patient acceptable symptom state: methodological issues. *J Rheumatol* 2005 October;32(10):2025-9.

Angst F, Aeschlimann A, Michel BA, Stucki G. Minimal clinically important rehabilitation effects in patients with osteoarthritis of the lower extremities. *J Rheumatol* 2002 January;29(1):131-8.

Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. *Arthritis Rheum* 2001 August;45(4):384-91.

Johnston, B.C., Thorlund, K., Schünemann, H.J. *et al.* Improving the interpretation of quality of life evidence in meta-analyses: the application of minimal important difference units. *Health Qual Life Outcomes* **8**, 116 (2010). <https://doi.org/10.1186/1477-7525-8-116>

T Pham, D van der Heijde, R.D Altman, J.J Anderson, N Bellamy, M Hochberg, L Simon, V Strand, T Woodworth, M Dougados. OMERACT-OARSI Initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. *Osteoarthritis and Cartilage*. Volume 12, Issue 5, 2004, Pages 389-399. <https://doi.org/10.1016/j.joca.2004.02.001>.

K. Please see the statistical methods provided above.

L. Please see the statistical methods provided above.

M. Please see the statistical methods provided above.

N. Please see the statistical methods provided above.

O. Please see the statistical methods provided above.

P. Please see the statistical methods provided above.

Q. Please see the statistical methods provided above.

R. Please see the statistical methods provided above.

- S. While other systematic review bibliographies are referenced to ensure that we capture all relevant literature, only primary studies are included in the review.
- T. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.
- U. Please see the statistical methods provided above.
- V. Please see the statistical methods provided above; anchor based MID was used for each PICO question.
- W. No response.
- X. No response.
- Y. Please see the statistical methods provided above.
- Z. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.
- AA. No response.
- BB. Please see the statistical methods provided above.
- CC. Walking pain was used because this was the outcome used by the study: VAS scale pain when walking. It is a non-specific measure but is validated. The reason it was important to specifically define the measure used was not to insinuate more specific functional outcome improvements by not specifying the measure used in the study.
- DD. While other systematic review bibliographies are referenced to ensure that we capture all relevant literature, only primary studies are included in the review.
- EE. No response.
- FF. Please see the statistical methods provided above.
- GG. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.
- HH. No response.
- II. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.
- JJ. No response.
- KK. No response.
- LL. No response.

MM. No response.

NN. No response.

OO. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

PP. No response.

QQ. No response.

RR. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

SS. No response.

TT. No response.

UU. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

VV. No response.

WW. No response.

XX. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

YY. No response.

ZZ. No response.

AAA. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

BBB. No response.

CCC. Please see the statistical methods provided above.

DDD. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

EEE. No response.

FFF. Please see statistical methods provided above.

GGG. No response.

HHH. No response.

III. Please see the statistical methods provided above.

JJJ.No response.

KKK. No response.

LLL. Please see statistical methods provided above.

MMM. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

NNN. No response.

OOO. Please see the statistical methods above.

PPP. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

QQQ. No response.

RRR. Please see the statistical methods provided above.

SSS. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

TTT. Oral Narcotics vs Control evidence tables begin on 1131.

UUU. The work group believes based on the evidence, there is no role for any type of narcotic in the treatment of osteoarthritis of the knee. The evidence would demonstrate it does not provide benefit to patients with osteoarthritis of the knee and in fact demonstrates harm, so the work group would not encourage its use even in the mentioned scenarios.

VVV. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

WWW. Following the Review Period, the work group reconsidered this recommendation and removed the terms 'vast majority.'

XXX. Following the Review Period, the work group reconsidered this recommendation and downgraded the strength to Moderate.

YYY. No response.

ZZZ. No response.

AAAA. No response.

BBBB. No response.

CCCC. Please see the statistical methods provided above.

DDDD. Other systematic reviews are referenced via manual bibliography review to ensure that all relevant literature has been captured; only primary studies are included in AAOS reviews.

EEEE. Other systematic reviews are referenced via manual bibliography review to ensure that all relevant literature has been captured; only primary studies are included in AAOS reviews.

FFFF. Following the Review Period, the work group reconsidered the recommendation and downgraded the strength to Moderate.

GGGG. No response.

HHHH. Other systemic reviews are referenced via manual bibliography review to ensure that all relevant literature has been captured; only primary studies are included in AAOS reviews.

IIII. Other systemic reviews are referenced via manual bibliography review to ensure that all relevant literature has been captured; only primary studies are included in AAOS reviews.

JJJJ. The Baltzer paper has been added to the reference list. The inclusion criteria (found in eAppendix 1) specified that studies should have 30 or more patients per group, a minimum follow-up time of 4 weeks, and have a population of at least 80% adult osteoarthritis patients.

KKKK. No response.

LLLL. Please see statistical methods provided above.

MMMM. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

NNNN. No response.

OOOO. Please see the statistical methods provided above.

PPPP. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

QQQQ. The results between IA-PRP vs IA-HA diverged after 6 months. Most studies showed similar results between IA-PRP and IA-HA at six months, except one (Yaradilimis 2020) where the LR-PRP total WOMAC was better at all time points than the IA HA. Both the patients in the IA HA and IA PRP improved in total WOMAC at six months. Patients in the IA-PRP-arms maintained improvement after 6

months at the 9- OR 12-months mark for total WOMAC vs. IA-HA which started to have a worsening score.

RRRR. The work group utilized the Evidence-to-Decision framework in their deliberations and the drafting of recommendations.

SSSS. Work group members are asked to declare all financial FCOI as described in the FCOI Policy found here <https://www.aaos.org/quality/research-resources/methodology/>.

TTTT. No response.

UUUU. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

VVVV. No response.

WWWW. The Lavage/Debridement recommendation was present in the 2013 guideline and was updated accordingly.

XXXX. No response.

YYYY. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

ZZZZ. The work group utilized the GRADE Evidence-to-Decision framework when formulating the final recommendations and determining the strength of recommendation.

AAAAA. No response.

BBBBB. No response.

CCCCC. No response.

DDDDD. The work group discussed the recommendation language and elected to keep the definition of “appropriately indicated patients” in the rationale.

EEEEE. No response.

FFFFF. No response.

GGGGG. Following the Review Period, the work group reconsidered the HA recommendation and provided clarity within the recommendation language that it is not recommended as a first line treatment.

HHHHH. The work group defined the appropriately indicated patient as patients with mild-to-moderate knee OA and an MRI confirmed meniscal tear who have previously failed appropriate conservative treatment such as physical therapy, corticosteroid injections, and a course of non-steroidal anti-inflammatory medications. The inclusion criteria (found in eAppendix 1) specified that studies should have

30 or more patients per group, a minimum follow-up time of 4 weeks, and have a population of at least 80% adult osteoarthritis patients.

IIII. No response.

JJJJ. No response.

KKKK. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature.

LLLL. No response.

MMMM. No response.

NNNN. No response.

OOOO. No response.

PPPP. The work group discussed the supporting evidence as well as all domains of the Evidence-to-Decision Framework at the final meeting to determine recommendation strength. The negative HA recommendation is in accordance with the supporting evidence; however, the work group has used the framework to downgrade the strength. The arthroscopic meniscectomy recommendations defines indicated patients as "... patients with mild-to- moderate knee OA and an MRI confirmed meniscal tear who have previously failed appropriate conservative treatment such as physical therapy, corticosteroid injections, and a course of non-steroidal anti-inflammatory medications."

QQQQ. When the evidence required to perform a meta-analysis is unavailable, recommendations are based on a systematic review of the relevant literature. The work group utilized the GRADE Evidence-to-Decision framework during their deliberations and when formulating the final recommendations. Please see the included statistical methods and the full methods section of the guideline for additional information.

Reviewer #17, Vinod Dasa, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
17	Vinod Dasa, M.D.	Key Informant Panelist, American Academy of Orthopaedic Surgeons	A. Should you add this statement as well for acetaminophen: "when not contraindicated"? B. For the HA injections, was an analysis done of only the papers w KL 1-3 or did that analysis incl studies w kl 4?

Workgroup Response to Reviewer #17

Dear Vinod Dasa, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. The workgroup has edited the recommendation to contain "when not contraindicated," into the oral acetaminophen recommendation.
- B. The majority of the supporting evidence covered KL1-3, with one article included in the OARSI outcome analysis which had KL4. The work group highlighted the need for future research with more detailed subgroup stratification of osteoarthritis severity.

Reviewer #18, Luis Pulido, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
18	Luis Pulido, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. The guideline is a complete resource of the most recent literature on multiple non surgical treatment modalities for patients with knee osteoarthritis. I strongly agree with the above-mentioned questions after reading and reviewing the OAK CPG draft.</p> <p>B. I have one comment and proposed change to the group. There is no reason or clarity on the order/rank of the interventions evaluated and graded. Orthotics are first on the list, followed by supplements, topical medications, rehabilitation therapies, Self management, education, weight loss, acupuncture and nerve stimulation, oral medications and IA injections. I recommend to modify the presentation of the CPG and present it based on the evidence rank and effect of intervention, from stronger evidence to lower evidence of intervention. For example, The first interventions listed have a Strong recommendation AND a positive response to reduce pain in the treatment of knee osteoarthritis, followed by the interventions with moderate, limited and consensus. The bottom of the list will have the strong evidence AND a negative response to reduce pain (Not recommended) in the treatment of knee osteoarthritis. The hierarchy and rank based on evidence should help with the EBM message and application in clinical practice.</p>

Workgroup Response to Reviewer #18

Dear Luis Pulido, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. The recommendations are presented in the order by which the PICO questions were created. Additional attention to this order will be applied to future guidelines.

Reviewer #19, Fred Nelson, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
19	Fred Nelson, M.D.	American Academy of Orthopaedic Surgeons	<p>Notes Guidelines</p> <p>A. Lines 519-525: Is this up to date? Seems low</p> <p>B. Lateral sole or heel wedges (built into heel)</p> <p>C. Line 828: The assumption is that canes were used on ipsilateral side based on instruction. One article did show better force reduction with contralateral use, similar to hip. Another study showed no difference. Chan GN, Smith AW, Kirtley C, Tsang WW. Changes in knee moments with contralateral versus ipsilateral cane usage in females with knee osteoarthritis. Clin Biomech (Bristol, Avon). 2005 May;20(4):396-404. doi: 10.1016/j.clinbiomech.2004.12.005.</p> <p>D. Lines 996-1035: I have real concerns with the strong recommendation. Odds are, the research was done on 3% diclofenac which most insurance does not support. The 1% may not have as strong an effect. Add to that lines 1009-1010 state “However, inconsistent evidence suggests no significant difference in pain and adverse events between topical NSAIDs and control.”</p> <p>E. Lines 1186-1187: “Future research should examine delivery methods designed to increase access for patients (e.g., online 1187 delivered programs,” The pandemic shut down our osteoarthritis classes. One good side effect of the pandemic is the spotlight shining on the huge internet disparities. Over the year that gap is being closed, making these classes more available to people with limited finances and transportation. This is an opportunity for the Academy to promote this type of research. Wow, no side effects. This also applies to patient education, which follows.</p> <p>F. Line 1231: Relative to weight loss this is an effect that is disease modification. Gersing AS, Solka M, Joseph GB, Schwaiger BJ, Heilmeyer U, Feuerriegel G, Nevitt MC, McCulloch CE, Link TM. Progression of cartilage degeneration and clinical symptoms in obese and overweight individuals is dependent on the amount of weight loss: 48-month data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2016 Jul;24(7):1126-34. doi: 10.1016/j.joca.2016.01.984. PMID: 26828356 PMCID: PMC4907808</p>

- | | | |
|--|--|--|
| | | <p>G. Line 1632-1637: Albeit NSAID are a cardiac issue this section is on acetaminophen. Here the issue is liver disease and dosage beyond 3 gm per day to be avoided.</p> <p>H. Line 1774: In the suggestion for future studies. It might be useful to look for differences in specific age and OA stage groups. Case in point would be the response of military and civilian industrial labor patient who have minimal radiographic change and trying to complete several years to retirement.</p> <p>I. Line 1794-1794: Review usefulness of extended-release corticosteroids in diabetic relative to costs</p> <p>J. Line 1825-1933: PRP well done. It is preparation versus category patient.</p> <p>K. Line 2004-2006: Future research should sort out effectiveness when other treatments have failed and on end stage disease in patient unable to have TKA (Age, comorbidities).</p> <p>L. Lines 2138-2142: Excellent! I know that there was a paper on people with mechanical locking versus those without, randomized, and to my surprise there was no difference in the long run. Can not find that paper.</p> <p>M. Line 2235: After the word “versus” add osteotomy. Also, consider the cost of the vocational and functional downtime for osteotomy compared to TAK.</p> <p>N. Line 2256: Not likely to happen, but the idea of a national osteotomy registry would be useful.</p> <p>O. General: Not mentioned in these reviews is the use of the new computer driven PROMIS scores.</p> |
|--|--|--|

Workgroup Response to Reviewer #19

Dear Fred Nelson, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for your comment. The draft has been modified.
- B. The majority of supporting evidence utilizes lateral insoles (ridgid) with one article looking at strapped insole with a shoe.
- C. The Chan et al. study was not included due to not having met the inclusion criteria of 30 patients per group.
- D. The supporting evidence for this recommendation included four studies that used 1% topical treatment.
- E. The work group has edited the rationale for the Patient Education recommendation to include more information.
- F. The Gersing et al. article did not fit the inclusion criteria and was excluded because the patient population was not specific to patients with osteoarthritis of the knee.
- G. Corrections have been made to the oral NSAIDs and acetaminophen rationales to only discuss each respective medication in the rationales.
- H. Osteoarthrosis severity was discussed by the work group but there wasn't enough evidence available with which to create a directional statement. The work group included this in the future research.
- I. This analysis was not included in the a priori scope as determined by the work group members.
- J. Thank you for your comment.
- K. Verbiage has been added to the future research section regarding end stage disease and patients unable to have total knee arthroplasty.
- L. Thank you for the positive feedback.
- M. Thank you for your comment. The draft has been modified.
- N. No response.
- O. PROMIS was not included in the scope of this guideline as defined by the work group.

Reviewer #20, Charles Hummer, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
20	Charles Hummer, M.D.	Key Informant Panelist, American Academy of Orthopaedic Surgeons	<p>A. For the Denervation therapy section, I do not see consideration of potential adverse impact on subsequent surgical treatment (eg. TKA); I realize that there may be no studies examining this, but perhaps suggesting this as an opportunity for future research might be worthwhile. (line 1935)</p> <p>B. For the Hyaluronic Acid and Platelet rich plasma sections, I do not see any mention of combination therapies. Perhaps mention of combination therapies as an opportunity for future research might be worthwhile. (lines 1714 and 1827)</p> <p>C. I commend the voting work group on their efforts and analysis. As a practitioner, I do make note that my personal experience with use of intra-articular HA for treatment of up to KL grade 3 OA of the knee is not in line with the recommendation regarding this intervention; I have found significant benefit for some patients in this category (anecdotal personal observation).</p>

Workgroup Response to Reviewer #20

Dear Charles Hummer, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. The work group did not feel that this addition was warranted.
- B. This analysis was not included in the a priori scope as determined by the work group members. The proposal for an addition to the future research section was examined by the workgroup and deemed not necessary.
- C. Thank you for the positive feedback.

Reviewer #21, Barry Kraushaar, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
21	Barry Kraushaar, M.D.	Board of Councilors, American Academy of Orthopaedic Surgeons	<p>A. I started with an open document for comments. As I read the initial guidelines I made some questions. After going through the explanatory sections I feel that these are valuable and central points that really need to be promoted across the orthopedic community. Great job. I do see the comments on Hyaluronic acid (1714) as a bit contradictory - It appears that the injections did not meet clinically significant levels, yet there is movement towards acceptance. Please re-read this one and see if it is worded squarely. Thanks.</p> <p>B. The reviewers of PRP vs HA(1827) did a great service in summarizing a very complex discussion.</p> <p>C. In the meniscectomy article (2070) it is hard to decide whether the reviewers are supporting the title because saying that meniscectomy is as effective as PT for mild to moderate OA is not really a ringing endorsement of meniscectomy. Its a fencepost.</p> <p>D. Overall Excellent and useful. We need to use these guidelines to help Orthopedic Surgeons with insurance denials. They are much more powerful than the members of the insurance boards who use money-saving over effectiveness as criteria.</p>

Workgroup Response to Reviewer #21

Dear Barry Kraushaar, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback. Following the Review Period, the work group reconsidered the recommendation and clarified the statement.
- B. Thank you for the positive feedback.
- C. In line with the supporting evidence, the work group recommends this intervention only for indicated patients. Indicated patients are defined as "... patients with mild-to- moderate knee OA and an MRI confirmed meniscal tear who have previously failed appropriate conservative treatment such as physical therapy, corticosteroid injections, and a course of non-steroidal anti-inflammatory medications.
- D. Thank you for the positive feedback.

Reviewer #22, Bernard Roehr, M.D., MHCDS

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
22	Bernard Roehr, M.D., MHCDS	American Academy of Orthopaedic Surgeons	<p>A. I found this CPG extremely well done and offer the highest praise to the workgroup that produced it!</p> <p>B. There is a minor typographical error in line 900 (varus instead of various).</p> <p>C. Page 65, lines 1982-2006 do not seem to fit correctly. They refer to intra-articular therapies when the previous page is discussing Denervation Therapy.</p> <p>D. There is a minor grammar error in line 2182. Perhaps it should "perhaps the closest" instead.</p> <p>E. Overall, an outstanding body of work!</p>

Workgroup Response to Reviewer #22

Dear Bernard Roehr, M.D., MHCDS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. Thank you for your comment. The draft has been modified.
- C. Thank you for your comment. The draft has been modified.
- D. Thank you for your comment. The draft has been modified.
- E. Thank you for the positive feedback.

Reviewer #23, Kenneth Jaffe, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
23	Kenneth Jaffe, M.D.	American Academy of Orthopaedic Surgeons	A. Line 314 Hyaluronic Acid-Strength of Recommendation-“Strong”. Continues to be a Bias by AAOS as to which articles were selected as in 2013. Did not explain adequately. Should have stated upfront that it could be used in certain patients

Workgroup Response to Reviewer #23

Dear Kenneth Jaffe, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Following the Review Period, the work group reconsidered this recommendation and downgraded the strength to Moderate.

Reviewer #24, Douglas Naudie, M.D., FRCSC

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
24	Douglas Naudie, M.D., FRCSC	The Knee Society	<p>A. In general, the CPG on Management of Osteoarthritis of the Knee (Non-Arthroplasty) is well-written, comprises excellent methodology, and adequately includes articles for assessment.</p> <p>B. However, the "limited" strength of recommendation for high tibial osteotomy should be re-evaluated. Clinical practice guidelines typically rely heavily on randomized trials. The 2014 Cochrane review on high tibial osteotomy (HTO) emphasized that no study had previously compared tibial osteotomy to conservative treatment. In the rationale for the recommendation for tibial osteotomy (lines 2182-2189), the 2017 paper by Van Outeren is referenced and supports the effectiveness for use of HTO compared to non-operative methods. Recent observational studies (prospective cohorts and national registries) suggest large, clinically-important improvements in pain and function (and gait biomechanics) 5 years post HTO (Birmingham et al. 2017); the vast majority of patients (depending on preoperative characteristics) avoid knee replacement 10 years post HTO (Primeau et al 2021; Niinimaki et al 2012; W-Dahl et al 2012); and when categorized by type of complication, severe adverse event rates are very low for HTO (Martin et al 2014). There are also modeling studies that suggest greater use of HTO would be cost-effective (Konoka et al 2015; Smith et al 2017).</p> <p>References:</p> <ul style="list-style-type: none"> • Reinoud W Brouwer, Maarten R Huizinga, Tijs Duivenvoorden, Tom M van Raaij, Arianne P Verhagen, Sita MA Bierma-Zeinstra, Jan AN Verhaar. Osteotomy for treating knee osteoarthritis, Cochrane Musculoskeletal Group. Cochrane Database Syst Rev. 2014 Dec; 2014(12): CD004019. • Birmingham TB, Moyer R, Leitch K, Chesworth B, Bryant D, Willits K, Litchfield R, Fowler PJ, Giffin JR. Changes in biomechanical risk factors for knee osteoarthritis and their association with 5-year clinically important improvement after limb realignment surgery. Osteoarthritis and Cartilage. 2017 Dec 1;25(12):1999-2006. • Primeau CA, Birmingham TB, Leitch KM, Willits KR, Litchfield RB, Fowler PJ, Marsh JD, Chesworth BM, Dixon SN, Bryant DM, Giffin JR. Total knee replacement after high tibial osteotomy: time-to-event analysis and predictors. Canadian Medical Association Journal. 2021 Feb 1;193(5):E158-66.

- Niinimäki TT, Eskelinen A, Mann BS, Junnila M, Ohtonen P, Leppilahti J. Survivorship of high tibial osteotomy in the treatment of osteoarthritis of the knee: Finnish registry-based study of 3195 knees. *The Journal of bone and joint surgery. British volume.* 2012 Nov;94(11):1517-21.
- W-Dahl A, Robertsson O, Lohmander LS. High tibial osteotomy in Sweden, 1998–2007: a population-based study of the use and rate of revision to knee arthroplasty. *Acta orthopaedica.* 2012 Jun 1;83(3):244-8.
- Martin R, Birmingham TB, Willits K, Litchfield R, LeBel ME, Giffin JR. Adverse event rates and classifications in medial opening wedge high tibial osteotomy. *The American Journal of Sports Medicine.* 2014 May;42(5):1118-26.
- Konopka JF, Gomoll AH, Thornhill TS, Katz JN, Losina E. The cost-effectiveness of surgical treatment of medial unicompartmental knee osteoarthritis in younger patients: a computer model-based evaluation. *The Journal of Bone and Joint Surgery. American volume.* 2015 May 20;97(10):807.
- Smith WB, Steinberg J, Scholtes S, Mcnamara IR. Medial compartment knee osteoarthritis: age-stratified cost-effectiveness of total knee arthroplasty, unicompartmental knee arthroplasty, and high tibial osteotomy. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2017 Mar 1;25(3):924-33.

C. I would recommend these guidelines for use in clinical practice with the exception of the limited strength of recommendation for tibial osteotomy.

Workgroup Response to Reviewer #24

Dear Douglas Naudie, M.D., FRCSC

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. This recommendation was downgraded from moderate strength to limited strength due to inconsistency in findings. The supporting evidence found both improvement and no significant change in patient outcome.
- C. Thank you for your comment.

Reviewer #25, Alexandra Page, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
25	Alexandra Page, M.D.	Board of Directors, American Academy of Orthopaedic Surgeons	<p>A. Overall excellent work, including the likely contentious topic of hyaluronic acid.</p> <p>B. The format for reporting on each treatment option is not uniformly applied. For example, Benefits/Harms, Cost Effectiveness/Resource Utilization, Feasibility are provided for interventions such as a cane, bracing, oral supplements, and neuromuscular training. Minor risks of oral medication or increased pain or muscle soreness from exercise are noted as harms. However for the invasive HA, PRP, or steroid injection the CPG notes "there are no harms with implementing". The CPG comments on the Cost effectiveness of canes, dietary supplements and other low-cost interventions, yet the section is missing on the more expensive surgical interventions of Lavage/Debridement and Partial Meniscectomy.</p> <p>C. For Hyaluronic Acid, more clarity may help surgeons with decision making. The intervention is not recommended for the vast majority of patients. Supporting rationale does not make clear the minority pts who might benefit. Acceptability indicates that there should be no issues implementing this recommendation because intra-articular treatments are commonly utilized. Yet as I understand the recommendation, it strongly supports NOT using HA injections. Benefits/Harms could be addressed for this invasive treatment. Advising against an invasive, non-effective treatment has clear benefit; for the minority pts who might benefit there are clear risks.</p> <p>D. For Acupuncture, Strength of Recommendation is Limited, but the Rationale (lines 1382-83, 1388-89) concludes "apply a moderate strength of recommendation".</p>

Workgroup Response to Reviewer #25

Dear Alexandra Page, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. The work group did not opt to include additional information regarding potential harms or cost implications.
- C. Following the Review Period, the work group reconsidered this recommendation and clarified the statement.
- D. Thank you for your comment. The draft has been modified.

Reviewer #26, Matthew Abdel, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
26	Matthew Abdel, M.D.	Board of Directors, American Academy of Orthopaedic Surgeons	A. This was very well done, of the highest scientific rigor, and based in evidence.

Workgroup Response to Reviewer #26

Dear Matthew Abdel, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A. Thank you for the positive feedback.

Reviewer #27, Alison Chang, PT, DPT, MS

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
27	Alison Chang, PT, DPT, MS.	Key Informant Panelist, American Academy of Orthopaedic Surgeons	<p>A. This draft is excellent. The summary recommendation layout is easy to follow and enables a quick read to grasp the main salient points. The layered presentation is user-friendly. Clinicians can efficiently overview all the summary of recommendations on Pages 7-14, then read detailed reviews on Pages 25-74 if they choose to. I also really appreciate the supplemental data and meta-analyses in the appendices. The subheadings of Benefits/Harms of Implementation, Outcome Importance, Cost Effectiveness/Resource Utilization, Acceptability, Feasibility, and Future Research are thoughtful additions when considering implementing a particular treatment.</p> <p>Here are my comments.</p> <p>B. For Oral/Dietary Supplements, tumeric, ginger extract, glucosamine, chondroitin, and Vitamin D were appraised and discussed. Many patients have inquired about the efficacy oral and/or topical CBD. Are there any evidence to share in the CPG?</p> <p>C. Topical Capsaisin is another commonly inquired treatment. Please consider including it in the CPG.</p> <p>D. Accumulating evidence on the role of central sensitization and psychosocial factors in patients with chronic knee symptoms supports a comprehensive management integrating physical, psychosocial, and mind-body domains. I noted that cognitive behavioral therapy was discussed, but no review of Tai Chi, a mind-body exercise form, was included. Tai Chi has been strongly recommended in the recent American College of Rheumatology/Arthritis Foundation Guidelines for the management of knee and/or hip OA (Kolasinski et al., 2020).</p> <ul style="list-style-type: none"> • Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. <i>Arthritis Care Res (Hoboken)</i>. 2020;72(2):149-162. doi:10.1002/acr.24131 <p>E. Stem cell therapy was proposed in the initial PICO discussion, but was not covered in this CPG. This is a frequent asked question in clinical encounters. Arthritis Foundation has posted a “Stem Cell Guidance” for patients (https://www.arthritis.org/science/events-publications/stem-cell-guidance). As many surgeons utilize this intra-articular therapy, it may be informative to provide critical appraisal and guidance on this topic.</p>

- | | | |
|--|--|--|
| | | <p>F. Page 24: The second box of the flow chart went from 2425 to 617 after excluding 1761 articles. $2425-1761=664$, not 617. I may have missed something. Please consider fixing this discrepancy.</p> <p>G. Page 30: Does the brace recommendation differentiate between tibiofemoral vs. patellofemoral compartment disease? Does it differentiate between unloading knee brace vs. simple neoprene sleeve?</p> <p>H. Page 51, Line 1576: “the lowest effective dose for the shortest duration possible for the patient”. This is not a suggestion for modification, but a question. Given that knee OA disease course often lasts a decade or more before arthroplasty, should we recommend only use oral NSAIDs to calm flare-ups, rather than using on a regular basis? Uncertain if any study exists to address this question.</p> <p>I. Page 59: Does repetitive administration of Intra-articular corticosteroid injection negatively impact cartilage health? Is there any recommendation for the frequency of injection per year?</p> <p>J. Page 64, Denervation Therapy - Please provide the publication year for all citations in this section.</p> <p>K. Page 66, Lavage/Debridement - Please provide the publication year for all citations in this section.</p> <p>L. Page 163 in Appendix 2 appears to be out of place.</p> |
|--|--|--|

Workgroup Response to Reviewer #27

Dear Alison Chang, PT, DPT, MS,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. CBD was not included in the scope of this guideline as defined by the work group.
- C. Topical Capsaisin was discussed by the work group but there wasn't enough evidence available with which to create a directional statement.
- D. Tai Chi was discussed by the work group but there wasn't enough evidence available with which to create a directional statement.
- E. Stem cell therapy was not included in the scope of this guideline as defined by the work group.
- F. Thank you for your comment. The draft has been modified.
- G. The majority of the supporting evidence utilizes patellofemoral compartment disease with one article looking at tibiofemoral. The majority of the evidence looks at unloading knee brace. Kirkley (1999) compared unloading knee brace to neoprene sleeve.
- H. The work group felt that the lowest effective dose for the shortest duration possible for the patient is a clinical judgement.
- I. Frequency of injection per year was not included in the scope of this guideline as defined by the work group.
- J. Thank you for your comment. The draft has been modified.
- K. Thank you for your comment. The draft has been modified.
- L. No response.

Reviewer #28, Ajay Srivastava, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
28	Ajay Srivastava, M.D.	Committee on Evidence-Based Quality and Value, American Academy of Orthopaedic Surgeons	<p>A. Overall, I agree with the recommendations. I commend the team for their commitment and hard work.</p> <p>B. I think using the word "may be helpful" in recommendations with limited evidence could be interpreted by general public as positive recommendation while in reality we do not know. For example, regarding oral/dietary supplements, line 156 "The following supplements may be helpful in reducing pain and improving function for patients with mild to moderate knee osteoarthritis; however, the evidence is inconsistent/limited and additional research clarifying the efficacy of each supplement is needed". The statement could be reworded as "There is limited evidence that following supplements are helpful in reducing pain and improving function....." and so for all of them with limited evidence. This kind of language allows us to state the evidence while not giving an impression that we are supporting this intervention. I think medical personnel can understand the new ones, but it would be helpful for general public.</p>

Workgroup Response to Reviewer #28

Dear Ajay Srivastava, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. The recommendations are formulated as action statements rather than conclusion statements, with 'may' being the standard language for limited strength recommendations.

Reviewer #29, Laura Bruse, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
29	Laura Bruse, M.D.	American Academy of Orthopaedic Surgeons	<p>A. Lines 517 to 525: lines 518 BURDEN OF DISEASE 519- Comment: There is no dimorphism stated, or differences between males and females in the specific recommendations even though is stated women (females) may have a higher prevalence of osteoarthritis. Is it the intention that the CPG be applied or any of the recommendations be given to males and females equally? Will future studies bear any differences between males and females with regard to the treatment responses?</p> <p>B. Lines 907-914- Comment: It may be informational to know if the brace affect the progression of arthritis by altering the kinematics which in turn then affects development of arthritis at the cellular level.</p> <p>C. Lines 921-929 and Lines 990 to 995 Future Research- Comment: Could future research be made more informational and educational to patients if it also included how the proposed mechanism of action of each of the supplements can affect osteoarthritis and how each supplement works biochemically to inhibit/affect progression of the osteoarthritis or modify symptoms.</p> <p>D. Lines 1012 to 1015: Comment: Mechanism of action? Topically how do the topical medications potentially harm those with chronic kidney disease, coronary artery disease, and congestive heart failure? Does it get absorbed and affect these organs directly? If so, this would be informational and educational for the providers and patients.</p> <p>E. 1037 Supervised Exercise: Lines 1095-1101: Future Research- Comment: Future should include addressing whether obesity precludes or affects the ability to participate in exercise in those with knee osteoarthritis.</p> <p>F. 1137 Self-Management: Lines 1185-1187: Future Research- Comment: Are there any psychological factors which may influence non-participation in self-management? Has this been addressed or examined?</p> <p>G. 1189 Patient Education: Lines 1191-1192- Comment: At what grade and educational level for this information is recommended? Has the grade level and education level been addressed or evaluated?</p>

- | | | |
|--|--|--|
| | | <p>H. 1333 Laser Treatment: Lines 1135-1136- Comment: What is the mechanism of approved laser treatment for which this is proposed to help? Are there any contra-indications? Can this be commented on in future research, lines 1359-1360.</p> <p>I. 1363 Acupuncture: Lines 1413-1416- Comment: how does acupuncture work to relieve pain and improve function in osteoarthritis?</p> <p>J. Lines 1455-1458: Comment: How do these modalities work and are there any modifiable factors which may identify responders and non-responders for various modalities? Could the explanation for how these modalities are proposed to work be added to future research? Lines 1500-1503</p> <p>K. Line 1505: Extracorporeal Shockwave Therapy: Lines 1514-1521- Comment: What is the proposed mechanism of this modality?</p> <p>L. Line 1825: Platelet-rich Plasma- Comment: It is important to know how PRP may work. Can an explanation be placed to state how PRP improves pain and function? Or could it be included in future research?</p> <p>M. 1976- 1980 Question: Is denervation therapy an intra-articular procedure?</p> <p>N. Line 1935: Denervation Therapy: Comment: Are there benefits, potential harms for future procedures for someone who already has had an ablation procedure? Does this influence future total knee replacement? Or other surgical intervention for osteoarthritis like arthroscopy, meniscectomy due to denervation about the knee and in the soft tissue envelope?</p> <p>O. Line 2258: Dry Needling- Comment: Does research include any proposed mechanism of action? What is the present known proposed mechanism of action for which this modality reduces pain/improves function and thus improved knee osteoarthritis?</p> <p>P. Thanks for the opportunity to participate in this review</p> |
|--|--|--|

Workgroup Response to Reviewer #29

Dear Laura Bruse, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. At the present time, the best available evidence does not differentiate between males and females. Although it is certainly an important topic, addressing the effectiveness for treatments specific to males or females is far from making it to clinical research. Currently, the most recently highlighted studies on this topic have not come from the area of osteoarthritis of the knee and still mostly are focused on animal studies. Therefore, it is not yet applicable to a clinical practice guideline focused on the best available evidence when we lack evidence on the topic.
- B. This analysis was not included in the priori scope as determined by the work group member.
- C. The discussion of proposed mechanisms is outside of the scope of future research. The purpose of the future research section is to help highlight what studies are necessary to improve the strength of the recommendation. Since an improved understanding of the mechanism of action might be beneficial, it doesn't necessarily translate to clinical effectiveness which is what would "move the needle" on the strength of the recommendation.
- D. When selecting a topical NSAID, absorption and bioavailability are important because of heterogeneity among topical drug formulations. However, topical NSAIDS limit systemic absorption and associated side-effects and drug interactions compared to oral NSAIDs.
- E. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.
- F. Psychological factors were discussed by the work group but there wasn't enough evidence available with which to create a directional statement.
- G. Education level was not included in the scope of this guideline as defined by the work group.
- H. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.
- I. This recommendation was based on the findings of Chen 2013, Suarez-Almazor 2010, Mavrommatis 2012, Berman 2004, Hinman 2014, Vas 2007, and Berman 1999.
- J. The available evidence did not specify the mechanism of action. The work group did not elect to add this to the future research section for this recommendation.
- K. The supporting evidence did not address mechanisms of action or any factors that could identify responders from non-responders. The future research section included studies that include factors to identify responders from non-responders and has been amended to include future research to determine the mechanisms of action in human subjects.

- L. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.
- M. Denervation therapy is not an intra-articular procedure. The draft has been modified.
- N. This analysis was not included in the a priori scope as determined by the work group members.
- O. The supporting evidence focused on clinical outcomes; however, the authors of the some supporting studies acknowledged that although the mechanisms of action are not fully understood, possible mechanisms include promotion of restorative processes in bone and cartilage through angiogenic, anti-edema, anti-inflammatory, anti-apoptotic and trophic effects. (Ediz 2018, Uysal 2020). Zhong 2019 reported some increase T2 signaling in cartilage after treatment which could suggest some structural degradation but in the discussion they state the amount reported was said to remain in normal limits so no clear evidence of either improvement or harm from this study. The future research section expresses the need for studies that examine the disease-modifying effects of the treatment.
- P. Thank you for participating.

Reviewers #30, Stephen Weber, M.D. and Louis McIntyre, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
30	Stephen Weber, M.D.; Louis McIntyre, M.D.	Arthroscopy Association of North America	<p>A. Overall, a noble goal, but the CPG process falls short of the actual purpose which is to provide guidance to facilitate clinical decisions in treating actual patients. Despite the AAOS insistence that these CPGs should not be permitted to deny coverage for treatment, this has been the case with several of the CPGs, and this one will be no exception. Question 3 therefore fails, as the target audience has become insurers and other payors. The AAOS has been ineffectual in curing this and it has become a significant barrier to patient care. Patients are harmed when they cannot access safe and effective treatments for an incurable disease.</p> <p>B. Another problem which has become increasingly evident is the flawed nature of MCID. This creates strong disagreement with the AANA reviewers. In questions 10-12 MCIDs create issues with the methods, validity of the conclusions, and the outcome of the statistical methods. The casual reader will be unaware of the nuances of MCIDs, which vary widely depending on the technique used to determine them (anchor based versus other) and what population and diagnosis they are applied to. The MCID of some common orthopedic PROs can vary by orders of magnitude depending on the diagnosis. These problems led Dekker to state that “MCIDs are not fit for purpose” (Dekker J. The minimal clinically important difference re-considered. Osteoarthritis Cartilage. 2019 Oct;27(10):1403-1404). Deciding a Strong Recommendation based on failing to meet what is increasingly recognized as a flawed benchmark is frustrating and not good science. MCID as a standard is flawed and any recommendation based on MCID therefore shares that flaw.</p> <p>C. AANA reviewers’ concerns rest with the Strong Recommendation, “Hyaluronic acid is not recommended for the vast majority of patients with symptomatic osteoarthritis of the knee.” One should read this as hyaluronic acid IS recommended for some patients. The text of the recommendation clearly states, “However, as previous research reported benefits in their use, the group felt that a specific subset of patients might benefit from its use.” This statement amazingly contradicts the Strong Recommendation against HA. AAOS states that a Strong Recommendation “expresses how possible it is that a recommendation will be overturned by future evidence. It is very difficult for future evidence to overturn a recommendation that is based on many high quality randomized controlled trials that show a large effect.” It would appear that the “Strong Recommendation” ignores the panel’s conclusion that a subset might benefit. The major flaw with virtually all of the hyaluronic acid literature is the use of saline control. Increasing evidence points to the saline control being a poor choice, as saline alone</p>

			<p>shows about a 30% improvement in symptoms and is a poor choice for placebo (Bar-or et al. Use of Saline as a Placebo in Intra-articular Injections in Osteoarthritis: Potential Contributions to Nociceptive Pain Relief. The Open Rheumatology Journal, 2017, 11, 16-22). Despite the benefit of saline, virtually all these RCT show statistically significant improvement with hyaluronic acid. As RCTs with a more reasonable control group are carried out, and a better measure of clinical improvement other than MCID is applied, future studies almost certainly will overturn the existing data from prior, flawed RCTs. The contention that the science on Hyaluronic acid is settled presents potential inherent bias against HA in the AAOS process. In addition, we would ask that all AAOS Board members who recommend HA for their patients recuse themselves from the vote to approve this CPG as such an approval would be dishonest. In summary, the Strong Recommendation against is flawed, based on the methodology used by the AAOS. An honest recommendation based on the text would read “Hyaluronic acid may not be recommended for the majority of patients with symptomatic osteoarthritis of the knee but a specific subset of patients might benefit from its use.” This statement of course would not generate a strong recommendation against, but at least would be consistent with the text of the recommendation, and a nuanced review of the data. The Strong Recommendation against and the statement for this recommendation are seriously flawed, and AANA cannot support them.</p>
--	--	--	---

Workgroup Response to Reviewers #30

Dear Stephen Weber, M.D. and Louis McIntyre, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order they were listed.

- A. All AAOS CPGs specify that "This guideline is not intended for use as a benefits determination document. It does not cover allocation of resources, business and ethical considerations, and other factors needed to determine the material value of orthopaedic care." In addition to the standard disclaimer, the HA recommendation has been clarified with the verbiage "first line treatment" and downgraded to Moderate strength.
- B. Following the Review Period, this recommendation was downgraded to Moderate. Additional information has also been added to the statistical methods section of the full guideline draft.
- C. Following the Review Period, the work group reconsidered this recommendation. The recommendation was both reworded to provide additional clarity and downgraded to Moderate strength.

Reviewer #31, Rafael Sierra, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
31	Rafael Sierra, M.D.	The Knee Society	A. I reviewed the guideline in detail. I appreciate the summary of the findings as well as the details pertaining to how the recommendations were given, specifically when deciding to downgrade recommendations based on new data. B. Excellent work.

Workgroup Response to Reviewer #31

Dear Rafael Sierra, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. Thank you for the positive feedback.
- B. Thank you for the positive feedback.

Reviewer #32, Alexander Sah, M.D., FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
32	Alexander Sah, M.D.	Key Informant Panelist, American Academy of Orthopaedic Surgeons	A.

Workgroup Response to Reviewer #32

Dear Alexander Sah, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

A.

Reviewer #33, Benjamin Miller, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
33	Benjamin Miller, M.D., MS	Committee on Evidence-Based Quality and Value, American Academy of Orthopaedic Surgeons	<p>A. L 172 - The wording "should be used" is stronger than others (which state "could" or "may"). The way it is worded implies that topical NSAIDs must be utilized in all patients when not contraindicated. I would suggest using "could" rather than "should" unless the work group feels that this intervention should be standard of care in all patients.</p> <p>B. L 260 - The format and wording of the next 2 recommendations are different. Better to keep it consistent.</p> <p>C. There is inconsistency with noting "when not contraindicated" or not (e.g. NSAIDs and Tylenol). Make this consistent - it is not unreasonable to have as an assumption that any intervention that is contraindication should not be considered making it unnecessary to state.</p> <p>D. For HA, lavage, wedges - better to state whether they are effective at pain relief or functional preservation rather than stating that they are not recommended without reasons why. More like the oral narcotics one.</p> <p>E. Should dedicate a paragraph in the rationale to specifically explain why recommendations were downgraded with the EtD framework.</p> <p>F. L 1189 - Patient Education rationale appears incomplete compared to the others.</p> <p>G. L 1259 - Should define "manual therapy"</p>

Workgroup Response to Reviewer #33

Dear Benjamin Miller, M.D., MS

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. AAOS recommendations utilize standardized language to clearly communicate the strength of the recommendation. While work groups are not held to a singular language stem, 'should' is utilized with strong recommendations whereas 'could' is used with moderate strength recommendations and 'may' with limited strength recommendations.
- B. The workgroup used “and” instead of “and/or” for shockwave because the literature that was reviewed for it said it was beneficial for both pain and function.
- C. The work group chose to include the statement because the guidelines are not only meant for clinicians but also patients. Therefore, the work group elected to use that language out of concern of patients self-treating but not being aware of the black box warning for the medications.
- D. The rationale outlines clearly which studies were utilized for arriving at the conclusion. Most of the studies suggest that Lavage is neither effective at pain relief nor functional improvement and hence cannot be recommended
- E. Statements containing the reason(s) for downgrade via the Evidence-to-Decision Framework have been added to each of the downgraded recommendations.
- F. The workgroup has edited the rationale to the Patient Education recommendation.
- G. Thank you for your comment. The draft has been modified.

Reviewer #34, Matthew Landfried, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.
34	Matthew Landfried, M.D.	American Academy of Orthopaedic Surgeons	A. I feel the protocol for the study was good. I am not sure that article selection is complete. Choosing articles may contain some bias. not necessarily seen, but possible.

Workgroup Response to Reviewer #34

Dear Matthew Landfried, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. The full search strategy as well as work group determined inclusion criteria can be found in eAppendix 1.

Reviewer #35, Matthew Austin, M.D.

Reviewer Number	Reviewer Name	Society or committee you are representing	<p>Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline: The response(s) below also includes all editing suggestions received from the Additional Comments section of the structured review form.</p>
35	Matthew Austin, M.D.	Key Informant Panelist, American Academy of Orthopaedic Surgeons	<p>A. The members of the workgroup should be commended for their valuable and time-intensive efforts. The one serious concern that I have is related to applicability of these guidelines to patients with severe, symptomatic (KL Grade IV and indeed some KL Grade III) disease as most of the evidence reviewed includes only patient cohorts with KL I and II patients. I would respectfully suggest that the authors specifically state the patient population for which the recommendations are applicable based on the evidence. For example, the recommendation on bracing is currently worded:</p> <ul style="list-style-type: none"> • Braces: Brace treatment could be used to improve function, pain and quality of life in patients with knee osteoarthritis. <p>If the majority of patients in the studies supporting bracing were KL I and II patients then perhaps it would be better worded as:</p> <ul style="list-style-type: none"> • Braces: Brace treatment could be used to improve function, pain and quality of life in patients with KL Grade I-II knee osteoarthritis <p>B. Furthermore, if the evidence allows, the severity of symptoms should also be accounted for based upon the literature that was examined. Patients with mild-moderate symptoms (and those with symptoms of short duration) are very different than those with longstanding, severe symptoms with severe dysfunction. For example the recommendation on self-management currently is worded:</p> <ul style="list-style-type: none"> • Self-Management: Self-management programs are recommended to improve pain and function for patients with knee osteoarthritis. <p>However, a patient who can ambulate only 30 feet with severe, longstanding pain and a 20 degree flexion contracture is not a typical patient included in studies that have shown self-management to be effective. Therefore, the evidence does not support that the patient with severe disease be managed with self-management as opposed to surgical treatment. Keeping this in mind, perhaps an alternative wording could be:</p> <ul style="list-style-type: none"> • Self-Management: Self-management programs are recommended to improve pain and function for patients with mild to moderate symptomatic knee osteoarthritis without severe functional limitations. <p>C. In summary, I respectfully ask that the workgroup consider specifically tailoring each recommendation to the patient population referenced in the evidence used to develop that recommendation. This would include (if applicable):</p>

- | | | | |
|--|--|--|--|
| | | | <ul style="list-style-type: none">• KL Grade• Severity of symptoms• Duration of symptoms |
|--|--|--|--|

D. I cannot recommend the guidelines for use in clinical practice in their present form. However, if consideration is given to the points above I believe that these guidelines could be incredibly valuable to our patients and our membership.

Workgroup Response to Reviewer #35

Dear Matthew Austin, M.D.,

Thank you for your expert review of the Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. We will address your comments by guideline section in the order that you listed them.

- A. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.
- B. Thank you for your comment. The draft has been modified.
- C. The workgroup has taken this comment under consideration but ultimately opted not to make any changes to the wording of the guideline based on this feedback.
- D. Thank you for your comments.

Appendix A – Structured Review Form

Review Questions (REQUIRED)

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
1. The overall objective(s) of the guideline is (are) specifically described.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. The health question(s) covered by the guideline is (are) specifically described.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. The guideline's target audience is clearly described.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. There is an explicit link between the recommendations and the supporting evidence.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Given the nature of the topic and the data, all clinically important outcomes are considered.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. The patients to whom this guideline is meant to apply are specifically described.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. The criteria used to select articles for inclusion are appropriate.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. The reasons why some studies were excluded are clearly described.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. All important studies that met the article inclusion criteria are included.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. The validity of the studies is appropriately appraised.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. The methods are described in such a way as to be reproducible.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. The statistical methods are appropriate to the material and the objectives of this guideline.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
14. Health benefits, side effects, and risks are adequately addressed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. The writing style is appropriate for health care professionals.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. The grades assigned to each recommendation are appropriate.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the Guideline:

Would you recommend these guidelines for use in clinical practice? (REQUIRED)

- Strongly Recommend
- Recommend
- Would Not Recommend
- Unsure

Additional Comments regarding this clinical practice guideline?