Systematic Review on Noninvasive Nonpharmacological Treatment for Chronic Pain: Surveillance Report 2

Literature Update Period: October 2021 through December 2021

Background and Purpose

This is the second update for the 2020 report *Noninvasive Nonpharmacological Treatment for Chronic Pain*[1] (available at https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research), covering the period from October through December 2021. The 2020 report addressed benefits and harms of noninvasive nonpharmacological therapy for five common chronic pain conditions: low back pain (LBP); neck pain; knee, hip, or hand osteoarthritis (OA); fibromyalgia (FM); and tension headache. Given the clinical and public health importance of this topic, it is important to identify new evidence that could impact practice or policy. The purpose of this surveillance report is to identify new evidence published since the September 2021 report and to determine how the new evidence impacts findings of the 2020 report and Surveillance Report 1, which added evidence from August 2019 through September 2021 and was published on the Agency of Healthcare Research and Quality (AHRQ) website (available at https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research). A subsequent surveillance report is planned for April 2022 (based on evidence published through March 2022).

Scope

The scope and eligibility criteria established at the time of the original report[1] were utilized for this surveillance report; no changes were made. That report included randomized controlled trials (RCTs) reporting outcomes at least 1 month following the completion of treatment and focused on the use of active, single component, noninvasive nonpharmacological interventions (including exercise, mind-body practices, psychological therapies, mindfulness practices, manual therapies, physical modalities, acupuncture, and multidisciplinary rehabilitation) for adults with five common chronic pain conditions, LBP (Key Question 1), neck pain (Key Question 2), knee, hip, or hand OA (Key Question 3), FM (Key Question 4), and tension headache (Key Question 5). The report addressed:

- Whether the interventions work overall compared with sham, waitlist control, attention control, no treatment, or usual care.
- Whether the interventions work compared with pharmacological alternatives.
- How outcomes for individual interventions (e.g., acupuncture) compare with a common comparator (exercise for LBP, neck pain, OA, and FM; biofeedback for headache).

In addition, Key Question 6 addressed whether estimates of benefits and harms differ by age, sex, presence of comorbidities (e.g., emotional or mood disorders), or degree of nociplasticity/central sensitization.

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The full protocol for the original report including detailed inclusion criteria using the PICOTS (populations, interventions, comparisons, outcomes, timing, settings) framework (https://www.ncbi.nlm.nih.gov/books/NBK556223/table/ch3.tab1/?report=objectonly) and full Key Questions (https://www.ncbi.nlm.nih.gov/books/n/cer227/ch2/#ch2.s2) is available on the AHRQ website (https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/protocol) and on the PROSPERO systematic reviews registry (CRD42019132457).

Methods

Update searches were conducted to identify evidence published from October 2021 through December 2021. Search strategies from the original report were utilized,[1] and we searched the same databases as in the original report (Ovid® MEDLINE®, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews). In addition, to capture articles not yet indexed in MEDLINE, we supplemented the original search strategies with a previously developed[2] optimized (text-word only) search in pre-MEDLINE to identify studies not yet indexed with Medical Subject Headings (MeSH). As in the original report, searches on electronic databases were supplemented by review of reference lists of relevant articles. Search strategies are available in Appendix A.

As in the original review, one investigator screened citations identified through searches for eligibility for full-text review. (Key Questions and inclusion criteria are available in Appendix B.) In addition, to increase efficiency of abstract review, we utilized a machine learning classifier in conjunction with a second investigator to assist in conducting dual reviews. The machine learning classifier was previously shown to have 100 percent recall for identifying eligible studies in update searches for this review.[2] The machine learning classifier screened all citations; the second investigator performed dual review on all studies that the machine learning classifier did not classify as very low probability of eligibility. Any citation identified as potentially eligible by either investigator underwent full-text review to determine final eligibility.

We planned to utilize the same methods for data abstraction and quality assessment as for the 2020 review if new studies were identified. We would assess the risk of bias of RCTs using the approaches recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 8.5, Risk of Bias Tool)[3] and the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Research*,[4] in conjunction with criteria and methods developed by the Cochrane Back and Neck Group.[5] The decision to update meta-analyses from the original report would be based on the number and sample sizes of new studies eligible for meta-analysis (meta-analysis performed if new evidence was large relative to the studies in the original meta-analysis); consistency in findings between the new studies and the original meta-analysis (meta-analysis performed if findings from new evidence appear inconsistent and new studies were appropriate for pooling based on similarity in populations, interventions, and comparisons, in order to determine whether new studies impact conclusions); or whether new evidence could impact the strength of evidence (SOE) (meta-analysis performed if the SOE based on the original meta-analysis was low or insufficient and new evidence could increase the strength of evidence due to increased precision, quality, or other factors). The SOE was based on the totality of evidence (evidence in the original report plus new evidence from Surveillance Report 1) and determined using the methods described in the original report.

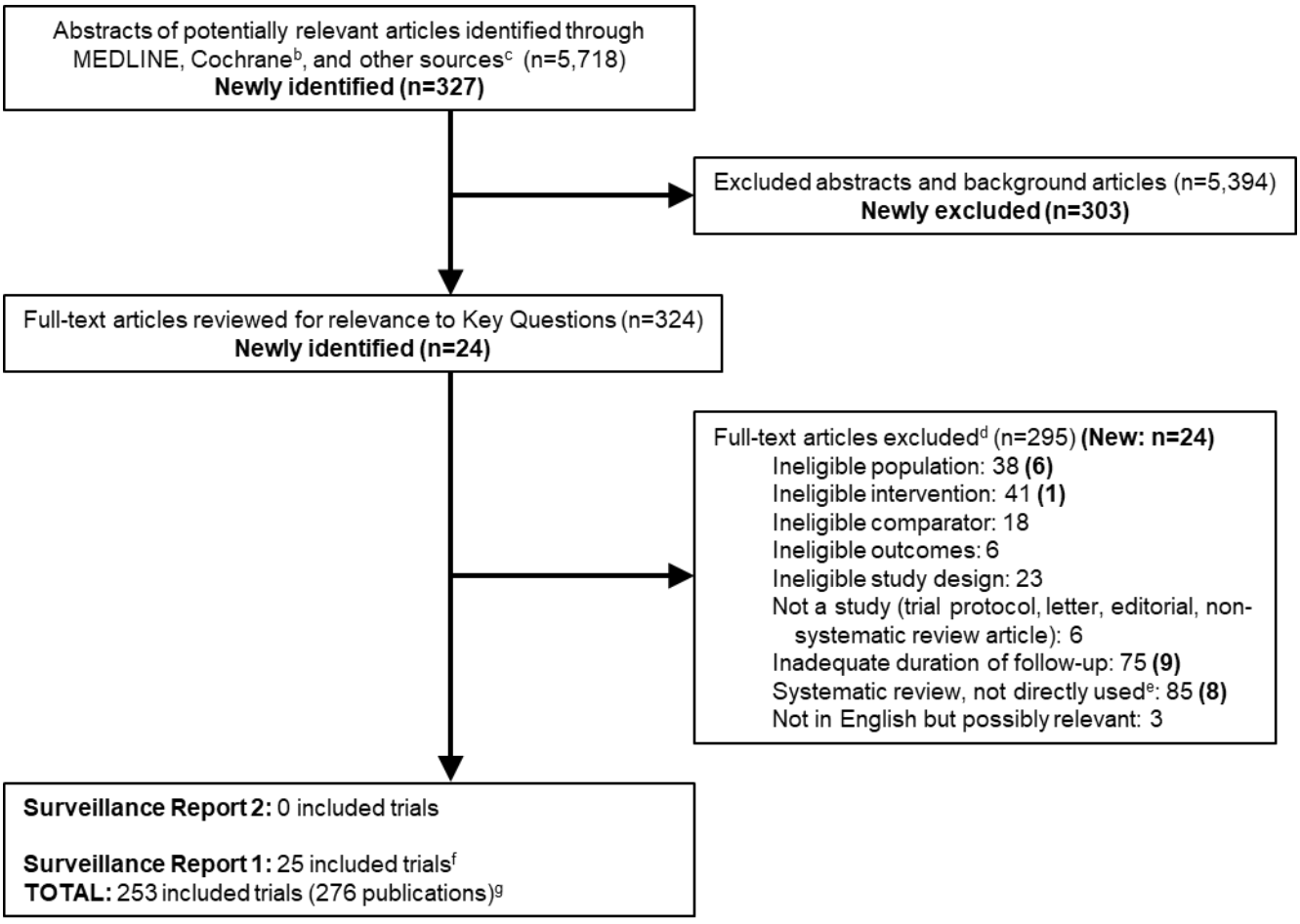
A list of studies included in Surveillance Report 1 is provided in Appendix C. Evidence tables providing data from those included studies are available in Appendix D, and quality assessments for each study are shown in Appendix E. A list of articles excluded at full-text

review for Surveillance Report 2 (current update), along with reasons for exclusion, is available in Appendix F. Updated and new meta-analyses from Surveillance Report 1 can be found in Appendix G.

Results

The search for Surveillance Report 2 from October through December 2021 yielded 327 citations and did not identify any new eligible trials (Figure 1). The primary reason for exclusion at full-text review was inadequate duration of followup postintervention in nine trials (i.e., followup <1-month postintervention). Reasons for exclusion for the remaining seven trials were ineligible population (6 trials; mixed chronic pain conditions and results not stratified by specific type, or not chronic pain) and ineligible intervention (1 trial; self-management). Additionally, we identified eight relevant systematic reviews that were not included as primary evidence, but the reference lists were reviewed for eligible studies.

Figure 1. Literature flow diagram[a]



[a] Search counts are for the update searches only, and the included studies total is from the original report and surveillance reports combined.
[b] Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
[c] Other sources include prior reports (i.e., Comparative Effectiveness Reviews, health technology assessments), reference lists of relevant articles, systematic reviews, etc.

[d] Publications may be included or excluded for multiple interventions.
[e] Used as source documents; studies checked for inclusion eligibility.
[f] Four followup publications to 3 trials included in the 2020 report were identified in Surveillance Report 1 (to Groessl 2017, Saper 2017 [chronic low back pain], and McCrae 2019 [fibromyalgia] included in the 2020 report). These publications reported only secondary outcomes of interest and were not summarized in Surveillance Report 1, but details can be found in Appendix D of that report.
[g] A total of 228 trials (in 247 publications) were included in the 2020 report.

Summary of Evidence

Given that no new evidence was identified for this update, the results presented below in Table 1 provide findings from studies identified in Surveillance Report 1, which focused on Key Questions and interventions with new evidence. The original full SOE table is available in the 2020 report (https://www.ncbi.nlm.nih.gov/books/n/cer227/appg/). Results details can be found in Surveillance Report 1 (https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research).

Table 1. Summary of conclusions and assessments informed by evidence published since the 2020 systematic review.

Condition: Intervention, Comparator	Outcome, Timing	Prior Review (2020)[a]	New in Surveillance Report 1[a]	Change
LBP: Exercise vs. UC, AC, or placebo	Function, short term	Small improvement SOE: Moderate 10 RCTs (N=940)	*2 fair-quality RCTs (N=147)[6,7] 1 small improvement[6], 1 large improvement[7]	No change in conclusions
	Function, intermediate term	No effect SOE: Low 5 RCTs (N=616)	*1 fair-quality RCT (N=96)[6] Small improvement	No change in conclusions
	Pain, short term	Moderate improvement SOE: Low 11 RCTs (N=981)	1 fair-quality RCT (N=111)[6] No effect	No change in conclusions
	Pain, intermediate term	Small improvement SOE: Low 5 RCTs (N=616)	1 fair-quality RCT (N=96)[6] No effect	No change in conclusions
LBP: Psychological therapies vs. UC	Function, short term	Small improvement SOE: Moderate 3 RCTs (N=906)	*2 fair-quality RCTs (N=146)[7,8] Large improvements[b]	Small improvement SOE: Low (downgraded one level)
	Function, intermediate term	Small improvement SOE: Moderate 3 RCTs (N=1,026)	*1 fair-quality RCT (N=116)[8] Moderate improvement	No change in conclusions
	Function, long term	Small improvement SOE: Moderate 3 RCTs (N=815)	*1 fair-quality RCT (N=124)[8] Moderate improvement	No change in conclusions
	Pain, short term	Small improvement SOE: Moderate 3 RCTs (N=906)	1 fair-quality RCT (N=112)[8] Small improvement	No change in conclusions
	Pain, intermediate term	Small improvement SOE: Moderate 3 RCTs (N=1,026)	1 fair-quality RCT (N=116)[8] Small improvement	No change in conclusions
	Pain, long term	Small improvement SOE: Moderate 3 RCTs (N=815)	1 fair-quality RCT (N=124)[8] Small improvement	No change in conclusions
LBP: Psychological therapies vs. exercise	Function, short term	No evidence at short term	1 fair-quality RCT (N=34)[7] No effect	Insufficient evidence

Condition: Intervention, Comparator	Outcome, Timing	Prior Review (2020)[a]	New in Surveillance Report 1[a]	Change
LBP: Physical modalities: LLLT vs. sham	Function, short term	Small improvement SOE: Low 1 RCT (N=56)	1 poor-quality RCT (N=34)[9] Large improvement	No change in conclusions
	Pain, short term	Moderate improvement SOE: Low 1 RCT (N=56)	1 poor-quality RCT (N=34)[9] Large improvement	No change in conclusions
LBP: Physical modalities: Burst TENS vs. continuous TENS vs. sham	Function, short term	No evidence	1 fair-quality RCT (N=73)[10] No effect	No effect SOE: Low
	Pain, short term	No evidence	1 fair-quality RCT (N=73)[10] No effect	No effect SOE: Low
LBP: Manual therapy: Spinal manipulation vs. sham, UC, AC	Function, short term	Small improvement SOE: Low 3 RCTs (N=704)	*1 fair-quality RCT (N=155)[11] No effect	No change in conclusions
	Pain, short term	No effect SOE: Low 3 RCTs (N=530)	1 fair-quality RCT (N=155)[11] No effect	No change in conclusions
LBP: Manual therapy: Massage vs. sham, UC, AC	Function, short term	Small improvement SOE: Moderate 6 RCTs (N=694)	1 fair-quality RCT (N=59)[12] No effect	No change in conclusions
	Pain, short term	Small improvement SOE: Moderate 5 RCTs (N=644)	1 fair-quality RCT (N=59)[12] No effect	No change in conclusions
LBP: Mind-body practices: Yoga vs. exercise	Function, short term	No effect SOE: Low 4 RCTs (N=559)	2 fair-quality RCTs (N=252)[13,14] No effect	No change in conclusions
	Pain, short term	No effect SOE: Low 5 RCTs (N=575)	2 fair-quality RCTs (N=252)[13,14] No effect	No change in conclusions
LBP: Acupuncture vs. sham, UC, or AC	Function, short term	Small improvement SOE: Low 4 RCTs (N=2,066)	1 fair-quality RCT (N=152)[15] Large improvement	No change in conclusions
	Pain, short term	Small improvement SOE: Moderate 5 RCTs (N=2,109)	1 fair-quality RCT (N=152)[15] Moderate improvement	No change in conclusions
Neck pain: Exercise vs. AC, WL, or NT	Function, short term	No effect SOE: Low 3 RCTs (N=444)	1 fair-quality RCT (N=43)[16] Moderate improvement	No change in conclusions
	Pain, short term	No effect SOE: Low 3 RCTs (N=444)	1 fair-quality RCT (N=43)[16] Large improvement	No change in conclusions
Neck pain: Manual therapy: Manipulation vs. sham	Function, short term	No evidence	1 fair-quality RCT (N=42)[16] Moderate improvement	Moderate improvement SOE: Low
	Pain, short term	No evidence	1 fair-quality RCT (N=42)[16] Large improvement	Large improvement SOE: Low
Neck pain: Manual therapy: Manipulation vs. exercise	Function, short term	No evidence	1 fair-quality RCT (N=43)[16] No effect	No effect SOE: Low
	Pain, short term	No evidence	1 fair-quality RCT (N=43)[16] No effect	No effect SOE: Low
Knee OA: Exercise vs. UC, AC, sham, or NT	Function, short term	Small improvement SOE: Moderate 8 RCTs (N=748)	*1 poor-quality RCT (N=84)[17] No effect	No change in conclusions

Condition: Intervention, Comparator	Outcome, Timing	Prior Review (2020)[a]	New in Surveillance Report 1[a]	Change
	Function, intermediate term	Moderate improvement SOE: Low 11 RCTs (N=879)	*1 fair-quality RCT (N=265)[18] No effect	No change in conclusions
	Function, long term	Small improvement SOE: Low 4 RCTs (N=1,199)	*2 fair-quality RCTs (N=342)[18,19] No effects	No change in conclusions
	Pain, short term	Small improvement SOE: Moderate 8 RCTs (N=748)	*1 poor-quality RCT (N=84)[17] Small improvement	No change in conclusions
	Pain, intermediate term	Moderate improvement SOE: Low 11 RCTs (N=879)	*1 fair-quality RCT (N=261)[18] No effect	No change in conclusions
	Pain, long term	Small improvement SOE: Low 4 RCTs (N=1,199)	*2 fair-quality RCTs (N=338)[18,19] No effects	No change in conclusions
Knee OA: Physical modalities: LLLT vs. sham or UC	Function, short term	Insufficient evidence 1 RCT (N=49)	*1 good-quality RCT (N=84)[20] Small improvement	Small improvement SOE: Low (upgraded one level)
	Function, intermediate term	Insufficient evidence 2 RCTs (N=109)	*1 good-quality RCT (N=84)[20] Small improvement	Small improvement SOE: Low (upgraded one level)
	Pain, short term	Insufficient evidence 2 RCTs (N=76)	*1 good-quality RCT (N=84)[20] No effect	No effect SOE: Low (upgraded one level)
	Pain, intermediate term	Insufficient evidence 2 RCTs (N=109)	*1 good-quality RCT (N=84)[20] Moderate improvement	No effect SOE: Low (upgraded one level)
Knee OA: Physical modalities: Continuous and pulsed US vs. sham	Function and pain, short term	No effect SOE: Low 3 RCTs (N=249)	1 good-quality RCT (N=75)[21] No effect	No change in conclusions
Knee OA: Physical modalities: Interferential current vs. sham	Function, short and intermediate term	No evidence	1 good-quality RCT (N=84)[20] No effect	No effect SOE: Low
	Pain, short and intermediate term	No evidence	1 good-quality RCT (N=84)[20] No effect	No effect SOE: Low
Knee OA: Manual therapies: Massage vs. UC	Function, short term	Insufficient evidence 1 RCT (N=125)	1 poor-quality RCT (N=60)[22] No effect	No change in conclusions
	Pain, short term	Insufficient evidence 1 RCT (N=125)	1 poor-quality RCT (N=60)[22] Small improvement	No change in conclusions
Knee OA: Mind-body therapies: Tai Chi vs. AC or UC	Function and pain, intermediate term	Insufficient evidence 1 RCT (N=40)	1 poor-quality RCT (N=92)[23] Moderate improvement	No change in conclusions
Knee OA: Mind-body therapies: Qigong vs. exercise	Function and pain, intermediate term	No evidence	1 fair-quality trial (N=68)[24] No effect	Insufficient evidence
Knee OA: Acupuncture vs. UC, NT, or sham	Function, short term	No effect SOE: Low 5 RCTs (N=944)	1 good-quality RCT (N=83)[25] No effect	No change in conclusions

Condition: Intervention, Comparator	Outcome, Timing	Prior Review (2020)[a]	New in Surveillance Report 1[a]	Change
	Pain, short term	No effect SOE: Low 6 RCTs (N=1065)	1 good-quality RCT (N=83)[25] No effect	No change in conclusions
FM: Exercise vs. UC, NT, sham, or AC	Function, short term	Small improvement SOE: Low 7 RCTs (N=410)	2 poor-quality RCTs (N=135)[26,27] No effect	No change in conclusions
FM: Manual therapy: Spinal manipulation vs. sham	Function, short and intermediate term	No evidence	1 fair-quality RCT (N=101)[28] No effect	No effect SOE: Low
	Pain, short and intermediate term	No evidence	1 fair-quality RCT (N=101)[28] No effect	No effect SOE: Low
FM; Mindfulness practices: MBSR, MAT vs. AC or WL	Function, intermediate term	Small improvement SOE: Low 1 RCT (N=148)	1 poor-quality RCT (N=98)[29] Small improvement	No change in conclusions
FM: Mind-body therapies: BBAT vs. UC	Pain, short and intermediate term	No evidence	1 fair-quality RCT (N=39)[30] No effect	Insufficient evidence
FM: Acupuncture vs. UC	Function, short term	No evidence	1 poor-quality RCT (N=67)[26] No effect	Insufficient evidence
FM: Acupuncture vs. exercise	Function, short term	No evidence	1 poor-quality RCT (N=67)[26] No effect	Insufficient evidence
FM: MDR vs. UC or WL	Function, short term	Small improvement SOE: Low 3 RCTs (N=381)	1 poor-quality RCT (N=64)[27] No effect	No change in conclusions
FM: MDR vs. exercise	Function, short term	No evidence	1 poor-quality RCT (N=64)[27] No effect	Insufficient evidence

* Meta-analysis updated.
Abbreviations: AC = attention control; BBAT = basic body awareness training; FM = fibromyalgia; LBP = low back pain; LLLT = low-level laser therapy; MA = meta-analysis; MAT = meditation awareness training; MBSR = mindfulness-based stress reduction; MDR = multidisciplinary rehabilitation; NT = no treatment; RCT = randomized controlled trial; SOE = strength of evidence; TENS = transcutaneous electrical nerve stimulation; UC = usual care; US = ultrasound; vs. = versus; WL = waitlist.
[a] The sample size (N) reported is as analyzed.
[b] One new trial, Shariat 2019, was an outlier and conclusions are based on inclusion of the one new fair-quality RCT (Ashar 2021) which increased heterogeneity leading to downgrade from moderate to low SOE.
[c] In the previous report, 3 RCTs were included that compared acupuncture with sham acupuncture and found a small improvement in function short term (moderate SOE).

Conclusions

A systematic review and two subsequent surveillance updates evaluated noninvasive nonpharmacological treatments for five common chronic pain conditions (LBP, neck pain, OA, FM, and tension headache). Exercise, multidisciplinary rehabilitation, acupuncture, low-level laser therapy, psychological therapies, mindfulness practices, and mind-body practices were most consistently associated with durable small to moderate improvements in function and pain for specific chronic pain conditions, although the data were sparse for many interventions.

Interventions or comparators for which there was low strength of evidence of no effect for improvements in function and/or pain were: transcutaneous electrical nerve stimulation (TENS) versus sham TENS in chronic LBP, spinal manipulation versus exercise for chronic neck pain,

inferential current versus sham for knee OA, and spinal manipulation versus sham manipulation for FM. Spinal manipulation was associated with improvements in function and pain short term compared with sham laser for chronic neck pain. There was very little evidence for chronic tension headache specifically. Harms were poorly reported across interventions. No serious intervention-related adverse events (e.g., leading to death or disability or requiring intensive medical attention) were identified; reported adverse events were generally minor and time limited.

No trials in pregnant or breastfeeding women with pre-existing chronic pain were identified.

No new evidence was identified for Surveillance Report 2. The next surveillance report is scheduled for April 2022.

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Disclaimers

This report is based on research conducted by the Pacific Northwest Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 75Q80120D00006). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Afterword

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis.

This and future quarterly progress reports will provide up-to-date information about the evidence base to inform health plans, providers, purchasers, government programs, and the healthcare system as a whole on the state of the science. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the website (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov. They will be considered in the next version of the report.

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Appendix Contents

Appendix A. Literature Search Strategies

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R), October through December 2021

1 exp Low Back Pain/ or ((back or spine or spinal) adj2 pain).ti,ab.
2 exp Chronic Pain/
3 Neck Pain/ or neck.ti,ab.
4 exp Osteoarthritis/ or osteoarthritis.ti,ab.
5 Headache/ or headache.ti,ab.
6 Fibromyalgia/ or fibromyalgia.ti,ab.
7 exp Exercise Therapy/
8 exp Physical Therapy Modalities/
9 exp Braces/
10 exp Mind-Body Therapies/
11 exp Acupuncture Therapy/
12 exp Rehabilitation/
13 exp Psychotherapy/
14 exp Musculoskeletal Manipulations/
15 (noninvasive or non-invasive or nonpharmacologic* or non-pharmacologic*).ti,ab.
16 (exercise or physical therapy or cognitive or behavioral or feedback or relaxation or acceptance or commitment or traction or ultrasound or stimulation or laser or magnet* or inferential or electromuscular or diathermy or heat or cold or manipulation or manual or craniosacral or mindfulness or meditation or mind-body or yoga or pilates or Qigong or acupuncture or functional restoration or multidisciplin* or interdisciplin*).ti,ab.
17 rh.fs.
18 or/1-6
19 or/7-17
20 18 and 19
21 randomized controlled trial.pt.
22 controlled clinical trial.pt.
23 clinical trials as topic.sh.
24 (random* or trial or placebo).ti,ab.
25 clinical trials as topic.sh.
26 exp animals/ not humans.sh.
27 or/21-25
28 27 not 26
29 20 and 28
30 limit 29 to english language
31 limit 30 to humans
32 31 and (20171$ or 2018$).dt,ed,ep.
33 meta-analysis.pt.
34 meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
35 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab.

36 ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab.
37 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab.
38 (data synthes* or data extraction* or data abstraction*).ti,ab.
39 (handsearch* or hand search*).ti,ab.
40 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab.
41 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab.
42 (meta regression* or metaregression*).ti,ab.
43 (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
44 (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
45 (cochrane or (health adj2 technology assessment) or evidence report).jw.
46 (meta-analysis or systematic review).ti,ab.
47 (comparative adj3 (efficacy or effectiveness)).ti,ab.
48 (outcomes research or relative effectiveness).ti,ab.
49 ((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab.
50 or/33-49
51 20 and 50
52 limit 51 to english language
53 limit 52 to humans
54 53 and (20171$ or 2018$).dt,ed,ep.
55 32 or 54

Database: EBM Reviews - Cochrane Central Register of Controlled Trials, October through December 2021
1 exp Low Back Pain/ or ((back or spine or spinal) adj2 pain).ti,ab.
2 exp Chronic Pain/
3 Neck Pain/ or neck.ti,ab.
4 exp Osteoarthritis/ or osteoarthritis.ti,ab.
5 Headache/ or headache.ti,ab.
6 Fibromyalgia/ or fibromyalgia.ti,ab.
7 exp Exercise Therapy/
8 exp Physical Therapy Modalities/
9 exp Braces/
10 exp Mind-Body Therapies/
11 exp Acupuncture Therapy/
12 exp Rehabilitation/
13 exp Psychotherapy/
14 exp Musculoskeletal Manipulations/
15 (noninvasive or non-invasive or nonpharmacologic* or non-pharmacologic*).ti,ab.
16 (exercise or physical therapy or cognitive or behavioral or feedback or relaxation or acceptance or commitment or traction or ultrasound or stimulation or laser or magnet* or inferential or electromuscular or diathermy or heat or cold or manipulation or manual or

craniosacral or mindfulness or meditation or mind-body or yoga or pilates or Qigong or acupuncture or functional restoration or multidisciplin* or interdisciplin*).ti,ab.
17 rh.fs.
18 or/1-6
19 or/7-17
20 18 and 19
21 limit 20 to yr="2017 -Current"
22 limit 21 to medline records
23 21 not 22
24 limit 23 to english language

Database: EBM Reviews - Cochrane Database of Systematic Reviews, October 2021 through December 2021
1 ((back or spine or spinal) adj2 pain).ti.
2 (neck adj2 pain).ti.
3 osteoarthritis.ti.
4 headache.ti.
5 fibromyalgia.ti.
6 (noninvasive or non-invasive or nonpharmacologic* or non-pharmacologic*).ti,ab. (295)
7 (exercise or physical therapy or cognitive or behavioral or feedback or relaxation or acceptance or commitment or traction or ultrasound or stimulation or laser or magnet* or inferential or electromuscular or diathermy or heat or cold or manipulation or manual or craniosacral or mindfulness or meditation or mind-body or yoga or pilates or Qigong or acupuncture or functional restoration or multidisciplin* or interdisciplin*).ti,ab.
9 6 or 7
10 8 and 9
11 limit 10 to new reviews

Appendix B. Key Questions and Inclusion and Exclusion Criteria

Key Questions

Key Question 1: Adults with chronic low back pain

Key Question 2: Adults with chronic neck pain

Key Question 3: Adults with osteoarthritis-related pain

Key Question 4: Adults with fibromyalgia

Key Question 5: Adults with chronic tension headache

Key Questions 1–5 incorporate the following subquestions:

a. What are the benefits and harms of noninvasive nonpharmacological therapies compared with sham treatment, no treatment, waitlist, attention control, or usual care?
b. What are the benefits and harms of noninvasive nonpharmacological therapies compared with pharmacological therapy (e.g., opioids, nonsteroidal anti-inflammatory drugs, acetaminophen, antiseizure medications, antidepressants, topical agents, medical cannabis, and muscle relaxants)?
c. What are the benefits and harms of noninvasive nonpharmacological therapies compared with exercise or, for headache, biofeedback?

The three-part format for Key Questions 1–5 reflects the following research concepts:

Part "a" answers the question of whether the various interventions work overall compared with sham, waitlist control, attention control, no treatment, or usual care. For this review, usual care was defined as care that might be provided or recommended by a primary care provider.

Part "b" answers the question of whether the various interventions work compared with pharmacological alternatives.

Part "c" answers the question of how outcomes for individual interventions (e.g., acupuncture) compare with a common comparator. Exercise is the most frequent comparison in the literature for many chronic pain conditions, so it provides a common comparator for analysis. It is also recommended in most guidelines for conditions including low back pain, neck pain, fibromyalgia, and osteoarthritis and is widely available. Exercise served as common comparator for these conditions. For chronic headache, biofeedback provided a common comparator for analysis.

Key Question 6: Do estimates of benefits and harms differ by age, sex, presence of comorbidities (e.g., emotional or mood disorders), or degree of nociplasticity/central sensitization?

Inclusion and Exclusion Criteria

Table B-1. Inclusion and exclusion criteria

PICOTS	Inclusion	Exclusion
Population **All KQs**	**General Inclusion Criteria** • Adults with the following chronic pain (defined as pain lasting 12 weeks or longer or pain persisting past the time for normal tissue healing) conditions: low back pain, neck pain, osteoarthritis pain, fibromyalgia, or tension headache. • Pregnant or breastfeeding women who have a history of chronic pain prior to pregnancy	**General Exclusion Criteria** • Acute pain • Children (<18 years), pregnant or breastfeeding women with pregnancy-related back or pelvic pain or who do not have chronic pain prior to pregnancy; • Patients with chronic pain related to "active" cancer, infection, inflammatory arthropathy, • <90% of study sample has the defined condition of interest or <90% received the treatment(s) of interest • Treatment for addiction • Pain at the end of life • Neuropathic pain
Population **KQ1**	**KQ1: Low back pain** • Adults with chronic, nonradicular low back pain	**KQ1: Low back pain** • Patients with radiculopathy • Low back pain associated with severe or progressive neurological deficits • Failed back surgery syndrome
Population **KQ2**	**KQ2: Neck pain** • Adults with chronic neck pain	**KQ2: Neck pain** • Patients with radiculopathy or myelopathy • Traumatic spinal cord injury • Neck pain associated with progressive neurological deficit, loss of strength
Population **KQ3**	**KQ3: Osteoarthritis** • Adults with osteoarthritis-related pain (primary or secondary osteoarthritis) of the hip, knee or hand	**KQ3: Osteoarthritis** • Other types of arthritis (e.g., rheumatoid) • Patients with joint replacement
Population **KQ4**	**KQ4: Fibromyalgia** • Adults with fibromyalgia	**KQ4: Fibromyalgia** • Conditions with generalized pain not consistent with fibromyalgia • Systemic exertion intolerance disease, (myalgic encephalomyelitis/chronic fatigue syndrome) • Somatization disorder (Briquet's syndrome)

PICOTS	Inclusion	Exclusion
Population KQ5	**KQ5: Headache** • Adults with primary chronic tension headache (International Classification of Headache Disorders, 3rd edition definition). ○ Primary headaches are attributed to the headache condition itself, not headache caused by another disease or medical condition. Tension headaches are the most common. Chronic headache is defined as 15 or more days each month for at least 12 weeks or history of headache more than 180 days a year.	**KQ5: Headache** • Migraine headache • Mixed headache (also known as coexistent tension and migraine headache, chronic daily headache, transformed migraine) • Trigeminal neuralgia • Cluster headache • Secondary headache types as defined in *The International Classification of Headache Disorders*, 3rd edition (i.e., headaches due to an underlying pathology such as cancer, prior medical procedures, temporomandibular joint disorders, neck pathology, cervicogenic headache, and medication over-use headache) • Traumatic brain injury
Interventions	**All KQs:** • Exercise (exercise as part of physical therapy, supervised exercise, home exercise, group exercise, formal exercise program) • Psychological therapies (cognitive and/or behavioral therapy, biofeedback, relaxation training) • Physical modalities (traction, ultrasound, transcutaneous electrical nerve stimulation, low-level laser therapy, interferential therapy, electro-muscular stimulation diathermy, superficial heat or cold, bracing for knee, back, neck, hand and magnets) • Manual therapies (musculoskeletal manipulation, massage) • Mindfulness practices (meditation, mindfulness-based stress reduction practices) • Mind-body practices (yoga, tai chi, qigong) • Acupuncture • Multidisciplinary/interdisciplinary rehabilitation[a]	**All KQs:** • Invasive nonsurgical treatments (e.g., injections, nerve block, spinal cord stimulators, parenterally-administered medications) • Surgical interventions (including minimally invasive surgical interventions) • Diet interventions or dietary supplementation • Studies evaluating incremental value of adding a noninvasive nonpharmacological intervention to another noninvasive nonpharmacological intervention • Self-management interventions or programs, self-management education programs • Others not listed for inclusion

PICOTS	Inclusion	Exclusion
Comparators	**<u>All KQs, subquestion a</u>** • Sham treatment • Waitlist • Usual care • No treatment • Attention control intended to control for nonspecific effects (e.g., time, attention, expectations); **<u>All KQs subquestion b</u>** • Commonly used nonopioid pharmacological therapy used to treat chronic pain [NSAIDS, acetaminophen, anti-seizure medications, antidepressants (SNRIs, TCAs), muscle relaxants (including benzodiazepines)] • Topical agents (lidocaine, diclofenac, capsaicin) • Medical cannabis (inhaled, oral, topical); phytocannabinoids (plant derived, THC and CBD); FDA approved synthetic cannabinoids [Dronabionol (THC), Nabilone (similar to THC)] • Opioid analgesics **<u>KQs 1-4, 6 subquestion c</u>** • Exercise[b] **<u>KQ 5, 6 subquestion c</u>** • Biofeedback[c]	**All KQs:** • Supplements (e.g., glucosamine, chondroitin, d-ribose, herbal or homeopathic treatments) • Invasive nonsurgical treatments (e.g., injections, nerve block, spinal cord stimulators, parenterally-administered medications) • Antidepressants not typically used for chronic pain including SSRIs and MAOIs • Anti-seizure medications not typically used to treat chronic pain including topiramate, lamotrigine, levetiracetam, phenytoin, valproic acid, zonisamide, tiagabine • Surgical interventions (including minimally invasive surgical interventions) • Studies evaluating incremental value of adding a noninvasive nonpharmacological intervention to another noninvasive nonpharmacological intervention • Comparisons within nonpharmacological intervention types (e.g., comparisons of different types of exercise with each other, different types of massage with each other) • Corticosteroids, biologic drugs • Salicylates (oral and topical) • Topical menthol preparations • Others not listed for inclusion
Outcomes	**All KQs:** Primary efficacy outcomes; we will focus on outcomes from validated measures for • Function/disability/pain interference[d] • Pain[d] Harms and Adverse effects Secondary outcomes • Psychological distress (including measures of depression and anxiety) • Quality of life • Opioid use • Sleep quality, sleep disturbance • Health care utilization	**All KQs:** • Intermediate outcomes (e.g., biomarkers for inflammation) • Other nonclinical outcomes
Timing	Duration of followup: short term (1 to <6 months), intermediate term (≥6 to <12 months) and long term (≥12 months); focus on longer term (>12 month) effects. Trials lasting ≥6 months that include a supervised intervention followed by continued home treatment as part of the intervention will be included even though the only followup occurs directly after the intervention.	• Studies with <1 month followup after treatment

PICOTS	Inclusion	Exclusion
Studies	Randomized controlled trials or high-quality systematic reviews of randomized controlled trials published in English; cross-over trials with random assignment of initial treatment will be considered.	**All KQs:** • Studies reporting on intermediate outcomes only • Nonrandomized studies • Abstracts, editorials, letters, conference proceedings • Duplicate publications of the same study that do not report on different outcomes • Single site reports from multicenter trials • White papers • Narrative reviews • Articles identified as preliminary reports when results are published in later versions • Indirect comparisons • Studies with fewer than 15 patients per treatment arm • Systematic reviews on treatment of chronic neck pain, fibromyalgia, chronic headache, or osteoarthritis that are of low methodological quality. Those that do not report outcomes or time frames of interest may be excluded. Systematic reviews may be excluded based on currency or relevance (e.g., if there is a substantial new body of evidence reflected in a later review).
Settings	Any nonhospital setting or in self-directed care	• Hospital care, hospice care, emergency department care

CBD = cannabidiol; FDA = Food and Drug Administration; KQ = Key Question; MAOI = monoamine oxidase inhibitor; NSAID = nonsteroidal anti-inflammatory drug; PICOTS = population, interventions, comparators, outcomes, timing and setting; SNRI = serotonin and norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; THC = tetrahydrocannabinol.

[a] Multidisciplinary rehabilitation (MDR) (also known as interdisciplinary rehabilitation), is defined as a coordinated program with biopsychosocial treatment components (e.g., exercise therapy and cognitive-behavioral therapy) provided by professionals from at least two different specialties. Functional restoration training is included as part of MDR.

[b] Different forms of exercise will not be compared to each other. Exercise will be compared with nonexercise interventions for low back pain, neck pain, fibromyalgia and osteoarthritis

[c] Different forms of biofeedback will not be compared to each other. Biofeedback will be compared with the noninvasive interventions for chronic headache

[d] The magnitude of effects for pain and function will be classified using the same system as in the AHRQ-funded noninvasive treatment for low back pain review recognizing that small effects using this system may not meet standard thresholds for clinically meaningful effects. A small effect was defined for pain as a mean between-group difference following treatment of 5 to 10 points on a 0- to 100-point visual analog scale (VAS), 0.5 to 1.0 points on a 0- to 10-point numeric rating scale, or equivalent; for function as a mean difference of 5- to 10-point difference on the 0- to 100-point Oswestry Disability Index (ODI) or 1 to 2 points on the 0- to 24-point Roland-Morris Disability Questionnaire (RDQ), or equivalent; and for any outcome as a standardized mean difference (SMD) of 0.2 to 0.5. A moderate effect was defined for pain as a mean difference of 10 to 20 points on a 0- to 100-point VAS, for function as a mean difference of 10 to 20 points on the ODI or 2 to 5 points on the RDQ, and for any outcome as an SMD of 0.5 to 0.8. Large/substantial effects were defined as greater than moderate. We will apply similar methodology to outcomes measures for the other condition. The clinical relevance of effects classified as small might vary for individual patients depending on preferences, baseline symptom severity, harms, cost, and other factors.

Appendix C. Included Studies List From Surveillance Report 1

No new eligible trials were identified during the recent surveillance period (for Surveillance Report 2). This list includes trials identified since the 2020 review and included in Surveillance Report 1.

1. Alqualo-Costa R, Rampazo EP, Thome GR, et al. Interferential current and photobiomodulation in knee osteoarthritis: A randomized, placebo-controlled, double-blind clinical trial. Clinical Rehabilitation. 2021 Apr 26:2692155211012004. doi: https://dx.doi.org/10.1177/02692155211012004. PMID: 33896234.
2. Ashar YK, Gordon A, Schubiner H, et al. Effect of Pain Reprocessing Therapy vs Placebo and Usual Care for Patients With Chronic Back Pain: A Randomized Clinical Trial. JAMA Psychiatry. 2021 Sep 29doi: 10.1001/jamapsychiatry.2021.2669. PMID: 34586357.
3. Bernal-Utrera C, Gonzalez-Gerez JJ, Anarte-Lazo E, et al. Manual therapy versus therapeutic exercise in non-specific chronic neck pain: a randomized controlled trial. Trials [Electronic Resource]. 2020 Jul 28;21(1):682. doi: https://dx.doi.org/10.1186/s13063-020-04610-w. PMID: 32723399.
4. Bravo C, Skjaerven LH, Espart A, et al. Basic Body Awareness Therapy in patients suffering from fibromyalgia: a randomized clinical trial. Physiotherapy theory and practice. 2019;35(10):919-29. PMID: CN-01980930.
5. Coste J, Medkour T, Maigne JY, et al. Osteopathic medicine for fibromyalgia: a sham-controlled randomized clinical trial. Therapeutic Advances in Musculoskeletal Disease. 2021;13:1759720X211009017. doi: https://dx.doi.org/10.1177/1759720X211009017. PMID: 33948127.
6. Garrido-Ardila EM, Gonzalez-Lopez-Arza MV, Jimenez-Palomares M, et al. Effectiveness of acupuncture vs. core stability training in balance and functional capacity of women with fibromyalgia: a randomized controlled trial. Clinical Rehabilitation. 2020 May;34(5):630-45. doi: https://dx.doi.org/10.1177/0269215520911992. PMID: 32204612.
7. Groessl EJ, Liu L, Schmalzl L, et al. Secondary Outcomes from a Randomized Controlled Trial of Yoga for Veterans with Chronic Low-Back Pain. Int J Yoga Therap. 2020 Jan 1;30(1):69-76. doi: 10.17761/2020-D-19-00036. PMID: 31509451.
8. Hu X, Lai Z, Wang L. Effects of Taichi exercise on knee and ankle proprioception among individuals with knee osteoarthritis. Research in Sports Medicine. 2020 Apr-Jun;28(2):268-78. doi: https://dx.doi.org/10.1080/15438627.2019.1663520. PMID: 31524502.
9. Joyce C, Roseen EJ, Keysor JJ, et al. Can Yoga or Physical Therapy for Chronic Low Back Pain Improve Depression and Anxiety Among Adults From a Racially Diverse, Low-Income Community? A Secondary Analysis of a Randomized Controlled Trial. Archives of Physical Medicine & Rehabilitation. 2021 Jun;102(6):1049-58. doi: https://dx.doi.org/10.1016/j.apmr.2021.01.072. PMID: 33556352.
10. Karakas A, Dilek B, Sahin MA, et al. The effectiveness of pulsed ultrasound treatment on pain, function, synovial sac thickness and femoral cartilage thickness in patients with knee osteoarthritis: a randomized, double-blind clinical, controlled study. Clinical Rehabilitation. 2020 Dec;34(12):1474-84. doi: https://dx.doi.org/10.1177/0269215520942953. PMID: 32715744.
11. Kholoosy L, Elyaspour D, Akhgari MR, et al. Evaluation of the Therapeutic Effect of Low Level Laser in Controlling Low Back Pain: A Randomized Controlled Trial. Journal of Lasers in Medical Sciences. 2020;11(2):120-5. doi: https://dx.doi.org/10.34172/jlms.2020.21. PMID: 32273951.

12. Kobayashi D, Shimbo T, Hayashi H, et al. Shiatsu for chronic lower back pain: Randomized controlled study. Complementary Therapies in Medicine. 2019 Aug;45:33-7. doi: https://dx.doi.org/10.1016/j.ctim.2019.05.019. PMID: 31331579.

13. Lam WC, Au KY, Qin Z, et al. Superficial needling acupuncture versus sham acupuncture for knee osteoarthritis: a randomized controlled trial. American Journal of Medicine. 2021 Jun 11;11:11. doi: https://dx.doi.org/10.1016/j.amjmed.2021.05.002. PMID: 34126097.

14. Lang AE, Hendrick PA, Clay L, et al. A randomized controlled trial investigating effects of an individualized pedometer driven walking program on chronic low back pain. BMC Musculoskeletal Disorders. 2021 Feb 19;22(1):206. doi: https://dx.doi.org/10.1186/s12891-021-04060-8. PMID: 33607979.

15. Luo Y, Yang M, Liu T, et al. Effect of hand-ear acupuncture on chronic low-back pain: a randomized controlled trial. Journal of traditional chinese medicine = chung i tsa chih ying wen pan. 2019;39(4):587-98. PMID: CN-02144857.

16. McCrae CS, Curtis AF, Miller MB, et al. Effect of cognitive behavioural therapy on sleep and opioid medication use in adults with fibromyalgia and insomnia. Journal of Sleep Research. 2020 12;29(6):e13020. doi: https://dx.doi.org/10.1111/jsr.13020. PMID: 32126156.

17. Messier SP, Mihalko SL, Beavers DP, et al. Effect of High-Intensity Strength Training on Knee Pain and Knee Joint Compressive Forces Among Adults With Knee Osteoarthritis: The START Randomized Clinical Trial. JAMA. 2021 02 16;325(7):646-57. doi: https://dx.doi.org/10.1001/jama.2021.0411. PMID: 33591346.

18. Michalsen A, Jeitler M, Kessler CS, et al. Yoga, Eurythmy Therapy and Standard Physiotherapy (YES-Trial) for Patients With Chronic Non-specific Low Back Pain: A Three-Armed Randomized Controlled Trial. Journal of Pain. 2021 Apr 20;20:20. doi: https://dx.doi.org/10.1016/j.jpain.2021.03.154. PMID: 33892154.

19. Munukka M, Waller B, Hakkinen A, et al. Effects of progressive aquatic resistance training on symptoms and quality of life in women with knee osteoarthritis: A secondary analysis. Scandinavian Journal of Medicine & Science in Sports. 2020 Jun;30(6):1064-72. doi: https://dx.doi.org/10.1111/sms.13630. PMID: 31999876.

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25. Roseen EJ, Gerlovin H, Femia A, et al. Yoga, Physical Therapy, and Back Pain Education for Sleep Quality in Low-Income Racially Diverse Adults with Chronic Low Back Pain: a Secondary Analysis of a Randomized Controlled Trial. Journal of General Internal Medicine. 2020 01;35(1):167-76. doi: https://dx.doi.org/10.1007/s11606-019-05329-4. PMID: 31667747.

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27. Thomas JS, Clark BC, Russ DW, et al. Effect of Spinal Manipulative and Mobilization Therapies in Young Adults With Mild to Moderate Chronic Low Back Pain: A Randomized Clinical Trial. JAMA Network Open. 2020 08 03;3(8):e2012589. doi: https://dx.doi.org/10.1001/jamanetworkopen.2020.12589. PMID: 32756930.

28. Xiao CM, Li JJ, Kang Y, et al. Follow-up of a Wuqinxi exercise at home programme to reduce pain and improve function for knee osteoarthritis in older people: a randomised controlled trial. Age & Ageing. 2021 02 26;50(2):570-5. doi: https://dx.doi.org/10.1093/ageing/afaa179. PMID: 32931545.

29. Yaksi E, Ketenci A, Baslo MB, et al. Does transcutaneous electrical nerve stimulation affect pain, neuropathic pain, and sympathetic skin responses in the treatment of chronic low back pain? A randomized, placebo-controlled study. The Korean journal of pain. 2021 Apr 01;34(2):217-28. doi: https://dx.doi.org/10.3344/kjp.2021.34.2.217. PMID: 33785674.

Appendix D. Evidence Tables

Shown in associated Excel files at https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research. Since Surveillance Report 2 identified no new studies, they are the same files as for Surveillance Report 1.

Appendix E. Quality Assessment

Shown in associated Excel files at https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research. Since Surveillance Report 2 identified no new studies, they are the same files as for Surveillance Report 1.

Appendix F. Excluded Studies List

1. Anan T, Kajiki S, Oka H, et al. Effects of an Artificial Intelligence-Assisted Health Program on Workers With Neck/Shoulder Pain/Stiffness and Low Back Pain: Randomized Controlled Trial. JMIR MHealth and UHealth. 2021 09 24;9(9):e27535. doi: https://dx.doi.org/10.2196/27535. PMID: 34559054. **Exclusion:** Ineligible population
2. Areerak K, Waongenngarm P, Janwantanakul P. Factors associated with exercise adherence to prevent or treat neck and low back pain: A systematic review. Musculoskeletal Science & Practice. 2021 04;52:102333. doi: https://dx.doi.org/10.1016/j.msksp.2021.102333. PMID: 33529988. **Exclusion:** Systematic Review used as source document
3. Avellanet M, Boada-Pladellorens A, Pages E, et al. A Comparative Study of a Novel Postural Garment Versus Exercise for Women with Nonspecific Cervical Pain: A Randomized Cross-over Trial. Spine. 2021 Nov 15;46(22):1517-24. doi: https://dx.doi.org/10.1097/BRS.0000000000004123. PMID: 34292213. **Exclusion:** Ineligible population
4. Bakken AG, Eklund A, Warnqvist A, et al. The effect of two weeks of spinal manipulative therapy and home stretching exercises on pain and disability in patients with persistent or recurrent neck pain; a randomized controlled trial. BMC Musculoskeletal Disorders. 2021 Oct 27;22(1):903. doi: https://dx.doi.org/10.1186/s12891-021-04772-x. PMID: 34706706. **Exclusion:** Inadequate duration of followup
5. Boonruab J, Poonsuk P, Damjuti W, et al. Myofascial Pain Syndrome Focused on the Upper Trapezius Muscle: A Comparative Randomized Controlled Trial of the Court-Type Traditional Thai Massage versus the Thai Hermit. Journal of Evidence-based Integrative Medicine. 2021 Jan-Dec;26:2515690X211030852. doi: https://dx.doi.org/10.1177/2515690X211030852. PMID: 34293959. **Exclusion:** Inadequate duration of followup
6. Bruck K, Jacobi K, Schmidt T. Fascial treatment versus manual therapy (HVLA) in patients with chronic neck pain: A randomized controlled trial. Journal of Back & Musculoskeletal Rehabilitation. 2021;34(6):997-1006. doi: https://dx.doi.org/10.3233/BMR-191731. PMID: 34092587. **Exclusion:** Inadequate duration of followup
7. Cho J, Lee E, Lee S. Upper cervical and upper thoracic spine mobilization versus deep cervical flexors exercise in individuals with forward head posture: a randomized clinical trial investigating their effectiveness. Journal of back and musculoskeletal rehabilitation. 2019;32(4):595-602. PMID: CN-01977722. **Exclusion:** Inadequate duration of followup
8. Dailey DL, Vance CGT, Rakel BA, et al. Transcutaneous Electrical Nerve Stimulation Reduces Movement-Evoked Pain and Fatigue: a Randomized, Controlled Trial. Arthritis & rheumatology (hoboken, N.J.). 2020;72(5):824-36. PMID: CN-02006043. **Exclusion:** Inadequate duration of followup
9. Dantas LO, Osani MC, Bannuru RR. Therapeutic ultrasound for knee osteoarthritis: A systematic review and meta-analysis with grade quality assessment. Brazilian Journal of Physical Therapy. 2021 Nov-Dec;25(6):688-97. doi: https://dx.doi.org/10.1016/j.bjpt.2021.07.003. PMID: 34535411. **Exclusion:** Systematic Review used as source document
10. Duarte N, Santos C, Hughes SL, et al. Feasibility and impact of Fit & Strong! Program in Portuguese older adults with osteoarthritis: a pilot randomized controlled trial. Geriatric nursing (New York, N.Y.). 2020;41(6):804-11. PMID: CN-02139995. **Exclusion:** Ineligible population
11. Hayden JA, Ellis J, Ogilvie R, et al. Exercise therapy for chronic low back pain. Cochrane Database of Systematic Reviews. 2021 09 28;9:CD009790. doi: https://dx.doi.org/10.1002/14651858.CD009790.pub2. PMID: 34580864. **Exclusion:** Systematic Review used as source document

12. Ibanez-Vera AJ, Garcia-Romero JC, Alvero-Cruz JR, et al. Effects of Monopolar Dielectric Radiofrequency Signals on the Symptoms of Fibromyalgia: a Single-Blind Randomized Controlled Trial. International journal of environmental research and public health. 2020;17(7) PMID: CN-02098575. **Exclusion:** Inadequate duration of followup

13. Kroll LS, Callesen HE, Carlsen LN, et al. Manual joint mobilisation techniques, supervised physical activity, psychological treatment, acupuncture and patient education for patients with tension-type headache. A systematic review and meta-analysis. Journal of Headache & Pain. 2021 Aug 21;22(1):96. doi: https://dx.doi.org/10.1186/s10194-021-01298-4. PMID: 34418953. **Exclusion:** Systematic Review used as source document

14. Kwon SH, Chung EJ, Lee J, et al. The Effect of Hamstring Relaxation Program on Headache, Pressure Pain Threshold, and Range of Motion in Patients with Tension Headache: A Randomized Controlled Trial. International Journal of Environmental Research & Public Health [Electronic Resource]. 2021 09 27;18(19):27. doi: https://dx.doi.org/10.3390/ijerph181910137. PMID: 34639438. **Exclusion:** Inadequate duration of followup

15. Lilje S, Eklund A, Wykman A, et al. Naprapathy versus orthopaedic standard care for common musculoskeletal disorders: an 8-year follow-up of a pragmatic randomized controlled trial in Sweden. Chiropractic & manual therapies. 2021 11 02;29(1):43. doi: https://dx.doi.org/10.1186/s12998-021-00400-6. PMID: 34727936. **Exclusion:** Ineligible population

16. Moller F, Ortiz-Munoz L, Irarrazaval S. Offloader knee braces for knee osteoarthritis. Medwave. 2021 Apr 28;21(3):e8115. doi: https://dx.doi.org/10.5867/medwave.2021.03.8114. PMID: 34038401. **Exclusion:** Systematic Review used as source document

17. Nelligan RK, Hinman RS, McManus F, et al. Moderators of the Effect of a Self-directed Digitally Delivered Exercise Program for People With Knee Osteoarthritis: Exploratory Analysis of a Randomized Controlled Trial. Journal of Medical Internet Research. 2021 10 29;23(10):e30768. doi: https://dx.doi.org/10.2196/30768. PMID: 34714252. **Exclusion:** Ineligible intervention

18. Samami E, Shahhosseini Z, Elyasi F. The Effect of Psychological Interventions on the Quality of Life in Women with Fibromyalgia: A Systematic Review. Journal of Clinical Psychology in Medical Settings. 2021 09;28(3):503-17. doi: https://dx.doi.org/10.1007/s10880-021-09794-0. PMID: 34216335. **Exclusion:** Systematic Review used as source document

19. Serrat M, Coll-Omana M, Albajes K, et al. Efficacy of the FIBROWALK Multicomponent Program Moved to a Virtual Setting for Patients with Fibromyalgia during the COVID-19 Pandemic: A Proof-of-Concept RCT Performed Alongside the State of Alarm in Spain. International Journal of Environmental Research & Public Health [Electronic Resource]. 2021 09 30;18(19):30. doi: https://dx.doi.org/10.3390/ijerph181910300. PMID: 34639600. **Exclusion:** Inadequate duration of followup

20. Susana CT, Maria TML, Pilar DS, et al. Effectiveness of self-applied acupressure for cervical pain of benign origin (EDIDO-CUH): a randomized controlled clinical trial. Acupuncture in Medicine. 2021 Oct;39(5):441-51. doi: https://dx.doi.org/10.1177/0964528420961398. PMID: 33280397. **Exclusion:** Ineligible population

21. Tan JS, Tikoft E, O'Sullivan P, et al. The Relationship Between Changes in Movement and Activity Limitation or Pain in People With Knee Osteoarthritis: A Systematic Review. Journal of Orthopaedic & Sports Physical Therapy. 2021 Oct;51(10):492-502. doi: https://dx.doi.org/10.2519/jospt.2021.10418. PMID: 34592828. **Exclusion:** Systematic Review used as source document

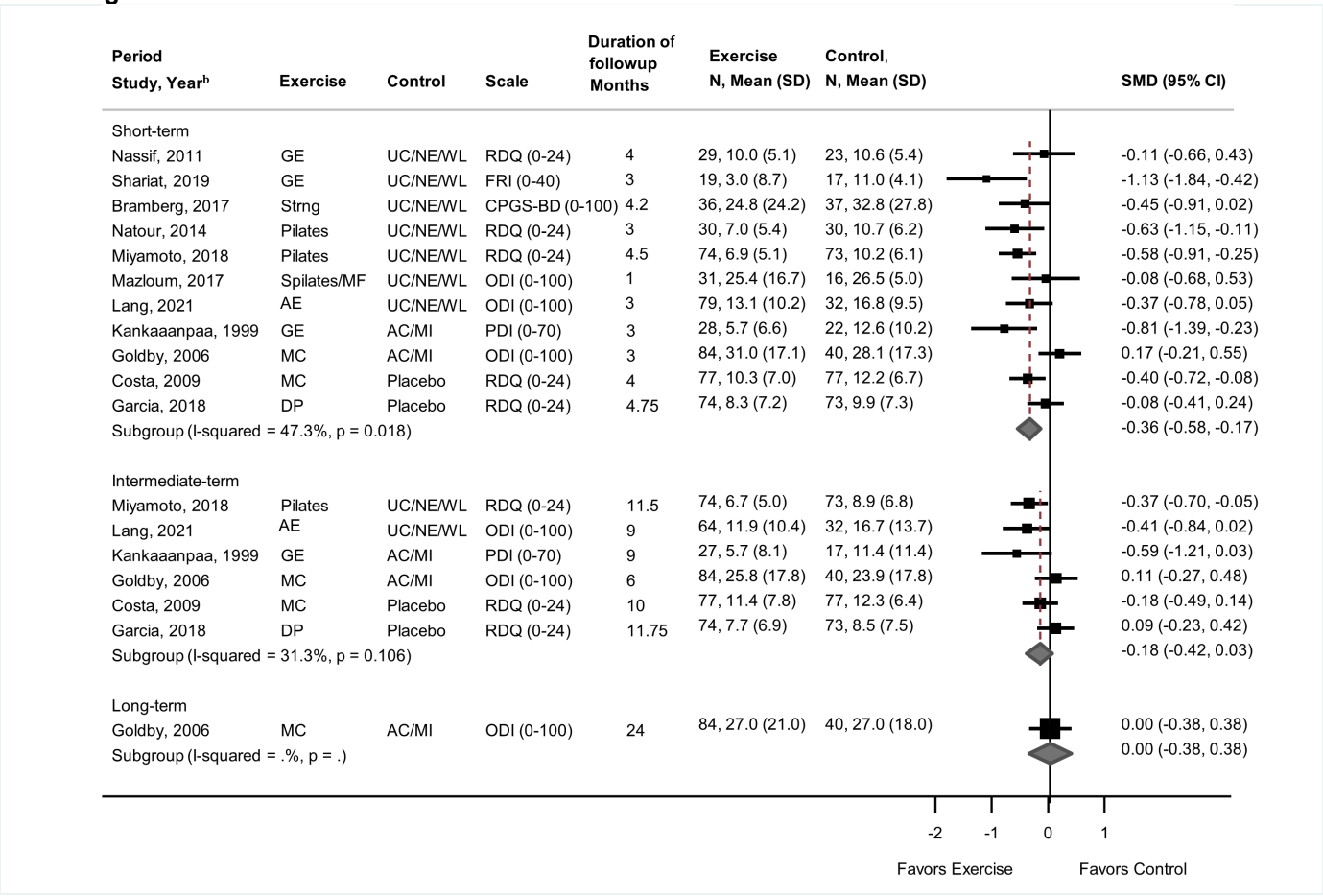
22. Ughreja RA, Venkatesan P, Balebail Gopalakrishna D, et al. Effectiveness of myofascial release on pain, sleep, and quality of life in patients with fibromyalgia syndrome: A systematic review. Complementary Therapies in Clinical Practice. 2021 Nov;45:101477. doi: https://dx.doi.org/10.1016/j.ctcp.2021.101477. PMID: 34507243. **Exclusion:** Systematic Review used as source document

23. Vasiliou VS, Karademas EC, Christou Y, et al. Acceptance and Commitment Therapy for Primary Headache Sufferers: A Randomized Controlled Trial of Efficacy. Journal of Pain. 2021 02;22(2):143-60. doi: https://dx.doi.org/10.1016/j.jpain.2020.06.006. PMID: 32682815. **Exclusion:** Ineligible population

24. Wang S, Chan PPK, Lam BMF, et al. Sensor-Based Gait Retraining Lowers Knee Adduction Moment and Improves Symptoms in Patients with Knee Osteoarthritis: a Randomized Controlled Trial. Sensors. 2021;21(16) PMID: CN-02306300 NEW. **Exclusion:** Inadequate duration of followup

Appendix G. Updated or New Meta-Analyses From Surveillance Report 1

Figure G-1. Exercise versus usual care, an attention control, or a placebo intervention for chronic low back pain: effects on function, excluding outlier trial[a]

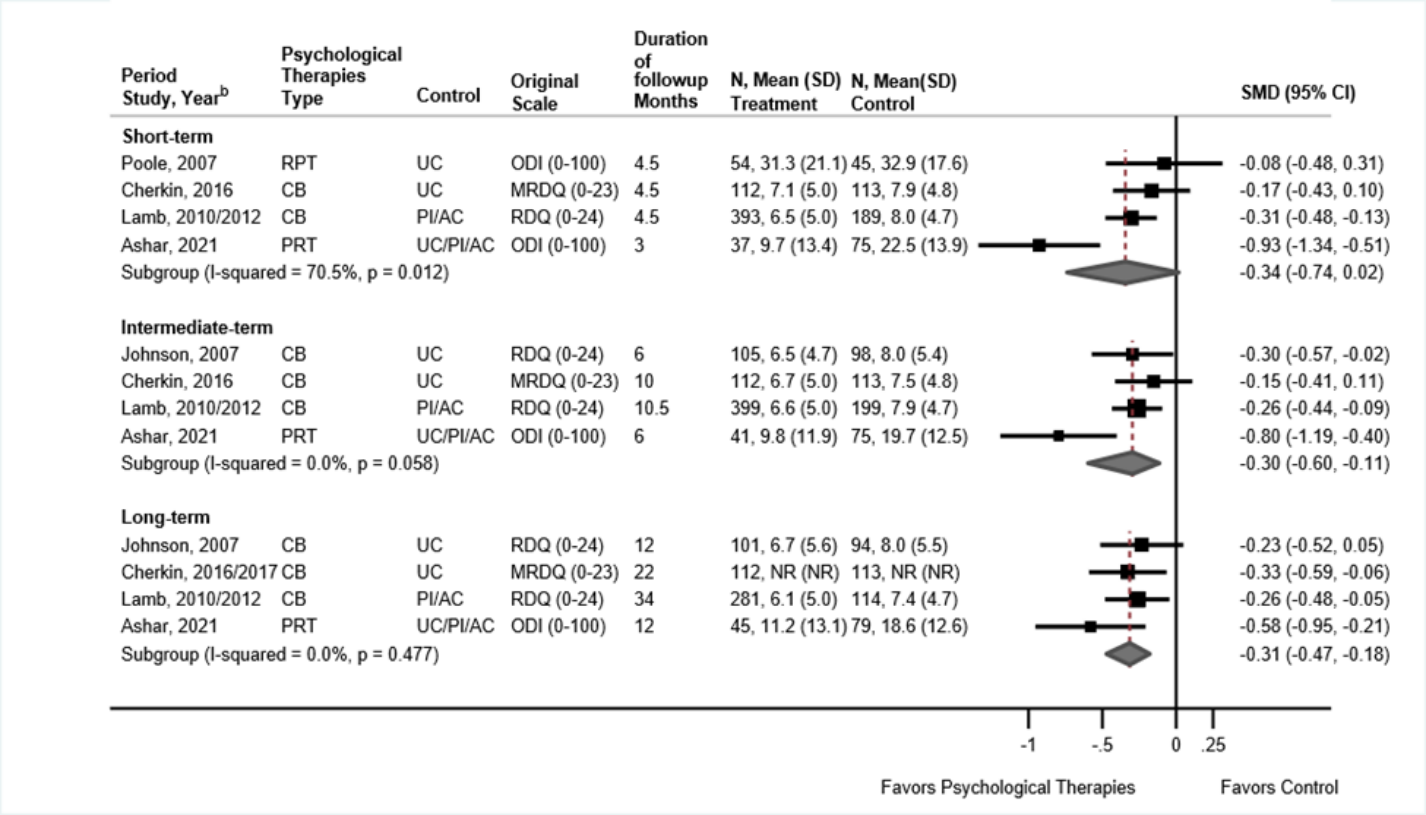


AC = attention control; AE = aerobic exercise (walking); CI = confidence interval; CPGS –BD =Von Korff Chronic Pain Grade Score Back Disability; DP = directional preference; GE= general exercise; MC = motor control; MF = mobility/flexibility; MI = minimal intervention; N = number; NE = no exercise; NM = neuromuscular re-education; ODI = Oswestry Disability Index; PDI = Pain Disability Index; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; Spilates = selective Pilates; Strng=Strength training; UC = usual care; WL = waitlist

[a] Areeudomwong 2017, included in prior report.

[b] New trials: Shariat 2019, Lang 2021

Figure G-2. Psychological therapy versus usual care or an attention control for chronic low back pain: effects on function, excluding outlier trial[a]

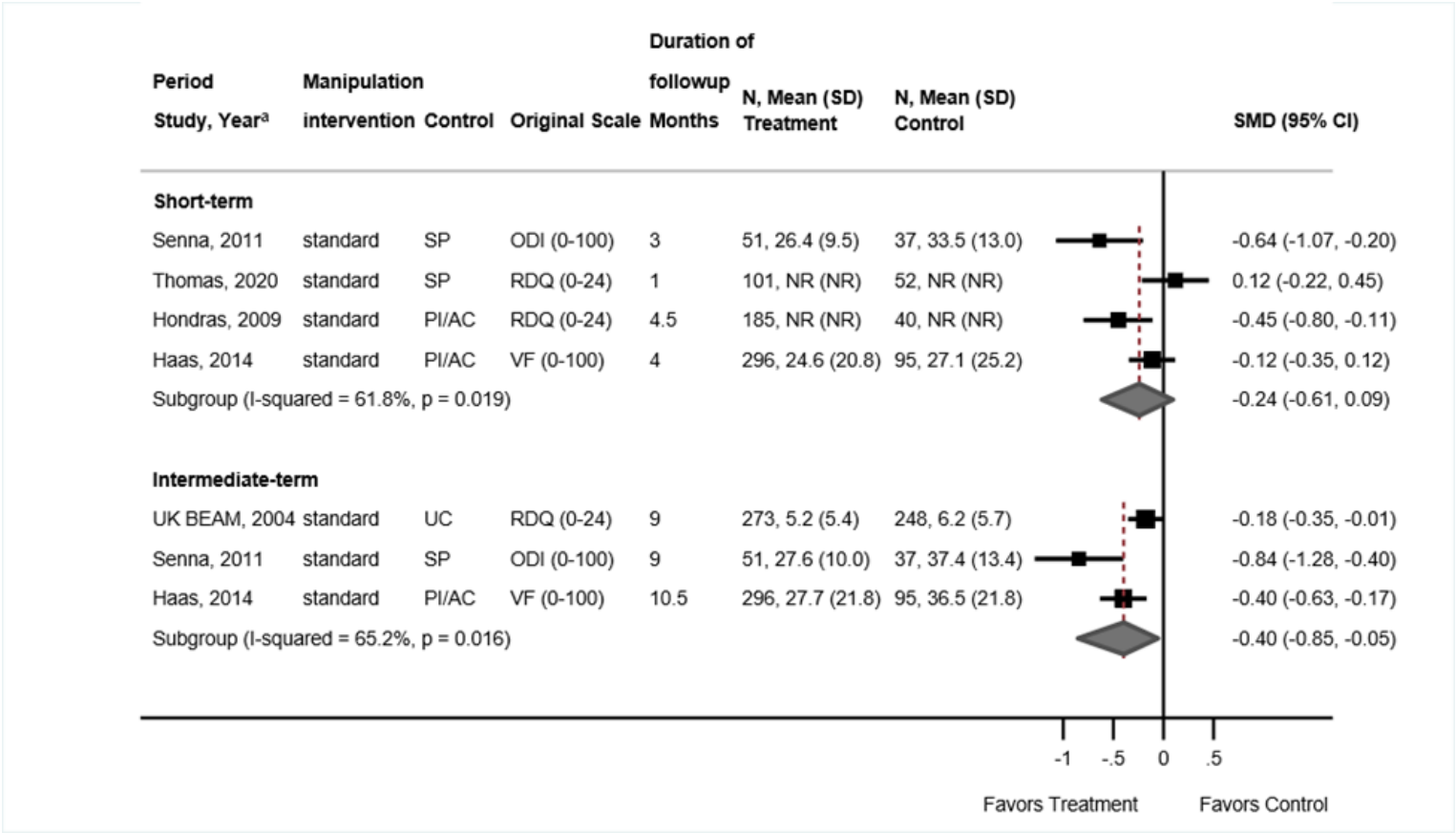


AC = attention control; CB = cognitive-behavioral therapy; CI = confidence interval; MRDQ = Modified Roland-Morris Disability Questionnaire; N = number; ODI = Oswestry Disability Index; PI = placebo intervention; PRT = pain reprocessing therapy; RDQ = Roland-Morris Disability Questionnaire; RPT = respondent therapy (progressive relaxation); SD = standard deviation; SMD = standardized mean difference; UC = usual care

[a] Shariat 2019, new trial.

[b] New trial: Ashar 2021

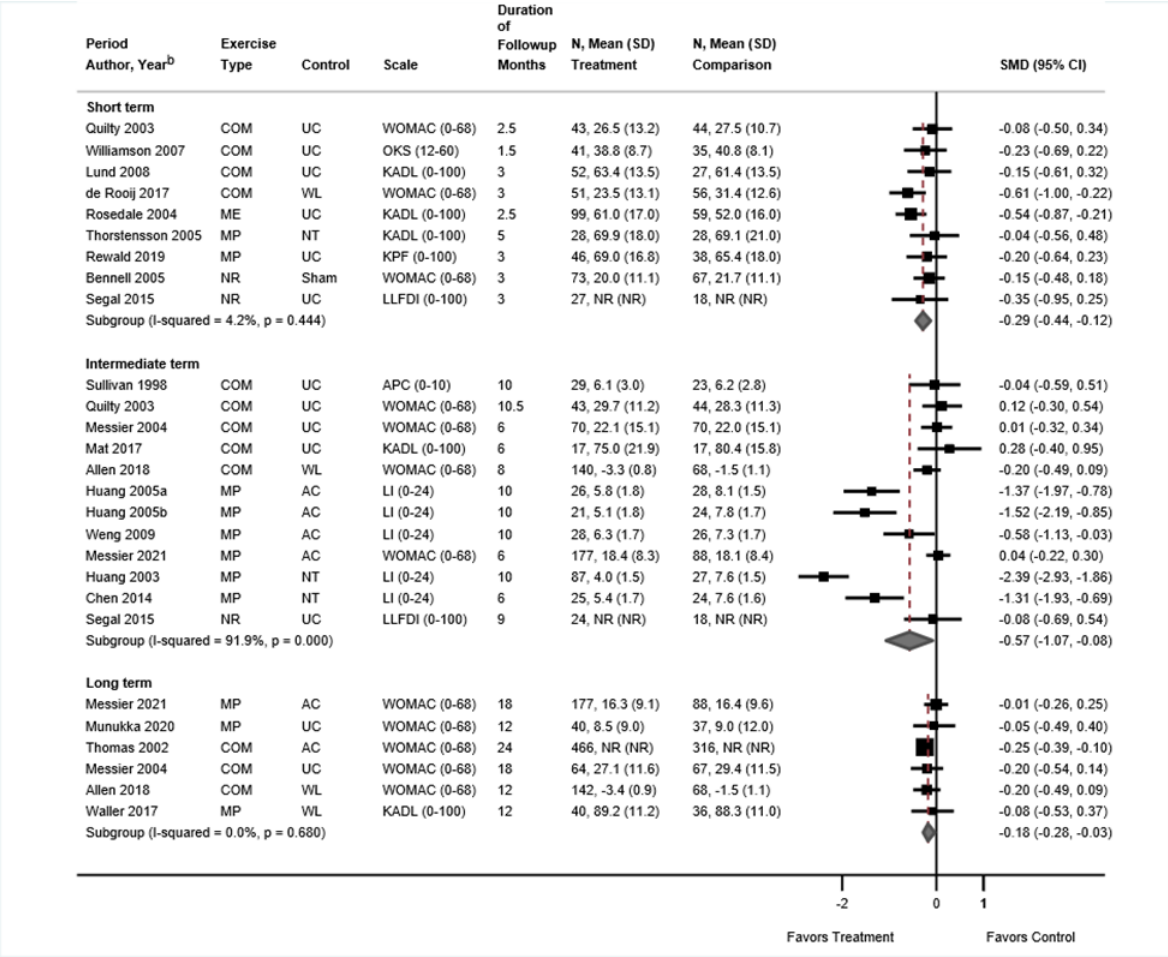
Figure G-3. Spinal manipulation versus sham manipulation, usual care, an attention control, or a placebo intervention for chronic low back pain: effects on function



AC = attention control; CI = confidence interval; N = number; ODI = Oswestry Disability Index; PI = placebo intervention; RDQ = Roland-Morris Disability Questionnaire; SD = standard deviation; SMD = standardized mean difference; SP= sham manipulation; UC = usual care; UK BEAM = UK Back pain exercise and manipulation trial; VF = Von Korff functional disability

[a] New trial: Thomas 2020

Figure G-4. Exercise versus usual care, no treatment, sham, or an attention control for osteoarthritis knee pain: effects on function, excluding outlier trial[a]

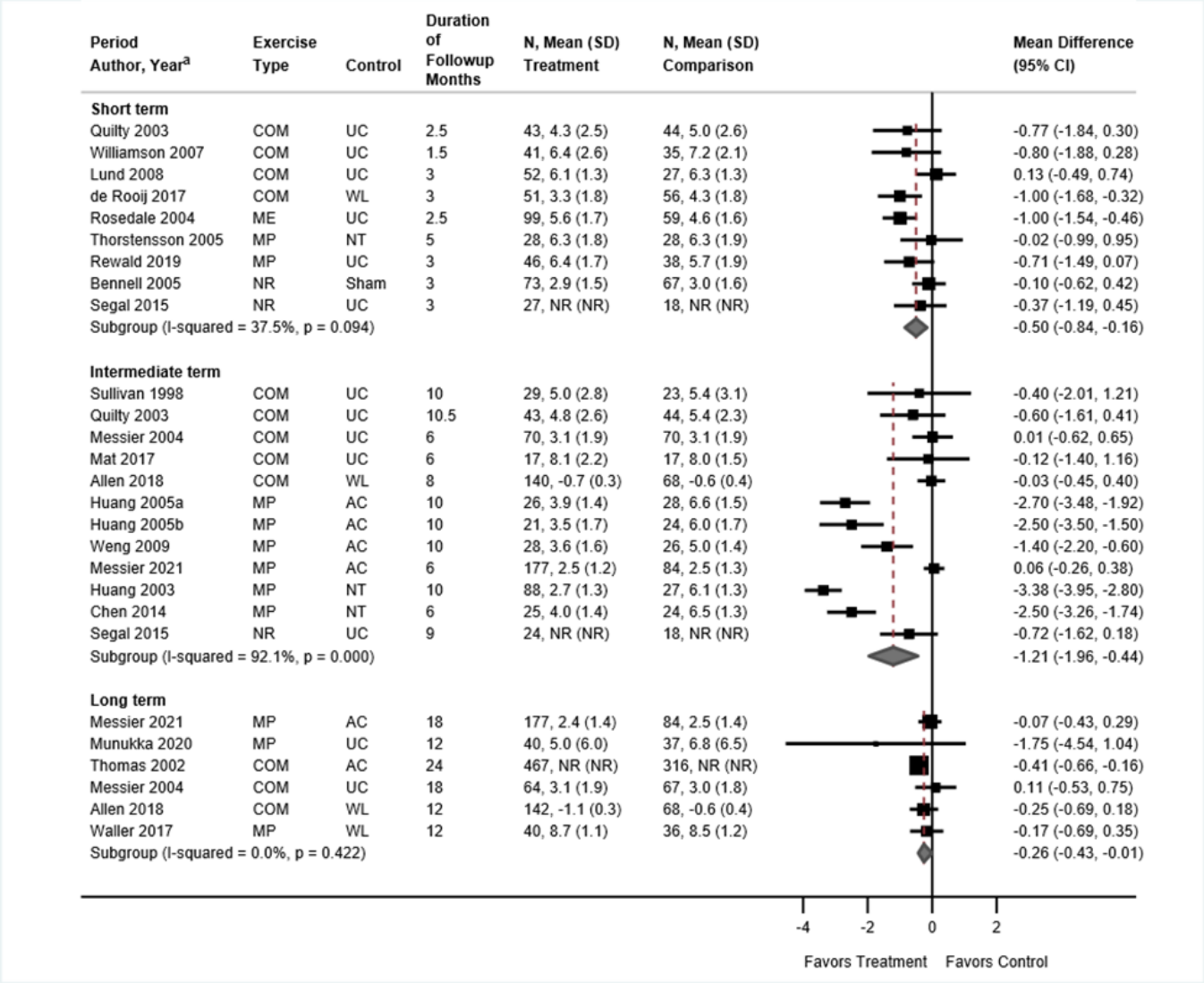


AC = attention control; APC = Arthritis Impact Measurement Scale (AIMS) physical activity component; CI = confidence interval; COM = combination exercise therapy; KADL = Knee Injury and Osteoarthritis Outcome Score (KOOS) ADL subscore; LI = Lequesne Index; LLFDI = Late Life Function and Disability Index Basic Lower Limb Function Score; ME = mobility exercise; MP = muscle performance exercise; NR = neuromuscular reeducation exercise; NT = no treatment; OKS = Oxford Knee Score; SD = standard deviation; SMD = standardized mean difference; UC = usual care; WOMAC = Western Ontario and McMaster's Universities Osteoarthritis Index

[a] Dias 2003, included in prior report.

[b] New trials: Messier 2021, Munukka 2020 and Rewald 2019.

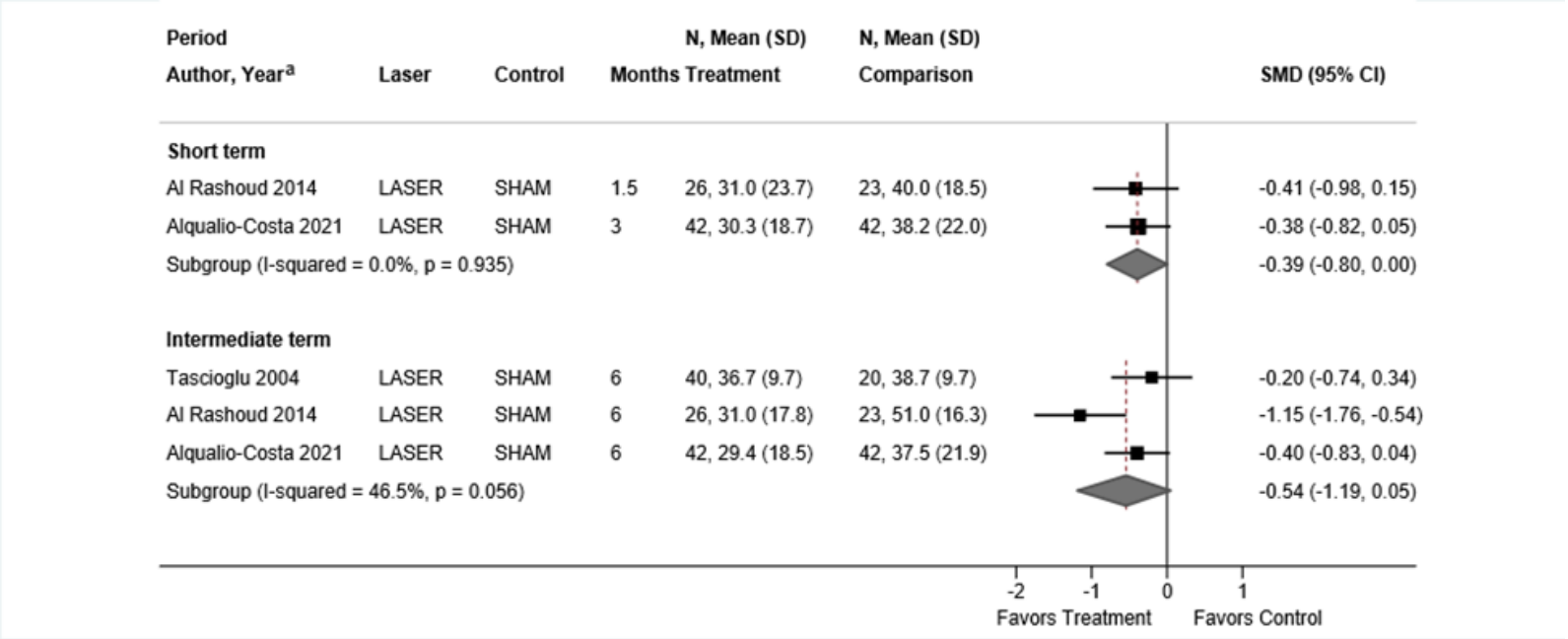
Figure G-5. Exercise versus usual care, no treatment, sham, or an attention control for osteoarthritis knee pain: effects on pain



AC = attention control; CI = confidence interval; COM = combination exercise therapy; ME = mobility exercise; MP = muscle performance exercise; NR = neuromuscular re-education exercise; NT = no treatment; SD = standard deviation; SMD = standardized mean difference; UC = usual care

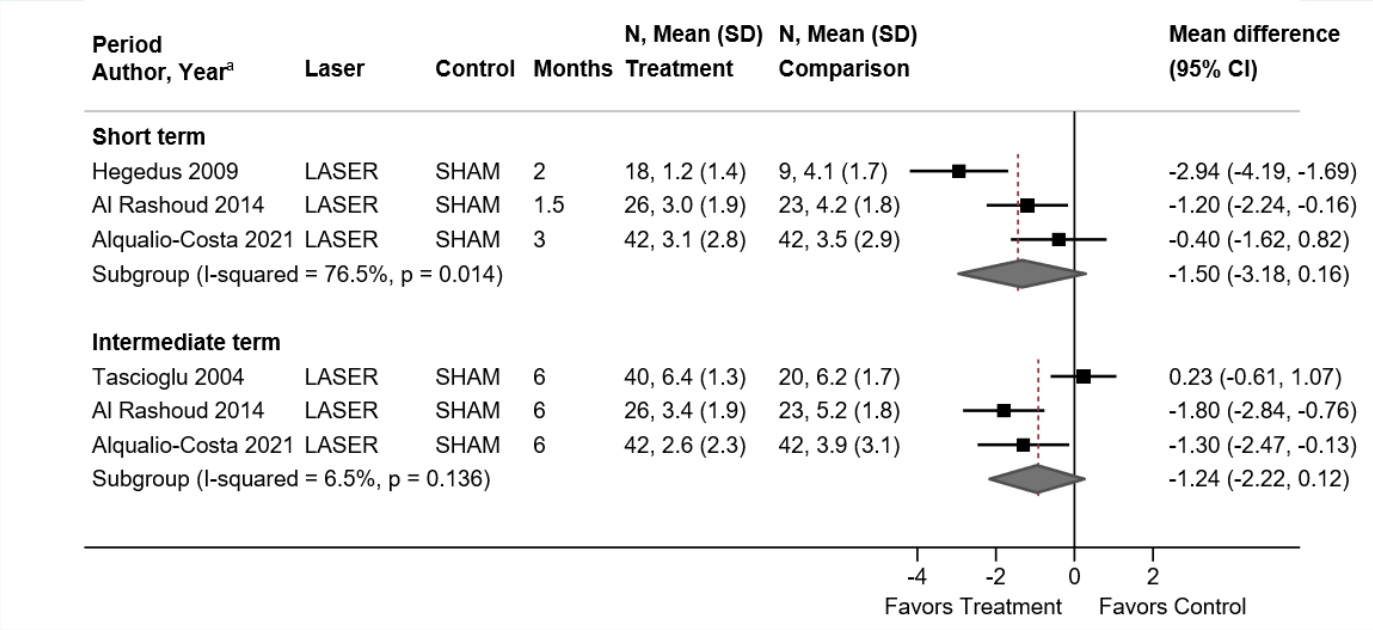
[a] New trials: Messier 2021, Munukka 2020 and Rewald 2019.

Figure G-6. Low-level laser therapy versus usual care or sham for osteoarthritis knee pain: effects on function (new meta-analysis)



CI = confidence interval; SD = standard deviation; UC = usual care
[a] New trial: Alqualio-Costa 2021

Figure G-7. Low-level laser therapy versus usual care or sham for osteoarthritis knee pain: effects on pain



CI = confidence interval; SD = standard deviation; UC = usual care
[a] New trial: Alqualio-Costa 2021