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### Appendix A – Search strategy

1.	exp Knee Joint/
2.	Knee/
3.	Cartilage, Articular/
4.	(knee* or patellofemoral or tibiofemoral).ti,ab.
5.	(knee and (articular or cartilage* or joint*)).ti,ab.
6.	or/1-5
7.	exp Osteoarthritis/
8.	(osteoarthritis* or arthritis* or OA or degenerat* or deteriorat* or disease* or DJD or lesion* or damage*).ti,ab.
9.	7 or 8
10.	6 and 9
11.	gonarthros#.ti,ab.
12.	10 or 11
13.	(non?surgical or conservative or pharmacologic* or non?pharmacologic*).ti,ab.
14.	exp Exercise/
15.	(exercise* or (physical adj1 activit*) or (weight adj1 loss) or (weight adj1 reduction)).ti,ab.
16.	exp Physical Therapy Modalities/
17.	Physical Therapy Specialty/
18.	((physical adj1 therap*) or physiotherapy or hydrotherapy or balneotherapy or (aquatic adj1 therapy) or rehab*).ti,ab.
19.	Transcutaneous Electrical Nerve Stimulation/
20.	(TENS or (transcutaneous adj3 stimulation)).ti,ab.
21.	Ultrasonic Therapy/
22.	((ultrasound or ultrason*) adj3 therap*).ti,ab.
23.	exp Acupuncture Therapy/
24.	acupuncture.ti,ab.
25.	exp Musculoskeletal Manipulations/
26.	((manual adj1 therap*) or (manipulative adj1 therap*)).ti,ab.
27.	Braces/
28.	Foot Orthoses/
29.	(brace* or bracing or orthos#s or insole* or (shoe adj1 insert*)).ti,ab.
30.	exp Glucosamine/
31.	exp Chondroitin/
32.	(glucosamine or chondroitin or nutraceutical* or ((nutritional or dietary) adj1 supplement*)).ti,ab.

33.	Capsaicin/
34.	capsaicin.ti,ab.
35.	exp Anti-Inflammatory Agents, Non-Steroidal/
36.	(NSAID* or (anti?inflammatory adj1 (drug* or agent*))).ti,ab.
37.	exp Analgesics/
38.	Acetaminophen/
39.	(analgesic* or acetaminophen or paracetamol).ti,ab.
40.	Analgesics, Opioid/
41.	opiod*.ti,ab.
42.	Viscosupplementation/
43.	Hyaluronic Acid/
44.	viscosupplement*.ti,ab.
45.	(hyaluron* or HA or IA?HA or hylan*).ti,ab.
46.	Cortisone/
47.	Adrenal Cortex Hormones/
48.	Glucocorticoids/
49.	(cortisone or glucocorticoid* or corticosteroid*).ti,ab.
50.	Platelet-Rich Plasma/
51.	Thrombocyte Rich Plasma/
52.	((platelet* or leu#ocyte* or thrombocyte* or plasma*) adj3 (rich* or enrich*)).ti,ab.
53.	(prp or prf or prgf*).ti,ab.
54.	or/13-53
55.	Exp Guideline/
56.	(guideline or practice guideline).pt.
57.	Meta-Analysis/
58.	meta-analysis.pt.
59.	(guideline* or recommendation* or treatment* or intervention* or management or therap*).ti,ab.
60.	meta?analy*.ti,ab.
61.	(systematic* adj1 review*).ti,ab.
62.	or/55-61
63.	12 and 54 and 62
64.	Exp Animals/ not Humans/
65.	Exp Case Reports/ or exp Case-Control studies/ or exp Cross-Sectional Studies/ or exp Retrospective Studies/ or exp Costs/ or exp Cost Analysis/ or exp Clinical Study/ or exp Multicenter Study/ or exp Congresses/
66.	Observational Study/ or Meeting Abstracts/

67.	(comment or congress* or consensus* or editorial or letter or meeting* or monograph or news* or case reports or clinical trial or multicenter study or meeting abstracts).pt.
68.	or/64-67
69.	63 not 68
70.	Limit 69 to English language
71.	Remove duplicates from 70

### **Inclusion Criteria**

The inclusion criteria were: 1) a guideline or meta-analysis that evaluated at least one nonsurgical intervention for knee OA (e.g., acupuncture, analgesics, bracing, intra-articular corticosteroid (IACS) injections, exercise, physical therapy, glucosamine and chondroitin (or other dietary supplements), insoles, intra-articular hyaluronic acid (IAHA) injections, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, platelet-rich plasma (PRP) injections, pulsed electromagnetic field (PEMF) therapy, serotonin and norepinephrine reuptake inhibitors (SNRIs), transcutaneous electrical nerve stimulation (TENS), ultrasound (US) therapy, weight loss), 2) referenced an MCID for pain on a continuous scale, 3) the nonsurgical intervention was compared to placebo or control, and 4) a full-text guideline or meta-analysis published in English.

### **Appendix B - Description of results in the AAOS guideline**

<b>Descriptive term</b>	<b>Condition for use:</b>
Clinically significant	Statistically significant and lower CI > MCID
Possibly clinically significant	Statistically significant and CIs contain MCID
Not clinically significant	Statistically significant and upper CI < MCID
True negative	Not statistically significant and upper CI < MCID
Inconclusive	Not statistically significant but CIs contain MCID

*CI, confidence interval; MCID, minimum clinically important difference.*

### Appendix C – Details of the included guidelines and meta-analyses

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p>Altman et al, 2016</p> <p><b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> IAHA  <b>Location:</b> United States  <b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Databases:</b> EMBASE, PubMed/Medline  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> During or after 1995  <b>Language restriction:</b> English  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> None  <b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups at 26 weeks. Conducted subgroup analyses by intervention characteristics.  <b>Software(s) used:</b> Online Excel tool  <b>Imputations/missing data:</b> Not reported</p>	<p>Unable to assess.</p>
<p>Arrich et al, 2005</p> <p><b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> IAHA  <b>Location:</b> Austria  <b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Databases:</b> BIOSIS, CINAHL, Cochrane Library, EMBASE, PubMed/Medline  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> No  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> No  <b>Language restriction:</b> No  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Assessed allocation concealment, degree of blinding, and intention-to-treat analysis  <b>Analysis:</b> Pairwise meta-analysis comparing outcomes between groups at 2-6, 10-14, 22-30, 44-60 weeks, with meta-regression based on study-level characteristics. Conducted subgroups analysis by intervention characteristics and sensitivity analysis based on trial quality.  <b>Software(s) used:</b> Not reported</p>	<p>VAS at rest, 2-6 weeks: ⊕○○○ VERY LOW</p> <p>VAS at rest, 10-14 weeks: ⊕⊕⊕○ MODERATE</p> <p>VAS at rest, 22-30 weeks: ⊕⊕⊕○ MODERATE</p> <p>VAS after exercise, 10-14 weeks: ⊕⊕⊕○ MODERATE</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
			<b>Imputations/missing data:</b> When variability was not reported, calculated from p values or confidence interval.	VAS after exercise, 22-30 weeks: ⊕⊕⊕○ MODERATE
Bannuru et al, 2011  <b>Study type:</b> Meta-analysis <b>Treatment(s) evaluated:</b> IAHA <b>Location:</b> United States <b>Outcome(s) evaluated:</b> Pain, Function, Stiffness	<b>Databases:</b> BIOSIS, CINAHL, Cochrane Library, EMBASE, Google Scholar, PubMed/Medline, Web of Science <b>Conferences:</b> AAOS, ACR, BSR, EULAR, ILAR, OARSI <b>Expert opinion:</b> Study authors, Product manufacturers <b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> No	<b>Study design:</b> RCT <b>Conference abstracts:</b> Yes <b>Publication date restriction:</b> No <b>Language restriction:</b> No <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> No	<b>Quality scale:</b> Assessed adequacy of randomization, allocation concealment, and blinding <b>Analysis:</b> Bayesian pairwise meta-analysis comparing change from baseline scores between groups at 2, 4, 8, 12, 16, 20, 24 weeks, with meta-regression based on study-level characteristics. <b>Software(s) used:</b> OpenBUGS, R <b>Imputations/missing data:</b> Estimated means and variances from median and range, and imputed standard deviation when needed	SMD, 4 weeks: ⊕⊕○○ LOW  SMD, 8 weeks: ⊕⊕○○ LOW  SMD, 12 weeks: ⊕⊕○○ LOW  SMD, 16 weeks: ⊕⊕⊕○ MODERATE  SMD, 24 weeks: ⊕⊕⊕○ MODERATE
Bannuru et al, 2015a  <b>Study type:</b> Network meta-analysis <b>Treatment(s) evaluated:</b> Acetaminophen, Corticosteroids, IAHA, NSAIDs, Placebo	<b>Databases:</b> Cochrane Library, EMBASE, Google Scholar, PubMed/Medline, Web of Science <b>Conferences:</b> AAOS, ACR, BSR, EULAR, ILAR, OARSI <b>Expert opinion:</b> Study authors, Product manufacturers	<b>Study design:</b> RCT <b>Conference abstracts:</b> Yes <b>Publication date restriction:</b> No <b>Language restriction:</b> No <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No <b>Age restriction:</b> No	<b>Quality scale:</b> Cochrane Risk of Bias <b>Analysis:</b> Bayesian network meta-analysis comparing change from baseline scores between groups at 3 months, with meta-regression based on study-level characteristics. Conducted sensitivity analysis for	Intra-articular placebo, WOMAC: ⊕⊕○○ LOW  Oral + topical placebo, WOMAC: ⊕⊕⊕○ MODERATE

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Location:</b> United States  <b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> clinicaltrials.gov, United States FDA</p>	<p><b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p>differential versus nondifferential placebo effects.  <b>Software(s) used:</b> OpenBUGS  <b>Imputations/missing data:</b> Not reported</p>	<p>Topical placebo, WOMAC:  ⊕⊕⊕○  MODERATE</p>
<p>Bannuru et al, 2015b   <b>Study type:</b> Network meta-analysis  <b>Treatment(s) evaluated:</b> Acetaminophen, Celecoxib, Corticosteroid, Diclofenac, IAHA, Ibuprofen, Naproxen, Placebo  <b>Location:</b> United States  <b>Outcome(s) evaluated:</b> Pain, Function, Stiffness</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, Google Scholar, PubMed/Medline, Web of Science  <b>Conferences:</b> AAOS, ACR, BSR, EULAR, ILAR, OARSI  <b>Expert opinion:</b> Study authors, Product manufacturers  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> clinicaltrials.gov, United States FDA</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> Yes  <b>Publication date restriction:</b> No  <b>Language restriction:</b> No  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Cochrane Risk of Bias  <b>Analysis:</b> Bayesian network meta-analysis comparing change from baseline scores between groups at 3 months, with meta-regression based on study-level characteristics. Conducted sensitivity analysis by type of outcome scale.  <b>Software(s) used:</b> OpenBUGS  <b>Imputations/missing data:</b> Not reported</p>	<p>Acetaminophen, WOMAC:  ⊕⊕⊕○  MODERATE  Celecoxib, WOMAC:  ⊕⊕⊕⊕  HIGH  Diclofenac, WOMAC:  ⊕⊕○○  LOW  Corticosteroid, WOMAC:  ⊕⊕○○  LOW  IAHA, WOMAC:  ⊕⊕○○  LOW  Intra-articular placebo, WOMAC:  ⊕○○○  VERY LOW  Ibuprofen, WOMAC:  ⊕⊕○○  LOW  Naproxen, WOMAC:  ⊕⊕⊕○  MODERATE</p>
<p>Bjordal et al, 2004   <b>Study type:</b> Meta-analysis</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, PubMed/Medline  <b>Conferences:</b> Yes, but not specified</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> Yes  <b>Publication date restriction:</b> No</p>	<p><b>Quality scale:</b> Jadad score  <b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups</p>	<p>WOMAC/VAS, 2-13 weeks:  ⊕⊕○○  LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Treatment(s) evaluated:</b> NSAIDs  <b>Location:</b> Norway  <b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Expert opinion:</b> Clinical experts  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Language restriction:</b> English, German, Scandinavian  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> ACR criteria and/or radiographic evidence  <b>Min. symptom duration:</b> 3 months  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p>at 2-13 weeks. Conducted subgroup analyses by treatment duration, type of outcome scale, and patients with flare up of symptoms.  <b>Software(s) used:</b> Comprehensive Meta-analysis  <b>Imputations/missing data:</b> If variance data not reported, calculated using sample size and other data such as p-values, t values, standard errors, or confidence intervals.</p>	
<p>Bjordal et al, 2007  <b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> Acupuncture, Low level laser therapy, PEMF, Static magnets, TENS, Ultrasound  <b>Location:</b> Norway  <b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Databases:</b> CINAHL, Cochrane Library, DARE, EMBASE, INAHTA, NGC, NICE, PEDro, PRODIGY Guidance, PubMed/Medline  <b>Conferences:</b> World Confederation of Physical Therapy, World Association of Laser therapy  <b>Expert opinion:</b> Yes, but not specified  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> Yes  <b>Publication date restriction:</b> No  <b>Language restriction:</b> English, German, Scandinavian  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> ACR criteria and/or radiographic evidence  <b>Min. symptom duration:</b> 3 months  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Jadad score  <b>Analysis:</b> Pairwise meta-analysis comparing changed from baseline scores between groups within 4 weeks and at 1-12 weeks post-treatment. Conducted subgroup analyses based on baseline pain, methodological quality, dosage, procedural recommendations, and funding sources.  <b>Software(s) used:</b> Review Manager  <b>Imputations/missing data:</b> If standard deviation not reported, re-calculated algebraically from the trial data of sample size and other variance data such as p-</p>	<p>Electro-acupuncture, VAS, 4 weeks: ⊕⊕⊕⊕ HIGH</p> <p>Low level laser therapy, VAS, 4 weeks: ⊕⊕○○ LOW</p> <p>Manual acupuncture, VAS, 4 weeks: ⊕⊕⊕○ MODERATE</p> <p>PEMF, VAS, 4 weeks: ⊕⊕⊕⊕ HIGH</p> <p>Static magnets, VAS, 4 weeks: ⊕⊕○○ LOW</p>



Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
			values, t- values, standard errors, or confidence intervals.	TENS, VAS, 4 weeks: ⊕⊕○○ LOW
<p>Brien et al, 2011</p> <p><b>Study type:</b> Meta-analysis</p> <p><b>Treatment(s) evaluated:</b> Dietary supplements (dimethyl sulfoxide, methylsulfonylmethane)</p> <p><b>Location:</b> United Kingdom</p> <p><b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Databases:</b> AMED, CINAHL, Cochrane Library, EMBASE, National Library for Health, PubMed/Medline, Scopus</p> <p><b>Conferences:</b> No</p> <p><b>Expert opinion:</b> No</p> <p><b>Reference list of relevant studies:</b> No</p> <p><b>Clinical trials registries:</b> clinicaltrials.gov, controlled-trials.com, actr.org.au, umin.ac.jp/ctr</p>	<p><b>Study design:</b> Quasi-RCT, RCT</p> <p><b>Conference abstracts:</b> No</p> <p><b>Publication date restriction:</b> No</p> <p><b>Language restriction:</b> No</p> <p><b>Min. sample size:</b> No</p> <p><b>Specific OA diagnostic criteria:</b> No</p> <p><b>Min. symptom duration:</b> No</p> <p><b>Age restriction:</b> No</p> <p><b>Min. follow-up:</b> No</p> <p><b>Study quality:</b> No</p> <p><b>BMI criteria:</b> No</p> <p><b>Other:</b> No</p>	<p><b>Quality scale:</b> Jadad score</p> <p><b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups at end of treatment.</p> <p><b>Software(s) used:</b> Not reported</p> <p><b>Imputations/missing data:</b> Not reported</p>	<p>VAS: ⊕○○○ VERY LOW</p>
<p>Christensen et al, 2007</p> <p><b>Study type:</b> Meta-analysis</p> <p><b>Treatment(s) evaluated:</b> Weight loss</p> <p><b>Location:</b> Denmark</p> <p><b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Databases:</b> CINAHL, Cochrane Library, EMBASE, PubMed/Medline, Scopus, Web of Science</p> <p><b>Conferences:</b> No</p> <p><b>Expert opinion:</b> No</p> <p><b>Reference list of relevant studies:</b> Yes</p> <p><b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT</p> <p><b>Conference abstracts:</b> Yes</p> <p><b>Publication date restriction:</b> No</p> <p><b>Language restriction:</b> No</p> <p><b>Min. sample size:</b> No</p> <p><b>Specific OA diagnostic criteria:</b> No</p> <p><b>Min. symptom duration:</b> No</p> <p><b>Age restriction:</b> No</p> <p><b>Min. follow-up:</b> No</p> <p><b>Study quality:</b> No</p> <p><b>BMI criteria:</b> No</p> <p><b>Other:</b> No</p>	<p><b>Quality scale:</b> Jadad score</p> <p><b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups, with meta-regression.</p> <p><b>Software(s) used:</b> Review Manager, SAS</p> <p><b>Imputations/missing data:</b> Not reported</p>	<p>SMD: ⊕⊕○○ LOW</p>
<p>Colen et al, 2012</p> <p><b>Study type:</b> Meta-analysis</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, PubMed/Medline</p> <p><b>Conferences:</b> No</p> <p><b>Expert opinion:</b> No</p>	<p><b>Study design:</b> RCT</p> <p><b>Conference abstracts:</b> No</p> <p><b>Publication date restriction:</b> No</p>	<p><b>Quality scale:</b> None</p> <p><b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups</p>	<p>VAS: ⊕⊕○○ LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Treatment(s) evaluated:</b> IAHA  <b>Location:</b> Belgium, the Netherlands  <b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Language restriction:</b> Included any paper that could be translated by the authors  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p>at 3 months. Conducted a subgroup analysis by IAHA brand.  <b>Software(s) used:</b> Review Manager  <b>Imputations/missing data:</b> Not reported</p>	
<p>Corbett et al, 2013  <b>Study type:</b> Network meta-analysis  <b>Treatment(s) evaluated:</b> Acupuncture, Aerobic exercise, Balneotherapy, Braces, Heat treatment, Ice/cooling treatment, Insoles, Interferential therapy, Laser/light therapy, Manual therapy, Muscle-strengthening, Neuromuscular electrical stimulation, PEMF, Pulsed electrical stimulation, Static magnets, Tai Chi, TENS, Weight loss</p>	<p><b>Databases:</b> Not reported  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> Yes, but not specified</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> No  <b>Language restriction:</b> No  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> Excluded trials that included patients with varus/valgus malalignment  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> ≥ 55 years  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Cochrane Risk of Bias  <b>Analysis:</b> Bayesian network meta-analysis comparing absolute scores between groups at end of treatment and 3 months. Conducted sensitivity analyses based on study-level characteristics.  <b>Software(s) used:</b> WinBUGS  <b>Imputations/missing data:</b> Not reported</p>	<p>Acupuncture, WOMAC: ⊕⊕○○ LOW</p> <p>Aerobic exercise, WOMAC: ⊕⊕○○ LOW</p> <p>Balneotherapy, WOMAC: ⊕⊕○○ LOW</p> <p>Braces, WOMAC: ⊕○○○ VERY LOW</p> <p>Heat treatment, WOMAC: ⊕⊕○○ LOW</p> <p>Ice/cooling treatment, WOMAC: ⊕○○○ VERY LOW</p> <p>Insoles, WOMAC:</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Location:</b> United Kingdom  <b>Outcome(s) evaluated:</b> Pain</p>				<p>⊕⊕○○ LOW</p>
				<p>Interferential therapy, WOMAC: ⊕⊕○○ LOW</p>
				<p>Laser/light therapy, WOMAC: ⊕⊕○○ LOW</p>
				<p>Manual therapy, WOMAC: ⊕⊕○○ LOW</p>
				<p>Static magnets, WOMAC: ⊕○○○ VERY LOW</p>
				<p>Tai Chi, WOMAC: ⊕⊕○○ LOW</p>
				<p>Neuromuscular electrical stimulation, WOMAC: ⊕○○○ VERY LOW</p>
				<p>PEMF, WOMAC: ⊕○○○ VERY LOW</p>
				<p>TENS, WOMAC: ⊕⊕○○ LOW</p>
				<p>Pulsed electrical stimulation, WOMAC: ⊕⊕○○ LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
				Sham acupuncture, WOMAC: ⊕⊕○○ LOW Weight loss, WOMAC: ⊕⊕○○ LOW
Dai et al, 2017  <b>Study type:</b> Cochrane review <b>Treatment(s) evaluated:</b> PRP, HA <b>Location:</b> Australia, Canada, the Netherlands <b>Outcome(s) evaluated:</b> Pain, Function	<b>Databases:</b> Pubmed, Embase, Scopus, Cochrane Library <b>Conferences:</b> No <b>Expert opinion:</b> No <b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> No	<b>Study design:</b> RCT <b>Conference abstracts:</b> No <b>Publication date restriction:</b> No <b>Language restriction:</b> English <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> ACR Diagnostic criteria <b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> No	<b>Quality scale:</b> Cochrane Risk of Bias <b>Analysis:</b> Pairwise random effects meta-analysis comparing pain and function at 6 and 12 months <b>Software(s) used:</b> Review Manager <b>Imputations/missing data:</b> Not reported	PRP, WOMAC: ⊕○○○ VERY LOW
Fransen et al, 2015  <b>Study type:</b> Cochrane review <b>Treatment(s) evaluated:</b> Exercise interventions <b>Location:</b> Australia, Canada, the Netherlands <b>Outcome(s) evaluated:</b> Pain, Function	<b>Databases:</b> CINAHL, Cochrane Library, EMBASE, PEDro, PubMed/Medline <b>Conferences:</b> No <b>Expert opinion:</b> No <b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> clinicaltrials.gov, World Health Organization	<b>Study design:</b> Quasi-RCT, RCT <b>Conference abstracts:</b> No <b>Publication date restriction:</b> No <b>Language restriction:</b> English <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No	<b>Quality scale:</b> Cochrane Risk of Bias <b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups at end of treatment, and at 2-6 and > 6 months. Conducted subgroup analyses based on intervention characteristics and sensitivity analyses based on study-level characteristics.	VAS: ⊕⊕⊕⊕ HIGH

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
		<b>Other:</b> No	<b>Software(s) used:</b> Review Manager <b>Imputations/missing data:</b> Reported no missing data.	
<p>Health Quality Ontario, 2005</p> <p><b>Study type:</b> Health technology assessment</p> <p><b>Treatment(s) evaluated:</b> IAHA (Hylan G-F 20/Synvisc)</p> <p><b>Location:</b> Canada</p> <p><b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, INAHTA, PubMed/Medline</p> <p><b>Conferences:</b> No</p> <p><b>Expert opinion:</b> No</p> <p><b>Reference list of relevant studies:</b> No</p> <p><b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> Economic evaluation, Meta-analysis, Non-RCT, RCT, Systematic Review</p> <p><b>Conference abstracts:</b> No</p> <p><b>Publication date restriction:</b> During or after 1966</p> <p><b>Language restriction:</b> English</p> <p><b>Min. sample size:</b> No</p> <p><b>Specific OA diagnostic criteria:</b> No</p> <p><b>Min. symptom duration:</b> No</p> <p><b>Age restriction:</b> No</p> <p><b>Min. follow-up:</b> No</p> <p><b>Study quality:</b> No</p> <p><b>BMI criteria:</b> No</p> <p><b>Other:</b> No</p>	<p><b>Quality scale:</b> Jadad score</p> <p><b>Analysis:</b> None</p> <p><b>Software(s) used:</b> Not applicable</p> <p><b>Imputations/missing data:</b> Not applicable</p>	<p>VAS, 1-4 weeks: ⊕○○○ VERY LOW</p>
<p>Jevsevar et al, 2015</p> <p><b>Study type:</b> Meta-analysis</p> <p><b>Treatment(s) evaluated:</b> IAHA</p> <p><b>Location:</b> United States</p> <p><b>Outcome(s) evaluated:</b> Pain, Function, Stiffness</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, PEDro, PubMed/Medline</p> <p><b>Conferences:</b> No</p> <p><b>Expert opinion:</b> No</p> <p><b>Reference list of relevant studies:</b> Yes</p> <p><b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT</p> <p><b>Conference abstracts:</b> No</p> <p><b>Publication date restriction:</b> No</p> <p><b>Language restriction:</b> English</p> <p><b>Min. sample size:</b> ≥ 30 patients per arm</p> <p><b>Specific OA diagnostic criteria:</b> No</p> <p><b>Min. symptom duration:</b> No</p> <p><b>Age restriction:</b> No</p> <p><b>Min. follow-up:</b> ≥ 4 weeks</p> <p><b>Study quality:</b> No</p> <p><b>BMI criteria:</b> No</p> <p><b>Other:</b> No</p>	<p><b>Quality scale:</b> Assessed type of control intervention, allocation concealment, blinding, intention-to-treat analysis, investigator bias</p> <p><b>Analysis:</b> Pairwise meta-analysis comparing scores between groups at 26 weeks, with meta-regression.</p> <p>Conducted a subgroup analysis by intervention characteristics.</p> <p><b>Software(s) used:</b> Stata</p> <p><b>Imputations/missing data:</b> Not reported</p>	<p>SMD: ⊕⊕○○ LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p>Jevsevar et al, 2013 (AAOS)</p> <p><b>Study type:</b> Guideline  <b>Treatment(s) evaluated:</b> All available therapies  <b>Location:</b> United States  <b>Outcome(s) evaluated:</b> Pain, Function, Stiffness, Composite score (WOMAC)</p>	<p><b>Databases:</b> CINAHL, Cochrane Library, EMBASE, PubMed/MEDLINE  <b>Conferences:</b> None  <b>Expert opinion:</b> None  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> None</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> During or after 1966  <b>Language restriction:</b> English  <b>Specific outcome measures:</b>  <b>Min. sample size:</b> ≥ 30 patients per arm  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> ≥ 4 weeks  <b>Study quality:</b> Excluded studies determined to have “very limited evidence strength”  <b>BMI criteria:</b> No  <b>Other:</b> Only validated “paper-and-pencil” outcome measures or those identified a priori by the work group as “critical”; excluded studies in which there was heterogeneity in patient characteristics or outcomes at baseline and authors did not statistically adjust for these differences</p>	<p><b>Quality scale:</b> 20-item questionnaire  <b>Analysis:</b> Bayesian network meta-analysis comparing change from baseline scores between treatments for continuous outcomes.  <b>Software(s) used:</b> WinBUGS  <b>Imputations/missing data:</b> Not reported.</p>	<p>Acupuncture, WOMAC/VAS, 4-26 weeks: ⊕⊕⊕○ MODERATE</p> <p>Corticosteroid, WOMAC/VAS: ⊕⊕⊕○ MODERATE</p> <p>Glucosamine, WOMAC: ⊕⊕⊕○ MODERATE</p> <p>Chondroitin sulfate, VAS: ⊕⊕⊕○ MODERATE</p> <p>IAHA. WOMAC: ⊕⊕⊕○ MODERATE</p>
<p>Jevsevar et al, 2018</p> <p><b>Study type:</b> Network meta-analysis</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, PubMed  <b>Conferences:</b> No  <b>Expert opinion:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> Search conducted in 2015  <b>Language restriction:</b> English</p>	<p><b>Quality scale:</b> Modified Cochrane Risk of Bias  <b>Analysis:</b> Bayesian network meta-analysis comparing change</p>	<p>Acetaminophen, SMD: ⊕⊕⊕○ MODERATE</p> <p>Celecoxib, SMD:</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Treatment(s) evaluated:</b> Acetaminophen, Celecoxib, Corticosteroid, Diclofenac, IAHA, Ibuprofen, Naproxen, PRP, Oral Placebo, IA Placebo</p> <p><b>Location:</b> United States</p> <p><b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Reference list of relevant studies:</b> Yes</p> <p><b>Clinical trials registries:</b> No</p>	<p><b>Min. sample size:</b> 30 per arm</p> <p><b>Specific OA diagnostic criteria:</b> No</p> <p><b>Min. symptom duration:</b> No</p> <p><b>Age restriction:</b> No</p> <p><b>Min. follow-up:</b> 28 days</p> <p><b>Study quality:</b> Studies assessed using appraisal criteria: randomization, allocation concealment, blinding, completeness of outcome data, selective reporting, and the presence of other biases such as conflicts of interest or industry funding, confounding factors or treatments, lack of intention-to-treat analysis when applicable, and significant differences in baseline measurements. Only articles fitting the best available evidence criteria were considered for each comparison.</p> <p><b>BMI criteria:</b> No</p> <p><b>Other:</b> No</p>	<p>from baseline scores between groups at 4 weeks.</p> <p><b>Software(s) used:</b> OpenBUGS</p> <p><b>Imputations/missing data:</b> No</p>	<p>⊕⊕⊕⊕ HIGH</p> <p>Diclofenac, SMD: ⊕⊕○○ LOW</p> <p>Corticosteroid, SMD: ⊕⊕⊕○ MODERATE</p> <p>IAHA, SMD: ⊕⊕⊕○ MODERATE</p> <p>Ibuprofen, SMD: ⊕⊕○○ LOW</p> <p>Naproxen, SMD: ⊕⊕⊕⊕ HIGH</p> <p>PRP, SMD: ⊕⊕○○ LOW</p>
<p>McCarthy et al, 2006</p> <p><b>Study type:</b> Meta-analysis</p> <p><b>Treatment(s) evaluated:</b> PEMF</p> <p><b>Location:</b> United Kingdom</p>	<p><b>Databases:</b> AMED, CINAHL, Cochrane Library, EMBASE, HealthSTAR, PEDro, PubMed/Medline, SPORTDiscus</p> <p><b>Conferences:</b> Yes, but not specified</p>	<p><b>Study design:</b> Non-RCT, RCT</p> <p><b>Conference abstracts:</b> Yes</p> <p><b>Publication date restriction:</b> During or after 1996</p> <p><b>Language restriction:</b> No</p> <p><b>Min. sample size:</b> No</p> <p><b>Specific OA diagnostic criteria:</b> No</p>	<p><b>Quality scale:</b> Jadad score</p> <p><b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups immediately post-treatment.</p> <p><b>Software(s) used:</b> Not reported</p> <p><b>Imputations/missing data:</b> Not reported</p>	<p>SMD: ⊕⊕○○ LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Expert opinion:</b> Yes, but not specified  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> Outcome measures must have been validated</p>		
<p>Moyer et al, 2015</p> <p><b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> Valgus bracing  <b>Location:</b> Canada  <b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Databases:</b> CINAHL, Cochrane Library, EMBASE, PubMed/Medline, Scopus, Science Direct, Web of Knowledge  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> No  <b>Language restriction:</b> English  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Cochrane Risk of Bias  <b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups at longest follow-up. Conducted subgroup analyses based on intervention characteristics and risk of bias, and sensitivity analyses based on study-level characteristics.  <b>Software(s) used:</b> Comprehensive Meta-analysis  <b>Imputations/missing data:</b> Used p-value if missing standard deviation.</p>	<p>SMD:  ⊕⊕⊕○  MODERATE</p>
<p>NICE 2014</p> <p><b>Study type:</b> Guideline  <b>Treatment(s) evaluated:</b> All available therapies  <b>Location:</b> United Kingdom  <b>Outcome(s) evaluated:</b> Pain, Function,</p>	<p><b>Databases:</b> AMED, Cochrane Library, EMBASE, PubMed/Medline  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> Non-RCT, Observational, RCT  <b>Conference abstracts:</b> Yes  <b>Publication date restriction:</b> No  <b>Language restriction:</b> English  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No</p>	<p><b>Quality scale:</b> Cochrane Risk of Bias  <b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups. Conducted subgroup analyses and sensitivity analyses by study time points and risk of bias.  <b>Software(s) used:</b> Review Manager</p>	<p>Unable to assess.</p>



Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
Stiffness, OMERACT-OARSI, PGA, QoL		<b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> No	<b>Imputations/missing data:</b> In cases where standard deviations were not reported, the standard error was calculated if the p-values or 95% confidence intervals were reported. If these statistical measures were not available then the methods described in section 16.1.3 of the Cochrane Handbook ‘Missing standard deviations’ were applied as the last resort.	
Richette et al, 2015  <b>Study type:</b> Meta-analysis <b>Treatment(s) evaluated:</b> IAHA <b>Location:</b> Belgium, France <b>Outcome(s) evaluated:</b> Pain, Function	<b>Databases:</b> Cochrane Library, EMBASE, PubMed/Medline <b>Conferences:</b> Yes <b>Expert opinion:</b> No <b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> Yes	<b>Study design:</b> RCT <b>Conference abstracts:</b> Yes <b>Publication date restriction:</b> No <b>Language restriction:</b> No <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> Only included studies with a low risk of bias <b>BMI criteria:</b> No <b>Other:</b> No	<b>Quality scale:</b> Assessed adequacy of randomization, allocation concealment, and blinding <b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups at 3 months. <b>Software(s) used:</b> R, Meta package <b>Imputations/missing data:</b> Not reported.	SMD, 12 weeks: ⊕⊕⊕⊕ HIGH
Rutjes et al, 2009  <b>Study type:</b> Cochrane review <b>Treatment(s) evaluated:</b> TENS <b>Location:</b> Switzerland	<b>Databases:</b> CINAHL, Cochrane Library, EMBASE, PEDro, PubMed/Medline <b>Conferences:</b> Yes, but not specified <b>Expert opinion:</b> Content experts and trialists	<b>Study design:</b> Quasi-RCT, RCT <b>Conference abstracts:</b> Yes <b>Publication date restriction:</b> No <b>Language restriction:</b> No <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No	<b>Quality scale:</b> Cochrane Risk of Bias <b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups at the end of the treatment period, with meta-regression. Conducted subgroup analyses based on	SMD, 4 weeks: ⊕○○○ VERY LOW

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> Yes, but not specified</p>	<p><b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> No</p>	<p>study-level and intervention characteristics. <b>Software(s) used:</b> Review Manager, Stata <b>Imputations/missing data:</b> Approximated means and measures of dispersion from figures in reports. If effect sizes could not be calculated, contacted authors for additional data.</p>	
<p>Rutjes et al, 2010</p> <p><b>Study type:</b> Cochrane review <b>Treatment(s) evaluated:</b> Ultrasound <b>Location:</b> Switzerland <b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Databases:</b> CINAHL, Cochrane Library, EMBASE, PEDro, PubMed/Medline <b>Conferences:</b> Yes, but not specified <b>Expert opinion:</b> Content experts and trialists <b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> Yes, but not specified</p>	<p><b>Study design:</b> Quasi-RCT, RCT <b>Conference abstracts:</b> Yes <b>Publication date restriction:</b> No <b>Language restriction:</b> No <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> No</p>	<p><b>Quality scale:</b> Cochrane Risk of Bias <b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups at the end of the treatment period. Conducted subgroup analyses based on study-level and intervention characteristics. <b>Software(s) used:</b> Review Manager, Stata <b>Imputations/missing data:</b> Used other available parameters to estimate effect size and variability.</p>	<p>SMD, 2-8 weeks: ⊕⊕○○ LOW</p>
<p>Rutjes et al, 2012</p> <p><b>Study type:</b> Meta-analysis <b>Treatment(s) evaluated:</b> IAHA <b>Location:</b> Switzerland</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, PubMed/Medline <b>Conferences:</b> Yes, but not specified <b>Expert opinion:</b> Yes, but not specified <b>Reference list of relevant studies:</b> Yes</p>	<p><b>Study design:</b> Quasi-RCT, RCT <b>Conference abstracts:</b> Yes <b>Publication date restriction:</b> No <b>Language restriction:</b> No <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No</p>	<p><b>Quality scale:</b> Assessed concealment of allocation, blinding of patients, use of a sham control, blinded outcome assessment, and intention-to-treat analyses <b>Analysis:</b> Pairwise meta-analysis comparing absolute</p>	<p>SMD: ⊕○○○ VERY LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Clinical trials registries:</b> Yes, but not specified</p>	<p><b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p>scores between groups at 3 months, with meta-regression. Conducted subgroups analyses based on study-level and intervention characteristics.  <b>Software(s) used:</b> Stata  <b>Imputations/missing data:</b> Used other available parameters to estimate effect size and variability.</p>	
<p>Schneider et al, 2012</p> <p><b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> Dietary supplement (chondroitin sulfate)  <b>Location:</b> France, Switzerland  <b>Outcome(s) evaluated:</b> Pain, Function, OMERACT-OARSI</p>	<p><b>Databases:</b> Cochrane Library, EMBASE, PubMed/Medline  <b>Conferences:</b> Yes  <b>Expert opinion:</b> Yes  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> Yes</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> Yes  <b>Publication date restriction:</b> No  <b>Language restriction:</b> No  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> 3 months  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Jadad score  <b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores and OMERACT-OARSI rates between groups at 3-6 months.  <b>Software(s) used:</b> Easy MA  <b>Imputations/missing data:</b> Not reported.</p>	<p>VAS:  ⊕⊕⊕○  MODERATE</p>
<p>Strand et al, 2015</p> <p><b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> IAHA  <b>Location:</b> United States</p>	<p><b>Databases:</b> EMBASE, PubMed/Medline  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> No  <b>Language restriction:</b> English  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No</p>	<p><b>Quality scale:</b> Jadad score  <b>Analysis:</b> Pairwise meta-analysis comparing absolute scores between groups at 4-13 and 14-26 weeks. Conducted subgroup analyses by study time points, patient characteristics,</p>	<p>SMD, 4-13 weeks:  ⊕○○○  VERY LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Outcome(s) evaluated:</b> Pain, Function</p>		<p><b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> Only included trials evaluating United States-approved products</p>	<p>sample size, and Jadad score, and sensitivity analysis by removing one study at a time.  <b>Software(s) used:</b> Comprehensive Meta-analysis  <b>Imputations/missing data:</b> Not reported</p>	<p>SMD, 14-26 weeks:  ⊕○○○  VERY LOW</p>
<p>Wang et al, 2012</p> <p><b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> Physical therapy interventions - Aerobic exercise, Aquatic exercise, Diathermy, Education program, Electrical stimulation, Massage, Orthotics, PEMF, Proprioception exercise, Strengthening exercise, Tai chi, Taping, Ultrasonography  <b>Location:</b> United States  <b>Outcome(s) evaluated:</b> Pain, Function, QoL</p>	<p><b>Databases:</b> AMED, Cochrane Library, Health and Psychosocial Instruments, PEDro, PubMed/Medline, Scirus, <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> clinicaltrials.gov</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> During or after 1970  <b>Language restriction:</b> English  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> Cochrane Risk of Bias  <b>Analysis:</b> Pairwise meta-analysis comparing scores between groups at &lt; 6, 6-13, 14-26, and &gt; 26 weeks, with meta-regression by study-level characteristics. Conducted subgroup analyses by patient characteristics and type of outcome scale.  <b>Software(s) used:</b> Stata  <b>Imputations/missing data:</b> Not reported</p>	<p>Aerobic exercise, SMD:  ⊕⊕○○  LOW</p> <p>Electrical stimulation, SMD:  ⊕⊕○○  LOW</p> <p>Strength exercises, SMD:  ⊕⊕○○  LOW</p> <p>Ultrasound, SMD:  ⊕⊕○○  LOW</p>
<p>Wang et al, 2015</p> <p><b>Study type:</b> Meta-analysis</p>	<p><b>Databases:</b> Cochrane Library, EBSCO, EMBASE, Google Scholar, PubMed/Medline, Science Direct  <b>Conferences:</b> No  <b>Expert opinion:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> No  <b>Language restriction:</b> English  <b>Min. sample size:</b> No</p>	<p><b>Quality scale:</b> Jadad score  <b>Analysis:</b> Pairwise meta-analysis comparing change from baseline scores between groups. Conducted subgroup analyses by patient characteristics.</p>	<p>Likert scale:  ⊕⊕⊕⊕  HIGH</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
<p><b>Treatment(s) evaluated:</b> Duloxetine (SNRI)  <b>Location:</b> China  <b>Outcome(s) evaluated:</b> Pain, Function, PGA</p>	<p><b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> clinicaltrials.gov</p>	<p><b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> 3 months  <b>Age restriction:</b> ≥ 40 years  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> Excluded trials with insufficient data</p>	<p><b>Software(s) used:</b> Review Manager  <b>Imputations/missing data:</b> Excluded trials with insufficient data.</p>	
<p>Warden et al, 2008  <b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> Bracing, Patellar taping  <b>Location:</b> United States  <b>Outcome(s) evaluated:</b> Pain</p>	<p><b>Databases:</b> CINAHL, EBM Reviews, Expanded Academic ASAP, PEDro, PubMed/Medline, SPORTSDiscus, Web of Knowledge  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> Quasi-RCT, RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> During or after 1980  <b>Language restriction:</b> English  <b>Min. sample size:</b> No  <b>Specific OA diagnostic criteria:</b> No  <b>Min. symptom duration:</b> No  <b>Age restriction:</b> No  <b>Min. follow-up:</b> No  <b>Study quality:</b> No  <b>BMI criteria:</b> No  <b>Other:</b> No</p>	<p><b>Quality scale:</b> PEDro scale  <b>Analysis:</b> Pairwise meta-analysis comparing scores between groups immediately post-treatment and at 3-12 weeks. Conducted sensitivity analyses by removing trials when heterogeneity was present and study time points.  <b>Software(s) used:</b> Review Manager  <b>Imputations/missing data:</b> Not reported</p>	<p>VAS:  ⊕⊕○○  LOW</p>
<p>Xu et al, 2017  <b>Study type:</b> Meta-analysis  <b>Treatment(s) evaluated:</b> PRP, IA-HA, IA placebo  <b>Location:</b> China  <b>Outcome(s) evaluated:</b> Pain, Function</p>	<p><b>Databases:</b> Medline, Embase, EBM reviews, Cochrane Library  <b>Conferences:</b> No  <b>Expert opinion:</b> No  <b>Reference list of relevant studies:</b> Yes  <b>Clinical trials registries:</b> No</p>	<p><b>Study design:</b> RCT  <b>Conference abstracts:</b> No  <b>Publication date restriction:</b> During or after 1980  <b>Language restriction:</b> English, Chinese  <b>Min. sample size:</b> at least 30 participants  <b>Specific OA diagnostic criteria:</b> No</p>	<p><b>Quality scale:</b> PEDro scale  <b>Analysis:</b> Pairwise meta-analysis comparing PRP to HA, and PRP to IA-placebo  <b>Software(s) used:</b> Review Manager  <b>Imputations/missing data:</b> Not reported</p>	<p>PRP WOMAC or IKDC:  ⊕○○○  VERY LOW</p>

Study Details	Search Details	Inclusion Criteria	Quality Assessment and Statistics	Quality of Evidence for Pain Assessments (GRADE)
		<b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> No		
Zeng et al, 2015  <b>Study type:</b> Network meta-analysis <b>Treatment(s) evaluated:</b> Celecoxib, Chondroitin, Glucosamine, Glucosamine plus Chondroitin <b>Location:</b> China <b>Outcome(s) evaluated:</b> Pain, Function	<b>Databases:</b> Cochrane Library, EMBASE, PubMed/Medline <b>Conferences:</b> No <b>Expert opinion:</b> No <b>Reference list of relevant studies:</b> Yes <b>Clinical trials registries:</b> clinicaltrials.gov, World Health Organization	<b>Study design:</b> RCT <b>Conference abstracts:</b> Not reported <b>Publication date restriction:</b> No <b>Language restriction:</b> English <b>Min. sample size:</b> No <b>Specific OA diagnostic criteria:</b> No <b>Min. symptom duration:</b> No <b>Age restriction:</b> No <b>Min. follow-up:</b> No <b>Study quality:</b> No <b>BMI criteria:</b> No <b>Other:</b> <20% loss to follow-up	<b>Quality scale:</b> Cochrane Risk of Bias <b>Analysis:</b> Bayesian network meta-analysis comparing change from baseline scores between groups at the last follow-up time point. Conducted sensitivity analyses by study-level characteristics. <b>Software(s) used:</b> WinBUGS, R, Stata <b>Imputations/missing data:</b> Not reported	Unable to assess.

AAOS, American Academy of Orthopaedic Surgeons; ACR, American College of Rheumatology; AMED, Allied and Complimentary Medicine Database; BSR, British Society for Rheumatology; BIOSIS, Biosciences Information Service; BMI, body mass index; CINAHL, The Cumulative Index to Nursing and Allied Health Literature; DARE, Database of Abstracts of Reviews of Effects; EMBASE, Excerpta Medica Database; EULAR, European League Against Rheumatism; FDA, Food and Drug Administration; IAHA, intra-articular hyaluronic acid; ILAR, International League of Associations for Rheumatology; INAHTA, International Network of Agencies for Health Technology Assessment; MEDLINE, Medical Literature Analysis and Retrieval System Online; NGC, National Guideline Clearinghouse; NICE, National Institute for Health and Care Excellence; NSAID, Nonsteroidal anti-inflammatory drug; OARSI, Osteoarthritis Research Society International; PEDro, Physiotherapy Evidence Database; PubMed, Public/Publisher MEDLINE; PEMF, pulsed electromagnetic field; PGA, patient global assessment; QoL, quality of life; RCT, randomized clinical trial; SAS, Statistical Analysis System; SMD, standardized mean difference; TENS, transcutaneous electrical nerve stimulation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

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### Appendix D - GRADE summary

<b>GRADE Quality of Evidence</b>	<b>Number of Outcomes (% within intervention type)</b>
<b>Nonpharmacological Interventions</b>	<b>46</b>
High	5 (10.9)
Moderate	6 (13.0)
Low	27 (58.7)
Very Low	8 (17.4)
<b>Intra-articular Interventions</b>	<b>29</b>
High	1 (3.4)
Moderate	10 (34.5)
Low	10 (34.5)
Very Low	8 (27.6)
<b>Oral Pharmacological Interventions</b>	<b>12</b>
High	2 (16.7)
Moderate	5 (41.7)
Low	5 (41.7)
Very Low	0 (0.0)
<b>Total</b>	<b>87</b>
High	8 (9.2)
Moderate	21 (24.1)
Low	42 (48.3)
Very Low	16 (18.4)



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