Comparative Effectiveness Review
Number 77

Effective Health Care Program

Physical Therapy Interventions for Knee Pain Secondary to Osteoarthritis

Executive Summary

Background

Osteoarthritis (OA), the most common form of arthritis,[1] is a progressive joint disorder characterized by gradual loss of cartilage.[2] Osteoarthritis of the knee afflicts 28 percent of adults over age 45[3] and 37 percent of adults over age 65 in the United States.[4] As a leading cause of disability among noninstitutionalized adults,[4] OA's prevalence, effect on health, and economic consequences are expected to increase dramatically during the next few decades as the population ages.[5]

OA treatments aim to reduce or control pain, improve physical function, prevent disability, and enhance quality of life.[6] Conservative treatment options include pain relievers, anti-inflammatory drugs, weight loss, general physical exercise, and physical therapy.[7,8] Optimal OA management combines pharmacologic treatments with physical therapy interventions[7-10] and, when conservative treatments fail, surgery.[7,8] Surgical treatments for knee OA include realignment osteotomy and knee replacements.[11] In the United States, about 556,400 knee replacement surgeries are performed annually.[11] By 2030, that number is projected to increase by 600 percent.[12]

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at **www.effectivehealthcare.ahrq.gov/reports/final.cfm**.

Comprehensive, up-to-date guidelines are available from the Osteoarthritis Research Society International (OARSI), the American Academy of Orthopedic

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Effective Health Care

Surgeons, and the National Institute for Health and Clinical Excellence. These guidelines recommend exercise (including local muscle strengthening and general aerobic fitness) as a core treatment for symptomatic osteoarthritis, regardless of patient age, comorbidity, pain severity, or disability.[7,8,13] Effectiveness has not been clearly established for other nonpharmacologic physical therapy interventions as adjunct to core treatment (e.g., thermal, manipulation, electrical nerve stimulation, and orthotics).[7]

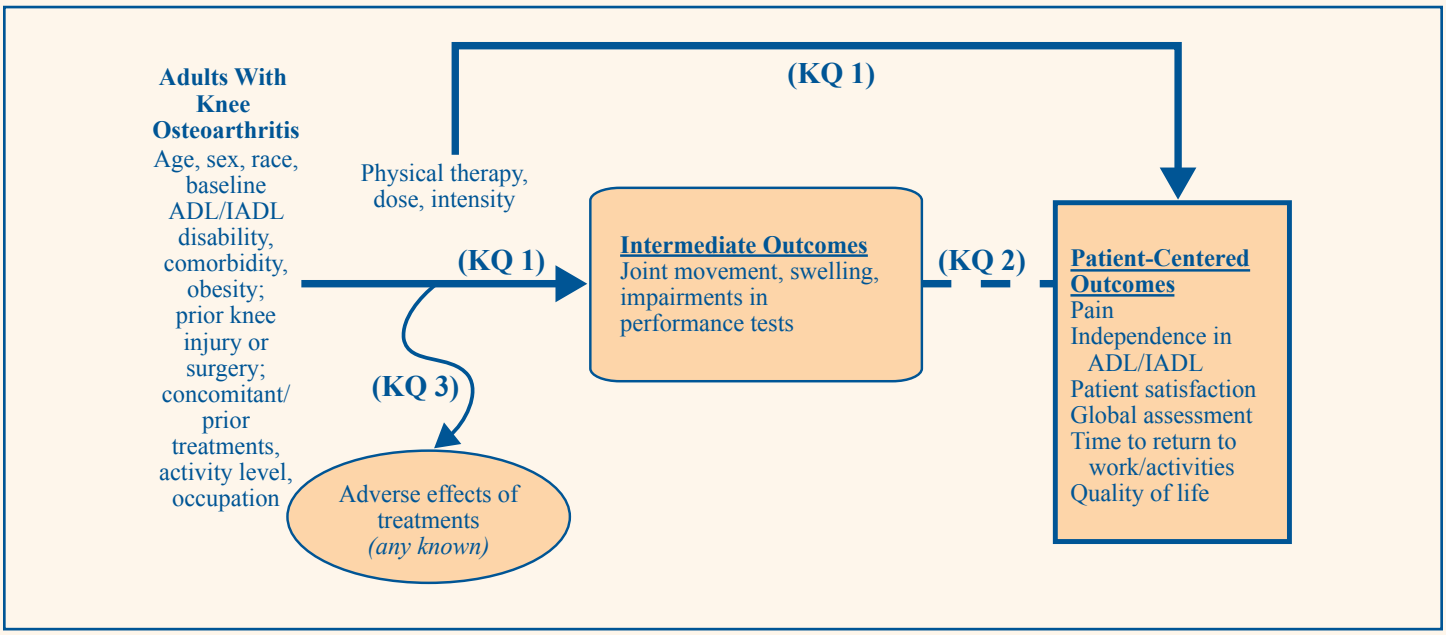
Patient-centered clinical outcomes include functional status, pain, and quality of life.[8] Consumers judge the success of physical therapy interventions by improvement in patient-centered outcomes.[14,15] Some consensus exists that clinical trials for symptomatic knee OA should examine patient-centered clinical outcomes and joint imaging.[16] However, published studies inconsistently define treatment success.[17-20] In practice, physical therapists evaluate treatment success using intermediate outcomes related to function, including instrumental measurements of gait, balance, and range of motion. Likewise, reimbursement is currently driven by functional outcomes, including gait, transfers, and activities of daily living. Yet, we are not certain whether these outcomes predict pain, disability, or quality of life.

This report synthesizes published evidence about the effectiveness of physical therapy for pain secondary to knee OA in adults. We focused on community-dwelling adults in ambulatory care settings and on interventions applicable to physical therapy practice. Our systematic review is intended to help clinicians, consumers, and policymakers make informed decisions based on synthesized evidence and other relevant factors.

Input From Stakeholders

We developed our Key Questions with stakeholder input as part of the Effective Health Care Program. We developed an analytic framework (Figure A) after discussions with key informants. Research questions were posted for public comment. Key informants recommended that we focus on patient-centered outcomes and physical therapy interventions relevant for clinical practice in the United States. Key informants also recommended that we review the intermediate outcomes with which physical therapists judge treatment success. Candidates to serve as Key Informants, technical experts, and Peer Reviewers were approved by the Task Order Officer from the Agency for Healthcare Research and Quality (AHRQ) after disclosure of conflicts of interest. We developed the protocol following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[21] (www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=637&pageaction=displayproduct), with input from members of the Technical Expert Panel (TEP).

Figure A. Analytic framework



ADL = activities of daily living; IADL = instrumental activities of daily living; KQ = Key Question

Objectives

For the topic of physical therapy interventions for adults with knee OA, our goal was to conduct (1) a comprehensive review of the literature about the association between intermediate and patient-centered outcomes and (2) a comprehensive synthesis of evidence of the clinical efficacy and comparative effectiveness of the interventions. We followed the principles from the Methods Guide for Effectiveness and Comparative Effectiveness Reviews from AHRQ (http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=318). We examined the following questions:

Key Question 1. What are the effectiveness and comparative effectiveness of available physical therapy interventions (without drug treatment) for adult patients with chronic knee pain due to OA on intermediate and patient-centered outcomes when compared to no active treatment or another active physical therapy modality?

a. Which patient characteristics are associated with the benefits of examined interventions of physical therapy on intermediate and patient-centered outcomes?

b. Do changes in intermediate and patient-centered outcomes differ by the dose, duration, intensity, and frequency of examined interventions of physical therapy?

c. Do changes in intermediate and patient-centered outcomes differ by the time of followup?

Key Question 2. What is the association between changes in intermediate outcomes with changes in patient-centered outcomes after physical therapy interventions?

a. What is the validity of the tests and measures used to determine intermediate outcomes of physical therapy on knee OA in association with patient-centered outcomes?

b. Which intermediate outcomes meet the criteria of surrogates for patient-centered outcomes?

c. What are the minimum clinically important differences of the tests and measures used to determine intermediate outcomes?

Key Question 3. What are the harms from physical therapy interventions available for adult patients with chronic knee pain due to osteoarthritis when compared to no active treatment or active controls?

a. Which patient characteristics are associated with the harms of examined physical therapy interventions?

b. Do harms differ by the duration of the treatment and time of followup?

Methods

Data Sources

We sought studies from a wide variety of sources, including MEDLINE® via OVID and PubMed®, the Cochrane Library, the Physiotherapy Evidence Database (PEDro), SCIRUS, Allied and Complementary Medicine (AMED), and the Health and Psychosocial Instruments bibliography database up to February 29, 2012. We conducted manual searches of reference lists from systematic reviews and eligible studies. The grey literature search included regulatory documents, conducted clinical trials, and abstracts presented in scientific meetings.

Study Selection

At least two investigators independently evaluated each study for eligibility. Disagreements were resolved by consensus. We defined the target population, eligible independent and dependent variables, outcomes, time, and setting following the PICOTS (Population, Intervention, Comparator, Outcomes, Timing, and Settings) framework developed in the protocol. We included original studies of adults with knee OA published in English after 1970. Eligible trials enrolled community-dwelling adults with knee OA and reported pain as an inclusion criterion and/or outcome. Eligible interventions fell within the scope of physical therapy practice, whether or not the articles clearly described the involvement of physical therapists or physical therapist assistants in a given study.[22] For analyses of efficacy, eligible comparators included sham stimulation, usual care, and no active treatment; for comparative effectiveness, eligible comparators were physical therapy interventions. Eligible patient-centered outcomes included knee pain, disability, quality of life, perceived health status, and global assessments of treatment effectiveness. Eligible intermediate outcomes

included composite function, joint function, gait function, strength, and transfers.

To minimize risk of bias and to obtain valid estimates of physical therapy benefits and harms, we focused on randomized controlled trials (RCTs). While randomization may distribute the effects of other treatments equally, their efficacy must still be taken into account. Moreover, some nonphysical therapy treatments, such as pain relievers, may in part mask the benefits of physical therapy, especially for pain. We also reviewed observational studies with multivariate adjustment for concomitant treatments and confounding factors.[23,24] We defined physical therapy and selected the interventions and methods to assess the outcomes in accordance with "Practice Pattern 4E: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Localized Inflammation" from the Guide to Physical Therapist Practice.[22]

For Key Question 2, we included any observational studies that reported the association between intermediate and patient-centered outcomes.

We defined the target population as community-dwelling adults with knee pain secondary to knee OA. We excluded studies involving children, adolescents, hospitalized patients, or patients in long-term care facilities; studies that included patients with knee or hip OA that did not separately report the outcomes in patients with knee OA; and studies that aimed to examine surgical or pharmacologic treatments for knee OA. We also excluded studies that examined physical therapy delivered via rehabilitation programs for adults with knee OA who had undergone knee arthroplasty within 6 months before the study. For Key Question 2, we did not review validation of tests in populations with diseases other than knee OA.

We defined harms as a totality of all possible adverse consequences of an intervention.[25] We included published and unpublished evidence of adverse effects with eligible interventions, regardless of how authors perceived causality of treatments.[25] We did not contact the primary investigators for further information or clarification about the methodology or results of the trials.

Data Extraction

We used standardized forms to extract data. We conducted a double independent quality control for the data extracted from RCTs. One reviewer abstracted an article and a second reviewer checked the data for accuracy. We abstracted minimum datasets for therapeutic studies. For categorical variables, we abstracted the number of events among treatment groups. We abstracted means and standard deviations of continuous variables. For RCTs, we abstracted the number randomized to each treatment group. We abstracted the time when the outcomes were assessed as weeks from randomization and the time of followup after treatments; we categorized followups as less than 6 weeks, 6 to 13 weeks, 14 to 26 weeks, or more than 26 weeks. For observational studies, we extracted relative measures of the association (relative risk, hazard ratio, odds ratio) with standard error or 95% confidence interval (CI), and reported adjustments for patient characteristics.

For the studies about the association between intermediate and patient-centered outcomes for Key Question 2, we abstracted the number of positive (true and false) and negative (true and false) with index diagnostic tests when compared with the reference standard.

We abstracted baseline patient characteristics, including eligible and mean age; mean body mass index; proportion of women and minorities; proportion with disability; proportions with severe knee OA, comorbidities, and multijoint OA; baseline physical activity level; occupation; and concomitant drug and physical therapy interventions. We abstracted settings and physical therapist supervision of the treatments. We abstracted type, dose, length, and intensity of physical therapy interventions when reported by the authors.

Risk of Bias Assessment and Strength of Evidence

Using a modified Cochrane risk of bias tool,[26] we evaluated risk of bias in individual studies according to their designs We evaluated random allocation of the subjects to treatment groups, adequacy of randomization and allocation concealment, masking of the treatment status for the outcome assessment, and intention-to-treat principles. We examined sponsorship and conflict of interest but did not increase risk of bias by using this information.

We defined RCTs as having medium risk of bias if one criterion was not met and high risk of bias if two or more criteria were not met.

We evaluated diagnostic studies for Key Question 2 using criteria from the Quality Assessment of Diagnostic Accuracy Studies.[27]

We assessed strength of evidence from therapeutic studies for each major outcome according to risk of bias, consistency, directness, and precision.[28] We focused on direct evidence from head-to-head RCTs. We downgraded strength of evidence if: (1) risk of bias was moderate or

high; (2) heterogeneity was statistically significant; or (3) estimates were inconsistent or imprecise. We defined treatment effect estimates as precise when pooled estimates had reasonably narrow 95% CIs and pooled sample size was greater than 400. When appropriate, we included strength of association[28] and upgraded the strength of evidence if the standardized effect size was more than 0.8. We defined strength of evidence as low when evidence was limited to an individual study with low or medium risk of bias, and we defined evidence as insufficient if drawn from single studies with high risk of bias.[28] We judged whether the overall body of available evidence allowed for conclusions that were sufficiently robust and resistant to bias and errors to guide clinical decisionmaking.[26]

We followed the criteria of the United States Preventive Services Task Force in assessing strength of evidence from observational studies that examined the association between patient-centered and intermediate outcomes.[29]

Applicability

We estimated the applicability of the sample by evaluating the selection of adults in observational studies and clinical trials. For each intervention study, we also examined setting (including the involvement of physical therapists or physical therapist assistants) and exclusion criteria.

Data Synthesis and Analysis

We synthesized and presented the evidence according to the classification of physical therapy interventions from the American Physical Therapy Association's (APTA's) Guide to Physical Therapist Practice.[22]

For categorical variables, we calculated rates, relative risk, and absolute risk differences. For continuous variables we calculated mean differences with 95% CI. We also calculated ratios of means that describe percentage differences in pain with active versus control interventions.[30] We calculated estimates by applying intention-to-treat principles. If we found more than one study from a particular trial, we used the results from the latest published papers.

We examined and synthesized evidence of other nonsurgical treatments for knee OA if reported in the studies. We then compared effects of the examined physical therapy interventions across the studies according to reported concomitant drug treatments. We conducted sensitivity and subgroup analyses according to concomitant drug treatments when the available data were suitable for pooling.

Using a standard preplanned algorithm, we explored heterogeneity by characteristics of clinical diversity, including age, sex, race, and baseline activities of daily living (ADL), instrumental activities of daily living (IADL), comorbidity, obesity, and significant skeletal abnormality.[31] We explored heterogeneity by treatment type, dose (when applicable), and duration, as well as by whether the control treatment included education or exercise. We performed subgroup analyses by the involvement of a physical therapist for all outcomes with aerobic or strengthening exercises but not with other interventions that were likely administered by physical therapists. We explored heterogeneity by disclosed conflict of interest[31] and by individual risk of bias criteria of individual studies rather than using a global risk of bias score.[32,33]

We focused on patient-centered outcomes, including pain, disability, and quality of life.[34] We categorized intermediate outcomes as measurements of gait, strength, balance, transfers, endurance, joint function, or composite measure of functional performance. We reviewed validity and reliability of the tests within the scope of physical therapy practice. Evidence of the association between intermediate and patient-centered outcomes of physical therapy interventions was synthesized from observational studies that adjusted for treatments and confounding factors. We synthesized evidence from the studies that reported diagnostic values of intermediate outcomes to predict clinical outcomes. In a separate analysis, we synthesized the evidence of the association between intermediate and clinical outcomes from linear, logistic, or Cox regression models.

Using Meta-analyst[35] and STATA[36] software at a 95% CI, we calculated differences in relative risk and absolute risk from the abstracted events, and we calculated nonstandard mean differences in continuous variables from the reported means and standard deviations. We used correction coefficients, forced intention to treat, and calculations for missing data as recommended by guidelines.[26] Using Cohen's criteria, we defined magnitude of the effect as small, middle, and large, corresponding 0-0.5, 0.5-0.8, and >0.8 standardized mean differences in standard deviation units.[37] Pooling criteria for Key Questions 1 and 3 required that interventions and outcomes be similarly defined.

We categorized eligible physical therapy interventions according to the way in which they were defined and ordered in APTA's Guide to Physical Therapist Practice.[22] To address differences in outcomes measures, we analyzed all eligible RCTs with the recommended standardization method instead of excluding valuable results from eligible

RCTs that used different measures of the outcomes.[38] We calculated standardized mean differences (SMDs) for different measures of the same outcome with Cohen and Hedges methods. We back transformed SMDs to mean differences[38] with several instruments: for disability, we used EQ-5D, a multiattribute, preference-based health status measuring instrument;[39] for quality of life, we used the 36-Item Short-Form Health Survey (SF-36);[40] for pain, we used the Visual Analog Scale (VAS);[41] for composite function, we used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) function score;[42] and for gait function, -we used walking speed.[41] We derived pooled standard deviations of EQ-5D and SF-36 from large population-based studies of noninstitutionalized adults.[39,40-42] We multiplied the SMDs by the among-person standard deviation to yield an estimate of the difference in mean outcome scores (with, versus without, intervention) on EQ-5D (0.38),[39] SF-36 (10.9),[40] VAS (22 in scale of 0 to 100),[41] WOMAC physical function (18.5),[42] and walking speed (0.2 m/s).[41] We categorized treatment effects from the studies by the clinical importance of differences in intermediate outcomes according to definitions of minimum clinically important differences (MCIDs) from published observational studies and evidence-based reports.[43] We categorized the results from each tested hypothesis as nonsignificant differences in continuous outcomes or as statistically significant differences of <20, 20–50, or >50 percent from control interventions.[44]

We tested consistency of the results by comparing the direction and strength of the association[28] and assessed heterogeneity of results using Chi square and I square tests.[45,46] We also explored heterogeneity with meta-regression and sensitivity analysis. Using four followup time categories, we performed meta-analyses based on examined physical therapy modalities and their combinations. We conducted subgroup analyses to examine the association between each component and treatment effect size. We reported the results from random effects models only[47] and chose the random effects model to incorporate in the pooled analysis differences across trials in patient populations, concomitant treatments, and definitions of interventions and outcomes.[31]

We qualitatively synthesized the evidence from poorly reported RCTs and observational studies. For studies that included knee and hip OA, we included the results in pooled analyses if we could isolate knee cases.

For Key Question 2, we summarized results of individual studies in evidence tables to analyze sensitivity, specificity, predictive values, diagnostic odds ratios, and predictive likelihood ratios, with a focus on the latter.[48,49] Ratios of 1 indicated that the tests did not provide a likelihood of accurate diagnosis.[49] Ratios of more than 10 provided large, and often conclusive, increases in the likelihood of an accurate diagnosis.[49]

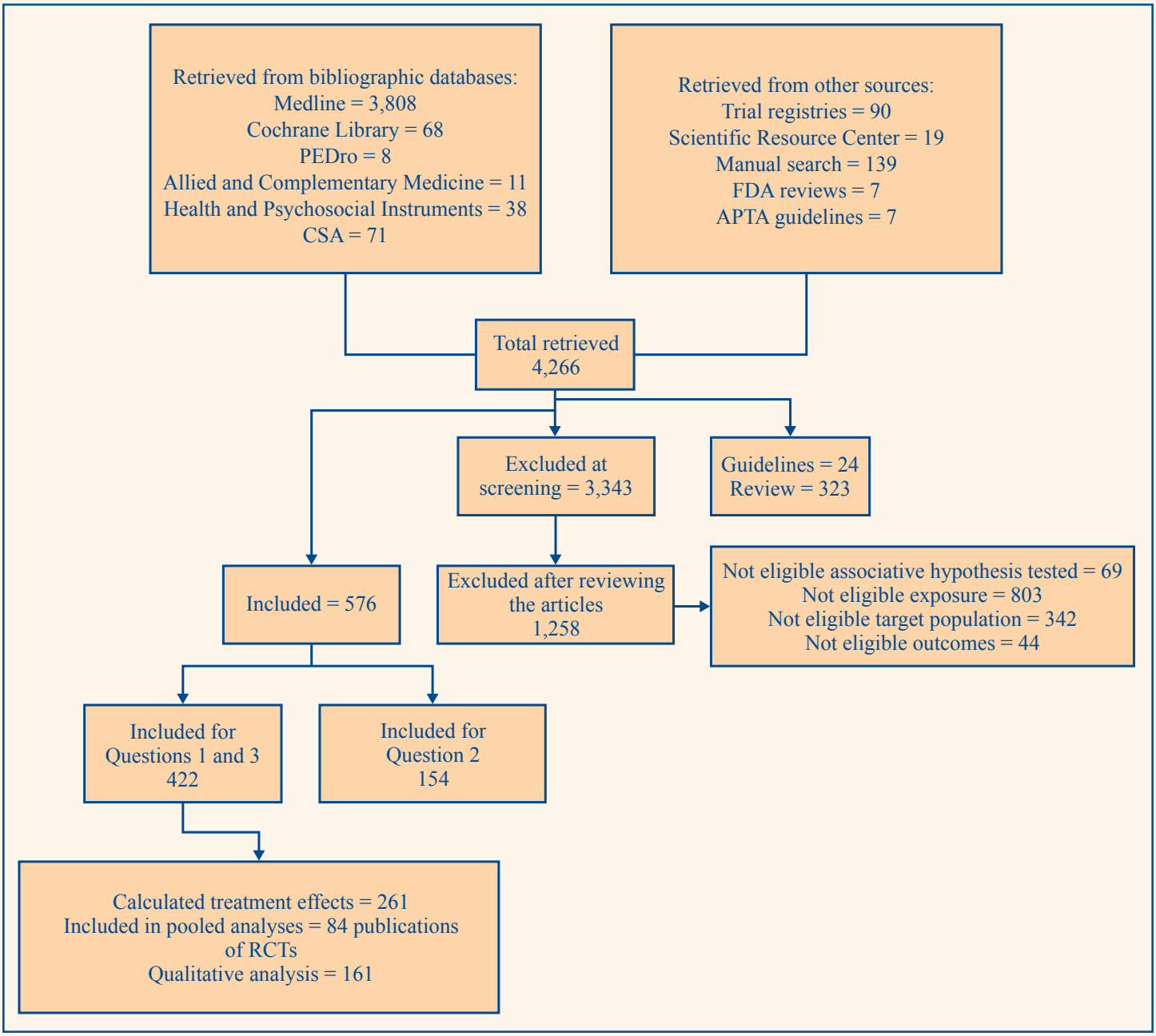
We tabulated each article for results of index diagnostic tests and reference standards. We evaluated validation and the proposed MCIDs in total scores when this information was available. To judge validity from the studies that reported correlation coefficients between index and reference methods, we categorized correlation as follows: weak correlations as <20 percent, medium correlation as 20-50 percent, strong correlation as 50-75 percent, and very strong correlation as >75 percent.[37] To answer the question of which intermediate outcomes met the criteria of surrogates for patient-centered outcomes, we used Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Criteria for Surrogate Endpoints.[44,50] We examined whether randomized trials of physical therapy interventions evaluated the association between intermediate outcome change and patient-centered outcome change.[50]

Results

Of 4,266 identified references, we included 576 references for this review (Figure B). For Key Questions 1 and 3, we synthesized evidence from 422 references. We calculated treatment effect from 261 references including 212 publications of 193 RCTs, and qualitatively analyzed 161 studies. Only 84 RCTs met pooling criteria and were included into meta-analyses. Definitions of physical therapy interventions and outcomes varied dramatically among studies; thus, only a small proportion of comparisons met pooling criteria. We prioritized pooled analyses and results at longest time of followup over nonpooled results and short followups. Most studies lasted 4 to 6 weeks, with a followup of 6 months.

Overall, RCTs had good applicability to our target population because they primarily recruited older adults with knee OA. More than 70 percent of the participants were female. Body mass index (BMI) of participants averaged 29 kg/m^2. In 100 RCTs (52 percent), subjects were taking anti-inflammatory drugs or pain relievers. Half the studies provided no information about exact pharmacologic treatments. Few studies specified that they excluded patients with prior knee surgery, and most did not report participants' occupation, knee injury, comorbidity, or duration of condition, or the proportion of subjects with baseline disability or who had undergone surgery.

Figure B. Study flow



APTA = American Physical Therapy Association; CSA = Cambridge Scientific Abstracts; FDA = U.S. Food and Drug Administration; PEDro = Physiotherapy Evidence Database; RCT = randomized controlled trials

Because the studies used different tools to measure the same outcomes, we used standardization in all pooled analyses. The studies examined continuous measures of the outcomes and rarely categorized the patients according to clinical importance of the changes.

The most common reasons for increased risk of bias were unmasking of the treatment status and no planned intention-to-treat analyses. Most RCTs had medium risk of bias.

Key Questions

Key Question 1. Effectiveness of Physical Therapy Interventions

We found very few statistically significant differences in outcomes between active and control treatments. Tables A and C show how many studies examined each outcome, estimated effect sizes, and our level of confidence that the evidence reflects a true estimate of the treatment effect that is not likely to be changed by future research. Tables B and D present our conclusions about effectiveness of physical therapy interventions.

In pooled analyses, we found low-strength evidence that core physical therapy interventions, including aerobic and aquatic exercise, improved disability measures; aerobic exercise and strengthening exercise reduced pain and improved function. In addition, ultrasound reduced pain and improved function. Proprioception exercise reduced pain, and tai chi improved function at short-term but not long-term followup. No single physical therapy improved all outcomes. We observed no benefits from specific education programs, diathermy, orthotics, or magnetic stimulation. Individual (nonpooled) RCTs failed to show consistent statistically significant, strong, or clinically important changes in outcomes. Individual small RCTs may fail to show statistically significant effects due to low statistical power. Strength of evidence was downgraded due to study risk of bias and heterogeneity in populations, treatments, and definitions of outcomes.

We described the interventions according to definitions and classification from APTA's Guide to Physical Therapist Practice.[22] For each examined intervention, we reported (1) the total number of eligible RCTs that contributed to our findings and (2) conclusions from the studies that contributed to the pooled analyses at the longest time of followup.

Specific Education Programs. We synthesized evidence from five RCTs; two RCTs with 511 participants contributed to the pooled analyses at the longest time of followup. The results of three articles from two RCTs that examined the effects of specific education programs provided low-strength evidence of no statistically significant effect on pain relief.

Aerobic Exercises. We synthesized evidence from 22 RCTs; 11 RCTs with 1,553 participants contributed to the pooled analyses at the longest time of followup. We found low-strength evidence that aerobic exercise resulted in statistically significant improvement in long-term pain and disability, but it did not improve psychological disability or health perception. Within 3 months, aerobic exercise improved composite function and gait function. At 12 months, the benefits of aerobic exercise continued for gait function, but not for composite function. A single RCT examined the effects of manual therapy combined with a standardized knee exercise program in the clinic and at home, and found statistically and clinically significant improvements in WOMAC total score and gait function.

Aquatic Exercises. We synthesized evidence from three RCTs with 348 participants that contributed to the pooled analyses at the longest time of followup. The studies provided low-strength evidence that aquatic exercise reduced disability, but it had no statistically significant effects on pain relief or quality of life.

Strengthening Exercises. We synthesized evidence from 17 RCTs; 9 RCTs with 1,982 participants contributed to the pooled analyses at the longest time of followup. Strengthening exercises had no statistically significant effect on disability (low-strength evidence). However, we observed a sustained improvement in pain relief, composite function, and gait function at 3 months through more than 12 months followup. Low-strength evidence demonstrated that strengthening exercises did not improve quality of life.

Tai Chi. Evidence from three RCTs with 167 participants contributed to the pooled analyses at the longest time of followup. Low-strength evidence from these small trials demonstrated that tai chi improved composite function measures around 3 months, but it had no statistically significant effect on pain or disability. Function did not improve further at 6 months followup.

Proprioception Exercises. Evidence from four RCTs with 247 participants contributed to the pooled analyses at the longest time of followup. These RCTs offered low-strength evidence that proprioception exercises led to pain relief, but they did not improve composite function or gait function.

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Specific Education Programs							
Pain 6-13 weeks Studies: 3; Subjects: 429 76-78	High	Direct	Inconsistent	Imprecise	NA	Low	0.09 (-0.42, 0.60) 2.0 (-9.2, 13.2)
Pain >26 weeks Studies: 2; Subjects: 511 76,79	High	Direct	Consistent	Precise	NA	Low	-0.09 (-0.32, 0.14) -2.0 (-7.0, 3.1)
Aerobic Exercise							
Disability <6 weeks Studies: 2; Subjects: 117 80,81	High	Direct	Inconsistent	Imprecise	Large	Low	**-1.70 (-3.27, -0.13)** **-0.65 (-1.24, -005)**
Disability 6-13 weeks Studies: 8; Subjects: 739 77,80-86	High	Direct	Inconsistent	Imprecise	NA	Low	-0.44 (-0.94, 0.05) -0.17 (-0.36, 0.02)
Disability 13-26 weeks Studies: 2; Subjects: 277 82,83	Medium	Direct	Consistent	Imprecise	NA	Low	0.12 (-0.11, 0.36) 0.05 (-0.04, 0.14)
Disability >26 weeks Studies: 4; Subjects: 806 54,83,87,88	High	Direct	Consistent	Precise	Small	Low	**-0.21 (-0.37, -0.04)** **-0.08 (-0.14; -0.02)**
Psychological disability 6-13 weeks Studies: 4; Subjects: 271 77,81,86,89	High	Direct	Inconsistent	Imprecise	NA	Low	-0.67 (-1.43, 0.1)
Pain <6 weeks Studies: 2; Subjects: 137 79,81	High	Direct	Inconsistent	Imprecise	NA	Low	-0.98 (-2.19, 0.24) -21.6 (-48.2, 5.3)
Pain 6-13 weeks Studies: 12; Subjects: 1,242 76,77,81-86,89-92	High	Direct	Inconsistent	Precise	Small	Low	**-0.32 (-0.55, -0.08)** **-7.0 (-12.1, -1.8)**

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Aerobic Exercise (continued)							
Pain 13-26 weeks Studies: 6; Subjects: 953 79,82,83,90-92	High	Direct	Consistent	Precise	NA	Low	-0.06 (-0.19, 0.06) -1.3 (-4.2, 1.3)
Pain >26 weeks Studies: 6; Subjects: 1,221 54,76,79,83,87,92	High	Direct	Consistent	Precise	Small	Low	**-0.21 (-0.35, -0.08)** **-4.6 (-7.7, -1.8)**
Function composite 6-13 weeks Studies: 3; Subjects: 351 64,89,92	Medium	Direct	Inconsistent	Imprecise	Large	Low	**-0.83 (-1.34, -0.32)** **-15.4 (- 24.8, -5.92)**
Function composite >26 weeks Studies: 3; Subjects: 826 54,79,92	Medium	Direct	Inconsistent	Precise	NA	Low	-0.18 (-0.44, 0.08) -3.33 (-8.14, 1.48)
Gait function < 6 weeks Studies: 3; Subjects: 220 80,81,90	High	Direct	Consistent	Imprecise	Small	Low	**-0.38 (-0.63, -0.13)** **-0.08 (-0.13, -0.03)**
Gait function 6-13 weeks Studies: 8; Subjects: 632 64,80,81,86,89-91,93	High	Direct	Consistent	Precise	Moderate	Low	**-0.57 (-0.75, -0.39)** **-0.11 (-0.15, -0.08)**
Gait function 13-26 weeks Studies: 3; Subjects: 459 79,90,91	High	Direct	Consistent	Precise	Small	Low	**-0.44 (-0.62, -0.26)** **-0.09 (-0.12, -0.05)**
Gait function >26 weeks Studies: 2; Subjects: 609 54,94	Medium	Direct	Consistent	Precise	Moderate	Low	-0.56 (-0.86, -0.25) -0.11 (-0.17, -0.05)
Health perception 6-13 weeks Studies: 2; Subjects: 62 81,89	High	Direct	Inconsistent	Imprecise	NA	Low	-1.38 (-3.08, 0.32)

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Aerobic Exercise (continued)							
Health perception >26 weeks Studies: 3; Subjects: 513 [83,87,88]	High	Direct	Consistent	Precise	NA	Low	-0.04 (-0.21, 0.14)
Aquatic Exercise							
Disability 6-13 weeks Studies: 2; Subjects: 99 [68,95]	Medium	Direct	Consistent	Imprecise	NA	Low	0.06 (-0.36, 0.49) 0.02 (-0.14, 0.19)
Disability 13-26 weeks Studies: 2; Subjects: 303 [95,96]	Medium	Direct	Consistent	Imprecise	Small	Low	**-0.28 (-0.51, -0.05)** **-0.11 (-0.19; -0.02)**
Pain 6-13 weeks Studies: 2; Subjects: 99 [68,95]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.25 (-0.64, 0.15) -5.5 (-14.1, 3.3)
Pain 13-26 weeks Studies: 2; Subjects: 303 [95,96]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.17 (-0.39, 0.06) -3.7 (-8.6, 1.3)
QL13-26 weeks Studies: 2; Subjects: 303 [95,96]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.10 (-0.32, 0.13) -1.06 (-3.51; 1.40)
Function composite 6-13 weeks Studies: 2; Subjects: 99 [68,95]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.03 (-0.51, 0.44) -0.56 (-9.44, 8.14)
Strengthening Exercise							
Disability 6-13 weeks Studies: 4; Subjects: 606 [95,97-99]	Medium	Direct	Inconsistent	Imprecise	NA	Low	-0.08 (-0.51, 0.35) -0.03 (-0.19, 0.13)
Disability 13-26 weeks Studies: 3; Subjects: 490 [95,98,100]	Medium	Direct	Consistent	Precise	Small	Low	**-0.19 (-0.36, -0.01)** **-0.07 (-0.14, -0.00)**

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Strengthening Exercise (continued)							
Disability >26 weeks Studies: 2; Subjects: 687 [54,98]	Medium	Direct	Inconsistent	Precise	NA	Low	-0.16 (-0.48, 0.16) -0.06 (-0.18; 0.06)
Pain 6-13 weeks Studies: 13; Subjects: 1,404 [63,95,97-99,101-108]	High	Direct	Inconsistent	Precise	Moderate	Low	**-0.63 (-0.87, -0.39)** **-13.9 (-19.1, -8.6)**
Pain 13-26 weeks Studies: 4; Subjects: 592 [95,98,100,109]	Medium	Direct	Consistent	Precise	Small	Low	**-0.35 (-0.51, -0.18)** **-7.7 (-11.2, -4.0)**
Pain >26 weeks Studies: 3; Subjects: 786 [54,98,105]	Medium	Direct	Inconsistent	Precise	Moderate	Low	**-0.68 (-1.23, -0.14)** **-15.0 (-27.1, -3.1)**
QL 6-13 weeks Studies: 2; Subjects: 194 [95,99]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.32 (-0.72, 0.07) -3.52 (-7.80, 0.77)
Function composite 6-13 weeks Studies: 6; Subjects: 521 [63,95,103,105,106,108]	Medium	Direct	Inconsistent	Precise	Large	Low	**-0.84 (-1.13, -0.56)** **-15.5 (-20.9, -10.4)**
Function composite 13-26 weeks Studies: 3; Subjects: 200 [95,100,109]	Medium	Direct	Consistent	Imprecise	Small	Low	**-0.35 (-0.61, -0.09)** **-6.48 (-11.3, -1.67)**
Function composite >26 weeks Studies: 2; Subjects: 394 [54,105]	Medium	Direct	Inconsistent	Imprecise	Large	Low	**-1.00 (-1.95, -0.05)** **-18.5 (-36.1, -0.93)**
Gait function 6-13 weeks Studies: 9; Subjects: 958 [63,98,101-103,106-108,110]	High	Direct	Inconsistent	Precise	Small	Low	**-0.47 (-0.78, -0.16)** **-0.09 (-0.16, -0.03)**

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Strengthening Exercise (continued)							
Gait function 13-26 weeks Studies: 2; Subjects: 494 98,109	Medium	Direct	Consistent	Precise	Small	Low	**-0.46 (-0.84, -0.08)** **-0.09 (-0.17, 0.02)**
Gait function >26 weeks Studies: 2; Subjects: 687 54,98	Medium	Direct	Consistent	Precise	Small	Low	**-0.39 (-0.59, -0.20)** **-0.08 (-0.12, -0.04)**
Tai Chi							
Disability 6-13 weeks Studies: 2; Subjects: 85 65,111	Medium	Direct	Consistent	Imprecise	NA	Low	-0.24 (-0.68, 0.2) -0.09 (-0.26, 0.08)
Disability 13-26 weeks Studies: 2; Subjects: 123 111,112	Medium	Direct	Consistent	Imprecise	NA	Low	-0.27 (-0.95, 0.41) -0.10 (-0.36, 0.16)
Pain 6-13 weeks Studies: 2; Subjects: 85 65,111	Medium	Direct	Consistent	Imprecise	NA	Low	-0.41 (-0.85, 0.03) -9.0 (-18.7, 0.7)
Function composite 6-13 weeks Studies: 2; Subjects: 85 65,111	Medium	Direct	Consistent	Imprecise	Small	Low	-0.44 (-0.88, 0.00) -8.14 (-16.3, 0)
Function joint 6-13 weeks Studies: 2; Subjects: 85 65,111	Medium	Direct	Consistent	Imprecise	NA	Low	-0.08 (-0.51, 0.36)
Proprioception Exercise							
Pain 6-13 weeks Studies: 3; Subjects: 198 105,106,113	High	Direct	Inconsistent	Imprecise	Moderate	Low	**-0.71 (-1.31, -0.11)** **-15.6 (-28.8, -2.4)**
Function composite 6-13 weeks Studies: 3; Subjects: 198 105,106,113	High	Direct	Inconsistent	Imprecise	NA	Low	-1.12 (-2.66, 0.41) -20.7 (-49.2, 7.59)

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Proprioception Exercise (continued)							
Gait function 6-13 weeks Studies: 3; Subjects: 181 106,113,114	High	Direct	Inconsistent	Imprecise	NA	Low	-0.96 (-2.00, 0.09) -0.19 (-0.4, 0.02)
Massage							
Function composite 6-13 weeks Studies: 2; Subjects: 94 115,116	High	Direct	Consistent	Imprecise	Moderate	Low	**-0.55 (-0.93, -0.18)** **-10.2 (-17.2, -3.33)**
Orthotics							
Gait function <6 weeks Studies: 4; Subjects: 101 117-120	High	Direct	Consistent	Imprecise	NA	Low	-0.01 (-0.22, 0.20) 0.00 (-0.04, 0.04)
Function composite <6 weeks Studies: 2; Subjects: 138 56,121	Medium	Direct	Inconsistent	Imprecise	NA	Low	-0.57 (-1.17, 0.02) -10.5 (-21.6, 0.37)
Taping: Elastic Subtalar Strapping							
Function composite 6-13 weeks Studies: 3; Subjects: 246 52,122,123	High	Direct	Consistent	Imprecise	Small	Low	**-0.27 (-0.53, -0.02)** **-5.00 (-9.81, -0.37)**
Electrical Stimulation							
Disability 6-13 weeks Studies: 2; Subjects: 98 124,125	Low	Direct	Consistent	Imprecise	NA	Moderate	-0.27 (-0.68, 0.14) -0.10 (-0.26; 0.05)
Pain <6 weeks Studies: 7; Subjects: 301 104,125-130	High	Direct	Consistent	Imprecise	Moderate	Low	**-0.71 (-0.98, -0.43)** -15.6 (-21.6, -9.5)
Pain 6-13 weeks Studies: 7; Subjects: 304 104,124,125,128,131-133	High	Direct	Consistent	Imprecise	NA	Low	-0.09 (-0.31, 0.14) -2.0 (-6.8, 3.1)

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Electrical Stimulation (continued)							
Pain 13-26 weeks Studies: 2; Subjects: 76 [132,133]	High	Direct	Consistent	Imprecise	Moderate	Low	**0.57 (0.09, 1.06)** **12.5 (2.0, 23.3)**
Global assessment 6-13 weeks Studies: 2; Subjects: 98 [124,125]	Low	Direct	Consistent	Imprecise	Small	Low	**-0.44 (-0.85, -0.02)**
Function composite 6-13 weeks Studies: 3; Subjects: 138 [124,125,131]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.08 (-0.43, 0.26) -1.48 (-7.96, 4.81)
Function joint <6 weeks Studies: 2; Subjects: 100 [125,130]	Medium	Direct	Consistent	Imprecise	NA	Low	-0.25 (-0.61, 0.11)
Function joint 6-13 weeks Studies: 2; Subjects: 98 [124,125]	Low	Direct	Consistent	Imprecise	NA	Moderate	-0.29 (-0.70, 0.12)
Gait function <6 weeks Studies: 4; Subjects: 191 [110,134-136]	High	Direct	Inconsistent	Imprecise	NA	Low	-0.19 (-0.69, 0.30) -0.04 (-0.14, 0.06)
Gait function 6-13 weeks Studies: 3; Subjects: 164 [110,131,133]	High	Direct	Consistent	Imprecise	NA	Low	0.06 (-0.23, 0.35) 0.01 (-0.05, 0.07)
Strength, measured as 120 degree extension 6-13 weeks Studies: 2; Subjects: 118 [131,133]	Medium	Direct	Inconsistent	Imprecise	NA	Low	-0.41 (-0.83, 0.01)
Strength, measured as 60 degree extension 6-13 weeks Studies: 2; Subjects: 146 [110,131]	High	Direct	Consistent	Imprecise	Moderate	Low	**-0.55 (-0.88, -0.22)**

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Pulsed Electromagnetic Fields							
Pain <6 weeks Studies: 2; Subjects: 145 137,138	Low	Direct	Consistent	Imprecise	NA	Moderate	0.01 (-0.41, 0.44) 0.2 (-9.0, 9.7)
Function composite <6 weeks Studies: 2; Subjects: 145 137,138	Low	Direct	Consistent	Imprecise	NA	Moderate	-0.13 (-0.60, 0.35) -2.41 (-11.1, 6.48)
Ultrasound							
Disability <6 weeks Studies: 2; Subjects: 157 139,140	Medium	Direct	Consistent	Imprecise	NA	Low	-0.39 (-0.79, 0.02) -0.15 (-0.30, 0.01)
Pain <6 weeks Studies: 2; Subjects: 157 139,140	Medium	Direct	Inconsistent	Imprecise	Moderate	Low	**-0.53 (-1.04, -0.03)** **-11.7 (-22.9, -0.7)**
Pain 6-13 weeks Studies: 4; Subjects: 227 131,141-143	Medium	Direct	Consistent	Imprecise	Moderate	Low	**-0.52 (-0.84, -0.19)** **-11.4 (-18.5, -4.2)**
Pain >26 weeks Studies: 2; Subjects: 160 141,142	Medium	Direct	Consistent	Imprecise	Moderate	Low	**-0.74 (-0.95, -0.53)** **-16.3 (-20.9, -11.7)**
Function composite 6-13 weeks Studies: 4; Subjects: 227 131,141-143	Medium	Direct	Inconsistent	Imprecise	NA	Low	-0.60 (-1.40, 0.20) -11.2 (-26.0, 3.72)
Function composite >26 weeks Studies: 2; Subjects: 160 141,142	Medium	Direct	Consistent	Imprecise	Large	Low	**-1.14 (-1.60, -0.69)** **-21.2 (-29.8, -12.8)**
Gait function <6 weeks Studies: 2; Subjects: 157 139,140	Medium	Direct	Inconsistent	Imprecise	NA	Low	-0.53 (-1.32, 0.25) -0.11 (-0.26, 0.05)

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Ultrasound (continued)							
Gait function 6-13 weeks Studies: 4; Subjects: 227 131,141-143	Medium	Direct	Inconsistent	Imprecise	Large	Low	**-1.13 (-2.08, -0.17)** **-0.23 (-0.42, -0.03)**
Gait function >26 weeks Studies: 2; Subjects: 160 141,142	Medium	Direct	Inconsistent	Imprecise	Large	Low	**-1.48 (-2.08, -0.89)** **-0.30 (-0.42, -0.18)**
Diathermy							
Disability <6 weeks Studies: 4; Subjects: 259 144-147	High	Direct	Consistent	Imprecise	NA	Low	-0.21 (-0.45, 0.02) -0.08 (-0.17, 0.01)
Disability 6-13 weeks Studies: 2; Subjects: 143 146,147	High	Direct	Consistent	Imprecise	NA	Low	-0.04 (-0.34, 0.25) -0.02 (-0.13, 0.09)
Pain <6 weeks Studies: 4; Subjects: 259 144-147	High	Direct	Inconsistent	Imprecise	Moderate	Low	**-0.53 (-0.96, -0.10)** **-11.7 (-21.1, -2.2)**
Pain 6-13 weeks Studies: 3; Subjects: 183 131,146, 147	High	Direct	Consistent	Imprecise	NA	Low	-0.01 (-0.27, 0.26) -0.2 (-5.9, 5.7)
Function composite <6 weeks Studies: 3; Subjects: 229 145-147	High	Direct	Inconsistent	Imprecise	NA	Low	-0.47 (-0.95, 0.02) -8.70 (-17.6, 0.37)
Function composite 6-13 weeks Studies: 3; Subjects: 183 131,146,147	High	Direct	Consistent	Imprecise	NA	Low	0.01 (-0.26, 0.27) 0.19 (-4.81, 5.00)

Table A. Effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences [SMDs] pooled with random effects models, using standardized units of differences-standard deviations) (continued)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
Diathermy (continued)							
Function joint <6 weeks Studies: 2; Subjects: 143 [146,147]	High	Direct	Consistent	Imprecise	NA	Low	0.20 (-0.10, 0.49)
Function joint 6-13 weeks Studies: 2; Subjects: 143 [146,147]	High	Direct	Consistent	Imprecise	NA	Low	0.16 (-0.14, 0.46)
Gait function <6 weeks Studies: 3; Subjects: 173 [144,146,147]	High	Direct	Consistent	Imprecise	NA	Low	-0.10 (-0.36, 0.17) -0.02 (-0.07, 0.03)
Gait function 6-13 weeks Studies: 3; Subjects: 183 [131,146,147]	High	Direct	Consistent	Imprecise	NA	Low	-0.14 (-0.40, 0.13) -0.03 (-0.08, 0.03)

CI = confidence interval; NA = not applicable; QL = quality of life

Note: Bold indicates significant differences when 95% CIs do not include 0; negative value means improvement; converted mean differences are in EQ-5D (0-1) for disability, in SF-36 (0-100) for quality of life, in Visual Analog Scale (0-100) for pain, in Western Ontario and McMaster Universities Osteoarthritis Index for physical function (0-100) for composite function, and in walking speed (m/s) for gait function.

Table B. Summary of effectiveness of physical therapy interventions for knee osteoarthritis		
Physical Therapy Intervention	**Studies/Subjects**	**Conclusions/Strength of Evidence**
Specific education programs	Studies=2/Subjects=511	Specific education programs improved health perception measures (L) but did not improve pain (L), disability (L), psychological disability (L), gait (L) and composite measures of function (L).
Aerobic exercises	Studies=11/Subjects=1,553	Aerobic exercises improved pain (L), disability (L), gait (L), and transfer (L) measures of function but did not improve psychological disability (L), global assessment (L), health perception (L), joint (L) and composite measures of function (L).
Aquatic exercises	Studies=3/Subjects=348	Aquatic exercises improved disability (L) but did not improve pain (L), psychological disability (L), quality of life (L), and composite measures of function (L).
Strengthening exercises	Studies=9/ Subjects=1,982	Strengthening exercises improved pain (L), global assessment (L), gait (L), transfer (L), and composite (L) function measures but did not improve disability (L), health perception (L), quality of life (L) and joint (L) function measures.
Tai Chi	Studies=3/Subjects=167	Tai Chi improved psychological disability (L) and composite (L) function measures, but did not improve pain (L), disability (L), quality of life (L), gait (L), and joint (L) function measures.
Proprioception exercises	Studies=4/Subjects=247	Proprioception exercises improved pain (L) but did not improve gait (L) and composite measures of function (L).
Massage	Studies=3/Subjects=162	Massage improved disability (L), joint (L), gait (L) and composite (L) function measures.
Joint mobilization	Studies=2/Subjects=83	Joint mobilization improved disability (L) and global assessment (L) but did not improve pain (L) and gait (L) function measures.
Joint mobilization with exercise	Studies=1/Subjects=134	Joint mobilization with exercise improved disability (L) but did not improve gait (L) function measures.
Orthotics	Studies=7/Subjects=364	Orthotics improved pain (L), disability (L), psychological disability (L), quality of life (L), and joint measures of function (L) but did not improve global assessment (L), gait (L) and composite (L) function measures.
Elastic subtalar strapping	Studies=3/Subjects=246	Elastic subtalar strapping improved composite function measures (L).
Taping	Studies=2/Subjects=105	Taping did not improve pain (L), disability (L), gait (L) and composite (L) function measures.
E-stim	Studies=7/Subjects=390	E-stim improved global assessment (L), but worsened pain (L), and did not improve disability (M), health perception (L), and gait (L), joint (M), transfer (L), and composite (L) function measures.
PEMF	Studies=4/Subjects=267	PEMF improved global assessment (L) but did not improve pain (M), disability (L), and gait (L), joint (L) and composite (M) function measures.
Ultrasound	Studies=6/Subjects=387	Ultrasound improved pain (L), gait (L) and composite (L) function measures but did not improve disability (L), and joint function measures (L).
Diathermy	Studies=5/Subjects=382	Diathermy did not improve pain (L), disability (L), psychological disability (L), global assessment (L), health perception (L), quality of life (L), and joint (L), gait (L) and composite (L) function measures.
Heat	Studies=3/Subjects=126	Heat improved disability (L) and quality of life (L), but did not improve pain (L), gait (L), joint (L), and composite (L) function measures.
Cryotherapy	Studies=2/Subjects=57	Cryotherapy did not improve disability (L), quality of life (L), and composite function measures (L).

E-stim = electrical stimulation; PEMF = pulsed electromagnetic fields

Note: Strength of evidence as L = low, M = moderate. Strength of evidence was determined according to four domains (risk of bias, directness, consistency, and precision).

Table C. Comparative effectiveness of physical therapy intervention on patient-centered outcomes (standardized mean differences pooled with random effects models, using standardized units of differences-standard deviations)

Outcome, Studies, Sample Size, References	Risk of Bias	Directness	Consistency	Precision	Strength of the Association	Strength of Evidence	Pooled Hedges Standard Mean Difference (95% CI) Converted Mean Difference (95% CI)
E-stim vs. Exercise							
Pain <6 weeks Studies: 2; Subjects: 81 104, 148	High	Direct	Inconsistent	Imprecise	NA	Low	-1.28 (-2.95, 0.40) -28.2 (-64.9, 8.8)
Gait function <6 weeks Studies: 2; Subjects: 81 110, 148	Medium	Direct	Inconsistent	Imprecise	NA	Low	0.20 (-1.15, 1.55) 0.04 (-0.23, 0.31)
Exercise Aquatic vs. Aerobic							
Pain 6-13 weeks Studies: 2; Subjects: 110 95, 149	Medium	Direct	Inconsistent	Imprecise	NA	Low	-0.44 (-1.22, 0.35) -9.7 (-26.8, 7.7)
Laterally vs. Neutrally Wedged Insole							
Function composite 6-13 weeks Studies: 2; Subjects: 383 51, 52	Medium	Direct	Consistent	Imprecise	NA	Low	-0.01 (-0.25, 0.25) -0.19 (-4.63, 4.63)

CI = confidence interval; E-stim = electrical stimulation; NA = not applicable

Note: Negative value means improvement; converted mean differences are in Visual Analog Scale (0-100) for pain, in Western Ontario and McMaster Universities Osteoarthritis Index for physical function (0-100) for composite function, and in walking speed (m/s) for gait function.

Table D. Summary of comparative effectiveness of physical therapy interventions for knee osteoarthritis		
Active vs. Control Physical Therapy Intervention	**Studies/Subjects**	**Conclusions/Strength of Evidence**
Aerobic exercises vs. strengthening exercises	Studies=1/Subjects=290	Aerobic exercises improved gait function measures (L) but did not improve pain (L), disability (L), transfer (L), and composite (L) function measures, compared to strengthening exercises.
Aquatic exercises vs. aerobic exercises	Studies=2/Subjects=110	Aquatic exercises did not improve pain (L), disability (L), gait (L) and composite (L) function measures, compared to aerobic exercises.
Proprioception exercises vs. strengthening exercises	Studies=1/Subjects=72	Proprioception exercises worsened composite function measures (L) and did not improve pain (L), gait function (L), compared to strengthening exercises.
Tai Chi vs. stretching exercises	Studies=1/Subjects=40	Tai Chi improved disability (L), psychological disability (L), and transfer function (L) but did not improve pain (L), global assessment (L), gait (L), joint (L), and composite (L) function measures, compared to stretching exercise.
Laterally vs. neutrally wedged insole	Studies=5/Subjects=613	Laterally wedged insole did not improve pain (L), disability (L), global assessment (L), quality of life (L), gait (L), joint (L), and composite function measures (L), compared to neutrally wedged insole.
Orthotics vs. brace	Studies=1/Subjects=91	Orthotics did not improve pain (L) and composite function measures (L), compared to brace.
E-stim vs. exercises	Studies=2/Subjects=81	E-stim improved joint (L) and composite (L) measures of function but did not improve pain (L) and gait (L) function, compared to exercises.
E-stim vs. ultrasound	Studies=1/Subjects=40	E-stim did not improve pain (L), gait (L) and composite (L) measures of function, compared to ultrasound.

E-stim = electrical stimulation

Note: Strength of evidence as L = low; strength of evidence was determined according to four domains (risk of bias, directness, consistency, and precision).

Massage. Evidence from three RCTs with 162 participants contributed to the pooled analyses at the longest time of followup. We found low-strength evidence that massage somewhat improved composite function.

Joint Mobilization. We synthesized evidence from three RCTs with 217 participants, but were unable to perform pooled analyses due to differences in outcomes examined, reporting formats, and time to followup. Individual studies showed that joint mobilization with or without exercise reduced disability.

Orthotics. Evidence from seven RCTs with 364 participants contributed to the pooled analyses at the longest time of followup. These RCTs demonstrated low-strength evidence that orthotics had no effect on short-term outcomes of composite function or gait function.

Therapeutic Taping. Three RCTs with 119 participants examined the effects of therapeutic taping and found no benefits for pain, disability, composite function, or gait function. Different reporting formats precluded pooled analyses. Individual RCTs suggested that taping might provide short-term pain relief.

Electrical Stimulation. We synthesized evidence from 15 RCTs, and seven RCTs with 390 participants contributed to the pooled analyses at the longest time of followup. Electrical stimulation resulted in statistically significant improved pain short term and at 3 months after starting the intervention. However, pain worsened at 6 months. We found low-strength evidence that at 3 months followup, global assessment and muscle strength (measured at 60 degree extension) improved significantly with electrical stimulation treatment. These statistically significant findings were consistent without substantial heterogeneity across the studies. Pooled analyses provided moderate-strength evidence of no improvement on disability or joint function and low-strength evidence of no improvement on gait or composite functional measures.

Pulsed Electromagnetic Fields. Evidence from four RCTs with 267 participants contributed to the pooled analyses at the longest time of followup. These RCTs offered moderate-strength evidence that pulsed electromagnetic fields (PEMFs) neither reduced pain nor improved composite function.

Ultrasound. Evidence from six RCTs with 387 participants contributed to the pooled analyses at the longest time of followup. We found low-strength evidence that ultrasound resulted in statistically significant reduction in pain with a moderate effect size and significantly improved composite function and gait function with a large effect size. Low-strength evidence also demonstrated that ultrasound did not improve disability.

Diathermy. We synthesized evidence from seven RCTs; five RCTs with 382 participants contributed to the pooled analyses at the longest time of followup. Low-strength evidence demonstrated that diathermy resulted in a statistically significant decrease in pain at 1 month, but the effect was statistically insignificant at 3 months. Low-strength evidence demonstrated that diathermy did not improve disability, composite function, joint function, or gait function.

Heat. We synthesized evidence from three RCTs with 126 participants, but were unable to perform a pooled analysis to draw robust conclusions.

Cryotherapy. We synthesized evidence from two RCTs with 57 participants, but were unable to perform a pooled analysis to draw robust conclusions.

The Role of Physical Therapist Involvement in Benefits With Exercises. We performed subgroup analyses by involvement of a physical therapist for all outcomes with aerobic or strengthening exercises. For most comparisons, effect sizes with the involvement of a physical therapist were larger than those without. Furthermore, the results in the physical therapist involvement group tended to be consistent without heterogeneity. Although the sample size of the subgroup with physical therapist involvement was smaller than the sample size of all pooled studies, our conclusions remain the same.

Clinical Importance of Treatment Effects With Physical Therapy Interventions. Original studies used a wide variety of pain measurements and thus required standardization in pooled analyses. This lack of consistency prevented us from being able to assess whether specific interventions resulted in benefits that were of clinical importance. To assess the clinical importance of pain reduction with interventions, we performed subgroup analyses with a subset of the studies that used the same VAS instrument for pain measures. We then compared mean reduction in pain with the cutoff for MCIDs in VAS as reported in observational studies. We found that electrical stimulation, diathermy, and ultrasound resulted in clinically significant short-term pain reduction.

In long-term followup, however, only strengthening exercise reduced pain with an effect size that exceeded the threshold of MCID.

To assess the clinical importance of improvements in disability and quality of life with physical therapy

interventions, we transformed SMDs to nonstandardized mean differences in EQ-5D or SF-36 (Table A).

Only aerobic and aquatic exercises led to statistically significant and clinically important benefits for disability (estimated EQ-5D improvements of 0.08 and 0.11, respectively). However, for quality of life, the benefits of aquatic and strengthening exercise were statistically insignificant (estimated SF-36 physical component summary improvements of 1.1 and 3.5, respectively).

As a part of the evidence synthesis, we also compared the differences in continuous measures of pain and disability reported in trials with the MCIDs determined in observational studies. We found few clinically important improvements. Aerobic exercise resulted in clinically important improvement in pain, disability, and joint function in the majority of individual RCTs.

Comparative Effectiveness of Physical Therapy Interventions. Single RCTs that examined comparative effectiveness of physical therapy interventions offered low-strength evidence for the majority of comparisons (Tables C and D). Aerobic and aquatic exercises had the same benefits for improving disability and pain, a finding consistent with the similar effect sizes demonstrated by these two interventions in efficacy studies. Tables E and F show pain and disability outcomes associated with each physical therapy intervention by strength of evidence. One study found no statistically significant differences between aerobic and strengthening exercises for disability and composite function, but gait function improved more with aerobic exercise. One study demonstrated that tai chi was better than stretching exercise for disability, psychological disability, global assessment, and transfer function.

We found no statistically significant differences between laterally and neutrally wedged insoles on composite function[51,52] or between orthotics and brace on composite function. A recent study showed that pain, disability, global assessment, quality of life, and joint function did not differ between laterally and neutrally wedged insoles. Several small studies found no statistically significant difference between electrical stimulation and exercise for pain relief and gait function. One study showed statistically insignificant differences between electrical stimulation and ultrasound for composite and gait function.

The studies of combined physical therapy modalities demonstrated no statistically significant benefits on the outcomes when compared with aerobic, strength, or proprioception exercise alone. Manual therapy added to aerobic exercise provided benefits similar to aerobic exercise alone.

Key Question 1a. Role of Patient Characteristics on Outcomes

The majority of subgroup analyses in individual RCTs lacked robust evidence and thus failed to permit definitive conclusions about the most effective physical therapy treatments in association with patient characteristics.

Compliance. Three RCTs showed that subgroups with high compliance tended to have better outcomes for exercise (aerobic, aquatic, and strengthening). The higher exercise compliance group had the lowest risk of incident ADL disability, a lower average depression score, a higher mean Quality of Well-Being Scale score, and greater improvements in both 6-minute walking distance and disability.

Age. Robust evidence was lacking for how age differences affect treatment outcomes because three studies were inconsistent with active and control treatments, outcomes, and definitions of age subgroups.

Malalignment. Low-strength evidence from two RCTs did not permit robust conclusions about how malalignment affects treatment outcomes. The RCTs found greater benefit in patients with the genu varus group and in those without malalignment.

Body Mass Index. Two RCTs provided inconsistent evidence about the role of BMI in predicting treatment effects. Improvement in function by lateral wedge insoles was better in adults of normal weight, while very obese participants (defined by the top tertile) experienced similar benefits from aerobic exercise interventions and resistance training programs.

Comorbidity. Evidence from individual studies did not permit robust conclusions about how treatment effects may be modified by comorbidity.

Sex. Evidence from individual studies did not permit robust conclusions about how treatment effects may differ between men and women. The five studies that reported clinical outcomes in male and female subgroups for exercise and orthotics[52-56] demonstrated no statistically significant differences in outcomes.

Race. Evidence from a single study was inconclusive for how racial differences affect treatment outcomes of exercise.

Severity. Baseline OA severity may modify the effects of physical therapy interventions on clinical outcomes. However, findings were inconsistent and varied across studies depending on the treatments, outcomes, and/or cutoff grades. Furthermore, RCTs reported post

hoc analyses of changes from baseline in functional measures among patients with different baseline severity scores. Clinical outcomes in severity subgroups were reported in seven RCTs, involving brace, insole, exercise (strengthening or range of motion), and weight reduction and/or electrical stimulation. Three RCTs found no consistent modification effect of baseline severity.

Key Question 1b. Association Between Dose/Duration/Intensity/Frequency of Examined Interventions and Intermediate/Patient-Centered Outcomes

For the majority of comparisons, evidence did not permit robust conclusions about the association between the dose/duration/intensity/frequency of examined interventions and outcomes.

Exercise. Included studies variously defined intensity of exercise, yet indicated equal benefits from low- and high-intensity exercise. One study using exercise compliance to examine the potential dose-response relationship between exercise frequency and outcomes showed that exercise for patients with knee OA should be done three times each week.

Orthotics. For patients with genu varus deformity from OA, medium duration (between 5 and 10 hours each day) of insole with subtalar strapping wear was better than short duration (fewer than 5 hours) and long duration (more than 10 hours).

Electrical Stimulation. We found no short-term clinical difference between low-frequency (2 Hz) and high-frequency (80 Hz) electrical stimulation. However, noxious stimulation decreased pain intensity more than innocuous stimulation. In one study, Burst Mode and High Rate stimulation had similar effects on stiffness and pain. Another study demonstrated that for reducing pain, 40 minutes was the optimal duration of electrical stimulation.

Ultrasound. Two RCTs showed that pulsed ultrasound was better than continuous ultrasound in improving disability, gait, and composite function measures.

Key Question 1c. Association Between Time of Follow-up and Intermediate/Patient-Centered Outcomes

The association between followup time and outcomes varied by treatments and outcomes of interest. The effects of aerobic, aquatic, and strengthening exercises and ultrasound did not differ at shorter versus longer followups. Further, in a combined analysis of aerobic, aquatic, strengthening, proprioception, and tai chi exercises, changes in intermediate and patient-centered outcomes did not differ by followup time (all p-values greater than 0.05). Results held consistent with or without inclusion of Tai Chi. Outcomes of pain, gait, and composite function after ultrasound did not differ by followup time. Electrical stimulation improved pain at short-term followup but significantly worsened pain at longer followups (p-value <0.001). In contrast, we observed that diathermy's benefits for disability increased with longer followups (p-value = 0.009).

Association Between Duration of Examined Interventions and Intermediate/Patient-Centered Outcomes. The duration of examined interventions varied broadly. For example, exercise programs ranged from 2 to 72 weeks. We found no statistically significant association between the duration of examined interventions and intermediate or patient-centered outcomes. In combined results for aerobic, aquatic, strengthening, proprioception, and tai chi exercises, changes in intermediate and patient-centered outcomes did not differ by the duration of the examined intervention, with all p-values greater than 0.05.

Key Question 2. Association Between Intermediate and Patient-Centered Outcomes

Evidence for the association between intermediate and clinical outcomes was limited to individual studies. We found substantial variability in definitions of index and reference methods, definitions of outcomes, and methods of examining diagnostic values and associations between intermediate and clinical outcomes.

We synthesized the evidence of association between intermediate and clinical outcomes from 43 studies that included 25,799 adults with knee OA. Disability measures were associated with gait, mobility restrictions, muscle strength, and range-of-motion measures, but the magnitude and clinical importance of the association were unclear.

Key Question 2a. Validity of the Tests and Measures Used To Determine Intermediate Outcomes of Physical Therapy on OA in Association With Patient-Centered Outcomes

Validation of the tests and measures used to determine intermediate outcomes of physical therapy on knee OA was reported in 66 studies of 14,563 adults. The studies used a variety of reference methods to judge validity according to statistically significant correlation coefficients. Only a small proportion of the studies demonstrated a strong (more than 50 percent) correlation between index and reference method measurements. Strength of correlation varied across validity types.

Key Question 2b. Which Intermediate Outcomes Meet the Criteria of Surrogates for Patient-Centered Outcomes?

None of the intermediate outcomes met surrogate criteria for patient-centered outcomes as defined by the OMERACT Criteria for Surrogate Endpoints. TEP members proposed gait as a feasible candidate for a surrogate endpoint. However, no study analyzed the association between gait and patient-centered outcomes of physical therapy for adults with knee OA. One RCT did conclude that knee pain and self-efficacy mediated the effects of exercise on stair-climb time. A single longitudinal study of elderly adults demonstrated that impaired gait and the Physical Performance Test were independent predictors of nursing home placement. Three cohort studies (the Einstein Aging Study, the Chinese Elderly Cohort, and the Women's Health and Aging Study) examined the association between gait and nursing home placement. However, the studies included adults with any etiology of gait problem, including neurological diseases or heart failure. Further, the definitions of "impaired gait" and magnitude of the association differed across the studies.

Key Question 2c. What are Minimum Clinically Important Differences of the Tests and Measures Used To Determine Intermediate Outcomes?

No RCTs of physical therapy interventions determined minimum clinically important differences (MCIDs). However, MCIDs in outcome measurements were reported in 30 observational studies of 13,138 adults. The studies used the anchor method, which compares patient perception of improvement with absolute change in scale score or with percentage difference from baseline levels. The percentage difference from baseline levels incorporated baseline severity of the diseases. MCIDs were available for 26 validated tools.

Few studies determined a Patient Acceptable Symptom State (PASS) for knee OA. PASS is defined as the highest level of symptom patients can tolerate and still be satisfied with treatment. The studies used the same anchor method for determining PASS as they did for determining MCIDs. The difference is in anchoring questions: MCID involves asking for patient perception of clinically important improvement while PASS involves asking patients whether they are satisfied with their functional status in relation to daily activities and quality of life. PASS was determined for three scales—WOMAC, VAS, and Patient Global Assessment.

Key Question 3. Harms From Physical Therapy Interventions Available for Adult Patients With Chronic Knee Pain Due to Osteoarthritis

Adverse events were uncommon and varied across interventions. Skin irritation was reported with brace, insole, taping, and electrical stimulation; swelling with brace, diathermy, and exercise; muscle soreness with electrical stimulation; throbbing sensation with diathermy, electrical stimulation, and PEMF; increased pain with diathermy, exercise, insole, and PEMF; falls with insole; and need for surgery with diathermy. Adverse events rates did not differ with statistical significance among treatment groups. Adverse events were not severe enough to deter participants from continuing treatment.

Discussion

Our report of patient-centered outcomes, including pain, disability, and quality of life with physical therapy interventions for adults with knee OA has implications for clinical practice. Our findings generally agree with previously published guidelines[8,13] and systematic reviews[17,19,57] that recommend exercise for adults with symptomatic knee OA. Few physical therapy interventions demonstrated any statistically significant effectiveness, and no single intervention improved all outcomes (Tables E and F). Pooled analyses demonstrated that diathermy, orthotics, and magnetic stimulation failed to show any benefits.

This review reflects the discrepancy between the recommended practice of physical therapy and the study designs used to examine the interventions. Current guidelines recommend that physical therapy be delivered with a combination of modalities.[22] Published research has focused instead on the marginal effects of individual physical therapy interventions. Our effort was further complicated by the fact that clinical care for adults with knee OA includes pharmacologic interventions,[58-60] while our review was limited to nonpharmacologic treatments. To address such complexity, we focused on randomized trials because these equally distribute concomitant treatments among treatment groups and thus provide valid estimates of effects of the examined interventions.

Randomized trials are the gold standard in establishing benefits from health care interventions.[61] However, applicability of findings is limited to similar settings, treatments, and patient populations. In our review, for example, randomization might equally distribute the effect of pain relievers (a common concomitant treatment), but it would not prevent the dampening of potential effects from

physical therapy interventions. The trials we examined rarely provided information about all other treatments patients might have received. Nor did the trials analyze outcomes separately in patient subgroups by concomitant treatments. We tried to examine the potential influence of pain medication on physical therapy outcomes for pain, but rare and inconsistent reporting of drug treatments impeded the evidence synthesis. Few studies provided information about sustained benefits at long-term followup. One recently published trial concluded sustained improvement in physical function at 30 months after a rehabilitation program combining self-management and exercise.[62] Heterogeneity in populations, treatments, and definitions of the outcomes downgraded strength of evidence to low or moderate in most cases.

Low-strength evidence resulted mainly from risk of bias: frequent exclusion of patients from the analysis, inadequate allocation concealment, and unmasked outcome assessment. In addition, small trials did not provide precise estimates of the treatment effects. Few studies reported masking of the outcome assessments.[63-68] We could not reproduce the results from several poorly reported studies, and we did not report evidence from individual studies with a high risk of bias. We did not synthesize the evidence from the trials that enrolled patients with knee or hip OA without separately reporting those outcomes. Many trials failed to provide sufficient detail about the nature and intensity of specific interventions or about the involvement of physical therapists, further impeding our ability to draw robust conclusions for decisionmaking.[69,70]

Variability in the definitions and measurements of outcomes presented another obstacle. Validated measurements of functional impairments relevant to physical therapy practice are listed in APTA's Guide to Physical Therapist Practice;[22] however, APTA's Guide recommends neither clinically important thresholds for such measures nor monitoring of treatment effects according to patient-centered outcomes. Most trials reported outcomes as average scores for all patients in each treatment group, with no evaluation of the clinical importance of the averages. Average scores do not reveal how many or which types of patients develop disability or experience clinically meaningful improvements in pain, function, or quality of life.

Furthermore, variability in the definitions of outcomes required us to calculate standardized mean differences. Statistically significant differences in this construct do not necessarily reflect the clinical importance of improvement in outcomes. OARSI has recommended evaluating treatment success according to patient-centered outcomes and clinically important differences in the WOMAC scale.[44,71] In addition, many studies have used the anchor method, which compares changes in scales with patient perception of improvement,[72,73] to determine MCIDs for the 26 validated tests. Yet, published studies of physical therapy interventions have not categorized patients according to meaningful improvements in pain, disability measures, or quality of life. Integrated approaches to evaluating the relationships between impairments in body structures and functions (e.g., strength, range of motion), physical activities (e.g., balance, walking), and participation in activities of daily living would allow better testing of patient-centered outcomes of disability and quality of life.

Treatment success should be measured not just by improvement in scales or performance tests, but by patient satisfaction with improvement in pain and function. The PASS tool is gaining favor as a valid and reliable approach across many areas of medical practice, including rheumatology.[74] PASS is used to identify the level of symptom state patients can tolerate while still considering their health satisfactory and their treatment successful. PASS is available for three scales: WOMAC, VAS for pain, and the Patient Global Assessment. Expanded use of PASS would help improve the quality of physical therapy practice, and increase the usefulness of studies examining physical therapy interventions.

Our report has implications for future research. First, consensus is needed regarding methods to judge benefits of physical therapy interventions.[75] Benefits should be defined as clinically important improvements in pain, independence in ADL, and quality of life. Treatment success should be estimated using rates of patient-centered outcomes. Through meta-analysis of individual patient data from previously conducted RCTs, researchers would be able to categorize patients according to the clinical importance of any changes they experienced. They would also be able to analyze rates of patient-centered outcomes. This would require that principal investigators of RCTs be willing to share their data. Individual patient data meta-analyses may also provide good estimates of treatment effects in patient subpopulations by age, comorbidity, severity of knee OA, and concomitant treatments. Future RCTs should examine comparative effectiveness of combined physical therapy treatments. Fully powered trials should examine comprehensive and multimodal interventions that more closely resemble physical therapy practice. Future studies should also analyze the effects of concomitant treatments such as pain relievers on pain and function.

Key Messages (see Tables E and F)

Key Question 1

- Effectiveness of physical therapy (PT) interventions.
  - Pooled analyses demonstrated the following results for core interventions:
    - Aerobic and aquatic exercise improved disability measures.
    - Aerobic and strengthening exercise reduced pain and improved function.
    - Proprioception exercise reduced pain.
  - Pooled analyses also found that:
    - Tai chi improved short-term function, but with no sustained benefit.
    - Ultrasound reduced pain and improved function.
  - Pooled analyses demonstrated that the following physical therapy interventions failed to show any benefits:
    - Specific education program.
    - Diathermy.
    - Orthotics.
    - Magnetic stimulation (PEMF).
  - Few physical therapy interventions were shown to be effective in general.
  - No single physical therapy intervention was shown to improve all examined outcomes.
  - Research focused on individual physical therapy interventions, in contrast with the common physical therapy practice of combining interventions.
  - Individual (nonpooled) randomized controlled trials (RCTs) failed to show consistent, statistically significant, strong, or clinically important changes in outcomes.
- Comparative effectiveness of physical therapy interventions.
  - Evidence about comparative effectiveness of physical therapy interventions was limited.
  - Pooled analyses demonstrated that:
    - Pain did not differ between aerobic and aquatic exercises.
    - Pain did not differ between electrical stimulation and exercise in pooled analyses.
  - Individual RCTs of other treatment comparisons found no consistent clinically important differences in outcomes and did not support robust conclusions about the best treatment option.
- Which patient characteristics are associated with the benefits of examined physical therapy interventions on intermediate and patient-centered outcomes?
  - Evidence from individual randomized controlled clinical trials did not support robust conclusions about differences in physical therapy effects by patient characteristics. Patients with high compliance tended to have a better treatment response with exercise interventions.
- Do changes in intermediate and patient-centered outcomes differ by the dose, duration, intensity, and frequency of examined physical therapy interventions?
  - The duration of examined interventions was not associated with better intermediate or patient-centered outcomes.
  - Evidence regarding the association between the dose/intensity/frequency of examined interventions and outcomes was not available for the majority of comparisons.
- Do changes in intermediate and patient-centered outcomes differ by the time of followup?
  - The effects of the treatments that significantly improved outcomes, including exercise (aerobic, aquatic, and strengthening) and ultrasound did not differ at shorter versus longer followup times.
  - Electrical stimulation provided short-term pain improvement, but significantly worsened pain at a longer followup.
  - Study risk of bias and heterogeneity in populations and treatments, including concomitant treatments, decreased the strength of evidence to low or moderate in most cases.

Key Question 2

- What is the association between changes in intermediate outcomes and changes in patient-centered outcomes after physical therapy interventions?
  - Gait, mobility restrictions, muscle strength, and range of motion measures were associated with disability measures.
  - Individual observational studies failed to provide strong evidence for determining which intermediate outcomes strongly and consistently predict patient-centered outcomes.
- What is the validity of the tests and measures used to determine intermediate outcomes of physical therapy on osteoarthritis (OA) in association with patient-centered outcomes?

Table E. Summary of pain outcome associated with each physical therapy intervention by strength of evidence

Physical Therapy Intervention	Moderate Strength of Evidence	Low Strength of Evidence
Education program		No improvement
Aerobic exercises		**Improvement**
Aquatic exercises		No improvement
Strengthening exercises		**Improvement**
Tai Chi		No improvement
Proprioception exercises		**Improvement**
Massage		
Joint mobilization		No improvement*
Joint mobilization + exercise		
Orthotics		**Improvement***
Elastic subtalar strapping		
Taping		No improvement*
E-stim		Worse
PEMF	No improvement	
Ultrasound		**Improvement**
Diathermy		No improvement
Heat		No improvement*
Cryotherapy		

E-stim = electrical stimulation; PEMF = pulsed electromagnetic fields.
* Result based on a single study.
Note: Bold = improvement.

  - Many articles reported validation, but few demonstrated a strong (more than 50 percent) correlation between index and reference method measurements.
  - Original studies concluded that tests are valid based on significance, not strength of correlation.

- Which intermediate outcomes meet the criteria of surrogates for patient-centered outcomes?
  - None of the intermediate outcomes met surrogate criteria for patient-centered outcomes.
- What are minimum clinically important differences (MCIDs) of the tests and measures used to determine intermediate outcomes?
  - MCIDs of the tests were determined using the anchor method, which compares changes in scales with patient perception of improvements. MCIDs were available as absolute change in score or as relative change as a percentage difference from baseline levels, the latter accounting for baseline severity of the disease.
  - The definition of Patient Acceptable Symptom State (PASS) that accounted for patient satisfaction was available for Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analog Scale (VAS) for pain, and for the Patient Global Assessment Scale. PASS defines the highest level of symptom state patients can tolerate and still be satisfied with their treatment.
  - Validated tools defined threshold values of clinical importance for evaluating treatment success in adults with knee OA. However, more often studies used continuous measures of the outcomes, providing an average score for all patients in each treatment group, with no evaluation of the clinical importance of these averages. Average scores do not reveal how many or which patients develop disability or experience clinically meaningful improvement in pain, function, or quality of life.

Table F. Summary of disability outcome associated with each physical therapy intervention by strength of evidence		
Physical Therapy Intervention	**Moderate Strength of Evidence**	**Low Strength of Evidence**
Education program		No improvement*
Aerobic exercises		**Improvement**
Aquatic exercises		**Improvement**
Strengthening exercises		No improvement
Tai Chi		No improvement
Proprioception exercises		
Massage		**Improvement***
Joint mobilization		**Improvement***
Joint mobilization + exercise		**Improvement***
Orthotics		**Improvement***
Elastic subtalar strapping		
Taping		No improvement*
E-stim	No inprovement	
PEMF		No improvement*
Ultrasound		No improvement
Diathermy		No improvement
Heat		**Improvement***
Cryotherapy		No improvement*

E-stim = electrical stimulation; PEMF = pulsed electromagnetic fields.
* Result based on a single study.
Note: Bold = improvement.

Key Question 3

- What are the harms from physical therapy interventions available for adult patients with chronic knee pain due to OA when compared with no active treatment or active controls?
  - Adverse events were uncommon, varied across interventions, and included skin irritation with brace/insole/tape/electrical stimulation; swelling with brace/diathermy/exercise; muscle soreness with electrical stimulation; warming/throbbing sensation with diathermy/electrical stimulation/ PEMF; increased pain with diathermy/exercise/ insole/PEMF; and falls with insole. Adverse events were not severe enough to deter participants from continuing treatment.

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Abbreviations

ADL	Activities of Daily Living
AHRQ	Agency for Healthcare Research and Quality
AMED	Allied and Complementary Medicine
APTA	American Physical Therapy Association
BMI	Body Mass Index
CI	Confidence Interval
EQ-5D	European Quality of Life-5 Dimension
E-stim	Electrical Stimulation
IADL	Instrumental Activities of Daily Living
MCID	Minimal Clinically Important Difference
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society
OMERACT	Outcomes Measures in Rheumatoid Arthritis Clinical Trials
PASS	Patient Acceptable Symptom State
PEDro	Physiotherapy Evidence Database
PEMF	Pulsed Electromagnetic Fields
PICOTS	Population, Intervention, Comparator, Outcome, Timing, and Setting
PT	Physical Therapy
RCT	Randomized Controlled Trial
SF-36	Medical Outcomes Study 36-Item Short-Form Health Survey
SMD	Standard Mean Difference
STATA	Statistics and Data Analysis Software
TEP	Technical Expert Panel
VAS	Visual Analog Scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Full Report

This executive summary is part of the following document: Shamliyan TA, Wang S-Y, Olson-Kellogg B, Kane RL. Physical Therapy Interventions for Knee Pain Secondary to Osteoarthritis. Comparative Effectiveness Review No. 77. (Prepared by the University of Minnesota Evidence-based Practice Center under Contract No. 290-2007-10064-I.) Rockville, MD: Agency for Healthcare Research and Quality. AHRQ Publication No. 12(13)-EHC115-EF. November 2012. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

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AHRQ Pub. No. 12(13)-EHC115-1
November 2012