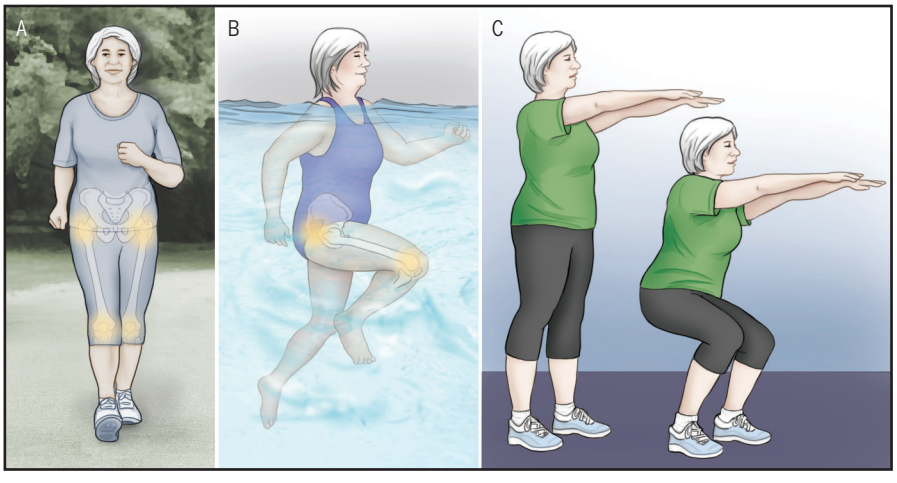
Exercise Is Essential for Osteoarthritis

The Many Benefits of Physical Activity

J Orthop Sports Phys Ther 2018;48(6):448. doi:10.2519/jospt.2018.0507

You may have heard the phrase "exercise is medicine." This may seem like a paradox, but for people with hip and knee osteoarthritis (OA), many high-quality research studies show that exercise therapy is very helpful in decreasing pain and improving joint motion. Physical activity and exercise also help prevent cardiovascular disease, type 2 diabetes, dementia, and many other health conditions. In fact, the right amount of physical activity has been shown to avert 35 health conditions and treat 26 chronic health conditions.

If you have hip and knee OA, you might not be getting enough physical activity and exercise throughout the day to stay healthy. A commentary published in the June 2018 issue of *JOSPT* highlights the importance of learning about the benefits of physical activity and exercise for improving your OA pain and preventing other chronic health conditions that often develop in those diagnosed with hip or knee OA.



STAY ACTIVE AND EXERCISE. If you have hip or knee osteoarthritis, exercise and physical activity may not only help improve your joint pain but can also boost your overall health and quality of life. Physical activity can be as simple as walking (A), biking, or water exercises (B). Strength training is critical to improving your function (C). Consult your physical therapist to design the right program for you.

This *JOSPT* Perspectives for Patients is based on an article by Skou et al, titled "Physical Activity and Exercise Therapy Benefit More Than Just Symptoms and Impairments in People With Hip and Knee Osteoarthritis" (*J Orthop Sports Phys Ther 2018;48(6):439-447. doi:10.2519/jospt.2018.7877*).

This Perspectives article was written by a team of *JOSPT*'s editorial board and staff. Deydre S. Teyhen, PT, PhD, Editor, and Jeanne Robertson, Illustrator.

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NEW INSIGHTS

The commentary's authors summarized 96 articles to best describe the benefits of exercise for those with hip and knee OA. The researchers reviewed the benefits of physical activity and exercise and how they often result in better outcomes than medications, injections, and surgery. The commentary specifically highlights the positive effects of exercise therapy in treating the symptoms of OA and discusses the "dose" (frequency, duration, and intensity) of supervised therapy and home exercises. Finally, the authors reviewed the evidence favoring physical activity for your overall health, including your heart, pancreas, and brain.

PRACTICAL ADVICE

The authors offer 7 key recommendations. (1) Exercise and physical activity should be tailored to your needs and preferences. (2) Consider water exercises if it is too painful to exercise on land. (3) Supervised exercise therapy over a 6-week period is often helpful to get you started. (4) Some people may need 12 weeks of supervised therapy to begin. (5) After you complete supervised therapy, you may need periodic "booster sessions" to help with long-term management of your OA pain and overall health. (6) Home exercises should be performed to optimize your outcomes. (7) You should be sure you understand how to manage flare-ups in pain and how to modify your exercises when pain increases.

The benefits of exercise and physical activity are numerous: they help fight cancer, heart disease, diabetes, and osteoporosis, and improve your mental health. Your physical therapist can help design the right program for you.

LETTER TO THE EDITOR-IN-CHIEF

Letters to the Editor are reviewed and selected for publication based on the relevance, importance, appropriateness, and timeliness of the topic. Please see submission guidelines at www.jospt.org for further information. J Orthop Sports Phys Ther 2018;48(6):514-515. doi:10.2519/jospt.2018.0202

THE ROOT METHOD AS FICTION: THE ORIGINAL REFERENCES

I commend Harradine, Gates, and Bowen for their Viewpoint titled "If It Doesn't Work, Why Do We Still Do It? The Continuing Use of Subtalar Joint Neutral Theory in the Face of Overpowering Critical Research,"[4] published in the March 2018 issue of *JOSPT*, in which the authors make a substantial and important statement about the continued professional application of the Root method for biomechanical orthotic prescription.[11-13] The authors point to the model as a "fiction" that is neither valid nor reliable. Most alarming and regrettable is the continued publication of the application of the Root method by both podiatrists and physical therapists. While this paper is timely and makes a valuable criticism of the state of the art, I was surprised and disappointed not to find any reference to the monumental commentary on the Root method by McPoil and Hunt[8] in 1995, or to the contributions to the same criticism by McPoil and Cornwall[7] in 1994 and Cornwall and McPoil[3] in 1995.

McPoil and Hunt[8] provided a nearly identical analysis and assessment of the Root method in an issue dedicated to the foot and ankle in this very journal (*JOSPT*) in 1995. In this article, McPoil and Hunt[8] cite poor reliability between evaluators in application of the Root method. Harradine et al,[4] in their Viewpoint, cite a study by Jarvis et al,[5] examining the reliability of the Root model. Jarvis et al,[5] in turn, cite McPoil and Cornwall[7] and Cornwall and McPoil[2,3] on the lack of reliability in measurement of the biomechanics of the subtalar joint and the gait cycle. McPoil and Hunt[8] also examined the only research referenced by Root and colleagues, the work of Wright et al[14] published in 1964, to explain the Root method's validity issues with normal foot alignment and subtalar joint positions during the gait cycle.

Wright et al[14] examined only 2 individuals, both male, raising questions of generalizability due to the small sample size and sex bias. McPoil and Hunt[8] suggest that Root misinterpreted Wright et al's[14] definition of the neutral position of the subtalar joint, which is actually "relaxed calcaneal stance position," rather than Root's "neutral subtalar joint position." Wright et al's[14] description of subtalar motion during the gait cycle was confirmed by McPoil and Cornwall in 1994.[7] McPoil et al[9] earlier demonstrated that Root's concept of subtalar neutral as a normal biomechanical pattern in the gait cycle was inaccurate, with only 17% of tested individuals demonstrating foot mechanics similar to that described by Root.

Interestingly, Harradine et al[4] also cite Lee[6] as a past historical review on the topic. The abstract from Lee's article states that the article "also discusses several important emergent models (the models of Dananberg, Kirby, Fuller, McPoil, Hunt, and Demp) that have gained increasing popularity among the podiatric and nonpodiatric clinical communities over the last 10 to 15 years."[6] Harradine et al,[4] therefore, reference articles that bridge the work of McPoil, Cornwall, and Hunt to the forefront, but fail to cite these primary sources that provide an overwhelming critique of the Root method.

The omission of these references likely reflects the 23 years since their publication in 1995. I believe that the publication by McPoil and Hunt[8] is one of the top 10 articles published in our profession, and has been a game changer for my career. That article by McPoil and Hunt[8] is one of those special articles published in *JOSPT* that contributes significantly to this journal's impact factor. McPoil and Hunt[8] deserve special mention, lest we fall victim to institutional amnesia.[10]

I commend *JOSPT* for publishing Harradine et al's[4] important editorial message to health care professionals working with musculoskeletal conditions of the lower kinetic chain. I agree that we should abandon the Root method and instead consider the adoption of other models for the examination and management of foot disorders, including the "tissue stress model" proposed by McPoil and Hunt.[8]

The greater tragedy is that Harradine et al[4] must remind us of the folly of our profession's continued use and promotion of the Root method nearly a generation after McPoil and Hunt[8] made a similar conclusion. Where is the evidence-based practice? The American Physical Therapy Association encourages evidence-based practice as follows: "The physical therapy profession recognizes the use of evidence-based practice (EBP) as central to providing high-quality care and decreasing unwarranted variation in practice. EBP includes the integration of best available research, clinical expertise, and patient values and circumstances related to patient and client management, practice management, and health policy decision-making."[1]

The physical therapy professional can't lay claim to an evidence-based practice if that practice continues to embrace a methodology based on a fiction, and if we fail to reform our practice in response to a preponderance of scientific evidence, then the method is invalid and unreliable.

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RESPONSE

Thank you for your letter and for highlighting the work by Cornwall and McPoil[1,2] and McPoil and Cornwall.[4] We are aware of their research but had not cited this work directly due to the word limit and reference restriction in an editorial-type publication. Instead, we focused[3] on more recent papers and a different approach to understanding why, in the presence of such critical work, the use of subtalar joint neutral theory is still so prevalent.

We do agree that Cornwall and McPoil's[1,2] and McPoil and Cornwall's[4] work was important in the development and progression of our understanding of how to treat the foot and ankle. Further interest and reading (hopefully as a result of our Viewpoint[3]) will lay bare their valuable contributions to any clinician or researcher.

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Physical Impairments in Adults With Ankle Osteoarthritis: A Systematic Review and Meta-analysis

STUDY DESIGN: Systematic review with meta-analysis.

BACKGROUND: Lower-limb osteoarthritis (OA) is associated with pain and reduced function. Most research focuses on hip and knee OA–related impairments; consequently, impairments that characterize ankle OA are not well understood.

OBJECTIVE: To systematically review available evidence of physical impairments in individuals with ankle OA.

METHODS: A comprehensive search of electronic databases was conducted from their inception to July 2017. Studies were screened using predefined inclusion/exclusion criteria. Studies that compared physical measures (excluding gait) between individuals with ankle OA and healthy controls or the unaffected ankle were included. Two reviewers rated studies for quality. Meta-analyses with random effects were conducted when appropriate.

RESULTS: Of 4565 identified studies (563 participants), 8 satisfied the inclusion criteria and 3 studies were included in meta-analyses. All studies evaluated a range of impairments at end-stage OA, and exhibited poor reporting of missing data, assessor blinding, and measurement validity. Meta-analyses revealed large impairments of ankle sagittal plane motion and strength. Evidence from single studies indicated large deficits of ankle frontal plane motion and strength, talar translation and rotation on arthrometry, balance, and electromyography of ankle joint muscles. There were also abnormal bony alignments and greater fatty infiltrate in all calf muscle compartments.

CONCLUSION: The results of this literature review suggest significant ankle motion, strength, and functional impairments in individuals with ankle OA. The strength of the conclusions is limited, due to the small number and methodological limitations of published studies.

LEVEL OF EVIDENCE: Symptom prevalence, level 1a. *J Orthop Sports Phys Ther 2018;48(6):449-459. Epub 7 Apr 2018. doi:10.2519/jospt.2018.7569*

KEY WORDS: *ankle joint, osteoarthritis, physical impairment, systematic review*

Osteoarthritis (OA) is one of the most prevalent and costly[3,73] health conditions and causes of disability.[5,63,82] The World Health Organization estimates that 80% of people with OA are limited in their movement, and 25% are unable to perform many daily activities.[94] Ankle OA affects approximately 70 million people worldwide.[73] It is predominantly associated with previous ankle trauma, including ankle sprains[22,23,33,84] and fractures.[5,70] Given that ankle sprains are the most common injury among sportspeople and the most common injury seen in US emergency departments,[23,24,89] the incidence of ankle OA is a considerable health concern. There is evidence that individuals with posttraumatic ankle OA report higher levels of disability, measured by the ankle osteoarthritis scale, relative to age-matched controls.[91] Studies investigating quality of life indicate that mental and physical disability associated with ankle OA is similar to that of individuals with end-stage hip OA,[21] renal disease, radiculopathy, and congestive heart failure.[71] Due to the posttraumatic origin of ankle OA, it affects a younger population than OA of other joints.[5,70] The disability associated with ankle OA may negatively impact earning potential and the ability to meet familial obligations.

In contrast to hip and knee OA, management options for ankle OA are limited, with lower success rates and less favorable long-term outcomes following surgical intervention.[16,43,65,68,75] Physical therapy is frequently used to manage pain and disability associated with OA.[60] The goals of intervention are often achieved by addressing physical impairments, such as low muscle strength/endurance, limited range of motion (ROM), and poor balance,[7,35,36] which improves pain and function.[19,72] Recent International Ankle Consortium recommendations highlight the need to address and raise awareness and understanding of consequences of lateral ankle sprain,[23,24] of which ankle OA is one. At the moment, it is challenging to determine which impairment

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should take priority as a therapeutic target for patients with ankle OA. Consistent with International Ankle Consortium recommendations,[23,24] an improved understanding of the scope and extent of physical impairments in persons with ankle OA is required. Further, understanding key impairments in ankle OA will inform the selection of outcome measures and the development of nonsurgical interventions for studies investigating disease management. This systematic review aimed to document reported physical impairments in adults with ankle OA, by comparing affected and unaffected sides in adults with unilateral ankle OA and healthy controls.

METHODS

Design

The protocol for this review was registered with the International Prospective Register of Systematic Reviews (PROSPERO registration number CRD42016036720). The following variations from the protocol were implemented: (*a*) gait-related outcomes were excluded from this review, as they were deemed of sufficient quantum to warrant a separate review; and (*b*) the I^2 statistic was used as the indicator of statistical homogeneity instead of the chi-square statistic. Reporting was conducted in accordance with the Meta-analysis Of Observational Studies in Epidemiology criteria[78] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement.[27,55]

Search Strategy

A comprehensive search strategy was devised in collaboration with a medical librarian. Three sets of entry strings were combined with AND. The first set of terms included synonyms for ankle OA, and the second set specified anatomical location. The terms in each set were combined using OR. Those 2 sets of search strings were combined using AND to a third search string consisting of physical outcomes and synonyms (ROM, muscle strength, balance, and proprioception). Finally, a set of NOT terms (searched in titles and abstracts) was used to exclude animal, cadaveric, and pediatric studies, and papers investigating unrelated health conditions, such as anterior cruciate ligament injury, patellofemoral pain, or hallux valgus. PubMed, Embase, CINAHL, Web of Science, and SPORTDiscus databases were searched, with no language or date restriction. The detailed search algorithms for different databases are presented in **APPENDIX A** (available at www.jospt.org).

Eligibility Criteria

Retrieved titles and abstracts were screened for eligibility using the following criteria: (1) the study investigated physical impairments associated with ankle OA, and (2) the study compared physical impairments between individuals with and without ankle OA or compared the affected and unaffected sides in individuals with ankle OA. Intervention studies were eligible for inclusion if preintervention measures were compared to individuals without ankle OA or to the unaffected side. Studies of different types of arthritis (eg, rheumatoid arthritis, septic arthritis) were only included if data for ankle OA were reported separately. Case reports, descriptions of surgical techniques, and abstracts from scientific meetings were excluded.

Study Selection

One author (M.M.) screened all articles identified in the literature search using the predefined inclusion and exclusion criteria. A second author (M.D.S.) screened a randomly selected 5% of the total studies. Full articles were retrieved and screened when inclusion could not be determined by reading the title and abstract. Translations were sought to determine the eligibility of 5 non-English publications (3 French, 1 German, and 1 Korean), 1 of which was eligible. Reference lists of all eligible studies were manually screened for potential studies not found by the electronic database search. The final eligibility of selected publications was determined by consensus with all authors.

Assessment of Study Quality and Risk of Bias

Quality assessment of all eligible studies was completed using the Epidemiological Appraisal Instrument (EAI).[20] The EAI has demonstrated good/excellent validity and good to excellent intrarater and interrater reliability.[20] Ten of the original EAI items (related to intervention, randomization, and follow-up) were not used, because they did not apply to cross-sectional and case-control study designs. Two reviewers (M.M. and D.A.M.) independently rated each article after deidentification by removal of authors, journal, and title. Scores were compared for consensus, and disagreements were resolved by a third investigator (although this was not necessary). The overall score was recorded as an average of the scores from all applicable items (range, 0-1).

Data Extraction

Data from eligible studies were extracted into a predesigned evidence table by one reviewer (M.M.) and verified by a second (D.A.M.). The following data were extracted from eligible studies: authors, publication year, country, study objectives as stated by the authors, study design, OA definition/diagnosis, population characteristics, comparisons made, outcome measures, measurement tools used, and study findings (values expressed as mean ± SD).

Data Analysis

Kappa statistics were used to report the interrater reliability between the 2 assessors for study selection and quality assessment. Interrater reliability was categorized as poor (less than 0.00), slight (0.00-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80), or almost perfect (0.81-1.00).[44] Data were analyzed using SPSS Version 17 software (IBM Corporation, Armonk, NY).

Studies with similar outcome measures and methods were considered for meta-analyses using RevMan 5 (The

Nordic Cochrane Centre, Copenhagen, Denmark). Heterogeneity was assessed by inspecting the I^2 statistic and was considered unacceptably high for values greater than 75%.[13] When homogeneity was less than or equal to 75%, data were pooled in a statistical meta-analysis with random effects.

Data representing point estimates of effect are presented as standardized mean differences (SMDs) and their confidence intervals (CIs) in tabular format, and in forest plots where appropriate. The SMD was calculated as the difference between ankle OA and control group means divided by the pooled standard deviation for all outcomes. For papers in which the standard deviation was not available, it was calculated as the product of the standard error of the mean and the square root of the sample size.[31] Differences in outcomes between the affected side in individuals with ankle OA and controls were calculated such that negative differences indicated that the measure for ankle OA was lower relative to controls, and positive differences indicated the opposite. Between-group differences were considered significant if the 95% CI did not contain zero. Effect sizes were interpreted as small (SMD greater than 0.2), medium (greater than 0.5), and large (greater than 0.8).[11] The SMD (CI) is reported throughout the text to provide a point estimate of effect for comparisons between measures with different units.

RESULTS

Study Selection

The search identified 4565 results, with 3439 unique studies remaining after removal of duplicates. After screening titles and abstracts, 28 full-text articles were assessed for eligibility. It was decided to exclude gait-related measures (n = 14) from this review, due to the quantum of papers, which warrants a separate review. Corresponding authors were contacted when information unavailable in the paper was needed to determine eligibility.[85,86,91] Eight studies met the eligibility criteria (**FIGURE 1**). There were no disagreements between the 2 reviewers in the eligibility assessment (undertaken on a random 5% [n = 172] of the studies identified). A subsequent manual reference list search of included studies did not reveal any additional studies.

Assessment of Study Quality and Risk of Bias

There were no disagreements between the 2 raters among the 264 quality assessment items rated (κ = 1.000, P<.01). The EAI quality assessment demonstrated a median score of 0.36 out of 1 (range, 0.30-0.56) (**APPENDIX B**, available at www.jospt.org). Descriptions of the research objectives,[29,38,47,48,58,86,90,91] study design,[29,38,47,48,58,86,90,91] main outcomes,[29,38,48,58,86,91] standardized assessment of outcomes,[29,38,48,58,86,90] and key findings[29,38,47,48,58,86,90,91] were addressed in most studies. The items that were not well addressed were a priori sample-size calculation,[90] missing data and dropouts,[29] and assessor blinding.[38] Three studies[38,86,90] collected prior history of ankle injuries as a contributing factor to OA development, but only 1 study[86] included this information in the analysis. No study reported the results by age or sex. Only 2 studies reported the validity of their main measures,[58,90] and 2 provided information about the psychometric properties of the physical impairment measures.[47,86]

Study Characteristics

All studies were published between 2006 and 2013 and conducted in the following geographical locations: Switzerland (n = 2),[58,90] Korea (n = 2),[47,48] Japan (n = 1),[29] the United States (n = 2),[38,91] and Canada (n = 1).[86] There were a total of 343 participants with ankle OA and 220 controls across studies. Individual study sample sizes ranged from 10 (5 ankle OA and 5 controls)[91] to 154 (104 ankle OA and 50

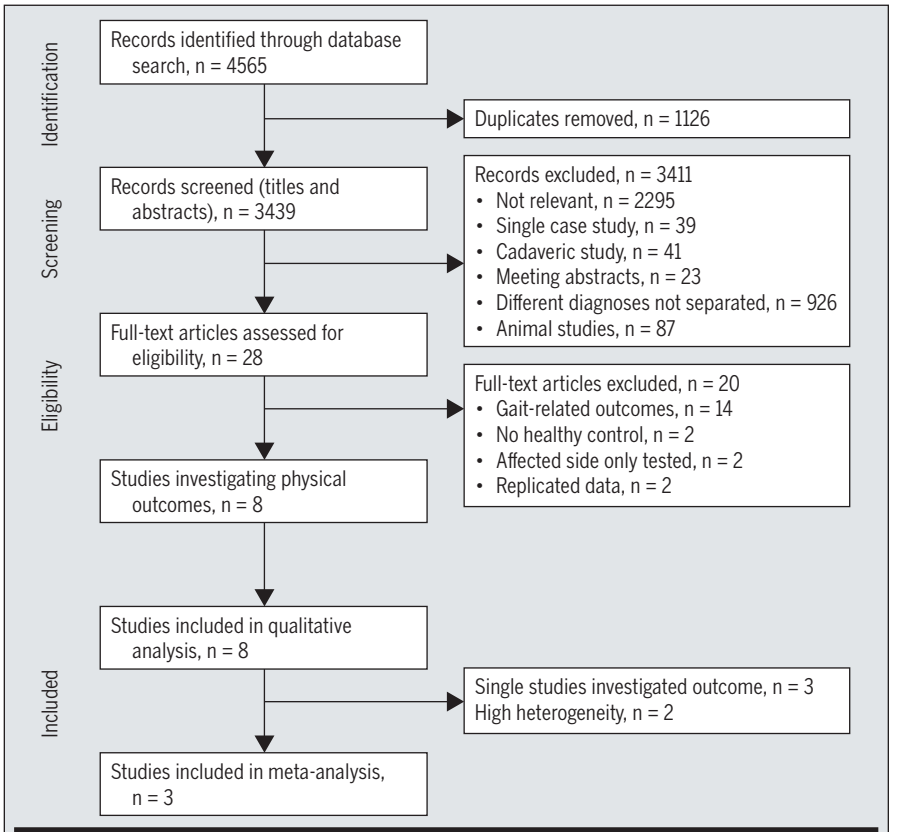


FIGURE 1. PRISMA 2009 flow diagram for the selection process.

controls) participants.[47] Seven studies compared data between individuals with ankle OA and controls,[29,38,47,48,58,86,91] and 4 studies compared the affected and unaffected ankles in individuals with ankle OA[38,58,86,90] (with 3 studies reporting both comparisons[38,58,86]).Characteristics of studies included in the review are presented in the **TABLE**.

OA Diagnosis

The majority of studies used radiographic imaging to establish the presence of OA (n = 7).[29,38,47,48,86,90,91] One study did not specify the method of establishing OA diagnosis.[58] Four studies[29,48,86,90] reported radiographic classification criteria used to establish a diagnosis of ankle OA, and 3 studies did not specify how the radiographs were evaluated.[38,47,91] No study provided information on reliability of the radiographic classification system.

The radiographic classifications used were the 3-stage Morrey and Wiedeman[56] classification (n = 2)[86,90] and the modified 5-stage Takakura classification[80] (n = 2).[29,48] The Morrey and Wiedeman and the modified Takakura classification systems have similar early-stage (1 and 2) OA definitions (eg, early sclerosis, minimum narrowing, and osteophyte formation). The modified Takakura classification includes an intermediate stage 3 OA classification that further differentiates the extent of joint space narrowing and subchondral bone contact. The advanced-stage OA is similar in both classifications (eg, gross deformity, ankyloses, no joint space, and bone contact). For this systematic review, ankle OA radiographic severity was collapsed to 3 categories incorporating both classifications: mild (stage 1), moderate (stage 2), and advanced OA (stages 3-4) (**APPENDIX C**, available at www.jospt.org).

Meta-analyses

Three studies contributed data to the meta-analyses of total sagittal plane ROM, calf circumference, and maximal voluntary isometric dorsiflexion (DF) and plantar flexion (PF) strength. Data (SMD and CI) are presented in forest plots (**FIGURES 2** and **3**). Large effects were identified for sagittal plane ROM (2 studies[86,90]) and maximal voluntary isometric strength (2 studies[58,86]). Pooled data indicate less sagittal plane ROM on the affected compared to the unaffected side in individuals with ankle OA, and lower maximum ankle DF and PF torque on the affected side in individuals with ankle OA compared to controls.

TABLE Characteristics of Studies Included in the Review

Study	Country	EAI Quality Score	OA Cases*	Control Cases*	Outcomes Investigated	Results
Hayashi et al[29]	Japan	0.56	n = 80 (15 male, 65 female) Age, 64 y (32-85 y)	n = 50 (10 male, 40 female) Age, 39 y (13-86 y)	Radiographic bony alignment	Progressive increased TPC angle from mild OA to moderate OA, then decreased in advanced OA, compared to controls Lower TTS and TAS angles in all stages of ankle OA compared to controls Smaller TAS and TLS angles in individuals with ankle OA compared to controls Greater TMM angle in advanced OA and less TTS angle in moderate and advanced ankle OA compared to controls
Hubbard et al[38]	United States	0.33	n = 8 (4 male, 4 female) Age, 51.8 ± 11.41 y	n = 8 (4 male, 4 female) Age, 51.5 ± 11.2 y	Mechanical stability DF/PF and inversion/eversion muscle torque Static balance	Less anterior displacement on the affected ankle compared to the unaffected ankle in individuals with ankle OA and controls Less inversion and eversion rotation on the affected compared to the unaffected ankle in individuals with ankle OA and controls No difference in posterior displacement between sides or groups Greater total center-of-pressure displacement and total velocity Greater mediolateral velocity and anteroposterior sway in individuals with OA compared to controls Weaker DF, PF, inversion, and eversion on the affected ankle compared to the unaffected ankle in individuals with ankle OA and controls
Lee et al[47]	Korea	0.36	n = 104 (72 male, 32 female) Age, 62 y (22-77 y)	n = 50	Radiographic bony alignment	Smaller tibiotalar ratio† in individuals with ankle OA than in controls
Lee et al[48]	Korea	0.39	n = 98 (47 male, 51 female) Age, 58.2 y (43-78 y)	n = 80 (57 male, 23 female) Age, 23.4 y (18-25 y)	Radiographic bony alignment	Greater talar tilt angle on affected ankle than in controls Smaller TAS and TLS angles, and an increase in TMM angle, as the stage of OA progressed compared to controls
Nüesch et al[58]	Switzerland	0.35	n = 12 (6 male, 6 female) Age, 56.60 y	n = 12 (7 male, 5 female) Age, 48.41 y	Calf circumference DF/PF muscle torque	No difference in calf circumference on the affected side compared to the unaffected side and controls Significant DF/PF weakness on the affected side compared to controls

Table continues on page 453.

Outcomes From Single Studies

Single studies assessed ROM, torque, calf circumference, ankle arthrometry, bony alignment, muscle electromyography (EMG), calf cross-sectional area (CSA), and fatty infiltration in calf muscles in individuals with ankle OA compared to controls or the individual's unaffected side. Pooling of data was not possible due to differences in reported outcomes or methods of measurement, or high heterogeneity. All data pertaining to effect sizes for outcomes are presented in **APPENDIX D** (available at www.jospt.org), and outcomes with large effect sizes are reported below.

Range of Motion One study compared total ankle DF and PF (sagittal) ROM and inversion and eversion (frontal) ROM between individuals with ankle OA and controls, with frontal plane ROM also compared between sides in individuals with ankle OA[86] (sagittal plane ROM reported in meta-analysis). Large effects were found for less frontal and sagittal plane ROM in individuals with ankle OA compared to controls, and less frontal plane ROM in individuals with ankle OA compared to the unaffected side.[86]

Ankle Arthrometry One study[38] used a portable ankle arthrometer (Blue Bay Research Inc, Navarre, FL) to measure anterior-to-posterior displacement and inversion-to-eversion rotation. Large SMDs indicated less anterior displacement and inversion and eversion rotation on the affected ankle in people with OA compared to the unaffected ankle and controls. Eversion rotation was also less on the unaffected side in individuals with ankle OA than in controls.

Calf CSA and Fatty Infiltration One magnetic resonance imaging study[90] quantified CSA and fatty infiltration in the medial and lateral gastrocnemius and soleus muscles and the anterior, lateral, and deep posterior compartments of the calf in individuals with ankle OA. Large effects indicated smaller soleus CSA, smaller overall anatomical calf CSA, and greater fatty infiltration in all muscles/compartments in the affected compared to the unaffected side in individuals with ankle OA.

TABLE Characteristics of Studies Included in the Review (continued)

Study	Country	EAI Quality Score	OA Cases*	Control Cases*	Outcomes Investigated	Results
Valderrabano et al[86]	Canada	0.36	n = 15 (6 male, 9 female) Age, 53.3 y (33-74 y)	n = 15 (6 male, 9 female) Age, 52.9 y (27-65 y)	Total DF/PF ROM Calf circumference DF/PF muscle torque Surface EMG amplitude and frequency during muscle maximum voluntary contraction	Less total DF/PF ROM on the affected side compared to the unaffected side No difference in calf circumference on the affected side compared to the unaffected side and controls Significant DF/PF weakness on the affected side compared to the unaffected side and controls No difference in calcaneal alignment between individuals with moderate to advanced OA and controls or between sides in individuals with OA Mean EMG frequency was lower for all tested muscles on the affected compared to the unaffected side in individuals with ankle OA Lower anterior tibial and medial gastrocnemius EMG frequencies in individuals with ankle OA compared to controls Lower medial gastrocnemius, but not anterior tibial, peroneus longus, or soleus, EMG amplitude in individuals with ankle OA compared to controls
Wiewiorski et al[90]	Switzerland	0.41	n = 21 (10 male, 11 female) Age, 35-76 y	Unaffected side	Total DF/PF ROM Calf circumference Muscle cross-sectional area Muscle fatty infiltration	Less total DF/PF ROM and lower calf circumference on the affected side compared to the unaffected side Greater fatty infiltration and smaller overall anatomical cross-sectional area in all compartments and muscles on the affected compared to the unaffected side in individuals with ankle OA Smaller cross-sectional area for the soleus and the deep posterior muscles on the affected compared to the unaffected side
Wikstrom and Anderson[91]	United States	0.30	n = 5 Age, 63.4 ± 11.3 y	n = 5 Age, 60.0 ± 3.0 y	Standing balance	Greater anteroposterior sway in individuals with OA compared to controls

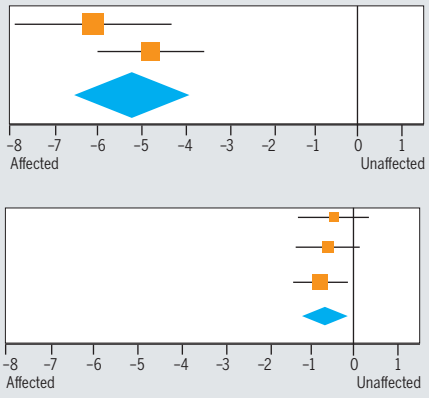
Abbreviations: DF, dorsiflexion; EAI, Epidemiological Appraisal Instrument; EMG, electromyography; OA, osteoarthritis; PF, plantar flexion; ROM, range of motion; TAS, angle between the tibial shaft and tibial articular surface in the frontal plane on weight-bearing X-ray; TLS, angle between the tibial shaft axis and the articular surface of the tibial shaft in the sagittal plane on weight-bearing X-ray; TMM, angle between the distal third of the tibial shaft and the medial malleolar joint surface; TPC, angle between the tibial shaft axis and the articular surface of the posterior facet of the calcaneus; TTS, angle between the tibial shaft and the articular surface of the talar dome.

**Values for age are mean, mean ± SD, mean (range), or range.*

†Ratio into which the mid-longitudinal axis of the tibial shaft divides the longitudinal talar length.

Affected Side Versus Unaffected Side in Individuals With Osteoarthritis

Measure/Study	Affected Mean ± SD	Affected Total, n	Unaffected Mean ± SD	Unaffected Total, n	Weight	SMD IV, Random (95% CI)
Total DF/PF ROM, deg						
Valderrabano et al[86]	16.0 ± 7.6	15	56.7 ± 5.23	15	37.2%	−6.07 (−7.87, −4.27)
Wiewiorski et al[90]	18.1 ± 9.15	21	56.0 ± 6.25	21	62.8%	−4.75 (−5.97, −3.52)
Total*		36		36	100.0%	−5.24 (−6.49, −3.98)
Calf circumference, cm						
Nüesch et al[58]	38.19 ± 2.36	12	39.42 ± 2.74	12	25.6%	−0.46 (−1.28, 0.35)
Valderrabano et al[86]	32.7 ± 3.45	15	34.8 ± 3.44	15	31.5%	−0.59 (−1.33, 0.14)
Wiewiorski et al[90]	33.2 ± 2.65	21	35.3 ± 2.76	21	42.9%	−0.76 (−1.39, −0.13)
Total†		48		48	100.0%	−0.63 (−1.04, −0.22)

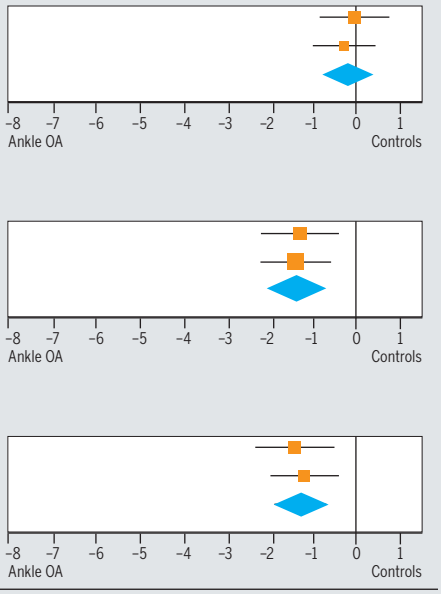


Abbreviations: CI, confidence interval; DF, dorsiflexion; IV, independent variable; PF, plantar flexion; ROM, range of motion; SMD, standardized mean difference.
**Heterogeneity: $\tau^2 = 0.26$, $\chi^2 = 1.42$, $df = 1$ ($P = .23$), $I^2 = 30\%$.*
†Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.34$, $df = 2$ ($P = .84$), $I^2 = 0\%$.

FIGURE 2. Forest plots for outcomes between affected and unaffected sides in individuals with ankle osteoarthritis.

Affected Side of Individuals With OA Versus Controls

Measure/Study	Ankle OA Mean ± SD	Ankle OA Total, n	Control Mean ± SD	Control Total, n	Weight	SMD IV, Random (95% CI)
Calf circumference, cm						
Nüesch et al[58]	38.19 ± 2.36	12	38.29 ± 2.67	12	44.7%	−0.04 (−0.84, 0.76)
Valderrabano et al[86]	32.7 ± 3.45	15	33.6 ± 2.8	15	55.3%	−0.28 (−1.00, 0.44)
Total*		27		27	100.0%	−0.17 (−0.71, 0.36)
Maximal voluntary isometric DF, Nm						
Nüesch et al[58]	11.1 ± 7.96	12	26.3 ± 13.86	12	44.9%	−1.30 (−2.19, −0.40)
Valderrabano et al[86]	16.4 ± 4.9	15	27.1 ± 9.4	15	55.1%	−1.39 (−1.95, −0.75)
Total†		27		27	100.0%	−1.35 (−1.95, −0.75)
Maximal voluntary isometric PF, Nm						
Nüesch et al[58]	20.9 ± 7.62	12	36.9 ± 13.51	12	42.6%	−1.41 (−2.32, −0.50)
Valderrabano et al[86]	15.8 ± 7.6	15	30.7 ± 15.5	15	57.4%	−1.19 (−1.97, −0.40)
Total‡		27		27	100.0%	−1.28 (−1.88, −0.69)



Abbreviations: CI, confidence interval; DF, dorsiflexion; IV, independent variable; OA, osteoarthritis; PF, plantar flexion; SMD, standardized mean difference.
**Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.19$, $df = 1$ ($P = .66$), $I^2 = 0\%$.*
†Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.02$, $df = 1$ ($P = .88$), $I^2 = 0\%$.
‡Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.13$, $df = 1$ ($P = .72$), $I^2 = 0\%$.

FIGURE 3. Forest plots for outcomes between individuals with ankle osteoarthritis and controls.

Joint Torque Comparison of DF and PF torque between sides in individuals with ankle OA indicated lower torque on the affected than on the unaffected side.[86] Ankle DF, PF, and inversion and eversion torque normalized to body weight was less on the affected and unaffected ankles in individuals with OA compared to controls.[38] There were also large deficit effects for normalized eversion and inversion torque on the affected compared to the unaffected side in individuals with ankle OA.

Muscle EMG Large SMDs from 1 study indicated lower medial gastrocnemius EMG amplitude and lower anterior tibial and medial gastrocnemius muscle EMG frequencies on the affected side in individuals with ankle OA compared to controls.[86] Electromyography frequency on the affected side was also lower for the medial gastrocnemius, soleus, and peroneus longus compared to the unaffected side.

Standing Balance Balance during double-leg stance was assessed in 2 studies using different testing methodology and outcomes.[38,91] Data indicated greater total center-of-pressure displacement and velocity,[38] mediolateral velocity,[38] and anteroposterior sway[91] in individuals with OA compared to controls.

Bony Alignment Alignment data were identified in 4 studies using radiographic[29,47,48] or goniometric measures.[86] The angle between the distal third of the tibial shaft and the joint surface of the medial malleolus was greater in those with advanced OA,[29,48] and the angle between the tibial shaft and the articular surface of the talar dome was less for those with moderate and advanced ankle OA compared to controls, both measures indicating greater varus in those with ankle OA. Individuals with moderate and advanced ankle OA also had a greater angle between the articular surface of the talar dome and the posterior facet of the calcaneus than did controls.[29] The angles between the tibial shaft and tibial articular surface in the frontal and sagittal planes were assessed in 2 studies,[29,48] which could not be pooled due to high heterogeneity (I^2 values greater than 75%). Large effects indicated that the angle between the tibial shaft and tibial articular surface in the frontal plane (2 studies[29,48]) and sagittal plane (1 study[48]) was smaller for individuals with moderate and advanced ankle OA compared to controls. The tibiotalar ratio (the mid-longitudinal axis of the tibial shaft divided by that of the talus)[47] was smaller in individuals with advanced ankle OA than in controls. The SMDs for talar tilt angle (the angle between talocrural joint surfaces with the ankle in supination[69]) could not be calculated due to a standard deviation of zero in the control group.[48]

DISCUSSION

This systematic review synthesized data from 8 studies investigating physical impairments in individuals with ankle OA compared to controls or the unaffected side. The quality appraisal highlighted a general lack of reporting missing data, assessor blinding, and measurement validity. Meta-analyses of 3 studies provided evidence of less sagittal plane ROM and smaller calf circumference on the affected compared to the unaffected side in individuals with ankle OA, and lower ankle torque production in individuals with ankle OA compared to controls. Evidence from single studies reported less total frontal plane ROM, lower frontal plane torque production, and less talar translation and rotation on arthrometry on the affected compared to the unaffected side in people with ankle OA and to controls. Single studies also reported more fatty infiltration, smaller muscle CSA, and a shift toward lower EMG frequencies for some muscles that influence ankle movements on the affected compared to the unaffected side, with differences in bony alignment on the affected ankle compared to controls.

Ankle OA impairments are likely present as elements of a complex pathoetiologic paradigm. Limited joint mobility is one of the clinical signs of OA[10,76,77,87] and is commonly present after an ankle sprain.[34,62] Large ROM differences are present between affected and unaffected ankles in individuals with ankle OA[86,90] and between the affected ankle in individuals with ankle OA and controls.[86] Limited motion may be due to factors such as shortened musculotendinous structures (ie, shortened gastrocnemius-soleus complex),[17,18] limited accessory or physiological joint motions (ie, limited talar glide)[8,12,45] due to degeneration or capsular restriction,[14] or chronic inflammation or pain.[93] Consistent with restricted ankle ROM, individuals with ankle OA have less anterior talar translation and inversion and eversion rotation on arthrometry compared to controls. Those findings suggest that ROM deficits in individuals with ankle OA are related to joint restriction, in addition to potentially shortened musculotendinous structures. Because only total ankle ROM is reported, it is unclear whether ROM deficits at the ankle are due to PF restriction, DF restriction, or both. This is important because reduced ankle DF has been associated with impaired gait and compromised balance and function.[2,15,25,26,52,88] An improved understanding of underlying mechanisms of movement restriction could lead to improved patient management.

Large differences in isometric PF, DF, inversion, and eversion torque production were found between the affected side in individuals with ankle OA and controls. Lower PF torque production is consistent with findings of lower medial gastrocnemius EMG amplitude and frequency in individuals with ankle OA (affected side) compared to controls. The relationship between lower torque production in other directions of ankle movement and EMG amplitude/frequency of relevant muscles was not readily apparent, and the interpretation of altered EMG findings is unclear. Lower EMG amplitude and muscle strength may be due to an inability of the central nervous system to fully activate the muscle[37] (arthrogenous muscle inhibition), which has been shown

in knee OA,[40,59] post knee trauma,[39] in acute ankle sprains,[41] and in functional ankle instability.[51] Osteoarthritis-related muscle inhibition is thought to occur due to pain,[1,28,59] joint immobilization,[86] and altered sensory output accompanying articular cartilage structural changes.[42,61]

Weaker muscles and lower muscle activation may contribute to, or be a consequence of, muscle atrophy. Calf circumference was smaller on the affected compared to the unaffected side in individuals with ankle OA, but not between individuals with ankle OA and controls. The difference in calf circumference between the affected and unaffected sides in individuals with ankle OA[58,86,90] was driven by the findings of Wiewiorski et al.[90] Greater fatty infiltration and smaller posterior muscle size[90] may contribute to smaller calf circumference and muscle weakness on the affected side in individuals with ankle OA. The hypertrophy/increased muscle CSA on the unaffected side in individuals with ankle OA may be an adaptation related to increased use of the unaffected side in individuals with unilateral ankle OA.

Although only investigated in studies with small sample sizes,[38,91] balance was impaired in individuals with ankle OA compared to controls. Standing balance[4,46] and proprioception[49,66,92] deficits are also observed in ankle sprains. Reduced joint motion,[9,52] weak muscles,[6] and pain[32] could contribute to compromised balance in ankle OA. As impaired balance is linked with falls,[6,57,67] this may suggest an increased risk of falls in this population. Further research to understand specific elements of balance impairment and evaluate the incidence of falls in people with ankle OA is needed.

Individuals with ankle OA commonly present with concomitant varus hindfoot.[79,80] This shift in alignment alters the normal load bearing across the ankle joint, resulting in asymmetrical load distribution.[81,83] A direct correlation between the extent of malalignment and amount of degenerative changes at the ankle has been reported.[64] Key findings from data on tibiocalcaneal and tibiotalar angles suggest that the progressive subtalar joint valgus inclination is an attempt to compensate for tibial varus. It is unclear whether the malalignment was pre-existing and possibly contributed to ankle OA, or was a consequence of ankle OA. In individuals with knee joint OA, malalignment predicts decline in physical function,[74] but the effect of alignment on physical function in individuals with ankle OA is yet to be explored.

A number of factors must be considered when interpreting the findings from this systematic review. First, many studies used a convenience sample of individuals with end-stage OA awaiting surgical intervention.[29,47,58,90] These participants likely have the most severe symptoms and impairments related to ankle OA, which may not represent the broader population with ankle OA and limits generalizability of data. Further research investigating impairments present in the earlier stages of ankle OA is warranted. Second, pooling data and comparison between studies were limited by the populations, comparisons made, and single studies that assessed many measures (eg, weighted muscle torque,[38] calf CSA,[90] balance,[38] muscle EMG,[86,90] and mechanical instability[38]). Third, some studies compared individuals with ankle OA to controls, whereas others compared data between affected and unaffected sides in individuals with ankle OA. Evidence from other musculoskeletal conditions of bilateral impairments in individuals with unilateral problems[30,50,53,54] suggests that comparison to the unaffected side may not be the most appropriate approach to study impairments in individuals with ankle OA.

Fourth, while there were methodological limitations in the research of physical impairments in individuals with ankle OA, the included studies offered insight into OA-related impairments that should be explored by further research. The assessment of study quality highlights the need for future studies to specify the validity of outcome measures, to include an unaffected control group, to recruit individuals with OA from the general population to optimize generalizability of findings, and to consider demographics and stage of OA in analyses. Investigation of direction-specific ROM deficits and performance of functional tasks (eg, walking and stairs) is needed. Further, longitudinal study designs are necessary to understand the development and progression of physical impairments in individuals with different stages of ankle OA. Finally, to our knowledge, this review is the first to study impairments in ankle OA; it has employed a comprehensive strategy with terms that cast a broad net over the literature. However, it might have missed relevant articles with different key words, an unclear or covert title or abstract, or studies not indexed in the specified databases.

CONCLUSION

This systematic review assessed the literature and identified issues with methodological quality of studies investigating physical impairments in individuals with ankle OA. Meta-analyses indicated large impairments in ankle DF and PF ROM and torque in individuals with ankle OA compared to controls. Single studies suggest that altered joint alignment, impaired standing balance and EMG activity, and limited arthrokinematic movements may be characteristic of ankle OA. Considerations of these impairments may lead to improved outcomes in the management of individuals with ankle OA. Further high-quality research is needed to better understand impairments in the different stages of ankle OA, particularly early OA, which has received little attention in the literature, and the relation between specific impairments, function/disability, and quality of life. ◉

KEY POINTS

FINDINGS: Physical impairments are evident in the affected and unaffected sides in individuals with ankle osteoarthritis (OA) compared to controls. In terms

of mobility, ankle joints affected by OA are stiffer, with less range of motion and translation. Leg muscle weakness and fatty infiltrate, along with altered neuromuscular function, are characteristic of individuals with ankle OA. Balance deficits are also present in this population.

IMPLICATIONS: Identified physical impairments associated with ankle OA would likely compromise physical capacity. Targeted interventions to address those specific impairments in torque production, range of motion, and mechanical and sensorimotor outcomes may lead to improved outcomes.

CAUTION: Data pooling was not always possible due to single studies assessing the measure or different variables collected between studies. Thus, meta-analyses only included a small number of studies, which had small sample sizes. This review has not identified different outcomes between stages of OA. Further research is required to assess the impact of ankle OA on individuals with early-stage disease.

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APPENDIX A

SEARCH TERMS

tibiotalar OR talofibular OR talotibial OR talocrural OR talocalcaneal OR ankle
AND
osteoarthritis OR osteoarthrosis OR osteo-arthritis OR osteo-arthrosis OR arthrosis
AND
"force plate" OR muscle OR kinematic OR kinematics OR kinetics OR kinetic OR kinesthe* OR valgus OR varus
OR atrophy OR isometric OR isotonic OR isokinetic OR strength OR weakness OR dynamometer OR power OR force OR endurance OR speed OR fatigue OR contraction OR EMG OR latency OR electromyograph* OR activation OR laxity OR stiffness OR displacement OR "anterior drawer" OR motion OR "range of movement"
OR dorsiflex* OR plantarflex* OR inver* OR ever* OR supinat* OR pronat* OR flex OR flexor* OR flexion OR extens* OR adduct* OR abduct* OR "reaction time" OR "joint position" OR sensorimotor OR "movement detection" OR accelerometer OR "stride length" OR cadence OR stability OR control OR arthrometer OR balance OR proprioception OR postur* OR coordinate* OR "center of mass" OR "centre of mass" OR "center of pressure" OR "centre of pressure" OR gait OR walk* OR locomot* OR step OR steps OR stepping OR hop
OR hops or hopping OR jump* OR run OR instability

NOT Terms

Cadaver OR cadaveric OR rabbit OR rat OR rats OR mouse OR mice OR Paediatric OR pediatric OR juvenile OR child OR children OR "Cruciate ligament" OR Cruciate OR "Collateral ligament" OR meniscus OR menisci OR hip OR patellofemoral OR Diabetic OR diabetes OR Rheumatic OR "rheumatoid arthritis" OR Rheumatologic
OR rheumatism OR Hallux OR "hallux rigidus" OR "hallux valgus" OR "hallux limitus" OR "hallux varus" OR Cancer or tumor

Database Search Algorithm

Search in PubMed

Main search terms linked with "AND"
"NOT" review in "publication type" search field
Combining the NOT term sets resulted in higher numbers hence the option to search each set of terms independently.
"NOT" term sets searched independently in "title/abstract" search field:
Cadaver OR cadaveric OR rabbit OR rat OR rats OR mouse OR mice Paediatric OR pediatric OR juvenile OR child OR children
"Cruciate ligament" OR Cruciate OR "Collateral ligament" OR meniscus OR menisci OR hip OR patellofemoral
Diabetic OR diabetes
Rheumatic OR "rheumatoid arthritis" OR Rheumatologic OR rheumatism
Hallux OR "hallux rigidus" OR "hallux valgus" OR "hallux limitus" OR "hallux varus" Cancer or tumor

Search in SPORTDiscus

Notes: Relevant search fields for our set of NOT terms were either in title, subjects (descriptor) or abstract.
I removed the term review from "title" (subject field).
Experimented removing the terms from titles and again from abstracts and identified the difference.
Removing the terms from abstracts included all terms that were removed from titles. Hence NOT terms were removed from abstracts (subject field)

Search in CINAHL

Notes: Search fields are different in CINAHL with an option to select human in the "search option" table as well as the option to search "publication type" in the search field.
I removed the term review from "publication type" (search field).
Experimented removing the terms from titles and again from abstracts and identified the difference.
Removing the terms from abstracts included all terms that were removed from titles. Hence NOT terms were removed from abstracts (subject field)

Search in Embase

Notes: There are no specific search fields to select from.
The main Boolean operators listed are AND and OR.
I searched for the different sets of main terms independently then I combined them with AND.
When I typed the# presenting the combined main searches followed by NOT terms e.g. #4 NOT Cadaver OR cadaveric OR rabbit OR rat OR rats OR mouse OR mice, the numbers were higher instead of being lower.
I then searched for the different sets of NOT terms separately.

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Within the entry box I typed the # presenting the combined main searches followed it with NOT and the # representing search results for each set of NOT terms.
Same results was achieved by typing # presenting the combined main searches followed by NOT and all NOT terms in brackets.
NOT and the # representing search results for each set of NOT terms.

Search in Web of Science

Notes: Relevant search fields for our set of NOT terms were either in title or topic.
Search main terms linked with "AND"
"NOT" in title:
Cadaver OR cadaveric OR rabbit OR rat OR rats OR mouse OR mice
Paediatric OR pediatric OR juvenile OR child OR children
"Cruciate ligament" OR Cruciate OR "Collateral ligament" OR meniscus OR menisci OR hip OR patellofemoral
Diabetic OR diabetes
Rheumatic OR "rheumatoid arthritis" OR Rheumatologic OR rheumatism
Hallux OR "hallux rigidus" OR "hallux valgus" OR "hallux limitus" OR "hallux varus"
Refining to web of science subject category and document type is possible only after the search is done.
Review, letter, meeting abstracts, book chapters, editorial material, reprints and proceedings paper (document types) were excluded from the results.

APPENDIX B

RESULTS OF METHODOLOGICAL QUALITY ASSESSMENT

Item*	Hayashi et al[29]	Hubbard et al[38]	Lee et al[48]	Lee et al[47]	Nüesch et al[58]	Valderrabano et al[86]	Wiewiorski et al[90]	Wikstrom and Anderson[91]
1. Is the hypothesis/aim/objective of the study clearly described?	Y	Y	Y	Y	Y	Y	Y	Y
2 Are all the exposure variables clearly described?	Y	N	Y	N	N	P	P	N
3. Are the main outcomes clearly described?	Y	Y	Y	Y	Y	Y	P	Y
4. Is the study design clearly described?	P	Y	P	Y	P	P	Y	Y
5. Is the source of subject population clearly described?	Y	N	P	Y	P	N	Y	N
6. Are the eligibility criteria for subject selection clearly described?	Y	Y	Y	Y	Y	Y	Y	Y
7. Are the participation rates reported? Are ascertainments of record availability described?	Y	N	N	Y	N	N	N	N
8. Are the characteristics of study participants described?	P	P	P	P	P	Y	P	P
9. Have the characteristics of subjects lost after entry into the study or subjects not participating from among the eligible population been described? Have the details of unavailable records been described?	N	N	N	P	N	N	N	N
11. Are the important covariates and confounders described in terms of individual variables?	P	P	P	P	P	P	P	P
13. Are the statistical methods clearly described?	Y	N	Y	Y	P	N	N	P
14. Are the main findings of the study clearly described?	Y	Y	Y	Y	Y	Y	Y	Y
15. Does the study provide estimates of the random variability in the data for the main outcomes (ie, confidence intervals, standard deviations)?	Y	Y	Y	Y	Y	Y	Y	P
16. Does the study provide estimates of the statistical parameters (eg, regression coefficients or parameter estimates such as odds ratios or mean differences)?	N	N	Y	N	N	Y	N	N
17. Are sample-size calculations performed and reported?	N	N	N	N	N	Y	Y	N
18. Is the comparison/reference group comparable to the exposed group?	P	Y	N	N	P	P	N	P
19. Is the participation rate adequate? Is the ascertainment of record availability adequate?	Y	N	U	Y	U	U	U	U
20. Are the study subjects from different groups recruited over the same period of time?	U	N	N	N	U	U	Y	U
21. Are subject losses or unavailable records after entry into the study taken into account?	Y	N	N	N	N	N	N	N
25. Are the exposure variables reliable?	U	U	U	U	U	U	U	U
26. Are the exposure variables valid?	U	U	U	U	U	U	U	U
27. Are the methods of assessing the exposure variables similar for each group?	Y	N	Y	U	U	N	Y	N
29. Are the observers blinded to subject groupings when the exposure assessment was made or the disease status of subjects when conducting exposure assessment?	N	Y	N	N	N	N	N	N
31. Are the main outcome measures reliable?	Y	Y	U	U	Y	U	U	U
32 Are the main outcome measures valid?	U	N	U	U	Y	U	Y	Y
33. Are the methods of assessing the outcome variables standard across all groups?	Y	Y	Y	U	Y	Y	Y	Y
34. Are the observations taken over the same time for all groups?	U	U	U	U	U	U	U	U
35. Is prior history of disease and/or injury collected and included in the analysis?	N	P	N	N	N	Y	P	P

APPENDIX B

Item*	Hayashi et al[29]	Hubbard et al[38]	Lee et al[48]	Lee et al[47]	Nüesch et al[58]	Valderrabano et al[86]	Wiewiorski et al[90]	Wikstrom and Anderson[91]
36. Is there adequate adjustment for covariates and confounders in terms of individual variables in the analyses?	N	N	N	N	N	N	N	N
40. Are outcome data reported by levels of exposure?	Y	N	Y	N	N	N	N	N
41. Are the outcome/exposure data reported by subgroups of subjects?	N	N	N	N	N	N	N	N
42. Can the study results be applied to the eligible population?	Y	U	U	Y	U	U	U	U
43. Can the study results be applied to other relevant populations?	P	U	U	P	U	U	U	U
Quality score (0-1)	0.56	0.33	0.39	0.36	0.35	0.36	0.41	0.30

Abbreviations: N, no; P, partial; U, unable to determine; Y, yes.
**From the Epidemiological Appraisal Instrument.[20]*

APPENDIX C

TABLE 1
Stages of Ankle OA in 2 Classification Systems and the Adopted Stages for the Current Systematic Review

Stage	Morrey and Wiedeman[56] Classification	Modified Takakura Classification[80]*	Adopted Grouping
0	Normal	...	...
1	Minimum narrowing and osteophyte formation	Early sclerosis and formation of osteophytes; no joint space narrowing	Mild OA
2	Moderate narrowing and osteophyte formation	Narrowing of the medial joint space	Moderate OA
3	Gross deformity and ankylosis	a. Obliteration of the medial joint space, with subchondral bone contact limited to the medial malleolus b. Subchondral bone contact extending to the roof of the dome of the talus	Advanced OA
4	...	Obliteration of the entire joint space, resulting in bone contact throughout the ankle	

Abbreviation: OA, osteoarthritis.
**From Lee et al.[48]*

TABLE 2
Adopted Stages for the Current Systematic Review

Stage	Description
Mild	Early sclerosis, minimum joint space narrowing, and osteophyte formation
Moderate	Moderate narrowing and osteophyte formation
Advanced	Obliteration of the entire joint space, subchondral bone contact/ankylosis

APPENDIX D

PHYSICAL OUTCOMES COMPARED BETWEEN THE AFFECTED SIDE IN PEOPLE WITH ANKLE OSTEOARTHRITIS VERSUS THE UNAFFECTED SIDE OR HEALTHY CONTROLS

Outcome/Stage of OA	Affected Side*	Unaffected Side*	Between Sides†	Healthy Controls*	Affected Side Versus Controls†	Unaffected Side Versus Controls†
TMM, deg[48]						
Moderate	24.9 ± 2.8 (n = 68)			22.6 ± 6.1 (n = 80)	0.47 (0.14, 0.80)	
Advanced	28.78 ± 8.58 (n = 87)			22.6 ± 6.1 (n = 80)	0.82 (0.50, 1.14)	
TTS, deg[29]						
Mild	85.3 ± 2.6 (n = 26)			87.2 ± 2.8 (n = 62)	−0.69 (−1.16, −0.22)	
Moderate	82.7 ± 3.5 (n = 39)			87.2 ± 2.8 (n = 62)	−1.45 (−1.90, −1.00)	
Advanced	77.44 ± 7.6 (n = 68)			87.2 ± 2.8 (n = 62)	−1.66 (−2.07, −1.26)	
Talar tilt, deg[48]						
Moderate	2.5 ± 2.8 (n = 68)			0 ± 0 (n = 80)		
Advanced	5.4 ± 5.3 (n = 87)			0 ± 0 (n = 80)		
TPC, deg[29]						
Mild	88.2 ± 6.1 (n = 26)			88.3 ± 5.8 (n = 62)	−0.02 (−0.47, 0.44)	
Moderate	91.0 ± 8.7 (n = 39)			88.3 ± 5.8 (n = 62)	0.38 (−0.02, 0.78)	
Advanced	84.1 ± 10.9 (n = 68)			88.3 ± 5.8 (n = 62)	−0.47 (−0.82, −0.12)	
SIA, deg[29]						
Mild	2.9 ± 7.0 (n = 26)			1.5 ± 5.9 (n = 62)	0.22 (−0.24, 0.68)	
Moderate	8.0 ± 8.6 (n = 39)			1.5 ± 5.9 (n = 62)	0.91 (0.49, 1.33)	
Advanced	6.6 ± 9.0 (n = 68)			1.5 ± 5.9 (n = 62)	−10.93 (−12.33, −9.54)	
TAS, deg[29]						
Moderate	84.5 ± 3.1 (n = 39)			87.4 ± 2.7 (n = 62)	−1.01 (−1.43, −0.58)	
Advanced	82.7 ± 3.7 (n = 68)			87.4 ± 2.7 (n = 62)	−1.43 (−1.82, −1.05)	
TAS, deg[48]						
Moderate	86.9 ± 2.4 (n = 68)			88.9 ± 2.4 (n = 80)	−0.83 (−1.17, −0.49)	
Advanced	84.9 ± 4.4 (n = 87)			88.9 ± 2.4 (n = 80)	−1.09 (−1.41, −0.76)	
TLS, deg[29]						
Moderate	80.4 ± 3.2 (n = 39)			81.13 ± 2.8 (n = 62)	−0.24 (−0.65, 0.16)	
Advanced	78.4 ± 5.2 (n = 68)			81.13 ± 2.8 (n = 62)	−0.64 (−0.99, −0.29)	
TLS, deg[48]						
Moderate	76.8 ± 3.5 (n = 68)			79.8 ± 3.8 (n = 80)	−0.81 (−1.15, −0.48)	
Advanced	72.4 ± 4.8 (n = 87)			79.8 ± 3.8 (n = 80)	−1.69 (−2.05, −1.34)	
Hindfoot alignment, deg[48‡]						
Moderate	0.5 ± 8.1 (n = 68)			−0.5 ± 5.4 (n = 80)	0.15 (−0.18, 0.47)	
Advanced	5.3 ± 8.63 (n = 87)			−0.5 ± 5.4 (n = 80)	0.79 (0.48, 1.11)	
Calcaneal alignment, deg[86§]						
Moderate and advanced	3.0 ± 8.9 (n = 15)	7.0 ± 3.55 (n = 15)	−0.57 (−1.31, 0.16)	4.6 ± 1.24 (n = 15)	−0.25 (−0.96, 0.47)	
Tibiotalar ratio[47‖]						
Advanced	28.3 ± 2.47 (n = 104)			35.0 ± 3.0 (n = 50)	−2.51 (−2.95, −2.07)	
Total ROM, deg						
Inversion/eversion[86]						
Moderate and advanced	19.7 ± 11.1 (n = 15)	43.3 ± 10.97 (n = 15)	−2.08 (−2.99, −1.17)	50.7 ± 8.4 (n = 15)	−3.07 (−4.16, −1.97)	−0.74 (−1.48, 0.01)
Dorsiflexion/plantar flexion[86]						
Moderate and advanced	16.0 ± 7.6 (n = 15)	56.7 ± 5.23 (n = 15)	−6.07 (−7.87, −4.27)	58.7 ± 5.2 (n = 15)	−6.39 (−8.27, −4.52)	−0.37 (−1.10, 0.35)

Table continues on page A7.

APPENDIX D

Outcome/Stage of OA	Affected Side*	Unaffected Side*	Between Sides†	Healthy Controls*	Affected Side Versus Controls†	Unaffected Side Versus Controls†
Dorsiflexion/plantar flexion[90]	18.1 ± 9.15 (n = 21)	56.0 ± 6.25 (n = 21)	−4.75 (−5.97, −3.52)			
Mechanical stability						
Anterior displacement, mm[38] (anterior load applied)	7.1 ± 1.9 (n = 8)	10.6 ± 1.5 (n = 8)	−1.93 (−3.18, −0.69)	11.2 ± 1.8 (n = 8)	−2.09 (−3.38, −0.81)	−0.34 (−1.33, 0.65)
Posterior displacement, mm[38]	4.6 ± 1.3 (n = 8)	5.0 ± 1.3 (n = 8)	−0.29 (−1.28, 0.70)	4.9 ± 0.58 (n = 8)	−0.28 (−1.27, 0.70)	0.09 (−0.89, 1.07)
Inversion rotation, deg[38]	21.6 ± 6.4 (n = 8)	31.1 ± 4.5 (n = 8)	−1.62 (−2.80, −0.45)	33.0 ± 2.1 (n = 8)	−2.26 (−3.60, −0.93)	−0.51 (−1.51, 0.49)
Eversion rotation, deg[38]	9.4 ± 2.8 (n = 8)	15.2 ± 5.1 (n = 8)	−1.33 (−2.45, −0.22)	21.3 ± 5.6 (n = 8)	−2.54 (−3.95, −1.13)	−1.08 (−2.15, −0.01)
Calf circumference, cm						
Calf circumference[58]	38.19 ± 2.36 (n = 12)	39.42 ± 2.74 (n = 12)	−0.46 (−1.28, 0.35)	38.29 ± 2.67 (n = 12)	−0.04 (−0.84, 0.76)	0.41 (−0.40, 1.22)
Calf circumference[86]						
Moderate and advanced	32.7 ± 3.45 (n = 15)	34.8 ± 3.44 (n = 15)	−0.59 (−1.33, 0.14)	33.6 ± 2.8 (n = 15)	−0.28 (−1.00, 0.44)	0.37 (−0.35, 1.10)
Calf circumference[90]						
Moderate and advanced	33.2 ± 2.65 (n = 21)	35.3 ± 2.76 (n = 21)	−0.76 (−1.39, −0.13)			
CSA, cm^2						
Anterior tibial muscle group[90¶]						
Moderate and advanced	10.3 ± 2.6 (n = 21)	11.0 ± 2.9 (n = 21)	−0.25 (−0.86, 0.36)			
Peroneal muscle group[90#]						
Moderate and advanced	5.8 ± 1.7 (n = 21)	6.5 ± 1.5 (n = 21)	−0.43 (−1.04, 0.18)			
Deep posterior muscles[90**]						
Moderate and advanced	4.5 ± 1.3 (n = 21)	5.4 ± 1.5 (n = 21)	−0.63 (−1.25, −0.01)			
Gastrocnemius medialis muscle[90]						
Moderate and advanced	12.0 ± 3.3 (n = 21)	13.3 ± 3.5 (n = 21)	−0.37 (−0.99, 0.24)			
Gastrocnemius lateralis muscle[90]						
Moderate and advanced	5.7 ± 2.0 (n = 21)	6.7 ± 2.0 (n = 21)	−0.49 (−1.11, 0.12)			
Soleus muscle[90]						
Moderate and advanced	18.6 ± 5.4 (n = 21)	24.7 ± 6.0 (n = 21)	−1.05 (−1.70, −0.40)			
Anatomical calf CSA[90]						
Moderate and advanced	57.0 ± 13.4 (n = 21)	67.5 ± 11.9 (n = 21)	−0.81 (−1.44, −0.18)			
Fatty infiltration						
Anterior tibial muscle group[90¶]						
Moderate and advanced	1.3 ± 0.8 (n = 21)	0.4 ± 0.5 (n = 21)	1.25 (0.58, 1.92)			
Peroneal muscle group[90#]						
Moderate and advanced	1.4 ± 0.6 (n = 21)	0.5 ± 0.5 (n = 21)	1.60 (0.90, 2.30)			
Deep posterior muscles[90**]						
Moderate and advanced	1.4 ± 0.8 (n = 21)	0.2 ± 0.4 (n = 21)	1.86 (1.13, 2.60)			
Gastrocnemius medialis muscle[90]						
Moderate and advanced	1.3 ± 0.5 (n = 21)	0.6 ± 0.6 (n = 21)	1.24 (0.58, 1.91)			
Gastrocnemius lateralis muscle[90]						
Moderate and advanced	1.1 ± 0.7 (n = 21)	0.4 ± 0.5 (n = 21)	1.13 (0.47, 1.78)			
Soleus muscle[90]						
Moderate and advanced	2.5 ± 0.5 (n = 21)	0.8 ± 0.6 (n = 21)	3.02 (2.11, 3.93)			

Table continues on page A8.

APPENDIX D

Outcome/Stage of OA	Affected Side*	Unaffected Side*	Between Sides†	Healthy Controls*	Affected Side Versus Controls†	Unaffected Side Versus Controls†
Maximal isometric torque						
Dorsiflexion[86]						
Moderate and advanced	16.4 ± 4.9 (n = 15)	25.9 ± 8.2 (n = 15)	−1.37 (−2.17, −0.56)	27.1 ± 9.4 (n = 15)	−1.39 (−2.20, −0.58)	−0.13 (−0.85, 0.58)
Dorsiflexion[58]	11.1 ± 7.96 (n = 12)			26.3 ± 13.86 (n = 12)	−1.30 (−2.19, −0.40)	
Plantar flexion[86]						
Moderate and advanced	15.8 ± 7.6 (n = 15)	25.6 ± 7.4 (n = 15)	−1.27 (−2.07, −0.48)	30.7 ± 15.5 (n = 15)	−1.19 (−1.97, −0.40)	−0.41 (−1.13, 0.32)
Plantar flexion[58]	20.9 ± 7.62 (n = 12)			36.9 ± 13.51 (n = 12)	−1.41 (−2.32, −0.50)	
Isometric strength, Nm/kg						
Plantar flexion[38]	0.18 ± 0.09 (n = 8)	0.22 ± 0.07 (n = 8)	−0.47 (−1.47, 0.53)	0.39 ± 0.1 (n = 8)	−2.09 (−3.37, −0.80)	−1.86 (−3.09, −0.63)
Dorsiflexion[38]	0.16 ± 0.05 (n = 8)	0.20 ± 0.06 (n = 8)	−0.68 (−1.70, 0.33)	0.36 ± 0.1 (n = 8)	−2.39 (−3.76, −1.02)	−1.83 (−3.06, −0.61)
Inversion[38]	0.09 ± 0.03 (n = 8)	0.14 ± 0.04 (n = 8)	−1.34 (−2.45, −0.22)	0.22 ± 0.04 (n = 8)	−3.48 (−5.17, −1.78)	−1.89 (−3.13, −0.65)
Eversion[38]	0.10 ± 0.03 (n = 8)	0.14 ± 0.03 (n = 8)	−1.26 (−2.36, −0.16)	0.22 ± 0.04 (n= 8)	−3.21 (−4.82, −1.60)	−2.14 (−3.44, −0.84)
Muscle EMG amplitude, μV						
Anterior tibial muscle[86]						
Moderate and advanced	39.8 ± 21.9 (n = 15)	67.8 ± 53.4 (n = 15)	−0.67 (−1.41, 0.07)	62.6 ± 43.4 (n = 15)	−0.65 (−1.38, 0.09)	
Medial gastrocnemius[86]						
Moderate and advanced	6.9 ± 10.9 (n = 15)	20.2 ± 23.0 (n = 15)	−0.72 (−1.46, 0.02)	24.7 ± 19.0 (n = 15)	−1.12 (−1.90, −0.34)	−0.21 (−0.93, 0.51)
Peroneus longus[86]						
Moderate and advanced	14.1 ± 19.4 (n = 15)	26.9 ± 25.3 (n = 15)	−0.55 (−1.28, 0.18)	33.0 ± 43.3 (n = 15)	−0.55 (−1.28, 0.18)	−0.17 (−0.88, 0.55)
Soleus[86]						
Moderate and advanced	19.9 ± 55.6 (n = 15)	17.9 ± 25.1 (n = 15)	0.05 (−0.67, 0.76)	25.7 ± 29.4 (n = 15)	−0.13 (−0.84, 0.59)	−0.28 (−1.00, 0.44)
Muscle EMG frequency, Hz						
Anterior tibial muscle[86]						
Moderate and advanced	119.4 ± 31.8 (n = 15)	142.0 ± 29.1 (n = 15)	−0.72 (−1.46, 0.02)	144.9 ± 26.1 (n = 15)	−0.85 (−1.61, −0.10)	−0.10 (−0.82, 0.61)
Medial gastrocnemius[86]						
Moderate and advanced	159.2 ± 19.9 (n = 15)	186.5 ± 26.7 (n = 15)	−1.13 (−1.91, −0.35)	184.8 ± 23.8 (n = 15)	−1.14 (−1.91, −0.36)	0.07 (−0.65, 0.78)
Peroneus longus[86]						
Moderate and advanced	147.5 ± 35.4 (n = 15)	176.1 ± 31.7 (n = 15)	−0.83 (−1.58, −0.08)	159.8 ± 28.6 (n = 15)	−0.37 (−1.09, 0.35)	0.53 (−0.20, 1.26)
Soleus[86]						
Moderate and advanced	124.2 ± 33.1 (n = 15)	150.1 ± 21.0 (n = 15)	−0.91 (−1.67, −0.15)	146.8 ± 32.6 (n = 15)	−0.67 (−1.41, 0.07)	0.12 (−0.60, 0.83)
CoP total displacement, mm[38]	219.5 ± 193.6 (n = 8)			27.0 ± 6.6 (n = 8)	1.33 (0.21, 2.44)	
CoP total velocity, mm/s[38]	36.8 ± 16.4 (n = 8)			11.4 ± 2.1 (n = 8)	2.05 (0.78, 3.33)	
CoP ML displacement, mm[38]	2.8 ± 4.5 (n = 8)			0.88 ± 0.55 (n = 8)	0.57 (−0.44, 1.57)	
CoP AP displacement, mm[38]	1.9 ± 2.2 (n = 8)			0.35 ± 0.4 (n = 8)	0.93 (−0.12, 1.97)	
CoP ML velocity, mm/s[38]	0.53 ± 0.61 (n = 8)			0.01 ± 0.09 (n = 8)	1.13 (0.05, 2.21)	
CoP AP velocity, mm/s[38]	0.68 ± 0.83 (n = 8)			0.15 ± 0.13 (n = 8)	0.84 (−0.19, 1.88)	
AP sway, cm[91]	3.94 ± 1.36 (n = 5)			2.31 ± 0.25 (n = 5)	1.51 (0.01, 3.01)	
ML sway, cm[91]	2.14 ± 1.03 (n = 5)			1.02 ± 0.21 (n = 5)	1.36 (−0.10, 2.82)	

Abbreviations: AP, anteroposterior; CoP, center of pressure; CSA, cross-sectional area; EMG, electromyography; ML, mediolateral; ROM, range of motion; SIA, angle between the articular surface of the talar dome and the posterior facet of the calcaneus; TAS, angle between the tibial shaft and tibial articular surface in the frontal plane on weight-bearing X-ray; TLS, angle between the tibial shaft axis and the articular surface of the tibial shaft in the sagittal plane on weight-bearing X-ray; TMM, angle between the distal third of the tibial shaft and the medial malleolar joint surface; TPC, angle between the tibial shaft axis and the articular surface of the posterior facet of the calcaneus; TTS, angle between the tibial shaft and the articular surface of the talar dome.

**Values are mean ± SD.*

†Values are standardized mean difference (95% confidence interval).

‡The angle between the tibial and calcaneal axes.

§Alignment was measured with a goniometer in standing.

‖The ratio into which the mid-longitudinal axis of the tibial shaft divides the longitudinal talar length.

¶Tibialis anterior, extensor digitorum, and hallucis longus.

#Peroneus longus and brevis.

***Tibialis posterior, flexor digitorum longus, and flexor hallucis longus.*

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Outcomes in Distressed Patients With Chronic Low Back Pain: Subgroup Analysis of a Clinical Trial

There is growing evidence that screening for risk factors and matching interventions accordingly can improve outcomes in individuals with low back pain (LBP).[9] There is a need to find cost-effective interventions for subgroups of patients with LBP who also have psychological obstacles to recovery, such as depression, anxiety, catastrophic thinking, and fear of activity.[12] Depression and anxiety, in this context, are usually measured through self-report of symptoms and are indicators of distress rather than diagnoses of a clinical condition. This subanalysis focuses on a combined measurement of depression and anxiety symptoms, conceptualized as distress, and measured through the Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12) mental health subscale.

STUDY DESIGN: Subgroup analysis of a controlled clinical trial.

BACKGROUND: Current evidence suggests that people with chronic low back pain who are distressed may require different interventions than do those who are not distressed. Recently, the enhanced transtheoretical model intervention (ETMI) reported significant improvements in disability and pain and increased physical activity in patients with chronic low back pain compared to physical therapy as usual.

OBJECTIVES: To compare outcomes between ETMI and physical therapy interventions for participants with and without self-reported distress.

METHODS: We tested the interaction between intervention (ETMI versus physical therapy) and distress status (using the Medical Outcomes Study 12-Item Short-Form Health Survey cut point), and performed between-group comparisons on 3 separate outcomes (disability, pain, and physical activity) at 3 and 12 months.

RESULTS: In the ETMI group, 57 of 108 participants were considered distressed, versus 62 of 106 participants in the physical therapy group. The interaction between intervention and distress at 12 months was significant. Participants improved with both interventions, but the magnitude of change in distressed participants who received ETMI was larger than that in distressed participants who received physical therapy (mean ± SD difference from baseline in disability of 6.1 ± 6.1 in the ETMI group, compared with 3.4 ± 6.7 in the physical therapy group).

CONCLUSION: The enhanced transtheoretical model intervention was significantly more effective than physical therapy in participants with distress. The trial was registered in *ClinicalTrials.gov* (NCT01631344).

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KEY WORDS: *chronic low back pain, physical activity, physical therapy, psychological distress, transtheoretical model*

In a prospective pragmatic controlled trial,[4] we compared an intervention for people with chronic LBP (CLBP) based on an enhanced transtheoretical model intervention (ETMI) (n = 109) to physical therapy treatment as usual (TAU) (n = 111). The results[4] suggest that ETMI may significantly decrease pain and disability and increase physical activity compared to TAU. The ETMI was based on behavior change principles tailored to each patient's motivation and readiness for change.[16] It addresses fear avoidance through exposure to the feared activity and includes explicit statements aimed at increasing self-efficacy for physical activity. Although the ETMI did not explicitly elicit and address psychological risk factors, it may prove more beneficial for distressed patients than physical therapy alone, because treatment involves a process of addressing cognitions. The theoretical principles imply that changes in self-efficacy and beliefs will result in behavioral changes (increased physical activity). While this ETMI did not directly target distress, it may address the disengagement from daily activity associated with distress, resulting in increased activity and engagement in life. The aim of this subgroup analysis was to test the difference in change in disability (primary outcome), pain, and physical activity between patients who

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present with and without distress, within and between ETMI and TAU treatment allocations.

METHODS

Details of the full clinical trial have been described in a previous study.[4] This analysis of trial data compared outcomes between subgroups according to the presence of distress determined through baseline measures of the mental health subscale of the SF-12, using the recommended cut point of 45.6,[18] which has previously been used to determine the presence of depressive disorders. This cut point was validated in a representative sample of more than 21 000 noninstitutionalized people across 6 European countries against psychiatric *Diagnostic and Statistical Manual of Mental Disorders* criteria.[18]

We used this SF-12 cut-point as an indication of distress in our study sample. The SF-12 items explore how emotional problems interfere with work, social life, and activities and ask participants to report whether they feel calm and peaceful, energetic, or down-hearted and blue. The SF-12 measure can be regarded as representing both anxiety and depressive symptoms, which are highly correlated in people with chronic pain.[20]

The trial recruited people with CLBP between the ages of 22 and 55 years who were referred to physical therapy. The age restriction was based on previous studies that have reported a failure to change behavior among groups of older participants.[3] There were 8 participating centers, with 11 physical therapists providing ETMI and 23 physical therapists providing TAU. Treatment of patients in the TAU group was not restricted, standardized, or limited in the number of therapy sessions. Allocation to treatment group was determined by a central, independent telephone center according to the first available physical therapist within the closest geographical location to the patient. Patients were excluded if they had rheumatic diseases, tumors, fractures, fibromyalgia, LBP after an automobile or work accident, or previous spinal surgery, were pregnant, or had Hebrew-language fluency difficulties.

The research proposal was approved by the Ethics Committee of Maccabi Healthcare Services, a public health organization in Israel, and the Ethics Committee of Tel Aviv University. Participants signed an informed-consent form prior to their inclusion in the study. The trial was registered in *ClinicalTrials.gov* (NCT01631344).

Intervention

The ETMI focused on known obstacles to engaging in physical activity, including low motivation, low self-efficacy, and fear of movement. The guiding model was the transtheoretical model of behavior change,[15] and physical therapists were trained to match participants' readiness to contemplate or plan their engagement in physical activity. In addition, the ETMI included standardized statements about the value of engaging in physical activity as a preventative strategy and treatment for LBP, and for those who feared walking (the most commonly chosen activity), the intervention included in vivo exposure[19] and graded activity.[11]

Outcome Measures

All measures were taken at baseline and at 3 and 12 months. The primary clinical outcome was the effect of treatment on the Roland-Morris Disability Questionnaire (RMDQ) score,[14] with scores ranging from 0 to 23 and higher scores indicating more severe disability. Secondary outcomes included the numeric pain-rating scale[6] (NPRS), which measures worst pain and average pain in the last week on an 11-point scale ranging from

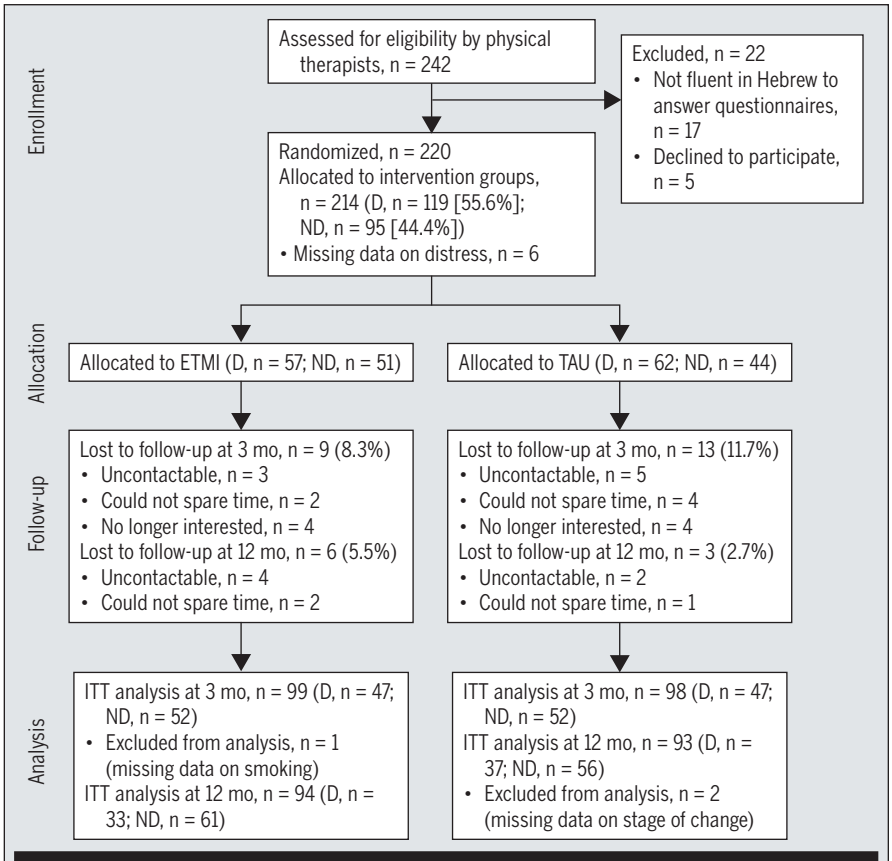

FIGURE. Participant flow through the controlled trial. Abbreviations: D, distressed; ITT, intention to treat; ND, nondistressed; TAU, physical therapy treatment as usual.

0 (no pain at all) to 10 (unbearable pain), and the Baecke Physical Activity Questionnaire[1] (BPAQ), a measure of intensity of physical exercise, with scores ranging from 1 (very low intensity) to 5 (very high intensity).

Statistical Analysis

Analysis was conducted using SPSS Version 22 (IBM Corporation, Armonk, NY). We compared outcomes via a 2-by-2 analysis of covariance (ANCOVA), with baseline pain, disability, and physical activity as covariates in each model. Analyses were conducted separately for each of the dependent variables, which were disability (RMDQ), pain (NPRS), and physical activity (BPAQ). The main hypothesis to be tested was an interaction between group (ETMI or TAU) and distress status (distressed or nondistressed) for each outcome. Effect sizes were calculated using the Cohen *d*: (M2 – M1)/SD pooled.[7] All *P* values are reported as 2-sided alpha.

RESULTS

Overall, 220 patients were eligible to participate. Of these, 214 provided scores on the SF-12, were randomly allocated to treatment groups, and were included in the analysis (**FIGURE**). At 12 months, 85.9% provided follow-up data. Among those who provided follow-up data, missing observations were less than 1% of the responses and were therefore omitted from the analyses.[5] Description of baseline variables is presented in **TABLE 1.** At baseline, 55.6% of participants with CLBP scored below the cut point for the SF-12, indicating high levels of distress. The proportion of distressed participants did not differ between the ETMI (57/108) and TAU (62/106) groups (**FIGURE**).

The results for the ANCOVA analyses are presented in **TABLE 2.** The interaction between subgroup (with and without distress) and intervention (ETMI or TAU) was significant (P = .001) for disability scores at 3 months (mean difference on RMDQ, 3.3; 95% confidence interval [CI]: 1.3, 5.3; P = .001) and at 12 months (mean difference on RMDQ, 4.0; 95% CI: 1.8, 6.3). The mean ± SD change from baseline to 12 months in the ETMI group was 6.1 ± 6.1 for distressed participants and 6.9 ± 5.5 for nondistressed participants. For the TAU intervention, mean ± SD change from baseline was 3.4 ± 6.7 for distressed participants and 4.5 ± 5.7 for nondistressed participants.

TABLE 1 Baseline Demographics and Clinical Characteristics of Participants*

	Nondistressed		Distressed	
	ETMI (n = 51)	TAU (n = 44)	ETMI (n = 57)	TAU (n = 62)
Age, y	41.6 ± 7.0	40.8 ± 7.3	42.8 ± 7.9	42.8 ± 6.7
Female sex, n (%)	27 (52.9)	24 (54.5)	28 (49.1)	37 (59.7)
Education (years completed), n	14.6 ± 2.5	15.1 ± 2.7	14.2 ± 2.8	14.7 ± 2.6
Body mass index, kg/m^2	26.9 ± 5.2	25.8 ± 4.8	25.3 ± 4.3	26.3 ± 5.2
Smokers, n (%)	9 (17.6)	5 (11.4)	7 (12.3)	9 (14.5)
RMDQ	9.1 ± 4.6	9.8 ± 5.0	10.7 ± 5.2	10.8 ± 5.3
Worst pain†	6.3 ± 2.6	6.4 ± 2.2	6.3 ± 2.7	6.6 ± 2.3
Average pain†	4.8 ± 2.1	4.6 ± 1.9	5.0 ± 2.2	5.2 ± 2.2
BPAQ	1.9 ± 1.7	2.0 ± 1.7	1.8 ± 1.4	1.9 ± 1.7

Abbreviations: BPAQ, Baecke Physical Activity Questionnaire; ETMI, enhanced transtheoretical model intervention group; RMDQ, Roland-Morris Disability Questionnaire; TAU, physical therapy treatment as usual group.
**Values are mean ± SD unless otherwise indicated.*
†In the last week, assessed on an 11-point numeric pain-rating scale ranging from 0 (no pain at all) to 10 (unbearable pain).

The interaction between intervention and distress status on secondary outcomes was significant at 3 months for pain and physical activity, with the ETMI being superior to TAU in the distressed group only. Changes in nondistressed participants did not differ between those receiving the ETMI and TAU interventions on any measures at 3 months or on measures of pain and physical activity at 12 months (**TABLE 2**).

DISCUSSION

We found significant improvements in disability and physical activity after 3 and 12 months in distressed participants who were treated using ETMI in comparison with those undergoing a more traditional physical therapy approach. The reduction in disability among participants in the distressed subgroup who received ETMI was above the cut-points for clinically meaningful change in disability (2.5 points).[14,18]

In nondistressed participants, those who received ETMI had lower disability at 12 months than those who received physical therapy, but other outcomes (pain and physical activity) did not differ from those in participants who received physical therapy.

By comparison, in the STarT Back[9] trial, the group with high psychosocial risk had a mean change in RMDQ of 5.9 at 12 months for the intervention matched to the psychosocial factors versus 4.8 in those who received a more classic physical therapy approach. In the current study, at 12 months, distressed participants in the ETMI group reported a mean change in RMDQ score of 6.12, and those in the TAU group reported a mean change of 3.4. At 12 months, the standardized effect size between the distressed groups was 0·70. Distressed participants treated with the ETMI also showed significantly increased physical activity compared to those in the TAU group. Physical therapy, in contrast, was more effective in nondistressed participants than in those with distress.

TABLE 2 The Difference in Pain and Disability Between Distressed and Nondistressed Patients With CLBP at Baseline, 3 Months, and 12 Months in ETMI Versus TAU Groups*

	Nondistressed			Distressed			
	ETMI	TAU	*P* Value	ETMI	TAU	*P* Value	Mean Difference (95% CI)
Baseline	n = 51	n = 44		n = 57	n = 62		
RMDQ	9.1 ± 4.6	9.8 ± 5.0	.48	10.7 ± 5.2	10.8 ± 5.3	.87	
Worst pain†	6.3 ± 2.6	6.4 ± 2.2	.89	6.3 ± 2.7	6.6 ± 2.3	.58	
Average pain†	4.8 ± 2.1	4.6 ± 1.9	.67	5.0 ± 2.2	5.2 ± 2.2	.61	
BPAQ	1.9 ± 1.7	2.0 ± 1.7	.76	1.8 ± 1.4	1.9 ± 1.7	.74	
3 mo	n = 52	n = 51		n = 47	n = 47		
RMDQ	4.8 ± 4.0	5.4 ± 4.3	.49	4.6 ± 5.3	8.3 ±6.9	<.01‡	3.3 (1.3, 5.3)
Worst pain†	4.5 ± 2.9	4.1 ± 2.8	.54	3.9 ± 3.1	5.2 ± 3.2	.04‡	1.2 (0.03, 2.4)
Average pain†	2.7 ± 2.0	2.9 ± 2.2	.72	2.6 ± 2.4	4.0 ± 2.8	.01‡	1.2 (0.2, 2.1)
BPAQ	2.0 ± 1.5	1.8 ± 1.6	.56	2.3 ± 1.6	1.6 ± 1.7	.01‡	0.7 (0.1, 1.2)
12 mo	n = 61	n = 56		n = 33	n = 37		
RMDQ	3.3 ± 4.1	5.0 ± 4.1	.02‡	3.1 ± 5.0	7.4 ± 7.0	<.01‡	4.0 (1.8, 6.3)
Worst pain†	3.5 ± 3.0	4.4 ± 2.9	.10	3.4 ± 3.3	4.9 ± 3.4	.06	1.4 (−0.07, 2.8)
Average pain†	2.3 ± 2.3	2.8 ± 2.3	.19	2.3 ± 2.8	3.4 ± 2.6	.11	0.9 (−0.2, 2.0)
BPAQ	2.9 ± 0.8	3.0 ± 0.7	.50	3.3 ± 1.0	2.7 ± 0.7	<.01‡	0.8 (0.2, 1.3)

Abbreviations: BPAQ, Baecke Physical Activity Questionnaire; CI, confidence interval; CLBP, chronic low back pain; ETMI, enhanced transtheoretical model intervention group; RMDQ, Roland-Morris Disability Questionnaire; TAU, physical therapy treatment as usual group.
**Values are mean ± SD unless otherwise indicated.*
†In the last week, assessed on an 11-point numeric pain-rating scale ranging from 0 (no pain at all) to 10 (unbearable pain).
‡Significant (P≤.05).

These findings raise questions about the process of care for people with CLBP and suggest that physical therapists may require further training to recognize and address psychological obstacles to recovery. Training in psychologically informed practice may not require extensive training. The ETMI demonstrates that the principles of behavioral change can be learned and implemented in practice after 2 days of training. Evidence from the STarT Back trial suggests that screening for psychosocial factors and matching treatment accordingly is more effective than physical therapy provided without stratification for psychosocial factors. The current study suggests that both distressed and nondistressed participants improve equally in some outcomes (engagements with physical activity and disability) in response to a single intervention.

The findings from the ETMI are particularly promising considering the short training required and the low dose of the intervention, because physical therapists trained and reached competence at using the ETMI in 2 training days, and the intervention was effective at small doses (mean intervention sessions, 3.5; 95% CI: 3.2, 3.9).[4]

The findings of this study should be viewed with caution, primarily because the parent trial was not designed to test the hypothesis under investigation and was not powered for subgroup analysis. We also note that the ETMI is a multicomponent intervention, and the design of the trial did not enable testing of which component was most effective at improving outcomes.

The number of distressed participants in this study, using the recommended cut point for the SF-12, was high (55.6%), but not without precedent. While larger surveys of individuals with CLBP have suggested a prevalence of around 13%,[8] other studies have reported rates of around 55%,[15] and the rate of major depression has been reported to be 4 times greater in people with chronic back pain than in the general population.[17] The problems surrounding the diagnosis, measures, and conceptualization of depression in people with chronic pain are well known.[2,10,13] Because several items in the SF-12 ask about anxiety symptoms and other items ask about interference with work, daily activities, and social life, the SF-12 may represent a composite measure of pain interference interacting with distress. Therefore, we have conceptualized a subgroup of people who have elevated pain-related distress that may be an obstacle to recovery. Future work should include other known obstacles to recovery, such as fear avoidance and catastrophic thinking.

Whether an ETMI is particularly effective in patients who have psychosocial obstacles to recovery, including elevated distress, remains to be confirmed in future trials. A systematic review[8] of the evidence on the effectiveness of behavioral interventions in patients with CLBP concluded that these interventions appear to

be appropriate only for people who show indicators of significant psychosocial issues. The results of our study suggest that an ETMI is effective for those with distress, at least in reference to certain outcomes, such as reducing disability. The patients in the present study were recruited from primary care and likely to present with less complex problems than those referred to secondary care pain services.

CONCLUSION

Although patients with CLBP in both interventions improved, the ETMI was more effective than physical therapy for distressed participants in reducing disability, improving pain, and increasing physical activity. For nondistressed participants, an ETMI may be more effective than usual treatment in reducing disability (based on absolute values at 12 months), but no more effective in improving pain or physical activity. However, this study represents post hoc analysis of an age-specific subgroup of patients with CLBP, and future trials are needed to replicate the effect and to extend the findings through the use of planned subgroup analysis. ◉

KEY POINTS

FINDINGS: A large proportion of patients seen by physical therapists were classified as distressed (55.6%). Both physical therapy and the ETMI improved outcomes, but the magnitude of change was larger in the ETMI group, especially for participants with distress.

IMPLICATIONS: Physical therapists should be aware of psychological obstacles to recovery such as distress, and consider possibly adapting a more behavioral approach to these patients.

CAUTION: It is not possible to establish whether an ETMI is the optimal intervention for distressed patients with CLBP. The findings in this study are based on post hoc analysis and small samples, and are subject to the methodological limitations inherent in the original trial.

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Bed Rest for Sciatica: A Closer Look at the Evidence

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When managing acute nonspecific low back pain (LBP), bed rest is commonly discouraged as a form of therapy. Indeed, avoiding bed rest is recommended in numerous clinical practice guidelines pertaining to the management of acute nonspecific LBP in a primary care setting. A systematic review from Arnau et al[1] compared national guidelines from 13 different countries and reported recommendations ranging from "discourage even if pain is severe" to considering bed rest "harmful for more than 2 days." Such recommendations stem from consistent evidence that advice to stay active leads to better symptomatic and functional outcomes in both the short and long term for people with acute LBP.[4]

However, when the picture includes radiating leg pain arising from the lumbar spine, the evidence is less robust. In fact, only a minority of guidelines included in the review from Arnau et al[1] tailored their recommendations to differentiate between acute nonspecific LBP, acute LBP with radiating leg pain, and the combination of both. According to the authors, "Only three guidelines [out of thirteen] included recommendations for pain radiating in the leg."[1] This suggests that, in a clinical context, automatically extending the same recommendations for acute nonspecific LBP to patients with radiating leg pain may not be justified.

This discrepancy in the level of evidence may derive from 2 important aspects of the literature pertaining to LBP complicated by radiating leg pain. First, there is a paucity of studies specifically investigating bed rest as part of the management of radiating leg pain. The effects of recommendations to stay active versus resting in bed on sciatica, defined as "low back pain with verified neurological deficits," were addressed by a Cochrane review in 2010.[4] The review identified 10 randomized controlled trials concerning bed rest for LBP, of which only 2 (Vroomen et al[16] and Hofstee et al[8]) related to radiating leg pain. The authors concluded that, "For patients with sciatica, little or no difference is seen between advice to rest in bed and advice to stay active."[4] This is true for both pain levels and functional status up to a follow-up period of 3 months, even when individuals rested in bed for the entire first week of the study or when they were asked to lie in bed as much as possible for 3 months. As such, it is apparent that the literature is less dogmatic regarding the avoidance of bed rest when radiating leg pain is the dominant clinical feature. Again, it is important to recognize that the evidence regarding the effect of bed rest for radiating leg pain with verified neurological deficit has been investigated in only these 2 randomized controlled trials.[8,16]

Second, an additional observation from the randomized controlled trials from Vroomen et al[16] and Hofstee et al[8] is that the effects of bed rest were evaluated in a selected population presenting with acute LBP complicated by radiating leg pain. However, radiating leg pain may arise from several different pathophysiological mechanisms (**TABLE**). *Sciatica*, an arcane term used indiscriminately by clinicians and the public to refer to back-related leg pain, is used to encompass all forms, but is neither diagnostic nor epistemologically accurate.[13] This is probably due to a lack of consensus over a universally accepted definition of sciatica, the absence of widely accepted diagnostic criteria, and a poor understanding of the underlying pathophysiology.[6,9] The current definition of sciatica considers it a disease of the peripheral nervous system[5,14] that is consistent with lumbar radiculopathy. This means that the symptoms specifically arise from a disturbance or pathology of lumbosacral spinal nerves, which contrasts with somatic referred pain from lumbar osteoarticular or musculotendinous structures. While sciatica has been reported to affect up to

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43% of the general population, this lifetime prevalence estimate may be inflated; with careful examination, the prevalence of leg pain arising from a disease of the peripheral nervous system drops to about 4.8%.[6,9] Also to consider are the inclusion criteria of the 2 randomized controlled trials evaluating the effects of bed rest on radiating leg pain, which did not account for lower-limb pain location or the presence of neurological signs that would be mandatory requirements for a diagnosis of painful radiculopathy.[8,16] Instead, only a quarter of the selected participants exhibited neurological deficits.[16] Hence, a neurological source for leg pain was not adequately established, and it is reasonable to believe that the radiating pain might have corresponded more to somatic pain referred from musculoskeletal structures or arising from nonconducting neural tissue. In conclusion, this may explain the inconclusive results with respect to the effect of bed rest on patients presenting with lumbar spine–related leg pain.

From a biopsychosocial perspective, the importance of encouraging activity and participation in work and everyday life to improve long-term outcomes has been well established in patients with acute nonspecific LBP. However, it is premature to say that bed rest has a detrimental effect on pain and functional status in patients with radiating leg pain or radiculopathy, particularly where there is evidence of neurological deficits. Animal experimental evidence suggests that immediate or early exercise or passive movement following different types of nerve injury may help to reduce the development of neuropathic pain and may aid in recovery of nerve physiology.[2,7,11,15] Nonetheless, this remains to be confirmed in humans. In another animal experimental study,[15] there is evidence that delaying exercise by up to 4 weeks from the onset of nerve injury did not impact the beneficial effects of such activity in terms of nerve recovery and neuropathic pain amelioration. It is likely that prolonged bed rest is detrimental to health, inducing both musculoskeletal and cardiovascular deconditioning, as well as having a psychological impact on patients; however, short recovery periods in antalgic postures, including lying in bed, are not likely to be as harmful and may represent an important self-management strategy for patients. Further research is required to classify limb pain according to current evidence-based classification systems and to determine whether different forms of neural disorders respond in a similar way to bed rest in people with acute nonspecific LBP.

Leg pain due to neural tissue involvement is typically a very painful disorder. As such, in a clinical setting, allowing short recovery periods in bed as a pain management strategy while discouraging prolonged rest as a form of therapy may not be contraindicated, particularly when the alternatives—such as drug management—do not provide convincing benefit compared with a placebo,[10,12,17] and where opioids may even prolong neuropathic pain[3,7] or lead to addiction. Further studies are required to determine whether the prescription of bed rest has any place in the management of patients with radiating leg pain and radiculopathy, classified according to current evidence-based guidelines. ◉

TABLE Pathophysiological Mechanisms of Radiating Leg Pain

	Clinical Definition	
Clinical Characteristics	**Low Back Pain Plus Somatic Referred Leg Pain**	**Painful Radiculopathy**
Likely source of nociception	Nonneural tissue	Neural tissue
Predominant pain state	Nociceptive	Neuropathic
Bedside neurological examination	Normal (although weakness can occur due to pain inhibition)	Diminished sensation, reflex, or muscle power in an anatomically related nerve root pattern

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Optimal Screening for Prediction of Referral and Outcome (OSPRO) for Musculoskeletal Pain Conditions: Results From the Validation Cohort

STUDY DESIGN: Observational, prospective cohort.

BACKGROUND: Musculoskeletal pain is a common reason to seek health care, and earlier nonpharmacological treatment and enhancement of personalized care options are 2 high-priority areas. Validating concise assessment tools is an important step toward establishing better care pathways.

OBJECTIVES: To determine the predictive validity of Optimal Screening for Prediction of Referral and Outcome (OSPRO) tools for individuals with neck, low back, shoulder, or knee pain.

METHODS: A convenience sample (n = 440) was gathered by Orthopaedic Physical Therapy-Investigator Network clinics (n = 9). Participants completed demographic, clinical, and comorbidity questionnaires and the OSPRO tools, and were followed for 12-month outcomes in pain intensity, region-specific disability, quality of life, and comorbidity change. Analyses predicted these 12-month outcomes with models that included the OSPRO review-of-systems (OSPRO-ROS) and yellow flag (OSPRO-YF) tools and planned covariates (accounting for comorbidities and established demographic and clinical factors).

RESULTS: The 10-item OSPRO-YF tool (baseline and 4-week change score) consistently added to predictive models for 12-month pain intensity, region-specific disability, and quality of life. The 10-item OSPRO-ROS tool added to a predictive model for quality of life (mental summary score), and 13 additional items of the OSPRO-ROS+ tool added to prediction of 12-month comorbidity change. Other consistent predictors included age, race, income, previous episode of pain in same region, comorbidity number, and baseline measure for the outcome of interest.

CONCLUSION: The OSPRO-ROS and OSPRO-YF tools statistically improved prediction of multiple 12-month outcomes. The additional variance explained was small, and future research is necessary to determine whether these tools can be used as measurement adjuncts to improve management of musculoskeletal pain. *J Orthop Sports Phys Ther 2018;48(6):460-475. Epub 7 Apr 2018. doi:10.2519/jospt.2018.7811*

KEY WORDS: *OSPRO, outcomes, prognosis, red flag, yellow flag*

Musculoskeletal pain is a common reason to seek health care, and a national initiative has provided guidance on priorities for improving management of this costly and disabling condition.[33] Two elements stressed in progressive pain-management strategies are earlier nonpharmacological treatment[13,44] and enhancement of personalized/tailored care options.[33] Physical therapists can meet the demands of these initiatives by developing concise assessment tools to aid in clinical decision making for these elements.[27] In musculoskeletal pain management, there are 2 important components of almost every patient encounter: identification of symptoms that may indicate coexisting systemic pathology[15] and consideration of pain-associated distress and coping styles.[49] These components are important to consider, because their results could alter an episode of care by indicating the need for additional diagnostic testing before starting traditional nonpharmacological treatment,[14,28] either alone or supplemented with principles of psychologically informed practice.[5,31,42]

The Orthopaedic Physical Therapy-Investigator Network (OPT-IN) was formed to develop and validate concise assessment tools for individuals with a primary complaint of neck, shoulder, low back, or knee pain. The OPT-IN provided the clinical infrastructure necessary to recruit for

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the Optimal Screening for Prediction of Referral and Outcome (OSPRO) development and validation cohorts. The OSPRO cohort studies occurred in sequence, with the development cohort (a cross-sectional study for tool development) and the separately recruited validation cohort (a longitudinal study to test the predictive validity of the newly developed tools). The instruments were directly aligned with assessment of examination components that could influence a care episode. A review-of-systems (OSPRO-ROS) tool was developed for assessing symptoms of systemic pathology,[19] and a yellow flag (OSPRO-YF) tool was developed to assess psychosocial aspects of pain vulnerability and resilience.[39] Details on the OSPRO-ROS and OSPRO-YF tools have been previously reported[19,39] and will be described in more detail in the Methods section.

Though the development of the OSPRO-ROS and OSPRO-YF tools was encouraging, all prior work was done in a cross-sectional manner.[19,39] Because longitudinal studies provide a more optimal design to test the capabilities of these tools and to determine their predictive validity for outcomes relevant to clinical decision making, the purpose of the current paper was to report the primary analyses of the OSPRO validation cohort in individuals with a primary complaint of neck, low back, shoulder, or knee pain. These analyses involved prediction of 12-month pain, quality of life, region-specific disability, and comorbidity outcomes. Predictive models were built to determine the contribution of the OSPRO tools to 12-month outcomes after demographic, clinical, and baseline variables were already considered. In addition, we analyzed the interaction between anatomical region and the OSPRO tools to determine whether the performance of the tool would vary based on the primary site of pain. This approach provided a relatively high bar to determine the predictive validity of the new tools, because the models included previously established predictive factors and anatomical region as planned covariates. Based on prior studies showing that change in psychological factors may improve outcome prediction for low back pain,[4,26,55,57] 4-week change in the OSPRO-YF tool was entered into the last step of the prediction models. Our primary hypotheses were that the OSPRO-YF tool would improve prediction of pain and disability outcomes, while the OSPRO-ROS tool would improve prediction of quality of life and comorbidity outcomes.

METHODS

Overview

The OSPRO validation cohort study was approved by the University of Florida Human Subjects Institutional Review Board, and all participants provided consent to participate in the study. A convenience sample was gathered by participating OPT-IN clinics (n = 9) for the months of December 2014 through December 2015. The OPT-IN clinics that participated in data collection represented 5 of 8 geographic regions in the United States, including the Mideast, Southeast, Great Lakes, Rocky Mountain states, and Far West. The majority of the patients (275/440, 62.5%) were recruited from clinics in the Southeast region. The New England, Plains, and Southwest regions were not represented. An attempt was made to achieve a balance of patients from urban and rural settings over the entire OPT-IN; however, for pragmatic reasons, that balance could not be provided within each geographic region. Methodological details for the OSPRO validation cohort have been previously reported in a cohort-profile paper.[20] The current paper presents an abbreviated version of the methods that allows for interpretation of the primary analyses.

Participants

Inclusion Criteria Physical therapists determined the eligibility of participants at the initial evaluation using matching criteria from the development cohort.[19,39] Patients between 18 and 65 years of age were eligible to participate in this study if they (1) were seeking outpatient physical therapy treatment for musculoskeletal pain; (2) had primary complaints involving the cervical spine, lumbar spine, shoulder, or knee; and (3) were able to read and comprehend the English language (this criterion was necessary due to the large number of self-report forms).

Exclusion Criteria Patients were excluded from study participation for any diagnosis indicative of (1) widespread chronic pain syndrome (eg, fibromyalgia or irritable bowel syndrome), (2) neuropathic pain syndrome (eg, complex regional pain syndrome or diabetic neuropathy), (3) psychiatric history (currently in care of mental health care provider or taking 2 or more prescription psychiatric medications), (4) cancer (currently receiving treatment for active cancer), or (5) neurological disorder (eg, stroke, spinal cord injury, or traumatic brain injury).

Baseline and follow-up data collection was conducted online at the clinic or at home (based on individual preference), and the participants completed all survey assessments on the study website. Eligible participants were directed to a secure, University of Florida–hosted website for the informed-consent process and baseline assessment. All assessments were self-report and completed electronically by the participant in a deidentified manner.

Follow-ups were at 4 weeks, 6 months, and 12 months, and participants were notified of a pending assessment by an e-mail that directed them back to the study website to complete their follow-up assessment. If participants did not complete their follow-up assessment within 1 week of the first e-mail notification, then an additional e-mail reminder was sent each week for up to 3 weeks. Participants who were not responsive to any of these e-mail reminders were contacted by telephone. Only 12-month data were reported in this paper, and there are no plans to report the 6-month data separately.

Predictive Measures

Demographic and Clinical Information Participants completed a standard intake form previously used in our clinical

studies[3,23] to collect information including age, sex, race, income, employment, education, insurance, geographic region, pain location, pain duration, pain onset type, previous episode in same location, and history of surgery. Historical data included the anatomical location of the pain, onset of symptoms, duration of symptoms, previous episodes in same anatomical region, and previous treatments.

Comorbidities Health history was determined with the Charlson and functional comorbidity indices.[9,24] For analysis purposes, a comorbidity count was derived by adding a unique number of comorbidities reported (ie, similar comorbidities reported in both indices were only counted once). The number of comorbidities reported at baseline was used as a covariate.

OSPRO Tools

Review of Systems The OSPRO-ROS tool includes standard symptom descriptors previously used to aid in screening for potential systemic involvement.[19] It includes questions related to symptoms of the cardiovascular, gastrointestinal, endocrine, nervous, integumentary, pulmonary, and musculoskeletal systems that were identified based on their ability to predict any 1 positive response to a larger item bank. The accuracy of the 10- and 23-item versions of the OSPRO-ROS tool differed in predicting a positive response to the larger item bank[19]; therefore, these versions were considered separately in predictive analyses. The OSPRO-ROS tool was scored by summing the positive responses, which provided a potential range of 0 to 23 when all 23 items were used. Higher OSPRO-ROS scores indicate higher levels of red flag symptom complaints. In this analysis, we separated the 23 items to determine whether they uniquely contributed to outcomes of interest; therefore, OSPRO-ROS refers to the first 10 items of the tool and OSPRO-ROS+ refers to the additional 13 items.

Yellow Flags The OSPRO-YF tool includes items from pain-vulnerability domains (negative affect and fear avoidance) and pain-resilience domains (positive affect and self-efficacy) to aid in the efficient identification of pain-associated psychological distress and coping.[39] The OSPRO-YF tool estimates scores for full-length parent questionnaires with increased accuracy based on 10- and 17-item versions of the tool. The OSPRO-YF tool was considered in predictive analyses by testing the 10-item version and additional 7 items separately.[39] The OSPRO-YF tool was scored by summing all item responses from the original parent questionnaires on the original scale, with pain-resilience items reverse scored, providing a potential score range of 6 to 89 when all 17 items are used. Higher OSPRO-YF scores indicate higher psychological distress, as demonstrated by higher pain vulnerability and lower pain resilience.

Outcome Measures

Outcome measures were captured at baseline and at 12-month follow-up. The baseline value of a given measure was included in the corresponding prediction model for 12-month outcomes. Pain intensity was assessed with the 0-to-10 numeric pain-rating scale (NPRS), with 0 indicating no pain and 10 the worst pain imaginable. Participants rated their current pain intensity, as well as their best (lowest) and worst (highest) pain intensity over the past 24 hours.[6,10,35] The average of these 3 NPRS scores was used to represent pain intensity in these analyses.

Region-specific disability was assessed by participants completing 1 of the following questionnaires that matched the primary site of pain complaint: (1) Neck Disability Index,[53] (2) Oswestry Disability Questionnaire,[17] (3) shortened version of the Disabilities of the Arm, Shoulder and Hand questionnaire,[2] or (4) International Knee Documentation Committee Subjective Knee Evaluation Form.[34] The individual region-specific measures were included in the analysis as *z* scores due to different scaling, and were thus able to be included in the same predictive models, consistent with analyses from the OSPRO development cohort.[7]

The Medical Outcomes Study 8-Item Short-Form Health Survey was used as a general quality-of-life measure and reported as the corresponding Physical Component Summary (PCS) and Mental Component Summary (MCS) scores.[18,38] Comorbidity at 12 months was included as an outcome measure to determine change in disease burden and assessed in the same manner described in the Predictive Measures section.

Data Analysis

Our primary analyses assessed the accuracy of the OSPRO-ROS and OSPRO-YF tools in predicting 12-month outcomes. Separate general linear models were fitted for the continuous outcome measures of 12-month pain intensity, region-specific disability, quality of life, and comorbidity, using the OSPRO tools as planned fixed effects. Before OSPRO tools were considered, we entered planned covariates into each prediction model, including, for example, age, sex, race, income, employment, education, type of insurance, geographic region, pain location, pain duration, pain onset type, previous episode in same location, history of surgery, comorbidities, and the corresponding outcome measure at baseline (full set reported in **TABLE 1**). This modeling approach is consistent with other reports in the literature[3,16,25] and resulted in the following model structure, applied consistently for each outcome of interest:

- Block 1: demographic, clinical, and comorbidity
- Block 2: baseline dependent variable
- Block 3: OSPRO tools, short version (10-item versions of the OSPRO-ROS and OSPRO-YF)
- Block 4: OSPRO tools, longer version (13 additional items for the OSPRO-ROS and 7 additional items for the OSPRO-YF)
- Block 5: OSPRO-YF 4-week change score

After block 5, interaction terms for OSPRO-YF and OSPRO-ROS tools by anatomical region were included in the

TABLE 1 Descriptive Summary of OSPRO Validation Cohort

Variable	Overall Sample (n = 440)	Missing 12-mo Follow-up (n = 161)	Completed 12-mo Follow-up (n = 279)	*P* Value
Demographics				
Age, y*				.024
Mean ± SD	45.2 ± 15.8	43.1 ± 15.3	46.5 ± 16.0	
Median (range)	45 (18-75)	42 (18-74)	47 (18-75)	
Sex, n (%)				.145
Male	164 (37.3)	69 (42.9)	95 (34.1)	
Female	275 (62.5)	92 (57.1)	183 (65.6)	
Prefer not to answer	1 (0.2)		1 (0.4)	
Race, n (%)				.121
American Indian/Alaska Native	3 (0.7)	1 (0.6)	2 (0.7)	
Asian	25 (5.7)	8 (5.0)	17 (6.1)	
Black or African American	62 (14.1)	32 (19.9)	30 (10.8)	
White	343 (78.0)	117 (72.7)	226 (81.0)	
Don't know/prefer not to answer	7 (1.6)	3 (1.9)	4 (1.4)	
Ethnicity, n (%)				.310
Hispanic or Latino	31 (7.0)	10 (6.2)	21 (7.5)	
Not Hispanic or Latino	376 (85.5)	135 (83.9)	241 (86.4)	
Don't know/prefer not to answer	33 (7.5)	16 (9.9)	17 (6.1)	
Income, n (%)*				.004
Less than $20000	59 (13.4)	29 (18.0)	30 (10.8)	
$20000 to $35000	53 (12.0)	14 (8.7)	39 (14.0)	
$35001 to $50000	50 (11.4)	17 (10.6)	33 (11.8)	
$50001 to $70000	56 (12.7)	24 (14.9)	32 (11.5)	
Greater than $70000	156 (35.5)	44 (27.3)	112 (40.1)	
Don't know/prefer not to answer	66 (15.0)	33 (20.5)	33 (11.8)	
Employment, n (%)*				.007
Full-time employed	237 (53.9)	88 (54.7)	149 (53.4)	
Part-time employed	62 (14.1)	21 (13.0)	41 (14.7)	
Unemployed	61 (13.9)	31 (19.3)	30 (10.8)	
Retired	58 (13.2)	11 (6.8)	47 (16.8)	
Prefer not to answer	22 (5.0)	10 (6.2)	12 (4.3)	
Education, n (%)*				<.0001
Less than high school	11 (2.5)	10 (6.2)	1 (0.4)	
Graduated from high school	38 (8.6)	21 (13.0)	17 (6.1)	
Some college	112 (25.5)	49 (30.4)	63 (22.6)	
Graduated from college	120 (27.3)	41 (25.5)	79 (28.3)	
Some postgraduate coursework	56 (12.7)	15 (9.3)	41 (14.7)	
Completed postgraduate degree	97 (22.0)	23 (14.3)	74 (26.5)	
Prefer not to answer	6 (1.4)	2 (1.2)	4 (1.4)	
Insurance, n (%)*				.009
Private	273 (62.0)	93 (57.8)	180 (64.5)	
Medicare	52 (11.8)	13 (8.1)	39 (14.0)	
Medicaid	19 (4.3)	9 (5.6)	10 (3.6)	
Workers' compensation	14 (3.2)	8 (5.0)	6 (2.2)	
Disability	4 (0.9)	3 (1.9)	1 (0.4)	
Uninsured	7 (1.6)	5 (3.1)	2 (0.7)	
Other	45 (10.2)	15 (9.3)	30 (10.8)	
Unknown/prefer not to answer	26 (5.9)	15 (9.3)	11 (3.9)	

Table continues on page 464.

TABLE 1 Descriptive Summary of OSPRO Validation Cohort (continued)

Variable	Overall Sample (n = 440)	Missing 12-mo Follow-up (n = 161)	Completed 12-mo Follow-up (n = 279)	*P* Value
Clinic site, n (%)*				.025
Portland, OR	20 (4.5)	4 (2.5)	16 (5.7)	
Los Angeles, CA	61 (13.9)	18 (11.2)	43 (15.4)	
Greenville, SC	86 (19.5)	28 (17.4)	58 (20.8)	
Boulder, CO	17 (3.9)	1 (0.6)	16 (5.7)	
Jacksonville, FL	50 (11.4)	21 (13.0)	29 (10.4)	
Gainesville, FL	139 (31.6)	59 (36.6)	80 (28.7)	
Philadelphia, PA	20 (4.5)	7 (4.3)	13 (4.7)	
Chicago, IL	24 (5.5)	13 (8.1)	11 (3.9)	
Terra Haute, IN	23 (5.2)	10 (6.2)	13 (4.7)	
Anatomical region, n (%)				.375
Neck	98 (22.3)	39 (24.2)	59 (21.1)	
Low back	118 (26.8)	46 (28.6)	72 (25.8)	
Shoulder	107 (24.3)	41 (25.5)	66 (23.7)	
Knee	117 (26.6)	35 (21.7)	82 (29.4)	
Pain duration, d				.955
Mean ± SD	413.8 ± 1757.6	506.5 ± 1454.1	360.2 ± 1911.4	
Median (range)	90 (0-29565)	90 (0-10000)	90 (1-29565)	
Onset of symptoms, n (%)*				.028
Gradual	239 (54.3)	74 (46.0)	165 (59.1)	
Sudden	138 (31.4)	60 (37.3)	78 (28.0)	
Traumatic	63 (14.3)	27 (16.8)	36 (12.9)	
Previous episodes in past year, n (%)				.187
Yes	224 (50.9)	81 (50.3)	143 (51.3)	
No	185 (42.0)	64 (39.8)	121 (43.4)	
Do not remember	31 (7.0)	16 (9.9)	15 (5.4)	
Surgery for primary complaint, n (%)				.094
Yes	83 (18.9)	37 (23.0)	46 (16.5)	
No	357 (81.1)	124 (77.0)	233 (83.5)	
Unique number of comorbidities				.158
Mean ± SD	2.1 ± 2.3	1.9 ± 2.1	2.2 ± 2.3	
Median (range)	1.5 (0-13)	1 (0-13)	2 (0-11)	
Distribution of comorbidities, n (%)				.437
0	134 (30.6)	55 (34.2)	79 (28.5)	
1	85 (19.4)	31 (19.3)	54 (19.5)	
2+	219 (50.0)	75 (46.6)	144 (52.0)	
OSPRO-ROS				
10-item score (0-10)				.515
Mean ± SD	2.7 ± 2.4	2.8 ± 2.5	2.6 ± 2.3	
Median (range)	2 (0-10)	2 (0-10)	2 (0-10)	
13-item score (0-13)				.924
Mean ± SD	1.2 ± 1.8	1.4 ± 2.1	1.2 ± 1.6	
Median (range)	1 (0-12)	1 (0-12)	1 (0-9)	
23-item score (0-23)				.631
Mean ± SD	3.9 ± 3.8	4.2 ± 4.3	3.8 ± 3.5	
Median (range)	3 (0-21)	3 (0-21)	3 (0-17)	

Table continues on page 465.

TABLE 1 Descriptive Summary of OSPRO Validation Cohort (continued)

Variable	Overall Sample (n = 440)	Missing 12-mo Follow-up (n = 161)	Completed 12-mo Follow-up (n = 279)	*P* Value
OSPRO-YF*				
10-item score (3-53)				.033
Mean ± SD	17.4 ± 6.7	18.4 ± 7.2	16.9 ± 6.3	
Median (range)	17 (4-47)	18 (4-47)	16 (4-40)	
7-item score (3-46)				.005
Mean ± SD	14.9 ± 5.5	15.9 ± 6.3	14.3 ± 4.9	
Median (range)	15 (3-34)	16 (3-34)	15 (3-28)	
17-item score (6-89)				.009
Mean ± SD	32.4 ± 11.2	34.3 ± 12.5	31.2 ± 10.3	
Median (range)	32 (8-81)	33 (8-81)	31 (9-68)	
Average pain intensity (0-10)*				<.001
Mean ± SD	4.2 ± 2.0	4.8 ± 2.3	3.9 ± 1.7	
Median (range)	4 (0-9.7)	4.7 (0-9.7)	3.7 (0-8)	
Quality of life (0-100)				
Physical Component Summary				.138
Mean ± SD	42.7 ± 8.5	41.9 ± 9.1	43.2 ± 8.1	
Median (range)	43.7 (22.4-59)	42.1 (22.4-58.6)	44.4 (24.9-59)	
Mental Component Summary				.070
Mean ± SD	50.9 ± 9.1	49.9 ± 9.3	51.5 ± 9.0	
Median (range)	53 (22.6-68.8)	51.8 (26-65.7)	53.7 (22.6-68.8)	
Neck Disability Index (0-100)*				.045
Mean ± SD	28.6 ± 16.1	31.8 ± 15.6	26.5 ± 16.3	
Median (range)	24 (2-76)	30 (2-62)	22 (2-76)	
Revised Oswestry Disability Questionnaire (0-100)				.279
Mean ± SD	28.7 ± 18.2	30.7 ± 18.8	27.4 ± 17.9	
Median (range)	26 (0-86)	31 (0-86)	24 (2-82)	
QuickDASH (0-100)				.071
Mean ± SD	38.8 ± 20.1	43.6 ± 22.5	35.8 ± 17.9	
Median (range)	34.1 (2.3-97.7)	43.2 (2.3-97.7)	31.8 (6.8-77.3)	
IKDC total score (0-100)				.908
Mean ± SD	39.6 ± 15.7	39.6 ± 17.6	39.6 ± 14.9	
Median (range)	39.2 (7.2-77.3)	38.1 (15.5-73.2)	39.2 (7.2-77.3)	
Region-specific disability (*z* score)*				.032
Mean ± SD	0.4 ± 0.9	0.6 ± 1.0	0.4 ± 0.9	
Median (range)	0.3 (−1.6-3.6)	0.5 (−1.3-3.6)	0.2 (−1.6-3.4)	

Abbreviations: IKDC, International Knee Documentation Committee Subjective Knee Evaluation Form; OSPRO, Optimal Screening for Prediction of Referral and Outcome; OSPRO-ROS, Optimal Screening for Prediction of Referral and Outcome review-of-systems tool; OSPRO-YF, Optimal Screening for Prediction of Referral and Outcome yellow flag tool; QuickDASH, shortened version of the Disabilities of the Arm, Shoulder and Hand questionnaire.
**Variable differs based on follow-up status.*

models to investigate the specificity of their use based on primary site of pain complaint. Predictive analyses were first conducted with completed cases in full (all covariates) and parsimonious (backward-selection) models. Missing 12-month outcomes were then accounted for using regression imputation.[47] Considering that the data might not have been missing at random, we also performed regressions inversely weighted by inclusion (nonmissing) probability, which was estimated based on logistic regressions with logit link and predictors that included age, education, type of insurance, pain onset type, and baseline dependent variable.[8] Therefore, this paper reported results from completed cases, regression imputation, and inverse probability weighted. Presenting the results in this manner remained true to the original analysis plan, while also presenting models that appropriately accounted for loss to follow-up.

Power Analysis

There are no uniform standards for determining sample size in cohort studies. For the OSPRO studies, sample-size estimates were based on precision for the assessment tools. The sample size was calculated so that 95% confidence intervals for the accuracy of predicting the 23-item version of the OSPRO-ROS tool from the abbreviated 10-item version would have a maximum width of ±5%. Specifically, we required that sample size (n) satisfy $\sqrt{(p \times [1-p]/n)} \times 1.96 < 0.05$, where p is the prediction accuracy. This calculation yielded 385 patients with neck, shoulder, low back, or knee pain. An estimate of 20% loss to follow-up at 1 year resulted in a required total sample size of 462, or approximately 115 patients for each anatomical region.

RESULTS

Recruitment and Follow-up Summary

A descriptive summary of the OSPRO validation cohort is reported in **TABLE 1**, and additional data are available in the cohort profile paper.[20] A total of 440 participants completed baseline measures with primary complaints of neck (n = 98, 22.3%), shoulder (n = 107, 24.3%), low back (n = 118, 26.8%), or knee (n = 117, 26.6%) pain. A total of 279 (63.4%) participants completed the 12-month follow-up with primary complaints of neck (n = 59, 21.1%), shoulder (n = 66, 23.7%), low back (n = 72, 25.8%), or knee (n = 82, 29.4%) pain. While there were no differences in follow-up rates by anatomical region, there were several differences between those who completed the 12-month follow-up and those who did not (**TABLE 1**).

Those who completed the follow-up were more likely to be older, have higher income, and have completed higher levels of education. There were differences in insurance type, clinic site, and onset of symptoms based on 12-month follow-up. Finally, those who completed the follow-up had lower scores on the OSPRO-YF, neck disability, pain intensity, and composite z score for region-specific disability. Those who did not complete the follow-up for this study were more likely to have lower income and education levels, to be uninsured or on disability, to be covered by Medicaid or workers' compensation, and to be experiencing higher pain and pain-associated distress. All variables reported in **TABLE 1** were planned as covariates, so no additional covariates were added to the prediction models based on differences in follow-up rates.

Overall Model Performance

Overall performance for completed cases, regression imputation, and inverse probability–weighted models is summarized in **TABLE 2**, and individual predictors across these models are summarized in **TABLE 3**.

There was a consistent pattern in the prediction of 12-month pain, disability, and quality-of-life outcomes. The baseline value of the outcome of interest explained most of the additional variance, after accounting for demographic and clinical variables. The 10-item version of the OSPRO-YF tool explained variance beyond baseline scores, and the 10-item version of the OSPRO-ROS tool explained only the additional variance in MCS scores. The additional amount of variance explained at baseline by OSPRO tools was small (increment range, 0.01-0.07). When the 4-week change in the 10-item OSPRO-YF tool was added to prediction models, it explained additional variance in 12-month pain, disability, and quality-of-life outcomes. Again, the overall amount of variance added was smaller than change scores (increment range, 0.04-0.07).

The pattern for predicting 12-month comorbidity change differed from the other outcome measures. Baseline number of comorbidities still explained the most additional variance after accounting for demographic and clinical variables; however, only the 13 additional items from the OSPRO-ROS+ tool explained variance in the models predicting 12-month comorbidity change.

Individual Predictors of Outcome

Parsimonious models were used to identify individual predictors, because they provided a conservative estimate of the overall model's predictive ability (parsimonious models had the lowest total variance explained) (**TABLE 2**). Parsimonious models were deemed appropriate for identifying individual predictors due to a lower-than-anticipated follow-up rate at 12 months, which suggests that the full models would have been overfitted had all the covariates been included. Finally, we wanted to preserve the efficiency in identifying (ie, reporting the fewest) individual predictors and to avoid overreporting individual predictors. Fewer individual predictors make the building of future risk models easier by better prioritizing the collection of clinical data. Results from completed cases and regression imputation models were reported to allow for direct comparisons of model stability.

Model parameters for individual predictors are provided in detail in **TABLE 4** (pain intensity and region-specific disability), **TABLE 5** (quality of life), and **TABLE 6** (comorbidity). The estimates provided in **TABLES 4** through **6** represent how much the outcome variable would be expected to change per 1 unit of change in a given predictor variable. For example, for the 12-month pain intensity outcomes in **TABLE 4**, the estimate for "previous episode" as a categorical predictor is 0.83 (completed-cases model). This means that a response of yes to "previous episode" would increase the expected 12-month pain intensity score by an additional 0.83 points on the NPRS compared to a response of no. As another example from **TABLE 4**, baseline pain intensity is a continuous predictor with an estimate of 0.41 (completed-cases model). This means that a baseline pain intensity score of 6 would be predicted to be 2.05 points higher (5 × 0.41) at 12 months on the NPRS compared to a baseline pain intensity score of 1. A summary of individual predictors for each outcome is provided below.

12-Month Pain Intensity Previous episode in same region, baseline pain in-

TABLE 2 Model Performance for OSPRO Tools Predicting 12-Month Clinical Outcomes

Dependent Variable (12 mo)/Predictive Models	Pain Intensity*	Region-Specific Disability†	PCS‡	MCS‡	Comorbidity§
Block 1: demographic, clinical, and comorbidity					
Completed cases	.276‖	.368‖	.314‖	.291‖	.677‖
Regression imputation	.305‖	.352‖	.291‖	.311‖	.519‖
Inverse probability weighted	.306‖	.397‖	.299‖	.312‖	.463‖
Block 2: baseline dependent variable					
Completed cases	.374¶	.516¶	.402¶	.435¶	
Regression imputation	.407¶	.485¶	.376¶	.433¶	
Inverse probability weighted	.406¶	.549¶	.385¶	.425¶	
Block 3: OSPRO-YF (10 items), OSPRO-ROS (10 items)					
Completed cases	.406¶	.544	.467¶	.483¶	.705¶
Regression imputation	.422¶	.501¶	.413¶	.453¶	.530¶
Inverse probability weighted	.442¶	.580¶	.452¶	.473¶	.485¶
Block 4: OSPRO-YF (7 items),# OSPRO-ROS (13 items)#					
Completed cases	.427	.559	.497	.491	.730
Regression imputation	.436	.504	.429	.460	.541¶
Inverse probability weighted	.461	.592	.478	.478	.502
Block 5: OSPRO-YF (4-wk change)					
Completed cases	.456	.587¶	.531¶	.522¶	.732¶
Regression imputation	.458¶	.536¶	.469¶	.501¶	.544¶
Inverse probability weighted	.507	.628¶	.550¶	.554¶	.700
Parsimonious model (backward selection)					
Completed cases	.317‖	.458‖	.417‖	.412‖	.626‖
Regression imputation	.369‖	.467‖	.353‖	.424‖	.444‖
Inverse probability weighted	.350‖	.491‖	.433‖	.430‖	.613‖

Abbreviations: MCS, Mental Component Summary; OSPRO, Optimal Screening for Prediction of Referral and Outcome; OSPRO-ROS, Optimal Screening for Prediction of Referral and Outcome review-of-systems tool; OSPRO-YF, Optimal Screening for Prediction of Referral and Outcome yellow flag tool; PCS, Physical Component Summary.

**Pain intensity was measured on a 0-to-10 numeric pain-rating scale.*

†Region-specific disability was from z scores derived from validated questionnaires for neck, shoulder, back, and knee disability.

‡The PCS and MCS were from the Medical Outcomes Study 8-Item Short-Form Health Survey.

§Comorbidity change was from the Charlson and functional comorbidity indices.

‖R^2: P<.05 (first step of model).

¶R^2 increment: P<.05 (compared to previous step).

#Additional items in longer versions of the corresponding tool.

tensity, and the OSPRO-YF tool (10-item and 4-week change) were predictors in the inverse probability–weighted model (**TABLE 4**). These predictors matched the completed-cases model, while the regression imputation model also included educational level.

12-Month Region-Specific Disability The inverse probability–weighted model included sex, race, comorbidity, baseline score, and OSPRO-YF tool (10-item and 4-week change) as individual predictors (**TABLE 4**). These predictors matched the completed-cases model. The regression imputation model included different demographic factors for predictors (eg, age and previous episode) and also considered anatomical region. The nature of the interaction indicated that prediction of disability outcomes at the shoulder region differed from those at the knee; otherwise, individual predictors matched those of the other models.

12-Month PCS Race, comorbidity, baseline PCS score, and the OSPRO-YF tool (10-item and 4-week change) were predictors in the inverse probability–weighted model (**TABLE 5**). These predictors matched those of the completed-cases model, and the regression imputation model differed by including age (instead of race) as an individual predictor.

12-Month MCS The inverse probability–weighted model included age, baseline MCS score, 10-item OSPRO-ROS, and the OSPRO-YF tool (10-item and 4-week change) as individual predictors (**TABLE 5**). These predictors matched the completed-cases model, and the regression imputation model included income as an additional individual predictor.

TABLE 3 Predictors of 12-Month Clinical Outcomes from Completed Cases and Regression Imputation Approaches

Model Type	Demographic, Clinical, and Comorbidity	Baseline Dependent	Baseline OSPRO, Short	Baseline OSPRO, Long	4-wk Change, OSPRO-YF	Region, Interaction
Pain intensity (0-10)*						
Completed cases	Previous episodes	Yes	YF-10		Yes	
Regression imputation	Income, previous episodes	Yes	YF-10		Yes	
Inverse probability weighted	Race, previous episodes	Yes	YF-10			ROS-10
Region-specific disability†						
Completed cases	Sex, race, comorbidity	Yes	YF-10		Yes	
Regression imputation	Age, previous episodes, anatomical region, comorbidity	Yes	YF-10		Yes	YF-10
Inverse probability weighted	Race, income, previous episodes	Yes	YF-10		Yes	
PCS‡						
Completed cases	Race, comorbidity	Yes	YF-10		Yes	
Regression imputation	Age, comorbidity	Yes	YF-10		Yes	
Inverse probability weighted	Race, income, anatomical region, comorbidity	Yes	YF-10		Yes	
MCS‡						
Completed cases	Age	Yes	ROS-10, YF-10		Yes	
Regression imputation	Age, income	Yes	ROS-10, YF-10		Yes	
Inverse probability weighted	Age, income, education	Yes	YF-10		Yes	
Comorbidity§						
Completed cases		Yes		ROS+		
Regression imputation	Age	Yes		ROS+		
Inverse probability weighted	Education	Yes		ROS+		

Abbreviations: MCS, Mental Component Summary; OSPRO, Optimal Screening for Prediction of Referral and Outcome; OSPRO-YF, Optimal Screening for Prediction of Referral and Outcome yellow flag tool; PCS, Physical Component Summary; ROS+, additional 13 items of the review-of-systems tool; YF-10 or ROS-10, 10-item version of the tool.
**Measured on a 0-to-10 numeric pain-rating scale.*
†Region-specific disability was from z scores derived from validated questionnaires for neck, shoulder, back, and knee disability.
‡The PCS and MCS were from the Medical Outcomes Study 8-Item Short-Form Health Survey.
§Comorbidity was from the Charlson and functional comorbidity indices.

12-Month Comorbidity Education, baseline number of comorbidities, and the 13 additional items of the OSPRO-ROS+ were individual predictors in the inverse probability–weighted model (**TABLE 6**). The completed-cases model included only the baseline number of comorbidities and 13 additional items of the OSPRO-ROS+, and the regression imputation model included age, the baseline number of comorbidities, and 13 additional items of the OSPRO-ROS+.

DISCUSSION

Analyses from the OSPRO validation cohort provided additional information on the use of concise assessment tools for prediction of musculoskeletal pain outcomes. The 10-item OSPRO-YF added statistically to the prediction of 12-month pain intensity, disability, and quality of life (physical and mental), a finding consistent with other concise tools for pain-associated distress (eg, the Örebro Musculoskeletal Pain Questionnaire[32,41] and STarT Back Tool[29,30]). The 10-item OSPRO-ROS tool added statistically to the prediction of 12-month quality-of-life (mental) outcomes, while the 13-item OSPRO-ROS+ tool added statistically to the prediction of comorbidity status outcomes. The present study's findings on the OSPRO-ROS and OSPRO-ROS+ are novel, as there are no other tools available that we are aware of for direct comparison, and these data provide preliminary support for the predictive validity of these tools. All predictive models included demographic, clinical, and baseline variables as planned covariates, consistent with previous modeling strategies.[3,21,25] The OSPRO tools added a relatively small amount of variance to models containing covariates (ie, demographic and clinical factors, comorbidity, and baseline outcome scores), as in another report that focused on psychological measures.[16] Therefore, the OSPRO tools may have limited potential to enhance clinical decision making, when considered in conjunction with demographic variables and baseline outcome scores.

TABLE 4 Parameters for Individual Predictors of Pain Intensity and Region-Specific Disability

Measure/Completed Cases	Estimate	Regression Imputation	Estimate	Inverse Probability Weighted	Estimate
12-mo pain intensity*					
Intercept	−0.91	Intercept	−0.34	Intercept	−1.12
		Education			
		High school or lower (reference)			
		Some college	0.84		
		Graduated from college	−0.01		
		Some postgraduate coursework	0.05		
		Completed postgraduate degree	−0.22		
		Prefer not to answer	−0.31		
Previous episode, yes (reference, no)	0.83	Previous episode, yes (reference, no)	0.61	Previous episode, yes (reference, no)	0.89
Baseline pain intensity	0.41	Baseline pain intensity	0.35	Baseline pain intensity	0.43
OSPRO-YF (10 items)	0.07	OSPRO-YF (10 items)	0.05	OSPRO-YF (10 items)	0.08
OSPRO-YF (change)	0.08	OSPRO-YF (change)	0.06	OSPRO-YF (change)	0.08
12-mo region-specific disability†					
Intercept	−1.22	Intercept	−1.41	Intercept	−1.30
Sex, male (reference, female)	−0.29	Age, y	0.01	Sex, male (reference, female)	−0.31
Race		Previous episode, yes (reference, no)	0.28	Race	
White (reference)				White (reference)	
American Indian/Alaska Native	1.06			American Indian/Alaska Native	0.97
Asian	−0.16			Asian	−0.16
Black or African American	0.26			Black or African American	0.32
Prefer not to answer	2.22			Prefer not to answer	2.48
		Anatomical region			
		Knee (reference)			
		Neck	−0.01		
		Low back	−0.13		
		Shoulder	−0.76		
Comorbidity (baseline)‡	0.08	Comorbidity (baseline)‡	0.06	Comorbidity (baseline)‡	0.08
Baseline *z* score	0.35	Baseline *z* score	0.34	Baseline *z* score	0.36
OSPRO-YF (10 items)	0.03	OSPRO-YF (10 items)	0.01	OSPRO-YF (10 items)	0.04
OSPRO-YF (change)	0.04	OSPRO-YF (4-wk change)	0.04	OSPRO-YF (change)	0.04
		Anatomical region by yellow flag			
		Knee (reference)			
		Neck	0.03		
		Low back	0.02		
		Shoulder	0.06		

Abbreviation: OSPRO-YF, Optimal Screening for Prediction of Referral and Outcome yellow flag tool.
**Pain intensity was from a 0-to-10 numeric pain-rating scale.*
†Region-specific disability was from z scores derived from validated questionnaires for neck, shoulder, back, and knee disability.
‡Comorbidity included unique number from the Charlson and functional comorbidity indices.

The OSPRO tools are intentionally concise and consistently contributed to outcome prediction across a variety of domains in the parsimonious prediction models. Therefore, these tools could be useful measurement adjuncts for health systems developing clinical pathways to determine the appropriateness of nonpharmacological pain management,[44] to facilitate the delivery of psychologically informed treatment options,[42] and to assess the impact of disease burden on patient-management strategies.[48] However, the individual clinical relevance (if any) of the OSPRO tools will need to be determined in follow-up studies in additional cohorts.

The 10-item OSPRO-YF tool consistently contributed a small amount of additional variance to the predictive models for 12-month pain intensity,

TABLE 5 Parameters for Individual Predictors of Quality of Life

Measure/Completed Cases	Estimate	Regression Imputation	Estimate	Inverse Probability Weighted	Estimate
12-mo PCS*					
Intercept	45.33	Intercept	48.14	Intercept	47.1
Race		Age, y	−0.07	Race	
White (reference)				White (reference)	
American Indian/Alaska Native	−4.67			American Indian/Alaska Native	−5.12
Asian	3.26			Asian	3.51
Black or African American	−3.16			Black or African American	−2.94
Prefer not to answer	−18.76			Prefer not to answer	−19.58
Comorbidity (baseline)†	−0.83	Comorbidity (baseline)†	−0.54	Comorbidity (baseline)†	−0.92
Baseline PCS score	0.27	Baseline PCS score	0.23	Baseline PCS score	0.24
OSPRO-YF (10 items)	−0.37	OSPRO-YF (10 items)	−0.33	OSPRO-YF (10 items)	−0.40
OSPRO-YF (change)	−0.40	OSPRO-YF (change)	−0.38	OSPRO-YF (change)	−0.41
12-mo MCS*					
Intercept	38.76	Intercept	34.15	Intercept	38.93
Age, y	0.09	Age, y	0.07	Age, y	0.08
		Income			
		<$20000 (reference)			
		$20000-$35000	4.71		
		$35001-$50000	6.40		
		$50001-$75000	4.88		
		>$75000	6.33		
		Prefer not to answer	5.29		
Baseline MCS score	0.34	Baseline MCS score	0.28	Baseline MCS score	0.35
OSPRO-ROS (10 items)	−0.58	OSPRO-ROS (10 items)	−0.34	OSPRO-ROS (10 items)	−0.65
OSPRO-YF (10 items)	−0.42	OSPRO-YF (10 items)	−0.28	OSPRO-YF (10 items)	−0.43
OSPRO-YF (change)	−0.41	OSPRO-YF (change)	−0.38	OSPRO-YF (change)	−0.41

Abbreviations: MCS, Mental Component Summary; OSPRO-ROS, Optimal Screening for Prediction of Referral and Outcome review-of-systems tool; OSPRO-YF, Optimal Screening for Prediction of Referral and Outcome yellow flag tool; PCS, Physical Component Summary.
**The PCS and MCS were from the Medical Outcomes Study 8-Item Short-Form Health Survey (0-100 scale).*
†Comorbidity included unique number from the Charlson and functional comorbidity indices.

region-specific disability, and quality-of-life (mental and physical) outcomes. This finding shows a predictive ability similar to that of the aforementioned assessment tools (eg, Örebro Musculoskeletal Pain Questionnaire[32,41] and STarT Back Tool[29,30]), and a recent study suggests that it is unlikely that any single screening tool would be superior for prediction when compared with other screening tools.[37]

A few caveats deserve mention in interpreting results from this cohort. First, the OSPRO-YF tool is predictive of multiple outcome domains, while the other assessment tools tend to have stronger predictive capabilities for functional outcomes.[36] Second, the OSPRO-YF tool included items for pain resilience, a dimension not captured by the other tools but that may be relevant for predicting pain-related outcomes. Third, the OSPRO-YF tool can be used as a total score (as in the analyses of the present study) or as estimate scores of the 11 full-length parent questionnaires for negative mood, fear avoidance, and positive coping style (as in the development paper[39]). However, we acknowledge that the predictive contributions of the OSPRO tools to outcomes were small in magnitude and that additional research must be completed to provide informed recommendations for clinical use.

The contribution of the 10-item OSPRO-YF 4-week change score to outcome prediction expands the concept of treatment monitoring for individuals with neck, shoulder, and knee pain. Considering an immediate change in pain-associated psychological distress may improve prediction of longer-term clinical outcomes. Treatment monitoring via change in psychological measures has been established for patients with low back pain.[26,43,50,55,56] In this cohort, we considered the OSPRO-YF tool for its treatment-monitoring capacity across

TABLE 6 Parameters for Individual Predictors of Comorbidity Status

Measure/Completed Cases	Estimate	Regression Imputation	Estimate	Inverse Probability Weighted	Estimate
12-mo comorbidity change					
Intercept	−0.16	Intercept	−0.34	Intercept	−0.38
		Age, y	0.01		
Comorbidity (baseline)*	−0.79	Comorbidity (baseline)*	−0.87	Comorbidity (baseline)*	−0.79
OSPRO-ROS+ (13 items)	0.19	OSPRO-ROS+ (13 items)	0.14	OSPRO-ROS+ (13 items)	0.25
				Education	
				High school or lower (reference)	
				Completed postgraduate degree	−0.02
				Some postgraduate coursework	−0.03
				Graduated from college	0.17
				Some college	0.72
				Prefer not to answer	4.32

Abbreviation: OSPRO-ROS+, additional 13 items from the long version of the Optimal Screening for Prediction of Referral and Outcome review-of-systems tool.
**Comorbidity was from the Charlson and functional comorbidity indices.*

several other musculoskeletal pain conditions. The 4-week change in the 10-item OSPRO-YF tool consistently contributed a small amount of additional variance to the prediction of 12-month outcomes for pain intensity, region-specific disability, and quality of life. The contribution of the OSPRO-YF change score, while small in magnitude, was of equal weight to the baseline score for a given prediction model. This finding suggests that, to enhance outcome prediction via treatment monitoring, psychological assessments should be structured to capture baseline status and a follow-up measure, because they both equally contributed to the outcome of interest.

The 10-item OSPRO-ROS tool was narrower in its predictive scope by being specific to 12-month quality of life (mental). The finding for MCS scores suggests that the OSPRO-ROS (short version) can be used in tandem with the OSPRO-YF tool for better accuracy on mental health outcomes. The 10-item OSPRO-ROS tool correlated with depressive symptoms in the cross-sectional development cohort,[19] and this was a corroborative finding in the longitudinal validation cohort. These findings suggest that, though the items of the OSPRO-ROS are focused on red flag symptomatology, there is a link between these symptoms and overall mental health status, even after other psychological factors are considered (by the OSPRO-YF tool in these analyses).

The additional 13 items from the OSPRO-ROS+ contributed small amounts of additional variance to the prediction of 12-month comorbidity change. Red flag symptom assessment has traditionally been geared toward determining existing pathology, but this strategy has been questioned due to low accuracy.[14,52] An alternate approach to red flag assessment is to determine the association with change in medical, health, or disease status.[19,46] In these analyses, we focused on whether the 10-item OSPRO-ROS tool and the additional 13 items from the OSPRO-ROS+ were predictive of 12-month comorbidity change. Comorbidity status was selected because musculoskeletal pain burden may be exacerbated by the presence of multiple comorbid conditions, which can independently influence the trajectories of perceived health status, functional impairment, and disability.[45,51,54] As a result, there is surging interest in the implications that multiple comorbidities (ie, multimorbidity) have for individual patient care and decision making.[1] To better understand the impact of multimorbidity and to more clearly define who may be at risk for poor outcomes, physical therapists and other health care providers will need assessment tools that provide a reasonable estimate of future disease burden. Information on future disease burden can then be combined with other existing methods for predicting clinical outcomes, resulting in an approach that generates care pathways to address issues specific to multimorbidity. The additional 13 items of the OSPRO-ROS+ predicted 12-month comorbidity change, adding to models that already included the baseline number of comorbidities. This is an encouraging finding that could aid future clinical decision making for value-based care in musculoskeletal pain,[40,48] but it will need to be investigated in additional studies for replication.

The OSPRO tools added statistically to the prediction of outcomes after considering baseline outcome scores, but contributions may have limited clinical relevance. For example, the baseline 10-item OSPRO-YF score (range, 3-53) would have to vary by 30 points to correspond with a 2-point difference in 12-month pain intensity outcome. This suggests that the OSPRO-YF could be used to refine a prediction after an initial trajectory is determined by a baseline pain-intensity score. Large differences in

baseline OSPRO-YF or OSPRO-ROS scores are needed to predict clinically relevant differences for other outcomes. In the case of the OSPRO-YF tool, the 4-week change score can be used to further refine outcome prediction, which may enhance its utility, but with the burden of additional measurement. Future utility of the OSPRO tools can only be determined by future studies that directly link their use to clinical decision making.

These findings did indicate that the OSPRO tools can be used broadly across individuals with neck, shoulder, low back, and knee pain. The present study found little evidence of the influence of anatomical region on the OSPRO-YF and the OSPRO-ROS tools. These findings were similar to those of our previous work in depressive symptoms,[21] fear-avoidance beliefs,[22] and pain-associated distress.[7] The finding that the influence of psychological symptoms on clinical outcomes is not region dependent has been reported in other cohorts.[11,12] However, the regression imputation analyses did indicate a potential for differences based on disability measures that are specific to anatomical region. For example, our analyses indicated that slightly higher 12-month disability scores would be expected for shoulder pain compared to knee pain, given the same baseline OSPRO-YF score. This finding, which suggests the need to consider anatomical specificity in yellow flag assessment, converges with the initial validation of a modified STarT Back Tool.[29] The reasons for these contrasting findings from the regression imputation models cannot be determined or resolved within this cohort. However, they do provide focus for future study in this area by determining whether OSPRO tool interpretation needs to be adjusted based on anatomical region when the outcome of interest is region-specific disability.

Primary limitations of the OSPRO validation cohort, including convenience sampling and lack of individual treatment parameters, have been described in the cohort profile paper.[20] Another primary limitation is that we did not include specific medical diagnoses or severity of injury in the predictive models; therefore, these predictive models may not be applicable when a specific medical diagnosis is a strong predictor of clinical outcomes. An additional limitation of this analysis was the follow-up rate of 63.4%, which was lower than anticipated. Furthermore, there were multiple differences between those who completed follow-up and those who did not. These predictive models may need to be adjusted to account for those participants who identify as nonwhite, report lower income and education levels, are uninsured, receive Medicaid or workers' compensation, and report higher levels of pain and pain-associated distress. To account for this lower-than-anticipated and differential follow-up rate, we were transparent in interpreting results from parsimonious models (to avoid reporting overfitted models) that accounted for the missing data (to avoid loss-to-follow-up bias). The completed-cases and imputed models most often showed very good convergence, but these analyses indicated that the prediction of comorbidity outcomes was most affected by the loss to follow-up. Another limitation is that all outcomes for these analyses were self-reported. Future studies should consider incorporating a corresponding physical performance measure and medical record verification of the 12-month comorbidity status. Finally, the present analysis did not weight the OSPRO-YF tool based on its different components (eg, negative affect, fear avoidance, and positive coping). Therefore, a limitation in interpreting the OSPRO-YF tool score is not knowing which individual components may be better targeted for intervention approaches or whether there are dominant components of the OSPRO-YF tool for predicting outcomes.

The OSPRO validation cohort generated several areas for future research. First, the musculoskeletal conditions recruited in this cohort were selected because they were highly prevalent and commonly treated by physical therapists in outpatient settings. Future study of the OSPRO tools in less prevalent patient groups is necessary to determine refinements to the existing tools. Second and specific to the OSPRO-ROS tool, there may be an interest in determining whether the tool can be used to identify the need for additional diagnostic testing. Although this direction was not our intent in the validation cohort, the OSPRO-ROS tool could be investigated in appropriately designed future studies for improving diagnostic accuracy in identifying systemic pathology. Third and specific to the OSPRO-YF tool, future study should investigate whether relevant domains not originally included in the tool's development (eg, perceived injustice and optimism) would improve the predictive performance of the tool. Finally, the original OSPRO tool development did not include item response theory, and using such an analytical approach could generate different tools to compare performance in future predictive testing.

Future work should determine whether or how OSPRO tools may improve clinical decision making for musculoskeletal pain. The OSPRO tools could be used to direct tailored treatment options for higher pain-associated psychological distress linked to poor outcomes or for symptom reports indicating increased disease burden. The current study was predictive, but future studies could investigate whether these tools may be used to identify responders via treatment-effect modification or to verify their use as treatment-monitoring tools via mediation analyses. Another area of future work is to incorporate the OSPRO tools into existing electronic health records and/or patient registries. The OSPRO tools provide a concise way to capture relevant risk-adjustment parameters that are often missing from large-scale data sets on musculoskeletal pain. Pragmatic use of these tools would allow for more precise estimates of their predictive capabilities for clinical outcomes and exploration of their ability to predict future health care utilization. For example, these tools could be used to identify patients

who start in a nonpharmacological care pathway, then transition to higher-risk options like opioids, injections, or surgery. Earlier identification of these patients may allow for additional tailored strategies to prevent unwarranted utilization of high-risk, low-benefit treatments for musculoskeletal pain.

CONCLUSION

The primary analyses from the OSPRO validation cohort demonstrated that the OSPRO tools added statistically to the prediction of 12-month outcomes for common musculoskeletal pain conditions. The 10-item OSPRO-YF tool, designed to assess negative mood, fear avoidance, and positive-coping styles, improved prediction of 12-month pain intensity, region-specific disability, and quality of life (physical and mental). The 10-item OSPRO-ROS tool, designed to assess red flag symptomatology, improved prediction of 12-month quality of life (mental). The additional 13 items from the OSPRO-ROS+ improved prediction of 12-month comorbidity status. The OSPRO tools contributed small amounts of variance to prediction models that included demographic and clinical factors, comorbidity, and baseline scores. The OSPRO validation cohort was not designed to be a definitive study, so future research is needed to determine whether these tools have a role in improving clinical decision making for better management of musculoskeletal pain. ◉

KEY POINTS

FINDINGS: The baseline score and 4-week change in the 10-item Optimal Screening for Prediction of Referral and Outcome yellow flag (OSPRO-YF) tool improved statistically the prediction of 12-month pain intensity, region-specific disability, and quality of life (physical and mental) outcomes. The baseline score of the 10-item Optimal Screening for Prediction of Referral and Outcome review-of-systems (OSPRO-ROS) tool statistically improved the prediction of 12-month quality of life (mental), and the additional 13 items in the OSPRO-ROS+ statistically improved the prediction of comorbidity change.

IMPLICATIONS: The OSPRO tools can be used for baseline assessment and treatment monitoring for commonly occurring musculoskeletal conditions (ie, neck, shoulder, low back, or knee pain). The OSPRO tools contributed to outcome prediction, but their contribution to the models was small in magnitude. It is our assertion that the OSPRO tools may be used for directing care in pain-management pathways that deliver early nonpharmacological treatments, psychologically informed approaches, or want to consider the impact of multimorbidity.

CAUTION: The study sample was not recruited consecutively and there was high loss to follow-up; therefore, these results may not be entirely representative of patient populations. There is some evidence of anatomical specificity in these tools for predicting region-specific outcomes, which will need to be considered in future studies. Additional studies are needed to determine the utility of the OSPRO tools for clinical decision making.

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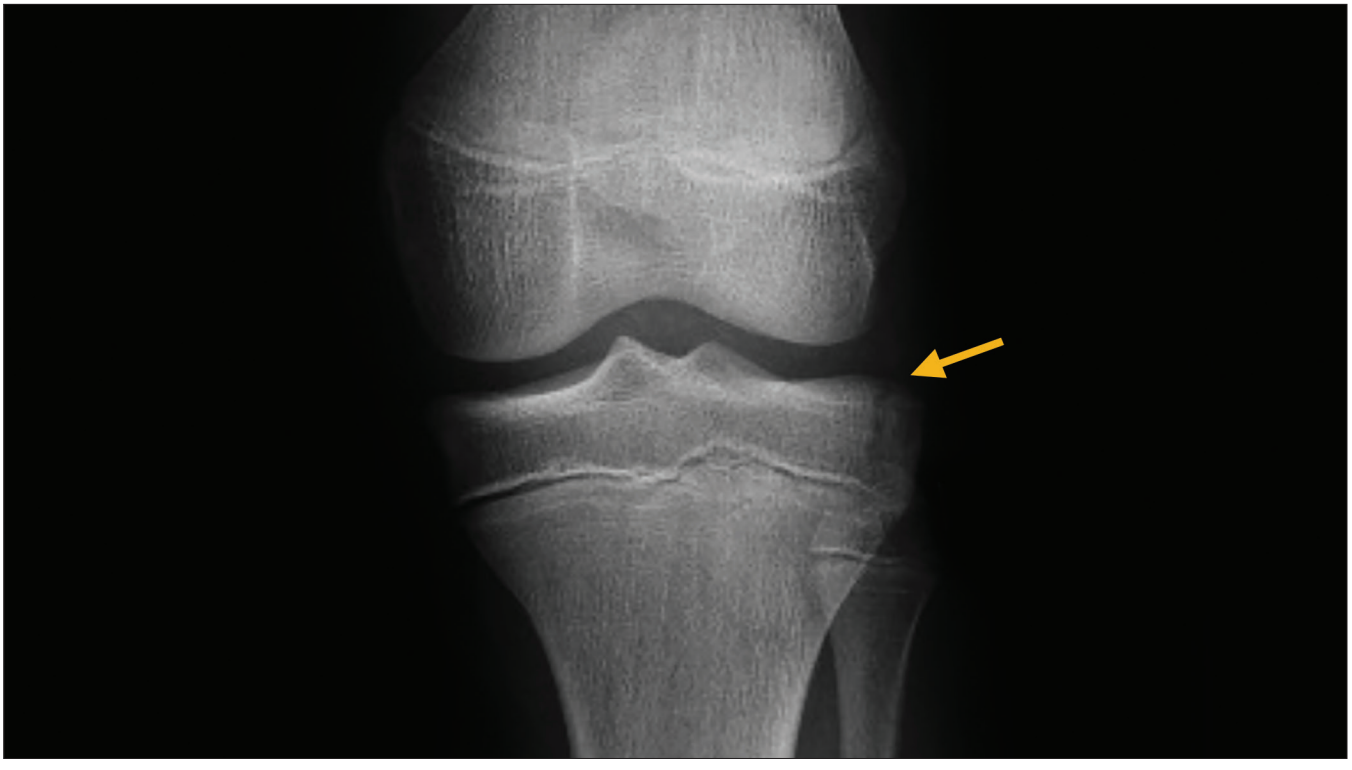

FIGURE. Anteroposterior radiograph of the left knee demonstrating an intra-articular, nondisplaced Salter-Harris type III fracture (arrow) of the left lateral tibial plateau.

Type III Salter-Harris Fracture After an Onside Kick

J. PARRY GERBER, PT, PhD, ATC, *Eastern Washington University, Cheney, WA.*

A 14-year-old male football player consulted a sports physical therapist with the primary goal of being able to play in next week's game. During practice 1 week prior, he reported being kicked in the front part of his left knee as he was trying to recover an onside kick. He could not recall twisting the knee, feeling a pop, or other injury details. He reported immediate knee pain and noticeable swelling within an hour after injury. He was initially treated by his coaching staff with ice and placed on crutches. The patient then reported that his knee was improving quickly, swelling was gone, walking was pain free, and pain with jogging was improving.

On examination, important findings included normal gait and knee range of motion, mild effusion detected via the swipe test, an inconclusive Lachman test due to guarding, and tenderness over the lateral joint line and proximal lateral tibia. Because of these findings in a 14-year-old adolescent, a radiological examination was recommended to rule out a tibia eminence or growth-plate fracture.

Radiographs revealed a nondisplaced type III Salter-Harris fracture of the lateral tibial plateau (**FIGURE**). The patient was placed in a straight-leg brace and on crutches (toe-touch weight bearing) for 4 weeks. He was allowed to do quadriceps setting exercise during this time.

Progressive rehabilitation followed, and he returned to running and jumping without pain or effusion 8 to 10 weeks post injury.

In children and teenagers, growth-plate injuries should be high on the list of differential diagnoses whenever there is trauma to and effusion in a joint.[1] In this case, results of imaging prevented the potentially deleterious effects of returning an injured athlete to competition prematurely.

J Orthop Sports Phys Ther 2018;48(6):511. doi:10.2519/jospt.2018.7868

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STEVEN J. KAMPER[1]

Engaging With Research: Linking Evidence With Practice

J Orthop Sports Phys Ther 2018;48(6):512-513. doi:10.2519/jospt.2018.0701

This is the first in a series of brief overviews covering discrete aspects of clinical research. The aim is to help clinicians become more proficient consumers of research and encourage appropriate incorporation of evidence into practice.

Debates concerning the why and how of evidence-based practice (EBP) occupy thousands of words in textbooks and journals and on the Internet. These discussions go beyond medicine into fields as diverse as education, finance, and social policy, to name a few. Regardless of your thoughts on EBP, there are at least 3 reasons why physical therapists should engage with research evidence:

1. The public expects medical care to be based in science.
2. If physical therapy wants to call itself a scientific profession, then relevant evidence must be generated and used in clinical practice.
3. Agencies that pay for services, such as insurers and government bodies, are increasingly making reimbursement contingent on providing evidence-based care.

Sometimes research results differ substantially from your own experience of the effectiveness of a particular treatment. This presents a challenge and begs the very reasonable question of why a physical therapist should be expected to prioritize evidence from a study over his or her own clinical experience.

Information recalled from clinical experience should be appraised and assessed for bias, just as information from research should be. So, it is important to understand the potential limitations and relevant biases.

Confirmation Bias

People tend to appraise and interpret information such that it reinforces their own beliefs. We overvalue information that supports our beliefs, ignore or forget information that contradicts them, and interpret ambiguous information in a way that favors our views. This is confirmation bias; it is not a character flaw of an individual, nor is it an attempt to justify one's actions. It is a sort of cognitive shortcut that our species has developed for more efficient day-to-day function. The problem is that it leads us astray in certain situations. For example, consider physical therapists who believe that (1) they are good at their job and (2) they have their patients' best interests at heart. What effect could confirmation bias have on these physical therapists' recollection of the effectiveness of their treatments?

Recall Bias

People have a tendency to better remember substantial or impressive events, as opposed to average or more common occurrences. In the context of clinical practice, this could lead to clearly remembering the patients who did spectacularly well (or spectacularly badly) and less clearly remembering those with an average outcome. So, when it comes time to apply previous experience to the next patient, the most likely outcome may be the one least likely to be recalled.

A related problem is that some patients will engage with therapy, while others will stop attending. Outcomes of the latter patients are usually unknown. Given the likelihood of confirmation bias, it is probable that dropouts are assumed to have done well (did not need more treatment), though the opposite may be true.

Clinical Observation

Let's say that you treat a patient with a particular intervention. The patient sees you a few times and, after 3 weeks, is much improved. The simplest interpretation is that what you did was effective. The problem is that the improvement may or may not be because of the treatment. There is a fundamental difference between change in outcome (clinical change over time) and treatment effect (clinical change over time that is due to treatment). In the clinic, you observe the change in outcome over 3 weeks, but only a part of that change is treatment effect. There are a number of factors that contribute to change in outcome, including those below (**FIGURE**).

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Natural History Many conditions resolve completely or to some extent on their own, particularly acute conditions. For example, a patient who presents with pain, swelling, and limited function the day after an ankle sprain will improve on those outcomes over the next 2 weeks. This is the case whether the patient receives intensive treatment, minimal treatment, ineffective treatment, or no treatment at all. Obviously, natural history varies according to condition, so the proportion of change in outcome due to natural history will vary from case to case.

Regression to the Mean Many conditions follow an episodic or fluctuating course. Patients have no symptoms or low-level symptoms most of the time, interspersed by exacerbations or flare-ups. Back pain and neck pain are common examples. People with these conditions generally seek care when symptoms are at their worst, that is, during an exacerbation. Because symptom severity is typically at or near its worst when they see a clinician, the next fluctuation in severity is most likely to be an improvement. In practice, this means they are more likely to improve after a consultation, regardless of intervention.

Placebo Effects Placebo effects are most likely due to manipulation of patient expectations and/or classical conditioning. Irrespective of the mechanism, placebo effects are attached to, but distinct from, the actions of any particular intervention; they are "portable" across different interventions.

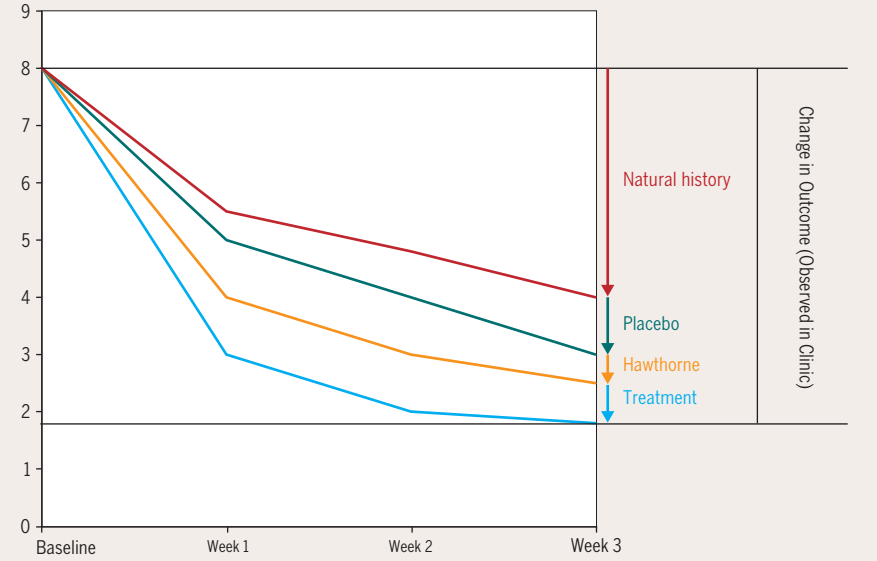

FIGURE. Deconstruction of outcome.

They can contribute to change in outcome but are different from treatment effect.

Polite Patients Most clinicians try to form a rapport with their patients. A result is that many patients don't want to "disappoint" their therapist by failing to respond to the therapist's sincere efforts to help them. This desire on behalf of patients can bias reports of outcome. Patients may appear to (and state that they) have improved more than they really have.

Summary

Well-executed EBP does not dismiss clinical experience. However, potential biases must be considered when appraising and applying information recalled from clinical experience. Similarly, EBP is not about picking holes in published studies. It involves carefully considering the nature and magnitude of biases that apply to all the information (from clinical experience and from research) that a clinician needs to consider in his or her reasoning process.

There is a misconception that EBP seeks to devolve clinical decision making to a cookbook. In reality, EBP asks more of clinicians, not less. It challenges them to accept flaws in their reasoning and recognize their own biases, and demands that they develop the skills to find, appraise, and integrate research evidence into their practice.

Evidence in Practice: A New Series for Clinicians

STEVEN J. KAMPER
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J Orthop Sports Phys Ther 2018;48(6):429. doi:10.2519/jospt.2018.0105

Physical therapists are expected to deliver their clinical services within the evidence-based practice (EBP) paradigm. While debate as to the optimal form of EBP in academic and professional circles is ongoing, the underlying principle is well accepted: clinical practice should be informed by the best available research evidence (integrated with clinical and patient values).[2] Despite the simplicity of the idea, EBP places considerable demands on physical therapists, and barriers to implementation are numerous.[1]

An absolute precondition for EBP is the capacity of every clinician to understand scientific research. Understanding a research article requires some familiarity with both the language and the methods used in the research world. From this foundation, the findings of studies can then be integrated with the specific patient and pathology knowledge that a physical therapist already possesses. There is no need to be a statistician or epidemiologist; a basic grasp of the way research works can enable clinicians to effectively use evidence in their practice. We want physical therapists to be able to read a paper (or watch a presentation), understand what is being said, pull out what is useful, and apply it in practice.

The aim of the "Evidence in Practice" series is to help practicing physical therapists build expertise in understanding research. Each article will focus on one feature of the research process and explain the basics concisely—less than 2 pages—in nontechnical language. Evidence in Practice articles will not delve into the complexity of scientific methodology; rather, the goal is to provide "bite-sized" explanations that cover the most important issues for interpreting research evidence. The focus will be on clinical research, as opposed to basic discovery research, to reflect the core purpose and readership of the *Journal*.

The articles in the series will cover a few broad topics: (1) the basics of identifying relevant research literature, such as asking a question, searching, and the types of research questions; (2) important principles and components of research, such as bias, randomization, blinding, odds and risk ratios, and outcome measures; and (3) the different types of studies that readers will encounter, including clinical trials, meta-analyses, subgrouping, and diagnostic studies.

It is our hope that Evidence in Practice becomes a valuable resource for clinicians attempting to meet the challenge of integrating research evidence into their care delivery. Like any new initiative, there is no certainty that we'll get the pitch and content right straightaway; so, starting with the first installment, titled "Engaging With Research: Linking Evidence With Practice," in this issue of the *Journal*, we invite your feedback on what we can do better.


[EVIDENCE IN PRACTICE]

STEVEN J. KAMPER[1]

Engaging With Research: Linking Evidence With Practice

J Orthop Sports Phys Ther 2018;48(6):512-513. doi:10.2519/jospt.2018.0701

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FIGURE. The first installment of Evidence in Practice appears on page 512 of this issue.

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Effectiveness of the McKenzie Method of Mechanical Diagnosis and Therapy for Treating Low Back Pain: Literature Review With Meta-analysis

STUDY DESIGN: Literature review with meta-analysis.

BACKGROUND: The McKenzie Method of Mechanical Diagnosis and Therapy (MDT), a classification-based system, was designed to classify patients into homogeneous subgroups to direct treatment.

OBJECTIVES: To examine the effectiveness of MDT for improving pain and disability in patients with either acute (less than 12 weeks in duration) or chronic (greater than 12 weeks in duration) low back pain (LBP).

METHODS: Randomized controlled trials examining MDT in patients with LBP were identified from 6 databases. Independent investigators assessed the studies for exclusion, extracted data, and assessed risk of bias. The standardized mean difference (SMD) and 95% confidence interval were calculated to compare the effects of MDT to those of other interventions in patients with acute or chronic LBP.

RESULTS: Of the 17 studies that met the inclusion criteria, 11 yielded valid data for analysis. In patients with acute LBP, there was no significant difference in pain resolution ($P = .11$) and disability ($P = .61$) between MDT and other interventions. In patients with chronic LBP, there was a significant difference in disability (SMD, −0.45), with results favoring MDT compared to exercise alone. There were no significant differences between MDT and manual therapy plus exercise ($P>.05$) for pain and disability outcomes.

CONCLUSION: There is moderate- to high-quality evidence that MDT is not superior to other rehabilitation interventions for reducing pain and disability in patients with acute LBP. In patients with chronic LBP, there is moderate- to high-quality evidence that MDT is superior to other rehabilitation interventions for reducing pain and disability; however, this depends on the type of intervention being compared to MDT.

LEVEL OF EVIDENCE: Therapy, level 1a. *J Orthop Sports Phys Ther 2018;48(6):476-490. Epub 30 Mar 2018. doi:10.2519/jospt.2018.7562*

KEY WORDS: *centralization, classification, directional preference, lumbar spine, manual therapy*

Low back pain (LBP) is the worldwide leading cause of years lived with disability, with an estimated point prevalence of 9.4% and a lifetime prevalence of up to 39%.[25,52,62] This negatively impacts the psychosocial health of those affected.[48] Moreover, with an aging population, LBP is expected to become more widespread.[26]

A variety of clinical practice guidelines have been developed for the treatment of LBP.[6,29,43] These guidelines propose a shift away from treatment of LBP primarily based on pathoanatomical principles in favor of a classification-based approach. This suggestion is largely based on several studies reporting that classifying patients led to improved clinical results.[14,15,31] However, a recent review has questioned the clinical effectiveness of subgrouping claims, due to trials that were underpowered and the poor quality of reporting.[55]

The McKenzie Method of Mechanical Diagnosis and Therapy (MDT) is a well-studied classification system. This assessment and treatment model has demonstrated good interexaminer reliability when classifying patients with LBP; however, evidence of its treatment effectiveness continues to be challenged. The MDT was designed to classify patients into 3 mechanical subgroups (derangement, dysfunction, or postural syndrome) or an "other" subgroup, by which to direct treatment.[23,36] Derangement, the most

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common subgroup, is associated with a rapid change in symptoms secondary to performance of a "directional-preference" exercise.[36] The directional preference of a patient is the direction in which a repeated movement and/or sustained position produces an improvement in symptoms. Those improvements may include centralization, a phenomenon in which symptoms down the lower extremity are progressively abolished in a distal to proximal direction.[64] The presence of centralization is associated with good prognosis in patients with LBP.[64] Furthermore, recent studies have shown that directional preference and centralization, when matched with adequate MDT treatment, result in better patient outcomes than treatment with general range-of-motion exercise.[31,47,50]

The latest meta-analysis to examine the effectiveness of MDT for LBP found limited evidence to support the use of MDT.[32] However, additional randomized controlled trials have since been published.[31,33,47] Moreover, the previous meta-analysis did not consider acute and chronic LBP separately. Because acute and chronic forms of LBP manifest differently, the treatment effect could be different.[19,44,51] A cutoff of 12 weeks to differentiate acute from chronic LBP has been used in previous systematic reviews and clinical practice guidelines.[4,37] Also, the previous meta-analysis compared MDT to passive therapy, which included a variety of interventions that might have different effects. Because the relative effectiveness of MDT could change based on the comparator intervention, MDT should be compared to each intervention type separately. The level of MDT training should also be considered, as it may impact interventions and risk-adjusted functional outcomes.[10] The objective of this meta-analysis was to determine the effectiveness of MDT provided by trained therapists compared to that of different types of comparator interventions for improving pain and disability in patients with acute and chronic LBP separately.

METHODS

The methodology for this review was based on the PRISMA statement,[39] and the data extraction form was informed by the Cochrane meta-analysis guidelines.[27]

Eligibility Criteria

Randomized controlled trials that examined the effectiveness of MDT for pain and disability in patients with LBP were included. There was no limit on publication date, and studies could be written in English or French. Exclusion criteria included duplicated data from other studies, other interventions combined with MDT where the effects could not be partitioned, and studies published in non–peer-reviewed journals. Only trials in which therapists were MDT trained were included. To be considered MDT trained, therapists were required to have participated in at least 1 course offered by the McKenzie Institute International focused on applying MDT to patients with LBP. This criterion was based on evidence that trained therapists are more reliable in classifying patients (κ = 0.7-0.9) than are therapists without certification (κ = 0.17-0.39).[28,49,65] Studies in which an MDT classification was not completed prior to the treatment were excluded, as a priori classification is an essential characteristic of the MDT approach.[36] Last, the comparator intervention had to be a typical rehabilitation intervention, such as manual therapy, exercise, or education. There was no review protocol published for this meta-analysis.

Information Sources

Six electronic databases (MEDLINE, Embase, CINAHL, Cochrane Database of Systematic Reviews, PsycINFO, and the Physiotherapy Evidence Database [PEDro]) were searched using 3 primary search strings: (1) MDT therapy, (2) low back/lumbar pain, and (3) randomized controlled trials. Related terms were included for each search string, and an example for the MEDLINE search is provided (**APPENDIX**, available at www.jospt.org). The first search was performed on November 12, 2015. A second search was performed on May 26, 2016, and a third search was performed on September 6, 2017 to provide an update of articles published since the first search. Additionally, references from the included studies and from previous systematic reviews/meta-analyses were searched manually, along with publications on the McKenzie Institute International website (www.mckenzieinstitute.org).

Study Selection

Titles and abstracts were screened independently by 2 reviewers (O.L., D.S.). When disagreements between reviewers occurred, they discussed the relevant abstract to reach a consensus. A third reviewer (S.R.) made the decision when a consensus could not be reached. The full articles were obtained for the selected abstracts and were reviewed again independently by 2 reviewers (O.L., D.S.). As before, a third reviewer (S.R.) made the decision to include the study in the analysis if a consensus could not be reached by the 2 initial reviewers.

Data Extraction

Data extraction was performed by 2 investigators (P.T.P., M.C.F.), who each independently extracted the data from all studies with the use of an extraction form. A customized data extraction form was developed for each of the 2 outcomes of interest, pain and disability. The data extraction form was a Microsoft Excel spreadsheet designed according to the Cochrane meta-analysis guidelines and adjusted to the needs of this meta-analysis.[27]

The following information was extracted from each study: (1) characteristics of the study (study duration, therapist MDT training, and the number of patients allocated to each group) and inclusion criteria, (2) type of intervention (including duration and frequency of the different interventions), and (3) type of outcome measures (including pain scores, disability scores, definitions and time of

data collections). Where the study sample included a mix of individuals with chronic and acute LBP, the average duration of LBP symptoms was used to determine whether they were acute or chronic. The comparison interventions were classified into "other interventions," placebo, or a subdivision of other interventions. Other interventions were defined as nonsurgical and noninvasive interventions within the scope of physical therapy practice (eg, exercise, manual therapy, and education). These interventions could be performed by physical therapists or other health professions. Other interventions were further subdivided into manual therapy, exercise, a combination of manual therapy and exercise, or education. Chronic LBP was defined as pain in the lumbar spine lasting more than 12 weeks. Acute LBP was defined as having a duration of pain less than 12 weeks. After having completed the extraction process, the investigators compared results and reached consensus on any discrepancies. A third investigator (S.R.) resolved disagreements if a consensus could not be reached. Once the extraction form was completed, the 2 investigators independently tested the form with the first 3 included studies. The results were then compared to ensure uniformity of the extraction process. When relevant data were missing from a study, the authors and coauthors were contacted via e-mail to request the missing information. If the data could not be obtained, the study was excluded from the analyses. For each study, pain and disability measures were extracted immediately after the MDT intervention or the comparison intervention, when the intervention was assumed to have the largest treatment effect.

Risk of Bias and Strength of Evidence

To evaluate risk of bias in individual studies, the methodological quality of the included studies was rated on the PEDro scale.[34] The PEDro scale has demonstrated acceptable reliability for the overall score (intraclass correlation coefficient = 0.680)[34] and validity.[7] The ratings were obtained from the PEDro website when available. Articles not indexed in the PEDro database were assessed by 2 raters (O.L., D.S.) and a third reviewer (S.R.) made the final decision if a consensus could not be reached.

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to assess the quality of the body of evidence for each outcome of this meta-analysis (pain and disability).[27] This evaluation was conducted by 2 raters (D.S., P.T.P.), and a third reviewer (O.L.) made the final decision if a consensus could not be reached. The quality of evidence was initially considered "high" and could be downgraded based on the following 5 factors: (1) limitation of design, (2) indirectness of evidence, (3) inconsistency of results, (4) imprecision of results, and (5) high probability of publication bias. Studies that did not reach a score of 5 on the PEDro scale could be downgraded for a limitation of design[41]; studies that possessed differences in populations, interventions, outcome measures, and indirect comparisons could be downgraded for indirectness; studies with effect estimates that were heterogeneous could be downgraded for inconsistency; and studies that had fewer than 400 participants could be downgraded for imprecision.

Statistical Analysis

Analyses were completed separately for patients with acute and chronic LBP. The effectiveness of MDT compared to other interventions, subdivisions of other interventions, or placebo were examined using random-effects models with statistical significance set at $P<.05$.[8,67] The standardized mean difference (SMD) and 95% confidence interval (CI) were calculated for each analysis. Random-effects models were utilized, because it was expected that there would be heterogeneity of the comparator interventions. The heterogeneity among studies was determined using the chi-square statistic with significance set at $P<.10$ and I^2. These analyses proceeded even if statistical heterogeneity was present. RevMan 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used for all statistical analyses.

When a study had 2 intervention groups that were compared to MDT (eg, manual therapy and education), the intervention that was considered to contribute most (eg, manual therapy) was included in the primary analysis. However, in these cases, a sensitivity analysis was completed where the comparator groups were substituted. Both comparator groups could not be included in the same analysis to avoid artificially inflating the sample size. When medians and interquartile ranges (first and third) were provided, means were calculated by summing the median, first interquartile range, and third interquartile range and then dividing by 3. Standard deviation estimates were calculated from interquartile values and consideration of the study sample size.[63]

RESULTS

The literature search resulted in the identification of 758 publications, 678 from databases and 80 from reference lists (**FIGURE 1**). After removing duplicates, 2 independent reviewers screened 354 abstracts and selected 51 articles for full-text review. After review, 17 articles were retained for the meta-analysis; however, of these 17 studies, 4 did not provide sufficient data to be included in the statistical analyses. These 4 studies are summarized in **TABLE 1**.[1,20,46,53] No significant between-group differences were observed in pain and disability in 3 and 4, respectively, of the 4 studies excluded from the meta-analysis.[1,20,46,53] Attempts to contact the authors to provide additional data were not successful. One study that met the inclusion criteria was excluded from data analysis, because participants who were noncentralizers post randomization were only excluded from the intervention group.[41] This could have biased the treatment effect toward the MDT group, as a greater effect has been

shown when a directional-preference exercise is given to centralizers.[66] Also, because the modification occurred following allocation, the study could not be considered a randomized controlled trial. In this study, the findings of a significant between-group difference in improvement in pain and disability favoring MDT should be interpreted with caution.[41] One study with a mix of individuals with acute and chronic LBP[45] was included in the data analyses for chronic LBP, because most participants had recurrent episodes of LBP. For 1 study, medians and interquartile ranges were converted to means and standard deviations, respectively, as described in the Methods.[63] A summary of the meta-analysis is shown in **TABLE 2**.

Acute LBP: Primary Analysis of MDT Versus Other Interventions

Four studies compared MDT to other interventions in participants with acute LBP.[3,33,54,55] The other interventions included spinal manipulative thrusts, lumbar range-of-motion exercise,[54] joint mobilizations,[55] and first-line care (eg, advice to remain active and take acetaminophen, and assurance of a favorable prognosis).[33] Another study compared MDT to 2 other interventions: manipulations with strength and stretching home exercises, and an education booklet.[3]

Only 3 of 4 studies were included in the analysis of pain intensity.[33,54,55] The fourth study examined the bothersomeness of pain, numbness, and tingling, which was considered a different construct.[3] For the 3 included studies, tests of heterogeneity were not significant (**FIGURE 2A**). There was moderate-quality evidence of no significant (P = .11) difference in pain after the intervention period (SMD, −0.45; 95% CI: −0.99, 0.10) between MDT and the other interventions. Ratings were downgraded because of imprecision of results.

For the disability analysis, all 4 studies were included and tests of heterogeneity were not significant (**FIGURE 3A**).[3,33,54,55] There was high-quality evidence of no significant difference (P = .61) in disability after the intervention period between MDT and other physical therapy interventions (SMD, −0.07; 95% CI: −0.34, 0.20). The analysis included manipulations, with home exercises as the comparator intervention from the study that included 2 comparator interventions.[3] When the education booklet was included instead, no significant differences remained (P = .16).

Acute LBP: Subgroup Analysis

MDT Versus Manual Therapy Plus Exercise Three studies compared MDT to manual therapy plus exercise.[3,54,55] Comparator interventions included spinal manipulative thrusts with lumbar range-of-motion exercises,[54] joint mobilizations,[55] and manipulations with home exercises.[3] Only 2 of 3 studies were included in the pain intensity analysis.[54,55]

Tests of heterogeneity were not significant (**FIGURE 2B**). There was moderate evidence of a significant (P = .04) difference in pain after the intervention period, with results favoring MDT (SMD, −0.74; 95% CI: −1.45, −0.03). Ratings were downgraded because of imprecision of results. For the disability analysis, all 3 studies were included and tests of heterogeneity were not significant (**FIGURE 3B**).[3,54,55] There was moderate evidence of no significant difference (P = .36) in disability after the intervention period between MDT and manual therapy plus exercise (SMD, −0.24; 95% CI: −0.77, 0.28). Ratings were also downgraded because of imprecision of results.

MDT Versus Exercise None of the included studies compared MDT to exercise alone in participants with acute LBP.

MDT Versus Education Two studies compared MDT to an intervention that included only education in participants with acute LBP.[3,33] In 1 study, education was described as "first line care," and included advice to avoid bed rest and to remain active, assurance of a favorable prognosis, and advice to take acetaminophen.[33] This first-line care was provided

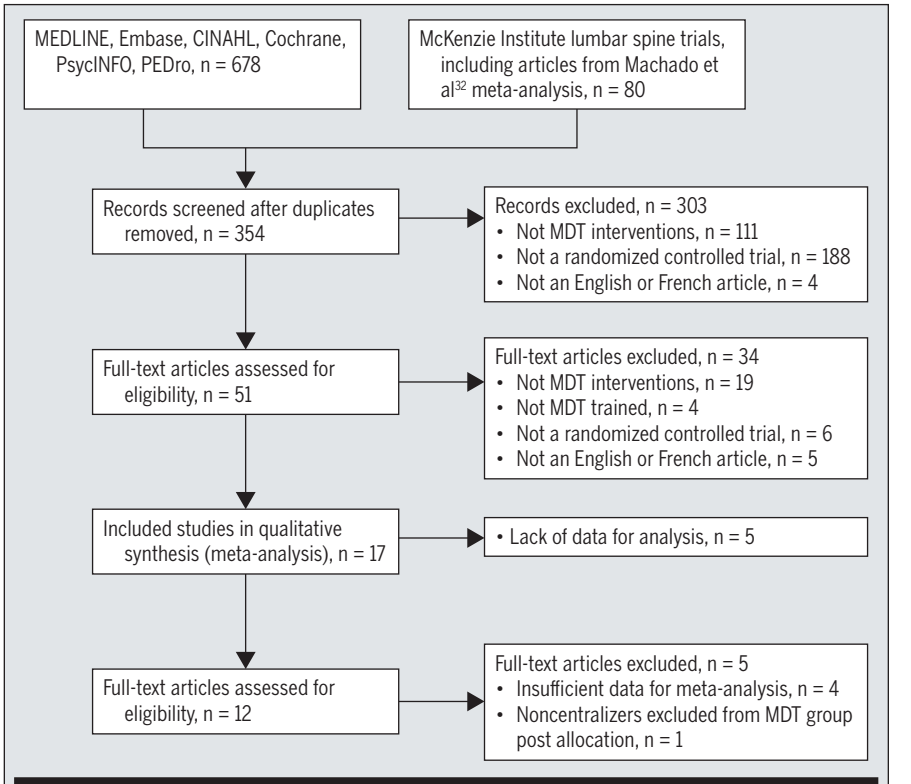

FIGURE 1. Flow diagram of search strategy and results. Abbreviation: MDT, Mechanical Diagnosis and Therapy.

to both the MDT group and the comparison group, who received no other treatments. The outcome variables for this study included both pain intensity and disability. The second study used an education booklet as the comparison intervention,[3] and had disability as an outcome measure, but not pain intensity.

As only 1 study assessed pain intensity,[33] no meta-analysis was performed. This study found that MDT plus first-line care resulted in a significant ($P = .02$), but small, improvement (0.7 on an 11-point numeric pain-rating scale; adjusted values) in pain intensity compared to first-line care only.

For the disability analysis, based on 2 studies,[3,33] tests of heterogeneity were not significant (**FIGURE 3C**). There was

TABLE 1 Summary of Inclusion and Exclusion Criteria, Intervention Groups, and Outcome Measures

Study (PEDro Score)	Participants (MDT Intervention)*	Participants (Other Interventions)*	Inclusion Criteria	Acute Pain (<12 wk) or Chronic Pain (>12 wk)	Intervention	MDT Level of Training	Outcomes
Bonnet et al[1] (7/10)†	n = 28; men, n = 17; women, n = 11; age, 48.8 ± 4.75 y; mean symptom duration, 46.1 mo	n = 26 men, n = 12; women, n = 14; age, 45.9 ± 5.1 y; mean symptom duration, 49.2 mo	Nonspecific LBP with or without radiation to lower extremity, ≥18 y of age	Mix	MDT: directional-preference exercises, can modify positions and/or add manual techniques Manual therapy plus exercise: active mobilizations in weight bearing and non–weight bearing, lower extremity stretching, proprioception in weight bearing, massage, TENS	Parts A and B	Pain: visual analog scale Disability: Oswestry Disability Questionnaire Outcomes evaluated after 1 wk
Cherkin et al[3] (8/10)	n = 133; men, n = 71; women, n = 62; age, 41.8 ± 11.5 y; mean symptom duration, 77% <6 wk	Education: n = 66; men, n = 38; women, n = 28; age, 40.1 ± 11.2 y; mean symptom duration, 72% <6 wk Manual therapy plus exercise: n = 122; men, n = 57; women, n = 65; age, 39.7 ± 9.4 y; mean symptom duration, 83% <6 wk	LBP with pain 7 d after initial physician visit, 20-64 y of age	Acute	MDT: directional-preference exercises, avoid symptom peripheralizing movements, home exercise program, education book, lumbar-support cushion Manual therapy plus exercise: chiropractic high-velocity, low-amplitude thrust manipulation; stretching and strengthening exercises; home exercise program Education: Educational booklet	Credentialed	Bothersomeness of back/leg pain, numbness/tingling: numeric rating scale Disability: modified Roland-Morris Disability Questionnaire Outcomes evaluated at 1, 4, and 12 wk
Garcia et al[17] (8/10)	n = 74; men, n = 16; women, n = 58; age, 53.7 ± 1.53 y; mean symptom duration, median of 21 mo (IQR, 28)	n = 74; men, n = 23; women, n = 51; age, 54.16 ± 1.57 y; mean symptom duration, median of 24 mo (IQR, 83)	Nonspecific LBP of ≥3 mo duration, 18-80 y of age	Chronic	MDT: directional-preference exercises, postural training, home exercise program, education Exercise: exercises aimed to improve mobility, flexibility, and strength; home exercise program; education	Credentialed	Pain: numeric rating scale Disability: Roland-Morris Disability Questionnaire Outcomes evaluated after 1, 3, and 6 mo
Gillan et al[20] (4/10)†	n = 19; sex, NA; age, NA; symptom duration, NA	n = 21; sex, NA; age, NA; symptom duration, NA	Acute LBP, <12 wk in duration, and a lateral shift of the lumbosacral spine	Acute	MDT: MDT approach, no further details given Education: nonspecific back massage and standard back care advice	Diploma	Disability: Oswestry Disability Questionnaire Outcomes evaluated after 1 and 3 mo
Long et al[31] (8/10)	n = 80; men, n = 39; women, n = 41; age, 42.86 ± 9.55 y; symptom duration, 13.7 ± 19.84 wk	Exercise: n = 80; men, n = 39; women, n = 41; age, 41.51 ± 10.76 y; symptom duration, 14.55 ± 17.6 wk Opposite MDT (experimental): n = 69; men, n = 35; women, n = 34; age, 42.19 ± 10.34 y; symptom duration, 17.65 ± 21.82 wk	LBP, with or without leg symptoms, with or without 1 neurological sign, directional preference, 18-65 y of age	Chronic	MDT: directional-preference exercise, avoid activities and positions that increase or radiate symptoms Exercise opposite MDT: unidirectional end-range lumbar exercises in opposite direction of directional preference and education Exercise: multidirectional, midrange lumbar exercises and stretches for the hip and thigh muscles, education	Credentialed and diploma	Back pain and leg pain: visual analog scale Disability: Roland-Morris Disability Questionnaire Outcomes evaluated after 2 wk

Table continues on page 481.

TABLE 1 Summary of Inclusion and Exclusion Criteria, Intervention Groups, and Outcome Measures (continued)

Study (PEDro Score)	Participants (MDT Intervention)*	Participants (Other Interventions)*	Inclusion Criteria	Acute Pain (<12 wk) or Chronic Pain (>12 wk)	Intervention	MDT Level of Training	Outcomes
Machado et al[33] (8/10)	n = 73; men, n = 35; women, n = 38; age, 47.5 ± 14.4 y; mean symptom duration, 66% <2 wk, 34% 2-6 wk	n = 73; men, n = 38; women, n = 35; age, 45.9 ± 14.9 y; mean symptom duration, 67% <2 wk, 33% 2-6 wk	Acute nonspecific LBP, pain between the 12th rib and buttock crease, with or without leg pain, <6 wk in duration, preceded by at least 1 mo without LBP in which the patient did not consult a health care practitioner, 18-80 y of age	Acute	MDT: first-line care, directional-preference exercises, postural correction and education, *Treat Your Own Back* book, lumbar roll, home exercise program Education: physician advice, acetaminophen; follow-up visit in 3 wk, earlier if necessary	Credentialed	Pain: numeric rating scale Disability: Roland-Morris Disability Questionnaire Function: Patient-Specific Functional Scale Outcomes evaluated after 1 and 3 wk
Moncelon and Otero[40] (5/10)	n = 7; men, n = 4; women, n = 3; age, NA; symptom duration, NA; age of both groups, 47 ± 11 y	n = 7; men, n = 5; women, n = 2; age, NA; symptom duration, NA	Chronic nonspecific LBP, directional preference, 18-70 y of age	Chronic	MDT: directional-preference exercises, home exercise program, pool therapy Manual therapy plus exercise: diaphragmatic breathing, lumbopelvic and coxofemoral mobilizations, paravertebral muscle strengthening, pool therapy	Parts A and B	Disability: Oswestry Disability Questionnaire Outcome evaluated after 1 wk
Murtezani et al[41] (8/10)†	n = 111; men, n = 83; women, n = 28; age, 48.8 ± 8.9 y; symptom duration, NA	n = 109; men, n = 42; women, n = 67; age, 47.5 ± 8.8 y; symptom duration, NA	Nonspecific LBP, pain between lower angle of scapulae and above the buttocks, with or without leg pain or neurological signs, >3 mo duration, 18-65 y of age	Chronic	MDT: directional-preference exercises, can add manual techniques, avoid motions that peripheralize symptoms, home exercise program Modalities: interferential current, ultrasound, heat	50 h of training, equivalent to 2 courses	Pain: visual analog scale Disability: Oswestry Disability Questionnaire Outcomes evaluated at 2 and 3 mo
Paatelma et al[45] (7/10)	n = 52; men, n = 37; women, n = 15; age, 44 ± 9 y; symptom duration, NA	Education: n = 37; men, n = 24; women, n = 13; age, 44 ± 15 y; symptom duration, NA Manual therapy: n = 45; men, n = 26; women, n = 19; age, 44 ± 10 y; symptom duration, NA	Nonspecific LBP with or without radiation to one or both lower extremities, employed, acute or chronic duration, 18-65 y of age	Mix	MDT: exercises with or without sustained end-range positions, manual techniques, education, *Treat Your Own Back* book, home exercise program Manual therapy plus exercise: high-velocity, low-amplitude thrust manipulation; specific mobilizations; stretching; spinal stabilization exercises; home exercise program Education: good prognosis of LBP, pain tolerance and remaining active, medication, early return to work, booklet	Credentialed	Pain: back and leg pain, visual analog scale Disability: Roland-Morris Disability Questionnaire Outcomes evaluated after 3, 6, and 12 mo

Table continues on page 482.

TABLE 1 Summary of Inclusion and Exclusion Criteria, Intervention Groups, and Outcome Measures (continued)

Study (PEDro Score)	Participants (MDT Intervention)*	Participants (Other Interventions)*	Inclusion Criteria	Acute Pain (<12 wk) or Chronic Pain (>12 wk)	Intervention	MDT Level of Training	Outcomes
Petersen et al[46] (7/10)†	n = 132; men, n = 70; women, n = 62; median (10th, 90th percentiles) age, 34.5 y (23.0, 52.1 y); median (10th, 90th percentiles) symptom duration, 8 mo (2.0, 95.7 mo)	n = 128; men, n = 72; women, n = 56; median (10th, 90th percentiles) age, 35 y (24.0, 51.6 y); median symptom duration (10th, 90th percentiles), 14 mo (2.7, 113.5 mo)	LBP with or without leg pain of >8 wk; radiograph, CT scan, or MRI taken within the preceding 2 y; 18-60 y of age	Mix	MDT: directional-preference exercises, can modify positions and/or add manual techniques Exercise: stationary bike and low-resistance exercises for lumbopelvic muscles, dynamic back strengthening exercises, stretching trunk and hip muscles Both groups: asked to continue exercising for a minimum of 2 mo after intervention	Credentialed, parts A-D	Pain: back and leg pain, Low Back Pain Rating Scale Disability: Low Back Pain Rating Scale Outcomes evaluated after 2, 4 , and 12 mo
Petersen et al[47] (7/10)	n = 175; men, n= 72; women, n = 103; age, 38 ± 10.4 y; symptom duration, 97 ± 230 wk	n = 175; men, n = 83; women, n = 92; age, 37 ± 9.4 y; symptom duration, 94 ± 181 wk	LBP, with or without leg pain, >6 wk; able to speak and understand Danish; clinical signs of disc-related symptoms; 18-60 y of age	Chronic	MDT: directional-preference exercise, no manual vertebral mobilizations, educational booklet and/or lumbar roll at therapist discretion Manual therapy plus exercise: manual techniques at therapist discretion (eg, vertebral mobilization/manipulation), self-manipulation, flexion/extension exercises and stretching, educational booklet Both groups: given stabilization/strengthening exercises at therapist discretion, given home exercise plan and encouraged to continue post intervention	Screening preran-domization: diploma Treatment: credentialed	Pain: numeric rating scale Disability: Roland-Morris Disability Questionnaire SF-36 Outcomes evaluated after 3, 5, and 12 mo
Sakai et al[53] (4/10)†	n = 25; men, n = 25; women, n = 0; age, 47.9 ± 13.1 y; symptom duration, 25.3 ± 17.5 mo	Control: n = 25; men, n = 25; women, n = 0; age, 44.4 ± 13.9 y; symptom duration, 20.3 ± 18.7 mo Medication: n = 24; men, n = 24; women, n = 0; age, 44.2 ± 12.2 y; symptom duration, 23.9 ± 20.4 mo	LBP, without radiating leg pain or numbness in lower extremity, of >6 mo; male >20 y of age	Chronic	MDT: MDT approach, no further details given Control: compress, no exercise Medication: 50 mg eperisone hydrochloride, 3 times a day after meals for 4 wk All groups: educational booklet, heat therapy, ultrasound, electrical muscle stimulation, traction, no use of NSAID or anti-inflammatory agent	Credentialed	Pain: visual analog scale, Faces Pain Scale-Revised Disability: SF-36 Outcomes evaluated after 2 and 4 wk
Schenk et al[54] (5/10)	n = 19; men, n = 7; women, n = 12; mean age, 39 y; mean symptom duration, 18 d	n = 12; men, n = 5; women, n = 7; mean age, 46 y; mean symptom duration, 15 d	LBP, at least 3 of 5 selection criteria from clinical prediction rules, ≥18 y of age	Acute	MDT: directional-preference exercises, home exercise program Manual therapy plus exercise: regional lumbopelvic thrust technique, hand-heel rock range-of-motion exercise Both groups: as of third session, directional-preference exercises at home on an hourly basis, exercise log	Credentialed	Pain: numeric rating scale Disability: Oswestry Disability Index Outcomes evaluated after 2 and 4 wk

Table continues on page 483.

TABLE 1 Summary of Inclusion and Exclusion Criteria, Intervention Groups, and Outcome Measures (continued)

Study (PEDro Score)	Participants (MDT Intervention)*	Participants (Other Interventions)*	Inclusion Criteria	Acute Pain (<12 wk) or Chronic Pain (>12 wk)	Intervention	MDT Level of Training	Outcomes
Schenk et al[55] (5/10)	n = 15; men, n = 7; women, n = 8; mean age, 40.1 y; symptom duration, 7 d to 7 wk	n = 10; men, n = 8; women, n = 2; mean age, 44.8 y; symptom duration, 7 d to 7 wk	Lumbar radiculopathy: symptoms originating in disc, peripheral to lumbar region, with or without neurological symptoms; posterior derangement	Acute	MDT: directional-preference exercises Manual therapy plus exercise: mobilization: passive movement to spinal segments Both groups: postural correction, ambulation on treadmill	Credentialed	Pain: visual analog scale Disability: Oswestry Disability Questionnaire Outcomes evaluated after third visit
Miller et al[38] (5/10)	n = 14; men, n = 7; women, n = 7; age, 44 ± 16 y; symptom duration, 20 ± 30 mo	n = 15; men, n = 8; women, n = 7; age, 54 ± 15 y; symptom duration, 32 ± 58 mo	Chronic LBP for >7 wk, 18 y of age or older	Chronic	MDT: postural correction, directional-preference exercises, and manual techniques Exercise: spine stabilization exercises (transversus abdominis and lumbar multifidus) Both groups: home exercise program according to grouping	Credentialed	Pain: short-form McGill Pain Questionnaire Disability: Functional Status Questionnaire Outcomes evaluated after 6 wk
Halliday et al[22] (7/10)	n = 35; men, n = 7; women, n = 28; age, 48.8 ± 12.1 y; median symptom duration, 26.6 wk (IQR, 22.3)	n = 35; men, n = 7; women, n = 28; age, 48.3 ± 14.2 y; median symptom duration, 37.7 wk (IQR, 28.8)	LBP localized between the 12th rib and the buttock crease, with or without referred pain into one or both legs and with or without sensory and or motor changes, for >3 mo; directional preference	Chronic	MDT: directional-preference exercises, postural education and lumbar roll, *Treat Your Own Back* book Exercise: motor control exercises of deep lumbar stabilizers, home exercise program	Credentialed	Pain: visual analog scale Disability: Patient-Specific Functional Scale Outcomes evaluated after 8 wk
Garcia et al[18] (8/10)†	n = 74; men, n = 16; women, n = 58; age, 57.5 ± 12.2 y; symptom duration, 36 ± 102 mo	n = 73; men, n = 19; women, n = 54; age, 55.5 ± 13.7 y; symptom duration, 48 ± 96 mo	Chronic nonspecific LBP, pain intensity of 3/10 on a numeric pain-rating scale, 18-80 y of age, and able to read Portuguese	Chronic	MDT: directional-preference exercises, specific end-range motion exercise, postural education, home exercise program, and *Treat Your Own Back* book Placebo: detuned pulsed ultrasound, detuned shortwave diathermy Both groups: given educational booklet *The Back Book*	Part A	Pain: numeric pain-rating scale Disability: modified Roland-Morris Disability Questionnaire Outcomes evaluated after 5 wk and 3, 6, and 12 mo

Abbreviations: CT, computed tomography; IQR, interquartile range; LBP, low back pain; MDT, Mechanical Diagnosis and Therapy; MRI, magnetic resonance imaging; NA, not available; NSAID, nonsteroidal anti-inflammatory drug; PEDro, Physiotherapy Evidence Database; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; TENS, transcutaneous electrical nerve stimulation.
**Values are mean ± SD unless otherwise indicated.*
†Not included in meta-analysis.

high-quality evidence of no significant (P = .45) difference in disability after the intervention period between participants treated with MDT or education (SMD, −0.09; 95% CI: −0.31, 0.14).

One study included in the review, despite lacking data for analysis, compared MDT to education[20] and found no significant between-group differences for changes in disability.

Chronic LBP: Primary Analysis of MDT Versus Other Interventions

Seven studies compared MDT to other interventions in participants with chronic LBP.[17,22,31,38,40,45,47] Exercise, combined

manual therapy and exercise, and education were the comparator interventions. One of the studies compared combined MDT and balneotherapy to combined exercise, manual therapy, and balneotherapy.[40] Another study had 2 comparator groups, manual therapy with exercise and education.[45]

Six of the 7 studies measured pain intensity.[17,22,31,38,45,47] Tests of heterogeneity were significant (**FIGURE 4A**). There was moderate evidence of a significant (P = .03) difference in pain after the intervention period, with the results favoring MDT (SMD, −0.33; 95% CI: −0.63, −0.03). The GRADE ratings were downgraded due to unexplained heterogeneity. This analysis included manual therapy with exercise as the comparator intervention from the study that included 2 comparator groups.[45] When education was included instead, significant differences remained (P = .03).

Disability was measured in all 7 studies.[17,22,31,38,40,45,47] Tests for heterogeneity were not significant (**FIGURE 5A**). There was high-quality evidence of a significant (P<.01) difference in disability after the intervention period, with the results favoring MDT (SMD, −0.28; 95% CI: −0.44, −0.12). This analysis included manual therapy, with exercise as the comparator intervention from the study that included 2 comparator groups.[45] When education was included instead, significant differences remained (P = .04).

Two studies included in the review, which lacked sufficient data to be included in the meta-analysis comparing MDT to modalities (heat, ultrasound, electrical muscle stimulation, and interferential current),[42,53] found significant between-group differences for changes in pain, with results favoring MDT; only 1 of these studies[42] found a significant difference in change in disability, with results favoring MDT.

TABLE 2 Summary of Meta-analysis Results

	Number of Studies	Mean Difference (95% CI)	*P* Value
Acute LBP			
MDT versus other interventions			
Pain	3	−0.45 (−0.99, 0.10)	.11
Disability	4	−0.07 (−0.34, 0.20)	.61
MDT versus manual therapy and exercise			
Pain	2	−0.74 (−1.45, −0.03)	.04
Disability	3	−0.24 (−0.77, 0.28)	.36
MDT versus education	2	−0.09 (−0.31, 0.14)	.45
Chronic LBP			
MDT versus other interventions			
Pain*	6	−0.33 (−0.63, −0.03)	.03
Disability	7	−0.28 (−0.44, −0.12)	<.01
MDT versus manual therapy and exercise			
Pain*	2	−0.26 (−0.73, 0.22)	.30
Disability	3	−0.11 (−0.29, 0.07)	.23
MDT versus exercise			
Pain*	4	−0.38 (−0.82, 0.05)	.08
Disability	4	−0.45 (−0.64, −0.25)	<.01
MDT versus education			
Pain (unable to calculate)	1		
Disability (unable to calculate)	1		
MDT versus placebo			
Pain (unable to calculate)	1		
Disability (unable to calculate)	1		

Abbreviations: CI, confidence interval; LBP, low back pain; MDT, Mechanical Diagnosis and Therapy.
**Significant heterogeneity.*

Chronic LBP: Subgroup Analysis

MDT Versus Manual Therapy Plus Exercise Three studies compared the effects of MDT to combined manual therapy plus exercise in participants with chronic LBP.[40,45,47] Manual therapy plus exercise interventions consisted of manipulation, mobilization, and lumbar range of motion/stretching exercises. Of the 3 studies, 2 measured pain intensity, and tests of heterogeneity were significant (**FIGURE 4B**).[45,47] There was moderate evidence of no significant (P = .30) difference in pain after the intervention period between interventions (SMD, −0.26; 95% CI: −0.73, 0.22). Ratings were downgraded because of unexplained heterogeneity. All 3 studies measured disability, and tests of heterogeneity were not significant (**FIGURE 5B**).[40,45,47] There was high-quality evidence of no significant (P = .23) difference in disability after the intervention period between interventions (SMD, −0.11; 95% CI: −0.29, 0.07).

One study that did not provide sufficient data to be included in the meta-analysis[2] compared MDT to manual therapy and exercise. The study found no significant between-group differences for change in pain intensity and disability after a 1-week intervention.

MDT Versus Exercise Four studies compared the effects of MDT and exercise on pain intensity in participants with chronic LBP.[17,22,31,38] Exercise programs consisted of group exercises,[17] midrange lumbar/stretching exercises,[31] or stabilization/motor control exercises.[22,38] One study had 2 comparison intervention groups consisting of either MDT exercise in the opposite direction as the directional preference or midrange lumbar/stretching exercises.[31] Only this latter group was included as the comparison to MDT in the

current analysis. All 4 studies measured pain intensity, and tests of heterogeneity were significant (**FIGURE 4C**).[17,22,31,38] There was moderate evidence of no significant difference in pain after the intervention period between interventions (SMD, −0.38; 95% CI: −0.82, 0.05). Ratings were downgraded because of imprecision of results. These 4 studies also examined disability. Tests of heterogeneity were not significant (**FIGURE 5C**). There was high-quality evidence of a significant difference ($P<.01$) in disability after the intervention period, with the results favoring MDT (SMD, −0.45; 95% CI: −0.64, −0.25.

One of the included studies did not provide sufficient data to be included in the meta-analysis; the authors found no significant between-group differences in change in pain and disability between patients treated with MDT versus exercise.[47]

MDT Versus Education Only 1 study compared MDT to an education intervention in participants with chronic LBP, and thus a meta-analysis could not be completed.[45] Education included advice to remain active. There was no significant difference in change in pain intensity or disability between MDT and education 3 months after initiating treatment.

MDT Versus Placebo One study compared MDT to a placebo intervention in participants with chronic LBP, and thus a meta-analysis could not be completed.[18] Both groups received a copy of *The Back Book* (Baltimore, MD: Johns Hopkins University Press) and 5 weeks of treatments that included 10 sessions in total. The placebo group was treated with detuned pulsed ultrasound for 5 minutes and detuned shortwave diathermy in pulse mode for 25 minutes, which did not provide any therapeutic benefit. There was a statistically significant difference between groups for change in pain intensity at the end of treatment, with results favoring the MDT group (adjusted mean difference, −1.00; 95% CI: −2.09, −0.01); however, the difference was only 1 point on a 0-to-10 visual analog scale, and likely not clinically significant.

Risk-of-Bias Assessment and Strength of Evidence

The articles' scores on the PEDro scale were all obtained through the PEDro database and ranged from 4 to 8 out of 10. There were 15 studies with a PEDro score of at least 5, and 2 studies with a score of less than 5. Due to the nature of the interventions, the providers could not be blinded to the interventions in any of the studies, which lowered the PEDro scores of the included articles. Blinding of the patients was reported in only 1 study.[18] Blinding of the assessor was reported in 9 of the studies.[1,17,20,22,31,33,41,47,55] The mean PEDro scale score for all studies was 6/10 (**TABLE 1**).

DISCUSSION

In patients with acute LBP, (1) MDT was no more effective than other interventions, (2) MDT yielded statistically and clinically significant better improvements in pain intensity compared to manual therapy plus exercise (though only 2 studies with small sample sizes were included in the analysis), and (3) no difference in improvement in disability was found between MDT and either manual therapy plus exercise or education. In those with acute LBP, the quality of evidence assessed with the GRADE ratings was moderate and high for the outcome of pain and disability, respectively; therefore, there is good-quality evidence showing that MDT is not clinically superior to other interventions in acute LBP to improve pain or disability.

In patients with chronic LBP, (1) MDT was more effective at reducing pain and disability than other rehabilitation interventions, (2) MDT was superior to exercise for reducing disability but not pain, and (3) MDT was not superior to combined manual therapy and exercise, or to education. Although superior, the effect size was small to moderate, indicating at least minimal clinical significance. The strength of evidence of these findings was moderate to high and was downgraded mainly due to significant heterogeneity between the included studies. The strength of evidence is further demonstrated by the PEDro scale scores higher than 5 for all studies contrib-

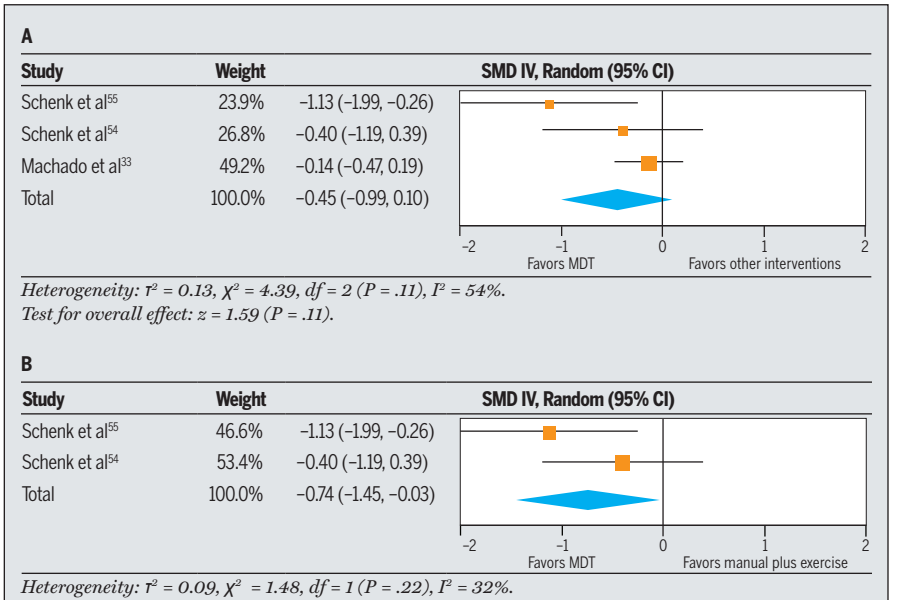

FIGURE 2. Forest plot of the effectiveness of MDT for improving pain in patients with acute low back pain in comparison to (A) other physical therapy interventions, and (B) a combination of manual therapy with exercise. The other physical therapy interventions included a combination of manual therapy with exercise or education. Abbreviations: CI, confidence interval; IV, independent variable; MDT, Mechanical Diagnosis and Therapy; SMD, standardized mean difference.

uting to statistical analysis. A PEDro scale score of 5 or higher is used as a common cutoff to evaluate the quality of a study.[7]

The current findings were different from those of the previous meta-analysis, which concluded that the MDT approach did not produce clinically significant differences in pain and disability in patients with LBP. Nine studies included in the current study were published after the last meta-analysis,[32] published in 2006 (**TABLE 1**).[1,18,22,33,40,45,47,53,54] There are 4 main differences between the previous and current meta-analyses. First, in the current meta-analysis, acute and chronic LBP were investigated separately. Chronic pain and acute pain manifest differently, because psychosocial factors are potentially more dominant in patients with chronic pain.[68] Second, the current meta-analysis only included studies in which therapists received MDT standardized training. When providing care based on MDT principles, trained therapists obtained better treatment outcomes than untrained therapists.[10] From the previous meta-analysis, 2 studies included therapists who were not trained in MDT.[5,12] Third, only studies in which classification was conducted a priori were included in the current meta-analysis. The basis of the MDT approach relies on the classification of a patient before providing treatment, such as directional-preference exercises. Thus, patients should be classified into 1 of the subgroups (derangement, dysfunction, postural, or other) prior to receiving a specific treatment to be considered an MDT treatment. The classification process was omitted in 5 of the included studies in the previous systematic review.[9,11,35,57,60] Thus, the current findings provided an updated meta-analysis of the effectiveness of MDT, and ensured that the included studies more closely followed the MDT program as intended.

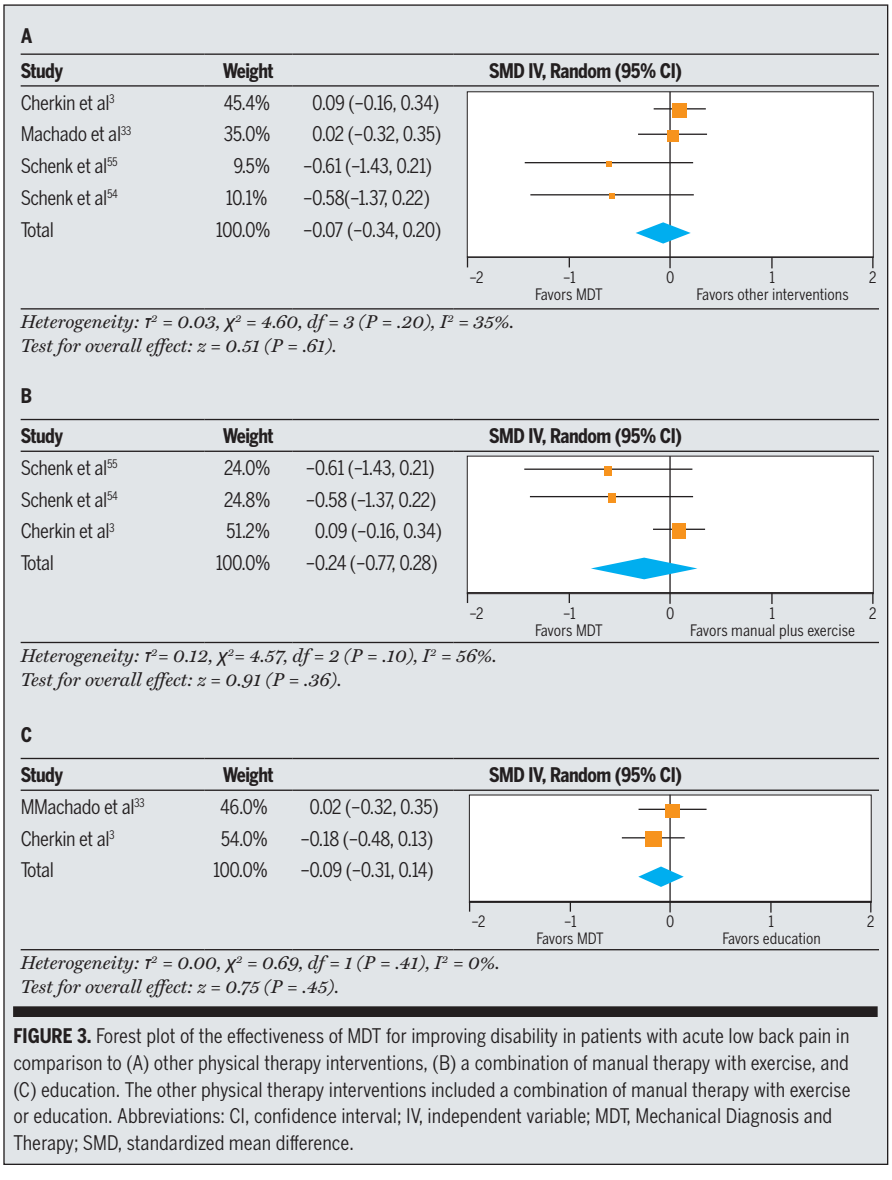

FIGURE 3. Forest plot of the effectiveness of MDT for improving disability in patients with acute low back pain in comparison to (A) other physical therapy interventions, (B) a combination of manual therapy with exercise, and (C) education. The other physical therapy interventions included a combination of manual therapy with exercise or education. Abbreviations: CI, confidence interval; IV, independent variable; MDT, Mechanical Diagnosis and Therapy; SMD, standardized mean difference.

In patients with acute LBP, we observed statistically significantly greater improvement in pain intensity when utilizing the MDT approach compared to the combination of manual therapy and exercise. Two studies in which directional-preference exercises were the primary means of treatment in the MDT group were analyzed.[54,55] Directional preference implies a rapid improvement in patient symptoms in response to a specific exercise.[36] This could explain the differences observed when comparing a symptom-based approach to a nonspecific exercise regimen, such as range-of-motion exercises, which may not address pain immediately. Analysis of the 2 included studies showed statistically significant differences in pain favoring MDT (**FIGURE 2**), with an SMD of 0.74 and a nonstandardized difference of 1.86 on the visual analog scale (analysis not presented), which would be considered clinically meaningful.[21] For acute LBP, no difference was observed for change in disability across the different methods of intervention, including education (**FIGURE 3**). This could be explained by the nature of acute LBP, in that most patients have a favorable prognosis, and that rapid reductions in both pain and disability are noted within 6 weeks of symptom onset.[37] For patients with acute LBP, MDT seemed to be more effective at reducing pain than manual therapy plus exercise; however,

therapists should be careful when using MDT exclusively, as the effect size was moderate for a small sample size, and other treatment approaches could yield similar results for disability in this population.

For patients with chronic LBP, MDT provided greater improvements in pain and disability compared to other interventions and exercise alone, but had similar outcomes compared to the combination of manual therapy and exercise. The SMD values represented a small treatment effect for the comparison of MDT to other interventions for pain (SMD, −0.33) and disability (SMD, −0.28); therefore, despite statistical significance, the clinical significance of the difference may be less meaningful. Other symptom-matched approaches have also demonstrated similar findings in patients with chronic LBP.[2,56]

Although effective in treating chronic LBP, MDT might not be any better than combined manual therapy plus exercise. It has been shown in treatment-based classification that patients who may benefit from specific exercise may also benefit from spinal manipulation.[58] Also, small treatment effects could be credited to the fact that a large group of patients may not fall into a distinct subgrouping and may benefit from a more generalized exercise program.[59] These patients are likely to be classified into the "chronic pain" category of the MDT classification. Because the meta-analysis did not evaluate each MDT subgroup separately, definite conclusions regarding the different treatment effectiveness outcomes are unknown. This latter subgroup is largely based on the presence of psychological factors and on patients not responding to mechanical-type treatments.[36] Also, MDT does not explicitly account for pain systems theory, specifically differentiating between pain that is central or peripheral in origin, and for a wider spectrum of psychological factors that could be present in patients with chronic LBP.[44,51] Regardless, although the treatment effects are small to moderate, MDT remains a viable option in reducing pain and disability in patients with chronic LBP.

However, there were some methodological issues in the included studies. Lower PEDro scale scores were often due to the nature of the studies: not allowing for blinding of the therapists and patients. The intention to treat was not met for 4 studies, and it was not clear how participants who dropped out were accounted for statistically.[1,20,22,38] Also, some studies included only the derangement subgroup for the MDT intervention, whereas others included all 3 mechanical syndromes. The fact that the 3 different subgroups had different prognoses could have impacted MDT's effectiveness. Furthermore, MDT was not compared to other classification approaches that tailor treatments based on clinical characteristics rather than pathoanatomical diagnoses, such as treatment-based classification and movement system impairments.[13,27]

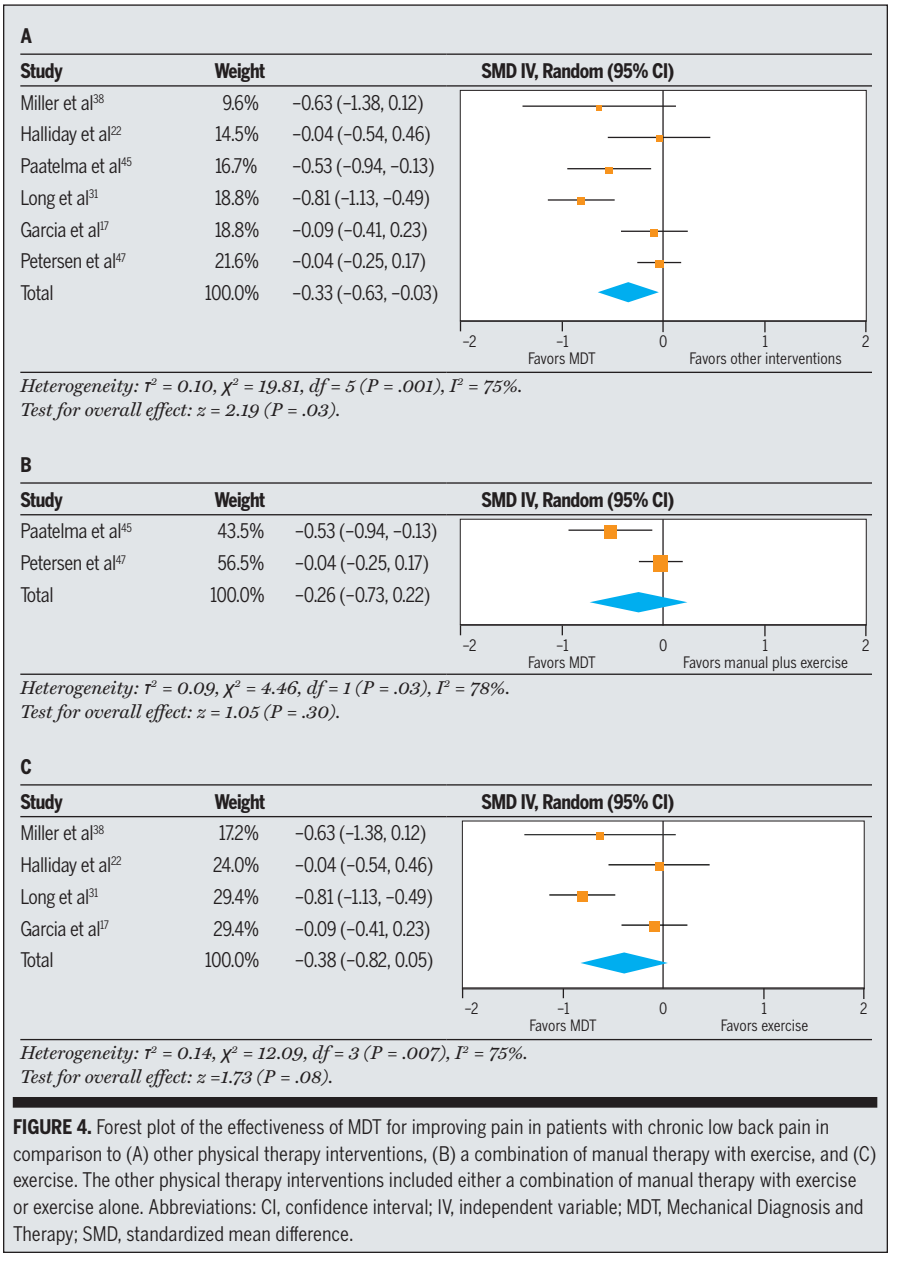

FIGURE 4. Forest plot of the effectiveness of MDT for improving pain in patients with chronic low back pain in comparison to (A) other physical therapy interventions, (B) a combination of manual therapy with exercise, and (C) exercise. The other physical therapy interventions included either a combination of manual therapy with exercise or exercise alone. Abbreviations: CI, confidence interval; IV, independent variable; MDT, Mechanical Diagnosis and Therapy; SMD, standardized mean difference.

These approaches have yielded similarly modest results, finding statistically insignificant improvements in outcome measures for both the classification-specific and the non–classification-specific groups.[24,61] However, this current review did find a significant difference between patient-matched treatment and generic exercise for disability in the short term for chronic LBP, albeit moderate.

CONCLUSION

There is moderate- to high-quality evidence that MDT is not superior to other rehabilitation interventions for reducing pain and disability in patients with acute LBP. In patients with chronic LBP, there is moderate- to high-quality evidence that MDT is superior to other rehabilitation interventions for reducing pain and disability; however, this depends on the type of intervention being compared to MDT, and the effect sizes were generally considered small to moderate, which means clinical significance needs to be determined. Although some evidence supported the use of MDT for assessing and treating LBP, therapists should be careful when using this approach exclusively, because other treatments have shown similar effectiveness, and a patient's values and preferences should be considered. ◉

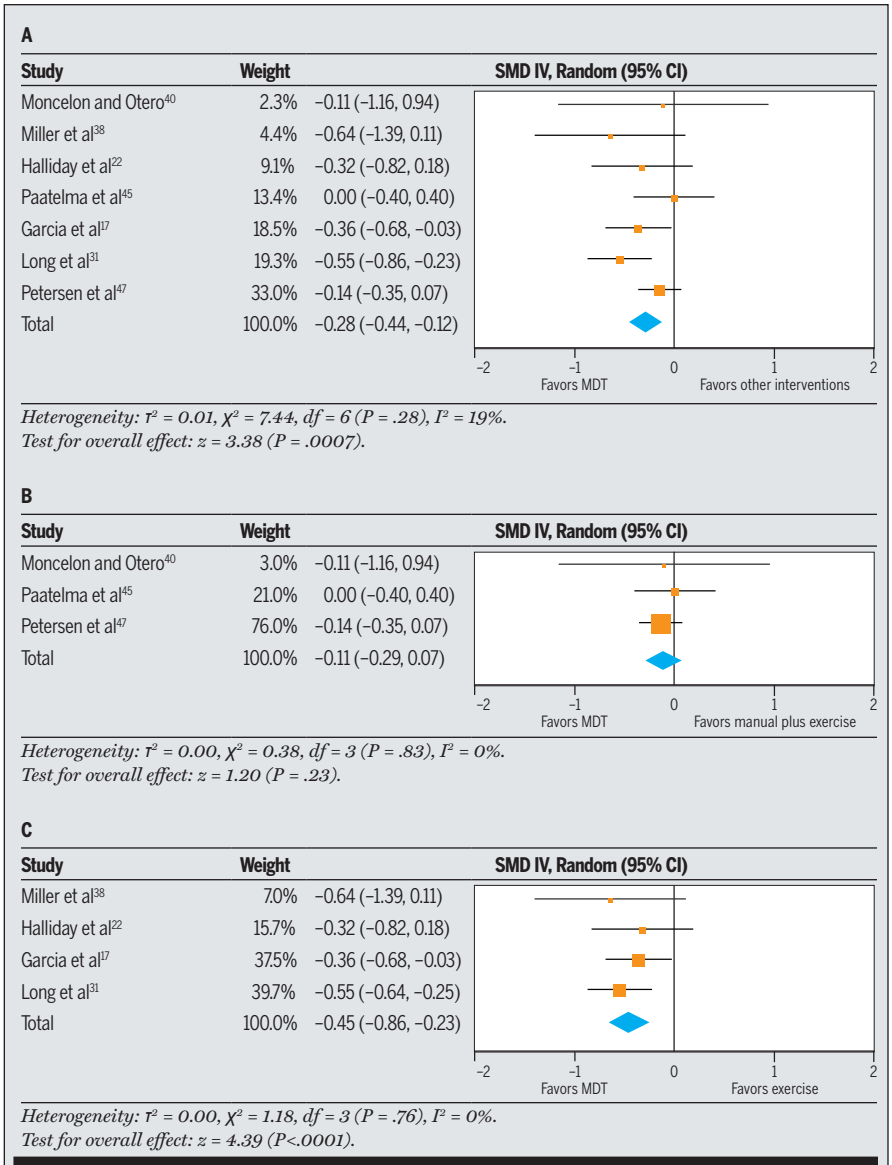

FIGURE 5. Forest plot of the effectiveness of MDT for improving disability in patients with chronic low back pain in comparison to (A) other physical therapy interventions, (B) a combination of manual therapy with exercise, and (C) exercise. The other physical therapy interventions included either a combination of manual therapy with exercise or exercise alone. Abbreviations: CI, confidence interval; IV, independent variable; MDT, Mechanical Diagnosis and Therapy; SMD, standardized mean difference.

KEY POINTS

FINDINGS: For reducing pain and disability in patients with acute low back pain (LBP), the McKenzie Method of Mechanical Diagnosis and Therapy (MDT) is not superior to other rehabilitation interventions. In patients with chronic LBP, however, MDT is superior to other rehabilitation interventions for reducing pain and disability; however, this depends on the type of intervention being compared to MDT. The treatment effect for MDT was generally small to moderate.

IMPLICATIONS: To treat patients with LBP, MDT may be used, although other intervention methods might offer a similar benefit.

CAUTION: Although statistically significant, clinical significance of MDT effects needs to be determined because the effect sizes found were small to moderate.

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APPENDIX

EXAMPLE OF A SEARCH CONDUCTED IN MEDLINE

Search String 1	Search String 2	Search String 3
1. McKenzie therap*.mp.	13. Low Back Pain/	34. randomized controlled trial.pt.
2. McKenzie method*.mp.	14. (low* back adj2 pain*).mp.	35. controlled clinical trial.pt.
3. McKenzie treatment*.mp.	15. lumbar pain.mp.	36. RCT.ti,ab.
4. McKenzie exerci*.mp.	16. lumbar strain.ti,ab.	37. random*.ti,ab.
5. centralization.mp.	17. lumbar sprain.ti,ab.	38. placebo.ti,ab.
6. extension exercise*.mp.	18. Back Pain/	39. trial.ti,ab.
7. flexion exercise*.mp.	19. (backache* or back ache*).ti,ab.	40. groups.ti,ab.
8. "mechanical diagnosis and therapy".mp.	20. discogenic pain.ti,ab.	41. or/34-40
9. MDT.mp.	21. dorsalgia.ti,ab.	
10. directional preference*.mp.	22. coccydynia.ti,ab.	
11. active therap*.mp.	23. Sciatica/	
12. or/1-11	24. sciatica.ti,ab.	
	25. Sciatic Neuropathy/	
	26. sciatic neuropath*.ti,ab.	
	27. Spondylosis/	
	28. spondylosis.ti,ab.	
	29. Spondylolysis/	
	30. spondylolysis.ti,ab.	
	31. Spondylolysthesis.ti,ab.	
	32. lumbago.ti,ab.	
	33. or/13-32	

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The Role and Value of Symptom-Modification Approaches in Musculoskeletal Practice

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Clinicians and researchers working in the same clinical area (eg, low back pain) often make recommendations on how best to manage patients, and these recommendations are often characterized by different clinical and philosophical approaches that range from biomechanical to psychological. The diversity of models of care in contemporary musculoskeletal physical therapy can be confusing for patients and practicing clinicians. There is, however, a common theme to many of these seemingly disparate models of care: symptom modification.

Symptom modification aims at reducing symptoms and improving function with a variety of clinical approaches. This Viewpoint explores the role of symptom modification in rehabilitation and specifically addresses (1) symptom modification within the kinesiopathological model of pain, (2) symptom modification in clinical practice, and (3) potential commonality in seemingly divergent models of clinical practice.

Clinicians are often confronted with conflicting advice in the literature and from advocates of a particular approach to the treatment of patients in pain. Finding common themes within these seemingly disparate approaches may help to reconcile these differences and potentially delineate commonality in contemporary practice. Symptom modification may serve as the overarching rationale for a variety of techniques and approaches used in contemporary practice.

Symptom Modification Within the Kinesiopathological Model of Pain

One goal of musculoskeletal practice has been to identify the structure associated with the patient's pain and symptoms. To achieve this, orthopaedic tests were developed to implicate a source of symptoms. The ability to achieve this goal has been challenged by multiple investigations that suggest that, in isolation or in combination, clinical tests are often incapable of identifying the structure associated with the symptoms with sufficient confidence. In addition, there is generally a poor correlation between the findings of imaging investigations and symptoms in the absence of trauma and sinister pathology. These 2 findings suggest that in many instances, musculoskeletal pain may be structurally and anatomically indeterminable. To address this uncertainty, clinicians and researchers have suggested that clinical practice could be guided by the identification and modification of potential kinematic, kinetic, or motor control impairments in musculoskeletal function, that is, a kinesiopathological approach.[10,33] The presumption is that the correction of movement to an assumed ideal movement and the correction of proposed impairments are necessary to alleviate pain and promote ideal function.

The identification of an impairment assumes that there is an ideal position or movement pattern and that deviations from this ideal predispose an individual to pain and may negatively impact recovery. A limitation of the kinesiopathological approach is the common research finding of an inconsistent rela-

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tionship between assumed impairments in posture, kinematics, kinetics, and motor control and pain and disability. For example, altered scapular kinematics are inconsistently linked to shoulder pain,[23] and altered scapular kinematics have been shown to not be predictive of future shoulder pain.[27] Conversely, other research has suggested that deviations in scapular kinematics do predispose athletes to future shoulder pain.[19] A poor relationship between spinal posture and neck pain[25] and shoulder pain[1] has been documented. Similarly, conflicting results have also been reported in the lower limb, with research findings suggesting increased hip adduction being associated with iliotibial band syndrome in runners.[7] Others have reported no relationship,[9] while some suggest that decreased hip adduction is linked with iliotibial band syndrome.[8] Within the same research study, inconsistencies in proposed kinematic flaws and their relationship to injury have also been documented. For example, in recreational runners, increased hip adduction has been prospectively linked to patellofemoral pain, but not to calcaneal eversion or hip internal rotation.[21] The inconsistent relationship between biomechanics and pain[24] challenges the existence of ideal movements and the use of an ideal movement standard to guide clinical decisions.

Further, while the process of attempting to change presumed kinematic or kinetic impairments or movement behaviors may be helpful in decreasing pain and disability, this is not always associated with changes in the assumed kinesiological dysfunction. For example, studies investigating shoulder kinematics following exercise interventions designed to change joint kinematics have often shown improvements in symptoms with little to no change in joint kinematics.[2,18,28] This Viewpoint recognizes that the clinical approach of changing movement parameters and assumed impairments may enjoy clinical success; therefore, an alternative rationale for changing movement behaviors and guiding changes in movement may be warranted, considering that the correction of the assumed impairment may not occur and may be unnecessary.

The hypothesis and contention of this Viewpoint is that kinematic behaviors may not be addressed with the goal of creating ideal or optimal movement relative to a standard of movement, but with a primary objective of altering symptoms. The corrected movement may then (1) be pain free, (2) permit the resumption of activities, or (3) function as a desensitizer for other movements.

Symptom Modification in Clinical Practice

Many approaches that use symptom modification have been based, in part, in a biomechanical/kinesiopathological paradigm, where it is assumed that pain may be a result of restricted joint movement, suboptimal alignment/control of anatomical structures, excessive structural loads, lack of stability, or inability to relax muscles during movement. Treatment based on changes in movement behaviors, and thus biomechanics, justifies the movement corrections based on symptom response alone. Across different treatment models, the hypotheses underpinning the models and the application of the procedures may appear polarized and contradictory. For example, to reduce lumbar symptoms, some modification models recommend bracing and others recommend relaxing the lumbar spine during functional activities, such as bending or squatting. Many approaches to symptom modification are described in the literature, and the approaches detailed in the **TABLE** highlight how seemingly different approaches have similar treatment components. The quotations describing each approach illustrate that the primary and common objective (the practical application) of part of the intervention is based on, and guided by, symptom modification. The proposed rationale for the movement modifier is often based on, or evolved from, biomechanics.

The common objective of these approaches is to identify movements that provoke symptoms and then to introduce a change to that movement. The rationale for the movement modifier, how the movement is explained to the patient, and how that change is delivered may differ across the approaches. All seem to agree, however, that the correct change is the one that eventuates in a reduction in pain and symptoms. Although these models appear to suggest that biomechanics may be partially relevant with respect to symptoms, the guiding rationale for the intervention is symptom modification and symptom control, not the assumed biomechanical correction. A biomechanical explanation, applied post hoc, may be hypothesized when attempting to explain the possible mechanism of the symptom modification.

This is well illustrated in the case series by Ikeda and McGill[13] and contrasted with the cognitive functional therapy approach.[30] Ikeda and McGill[13] identified pain-provocative movements and then made changes (movement modifiers) to the movements, with the intention of reducing pain during measures of muscle activity, kinematics, lumbar joint loads, and joint stability. The authors reported that each participant had different pain-provoking activities and different responses to suggested interventions (ie, movement modifications). In that case series, a number of movement modifications were attempted, and the "correct" modification was the one that changed symptoms. When identified, the authors then quantified spinal biomechanics during the activity now performed with less pain.[13]

For example, one participant experienced dramatic reductions in pain during a squat when taught to minimize lumbar spine flexion, increase hip flexion, and consciously increase the activation of the latissimus dorsi to create a "bracing" action. The authors reported that this new, less painful movement occurred with decreased lumbar flexion and increased mediolateral shear forces.[13] A second participant experienced pain with a sit-to-stand task. This pain was abolished

when the participant performed a movement modification consisting of abdominal bracing and attempting to minimize lumbar spine flexion while increasing hip flexion. However, instead of an increase in mediolateral shear (reported in the previous patient), a decrease in mediolateral shear was quantified.[13] Here we have a short-term clinical "success" based on symptoms with different response to mediolateral shear stability. Clinicians can't measure these biomechanical variables, and the complexity of these cases and what correlates with symptom changes suggest that the biomechanical variable cannot be used to guide the treatment.

Rather, it is symptom modification that is important, which is in turn influenced by changing biomechanics. But the correct biomechanical change may only be validated via symptom modification, not via an a priori goal (eg, changing mediolateral shear). Additionally, both successful movement modifications minimized the painful type of movement (spinal flexion). Thus, the correct movement strategy was avoiding the movement that hurt, that is, symptom modification. Using symptoms as a guide may be illustrated further when the "spine stability" approach is contrasted with the ostensibly different approach of the cognitive functional therapy research group.[30]

Cognitive functional therapy is an approach that aims to address the multidimensional nature of low back pain. Within this approach is a respect for biomechanical contributors to a patient's pain. Much like the previous "spine stability" approach, a cognitive functional therapy–trained clinician will perform a physical assessment to find painful postures (eg, sleeping, standing) and painful movements (eg, sit-to-stand, squatting, bending forward).

Cognitive functional therapy aims to address the multiple dimensions of pain, and one component of the intervention involves changing the movement behavior associated with pain. Many of the common movement modifications seen within the cognitive functional therapy approach for patients with pain associated with lumbar spine flexion contrast some of the strategies seen in the previously described "spine stability" approach. For example, a patient who experiences pain while performing lumbar spine flexion might be instructed to perform the painful task in a slightly different context or position.[20,30] This might involve spinal flexion while on all fours, sitting, or lying on the back. This slight change in technique might also be accompanied by changes in how the trunk muscles create or control that movement.

In contrast to the movement modifier involving spinal bracing, these clinicians might encourage a patient to bend with the trunk muscles more relaxed and/or with a focus on relaxed breathing. The correct way to move the spine or perform the task is not driven by an assumed ideal of spine function, but rather the chosen movement modification is justified via symptom modification. While cognitive functional therapy may have justified movement modification based on a biomechanical rationale, it appears that the model has expanded to also acknowledge the role of pain-inhibitory processes linked to reducing fear of pain using an interplay of disclosure of pain beliefs as well as emotional and physical impact of pain

TABLE Symptom Modification in Contemporary Clinical Practice

Name	Practical Application	Proposed Rationale
The Shoulder Symptom Modification Procedure[17]	"The person with shoulder symptoms informs the clinician if an individual procedure: partially or completely alleviates symptoms; has no change on symptoms; or makes symptoms worse"[17]	An aim of the Shoulder Symptom Modification Procedure is to assess the response to (1) changing the thoracic kyphosis, (2) changing scapular position, and (3) muscle contraction aiming to influence the glenohumeral joint. The rationale is not to produce a permanent change in posture but to use any positive change as a potential treatment technique, challenging the individual's previous experience of symptoms
Mobilization with movement[31]	"The technique is indicated if, during its application the technique enables the impaired joint to move freely without pain or impediment"[31]	An aim is to identify positional faults that occur secondary to injury and that lead to maltracking of the joint, resulting in symptoms such as pain, stiffness, or weakness[11]
Correction of "instability catches" and the "McGill" approach[13]	"A clinical kinesiologist then used verbal and manual cues to alter motion and muscle-activation patterns in attempt [sic] to immediately reduce or remove pain"[13]	Increasing the stiffness of the torso has been suggested to arrest micromovements of the spine to reduce pain in those with instability.[16] Minimizing spinal flexion and increasing torso stiffness during lifting or bending have been suggested to be optimal for spine mechanics[13]
Cognitive functional therapy[30]	"In this manner they were instructed to change old pain provocative movement behaviours and to reinforce their new functionally enhancing movement behaviours"[30]	Historically, interpretation of reductions in pain via cognitive functional therapy interventions was explained by a reframing of patients' beliefs about their spine, along with the unloading of pain-sensitive structures[3] via reducing abnormal tissue loading induced via unnecessary trunk muscle cocontraction or rigid spinal postures.[5] More recently, movement modifications along with other interventions may involve a process that commonly reduces pain responses during the exposure, creating opportunities to violate expectations that movement is painful and threatening, thereby facilitating inhibitory learning processes[32]

during the interview, combined with exposure to feared, avoided, or painful activities while reducing sympathetic responses, abolishing protective and safety behaviors, and normalizing body schema.[22]

The biomechanical justifications for both models appear to be vastly contradictory, but if viewed from the perspective of the apparent aim of both approaches, symptom modification, then the appropriate technique is the one that allows the movement to be performed with a reduction in the experience of pain. Thus, the approaches are quite similar in their practical applications, even though their views of ideal joint movement or the proposed mechanism of effect differ substantially. Both approaches may also contribute to improved outcomes by demonstrating to patients that they are able to control their pain, which in turn may influence self-efficacy, locus of control, emotional responses, and the resumption of meaningful and functional activities. Thus, components of the treatment that might appear driven and explained by biomechanics may lead to changes in pain via other contributors to sensitization.

Other symptom-modification approaches include mobilization with movement (MWM) and the Shoulder Symptom Modification Procedure (SSMP). Similar to cognitive functional therapy and Ikeda and McGill's case series,[13] a symptomatic movement or activity is identified, and then a modification is made to determine whether the symptoms are reduced during the movement. With MWM, the initial rationale for the treatment was historically based on aberrant joint arthrokinematics "related to minor positional faults that occur secondary to injury and that lead to mal-tracking of the joint, resulting in symptoms such as pain, stiffness, or weakness."[11] It should be noted that while this mechanical explanation has been proposed, proponents of MWM also suggest that other explanations for the possible mechanisms of action include the role of the endocrine, neurophysiological, and neuroimmune systems.[31] In practice, a painful movement is identified, and then a hand or treatment belt provides a force to either the region of the painful joint or a joint remote to the symptoms that has been determined to influence the pain. However, as the aberrant joint arthrokinematics or positional faults (much like measures of spine stability or shear loads) cannot be measured or assessed clinically and can only be hypothesized, as such, the changes in symptoms guide the intervention.

The SSMP is embedded within a comprehensive management package including advice, education, exercises for the rotator cuff, and, frequently, whole-body rehabilitation. When applying the SSMP,[17] a symptomatic movement is identified, and then the clinician makes various changes in 3 areas (thoracic spine, scapula, glenohumeral region) to determine whether shoulder-related symptoms change. While the initial rationale for those changes may have previously been driven by a potential kinesiological effect, it is the symptom modification that is of primary importance to guide treatment. Practically, the SSMP techniques are individual clinical experiments that aim to reduce symptoms. For example, pain may be experienced with shoulder flexion that is abolished with scapular repositioning. It could be hypothesized that this decrease in pain is due to alterations in the subacromial space, altered joint positioning, changes in muscle length-tension relationships, changes in neural tension, or reduced vascular compromise resulting in potentially less mechanical pressure on a sensitized structure. It is acknowledged and clearly stated that the mechanisms underpinning any reduction in symptoms using the SSMP are not known.[16] The intention is not to change posture but to use the change in symptoms as a way of challenging the individual's beliefs relating to the symptoms (eg, being told a rotator cuff tear will only respond to surgery), and then to use the technique that reduces symptoms in treatment (eg, repeating the previously symptomatic movement and incorporating the change into functional movements, aiming to disrupt pain memories). Many clinicians will have observed that after repeating this assistance and then slowly removing the assistance, the patient will still continue to have less pain, or the same patient may report reduced symptoms with multiple testing procedures. This may be due to a biomechanical overlap in the different techniques or to a nonbiomechanical effect of the modification procedure. Again, it is the symptom modification that drives the decision making, rather than an "ideal" biomechanical movement.

Symptom-modification applications are described in many other approaches. Those treating tendinopathy will often advocate 30 to 45 seconds of isometric loading.[26] This is essentially a symptom modifier to allow a person to function with less pain. Mechanical Diagnosis and Therapy[29] uses preferred-direction techniques that are essentially chosen for their ability to modify symptoms. Neurodynamic techniques that involve the movement of neural tissue are often chosen on the basis of finding and changing pain,[4] and running re-education may utilize changes in gait that modify symptoms.[6]

Symptom modification is the common thread among many seemingly disparate approaches used in contemporary musculoskeletal practice. Perhaps there is an unnecessary focus on the presumed differences between approaches, similar to the unexplored assumptions that have led to clinical differences in how spinal disorders are treated versus extremity disorders.[14] It is possible that common themes link the SSMP, cognitive functional therapy, the McGill approach, MWM, and other symptom-modifying approaches. A common aim is symptom reduction, which, if achieved, allows the individual to move with less pain. How this is achieved is unknown and may involve myriad multidimensional processes. People move differently when they experience pain,[12] and a reduction

in symptoms may permit changes to the way people move by decreasing the threat and fear associated with that movement. Modifying symptoms may demonstrate to patients that their pain is reducible or controllable, and may increase movement variability and may also influence the manner in which afferent information is processed. Alternative explanations suggest that moving with less pain results in an expectancy violation that might involve inhibitory learning processes that influence pain and fear.[32,34] Perhaps most importantly, all of the mentioned approaches appear to reduce symptoms via repeated movements that are then integrated into meaningful and functional activities for the patient.

Uncertainties With Symptom Modification

Although symptom reduction may be part of a comprehensive approach that addresses the multidimensional nature of pain, there are ongoing challenges and uncertainties associated with this approach.

1. Symptom modifiers are often used as a temporary desensitizer, yet it is unknown how long modifications need to persist to contribute to a meaningful change. There is evidence that movement modifications need to persist for pain or disability to be reduced.[20]
2. Are symptom-modification techniques necessary, and do they confer any additional benefit, or are other components of clinical management sufficient?
3. Symptom reduction should not always be seen as an end in itself, especially if there are additional requirements, such as strength training. However, a reduction in symptoms may then facilitate attainment of other treatment goals and aims.
4. Symptom reduction might not be possible, and attempting symptom change that does not achieve its goal may create hypervigilance or unreasonable patient expectations that ultimately become demotivating and sensitizing. The inability to modify symptoms may also cause consternation in the clinician that, in turn, may be imparted to the patient. This is also a potential issue with other forms of clinical management, such as long-term exercise programs that similarly fail to reduce symptoms. Appropriate education, advice, and explanations, together with appropriate clinician-patient interaction, should moderate this concern.
5. Modifying biomechanics may be beneficial for other reasons beyond symptom modification. Biomechanics may be relevant for performance benefits[15] and, perhaps, injuries to specific tissues where the load exceeds the ability of the structural properties of that tissue (eg, anterior cruciate ligament tears).

The Value of Symptom Modification

The commonality of the symptom-modification approach in contemporary musculoskeletal practice may in part be due to myriad variables:

1. Pain relief may be considered as an outcome desired by many patients and therapists.
2. Reducing the experience of pain with concomitant improvement in function may contribute to reducing the impact of negative influences, such as reduced self-efficacy, catastrophizing, locus of control, fear avoidance, and kinesiophobia.
3. Symptom modification may be utilized to promote or reinforce other educational messages related to pain. If the clinician is communicating educational information that pain is an alarm, is poorly related to damage, and can change, then symptom modification may be helpful in challenging potentially conflicting beliefs pertaining to pain, and may reduce the threat imposed by the symptoms.
4. If symptoms are reduced, then the patient may be able to repeat the task multiple times and introduce that movement into meaningful functional tasks, and, in so doing, "disrupt" the previous memory and association of that task with symptoms.[32,34]

Summary

Symptom modification is a commonly used approach in contemporary musculoskeletal practice and was born out of the realization that identifying the structural source of symptoms is generally not possible and that making movement modifications based on kinesiological ideals may be unnecessary and unsupported. The proponents of symptom-modification procedures have proposed seemingly divergent mechanisms to explain the technique. The definitive mechanisms underpinning any reduction in symptoms using these procedures are not clearly understood. Research on the uncertainties associated with this approach is needed to fully understand these commonly used procedures in contemporary clinical practice. ◉

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Differential Diagnosis in a Patient Presenting With Both Systemic and Neuromusculoskeletal Pathology: Resident's Case Problem

The American Physical Therapy Association Vision Statement for the Physical Therapy Profession is "transforming society by optimizing movement to improve the human experience."[1] The physical therapist is responsible for the evaluation and management of the movement system and should utilize best-practice standards to identify patients who fall within and outside the scope of physical therapy practice. Whether the patient is seen in a direct-access or referral setting, the physical therapist needs keen diagnostic skills and evidence-based screening strategies to differentiate conditions that require medical intervention from those that require physical therapy management.[28,40]

STUDY DESIGN: Resident's case problem.

BACKGROUND: Patients presenting with multiple symptomatic areas pose a diagnostic challenge for the physical therapist. Though musculoskeletal and nonmusculoskeletal symptoms typically present separately, they can occur simultaneously and mimic each other. Consequently, the ability to differentiate between musculoskeletal and nonmusculoskeletal symptoms is an important skill for physical therapists. The purpose of this resident's case problem was to describe the clinical-reasoning process leading to medical and physical therapy management of a patient presenting with upper and lower back pain, bilateral radiating arm and leg pain, and abdominal pain.

DIAGNOSIS: The patient was a 30-year-old woman referred to physical therapy for upper and lower back pain. A detailed history and thorough examination revealed that the patient had signs and symptoms consistent with a possible abdominal aortic aneurysm. She was referred for medical management and was diagnosed with symptomatic cholelithiasis. She subsequently had a cholecystectomy, which ultimately resolved her abdominal pain and reduced her pain in other areas significantly. Although many of her symptoms resolved postoperatively, her pain in other areas remained and was potentially musculoskeletal in origin. Following re-evaluation and 3 physical therapy treatments over a 2-month period, she was relatively symptom free at discharge and had achieved all functional rehabilitation goals.

DISCUSSION: This resident's case problem provides an opportunity to discuss the differential diagnosis, clinical reasoning, and outcome of a patient who presented with both systemic and neuromusculoskeletal pathology.

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KEY WORDS: *abdominal aortic aneurysm, abdominal pain, cholelithiasis, lower back pain*

Patients presenting with multiple symptomatic areas can pose a diagnostic challenge for the physical therapist. Though musculoskeletal and nonmusculoskeletal symptoms typically present separately, they can occur simultaneously and mimic each other. Consequently, the ability to differentiate between musculoskeletal and nonmusculoskeletal symptoms is an important skill for physical therapists.[3,5,28] When a patient is referred to physical therapy, the primary objective of the examination process is to determine whether (1) the patient can be treated primarily and independently by the physical therapist, (2) the patient needs multidisciplinary management that includes physical therapy intervention, or (3) the patient requires referral to another health care practitioner to obtain optimal care.[5,15]

During the patient interview, the physical therapist gains vital clues to the patient's condition by inquiring about the patient's symptoms, including their location, quality, behavior, and duration. The information gained from the interview guides the decision-making process and can help the therapist detect potentially serious pathology, choose which diagnostic tests or measures to use during the examination, and select the most

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appropriate intervention for the patient's current condition.[5] Symptom investigation through the patient interview can additionally help determine whether the patient's condition is primarily due to musculoskeletal causes, systemic pathologies, or a combination of the two presenting together.[6,18]

Lower back pain is a common complaint in the general population and ranks second to the common cold as the reason for primary care visits.[30] In a previous study, Jordan et al[34] highlighted the frequency of visits to primary care with complaints of musculoskeletal problems, showing that 1 in 7 of all consultations was for a musculoskeletal issue, 25% of those being specifically for lower back pain. Approximately 85% of the population in the United States has experienced lower back pain, and the point prevalence of lower back pain is 15% to 33%, representing an important economic burden.[9,13,29,39] Although lower back pain is frequently of musculoskeletal origin, it can also be a symptom of systemic pathology originating from cancer or from cardiac, renal, gastrointestinal, or gynecological conditions.[17,19,28,41,45,47,51,54] Upper back pain can also be from musculoskeletal causes, but cardiac, pulmonary, renal, and/or gastrointestinal pathologies are also prevalent in this region.[26,28]

Radiating arm or leg pain usually follows dermatomal or myotomal patterns due to direct irritation or involvement of a spinal nerve; however, myofascial pain may mimic radicular pathologies due to anatomically overlapping dermatomes.[5,18] Referred pain from systemic origin occurs because of dysfunction of the autonomous innervation of the body and generally follows the segmental innervation of the affected organ.[28] Abdominal pain can arise from various organ pathologies within the gastrointestinal, urogenital, and cardiovascular systems.[26,41,47,51] Patients who complain of radiating pain that does not follow a specific pattern and seems to affect entire extremities, or those who experience pain that is out of proportion to findings of the physical examination, may be experiencing inappropriate illness behavior or symptom magnification.[28,53]

Although it is not within the scope of physical therapy practice to diagnose systemic pathology, it is important for the physical therapist to recognize possible signs and symptoms consistent with systemic pathology, which may mimic or be obscured by musculoskeletal pain.[22,28,41,47,49,51] The purpose of this resident's case problem was to describe the clinical-reasoning process leading to a medical referral and subsequent intervention, including physical therapy, for a patient presenting with both systemic and neuromusculoskeletal pathology.

This resident's case problem involved a patient who presented with upper and lower back pain, bilateral radiating arm and leg pain, and abdominal pain. Due to the patient's multiple symptomatic areas, she required a careful differential examination to determine the possible sources of her pain. This differential diagnosis process resulted in the patient receiving initial medical intervention followed by physical therapy management.

DIAGNOSIS

Patient History

The patient was a 30-year-old Caucasian female homemaker and mother of 4 children. She stood 1.63 m tall and weighed 79 kg (body mass index, 30 kg/m^2). She enjoyed reading as a hobby and did not participate in any regular, formal exercise program. She was referred by her primary care physician to an outpatient orthopaedic physical therapy clinic with a medical diagnosis of "recurring bilateral scapular pain, lower back pain, and right posterior neck pain."

The patient's primary area of pain was her lower back, and she related a 15-year history of intermittent back pain, which had become more constant and sharp over the previous 2 months. She stated that the quality and intensity of her current lower back pain felt different from the back pain she had experienced previously. She denied any recent trauma or change in her normal daily activities that would explain her lower back pain. The patient stated that her upper back pain had started after she and her family moved 6 months prior to evaluation and was related to unpacking boxes. Her abdominal pain and left posterior lateral thoracic pain began 5 months prior to evaluation and initially resolved with the use of Prilosec medication, but returned 1 week prior to evaluation and were worsening. Finally, her radiating leg and arm pains had started 4 and 2 months prior to evaluation, respectively, but she denied any injury or change in activity that coincided with the onset of these symptoms. The only relationship among pain areas that the patient noted was that an increase in her lower back pain sometimes induced her bilateral leg symptoms, and that an increase in her upper back pain sometimes induced her bilateral arm symptoms. A body chart documenting the location, description, and intensity of her pain areas on her initial exam can be found in **FIGURE 1.**

The patient's history of previous pain episodes included left-sided torso pain following a car accident 12 years prior to evaluation, and some intermittent lower back pain during her menstrual periods. She denied any abnormal bleeding, discharge, or pain with her current menstrual cycles. The aggravating factors for her upper and lower back pain were lifting over 10 kg and sidebending motions. Her radiating arm symptoms would sometimes come on while riding in a car, but she was unsure what aggravated her leg symptoms. Her abdominal and left-sided torso pains were not aggravated by activity, and she denied any alteration in pain after meals, during exertional breathing, or with position changes. She related no successful easing factors other than being less active in general. She had tried heat, massage, and various pain medications, without relief of symptoms. Her 24-hour pain behavior was unremarkable except for morning stiffness in all joints, lasting 20 to 30 minutes.

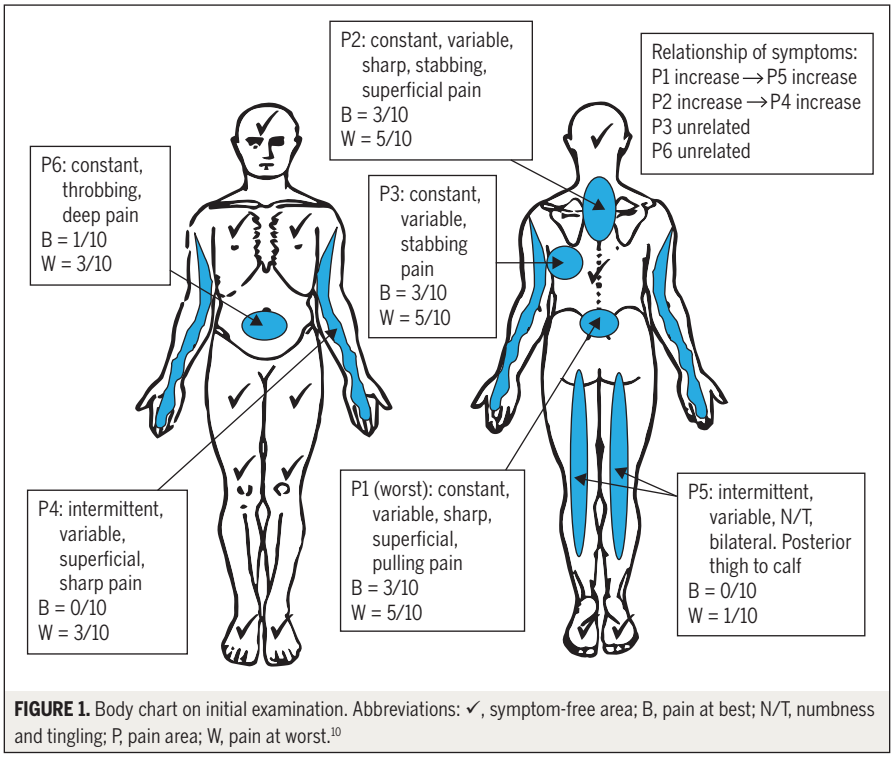

FIGURE 1. Body chart on initial examination. Abbreviations: ✓, symptom-free area; B, pain at best; N/T, numbness and tingling; P, pain area; W, pain at worst.[10]

The patient's surgical history included eye surgery, bilateral tubal ligation, and an appendectomy. She did not have any diagnostic imaging (radiographs or magnetic resonance imaging) as part of her medical work-up prior to her referral to physical therapy. A careful systems review was unremarkable, except that she reported increased sweating 2 to 3 times a week for the month prior to evaluation. She reported that this sweating would last all day and that she got relief from sitting in front of a fan. Her modified Oswestry Disability Index score was 30%, which indicates moderate disability. She did not drink alcohol, but did report that she had a 15 pack year history of smoking and that she currently smoked. The only medication she was currently taking was 800 mg of ibuprofen twice daily. Finally, the patient was screened for depression using 2 evidence-based questions.[2,37] She denied being bothered during the previous month by feeling down, depressed, or hopeless, or by having little interest or pleasure in doing things.

Physical Examination

During the patient interview and throughout the physical examination process, the patient appeared in no distress, despite her complaints of multiple pain areas. The patient demonstrated a nonantalgic gait, increased kyphotic thoracic spine and lordotic lumbar spine, and level pelvic landmarks in standing.[8] Her active ranges of motion in the lumbar, thoracic, and cervical spines were all within normal limits, except for causing some mild increased pain within the respective joints at the end ranges of motion. Her complaints of arm and leg pain were not reproduced with spinal motions. Repeated motion testing of the lumbar spine in both loaded and unloaded positions did not centralize or peripheralize her symptoms.

Her upper- and lower-quarter neurological screen revealed normal sensation, motor strength, and muscle stretch reflexes bilaterally. Pathological reflexes (Hoffmann, Babinski) and wrist and ankle clonus were also absent bilaterally. The straight leg raise test bilaterally did not reproduce any back or leg symptoms. The patient did, however, complain of a mild increase in her lower abdominal throbbing pain when lying in the supine position.

Abdominal palpation revealed tenderness in her right lower quadrant, with increasing pain toward the midline. The patient reported a strong, throbbing pulsation along her midline, which was increasingly tender with palpation. The transverse extent of the abdominal pulse was marked on either side of the midline and measured to have a total diameter of 5 cm. There is no consensus method for defining the cutoff point between a normal aorta and an abdominal aortic aneurysm (AAA); however, an infrarenal aortic diameter of 3 cm is commonly used.[7,35] The positive predictive value of palpation for an AAA of 3 cm or greater is 43%, but the sensitivity of palpation decreases with increased abdominal obesity.[35,52] The patient's abdominal adipose tissue did not appear of sufficient mass to affect the diagnostic utility of abdominal palpation. The patient had no swelling, ecchymosis, or abnormal temperature in the abdominal region, and had no rebound tenderness or abdominal rigidity. When the patient was asked to perform the abdominal drawing-in maneuver,[38,50] she complained of increasing abdominal and lower back pain. Upon further questioning, the patient again denied any changes to or abnormalities with her typical menstrual cycle, bowel and bladder function, or change in symptoms related to meals. The rest of the patient's exam was deferred and the orthopaedic manual physical therapy fellowship director was called in for a second opinion. The patient's history was given to the second physical therapist, who palpated the patient's abdomen and agreed with the finding of the atypically strong, wide, and bounding pulse.

Differential diagnosis at the end of the physical therapy examination included systemic origins of abdominal pain due to possible abdominal aortic pathology versus occult gastrointestinal or urogenital pathology. Although the diagnosis of

TABLE Factors That Were Present, Favoring a Specific Systemic Pathology, and Factors That Were Absent, Making the Diagnosis Less Likely

Possible Diagnosis	Present Factors Supporting the Diagnosis	Absent Factors Not Supporting the Diagnosis
Abdominal aortic aneurysm	Pain located in the abdomen and central lumbar region Palpable pulsating abdominal mass Pain described as pulsating or throbbing Sensation of a heartbeat when lying down Pain that increases with exertion Significant smoking history Obesity	Male sex Age greater than 50 years Familial history of abdominal aortic aneurysm or vascular claudication Patient unable to find comfortable position
Gallbladder pathology	Referred pain between the scapulae Pain with lying down Sweating Female sex Obesity	Pain in the mid epigastrium (heartburn) or right upper quadrant Referred pain to right shoulder Pain with respiratory inspiration Pain with upper-body movement Dark urine or light stools Pain after eating or intolerance to fatty foods Fever, chills, vomiting
Gastrointestinal pathology	Abdominal pain Sweating	Muscle guarding Abdominal rebound tenderness Abdominal rigidity Any movement aggravates pain Fever, chills, vomiting Pain relieved by sitting or leaning forward
Gynecological pathology	Lumbopelvic and lower abdominal pain	Cyclical pain, nausea, vomiting Dysmenorrhea Abnormal uterine bleeding or discharge

an AAA in a young woman is rare, the other systemic pathologies seemed less likely given the patient's history and review of systems (**TABLE**). An AAA was the most life-threatening diagnosis being considered and needed to be ruled out before other more likely diagnoses were addressed. The patient was also believed to have pain from musculoskeletal origins based on her history, but this was deemed of lesser priority for further examination and treatment. Based on the primary objective of the examination process, the patient required referral to another health care practitioner to obtain optimal care.[5,15]

The patient was informed that her symptoms required medical evaluation by a physician. Although the patient was apprehensive and more concerned, she agreed to be seen in the emergency department (ED) that day. She was escorted by the evaluating physical therapist to the ED, which was located in the same facility as the physical therapy department.

ED Examination

A copy of the patient's medical records from the ED was obtained following her examination there. Abdominal examination had been performed by a physician, who reported bilateral tenderness to the lower quadrants but no rebound tenderness or palpable mass. A pelvic exam had revealed thick, white discharge, and blood work had shown a positive beta-human chorionic gonadotropin (hCG) test, which is used to detect pregnancy.[48] Levels of the hCG hormone can first be detected by a normal blood test 11 days after conception. An hCG level of less than 5 mIU/mL is considered negative for pregnancy, and anything above 25 mIU/mL is considered positive for pregnancy.[48] The patient's hCG level was 50 mIU/mL. Pelvic ultrasound was performed and showed no intrauterine pregnancy, but revealed several mobile gallstones with shadowing. The liver, pancreas, uterus, and ovaries were all normal in appearance. Although the ultrasound showed gallstones, there was no sonographic evidence of acute cholecystitis. Differential diagnosis from the ED was ectopic pregnancy, bacterial vaginosis, and symptomatic cholelithiasis. The patient was given antibiotic medication (Rocephin and Cipro) in the ED and a consult to the gynecology and general surgery clinics.

Subsequent Medical Intervention

The patient was seen in the gynecology clinic 1 week after the ED visit to rule out ectopic pregnancy. The physician's documentation indicated a normal cardiovascular and respiratory systems exam, no abdominal masses, and a normal pelvic exam without blood or abnormal

discharge. A repeated beta-hCG test was positive, but trending downward (16.8 mIU/mL; 68% decrease from initial test 3 days earlier). Dart el al[14] found that patients with increasing beta-hCG values and indeterminate pelvic ultrasound examinations are at increased risk of ectopic pregnancy compared with patients with decreasing values, and concluded that patients are less likely to have ectopic pregnancies when the values decrease more than 50% over a 48-hour period. The gynecologist concluded that the patient had an early fertilization without implantation (ie, chemical pregnancy)[11] and determined that there were no signs of ectopic pregnancy. He predicted that the patient would likely have a normal menstrual period on her next cycle.

The patient was seen in the general surgery clinic 2 weeks after her ED visit. Six days later, a laparoscopic cholecystectomy was performed due to the patient's continued complaints of abdominal pain and the indeterminate physical examination findings. The patient had no complications from surgery, and, upon follow-up exams 10 days and then 1 month postoperatively with the general surgeon, the patient's complaints of abdominal pain (**FIGURE 1**, P6 area) had subsided.

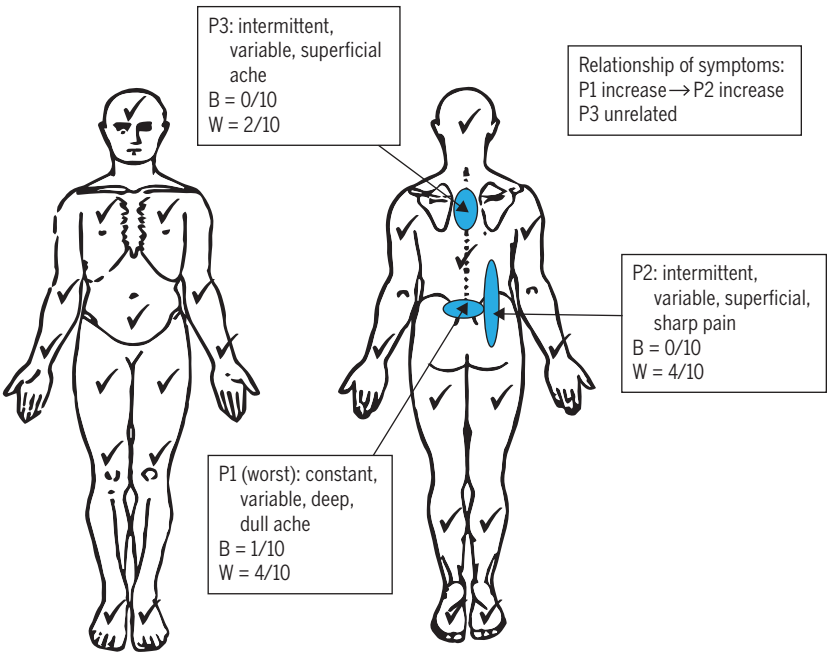

FIGURE 2. Body chart at 3-month follow-up. Abbreviations: ✓, symptom-free area; B, pain at best; P, pain area; W, pain at worst.[10]

Physical Therapy Intervention

The physical therapist contacted the patient 2 months postoperatively to follow up on her overall condition as well as the condition for which she was originally referred to physical therapy. The patient reported that she no longer had abdominal pain or bilateral arm or leg pain, and that her upper and lower back pains had improved, but were still present. The patient expressed a desire for further examination and physical therapy treatment, and was seen in the physical therapy clinic 2 days later (about 3 months after the initial physical therapy visit). The patient's current symptoms were re-evaluated. **FIGURE 2** shows that the location, description, and intensity of the patient's pain areas had decreased since the initial exam. The physical examination revealed signs and symptoms consistent with lumbar spine instability, including frequent episodes of lower back pain, aberrant motions with range-of-motion testing, a positive prone instability test, and hypermobility with spring testing.[16,24,33] The patient was subsequently classified into the stabilization subgroup for lower back pain and was given a home exercise program of lumbar stabilization exercises.[24,25,32] Two weeks later, she returned for a follow-up and reported significant improvement in her condition, and her Oswestry Disability Index score had improved to 10%, indicating mild disability. She was able to correctly demonstrate her lumbar stabilization exercises, and more functional movements of proper bending and lifting were incorporated into her exercise program. One month later, the patient was not able to attend a follow-up appointment, so the physical therapist contacted the patient by phone to check on her progress. The patient reported continued overall improvement in symptoms and function. **FIGURE 3** shows the pain areas the patient described. The patient reported that she could now perform all her household activities and care for her children without increased lower back pain. The patient was also able to verbally describe each of her exercises and stated that she was doing them daily. She was therefore discharged to self-management, as all of her rehabilitation goals had been met.

DISCUSSION

This resident's case problem describes the differential diagnosis, clinical reasoning, and successful outcome of a patient who presented with both systemic and neuromusculoskeletal pathology. It demonstrates the ability of physical therapists to recognize symptoms that originate from outside the musculoskeletal system and to appropriately initiate the diagnostic process, while providing musculoskeletal care consistent with best research evidence.

Nonmusculoskeletal Symptoms

The patient in this case problem presented with signs and symptoms consistent with an AAA; however, the patient's

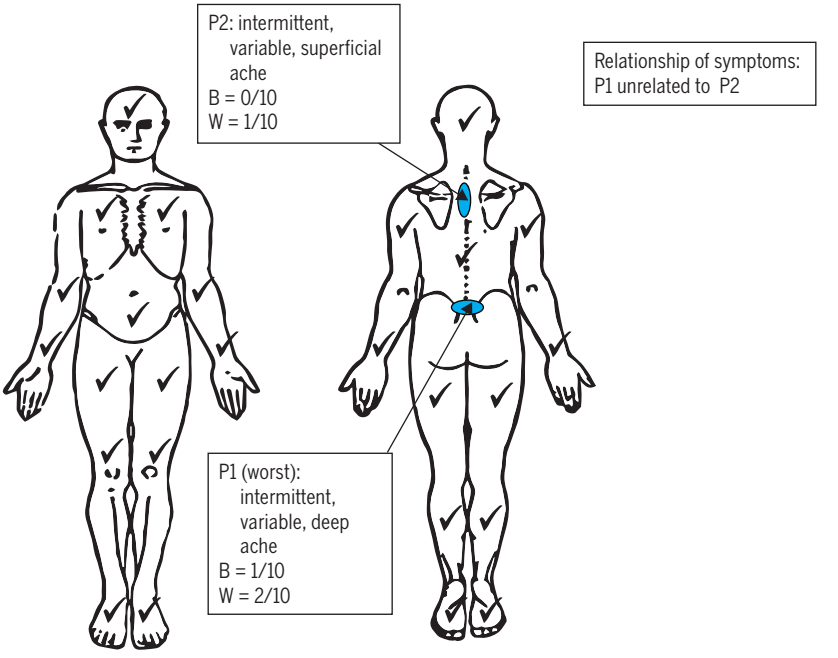

FIGURE 3. Body chart at 4-month follow-up. Abbreviations: ✓, symptom-free area; B, pain at best; P, pain area; W, pain at worst.[10]

young age and female sex made this diagnosis significantly less likely. Despite this, the patient did not initially present with conclusive signs and symptoms suggesting any gastrointestinal or urogenital pathology. Instead, her complaints of vague, throbbing abdominal and lower back pain, her increased sweating, and her physical signs of midline abdominal tenderness to palpation were all the therapist had to suggest that systemic pathology might be present. The **TABLE** describes the factors that favored a specific systemic pathology and the factors that were absent and thereby decreased the likelihood of each diagnosis.

Many of the 10 000 deaths each year in the United States attributed to AAA could be prevented with timely diagnosis and treatment.[27,42] An AAA is usually asymptomatic until rupture or increasing size draws the attention of the patient or examining provider.[12] A feeling of fullness or pulsations in the abdominal region may be early symptoms. In a review of 528 patients with AAA, Fielding et al[20] found that 91% of patients first had symptoms of abdominal pain and backache. Risk factors for developing AAA include male sex, increasing age, significant smoking history, hypertension, familial history of AAA or claudication, chronic obstructive airway disease, and increased weight.[4,12,23] However, Skibba et al[44] found that women had a higher frequency of AAA rupture than men at all size intervals. Given the life-threatening nature of an AAA, a prompt diagnosis is essential, as the consequence of a missed or delayed diagnosis could be fatal.[31] Careful abdominal palpation is the only maneuver of value in the physical examination to detect abnormal widening of the abdominal aorta.[35,52] Abdominal palpation is safe and has not been shown to cause rupture in patients with AAA. Fink et al[21] reported moderate overall accuracy in detecting AAA with abdominal palpation (sensitivity, 68%; specificity, 75%; positive likelihood ratio = 2.7; negative likelihood ratio = 0.43; interobserver agreement, 77%); however, in patients who have a waistline of less than 100 cm and whose AAA is large enough to warrant intervention (4 cm or larger), abdominal palpation is shown to be highly sensitive (82%-100%). Ultrasonography and computed tomography are now the procedures of choice for confirming the diagnosis of AAA, with sensitivity and specificity values close to 100%.[35,52] The 2 resident's case problems that include patients with AAA and lower back pain published to date[36,51] highlight the differential diagnosis and clinical-reasoning process required for patients presenting with both abdominal and lower back pain. In each of those studies, the cause of the patient's symptoms was found to be of visceral origin only. In this case problem, the patient's symptoms were more diffuse and complex, and likely caused by both visceral and musculoskeletal pathology. This case and the 2 previously published on AAA emphasize the importance of systematic screening and evaluation, knowledge of visceral referred pain patterns, and basic competence in abdominal palpation.

The second most likely nonmusculoskeletal diagnosis considered in this case was symptomatic cholelithiasis (the presence or formation of gallstones). Although this is one of the most frequent gastroenterological diagnoses, there are no published case studies by a physical therapist that identify this condition through medical screening. Patients with gallstones can present in a myriad of ways, ranging from no symptoms to life-threatening manifestations due to disease complications.[46] Symptoms from gallstones can mimic other abdominal pathology, making the diagnosis challenging based solely on the patient's history and areas of pain. Cholelithiasis is the fifth-leading cause of hospitalization among adults, and accounts for 90% of all gallbladder and duct diseases.[28] Risk factors for gallstones include increasing age, female sex, elevated estrogen levels, obesity, a high-cholesterol and low-fat diet, diabetes, and liver disease. Symptomatic gallstones may lead to acute cholecystitis, which may result in the

patient experiencing chills, low-grade fever, nausea, vomiting, and jaundice. Pain from gallbladder pathology can be localized to the upper right quadrant and epigastrium, and may be referred into the right shoulder and between the scapulae. Ultrasonography is the test of choice when evaluating a patient with suspected gallstones due to it being inexpensive, readily available, and highly accurate.[43]

Musculoskeletal Symptoms

As noted earlier, the patient's abdominal pain and bilateral arm and leg pain resolved after medical intervention, and only her lower back and upper back pain remained at follow-up with the physical therapist. Though it is difficult to determine which pathology caused each pain area, the fact that the patient reported musculoskeletal pain after her gallbladder and gynecological conditions had resolved lends evidence to the assumption that the patient had musculoskeletal back pain with coexisting gastrointestinal and gynecological pathology. Alternatively, referred pain from primary visceral pathology might have resulted in persisting musculoskeletal impairments and symptoms.[19,26] The use of a body chart or symptom map in documenting a patient's pain areas, as well as an understanding of common referral patterns for musculoskeletal and systemic pathologies, can assist the therapist in determining whether the condition is primarily due to musculoskeletal causes, systemic pathology, or a combination of the two presenting together.[5]

CONCLUSION

Differential diagnosis of patients presenting with multiple symptomatic areas can pose a significant challenge to physical therapists who practice in either direct-access or referral settings. This resident's case problem highlights that musculoskeletal and nonmusculoskeletal pathology can coexist and that systemic pathology can mimic musculoskeletal symptoms. By using systematic screening and evaluation methods, a physical therapist can appropriately determine whether a patient requires referral to another health care provider or can be independently managed by the physical therapist. ◉

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