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# All MCIDs Are Wrong, But Some May be Useful



Musculoskeletal research commonly uses the minimal clinically important difference (MCID) of various patient-reported outcomes (PROs) to guide clinical decision making in a value-based care paradigm.[35] Yet, the MCID is not without limitations, and it may not be an appropriate criterion when determining how clinically meaningful a clinically observed effect[5] is.

The terms and acronyms used to describe the idea of "a clinical change that is meaningful" are plentiful: MCID, clinically important difference, minimally clinically important change, clinically important change, and minimum clinically important improvement. The metrics are derived in different ways, and it is often unclear if these metrics are between-patient groups or within-patient groups. Even within the *MCID* phraseology adopted by the sports medicine field, there are different methods used to calculate the MCID.[6,7] Similar heterogeneity in reported MCID values[25] naturally leads to variability in how to interpret PROs. Baseline PRO values can also bias the MCID.[28,30,31]

Is it appropriate to use an imprecise measure to evaluate clinically meaningful change? We suggest that it is time to explore the underlying assumptions of anchored MCIDs calculated using a standard receiver operator curve (ROC) analysis and to propose an alternative methodology that may offer a more statistically valid and theoretically sound MCID calculation using an empirical data set.

**OBJECTIVE:** To demonstrate how to apply a baseline-adjusted receiver operator characteristic curve (AROC) analysis for minimum clinically important differences (MCIDs) in an empirical data set and discuss new insights relating to MCIDs.

**DESIGN:** Retrospective study.

**METHODS:** This study includes data from 999 active-duty military service patients enrolled in the United States Military Health System's Military Orthopedics Tracking Injuries and Outcomes Network. Anchored MCIDs were calculated using the standard receiver operator characteristic analysis and the AROC analysis for the Patient-Reported Outcome Measure Information System (PROMIS) Pain Interference and Defense and Veterans Pain Rating Scale (DVPRS). Point estimates where confidence intervals (CIs) crossed the 0.5 identity line on the area-under-the-curve (AUC) analysis were considered statistically invalid. MCID estimates where CIs crossed 0 were considered theoretically invalid.

**RESULTS:** In applying an AROC analysis, the region of AUC and MCID validity for the PROMIS Pain Interference score exists when the baseline score is greater than 61.0 but less than 72.3. For DVPRS, the region of MCID validity is when the baseline score is greater than 5.9 but less than 7.9.

**CONCLUSION:** Baseline values influence not only the MCID but also the *accuracy* of the MCID. MCIDs are statistically and theoretically valid for only a discrete range of baseline scores. Our findings suggest that the MCID may be too flawed a construct to accurately benchmark treatment outcomes. *J Orthop Sports Phys Ther 2022;52(6):401-407. doi:10.2519/jospt.2022.11193*

**KEY WORDS:** *clinical measurement (clinimetrics), implementation science/quality improvement, outcome measures, statistical analysis/research design*

## CONTEXT

There is no best practice for calculating MCID,[6] and despite widespread use of MCIDs, clinicians may not fully understand their derivations. At least 9 MCID calculation methods have been described.[4] In general, MCID calculation methods can be classified as either *distribution-based* or *anchor-based*.[6] Distribution-based MCIDs are derived from the standard error of measurement, standard deviation calculations from sample data, and/or the minimal detectable change.[4] While statistically straightforward, these methods are conceptually divorced from whether the change observed is clinically relevant to a patient's outcome.[6]

In anchor-based methods of determining clinical meaningfulness, clinical results are compared or *anchored* to changes in other measures. For example, an investigator might compare the change observed in a disease-specific questionnaire to the change observed in the Global Rating of Change Scale or patient ratings of satisfaction.[4,9,16,17] Objective outcomes such as health care consumption, return

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to work/sport, military deployability, or changes in other disease-related outcomes may also serve as anchors.[9,17] The MCID, extracted from an ROC curve analysis, attempts to balance sensitivity and specificity of the PRO to predict the anchor, which creates the *optimal cutoff score* delineating improved versus unimproved patients.[6] This is commonly accomplished through either the top-left corner method or Youden's J index.[19]

Studies using anchor-based calculations tend to demonstrate a high association between baseline PRO values and overall change scores, which, in turn, bias the anchored MCID.[8,21,27,28,31] This statistical phenomenon is known as regression-to-the-mean (RTM).[12] Regression to the mean can occur due to measurement error in the device, patient response variance, and/or ceiling and floor effects in measuring instrument when aggregated over repeated measurements.[2,36] RTM is conspicuously uncontrolled for in standard ROC curve analyses despite MCIDs using change scores as the predictor variable.[28] To mitigate the effects of RTM on the ROC analysis, we previously advocated for using baseline-adjusted ROC (AROC) analyses, a logical but infrequently referenced approach in the physical therapy literature.[28]

There are important limitations in both MCID calculation and interpretation. However, given the MCID's importance to payers, researchers, clinicians, and patients, many are loath to abandon it. Here, we suggest a path toward a more statistically and theoretically rigorous MCID interpretation. Our goals are to (1) show the application of an AROC analysis in an empirical data set; (2) discuss new insights relating to using MCIDs derived from this analysis; and (3) explore the broader implications of our results as they relate to physical therapy and sports medicine research.

## METHODS

The overarching framework for the Military Orthopedics Tracking Injuries and Outcomes Network (MOTION) has been previously described.[18] Briefly, the United States Military Health System has implemented a framework for the systematic delivery and data repository of PROs for use as a patient standard of care in the rehabilitation care community. The specific intervals at which PROs are delivered are subject to provider modifications but default to monthly intervals in the rehabilitation population.

Our retrospective analysis of standard of care data was approved by the Institutional Review Board at the Walter Reed National Military Medical Center (IRB #20-12031). We reported this manuscript in line with the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) reporting guideline for studies on measurement properties of PROMs, as a reporting guideline for studies on the MCID is currently lacking.[11]

### Data Description

Two of the primary PROs implemented in the rehabilitation population for MOTION are the PROMIS Pain Interference computer adaptive test[1] and the Defense and Veterans Pain Rating Scale (DVPRS).[3,20] Both are designed to measure the patient's perception of how pain interferes with various aspects of life (eg, sleep and physical activity); the DVPRS is scored on a 0-10 point scale, whereas the PROMIS Pain Interference computer adaptive test is normally distributed and population mean-centered at 50. A higher number indicates higher levels of pain interference in the life of the patient (ie, lower scores are better).

Patients also complete a military-specific *readiness* PRO as a part of their MOTION survey set. Depending on the specific service of the active-duty patient (eg, Army, Navy, Air Force, or Marine), the service member indicates if they feel they

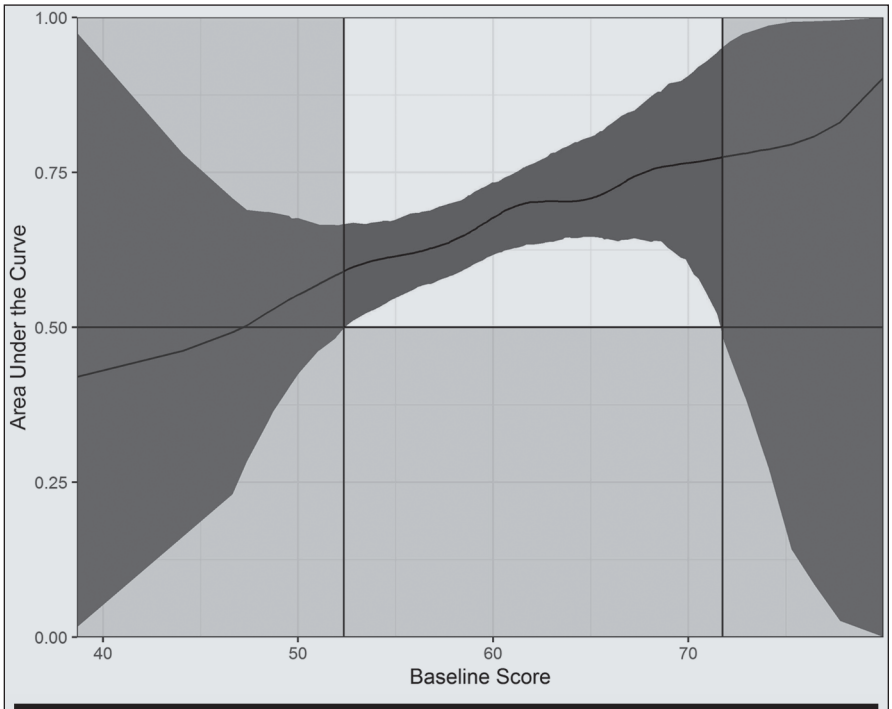


**FIGURE 1.** The baseline-adjusted AUC analysis for PROMIS Pain Interference. The black line surrounded by the dark gray band is the point estimate for the AUC, and the dark gray band is the 95% confidence intervals. The horizontal line at 0.50 represents the point at which an estimate is no better than random chance. The light gray sections represent when AUC point estimates are no better than random chance because the confidence intervals around that estimate cross the 0.50 threshold. Abbreviations: AUC, area under the curve; PROMIS, Patient-Reported Outcome Measure Information System.

are able to pass their specific physical fitness test, with or without modifications. They are also asked "If called for a six-month deployment today, my confidence to travel to/within a combat zone, carry/wear/use all required equipment and/or weapon, and perform required military duties for the duration of the six month deployment is:" with the patient answering on a 0-100 scale. For the purposes of setting up our anchor for the MCID analysis, the patient is said to have reached their positive outcome if they respond that they can pass their physical fitness test and are 60% or more confident in their ability to deploy in the next 6 months.

The first obtained data point from a patient is set as "day zero" and described as the "baseline score" throughout the rest of the analysis. Any following PRO completion times are benchmarked as "days since day zero" or days since that baseline visit. For our analysis, we were interested in the MCID necessary after a month of rehabilitation treatment. A month was defined as a PRO completed ≥20 days and ≤37 days post baseline visit. To calculate an MCID for the DVPRS or the PROMIS Pain Interference, it was required to have both the respective PRO's baseline and 1-month visit as well as the 1-month readiness survey completed.

### Sample Population

Our study included 999 unique patients: 753 males and 241 females with an average age of 29.5±7.8 years (5 patients recorded no demographic information). Eligibility criteria were visitation to an outpatient orthopedic or physical therapy clinic within the United States Military Health System between May 1, 2020, and July 26, 2021. The DVPRS analysis included data from 909 patients, and the PROMIS Pain Interference analysis includes data from 776 patients.

### Statistical Analysis

The anchored MCID calculations were performed using the standard ROC analysis and the AROC analysis. In the case of both analyses, the MCID was extracted from the ROC using Youden's J method, and 95% confidence intervals (CIs) were extracted using 1000 stratified bootstrap replications. Analyses where CIs cross the 0.5 identity line on an area-under-the-curve (AUC) analysis indicate that the point estimate is not better than random chance, and therefore statistically invalid. For theoretical purposes, it is not possible for an MCID to be both positive and negative; hence, MCID CIs crossing 0 indicate that the MCID is invalid for real-world use. It does not make theoretical sense to suggest that the MCID for the DVPRS is both -2 and +1; therefore, the associated MCID point estimate cannot be correct. Reporting of these analyses is consistent with recent guidelines.[28] The analyses were performed in the R programming language (version 4.0.2), using the following packages: dplyr,[34] tidyr,[14] ggplot2,[32] stringr,[33] lubridate,[13] pROC,[22] and npROCRegression.[23]

## RESULTS

Using the standard ROC-based method for MCID calculation, the PROMIS Pain Interference had an AUC of 0.55 (95% CI: 0.50, 0.59) and an MCID of -4.3 (95% CI: -9.8, 2.5). The DVPRS had an AUC of 0.59 (95% CI: 0.55, 0.63) and an MCID of -0.75 (95% CI: -2.5, 0.75). Based on the evaluation conventions stated in the "Statistical Analysis" section, the PROMIS Pain Interference MCID should be considered both statistically and theoretically invalid; in contrast, the DVPRS MCID would be considered statistically valid but theoretically invalid as the AUC was better than 0.5 but the MCID CIs cross 0.

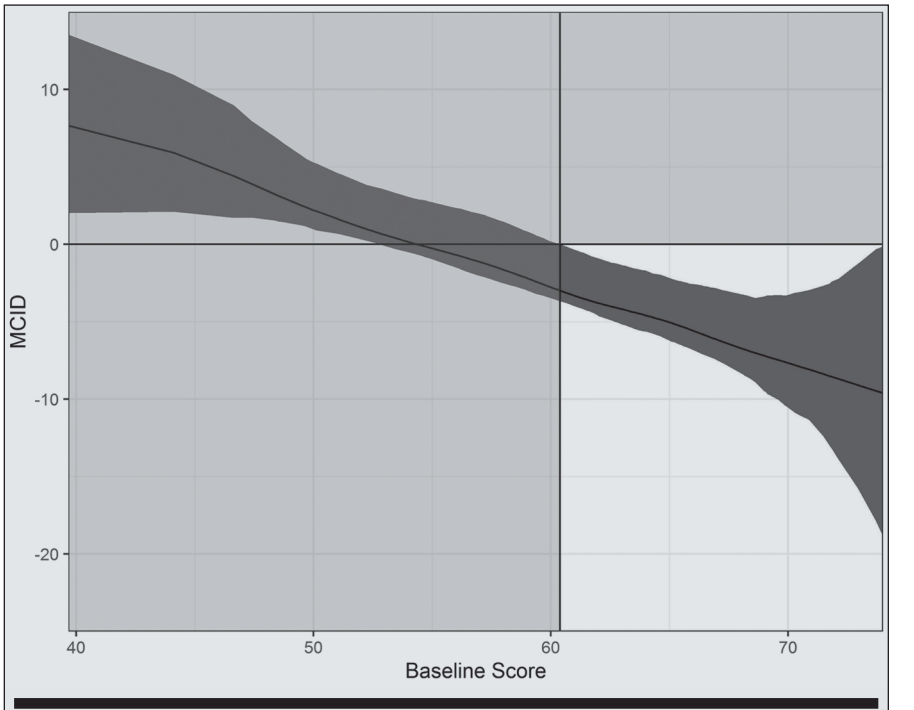


**FIGURE 2.** The baseline-adjusted MCID analysis for PROMIS Pain Interference. The black line surrounded by the dark gray band is the point estimate for the MCID, and the dark gray band is the 95% confidence intervals. The horizontal line at 0 reflects a threshold that should be considered when determining if the MCID estimate is theoretically reasonable or possible. The light gray sections represent when MCID estimates do not make theoretical sense because the confidence intervals around that estimate suggest that the MCID could be either positive or negative or when the point estimate does not make logical sense (eg, increases in pain interference are desirable to reach MCID). Abbreviations: MCID, minimum clinically important difference; PROMIS, Patient-Reported Outcome Measure Information System.

The statistical validity, as indicated by AUC, of the AROC method for MCID calculation can be seen reviewed for the PROMIS Pain Interference (**FIGURE 1**) and DVPRS (**FIGURE 3**) where the AUC estimate is surrounded by the 95% CIs (dark gray bands), and the light gray sections are regions indicating an MCID should not be interpreted because the AUC CIs cross 0.5, indicating that the estimate is no better than random noise.

The theoretical validity of the baseline-adjusted MCID, assessed by determining that the MCID cannot be both positive and negative at the same time and that the MCID makes theoretical sense, can be reviewed for the PROMIS Pain Interference (**FIGURE 2**) and DVPRS (**FIGURE 4**). In the figures assessing theoretical validity, the dark gray 95% CIs surround the MCID estimate line and the light gray sections are the areas in which the MCID does not make theoretical sense as the CIs cross zero, indicating that the MCID could be either positive or negative, or the MCID indicates that pain interference should get worse to reach MCID.

A statistically rigorous use of baseline-adjusted MCIDs should incorporate information from both the AUC and MCID figures (eg, **FIGURES 1 AND 2**) to determine when an MCID estimate is both statistically and theoretically valid (**TABLE 1**). Essentially, the overlapping areas of white between the AUC and MCID figures determine an overall region of MCID validity. In the case of PROMIS Pain Interference, the region of MCID validity is when the baseline score is greater than 61.0 but less than 72.3. For DVPRS, the region of MCID validity is when the baseline score is greater than 5.9 but less than 7.9. Within those regions of validity, the point estimate (black line) can be used to determine an appropriate MCID for clinical use.

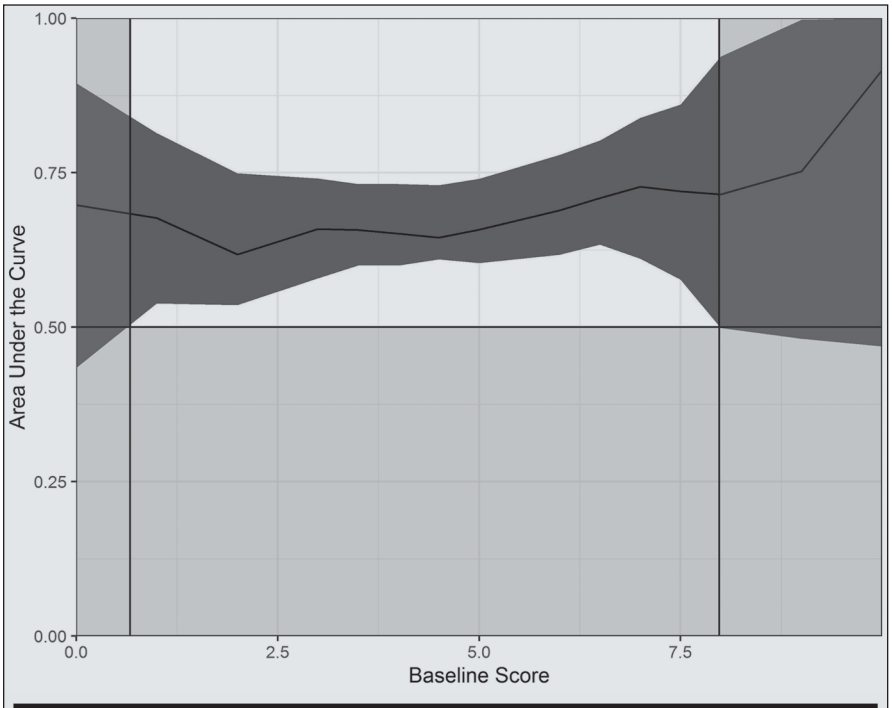


**FIGURE 3.** The baseline-adjusted AUC analysis for DVPRS. The black line surrounded by the dark gray band is the point estimate for the AUC, and the dark gray band is the 95% confidence intervals. The horizontal line at 0.50 represents the point at which an estimate is no better than random chance. The light gray sections represent when AUC point estimates are no better than random chance because the confidence intervals around that estimate cross the 0.50 threshold. Abbreviations: AUC, area under the curve; DVPRS, Defense and Veterans Pain Rating Scale.

## DISCUSSION

The aim of this investigation was to contrast MCID calculations and interpretations using standard versus baseline-adjusted ROC analyses using an empirical data set. These findings are applicable to within-subjects MCIDs and, therefore, should only be used for similar designs. Our findings support the validity of AROC analyses in MCID calculation, which we previously advocated as a means to mitigate RTM in MCID derivation.[28] Our analyses also demonstrate an equally consequential finding: baseline PRO values influence the *accuracy* of standard ROC analyses, fundamentally influencing the utility of the associated MCID. This is theoretically consistent with Riddle et al's[21] conclusions from 20 years earlier using stratified ROC curve analyses.

Consider the standard calculation of MCID for the PROMIS Pain Interference scale, anchored to whether a service member feels he or she is able to deploy. A standard ROC calculation generates an MCID of -4.3 with a wide CI that crosses zero (-9.8 to 2.5). Because the CI is large, crosses zero, and includes values indicating *increased* pain interference, we would not trust this MCID. Theoretically, we cannot accept an estimate whose CI indicates that the MCID could be *either* positive or negative. It is untenable to expect increased pain interference to be associated with a positive outcome. We observe an AUC of 0.55 (0.50–0.59). The AUC is a general measure of the effectiveness of the instrument (in this case, PROMIS Pain Interference) to predict the outcome (ability to deploy). An AUC of 0.5 indicates that the test instrument is no better than random chance. In this case, the PROMIS Pain interference has an AUC point estimate of 0.55 with the lower bound CI equal to random chance, indicating that the PROMIS Pain Interference scale is a poor predictor of deployability. Combining the results from both the AUC and MCID aspects of the unadjusted ROC analysis, we might

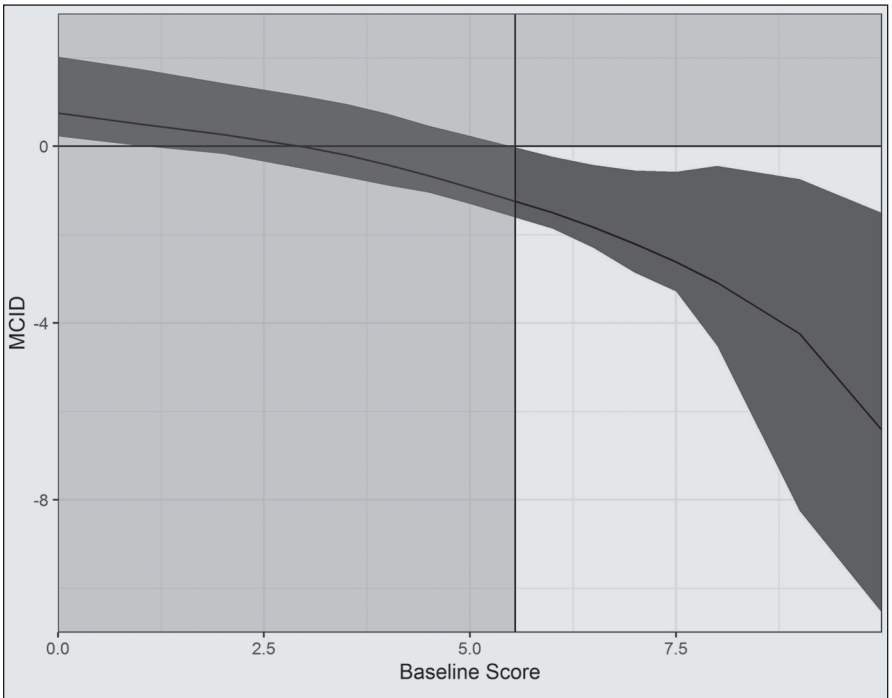


**FIGURE 4.** The baseline-adjusted MCID analysis for DVPRS. The black line surrounded by the dark gray band is the point estimate for the MCID, and the dark gray band is the 95% confidence intervals. The horizontal line at 0 reflects a threshold that should be considered when determining if the MCID estimate is theoretically reasonable or possible. The light gray sections represent when MCID estimates do not make theoretical sense because the confidence intervals around that estimate suggest that the MCID could be either positive or negative or when the point estimate does not make logical sense (eg, increases in pain are desirable to reach MCID). Abbreviations: DVPRS, Defense and Veterans Pain Rating Scale; MCID, minimum clinically important difference.

therefore disregard the PROMIS Pain Interference scale as impossible to create a valid MCID.

Yet, when we apply an AROC analysis, our conclusions are different. We find that (**FIGURE 2**) the CIs for the MCID are better than chance (ie, fail to cross zero) so long as the baseline score is greater than 60.4 and less than 72.3. This indicates a reliable MCID for subjects who report higher levels of pain interference at their initial visit. For baseline values less than 60.4 (less pain interference), the MCID estimate should be considered unreliable. Considering the AUC (**FIGURE 1**), we witness a similar phenomenon. CIs around the point estimate of the AUC are better than chance for PROMIS Pain Interference when values are greater than 61. The clinical implication is clearer but narrowly tailored: the user can calculate and apply an MCID for PROMIS Pain Interference but only for patients who report a level of baseline pain interference between 61 and 72.3 (**TABLE 1**). In our cohort, this represented 49% of the cohort or 378 out of 776 patients.

The story is similar for the DVPRS (**FIGURES 3 AND 4**). Using a standard ROC analysis, the DVPRS had an AUC of 0.59 (95% CI: 0.55, 0.63) and an MCID of -0.75 (95% CI: -2.5, 0.75). This AUC is only slightly better than chance, and the MCID is not theoretically sound, as the CIs crossed zero. The AROC analysis of the DVPRS yielded a variable AUC, often greater than 0.7, indicating improved accuracy over the standard ROC-curve calculation for baseline values between 0.7 and 7.9 (**FIGURE 3**). The AROC analysis also demonstrated point-estimate MCID values with 95% CIs not crossing zero when the baseline score is greater than 5.9. Therefore, the AROC MCID for DVPRS is valid and reliable when baseline scores are between 5.9 and 7.9, representing 34.4% of our cohort (313 out of 909 patients; **TABLE 1**).

## Implications

Standard MCID calculations can lead to overly optimistic or pessimistic conclusions when interpreting PROs. In contrast, AROC analyses provide more statistically and theoretically sound MCID values. We present evidence for a narrowly tailored MCID that takes baseline values into account. The ramifications of our findings are that a valid metric can only be calculated for a subset of the patients who fall within defined bounds of baseline scores; in our cohort, a valid MCID can be calculated for a third or half of the patients. At a basic level, this concept should not surprise clinicians or researchers; it has never been theoretically reasonable to have a 10-point scale with a static MCID of 3 and then expect a patient with a baseline score of 2 to "meet or exceed the MCID", as that would require them to score a -1 out

**TABLE 1** Baseline Score Ranges With Valid MCID Interpretations

| Outcome Measure | Baseline Score Range for 95% Confidence Interval AUC > 0.5 | Baseline Score Range for 95% Confidence Interval MCID Beyond Null | Baseline Score Range with Statistically & Theoretically Valid MCID |
|---|---|---|---|
| DVPRS | 0.7–7.9 | >5.9 | 5.9–7.9 |
| PROMIS-PI | >61.0 | 60.4–72.3 | 61.0–72.3 |

*Abbreviations: AUC, area under the curve; DVPRS, Defense and Veterans Pain Rating Scale; MCID, minimal clinically important difference; PROMIS-PI, Patient Reported Outcome Measure Information System – Pain Interference.*

of 10. Most importantly, our results highlight fundamental issues in musculoskeletal research where real-world variability is underemphasized. Investigators often fail to consider the statistical phenomena and theoretical assumptions that underlie MCID values. In addition, the vast majority of orthopedic PRO literature derives the MCID from a within-groups design,[10] and therefore, the common practice of using these MCIDs for between-group investigations is both theoretically improper and statistically invalid.

The ROC analysis, upon which an anchored MCID is based, is not natively designed to accommodate complex analyses or account for statistical issues, which often arise in clinical research and practice. At its core, the standard ROC analysis is a single-variable prediction model of a binary outcome. This begs the following questions: "Are your outcomes of interest really binary?" and "Is it reasonable to expect that one metric is sufficient to predict the likelihood of positive patient outcomes?" Our answer to both of these questions is a resounding "No". At the same time, when considering system-level identification of leading practices to improve delivery of quality health care, a simple measure is often needed. Our analysis shows a statistically and conceptually sound approach to using MCIDs as clinical benchmarks: all MCIDs are wrong, but some are useful.

### Future Directions

When considering what a valid next-level MCID-style metric might look like in musculoskeletal practice, it is best to consider what analytical frameworks have already been proposed and validated in other fields. Multivariable models may provide value over a univariate MCID, as they are able to incorporate information such as demographics or history of injury/illness while still calculating something akin to a "rate of change for clinical relevance", if that is desired.[29] If one were to adopt the "functional" and "dysfunctional" framework as proposed by Jacobson & Truax,[15] a multistate or state-transition model is a natural fit for this type of medical decision-making process.[26] Lastly, a greater focus on high-quality methodological approaches in the development and validation of complex medical decision-making frameworks and increased collaboration with authors from dedicated analytical backgrounds should lead to substantial gains in the effectiveness of future metrics gauging clinical relevance, especially given the low proportion of such authors in contemporary sports medicine studies.[24]

## CONCLUSION

A ROC analysis yielded more valid and accurate MCID values than the standard ROC curve analysis. When assessing PROs within groups, consider alternative methods such as multivariable models or AROC analyses.

### KEY POINTS

**FINDINGS:** Baseline patient-reported outcome values influence both the accuracy of the MCID derivation and the MCID value itself.

**IMPLICATIONS:** Researchers and health care information system designers should consider using a baseline-adjusted receiver operator characteristic curve to calculate MCIDs, and clinicians should seriously consider whether existing MCIDs are valid.

**CAUTION:** This is the first empirical data study using baseline-AROC curve analyses that demonstrates potential issues with standard MCIDs and the baseline-adjusted MCID remedy. Future studies are needed to prove that existing MCIDs are statistically and theoretically valid or else provide new MCIDs under the baseline-adjusted framework.

### STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** Matthew S. Tenan and Ian E. Lee were in charge of the acquisition of data. Matthew S. Tenan was in charge of analysis and/or interpretation of data. Christopher W. Boyer and Matthew S. Tenan were in charge of drafting the manuscript. All the authors contributed to the conception and design of the study, revised the manuscript critically for important intellectual content, and approved final the version of the manuscript to be published.

**DATA SHARING:** Individual patient data are available at the following link in CSV format: https://t.co/kRgyOWUSBv. All data used in the baseline-adjusted and standard ROC analysis for both DVPRS and PROMIS pain interference will be shared. No other documents will be available. *Data will be available on the* Open Science Framework where these data are hosted and has a guaranteed 50-year retention for the files. All analyses in this manuscript are freely available for anyone. Interested parties simply need to download at the following link: https://t.co/kRgyOWUSBv.

**PATIENT AND PUBLIC INVOLVEMENT:** Patients/athletes/public partners were not involved in this research.

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# Involving People With Lived Experience as Partners in Musculoskeletal Research: Lessons From a Survey of Aotearoa/ New Zealand Musculoskeletal Researchers

Health research aims to improve the lives of people who live with health conditions and use health services. In this Viewpoint, we (see panel 1 for a description of our team) argue that increased involvement of people as research partners is vital to increase the quality and impact of musculoskeletal research.

Many terms are used to describe the involvement of those with lived experience of health conditions or service use as partners in research (as opposed to as research participants), including partnership, patient and public involvement, patient research partners, consumer involvement, or community engagement.[8] Irrespective of the term, the key feature is the coproduction of research by researchers and those whose lives it aims to influence.[8] In this Viewpoint, we use the term *patient partner involvement*, consistent with previous *JOSPT* papers, but in our region, *consumer research partner* is commonly used.

**SYNOPSIS:** Involving patients as partners in research enables their concerns, perspectives, lived experiences, and priorities to be integrated into research. Involving patient partners improves research processes, outcomes, and translating findings into practice. Although musculoskeletal researchers consider that it is important to involve patient partners, few projects involve them. Researchers who involve patient partners report that the contributions of patient partners are very valuable, and researchers perceive the process to be less challenging than expected. Musculoskeletal research is staring at a significant unrealized opportunity to enhance the quality and impact of research and reduce research waste—think what the field could achieve if researchers and patients worked better together. A culture change is needed so that involving patient partners in musculoskeletal research becomes standard practice, expected and supported by funders, journals, research institutions, and researchers alike. *J Orthop Sports Phys Ther 2022;52(6):307-311. doi:10.2519/jospt.2022.10986*

**KEY WORDS:** *community-based participatory research, consumer research partner, cross-sectional studies, musculoskeletal diseases, patient and public involvement, patient participation, research design*

Patients can be involved as partners in all stages of the research process, from identifying a topic and meaningful outcomes to designing the study, acquiring the funding, conducting the research, analyzing and interpreting the data, disseminating and implementing the results, and evaluating the impact of the research.[3,4,6] Involving patients as partners with researchers and clinicians enables their concerns, perspectives, lived experiences, and priorities to be integrated into research,[2,6] increasing the relevance of the research and the likelihood that findings will be translated into improved health outcomes.[1-3,6]

Conversely, conducting research without involving patient partners contributes to research waste.[10] Wasteful practices arising from inadequate patient partner involvement include using outcome measures that fail to reflect patients' concerns, testing interventions that do not fit with the context and challenges of patients' lives, producing information materials that are hard to understand, misinterpreting key aspects of the data, and failing to effectively communicate the results of research.[1,2,4,6]

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**Box 1. Our Own Team**

We built a research team that included 3 consumer research partners (J.C., G.H., and B.H.) together with experienced musculoskeletal clinicians and researchers (B.D., N.D., and S.S.) and a medical student (J.H.T.). Consumer involvement and expertise shaped the research and ensured meaningful questions were asked. J.C. and G.H. are also partners in concurrent research projects. B.H. is a Consumer Advocate and Community Involvement Coordinator who connected with researchers through the Australia & New Zealand Musculoskeletal Clinical Trials Network. These consumer research partners were involved in the identification and prioritization of the study topic, research design, study management, carrying out the research, and dissemination of findings. All members of the team are authors on this Viewpoint.

## WHAT DOES PATIENT PARTNER INVOLVEMENT IN MUSCULOSKELETAL RESEARCH LOOK LIKE IN THE 2020S?

Less than 2% of rheumatology trials report patient and public involvement.[9] We were unable to identify any surveys of musculoskeletal researchers exploring their collaboration with patient partners. So, we surveyed patient partner involvement in musculoskeletal research in Aotearoa/New Zealand, including researcher experiences and perceptions of involving patient partners.

In late 2020, we surveyed 179 musculoskeletal researchers in Aotearoa/New Zealand (University of Otago Human Ethics Committee reference: D20/362). Seven in 10 were clinical researchers, and two thirds were based at a university. Details of researcher identification, flow through the study, and respondent characteristics are in the **SUPPLEMENTAL MATERIAL**.

### How Frequently Are Patient Partners Involved in Research Projects?

One in every 4 survey respondents had involved patient partners in at least 1 of their last 5 research projects. Of all respondents' last 5 musculoskeletal research projects, approximately 1 in every 10 projects (76 of 631 projects) involved patient partners. Patient partners were

**TABLE 1** Characteristics of Musculoskeletal Research Projects Involving Patient Partners (N = 76).

| Project Characteristic | n (Patient Partners or Projects) | Median (IQR) or Proportion (95% CI) Per Project |
|---|---|---|
| Total number of patients across all projects (n = 72 projects)[a] | 484 | 3 (2-10) |
| Total hours spent by patients on each project (n = 68 projects) | 2243 | 10 (4-30) |
| Stage of research involved[b] (n = 73 projects) | | |
| Identification and prioritizing of study topics/questions | 46 | 63% (51-74) |
| Research design | 47 | 64% (52-75) |
| Study management | 30 | 41% (30-53) |
| Carrying out the research | 41 | 56% (44-68) |
| Dissemination of findings | 22 | 30% (20-42) |
| Funding source[b] (n = 73 projects) | | |
| University | 16 | 22% (13-33) |
| Professional society | 13 | 18% (10-29) |
| Health Research Council | 12 | 16% (9-27) |
| Government | 10 | 14% (7-24) |
| No funding source[c] | 8 | 11% (5-20) |
| Patient organization | 7 | 10% (4-19) |
| Research foundation[c] | 6 | 8% (3-17) |
| Nongovernmental organization[c] | 5 | 7% (2-15) |
| Other | 9 | 12% (6-22) |
| Patient payment[b] (n = 75 projects) | | |
| Provided | 31 | 41% (30-53) |
| Vouchers | 15 | 20% (12-31) |
| Hourly rate | 7 | 9% (4-18) |
| Salary | 9 | 12% (6-22) |
| Other | 2 | 3% (0-9) |
| Patient named on funding application (n = 74 projects) | | |
| Yes | 26 | 35% (24-47) |
| Patient coauthorship (n = 75 projects) | | |
| Yes | 20 | 27% (17-38) |
| Not offered | 26 | 35% (24-47) |
| Offered, but declined | 3 | 4% (1-11) |
| Planned[c] | 12 | 16% (9-26) |
| Not planned[c] | 9 | 12% (6-22) |
| Yet to be published/no answer[c] | 4 | 5% (1-13) |
| Undecided[c] | 1 | 1% (0-7) |
| Value of patient contribution (n = 75 projects) | | |
| Extremely valuable | 45 | 60% (48-71) |
| Very valuable | 24 | 32% (22-44) |
| Moderately valuable | 4 | 5% (1-13) |
| Mildly valuable | 2 | 3% (0-9) |
| Not at all valuable | 0 | 0% (0-4) |

*Abbreviation: IQR, interquartile range.*
[a]*One project was described by 2 respondents, and respondents were unsure of the number of patient partners involved with 4 projects.*
[b]*Researchers could nominate more than 1 option.*
[c]*Categories were created from free-text data from the "Other" category.*

involved across all stages of research, but it was uncommon for patient partners to contribute to study management or dissemination of findings (**TABLE 1**). Researchers overwhelmingly viewed patient partner contributions as valuable.

### How Important Is Patient Partnership in Research?

Six in 10 respondents thought it was *very* or *extremely important* to involve patients as partners in research (**TABLE 2**). Although, among people who had experience working with patient partners, 8 in every 10 said it was important, compared to only half of the respondents who had no experience of patient partnership. A quarter of the respondents said it was *somewhat* or *extremely easy* to involve patients as research partners; people who had involved patient partners were more likely to say it was easy to involve patient partners than those with less experience of patient partnership.

### How Are Patient Partners' Contributions to Research Recognized?

Patient partners contributed a median of 10 hours per project, and most were unpaid. Of those who were paid, half received vouchers, and half received a salary or an hourly rate. Patient partners were coauthors on only one quarter of the publications arising from the research projects (some respondents indicated that they planned to involve patient partners as authors) (15 of 75 projects); most patient partners were not named on funding applications.

### Do Researchers Understand What Patient Partners Bring to the Table?

Some researchers appeared to misinterpret the meaning of *consumer research partner* and instead described research participants. This misunderstanding of true patient involvement as research partners appears to be widespread, with many studies reporting research participants in the "Patient and Public Involvement" sections of rheumatology papers.[9]

There is a dearth of research systematically exploring patient partner involvement in musculoskeletal research. We recommend similar surveys to ours be conducted in other countries to better understand current patient partner involvement and how this can be strengthened. Many researchers do not understand what patient partnership in research is or what it can look like. We recommend that future surveys provide comprehensive descriptions of what is and is not meant by the phrase *patient partner* (including vignette exemplars) before asking respondents to indicate whether such partners have been involved in their projects.

## MOVING FROM ENDORSEMENT TO ACTION

Many musculoskeletal researchers consider patient partner involvement as key to doing better research. But few are doing it. Here are some of our recommendations and experiences.

### Build Strong and Trusting Relationships

Identifying or connecting with the "right" patient partners is often cited as a key barrier. Our experience is that research participants who make contact outside of normal data collection (such as replying when summaries of research findings are shared) are often interested in research. These interactions are opportunities to build relationships that can be starting points for further collaboration.

Anxiety is often part of new relationships. Researchers may be anxious that patient partners will delay or derail the research process and need to trust that patient partners know what they are talking about and are motivated to improve research. Patient partners may feel in-

**TABLE 2** Importance and Ease of Involving Patient Partners in Musculoskeletal Research in Aotearoa/New Zealand Rated by Researchers Who Had and Had Not Previously Involved Patient Partners in Projects (N = 154).[a]

| | Importance, n (%; 95% CI) | | | | | | Ease, n (%; 95% CI) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Not at All Important | Slightly Important | Moderately Important | Very Important | Extremely Important | n | Extremely Difficult | Somewhat Difficult | Neither Easy nor Difficult | Somewhat Easy | Extremely Easy | n |
| **Involved patient partners in 1 or more of last 5 musculoskeletal research projects** | | | | | | | | | | | | |
| Involved patient partners | 0 (0%; 0-7) | 1 (3%; 0-13) | 5 (13%; 4-27) | 10 (26%; 13-42) | 23 (59%; 42-74) | 39 | 0 (0%; 0-7) | 14 (36%; 21-53) | 7 (18%; 8-34) | 16 (41%; 26-58) | 2 (5%; 1-17) | 39 |
| Had not involved patient partners | 5 (4%; 1-10) | 13 (11%; 6-19) | 39 (34%; 25-43) | 34 (30%; 21-39) | 24 (21%; 14-29) | 115 | 7 (7%; 3-13) | 34 (32%; 23-41) | 49 (46%; 36-56) | 14 (13%; 7-21) | 3 (3%; 1-8) | 107 |
| **Total** | 5 (3%; 1-7) | 14 (9%; 5-15) | 44 (29%; 22-36) | 44 (29%; 22-36) | 47 (31%; 23-38) | 154 | 7 (5%; 2-10) | 48 (33%; 25-41) | 56 (38%; 30-47) | 30 (21%; 14-28) | 5 (3%; 1-8) | 146 |

[a] *Twenty-five respondents exited the survey prior to answering these items.*

timidated by academic research teams or anxious that their thoughts and opinions will be considered silly or irrelevant and need to trust that researchers will treat them with respect and honesty. Trust is built through repeated positive and meaningful interactions. Giving feedback to patient partners about the value of their contributions and how these influence the research helps develop their confidence.

### Don't Expect Patient Partners to Speak on Behalf of *All* Patients

Patient partners cannot represent all people with their condition or experience. While it is ideal to have diversity in patient partners (and research teams more broadly), they should not feel the weight of representing any particular group. In some instances, it can be effective to involve people who work within support networks (like those linked to nongovernmental entities or social media groups) who understand issues faced by broader groups. Each team member brings specific skill sets and experience as well as other (often unexpected) skills that enhance the team and its work.

### Support and Highlight Patient Contributions

When planning meetings or setting deadlines, consider patient partners' other roles, health needs, and energy levels. Compensation for patient partners is important to promote equity, demonstrate respect for their expertise, and reduce barriers to their involvement. Compensation should be offered to all patient partners, but not all will accept. *JOSPT* has published excellent guidance to assist researchers to have respectful and meaningful compensation conversations.[7] Project timelines and budgets should allow for meaningful patient partner interaction and compensation.

Limited acknowledgment as authors on study publications reduces the visibility of patient partner involvement (when this occurs). Patient partners may not see coauthorship as necessary, so conversations about why this is important to academia and advancing scholarship that includes lived experience voices can be valuable. Describing the impact of collaboration with patient partners in publications highlights the way in which people with lived experience have contributed to, informed, and improved these projects as a key driver of success. This may help uplift other patient voices and encourage more patient partner involvement.

### Practice, Practice, Practice...to Get It Right

It is important to aspire to "get it [patient partnership] right," but it is equally important that researchers do not let fear of "getting it wrong" paralyze them. Like all areas of research practice, experience combined with curiosity, reflection, and critical appraisal results in learning and development. There are many frameworks and resources available to help researchers involve patient partners, including a range of resources published by *JOSPT*,[4,5] but the most important element is practice.

### Summary

A culture change is needed so that patient partner involvement in musculoskeletal research becomes standard practice. Researchers who partnered with patients found it valuable and less difficult than perceived by others. The low level of patient partner involvement represents a major unrealized opportunity to enhance the quality and impact of musculoskeletal research. To reduce waste and increase impact, patient partner involvement should be expected by funders, journals, research institutions, and researchers. Infrastructure should be developed to support it. Our experience is that once researchers and patient partners start working together, it opens opportunities not previously realized. Patient partnership is not only the right thing to do but also the bright thing to do.

### Key points

- Musculoskeletal researchers in Aotearoa/New Zealand consider patient partner involvement in research to be important, but few projects involve patients as research partners. When patients are involved as research partners, they make a valuable contribution.
- The low level of involvement of patient partners in musculoskeletal research misses an important opportunity to enhance musculoskeletal research.
- A research culture that expects patient partner involvement in musculoskeletal research needs to be developed worldwide, along with infrastructure to support this.
- Patient partner involvement in research needs to be appropriately acknowledged in publications to highlight and describe how people with lived experience have contributed to and informed these projects. ◉

## STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** All authors contributed to the conceptualization of the project and methodology as well as manuscript review and editing. Jaquille Haribhai-Thompson and Dr Darlow were involved in data collection and organization, data analysis, and writing the original draft.

**DATA SHARING:** A de-identified copy of the data related to the survey of musculoskeletal researchers in Aotearoa/New Zealand is available from the corresponding author upon reasonable request.

**PATIENT AND PUBLIC INVOLVEMENT:** Three consumer research partners (J.C., G.H., and B.H.) were members of the research team. J.C. and G.H. were partners in concurrent research projects. B.H. is a Consumer Advocate and Community Involvement Coordinator who connected with researchers through the Australia & New Zealand Musculoskeletal Clinical Trials Network. These partners were involved in the identification and prioritization of the study topic, research design, study management, carrying out the research, and dissemination of findings.

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**MORE INFORMATION**
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# Pain Science in Practice (Part 3): *Peripheral Sensitization*



In most cases, tissue injuries will lead to inflammation, which will lead to sensitization. From a neuroscience perspective, this is a way to explain *why we usually hurt when we are injured*. Peripheral sensitization is an essential principle in pain science, and it is associated with hyperalgesia, inflammation, and clinical pain conditions, including acute injuries and rheumatological diseases. This editorial explains peripheral sensitization, neurogenic inflammation, and the axon reflex, as well as the role of second messengers and peptidergic C-fibers.

The third editorial in the #JOSPTpainscienceinpractice series explains the first of three major principles in pain science: peripheral sensitization. This editorial emphasizes the relationship between peripheral sensitization and the inflammatory response. Remember that clinical pain is a complex phenomenon and that examples here are illustrative, not definitive.

## What Is "Sensitization"?

The International Association for the Study of Pain (IASP) defines *sensitization* as "Increased responsiveness of nociceptive neurons to their normal input, and/or recruitment of a response to normally subthreshold inputs." (see Glossary). Sensitization is neither a diagnosis nor a specific mechanism. It is "a neurophysiological term that can only be applied when both input and output of the neural system under study are known". Input can be studied by quantifying the stimulus (eg, pressure) and the action potentials in the neuron. In research in humans, it is rare to measure the stimulus and action potentials, but the IASP suggests that hyperalgesia or allodynia could be clinical correlates of sensitization. For more, see https://www.iasp-pain.org/resources/terminology/

## Focusing on C-fibers

The role of C-fibers is the focus of this editorial. However, the role of A-delta fibers, A-beta fibers, and some immune cells may be equally important, but it is less studied.

**SYNOPSIS:** In most cases, tissue injuries lead to inflammation and sensitization. From a neuroscience perspective, this is *why one usually hurts when one is injured.* Peripheral sensitization is an essential principle in pain science, and it is associated with hyperalgesia, inflammation, and clinical pain conditions, including acute injuries and rheumatological diseases. This editorial explains peripheral sensitization, neurogenic inflammation, and the axon reflex, as well as the role of second messengers and peptidergic C-fibers.
*J Orthop Sports Phys Ther 2022;52(6):303-306. doi:10.2519/jospt.2022.11202*

**KEY WORDS:** *musculoskeletal pain, neuroscience, pain, pain education*

The most remarkable feature of the nociceptive system is the ability to modify transmission of nociceptive signals. Peripheral sensitization is accepted as the dominant mechanism in *primary hyperalgesia*.[4] Peripheral (and central) sensitization occur following a sprain or fracture are present in classical tendinitis (ie, "inflamed tendons") and in more complex cases such as rheumatoid arthritis. A common feature of all these cases is the inflammatory process, which is strongly associated with peripheral (and central) sensitization. In the clinic, an acute inflammation will likely lead to localized tenderness (eg, evoked by palpation), which could be considered a clinical correlate of—albeit not equivalent to—hyperalgesia.

Part of the inflammatory response is due to neurogenic inflammation,[3] which is activated via the antidromic axon reflex in peptidergic C-fibers (see **FIGURE 1**). It is possible that neurogenic inflammation occurs in the absence of tissue injury, but its role in clinical conditions is unknown.

## TRPv1R: The Chili Receptor

Human C-fibers, which almost all express an ion channel known as *transient receptor potential vanilloid receptor 1* (TRPv1R), are the most abundant high-threshold neurons.[9] The C-fibers are thin, unmyelinated neurons surrounded by nonmyelinating Schwann cells (Remak bundles). Most C-fibers are *mechanosensitive*, meaning that in addition

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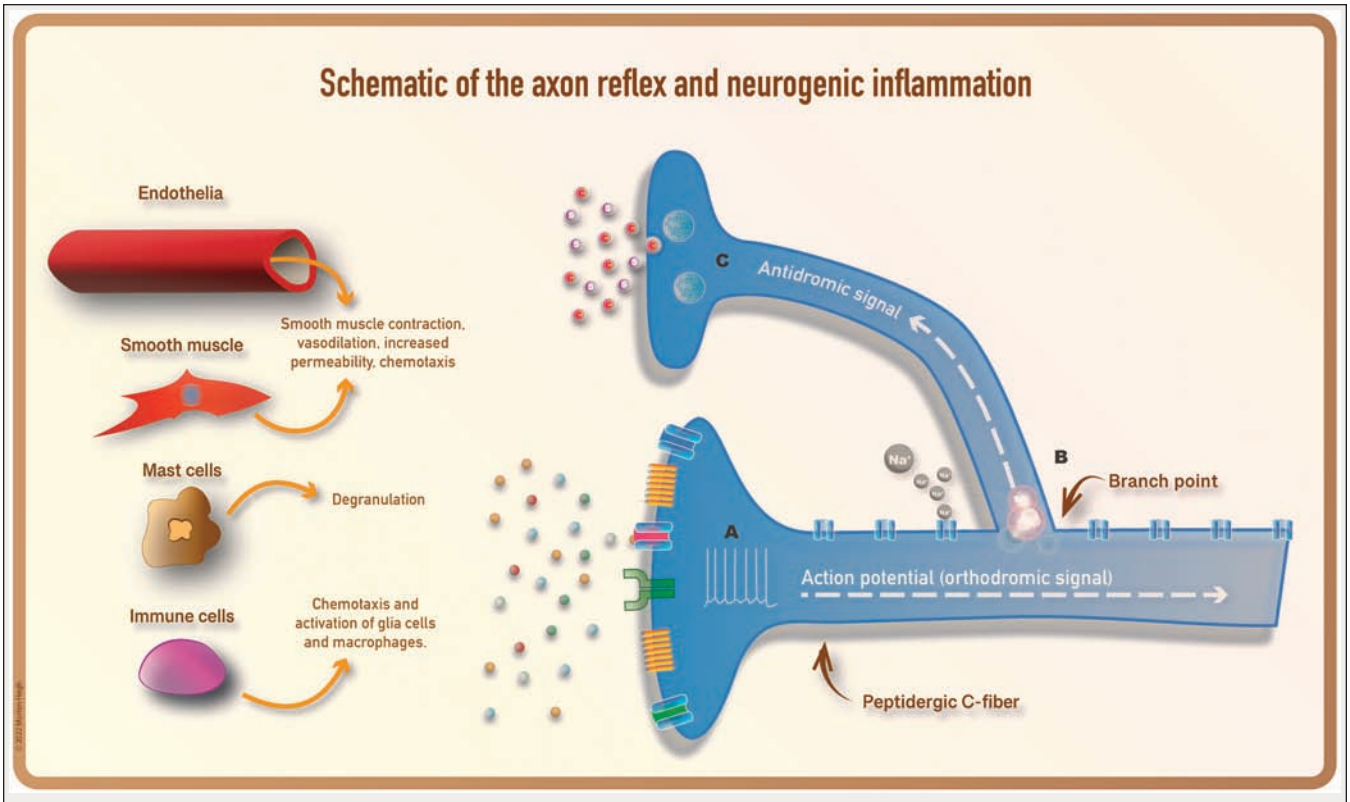


**FIGURE 1.** Axon reflex and neurogenic inflammation. Peptidergic C-fibers respond to activation (A) with an antidromic signal from the branching points to peripheral terminals of the branches (B) where it releases calcitonin gene-related peptide and Substance P (peptides) into the surrounding tissue. The peptides cause vasodilation, smooth muscle contraction, and increased capillary permeability, leading to local oedema and erythema. These peptides also facilitate an inflammatory response (and sensitization) by stimulating mast cells to degranulate (releasing, eg, histamine), activating macrophages and glia cells, and they have chemotactic abilities.[3]



to responding to heat (40°C-45°C) and/or cold (>20°C),[9] most also respond to low-threshold mechanical stimuli. Those that are *mechanoinsensitive* do not respond to stimuli in their naïve state but will respond to various noxious stimuli (including mechanical) when they become sensitized. This feature has given C-fibers the moniker "silent nociceptors".[9]

C-fibers express many different types of receptors besides the TRPv1R. However, much is known about the role of this specific receptor (see ADDITIONAL READING). Most people can relate to the TRPv1R receptor because it is also the receptor that is activated by capsaicin, the pungent agent in chili peppers. Interestingly, high concentrations of capsaicin can have a pain-relieving effect too. The discovery of desensitization of C-fibers by intense and prolonged stimulation of the TRPv1R ultimately led to the development and use of capsaicin-rich patches in patients with neuropathic pain symptoms. Depending on the concentration of the patches, application can desensitize and inactivate ion channels or ablate axon terminals.[1]

## Peptides and Neurogenic Inflammation

Most C-fibers contain peptides (*calcitonin gene-related peptide* and *Substance P*) as opposed to those that bind to IB4 and/or express the P2X3 receptor (non-peptidergic).[9] When peptidergic C-fibers are activated, an antidromic signal is sent from branch points back to the peripheral terminals where peptides are released into the surrounding tissue (ie, the axon reflex)[15] (**FIGURE 1**). The peptides exert an inflammatory response by triggering endothelial, smooth muscle, immune, and mast cells.[3] Due to negative feedback loops, neurogenic inflammation does not continue without relevant stimuli and dissipates until resolved.[13] A visual flare in the skin following a scratch exemplifies this process.

Neurogenic inflammation is vital for tissue healing[3] and resolving the inflammatory response.[7] In addition to tissue healing, neurogenic inflammation is involved in conditions including allergies and rheumatological, dermatological, and bowel diseases.[11] Neurogenic inflammation works in concert with the immune system and may play a role in some chronic pain conditions.[8]

## Peripheral Sensitization

Peripheral sensitization can result if algogens (eg, prostaglandin), cytokines (eg, tumor necrosis factor alpha), and neuro-

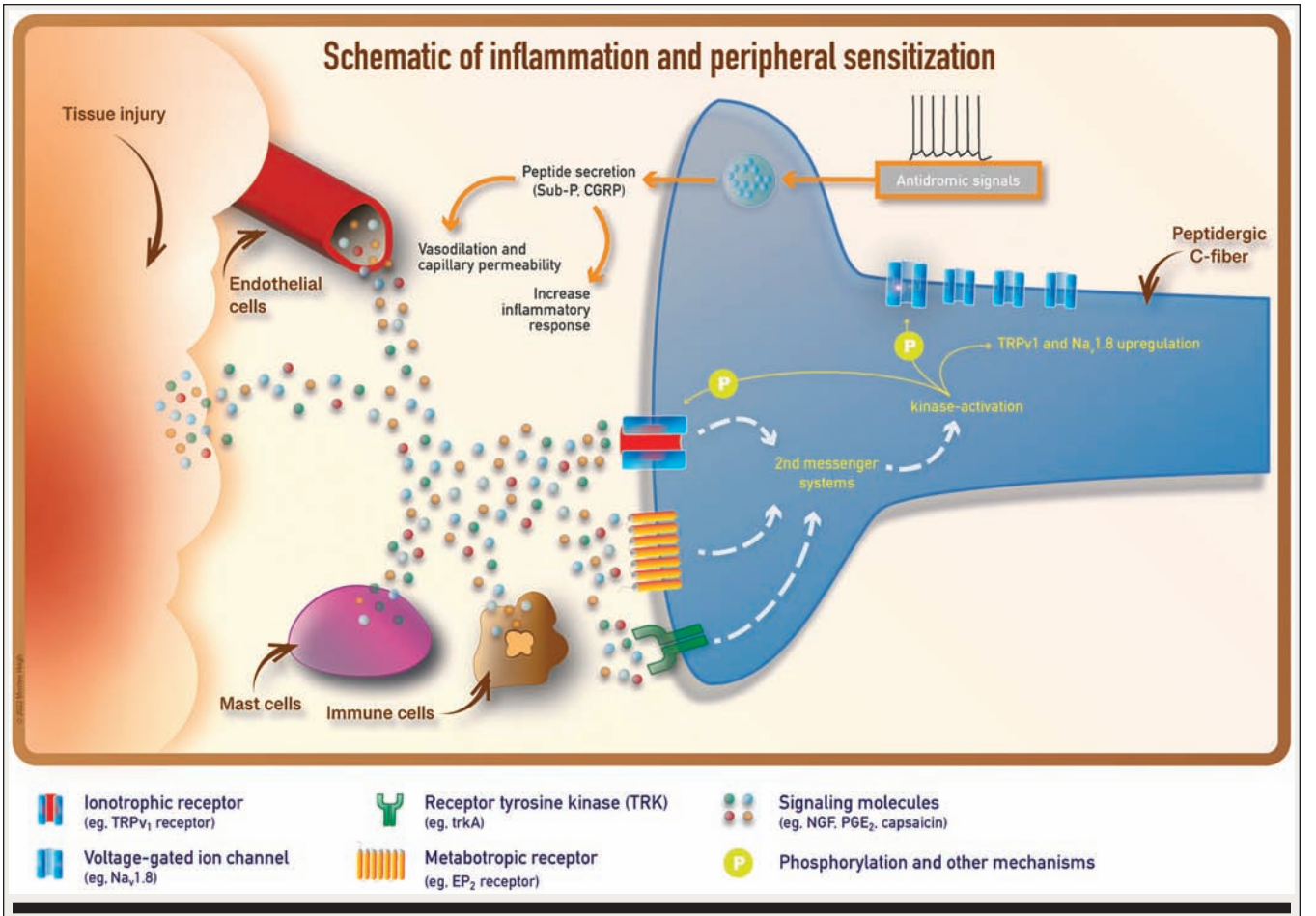


**FIGURE 2.** Inflammation and peripheral sensitization schematic. There are complex interactions between neurons, mast cells, endothelial cells, immune cells, and debris during tissue damage. Nociceptors (high-threshold receptors) respond to chemical signals from other cells (including nearby neurons) with signaling cascades that lead to phosphorylation, facilitation, and other processes responsible for increased responsiveness of the neuron. Abbreviations: $EP_2$, prostaglandin receptor; NGF, nerve growth factor; $PGE_2$, prostaglandin; TRPv1, transient receptor potential vanilloid 1.

trophic factors (eg, nerve growth factor) are released as these substances target receptors on the surface of the neurons. Algogens that bind to receptors sites activate *second messenger systems* (**FIGURE 2**). These messenger systems serve as a communication channel connecting information from the environment to inside the neuron. Second messengers include *calcium* ($Ca^{++}$), *cyclic AMP* (cAMP), and *inositol triphosphate* ($IP_3$), and their role is to facilitate changes within the neuron by activation of enzymatic processes such as *protein kinase A* (PKA), *phospholipase A* ($PLA_2$), *phospholipase C* (PLC), *calcium/calmodulin-dependent protein kinase* (CaMK), and others.[6] In C-fibers, the cascades include phosphorylation of the TRPv1Rs and facilitation of voltage-gated ion channels (NaV1.7-9), leading to increased action potential generation.[3,11] Increasing the possibility of triggering action potentials (peripheral sensitization) would ultimately lead to a barrage of nociceptive input into the spinal cord, kickstarting secondary hyperalgesia mechanisms.

Production and release of prostaglandins (eg, $PGE_2$) also depend on enzymatic processes: $PLA_2$ and PLC can hydrolyze *Arachidonic Acid* from the phospholipids inside the cell, which, in turn, is metabolized into *cyclooxygenases* (COX).[14] The active ingredient in non-steroidal anti-inflammatory drugs (NSAIDs) partly works by blocking the synthesis of $PGE_2$, thereby reducing pain associated with inflammation/peripheral sensitization.[2] However, even short-term use of NSAIDs is associated with an increased risk of thrombosis.[12]

Some C-fibers respond more strongly (ie, sensitization) during inflammation and can also increase their spontaneous activity. Similar patterns have been found in subgroups of patients who suffer from painful conditions where there is no signs of inflammation or tissue damage.[9] Peripheral sensitization is not always caused by inflammation but may also be part of a pathophysiological process.

Peripheral sensitization of C-fibers in the epidermis leads to *phenotypic changes*.

Pain can be evoked by innocuous stimuli such stroking with a cotton bud (ie, allodynia) and to noxious stimuli (eg, hyperalgesia).[3] However, neither allodynia nor hyperalgesia is a unique feature of primary hyperalgesia, and all pain descriptors should be considered (ie, neuropathic or nociplastic) when phenotypic changes are suspected clinically.

### Summary: Pain Science in Practice

Peripheral sensitization is never visible to the naked eye; hence, clinicians should look for signs of hyperalgesia (ie, abnormal evoked pain) and use the patient's history to put positive and negative findings into context. Signs of primary hyperalgesia (ie, relevant and local pain responses together with a relevant history) can be interpreted as a strong clinical suspicion of inflammation due to "overloading",[10] injury or a pathology[2] remembering that many orthopaedic tests are not tissue specific. In addition to pain responses, tests for structural integrity of ligaments, bones, muscles, etc, should be applied to rule out tissue damage whenever relevant.[5]

## STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** Dr Hoegh was responsible for the concept, drafting, and revisions of the manuscript and is a guarantor.

**DATA SHARING:** There are no data in this manuscript.

**PATIENT AND PUBLIC INVOLVEMENT:** No patients or members of the public were involved in this manuscript.

## GLOSSARY

**HYPERALGESIA:** Increased pain from a stimulus that normally provokes pain.

**SENSITIZATION:** Increased responsiveness of nociceptive neurons to their normal input and/or recruitment of a response to normally subthreshold inputs.

**PERIPHERAL SENSITIZATION:** Increased responsiveness and reduced threshold of nociceptive neurons (ie, C-fibers and A-fibers) in the periphery to the stimulation of their receptive fields.

**CENTRAL SENSITIZATION:** Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input. This may include dysfunctions in descending modulation but changes in function occur in central neurons only (ie, peripheral neurons are functioning normally).

**PHENOTYPIC CHANGES:** Phenotype refers to observable characteristics, eg, when light mechanical stimulation leads to the sensation of touch, and phenotypic changes refers to changes, eg, that light touch is experiences as painful (ie, allodynia).

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## ADDITIONAL READING

About the TRPV1 and Piezo2-receptors (Nobel Prize 2021):

The Nobel Prize in Physiology or Medicine 2021. NobelPrize.org. Nobel Prize Outreach AB 2022. (Retrieved on 15/03/2022), link: https://www.nobelprize.org/prizes/medicine/2021/summary/

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# Qualitative Research: Linking Evidence to Practice

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Qualitative research uses a rigorous approach to answer a descriptive research question with nonnumeric data. Studies typically involve analyzing the language that participants use to describe their experiences and perceptions. Separate quantitative and qualitative studies can address the same research area but not the same research question. For example, a quantitative study *estimates the likelihood* of false positive results on a diagnostic test; a qualitative study *describes the experience* of receiving a false positive diagnosis.

## Philosophical Approach

All research sits within philosophical approaches to how the world works (ontology) and how we know this (epistemology). The philosophical approach is quite consistent for quantitative studies, but it varies for qualitative studies. Assumptions underlying the philosophical approach influence the choice of methods and interpretation.[5]

## Qualitative Research

Qualitative research typically aligns more with one of two broad approaches.

**Interpretivist** Interpretivist approach assumes that everything is filtered through socially mediated influences such as language, shared meaning, and consciousness; hence, researchers are never completely unbiased. Researchers acknowledge their influence on the research and interpretation.

**Positivist** Positivist approach assumes that the study findings represent *truth* like quantitative research. A strict positivist stance is uncommon in qualitative research except occasionally in content analysis, where words or phrases are counted to calculate relationships between different concepts.[6]

**Analysis** A researcher might perform interviews with a group of marathon runners asking about barriers to complying with their training program. Thematic analysis from an interpretivist stance could seek to determine the importance of phrases and recognize the influence of the researcher's own views on the study conclusions. Thematic analysis from a (post) positivist stance might involve counting the number of times a word or phrase appeared in the data and generating themes to record the most common barriers.

## Qualitative Data

The data in qualitative studies are words as either the *content* or the *object* of analysis. Words are most commonly used as *content,* ie, proxies for experiences, and organized (coded) into themes, taxonomies, or maps. This involves methods such as thematic analysis, content analysis, or grounded theory. Methods using words as the *object* include conversation, performance, or narrative analyses.

## Key Components

**Research Question** Considerations regarding research questions apply equally to qualitative and quantitative research studies[1,3]: is the question clear, and is it important? If the research question is clear and important, the reader must establish whether qualitative methods are appropriate. Questions that aim to describe lived experiences or interpretations and deeper understanding of phenomena are most suited to qualitative methods. Questions investigating relationships between variables, treatment effectiveness, frequencies, or testing hypotheses require quantitative methods.

**Philosophical Approach** Philosophical assumptions adopted by researchers influence what is valued and how data are analyzed. Qualitative researchers should include information about their philosophical basis in the methods section. For example, classical grounded theory assumes that the researcher discovers theoretical concepts in the data (postpositivist). In a social constructionist (interpretivist) stance, knowledge is developed through interactions between the researcher and participants.

**Participants** Qualitative researchers are most interested in certain characteristics of a study sample rather than obtaining a representative sample,[2] which is critical in quantitative research. The characteristics of interest should be reported along with the description of the sample. For example, a study assessing enablers and barriers to adherence to an exer-

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cise program might specifically sample people who completed all the prescribed sessions and people that completed none or very few. The key point is that the characteristics of the participants are appropriate to the research question. The sample size requirement for qualitative research studies is typically much smaller than for quantitative research studies.

**Reflexivity** All researchers have personal perspectives and context that influence them. Explicit acknowledgment of biases is called reflexivity. Important factors might include gender, relationship to participants, experience, and professional background.

**Data Collection** Data are often collected in interviews, either structured or semistructured, individually, or as a focus group, and observations are often recorded. Knowing how information was recorded (notes, audio recordings, and video), who was present (alone, family, and group), interview location (home, hospital ward, and researcher's office), and how the interview was structured helps describe the participants' context. Researchers should also spell out why they stopped collecting data perhaps because no new information was emerging (saturation) or due to pragmatic reasons such as limited time, funding, or available participants. This helps readers judge whether there are sufficient data to answer the research question. Some studies allow participants the opportunity to review the data to ensure that they represent their perspectives; whether this was done should be specified.

**Analysis** It is not possible to appraise any study without clear reporting of analysis methods. Although there are many different qualitative analysis methods, most involve reading interview transcripts, breaking data into discreet units (coding), and then grouping similar codes together to create meaning. Coding can involve formal codebooks with definitions for each code developed beforehand, followed by a process where several coders agree on how data are coded. Other approaches use one or more coders generating codes based on what they find in the data (inductive coding).

## Summary

Good qualitative research starts with a clear and relevant question, and it requires alignment of methods. A major distinction between qualitative and quantitative research studies is the impact of philosophical stance, which has implications for assessing the quality of a qualitative study. Further, accessible information on qualitative studies is available in this *Journal of Orthopaedic and Sports Physical Therapy*[4] series, and in the study of Tracy and Hinrichs.[7]

## KEY POINTS FOR USING QUALITATIVE RESEARCH

**RESEARCH QUESTION:** Is the research question best answered using qualitative methods?

**PHILOSOPHICAL APPROACH:** Is the philosophical approach underpinning the study stated? Are the relevant assumptions considered in interpretation?

**SAMPLE:** Is there a clear explanation of how researchers selected the participants and description of their characteristics?

**REFLEXIVITY:** Are there statements about the researchers' relationship to participants, their professional background, and experience and description of strategies used to acknowledge and manage biases, eg, memo writing and self-interview?

**DATA COLLECTION:** Is there a description of how the researchers collected data, whether the structure of the interview plan changed in response to each interview, and how data were recorded?

**ANALYSIS:** Is there enough information to describe the process of converting raw data to conclusions?

## STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** Steven J. Kamper and Bronwyn Lennox Thompson drafted and revised the manuscript.

**DATA SHARING:** There are no data associated with this article.

**PATIENT PARTNERSHIP:** There was no patient consultation involved in this article.

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# ICON 2020—International Scientific Tendinopathy Symposium Consensus: A Scoping Review of Psychological and Psychosocial Constructs and Outcome Measures Reported in Tendinopathy Clinical Trials



**OBJECTIVE:** To identify and describe the psychological and psychosocial constructs and outcome measures used in tendinopathy research.

**DESIGN:** Scoping review.

**LITERATURE SEARCH:** We searched the PubMed, EMBASE, Scopus, Web of Science, PEDro, CINAHL, and APA PsychNet databases on July 10, 2021, for all published studies of tendinopathy populations measuring psychological and psychosocial factors.

**STUDY SELECTION:** Studies using a clinical diagnosis of tendinopathy or synonyms (eg, jumper's knee or subacromial impingement) with or without imaging confirmation.

**DATA SYNTHESIS:** We described the volume, nature, distribution, and characteristics of psychological and psychosocial outcomes reported in the tendinopathy field.

**RESULTS:** Twenty-nine constructs were identified, including 16 psychological and 13 psychosocial constructs. The most frequently-reported constructs were work-related outcomes (32%), quality of life (31%), depression (30%), anxiety (18%), and fear (14%). Outcome measures consisted of validated and nonvalidated questionnaires and 1-item custom questions (including demographics). The number of different outcome measures used to assess an individual construct ranged between 1 (emotional distress) and 11 (quality of life) per construct.

**CONCLUSION:** There was a large variability in constructs and outcome measures reported in tendinopathy research, which limits conclusions about the relationship between psychological and psychosocial constructs, outcome measures, and tendinopathies. Given the wide range of psychological and psychosocial constructs reported, there is an urgent need to develop a core outcome set in tendinopathy. *J Orthop Sports Phys Ther 2022;52(6):375-388. doi:10.2519/jospt.2022.11005*

**KEY WORDS:** *pain, psychology, tendinopathy/tendinitis*

Psychological and psychosocial factors are determinants of health, and they are associated with poor recovery in those with musculoskeletal conditions.[4-9] *Psychological* factors such as pain-related fear, catastrophizing, self-efficacy, and personality traits influence the experience of pain.[23,80,105,108,148] These factors are important prognostic indicators, treatment effect modifiers, or mediators of recovery of health across a range of musculoskeletal conditions and general disorders.[12,29,41,67,101,146,147,156] *Psychosocial* factors such as quality of life, employment, education, and social support are also prognostic indicators for musculoskeletal pain, but they have been scarcely investigated in tendinopathy.[73,88,112,171,181] For this review, we distinguished factors as either *psychological* or *psychosocial* constructs.

Exercise is the nonsurgical treatment of choice for tendinopathy.[125] Exercise interventions such as the Silbernagel concentric/eccentric program[151] and heavy slow resistance training[16] are associated with improved clinical outcomes in individuals with lower limb tendinopathy.[117]

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However, exercise is not a panacea: there are modest effects when comparing exercise to nonexercise interventions.[86] Studies evaluating exercise interventions have focused on the contribution of tendon structure or exercise parameters (eg, mode of contraction and exercise intensity) and their relationship to outcomes. However, evidence is conflicting about which exercise type or intensity is associated with superior outcomes in tendinopathy.[24,36,95,115] The long-held belief that improved clinical outcomes are associated with structural alterations following exercise interventions in tendinopathy is not supported.[60,128,172] These findings highlight the need to view tendinopathy from a multidimensional biopsychosocial perspective.

A recent systematic review[159] has found a weak-to-moderate association between psychological factors and pain, disability, and physical functional outcome in tendinopathy. The importance of psychological and psychosocial factors in tendinopathy has also been recently recognized by the International Consensus on Tendinopathy Group (ICON tendinopathy). The ICON tendinopathy consensus defined core outcome domains via a Delphi consensus study involving health care professionals and patients.[168] Psychological factors were included as 1 of the 9 core health-related outcome domains to assess tendinopathy clinical trials following the Delphi process.

While tendinopathy-specific outcome measures exist for many of the identified core outcomes (eg, function, disability, or pain), there is a lack of agreement on the most appropriate psychological outcome measures for tendinopathy. The Achilles tendinopathy consensus group (ICON Achilles, a subgroup of COS tendinopathy) only identified 3 studies in a recent systematic review that assessed psychological factors within prospective studies.[71] Unfortunately, *psychological* and *psychosocial* are sometimes used interchangeably in the literature, making it difficult to interpret which factor is under investigation. The ICON Psych Working Group was tasked with identifying psychological and psychosocial outcomes that have been used in tendinopathy research.

The ICON Psych Working Group's work will inform a subsequent Delphi study asking patients, clinicians, and researchers about the most important psychological and psychosocial constructs and outcome measures in tendinopathy. Future research should investigate the validity of existing psychological and psychosocial outcome measures in a tendinopathy-specific population to inform their use in research and clinical practice. These steps will build on the recommendations of ICON 2019 and facilitate more targeted interventions for this challenging musculoskeletal condition. Consequently, the aim of this scoping review was to outline the evidence concerning psychological and psychosocial *outcomes* in tendinopathy research. Due to the exploratory and descriptive nature of the question, a scoping review was the most appropriate review methodology to address the research question.[11]

## METHODS

The general purpose of scoping reviews is to identify and map the available evidence.[124,136,163,164] This aligns with the objectives of the ICON Psych Working Group. The study selection process is reported using the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.[164]

### Design

The scoping review was informed by the framework recommended by the Joanna Briggs Institute.[83] The framework provides guidance for the review process, including an initial identification of the research question and relevant studies, data extraction, presentation, and interpretation of results.[124,164] The scoping review followed the established 5-stage process as outlined by Arksey and O'Malley.[11]

### Stage 1: Identifying the Research Questions

Literature searches and multidisciplinary discussions were undertaken within the ICON Psych Working Group to inform and identify the research questions. Using a concept (psychological/psychosocial factors and outcome measures) and target population (tendinopathy), we formulated 4 broad research questions to guide the development of the scoping review as follows.

(1) Report all constructs and outcome measures used to assess psychological factors in tendinopathy research.
(2) Report the frequency of all constructs and outcome measures used to assess psychological factors in tendinopathy research.
(3) Report all constructs and outcome measures used to assess psychosocial factors in tendinopathy research.
(4) Report the frequency of the constructs and outcome measures used to assess psychosocial factors in tendinopathy research.

### Stage 2: Identifying Relevant Studies

An a priori decision was made to include a broad range of psychological and psychosocial constructs and the outcome measures used to evaluate these constructs that have been reported in the musculoskeletal literature.[54,116,166,181] Emotional, cognitive and behavioral factors were considered as *psychological* constructs, as previously defined by Linton and Shaw.[108] *Psychosocial* constructs considered were factors that align with the social determinants of health as per the World Health Organization definition: "Conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life".[181] The final categorization was not set a priori as it was dependent on the number of papers that reported the same constructs. Examples of psychological and psychosocial constructs that were considered are as follows.

#### Psychological Factors

- *Emotional factors* including, but not limited to, depression, distress, anxiety,

hypervigilance/somatization, stress, and anger
- *Cognitive factors* including, but not limited to, maladaptive beliefs, fear, kinesiophobia, catastrophizing, negative pain beliefs, and self-efficacy
- *Behavioral factors* including but not limited to avoidance, (negative) coping styles (negative), pain, or sleep interference

Definitions of all relevant psychological outcomes are outlined in **SUPPLEMENTAL FILE 1**.

### Psychosocial Factors

- *Quality of life*
- *Education*
- *Work-related constructs* including income, unemployment, type of work, full-time vs part-time employment, and return to work
- *Place of residence* urban versus rural
- *Race and ethnicity*
- *Socioeconomic status*
- *Social capital and networks* including social exclusion and social support

### Inclusion Criteria

- Studies using a clinical diagnosis of tendinopathy or synonyms (eg, jumper's knee or subacromial impingement) with or without imaging confirmation. The most commonly reported tendinopathies in the scientific literature were the focus of this review, including the following:
  - Achilles
  - Patellar
  - Gluteal
  - Hamstring
  - Lateral elbow
  - Rotator cuff
  - Plantar heel
- Participants >18 years old.
- A minimum sample of 10 participants with tendinopathy.
- All populations (ie, athletes, nonathletes, no restrictions on disease duration or any other factor).
- Any research design reporting quantifiable psychological or psychosocial outcome measures, including randomized trials, observational (cohort and cross-sectional) studies, and case series.

### Exclusion Criteria

- Studies that selectively recruited participants with tendon tears (partial or full thickness) or ruptures.
- Studies involving multiple musculoskeletal pathologies unless the tendinopathy cohort could be disaggregated from the overall cohort.
- Abstracts or conference papers.
- Animal studies and in vitro experiments.
- Studies where the full-text version was not available.

The literature search was performed on July 10, 2021, by 2 authors of the working group (MP and SMC). The search strategy involved MeSH terms and free-text words for tendinopathy clinical diagnoses, psychological factors, and psychosocial factors. The following online databases were searched: PubMed, EMBASE, Scopus, Web of Science, PEDro, CINAHL, and APA PsychNet. All identified articles were collected in Endnote and imported into Covidence (www.covidence.org). Duplicates were removed using an inbuilt function in Endnote and manually screened by one of the reviewers (MP) before being exported into Covidence. A list of search terms based on psychological and psychosocial factors defined previously is provided in **TABLE 1**.

### Stage 3: Study Selection

Titles and abstracts were evaluated by members of the ICON Psych Working Group. The working group split into pairs with each pair undertaking independent double screening of a proportion of the abstracts. The same process was completed for full-text screening of studies that passed the first screening stage. After both screening steps, the core group (SMA, MP, PM, AM, and CS) met to resolve any disagreements between the members of the broader ICON Psych Working Group. Additionally, the reference lists of the included full-text articles were examined to identify any further relevant studies not previously been found by the electronic search.

### Stage 4: Data Extraction—Charting the Data

Data were extracted per the guidelines outlined by the Joanna Briggs Institute.[83] The data extraction sheet is provided in the **APPENDIX**. Specifically, author information, type of study, tendon sites, age, sex, the type of psychological/psychosocial construct, and outcome measures were extracted. If possible, means (standard deviations) were extracted to support the

**TABLE 1** Search Constructs That Were Adapted for Each Search Strategy per Electronic Database

| 1. Tendinopathy | 2. Psychological Constructs | 3. Psychosocial Constructs |
|---|---|---|
| Tendinopathy OR bursitis OR rotator cuff OR shoulder impingement syndrome OR subacromial impingement OR elbow tendinopathy OR tennis elbow OR lateral epicondyl* OR gluteal tendin* OR greater trochanteric pain syndrome OR gluteal bursitis OR trochanteric bursitis OR lateral hip pain OR jumper's knee OR patellar tendin* OR achilles tendon OR tendoachilles OR Plantar fasc* OR heel pain | Psychological OR psycholog* response/ readiness/ distress OR mental health OR anxiety OR depression OR depressive disorder OR mood disorders OR fear OR fear of reinj* OR fear-avoidance OR kinesiophob* OR wakefulness OR vigilance OR hypervigilance OR stress OR emotions OR emotional distress OR catastrophi* OR self efficacy OR adaptation, psychological OR coping OR resilience OR self concept OR self-esteem OR optimism | Social support OR motivation OR social behaviour OR attitude OR goal setting OR perception OR mindfulness OR well-being OR empathy OR compassion OR education OR trust OR communication social class OR socioeconomic status OR culture OR ethnicity OR ethnic groups OR employment OR urban OR rural |
| **Full search** #1 AND (#2 OR #3) | | |

narrative synthesis. Given the iterative nature of scoping reviews, if additional data could be charted and extracted during this process, other categories of tables were added or table headings updated if needed. Data extraction was performed independently by the same pairs that undertook study selection; the core group discussed disagreements. The extraction framework was piloted by members of the core group (SMA, MP, PM, AM, and CS) on a small sample of studies to ensure consistency of application of the coding framework prior to completing the data extraction. The core group (SMA, MP, PM, AM, and CS) resolved any questions arising during this piloting process, and the data extraction framework was revised accordingly.

### Stage 5: Collating, Summarizing, and Reporting the Results

The aim was to report relevant information on the volume, nature, distribution, and characteristics of published studies in psychological and psychosocial factors in tendinopathy. Consequently, a descriptive-analytical method was used by applying a common analytical framework to all the primary research reports and collecting standard information on each study.[11,91] Where appropriate, medians were used to describe the central tendency of the extracted means to support the narrative synthesis. Results are presented as recommended by best practice using a map of the data in a logical, diagrammatic, or tabular form and/or in a descriptive format that aligned to the objectives and aim of the review.[136]

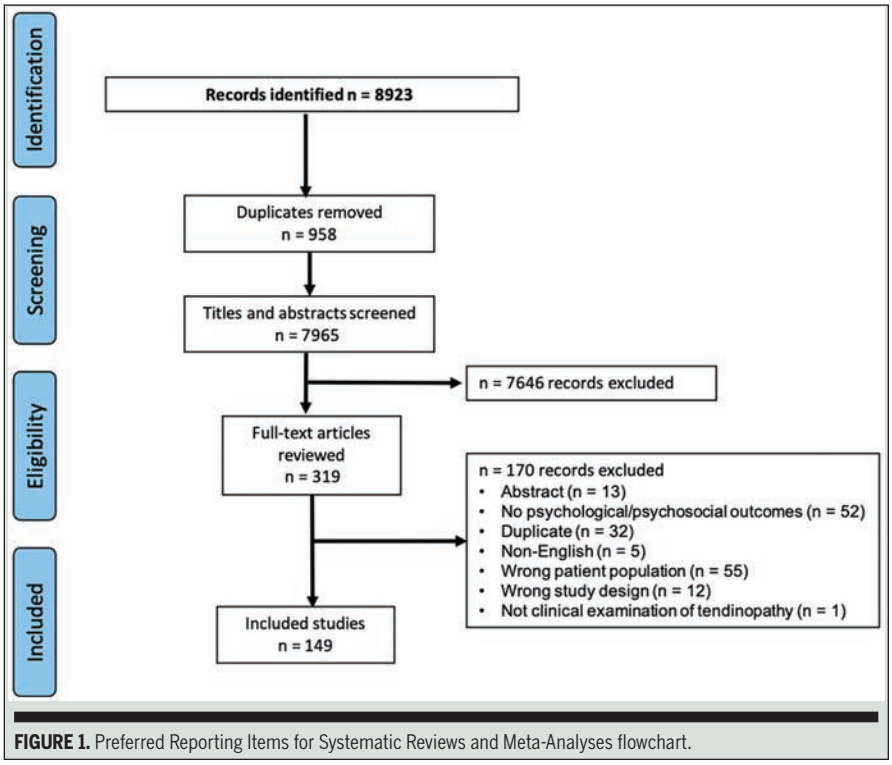


**FIGURE 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart.

## RESULTS

### Study Selection and Characteristics

The electronic search identified 8923 studies. After removing 958 duplicates, 7965 records were screened on title and abstract, with 319 included for full-text review. Finally, 149 studies were included (**FIGURE 1**). Of the 149 studies, 36 studies were randomized controlled trials, 98 observational (59 cohorts and 39 cross-sectional) studies, 7 case series, 3 audits, 1 repeated-measures design, 3 nonrandomized controlled trials, and 1 chart review. Most studied tendon sites were rotator cuff tendinopathy (studies = 62: n = 7327), followed by the lateral elbow tendinopathy (n = 40: n = 3965), Achilles tendinopathy (n = 19; n = 1739), plantar heel pain (n = 16: n = 935), and gluteal tendinopathy (n = 7: n = 27980). The median number of participants was 68, and the total number of participants with tendinopathy in the 149 studies was 42 046. Age was reported in 119/149 (80%) studies, with a mean age of 48 years. The average duration of symptoms was 19 months reported in 52/149 (35%) studies. The remaining studies reported symptoms as categories, reported median values, or did not report duration at all. Further details relating to the characteristics of the studies are outlined in **SUPPLEMENTAL FILE 2.**

### Psychological Factors

**Anxiety** Anxiety was investigated in 27/149 (18%) studies. The most common outcome measure was the Hospital and Anxiety Depression Scale (HADS) reported in 14/26 (54%) studies.[1,5-7,32,38,39,76,84,139,140,179,180] The HADS was originally developed as a self-report instrument to detect and measure the severity of depression and anxiety.[184] It has 2 separate subscales for anxiety and depression and has been used extensively with psychiatric, medical, rheumatological, and chronic pain patients (16). The HADS (15) comprises 14 items (7 items for depression and 7 items for anxiety) rated on a 4-point scale from 0 (*absence*) to 3 (*extreme*) with a total score of 42 (21 per subscale). A total score is generated for each anxiety and depression subscale, with higher scores indicating a higher level of anxiety or depression. The median anxiety score across 12 studies that reported means was 5.8/21 (range: 3-9.2). Tendon sites using the HADS varied: lateral elbow tendinopathy (n = 4), rotator cuff tendinopathy (n = 4), gluteal tendinopathy (n = 2), plantar heel pain (n = 2), and Achilles tendinopathy (n = 2). Five studies used the Depression, Anxiety and Stress Scale–Short Form (SF) 21 (DASS-21).[44,46,47,79,130] The median DASS score of 4 studies

reporting the mean was 4.2 (range: 3.8-12.20). The remaining studies used the Pain Anxiety Symptom Scale,[51,127,144] Symptom Check List-90,[167] Four-Dimensional Questionnaire,[96] MASS Mood Scale,[142] a single question from the Outcome Evaluation Questionnaire,[113] and a chart-based diagnosis.[135]

**Depression** Depression was investigated in 34/149 (23%) studies. The HADS was the most used outcome measure, reported in 12/34 (35%) studies.[1,5-7,32,76,84,121,139,140,178,179] The median of HADS mean score across studies was 3.9/21, with a range between 1.7 and 6.2. Tendon sites using the HADS varied: rotator cuff tendinopathy (n = 4), Achilles tendinopathy (n = 2), lateral elbow tendinopathy (n = 2), gluteal tendinopathy (n = 2), patellar tendinopathy (n = 1), and plantar heel pain (n = 1). The Beck Depression Inventory was used in 6 studies.[4,59,74,97,122,134] The mean score was specified in 4/6 studies. The median Beck Depression Inventory score across the studies was 10.2, ranging between 4.6 and 16.3. Tendon sites using the Beck Depression Inventory rotator cuff tendinopathy (n = 4), lateral elbow tendinopathy (n = 1), and plantar heel pain (n = 1). The Depression, Anxiety, and Stress Scale was used in 5 studies, and the median of reported mean scores was 7.2 (range: 6.4-9.9; n = 4).[44,46,47,79,130] The remaining studies used the Centre for Epidemiological Studies–Depression Scale (n = 3), Patient Health Questionnaire (n = 2), Four-Dimensional Symptom Questionnaire (n = 1), EuroQol 5-Dimension (EQ-5D) depression anxiety scale (n = 1), Outcome Evaluation Questionnaire (2 valid questions) (n = 1), and chart-based diagnosis (n = 1).

**Catastrophizing** Catastrophizing was investigated in 15/149 (10%) studies. The most common outcome measure was the Pain Catastrophizing Scale reported in 14/15 (93%) studies.[31,38,43,53,68,74,76,79,84,98,130,134] The catastrophizing pain scale is a 13-item self-report measure designed to assess catastrophic thinking related to pain. The Pain Catastrophizing Scale has several subscales: 3 items measuring magnification, 4 items measuring rumination, and 6 items measuring helplessness. The 13 items are rated on a 5-point Likert scale from 0 (*not at all*) to 4 (*all the time*). A total score of 30 indicates a clinically relevant level of catastrophizing.[160] The mean score was specified in 12/14 studies. The median score of means across studies was 13.6 with a range between 5 and 30. Tendon sites using the Pain Catastrophizing Scale varied: gluteal tendinopathy (n = 5), lateral elbow tendinopathy (n = 3), rotator cuff tendinopathy (n = 2), Achilles tendinopathy (n = 3), and plantar heel pain (n = 1). The other remaining study used the Pain-Related Self Statement Scale.[69]

**Fear** The psychological construct fear was investigated in 22/149 (13%) studies. The most common outcome measure reported was the Tampa Scale of Kinesiophobia (TSK), reported in 16/20 (75%) studies.[15,31,38-40,42,43,61,62,77,118,121,140,141,150,151] The TSK is a 17-item scale used to subjectively measure fear of movement and unhelpful beliefs about pain. The scale is based on the model of fear avoidance, fear of work-related injury, and fear of reinjury. The TSK has 17 items rated on a 4-point Likert-type scale.[63,170] The scale consists of 2 subscales: a harm factor and an activity avoidance factor. Total score ranges from 17 to 68, with a cutoff score of 37 or over being considered a high score.[170] Tendinopathy groups using the TSK varied: Achilles tendinopathy (n = 6), lateral elbow tendinopathy (n = 5), gluteal tendinopathy (n = 2), rotator cuff tendinopathy (n = 1), plantar heel pain (n = 1), and patellar tendinopathy (n = 1). The long-form TSK was used in 10 studies, while the SF TSK was reported in the remaining 6 studies.[15,31,38-40,141] The median score of means from the long-form TSK across the studies was 32, with scores ranging from 26.9 to 38.7, whereas the median of the SF was 36.6 (range: 24.3-37.2; n = 3). Four studies used the Fear Avoidance Beliefs Questionnaire with mean scores of 14 for the physical activity subcomponent, while a mean score of 17 was reported for the work subscale.[68,70,99,102] The remaining study exploring fear as a psychological construct used a single question taken from the Pain and Impairment Relationship Scale.[113]

**Mental Health** Mental health outcomes were reported in 14/149 (9%) studies. The most common outcome measure was the SF-36 measured in 9/14 (64%) studies.[2,3,46,48,58,59,82,161,183] The remaining studies used the SF-12 (n = 3)[132,153,158] and the SF-8.[102] Developed by RAND in 1992, the SF-36 is a 36-question survey derived from the Medical Outcomes Study, a multiyear study to explain variations in patient outcomes.[173] Scores for each domain range from 0 to 100, with a higher score defining a more favorable health state. The median of SF-36 means was 51.7, with a range of scores between 41.2 and 79.3 (n = 8), and the median of the SF-12 was 51.9 (range: 43.8-56.6; n = 4) Mental health was explored across a range of tendon sites, with SF-36 used in 1 study in individuals with Achilles tendinopathy, 3 studies in individuals with plantar heel pain, 3 studies in individuals with rotator cuff tendinopathy, and 2 studies in individuals with lateral elbow tendinopathy.

**Self-Efficacy** Self-efficacy was reported in 12/149 studies (8%). The most common outcome measure was the Pain Self- Efficacy Questionnaire, reported in 6/12 (50%) of the studies.[29,120,130,139,141,143] The Pain Self- Efficacy Questionnaire is used to assess confidence in performing activities while in pain. Participants rate how confidently they can perform activities described on a 7-point Likert scale, ranging from 0 (*not at all confident*) to 6 (*completely confident*). Total scores range from 0 to 60, where higher scores reflect stronger self-efficacy beliefs.[126,162] The median of reported means across these studies was 47.7, with a range of scores between 37.0 and 50.0. Tendon sites using the Pain Self-Efficacy Questionnaire varied: Achilles tendinopathy (n = 1), gluteal tendinopathy (n = 3), rotator cuff tendinopathy (n = 2), and patellar tendinopathy (n = 1). The remaining studies used a General Self-Efficacy Scale and[109,110] Chronic Pain Self-Efficacy Scale,[61] while the remaining 2 studies used 7-point ordinal scales.[26,100]

**Stress** Six studies 6/149 (4%) investigated the role of stress in tendinopathy. The most common outcome measure for this construct was the stress component of the Depression, Anxiety and Stress Scale–SF (DASS-21), used in 5 (83%) studies.[44,46,47,79,130] The DASS-21 is a set of 3 self-report scales designed to measure the emotional states of depression, anxiety, and stress. Each of the 3 DASS-21 scales contains 7 items, divided into subscales with similar content. Each component is assessed using a 4-point Likert scale ranging from 0 to 3. Recommended cut-off scores for conventional severity labels (normal, moderate, and severe) are described in the literature.[111] A higher score on the DASS-21 indicates greater severity or frequency of negative emotional symptoms. Four studies explored stress in individuals with plantar heel pain, while the remaining study by O'Leary et al[130] explored the role of stress in rotator cuff tendinopathy. The median of reported means across these studies was 10.3, with a range of scores between 8.5 and 15.7. Finally, 1 study[175] measured perceived stress in individuals with upper extremity tendinopathy using a Job Content Questionnaire.

**Emotional Distress** Emotional distress was reported in 3/149 (2%) studies, all of which were performed in cohorts with rotator cuff tendinopathy.[25,26,57] All studies used the Hopkins Symptom Checklist with mean scores being reported in 2 of the 3 studies; means ranged from 1.43 to 1.60.

**Other Psychological Variables** Other psychological variables that were reported across the studies included somatisization, perfectionism, psychological symptoms, mood state, neuroticism, patient expectations, and burnout (**SUPPLEMENTAL FILE 2**).

### Psychosocial Factors

**Education** Education level was reported in 9/149 (6%) studies[75,100,104,144,153,154,167,175,176] and years of education in 4 (3%, 4/145).[45,46,122,123] Education levels were mainly reported in categories.

**Quality of Life** Quality of life was reported in 54/149 studies (36%). The SF-36 was the most commonly reported outcome measure reported in 20 studies (37%, 20/54), including lateral elbow tendinopathy (n = 4), rotator cuff tendinopathy (n = 8), plantar heel pain (n = 6), and Achilles tendinopathy (n = 2). The SF-36 and the SF-12 (reported in n = 7 studies) are reported as general health/quality-of-life surveys reporting several subscales including a mental and social functioning subscale, which are reported in the "Mental Health" and "Other Psychosocial Outcomes" sections, respectively. The EuroQol, a 5-dimension quality-of-life scale, was used in 12/47 studies (26%),[28,35,36,38,68,84,100,114,120,131,140,178] including studies on rotator cuff tendinopathy (n = 6), Achilles tendinopathy (n = 2), lateral elbow tendinopathy (n = 1), plantar heel pain (n = 1), and gluteal tendinopathy (n = 2).

Of the 7 studies that reported means, the median of the mean index scores of the EuroQol was 0.7/1 (range: 0.5-0.7; n = 7). Other quality-of-life questionnaires included EQ-5D visual analog scale that ranged from 65.8 to 73/100 (n = 2), EQ-5D 3L (n = 1), World Health Organization Quality of Life (n = 3), Rotator Cuff Quality of Life (n = 2), Disabilities of the Arm, Shoulder and Hand (DASH)–Quality of Life (n = 1), Gothenburg Quality of Life (n = 1), Assessment of Quality of Life (n = 1), Foot and Ankle Outcome Score Quality of life component (n = 1), Western Ontario Osteoarthritis of the Shoulder index (n = 1), and The Western Ontario Rotator Cuff (n=1).

**Work-related outcomes** Work-related outcomes were reported by 49/149 studies (33%). Nine studies (18%) reported physical strain at work.[9,66,72,74,75,92,103,104,145] Types of physical strain included data on heavy loading and awkward postures measured with the Physical Workload Questionnaire (n = 2),[9,72] physical exposure measured with by trained ergonomic analysts (n = 1),[66] and categories of physical strain for example none, low, medium, high strain,[75] or lifting of heavy versus light loads.[92] Twelve studies (25%) reported psychosocial work factors that were assessed with the Karasek Job Content Questionnaire.[10,18,19,22,27,72,75,122,154,174,176] The Karasek Job Content Questionnaire produces work factor outcomes including job demands, decision latitude, social support, and job insecurity.[87] Duration of sick leave was reported by 7 studies[34,37,92,93,129,133,169] and return to work by 2 studies.[8,14] Employment status was reported in 8/49 (16%) studies.[37,52,89,93,144,157,165,175] The majority (>50%) of participants were currently employed, either full time (range: 62%-81%) or part time (range: 9%-15%). Employment type was reported in 9/49 (18%) studies.[17,18,27,68,85,89,106,119,123] Employment status and type of employment were presented descriptively, and as such, the vast majority of studies had not listed a description of the outcome or assessed these outcomes with a validated questionnaire. Examples of other work-related outcomes are job satisfaction, working ability, barriers to return to work, and sick leave benefits. All work-related outcomes can be found in **SUPPLEMENTAL FILE 2**. An overview of the psychological constructs for each domain is outlined in **FIGURE 2**.

**Other Psychosocial Variables** Other psychosocial variables that were reported included smoking status (n = 4), social functioning (n = 4), and emotional functioning (n = 3) - subscale of the SF-36, marital status (n = 2), confidence and social interaction scales of the DASH (n = 2), relations with other people measured with the SF - Brief Pain Inventory (n = 2), indigenous language (n = 1), and hobbies and activities (n = 1), sleep quality (n = 1), and coping strategies (n = 1). The median of social functioning means was 51.9/100 with a range from 43.8 to 56.6 (n = 4), and emotional role functioning ranged from 66.7 to 67.5/100 (n = 2).

## DISCUSSION

Our scoping review aimed to describe the psychological and psychosocial constructs and outcome measures that have been used in tendinopathy research. Twenty-nine common constructs were identified: 16 psychologi-

cal and 13 psychosocial. Psychological outcomes were more commonly reported, specifically, depression (30%), anxiety (18%), and fear (14%). Work-related outcomes were the most common psychosocial outcome (in 32% of studies). Outcome measures consisted of validated and nonvalidated questionnaires and 1-item custom questions or data were simply reflected by self-reported demographics. The number of outcome measures used to measure psychological and psychosocial constructs ranged between 1 (emotional distress) and 11 (quality of life) per construct. Large variability in constructs and outcome measures is likely to limit data pooling and conclusions about the relationships between psychological and psychosocial outcome measures with tendinopathy.

Measuring psychological factors in people with musculoskeletal conditions is important, but currently, most evidence arises from conditions other than tendinopathy. Depressive symptoms are related to higher levels of pain intensity, more functional limitation and disability, and worse prognosis,[13,137] and they predict the transition from acute to persistent in individuals with low back pain and neck pain.[107,138] Pain catastrophizing is associated with worsening physical disability, higher health care costs, and the amplification of pain sensitivity among patients with low back pain and joint pain.[55,56] Fear avoidance beliefs (kinesiophobia) are predictive of developing chronic low back pain,[64,65,94,149] poor work-related outcomes,[81,177] reduced function,[78,155] and higher health care use.[90] In tendinopathy, the current evidence is limited to cross-sectional studies outlining the relationship between psychological and psychosocial outcomes and the presence or severity of tendinopathy. A systematic review[159] investigated the strength of association between psychological factors and clinical outcome in tendinopathy. There was low to very low certainty evidence for an association between psychological factors and greater self-reported pain and disability as well as impaired physical function in people with tendinopathy. There was low to very low certainty evidence for an association between higher levels of self-efficacy and lower levels of pain intensity.[159] By highlighting current practices and limitations related to the measurement of these outcomes in tendinopathy, we are taking steps toward developing this priority research area for tendinopathy.

Although it is tempting to make direct comparisons between the baseline values for the various psychological and psychosocial outcomes reported in the review

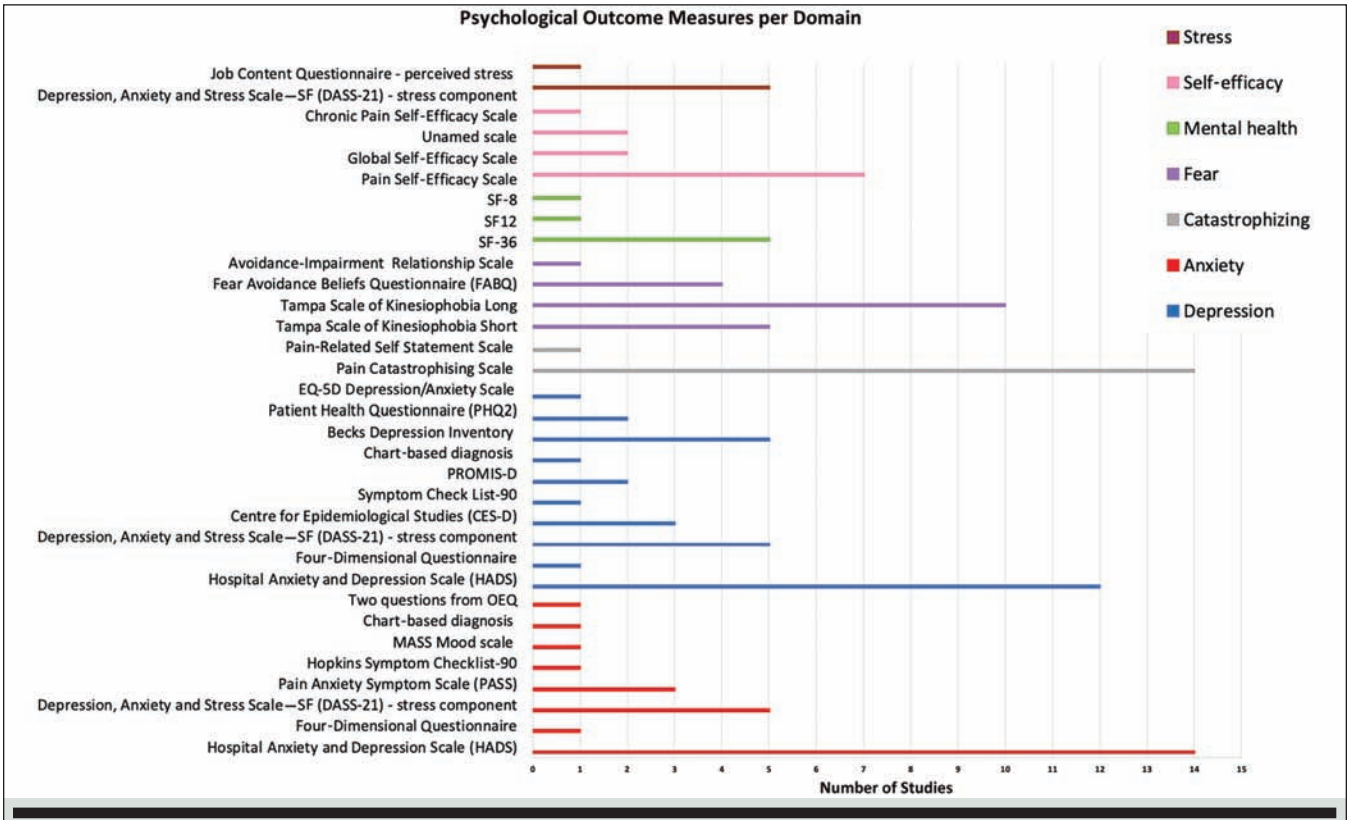


**FIGURE 2.** Psychological outcome measures per domain. EQ-5D, EuroQol 5-Dimension; OEQ, Outcomes and Experiences Questionnaire; PROMIS, Patient-Reported Outcome Measure Information System.

for people with tendinopathy to values reported in the literature for other musculoskeletal disorders, we urge caution. The psychological and psychosocial outcome measures reported in our review have not yet undergone psychometric evaluation in a population with tendinopathy. The outcome measures outlined in the review have been evaluated with participants with multiple pain sites (eg, widespread pain, headache, and leg pain), osteoarthritis, or in a population with persistent low back pain.[30] The measurement properties of an instrument are population specific and context specific, and they should be assessed before use in clinical research and practice in specific populations,[50] limiting direct comparisons with a tendinopathy population.

### Implications of Findings

The recent international tendinopathy consensus group (ICON tendinopathy) has included psychological factors as 1 of the 9 core domains for tendon research.[168] Our scoping review highlighted sparse reporting of psychological and psychosocial factors in tendinopathy studies and the use of varied outcome measures. The issue of heterogeneity of outcome reporting highlights the need to develop and apply core outcome sets in future tendinopathy trials. Further, outcome measures of core outcome sets should adequately meet the criteria of *truth* (ie, validity), *discrimination* (ie, reliability and sensitivity to change), and *feasibility* (ie, be applied and interpreted easily) in order to be meaningful and relevant for clinicians and researchers alike.[20]

### Developing a Core Outcome Set for Tendinopathy

We propose using a stepwise approach, the first step is to develop consensus on what constructs/domains to measure and report in future tendinopathy effectiveness studies. This consensus process is to be conducted using a modified Delphi method online survey to determine the core outcome set domains that are important to key stakeholders (patients, health care practitioners, and researchers). The domains then will be prioritized for their level of importance for clinical trials.[182] After a core outcome set is established, the working group will systematically assess the psychometric/clinimetric properties of the selected outcome measures to measure the core outcomes. Studies are only as credible as their outcome measures[21]; hence, to ensure credibility, the outcome measures must be validated in specific tendinopathy populations.[50] Establishing a core outcome set may lead to future research investigating whether psychological factors are prognostic factors, treatment effect modifiers, or mediators of recovery.[12,41,156] This may assist in identifying individuals with tendinopathy who may be at risk of poorer rehabilitation outcomes. Ultimately, this process will help inform clinical practice by identifying psychological factor(s) to consider or even address as part of a treatment intervention if it has been shown to mediate recovery.

### Strengths and Limitations

The scoping design allowed us to identify and map a broad and diverse topic. This is the largest and most comprehensive review using a collaborative approach on the topic of psychological and psychosocial factors in tendinopathy. All study designs were eligible for inclusion in this scoping review. The entire screening process was undertaken by 2 independent members of the ICON Psych Working Group.

A limitation is that data extraction was not conducted by 2 researchers but divided among members of the ICON Psych Working Group. Data were cross-checked by members of the core group before syntheses commenced. The review excluded tendon sites outside of the 7 sites defined (eg, peroneal), instead favoring the most common tendinopathies in the scientific literature, as agreed a priori. We acknowledge the findings should not be extrapolated to all tendon sites. Case series with fewer than 10 participants were excluded. There were no restrictions on the population or clinical/diagnostic criteria, which may have biased our findings.

We intended to provide an overview of the psychological and psychosocial literature in tendinopathies, and not to provide guidance on which constructs or instruments should be used in certain populations. Factors were set apart as either psychological or psychosocial factors by the steering committee, which may have led to reporting bias. The most common factors are individually reported, and raw data are provided in the supplemental files to minimize bias. Future studies should assess which psychological and psychosocial factors are important in research and clinical practice, accounting for diagnostic criteria and specific populations (eg, athletic vs nonathletic populations). The core group categorized factors, constructs, and measurement instruments to enable data synthesis, which is influenced by the core group's backgrounds, knowledge, and motivations. To minimize bias, all the raw data are available in **SUPPLEMENTAL FILE 2.**

## CONCLUSION

We identified 16 psychological and 13 psychosocial constructs. Work-related outcomes were the most common psychosocial outcome, reported in 32% studies. Quality of life (31%), depression (30%), anxiety (18%), and fear (kinesiophobia) (14%) were the most frequently reported psychological outcomes. Between 1 and 11 instruments were used to measure each construct. ◉

### KEY POINTS

**FINDINGS:** 149 studies were included in the review. Most studied tendon sites were rotator cuff tendinopathy (studies = 62), followed by the lateral elbow tendinopathy (n = 40), the Achilles tendinopathy (n = 19), plantar heel pain (n = 16), and gluteal tendinopathy (n = 7). Our review identified 16 psychological and 13 psychosocial constructs. Work-related outcomes were

the most common psychosocial outcome, reported in 32% studies. Quality of life (31%), depression (30%), anxiety (18%), and fear (kinesiophobia) (14%) were the most frequently reported psychological outcomes. Between 1 and 11 instruments were used to measure each reported psychological or psychosocial construct.

**IMPLICATIONS:** The recent international tendinopathy consensus group (ICON tendinopathy) has included psychological factors as 1 of the 9 core domains for tendon research. Our scoping review highlighted sparse reporting of psychological and psychosocial factors in tendinopathy studies and the use of varied outcome measures. Future research should investigate the validity of new and existing psychological and psychosocial outcome measures in a tendinopathy-specific population to inform their use in research and clinical practice.

**CAUTION:** Although it is tempting to make direct comparisons between the baseline values for the various psychological and psychosocial outcomes reported in the review for people with tendinopathy to values reported in the literature for other musculoskeletal disorders, we urge caution. The psychological and psychosocial outcome measures reported in our review have not yet undergone psychometric evaluation in a population with tendinopathy.

## STUDY DETAILS

**AUTHORS CONTRIBUTIONS:** The following authors Sean Mc Auliffe, Melanie Plinsinga, Peter Malliaras, Adrian Mallows, and Carl Stubbs were involved in all aspects of the review and consequently the core authorship team. All five authors (myself included) contributed equally to the review. It was agreed that equal authorship is attributed to this group followed the wider group as listed. I, Sean Mc Auliffe will remain the corresponding and first named author for referencing e.g. Mc Auliffe et al 2022.

**DATA SHARING:** The protocol for the review is available on Open Science Framework, a public, open-access repository (https://osf.io/ugamz/?view_only=79aa5fb96e9645b68f58dd4f1206f7f0).

**PATIENT AND PUBLIC INVOLVEMENT:** No patient and public representatives were involved in the scoping review process.

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# Risk Factors for Quadriceps Muscle Strain Injuries in Sport: A Systematic Review



Quadriceps muscle strain injuries are common across sports involving sprinting, repetitive kicking, and changes of direction.[46] While the burden of quadriceps muscle strain injury in sport is not as high as for hamstring injuries,[2,22] they still account for a considerable proportion of lower-limb muscle strain injuries: 5% of all time-loss injuries and 19% of all muscle injuries in men's professional football.[21] The match play incidence of quadriceps injury is 2.2 injuries per 1000 hours in rugby union.[9] In Australian football, quadriceps injuries account for 4.4 missed matches per team per season.[2] Quadriceps injuries are also common in basketball,[37] Gaelic football,[57] futsal,[40] and American football.[24]

Quadriceps injuries recur at rates of 15% in football[22] and up to 19% in Australian football.[2] Average time loss in football for index quadriceps muscle strain injury is equivalent to calf muscle strain, varying between 18 and 21 days with significantly higher mean absence in the event of reinjury.[22] There is little known about the prevalence or risk factors for quadriceps muscle strains in female athletes.

**OBJECTIVE:** To identify risk factors for quadriceps muscle strain injury in sport.

**DESIGN:** Risk factor systematic review.

**LITERATURE SEARCH:** A systematic search was conducted in the MEDLINE, CINAHL, Embase, AMED, AUSPORT, SPORTDiscus, PEDro, and Cochrane Library databases (from inception to September 2021).

**STUDY SELECTION CRITERIA:** Studies reporting prospective data to evaluate risk factors related to index and/or recurrent quadriceps muscle strain injury.

**DATA SYNTHESIS:** A risk-of-bias assessment (using a modified Quality in Prognosis Studies tool) was performed, and we used best-evidence synthesis to qualitatively synthesize the data to quantify relationships between risk factors and quadriceps muscle injury.

**RESULTS:** Sixteen studies were included, capturing 2408 quadriceps injuries in 11 719 athletes. Meta-analyses were not performed due to clinical heterogeneity. The dominant kicking leg (over 3154 individuals, 1055 injuries), a previous history of quadriceps muscle injury (6208 individuals, 975 injuries), and a recent history of hamstring strain (4087 individuals, 581 injuries) were intrinsic factors associated with quadriceps injury. Extrinsic factors relating to the preseason period and competitive match play increased quadriceps injury risk; participating at higher levels of competition decreased quadriceps injury risk. Age, weight, and flexibility (intrinsic factors) had no association with quadriceps injury.

**CONCLUSION:** Previous quadriceps injury, recent hamstring injury, the dominant kicking leg, and competitive match play were the strongest risk factors for future quadriceps muscle injury in sport.
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**KEY WORDS:** *lower extremity, muscle injury, muscle strain, quadriceps, risk factors, sport*

Despite the burden of quadriceps muscle strain injuries, there are limited studies that directly examine risk factors for quadriceps strain. A number of risk factors have been proposed in a narrative review,[46] but there is no systematic synthesis of the factors that may predispose an athlete to quadriceps muscle strain injury. Identifying risk factors for quadriceps muscle strain injury could assist clinicians when they are assessing and treating athletes and guide injury prevention and rehabilitation strategies. Our aim was to identify the risk factors for quadriceps muscle strain injury in sport.

## METHODS

This review was prepared and conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[47]

### Search Strategy

A systematic literature search was conducted across the following databases: MEDLINE, CINAHL, Embase, AMED, AUSPORT, SPORTDiscus, PEDro, and the Cochrane Library from inception to September 2021. Key words from the research question (quadriceps, sport, injury, and risk factors) and their synonyms were used to structure the search and mapped against medical subject headings where possible (**SUPPLEMENTAL APPENDIX 1**). Forward citation tracking, backward reference list scanning of included articles,

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and manual ahead-of-press searches were carried out.

### Study Selection

References were imported into EndNote X9 software (Thomson Reuters, USA), and duplicates were removed. Two reviewers (S.P. and T.P.) independently reviewed titles and abstracts using Covidence systematic review software (Veritas Health Innovation Ltd, Melbourne, Australia), and studies were identified for full-text review. The selection criteria were applied independently by both reviewers (S.P. and T.P.) against the full-text versions, and consensus was reached via discussion where required.

### Selection Criteria

**Participants/Injury** Included articles examined either an index injury (first presentation of quadriceps muscle injury) or recurrence (further quadriceps injury following index injury) of a quadriceps muscle strain injury in adult (over 18 years old) humans from sport or an athletically related activity (running, weight training, etc). Only studies presenting distinct data for specific quadriceps muscle strain injuries were examined. Traumatic or contusion-type injuries as well as injuries involving tendon pathologies or avulsions and surgical interventions (eg, quadriceps tendon graft) were excluded.

**Risk Factors** Studies must have presented discrete data for 1 or more variables and their association with risk of quadriceps muscle injury. Only intrinsic and extrinsic risk factors that were measured prospectively were included, although studies that presented non-modifiable risk factors that were analyzed retrospectively (eg, age at time of injury) were also deemed appropriate for inclusion.

**Study Design** Only studies from peer-reviewed sources and published in English with full-text versions available were included. Systematic reviews and studies with a prospective cohort design were included. Intervention studies were excluded to limit potential confounding. Non-systematic reviews, case studies, opinion articles, conference abstracts, and unpublished data were also excluded. Studies reporting injury incidence only for variables that required normalization against exposure data for interpretation of results (eg, preseason versus in-season exposure) were also excluded. This was to avoid inaccurate assumptions about the variable's relationship to quadriceps injury instead of its relationship to exposure.

### Data Collection and Analysis

**Data Extraction** Data were extracted with a focus on athletic participation, participant characteristics, study duration, method of quadriceps injury diagnosis, and specific intrinsic and extrinsic risk factors and their association with index or recurrent quadriceps muscle strain injury. Non-blinded reviewers (S.P. and T.P.) extracted data independently, and consensus was reached on the findings. Means, standard deviations, hazard ratios, risk ratios, and odds ratios were extracted. Where statistical analyses were not performed for the interaction of specific variables of interest, we extracted raw data and calculated mean differences and odds ratios where possible (**SUPPLEMENTAL APPENDIX 4**).

### Risk-of-Bias Assessment

A risk-of-bias assessment was performed by 2 independent reviewers (S.P. and T.P.) using a modified version of the Quality in Prognosis Studies (QUIPS) tool,[32,33] which has been used in recent systematic reviews examining muscle injury[28,29,56,59] and is recommended for systematic reviews of prognostic factors.[25]

Six areas of assessment were used to evaluate specific study design elements, with each area having specific criteria against which studies were appraised to identify potential sources of bias. These criteria were modified and agreed upon by the authors prior to assessment to reflect the relevant question of our review (**SUPPLEMENTAL APPENDIX 2**). Individual criteria within each area of assessment were scored "yes" or "no," with an area considered to have a high risk of bias if less than 75% of the responses within it were judged as "yes." An area was considered to have a low risk of bias if 75% or more of the responses within it were judged as "yes."

We calculated overall risk of bias for each study according to the number of areas that were deemed to be high risk. To be deemed to have an overall low risk of bias, a study must have had at least 5 of the 6 areas scored as "low risk," while also requiring a low risk-of-bias score for the area relating to outcome measurement (item 4). Studies not fulfilling this criterion were assessed as "high risk." This method has been described in other systematic reviews investigating risk factors for muscle injury.[28,29,55,59] Any disputes between the reviewers were resolved via consensus.

### Data Synthesis

We planned a meta-analysis of data from individual studies for potential risk factors for quadriceps muscle injury using a random-effects model. Where meta-analysis was not possible, a best-evidence synthesis of results was completed to identify the strength of evidence for the association between each risk factor and quadriceps muscle injury. The level of evidence was determined for each risk factor according to a hierarchy of information from the risk-of-bias assessment and the clinical results.[62,67] The best-evidence synthesis criteria have been used in recent muscle-related systematic reviews.[28,29,55,56,59]

1. Strong evidence: consistent results in 2 or more low–risk of bias studies, with generally consistent findings in 75% or more of the studies.
2. Moderate evidence: 1 low–risk of bias study and 1 or more high–risk of bias studies providing consistent findings or consistent findings reported in 2 or more high–risk of bias studies with consistent results in 75% or more of the studies.
3. Limited evidence: single-study findings from either a high–risk of bias or a low–risk of bias study.
4. Conflicting evidence: multiple studies (of either high risk or low risk of bias) that do not provide consistent results,

with consistent results in less than 75% of the studies.

# RESULTS

## Search Results

Initial searching returned a total of 4044 studies, with an additional 16 studies returned from citation tracking, ahead-of-press searches, and manual reference scanning. Following the removal of duplicates, the yield was reduced to 2293 studies. We assessed the full text of 91 studies and included 16 studies for review (**FIGURE 1**).[5,8,19-21,26,30,31,39,41,42,51-54,71] Reasons for exclusion are included in **SUPPLEMENTAL APPENDIX 3**.

## Description of Included Studies

A total of 2408 quadriceps injuries from a pool of over 11 719 athletes were captured, all from prospective cohort studies (**TABLE 1**). The majority of studies represented athletic populations from male cohorts across football (soccer)[5,8,20,21,26,30,31,39,41,42,71] and Australian football,[51,53,54] with single studies with participants from cricket,[52] and National Collegiate Athletic Association programs.[19]

## Data Analysis

Meta-analysis was precluded due to the limited number of eligible studies, the majority with a high risk of bias, heterogeneous expressions of risk estimates, different units of injury rate measurement, different approaches to the handling of continuous variables (eg, cutoff points for height, age), and the absence of raw data.

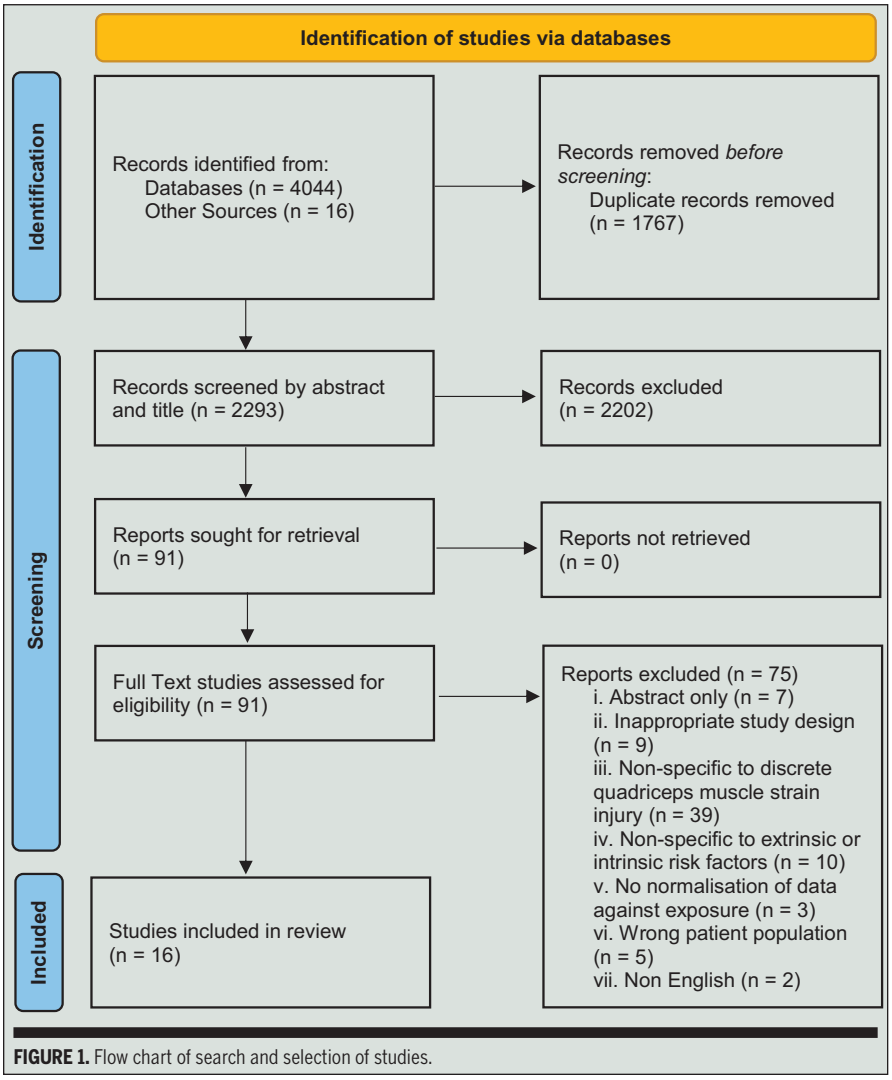


**FIGURE 1.** Flow chart of search and selection of studies.

## Risk-of-Bias Assessment and Best-Evidence Synthesis

Five studies were at low risk of bias; 11 were at high risk of bias (**TABLE 2**). The most common areas of bias across studies related to study confounding variables (14 of 16 [88%] studies were at high risk of bias) and measurement of study attrition (11 of 16 [69%] studies were at high risk of bias). The other sources of bias related to study participation (7 of 16 [44%] studies), outcome measurement (5 of 16 [32%] studies), statistical analysis and reporting (5 of 16 [32%] studies), and prognostic factor measurement (3 of 16 [19%] studies).

All studies reported univariable statistical analysis for most risk factors; 6 studies also presented further multivariable statistical methods (**TABLE 3**).

## Risk Factors for Quadriceps Muscle Injury in Athletes

**Chronological Age** There was strong evidence of no association between increasing age and quadriceps muscle strain injury in football (soccer) and Australian football athletes.

**Player Characteristics** The dominant or kicking leg had an increased risk of quadriceps strain injury when compared to the nondominant leg (strong evidence). Spinal alignment (thoracic Cobb's angle) had limited evidence of an association. There was no association between athlete body weight (strong evidence), flexibility (moderate evidence), or quadriceps eccentric strength (limited evidence) and quadriceps muscle strain injury. There was conflicting evidence for athlete height and athlete sex increasing the risk of quadriceps strain injury.

**History of Quadriceps Muscle Strain Injury** Any past history of quadriceps injury increased future injury risk (strong evidence). Recent quadriceps injury in the previous 8 weeks also elevated in-

**TABLE 1** Characteristics of Included Studies

| Study | Study Design | Sample/Sport | Number/Rate of Quadriceps Strain Injuries | Risk Factors | Injury Definition | Length of Tracking |
|---|---|---|---|---|---|---|
| Bengtsson et al (2013)[5] | Prospective cohort | First team players (n = 621, sex = male[a]) from 27 European professional football (soccer) teams from 10 countries | Quadriceps injuries (RR = 1.8/1000 hours of league match exposure) | Match load, grouped days recovery between matches, match characteristics | Acute time-loss quadriceps muscle injury diagnosed and recorded on an electronic injury registry by club medical staff | 2001-2012, 11 seasons |
| Bjørneboe et al (2010)[8] | Prospective cohort | Individual players with first team contract from 14 male Norwegian premier league football (soccer) teams (n = not reported, sex = male) | Quadriceps strains (n = 70) | Playing surface (grass vs artificial turf), training and match exposure | Acute time-loss quadriceps strain injury diagnosed and recorded on an injury form by a member of the club medical staff | 2004-2007, 4 seasons |
| Eckard et al (2017)[19] | Prospective cohort | Male and female collegiate student athletes participating in NCAA programs from 25 sports (n = not defined) | Quadriceps strains (n = 517) | Sex, event type (practice vs competition), time in season, type of sport | Quadriceps strain injuries reported by athletic trainers using the NCAA electronic health application—included both time loss and non–time loss injuries | 2009-2010 to 2014-2015 academic years, 6 seasons |
| Ekstrand et al (2011)[21] | Prospective cohort | Football (soccer) players (n = 2299, sex = male) from 51 European teams from 3 cohorts (UEFA Champions League, Swedish First League, European teams from top 2 playing home matches on artificial turf pitches) | Quadriceps muscle injuries (n = 485) | Age, leg dominance, time in match | Time-loss quadriceps muscle injury recorded by team medical staff on a standard injury form | 2001-2009, 9 seasons |
| Ekstrand et al (2011)[20] | Prospective cohort | Players (n = 767; 613 male, 154 female) from 20 first and second division football (soccer) teams from 8 European countries playing on third-generation artificial turf | Quadriceps strains (n = 96) | Playing surface, sex, event type (training vs match) | Time-loss quadriceps strain injuries reported by team medical staff on a standard injury form | 2003-2008, 7 seasons |
| Fousekis et al (2011)[26] | Prospective cohort | Players (n = 100, male) from 4 Greek National Soccer League third division teams | Quadriceps muscle strains (n = 7) | Age, weight, height, isokinetic muscle strength, flexibility, proprioception, anthropometry, knee joint stability, previous injuries | Time-loss noncontact quadriceps muscle strains recorded by the club physiotherapist on a standard questionnaire | 10 months, 1 season |
| Hägglund et al (2013)[30] | Prospective cohort | Players (n = 1401, sex = male[a]) from 26 professional football (soccer) clubs from 10 European countries | Quadriceps muscle injuries (n = 394) | Age, stature, mass, playing position, previous quadriceps muscle injury, previous other muscle injury, match-related factors, part of season, climate region | Time-loss quadriceps muscle injuries diagnosed and recorded by team medical staff on a standard injury form | 2001-2010, 9 seasons |
| Hallen and Ekstrand (2014)[31] | Prospective cohort | Professional football (soccer) teams from the top 2 divisions of 17 European countries (MRI results received from 21 clubs) (n = not defined, sex = male) | Quadriceps muscle injury with MRI examination (n = 103) | MRI grading | Time-loss quadriceps muscle injuries recorded by medical staff on a standard injury form—MRI examination performed within 24-48 hours of injury event | 2001-2013, 12 seasons |

*Table continues on next page.*

**TABLE 1** Characteristics of Included Studies (continued)

| Study | Study Design | Sample/Sport | Number/Rate of Quadriceps Strain Injuries | Risk Factors | Injury Definition | Length of Tracking |
|---|---|---|---|---|---|---|
| Kristenson et al (2013)[39] | Prospective cohort | Players (n = 1044, sex = male) from 32 clubs in the male Swedish and Norwegian football (soccer) premier leagues | Quadriceps muscle/tendon injury (acute n = 42, overuse n = 20) | Playing surface, event type (match vs training) | Time-loss quadriceps injuries recorded by a club medical team representative on a standardized form | 2010-2011, 2 seasons |
| Larruskain et al (2018)[41] | Prospective cohort | Spanish first division football (soccer) players (n = 85; male = 50, female = 35) from 1 professional club | Quadriceps strain injuries (n = 42) | Sex | Time-loss quadriceps injuries diagnosed by club medical staff and recorded in the club database | 2010-2015, 5 seasons |
| Lotfian et al (2017)[42] | Prospective cohort | Players (n = 244, sex not reported) from 16 clubs from the Iranian premier football (soccer) league | Quadriceps muscle injuries (n = 9) | Spinal alignment | Time-loss quadriceps injury, including strains, contusions, and overuse injuries, diagnosed and reported by the club doctor in an online platform | 2015-2016, 1 season |
| Orchard (2001)[51] | Prospective cohort | Elite Australian Rules football players (n = 1607, sex = male) from the AFL | Quadriceps muscle strains (n = 163) | History of quadriceps injury within previous 8 weeks, past quadriceps injury (>8 weeks ago), recent hamstring injury, age, height, weight, BMI, month of the year, dominant kicking leg, temperature on game day, rainfall in previous 7 days, evaporation in previous 7 days | Quadriceps strain injury causing a missed game clinically diagnosed by club medical staff and recorded via the AFL injury surveillance system | 1992-1999, 8 seasons |
| Orchard et al (2010)[52] | Prospective cohort | Professionally contracted Australian first-class cricket pace bowlers (n = 205, sex = male) | Quadriceps strains (n = 50) | Past history of lumbar stress fracture | Time-loss quadriceps injury diagnosed by team medical staff and recorded in the Cricket Australia Injury database | 1998-1999 to 2008-2009, 11 seasons |
| Orchard et al (2013)[54] | Prospective cohort | 229 827 Australian football player weeks from 17 AFL teams (n = not reported, sex = male) | Quadriceps strains (1.6-2.1/1000 hours) | Match climatic zone | Time-loss quadriceps injury diagnosed by club medical staff and recorded in the AFL Injury Database | 1999-2012, 4 seasons |
| Orchard et al (2020)[53] | Prospective cohort | Elite Australian football players (n = 3200, sex = male) from the AFL | Quadriceps muscle strain injuries (n = 418) | Recent quadriceps, hamstring, calf, and groin muscle strains within 8 weeks; previous quadriceps, hamstring, calf, and groin muscle injury occurring over 8 weeks ago; age; match level; substitution rule in place | Time-loss quadriceps injury diagnosed by club medical staff and recorded in the AFL Injury Database | 1992-2014, 23 seasons |
| Witvrouw et al (2003)[71] | Prospective cohort | Professional football (soccer) players (n = 146, sex = male) from 14 teams in the Royal Belgian Soccer Federation | Quadriceps muscle injuries (n = 13) | Leg dominance, quadriceps muscle flexibility | Time-loss quadriceps muscle injury documented by team physicians | 1999-2000, 1 season |

*Abbreviations: AFL, Australian Football League; BMI, body mass index; MRI, magnetic resonance imaging; n, number of participants; NCAA, National Collegiate Athletic Association; RR, rate ratio; UEFA, Union of European Football Associations.*
[a]*Sex not explicitly reported in the study but known from the data sample.*

**TABLE 2** Risk-of-Bias Assessment

| Study | Potential Risk-of-Bias Item[a] 1 | 2 | 3 | 4 | 5 | 6 | Risk of Bias |
|---|---|---|---|---|---|---|---|
| Bengtsson et al (2013)[5] | Low | High | Low | Low | High | Low | HIGH |
| Bjørneboe et al (2010)[8] | High | High | Low | Low | High | Low | HIGH |
| Eckard et al (2017)[19] | High | High | Low | High | High | Low | HIGH |
| Ekstrand et al (2011)[21] | Low | High | Low | Low | Low | Low | LOW |
| Ekstrand et al (2011)[20] | Low | High | Low | Low | High | Low | HIGH |
| Fousekis et al (2011)[26] | Low | Low | Low | High | High | Low | HIGH |
| Hägglund et al (2013)[30] | Low | Low | Low | Low | High | Low | LOW |
| Hallen and Ekstrand (2014)[31] | Low | High | Low | High | High | High | HIGH |
| Kristenson et al (2013)[39] | Low | Low | Low | Low | High | Low | LOW |
| Larruskain et al (2018)[41] | High | High | Low | Low | High | High | HIGH |
| Lotfian et al (2017)[42] | High | High | High | High | High | High | HIGH |
| Orchard (2001)[51] | Low | High | Low | Low | Low | Low | LOW |
| Orchard et al (2010)[52] | High | Low | High | Low | High | High | HIGH |
| Orchard et al (2013)[54] | High | High | Low | Low | High | Low | HIGH |
| Orchard et al (2020)[53] | Low | Low | Low | Low | High | Low | LOW |
| Witvrouw et al (2003)[71] | High | High | High | High | High | High | HIGH |
| Percentage of studies reporting high risk of bias | 7/16 (44%) | 11/16 (69%) | 3/16 (19%) | 5/16 (32%) | 14/16 (88%) | 5/16 (32%) | |

[a]*Potential risk-of-bias items: 1, study participation; 2, study attrition; 3, prognostic factor measurement; 4, outcome measurement; 5, study confounding; 6, statistical analysis and reporting.*

jury risk (strong evidence). There was no association with magnetic resonance imaging (MRI) grading of quadriceps muscle injury and recurrence rate (limited evidence).

**History of Other Injuries** Recent hamstring injury (within the previous 8 weeks) was associated with an increased risk of quadriceps muscle strain injury (strong evidence), although there was no association when accounting for hamstring injury history regardless of timing (limited evidence). Previous adductor strain, previous calf strain, and prior lumbar stress fracture had limited evidence for an association with quadriceps muscle injury.

**Match and Training Characteristics and Playing Schedule** The risk of quadriceps muscle injury was increased in matches compared to training (strong evidence), in the preseason compared to in-season (moderate evidence), and when competing in a congested schedule with decreased recovery between games (limited evidence). Injury risk decreased when participating in a higher level of competition (strong evidence) and when playing as a goalkeeper in football (limited evidence).

**Other Risk Factors** There was limited evidence of no association between temperature, rainfall on game day, evaporation in the previous week, maximum temperature, and month of the season with quadriceps muscle injury. There was a possible association between warmer climatic regions and injury risk (conflicting evidence), with some association with rainfall in the previous week (limited evidence) and quadriceps injury.

## DISCUSSION

A previous history of quadriceps muscle injury (both recent and prior) and a recent history of a hamstring strain were the strongest risk factors for quadriceps muscle strain injury. Athletes were at greater risk of quadriceps injury to their dominant (kicking) leg, with increased risk during competitive match play versus training. There was strong evidence that performing at a higher level of competition decreases quadriceps injury risk and moderate evidence of increased injury risk in the preseason period compared to the in-season period. There was strong evidence that player age and weight have no association with quadriceps muscle strain injury and moderate evidence that muscle flexibility has no association with quadriceps injury risk. There was conflicting evidence regarding the effect that sex, player height, playing surface, and climatic region have on quadriceps injury risk.

### Previous Injury as a Risk Factor for Quadriceps Strain in Sport

A past history of muscle injury is a nonmodifiable risk factor for hamstring,[28] calf,[29] and groin injury.[70] Our results confirm these findings for quadriceps muscle strain injury. Following muscle injury, maladaptive changes in the muscle can occur as a result of local tissue trauma and could negatively influence the capacity of the muscle to tolerate subsequent loads. Changes to muscle structure (decreased fascicle length,[65,66] decreased muscle volume,[4,58,61] and development of scar tissue[60]), along with ongoing neuromuscular inhibition,[27] and long-term deficits in muscle strength[14,49] have been demonstrated in previously injured quadriceps and hamstring muscles.[35,45,50] Quadriceps muscle architecture and angle of peak torque adapt in response to specific mechanical loads,[1,10,43] with reductions in rectus femoris fascicle length occurring following reduced exposure to eccentric load and periods of de-training from sport-specific tasks.[1] The reduced exposure to sport-specific stimuli following quadriceps or other lower-limb muscle injury may impact an athlete's ability to tolerate high levels of eccentric loading, especially kicking.

**TABLE 3** Results of Best-Evidence Synthesis

| Risk Factor | Studies | Participants (n) | Quadriceps Injuries (n) | Low Risk of Bias | | High Risk of Bias | | Association With Risk (increased ↑, decreased ↓, none =) | | Best-Evidence Synthesis | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Univariable | Multivariable | Univariable | Multivariable | ↑ / ↓ | = | Presence of Association | Level of Evidence |
| Age | 5 | 8607 | 1467 | 30,51,53 | | 21,26 | | | = 21,26,30,51,53 | No | Strong |
| Sex | 3 | 852+ | 655 | 20 | | 19,41 | | ↑ 19<br>↓ 20,41 | | Yes | Conflicting |
| Limb dominance | 4 | 3154+ | 1055 | 30,51 | | 21,71 | | ↑ 21,30,51 | = 71 | Yes | Strong |
| Player body mass/ weight | 3 | 3108 | 564 | 30,51 | | | 26 | | = 26,30,51 | No | Strong |
| BMI | 1 | 1607 | 163 | 51 | | | | | = 51 | No | Limited |
| Player height | 3 | 3108 | 564 | 30,51 | | | 26 | ↑ 51 | = 26,30 | Yes | Conflicting |
| Preseason period | 2 | 1401+ | 911 | 30 | | 19 | | ↑ 19,30 | | Yes | Moderate |
| Match vs practice | 4 | 1811+ | 655 | 20,39 | | 8,19 | | ↑ 8,19,20,39 | | Yes | Strong |
| Shorter between match recovery | 1 | 621 | NA | | | 5 | | ↑ 5 | | Yes | Limited |
| Level of competition | 2 | 4601 | 812 | | 30,53 | | | ↑ 30,53 | | Yes | Strong |
| Playing position | 1 | 1401 | 394 | | 30 | | | ↓ 30 | | Yes | Limited |
| Past history quadriceps injury | 3 | 6208 | 975 | | 30,51,53 | | | ↑ 30,51,53 | | Yes | Strong |
| Recent history quadriceps injury | 2 | 4807 | 581 | | 51,54 | | | ↑ 51,54 | | Yes | Strong |
| Recent hamstring injury | 2 | 4807 | 581 | | 51,53 | | | ↑ 51,53 | | Yes | Strong |
| Previous hamstring injury | 1 | 1401 | 394 | 30 | | | | | = 30 | No | Limited |
| Previous adductor injury | 1 | 1401 | 394 | | 30 | | | ↑ 30 | | Yes | Limited |
| Previous calf injury | 1 | 1401 | 394 | | 30 | | | ↑ 30 | | Yes | Limited |
| Previous lumbar stress fracture | 1 | 205 | 50 | | | 52 | | ↑ 52 | | Yes | Limited |
| Playing surface | 3 | 1044+ | 151 | 20,39 | | 8 | | ↓ 20 | = 8,39 | Yes | Conflicting |
| Time in match | 1 | 2299 | 485 | | | 21 | | ↑ 21 | | Yes | Limited |
| Eccentric strength | 1 | | | | | | 26 | | = 26 | No | Limited |
| Flexibility | 2 | 246 | 20 | | | | 26,71 | | = 26,71 | No | Moderate |
| MRI grading of injury | 1 | NA | 102 | | | 31 | | | = 31 | No | Limited |
| Spinal alignment | 1 | 244 | 9 | | | | 42 | ↓ 42 | | Yes | Limited |
| Low rainfall in previous 7 days | 1 | 1607 | 163 | | | | 51 | ↓ 51 | | Yes | Limited |
| Month of the year/ season | 1 | 1607 | 163 | | | 51 | | | = 51 | No | Limited |
| Rainfall on day of the game | 1 | 1607 | 163 | | | 51 | | | = 51 | No | Limited |
| Evaporation in previous 7 days | 1 | 1607 | 163 | | | 51 | | | = 51 | No | Limited |

*Table continues on next page.*

**TABLE 3** Results of Best-Evidence Synthesis (continued)

| Risk Factor | Studies | Participants (n) | Quadriceps Injuries (n) | Low Risk of Bias: Univariable | Low Risk of Bias: Multivariable | High Risk of Bias: Univariable | High Risk of Bias: Multivariable | Association With Risk (increased ↑, decreased ↓, none =): ↑ / ↓ | Association With Risk (increased ↑, decreased ↓, none =): = | Best-Evidence Synthesis: Presence of Association | Best-Evidence Synthesis: Level of Evidence |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Maximum temperature on day of game | 1 | 1607 | 163 | | | [51] | | | = [51] | No | Limited |
| Climatic region | 2 | 1401 | 394 | [30] | | [54] | | ↑ [54] | = [30] | Yes | Conflicting |
| Substitute rule in place (AFL) | 1 | 3200 | 418 | | [53] | | | ↓ [53] | | Yes | Limited |

*Abbreviations: +, includes studies where subject numbers were not reported; ↑, associated with increased risk of future quadriceps muscle strain; ↓, associated with decreased risk of quadriceps muscle strain injury; =, no association with future quadriceps muscle strain; AFL, Australian Football League; BMI, body mass index; MRI, magnetic resonance imaging; NA, not applicable.*



While there was limited evidence for no association between MRI grading of index quadriceps muscle injury and recurrence,[31] there is evidence that MRI assessment of the specific location and severity of quadriceps injury may be associated with changes in the rehabilitation interval.[3,11,15]

## Kicking as a Risk Factor for Quadriceps Strain in Sport

Kicking is proposed as a primary mechanism for quadriceps injury in football,[46] given the very high eccentric load requirements of the rectus femoris in the windup phase of the kick.[13] The higher incidence of quadriceps injuries in the dominant leg has been linked to heightened kicking demands.[16,64] Acute increases or fluctuations in kicking load may leave the dominant leg more at risk of quadriceps injury. Chronic exposure that does not exceed the load threshold of local quadriceps muscle tissue may generate specific protective muscular adaptations that enhance the muscles' ability to cope with this high-force activity. Graded reintroduction of kicking loads with controlled progression of the velocity component of kicking post quadriceps injury and periods of de-training has been suggested[69] to limit acute increases in load on the healing tissue and subsequent reinjury risk.

## Chronological Age as a Risk Factor for Quadriceps Strain

Unlike the hamstring and calf muscle groups where increased age has been strongly linked to an increased risk of muscle injury,[28,29] we identified no association between age and quadriceps muscle injury. The narrow age ranges of participants may contribute to the lack of association (we excluded youth athletes, and there were no data for senior or masters athletes), although studies included in this review have highlighted strong associations with increased age and injury risk in hamstring, calf, and groin muscle strain injuries in the same athlete populations.[21,30,51,53]

## No Association Between Player Characteristics and Quadriceps Strain in Sport

Player characteristics, such as weight, flexibility, and muscle strength, had varying evidence of no association with risk of quadriceps muscle strain. Improving the strength of the quadriceps muscle group has been reported as a strategy to mitigate future injury,[10,46] although only 1 high–risk of bias study has specifically investigated the link between eccentric strength and quadriceps injury.[26] As quadriceps strength is a trainable quality,[10,23,44] further investigation into the interactions between quadriceps strength and muscle architecture as well as the interventions that effectively alter these variables may be worthwhile. Regular monitoring of strength and flexibility across a season and in response to varying load exposures may be more suitable for determining a risk profile for quadriceps injury compared with a single baseline measure.[14]

## Sex Differences in Quadriceps Strain Injury Risk

The effect of sex on quadriceps injury risk was inconclusive, with conflicting evidence of injury rates in men's (increased rate in 1 low–risk of bias study[20]) and women's (increased rates in 2 high–risk of bias studies[19,41]) football (soccer) populations. Only 3 of the included studies had female participants.[19,20,41] The limited investigation of quadriceps injury in women's sport makes comparisons of injury risk between sexes difficult and should be prioritized in future research.

## Match and Training Characteristics

While variables related to individual player characteristics and environmental factors generally had limited evidence linking them to future quadriceps injury, external load variables such as match and preseason exposure were associated with quadriceps strain injury risk. Both

factors likely reflect an increased risk of injury due to changes in workload. Match play requires higher intensities of loading when compared to in-season training,[34,48,63] whereas the overall physiological load of a weekly training schedule is greater in the preseason than in-season period.[38] Acute spikes in kicking and sprinting loads occur early in the preseason following periods of decreased exposure and deconditioning in the off-season.

### Match Schedule and Level of Competition

A congested match schedule had limited evidence for an association with increased quadriceps injury risk.[5] Shorter recovery periods between matches have been linked with higher injury rates in football.[6,12,17] During periods of match congestion, increased muscle fatigue and decreased local muscle recovery prior to the subsequent match may contribute to quadriceps injury risk. The level of competition also influenced injury risk, with a greater risk identified in lower level competitions when compared to Union of European Football Associations Champions League and Australian Football League competition data.[30,53] The differences in match exposure, training loads, scheduling, game styles, and physical requirements between competition levels and their effect on quadriceps muscle recovery and function post competition may contribute to scenarios that increase the risk of quadriceps muscle injury.

### Sport and Position Played

The bias of studies included in this review toward football (soccer)[5,8,20,21,26,30,31,39,41,42,71] and Australian football[51,53,54] makes a case that specific movement patterns in these sports, possibly relating to kicking on the run, contribute to injury to the quadriceps muscles. There was limited evidence that football goalkeepers are at lower risk of quadriceps injury. Different kicking[69] and physical demands[18,68,72] are required from players in this position compared to field players. Higher quadriceps incidence rates have also been shown for backs when compared to forwards in rugby union match play,[9] which reinforces the relationship of injury risk to the physical and kicking demands of specific playing positions within each sport.

### Further Research

The limited evidence from studies with variable risk of bias indicates that future research analyzing specific risk factors for quadriceps muscle injury and their interactions in athletic populations is required. Further research in larger cohorts with wider age ranges, including female populations, that investigates the mechanism, location, and severity of quadriceps injury as well as the effect of injury on muscle architecture and capacity may be beneficial. Further analysis of the relationships between exposure to sport-specific loading variables (in particular, kicking) and quadriceps injury in preseason and match play conditions may also be of assistance to clinicians.

### Limitations

This review was prospectively planned but was not prospectively registered, and reviewers were not blinded during data extraction. These factors decrease the transparency of the review process and increase the possibility of bias. Language and publication bias are possible limitations given that only English language references were searched. The majority of studies were from male cohorts across 2 sports (predominately football [soccer] and Australian football), which limits generalizability of our results. The lack of data available precluded meta-analysis; the strength of our conclusions reflects the quality of included studies. A modified QUIPS framework was used to assess risk of bias in individual studies, although this method does not consider inconsistency, indirectness, or imprecision when assessing the certainty of evidence for individual factors and may overestimate the associations presented in this review.[36] Our conclusions reflect the small number of included studies and limited quality of evidence, which may reduce the strength of the identified associations and, clinically, may not represent all potential risk factors for quadriceps muscle strain injury.

### Clinical Implications

Understanding the risk factors for injury in sport is a key component of injury prevention strategies.[7] Athletes in kicking sports with a history of quadriceps injury or a recent hamstring injury may be at increased risk of future quadriceps injury and could benefit from specific monitoring or interventions focused on increasing quadriceps load tolerance. Understanding the complex interactions between risk factors and how these relationships may influence injury risk may be valuable to inform clinical practice in the prevention and management of quadriceps muscle strain injury.

## CONCLUSION

Recent and previous quadriceps injury, recent hamstring injury, the dominant kicking leg, and competitive match play were the strongest risk factors for future quadriceps muscle injury. Individual player characteristics, including age, weight, and flexibility, had no association with future quadriceps muscle strain.

### KEY POINTS

**FINDINGS:** A history of quadriceps injury and recent hamstring injury are strong risk factors for quadriceps muscle strain injury. The dominant kicking leg and competitive match play are also associated with an increased risk of injury. Individual player characteristics, particularly older age and weight, were not related to future quadriceps muscle strain injury.

**IMPLICATIONS:** Identification of athletes in kicking sports with a history of quadriceps injury in the dominant kicking leg can alert clinicians to which players may be at increased risk of future quadriceps injury. These athletes may benefit from focused load monitoring during periods

of greater injury risk (such as return to kicking in the preseason, during intense match play, or post injury) and from interventions focused on increasing quadriceps load tolerance.

**CAUTION:** This review was limited to a best-evidence synthesis of the literature due to high heterogeneity in the study methods and analysis types employed across the included articles. Data were taken from a small sample of studies with variable quality, across a limited number of sports (football [soccer] and Australian football), and therefore, generalizing the results to other sporting populations may be difficult.

## STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** Both authors were involved in the conception, design, study selection, quality assessment, data extraction, interpretation of the data, and preparation of the manuscript. Samuel Pietsch performed the literature search and wrote the first draft of the manuscript. Both of the authors have read and concur with the content in the final manuscript.

**DATA SHARING:** All data relevant to the study are included in the article or are available as online appendices.

**PATIENT AND PUBLIC INVOLVEMENT:** Patients or public partners were not involved in the design, conduct, or interpretation of this systematic review.



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# Benefits and Harms of Interventions With Surgery Compared to Interventions Without Surgery for Musculoskeletal Conditions: A Systematic Review With Meta-analysis



**OBJECTIVE:** To estimate the benefits and harms of interventions with and without surgery for musculoskeletal (MSK) conditions.

**DESIGN:** Intervention systematic review with meta-analysis of randomized controlled trials (RCTs).

**LITERATURE SEARCH:** MEDLINE, EMBASE, CINAHL, Web of Science, and CENTRAL, all up to January 7, 2021.

**STUDY SELECTION CRITERIA:** RCTs (English, German, Danish, Swedish, and Norwegian) of interventions with and without surgery conducted in any setting for any non-fracture MSK condition in adults (mean age: 18+ years) evaluating the outcomes on a continuous (benefits) or count (harms) scale. Outcomes were pain, self-reported physical function, quality of life, serious adverse events (SAEs), and death at 1 year.

**DATA SYNTHESIS:** Random-effects meta-analyses for MSK conditions where there were data from at least 2 trials.

**RESULTS:** One hundred RCTs (n = 12 645 patients) across 28 different conditions at 9 body sites were included. For 9 out of 13 conditions with data on pain (exceptions include some spine conditions), 11 out of 11 for function, and 9 out of 9 for quality of life, there were no clinically relevant differences (standardized mean difference of 0.50 or above) between interventions with and without surgery. For 13 out of 16 conditions with data on SAEs and 16 out of 16 for death, there were no differences in harms. Only 6 trials were at low risk of bias.

**CONCLUSION:** The low certainty of evidence does not support recommending surgery over nonsurgical alternatives for most MSK conditions with available RCTs. Further high-quality RCTs may change this conclusion. *J Orthop Sports Phys Ther 2022;52(6):312-344. doi:10.2519/jospt.2022.11075*

**KEY WORDS:** *exercise, orthopedics, placebos, randomized controlled trials, surgery, therapeutics*

Musculoskeletal (MSK) conditions affect around 1.5 billion people worldwide, with low back pain, neck pain, and osteoarthritis (OA) being some of the most common contributors to disability.[118] Since 2010, the burden from MSK conditions has increased by 20%, while low back pain and other MSK conditions are among the top 10 most important drivers of increasing burden of disease worldwide.[118] There is a clear need for safe and effective treatment options.

The balance of benefits and harms is an important consideration in shared decision making about interventions with and without surgery for MSK conditions. However, randomized controlled trials (RCTs) comparing interventions with and without surgery are less common for MSK conditions than in other fields in medicine.[61] In only 14% of trials of common MSK conditions comparing surgery to placebo surgery, nonsurgical intervention, or no intervention, there was a statistically significant and clinically relevant benefit for surgery.[37] The lack of supporting evidence for surgery was recently confirmed by an umbrella review of meta-analyses.[5] However, none of the previous reviews provided any effect sizes for benefits and

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harms for the different MSK conditions, which reduces transparency and hampers the interpretation of clinical implications.

High-quality RCTs comparing interventions with and without surgery have been published within different subgroups of MSK conditions, including meniscal tears,[55] knee OA,[110] femoroacetabular impingement syndrome,[35] shoulder impingement,[89] and lumbar spinal stenosis.[22] An updated, comprehensive overview and meta-analysis of these and other MSK conditions with effect sizes for the benefits and harms of interventions with and without surgery would support shared decision making about treatments for MSK conditions in clinical practice. Given the greater costs and risk of adverse events associated with surgery compared to the nonsurgical alternative for MSK conditions,[111,113] such overview would also provide decision makers with relevant information to prioritize which interventions to cover for specific conditions.

The aim of this systematic review was to estimate the benefits and harms of interventions with and without surgery for non-fracture MSK conditions. We extend existing knowledge by including more recent studies as well as outcomes on patient-reported pain, physical function, quality of life, and serious adverse events (SAEs) on some of the more common MSK conditions.

## METHODS

We followed the guidelines on performing systematic reviews in the *Cochrane Handbook for Systematic Reviews of Interventions*[41] and preregistered our review in the PROSPERO database (registration number CRD42015020805). In the PROSPERO registration, 2 systematic reviews are described, the other being a systematic review of surgical vs nonsurgical intervention of traumatic skeletal fractures in adults, which has been reported.[109] The present report conforms with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.[90] Patients were not included in the design, conduct, interpretation, and/or translation of the research.

### Search Strategy

We searched MEDLINE via PubMed, EMBASE via Ovid, CINAHL (including preCINAHL) via EBSCO, Web of Science via Web of Knowledge, and CENTRAL from inception to January 7, 2021. The search strategies were adjusted according to the individual database (see **SUPPLEMENTAL FILE S1**). To identify any additional trials, reference lists of the included trials as well as systematic reviews published in the last 10 years within the different MSK conditions were reviewed.

### Trial Selection

Four authors (S.T.S., E.P., A.B., and C.B.J.), independently and in pairwise comparison, assessed titles/abstracts for eligibility using selection criteria defined prior to the assessment of eligibility. If a trial was found eligible by at least 1 reviewer, the full text was retrieved. Three authors (E.P., A.B., and M.D.), independently and in pairwise comparison, evaluated the eligibility of the retrieved full-text trials, and consensus on inclusion was reached by discussion. In case of continued disagreement, a third author (C.B.J.) was consulted.

We included RCTs conducted in any setting evaluating the effect of surgical intervention in comparison with, or in addition to, nonsurgical intervention of MSK conditions in adults (mean age of trial participants: 18+ years). To be included, data that could be used for meta-analysis had to be available for pain, patient-reported physical function, quality of life, or SAE outcomes. Surgery was defined as a procedure that both changed the anatomy *and* required a skin incision or the use of an endoscopic technique.[120] A nonsurgical intervention was defined as any nonsurgical interventions, placebo interventions (including placebo surgery), or no-intervention controls. We included trials reported in English, German, Danish, Swedish, and Norwegian (ie, languages understood by the authors). No time restriction was applied for the analyses of benefits of interventions with and without surgery. However, due to increasing quality of surgery and anesthesia and expecting improved reporting of SAEs following the CONSORT (Consolidated Standards of Reporting Trials) statement published in 1996 and updated in 2001, only trials enrolling patients from 2000 were included in the harms analyses.

Trials investigating the effects of drug substances used perioperatively were excluded as it was outside the scope of the paper, whereas trials of joint distraction (not adhering to the definition of surgery), jaw disorders, and failed back surgery syndromes (including patients who already had unsuccessful surgery) were also excluded. Conference abstracts were also excluded. Sclerosant injections, radiofrequency denervation or related interventions, intradiscal electrothermal therapy, and chemonucleolysis were not considered surgical interventions.

### Outcomes

Our a priori defined outcomes were pain, patient-reported physical function, and quality of life for benefit and SAEs for harm. We prioritized data from multidimensional outcome measure instruments instead of unidimensional instruments, if data from more than 1 outcome measure were available for pain, patient-reported physical function, and quality of life. If available, pain intensity during activity was preferred over pain intensity at rest for unidimensional pain outcomes. SAEs were defined according to the U.S. Food and Drug Administration definition. SAEs were therefore defined as all adverse events that could significantly compromise the clinical outcome, result in significant disability or incapacity, require inpatient or outpatient hospital care, prolong hospital care, be life-threatening, or result in death.[116] Unless caused by an SAE, crossover from nonsurgical to surgical intervention was not considered an SAE.

### Data Extraction

A custom data extraction form was developed, and 3 authors (E.P., A.B., and M.D.) independently extracted data. Consensus on data extraction was reached by discussion. Data from the 12-month follow-up of the trials were preferred, as this is commonly used as the primary end point in trials of surgery of MSK conditions and as benefits from surgical and nonsurgical interventions are expected to be stable at 12 months.[83,112] If data were not available from a 12-month follow-up, data from the follow-up closest to 12 months were extracted. We extracted data on the number of patients randomized to interventions with and without surgery; sex; age; country of origin; pain; specific MSK condition; type of surgical and nonsurgical intervention; follow-up time; number of crossovers to surgical intervention from the nonsurgical group; number of patients not undergoing surgery in the surgical group; number of patients analyzed; mean effect and standard deviation (SD), standard error, or 95% confidence interval (CI), of pain, patient-reported physical function, and quality of life, when reported and for each group; number of SAEs in each group during follow-up; and deaths. If deaths were not mentioned in the report from the trials, death was considered as not having occurred.

### Risk-of-Bias Assessment

Risk of bias was assessed using the Risk of Bias 2.0 tool from the Cochrane Collaboration for trials that had results on benefits.[40] Two authors (E.P. and A.B.) independently assessed each of the following 5 domains: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in measurement of the outcome, and (5) bias in selection of the reported result. If multiple domains were judged as some concerns of risk of bias or if at least 1 domain was judged as high risk of bias, the overall risk of bias was judged as high, as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*.

For trials with results on SAEs, trial quality was assessed independently by the same authors using the 15-point McMaster tool for assessing quality of harms assessment and reporting in study reports (McHarm). A score greater than 9 was considered a high score and indicative of low risk of bias.[17]

Any discrepancies in the assessment of trial quality using the Risk of Bias 2.0 and McHarm tools were resolved by discussion or the involvement of a third author (C.B.J.).

### Data Synthesis and Statistical Methods

In meta-analyses, benefits were estimated as the standardized mean difference (SMD) to allow for pooling of the various outcomes used in the trials. The SMD was calculated as the difference in mean at follow-up in the surgical and nonsurgical groups divided by the pooled SD. As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*, the SD was estimated from the standard error, CI, or *P* value if it was not available.[41] If only the SD of the baseline score and the SD of the change score were available, these were used to estimate the SD of the final score.[41] The SMD was adjusted to Hedges's *g*, as Cohen's *d* tends to overestimate the effect in small studies.[41] The SMD was interpreted as proposed by Cohen,[19] ie, an SMD of 0.2 was small, an SMD of 0.5 was moderate, and an SMD of 0.8 was large. SMDs of 0.5 or larger were predefined as clinically relevant. Statistical heterogeneity was estimated as between-study variance ($\tau^2$) and $I^2$ measuring the proportion of variation (ie, inconsistency) in the combined estimates due to between-study variance. When $I^2$ is 0%, there is no inconsistency between results of individual trials, whereas inconsistency is maximal when $I^2$ is 100%.[41]

The risk of SAEs and death were estimated as relative risk (RR). Imputing half an event was used to handle zero events in either group.

Results of individual trials were pooled using a random-effects model (restricted maximum likelihood method) if at least 2 trials with relevant data on either of the outcomes were available within the individual MSK conditions.

*P* values less than .05 (2-sided) were considered statistically significant, and all analyses were carried out in Stata (Version 17.0; StataCorp LLC, College Station, TX) using the "meta" package.

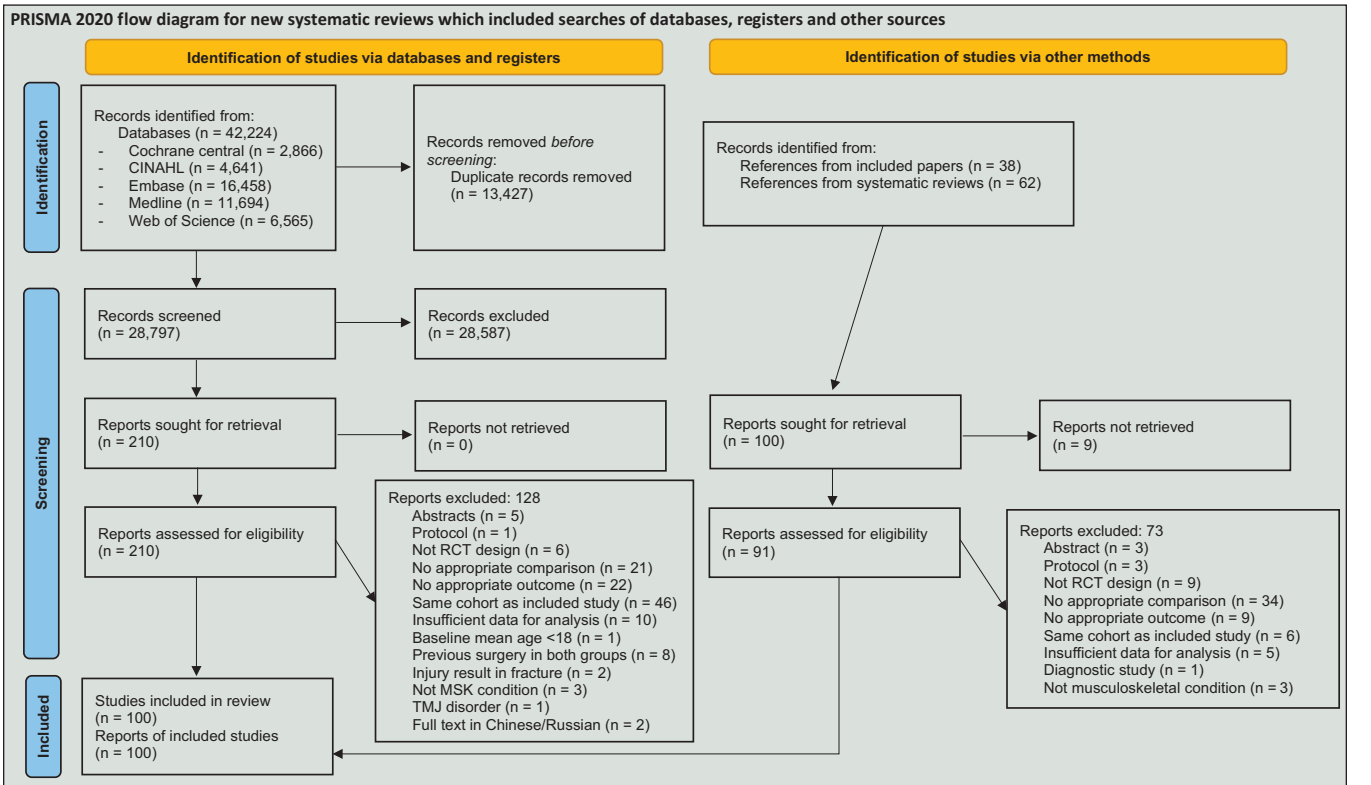
### Changes Made to the Protocol After the Initial PROSPERO Registration

A few changes were made to the protocol after the initial PROSPERO registration, but prior to conducting any analyses. This included adding the criterion to exclude trials involving patients with joint distraction, jaw disorders, and failed back surgery syndromes; excluding conference abstracts; using the updated Risk of Bias 2.0 tool from the Cochrane Collaboration instead of the older Cochrane tool; not conducting specified subgroup analysis; and restricting the language of papers to languages understood by the authors.

## RESULTS

### Characteristics of Included Trials

The literature search identified 42 224 hits; 100 were found in other sources (62 references from systematic reviews and 38 from included papers). After duplicate removal, 28 797 titles and abstracts were screened, which led us to retrieve 301 full texts. Following full-text screening, we included 100 trials (100 papers with 114 intervention comparisons) that had available data on pain, patient-reported function, quality of life, and/or SAEs (**FIGURE 1**). These trials were spread across 28 different categories of conditions at 9 body sites: *neck* (disc herniation, radiculopathy pain), *shoulder* (impingement and pain, rotator cuff tear, type II superior labral tear from anterior to posterior [SLAP] lesion, acromioclavicular dislocation, shoulder joint dislocation, frozen shoulder), *elbow* (lateral epicondylitis, ulnar neuropathy), *hand* (carpal tunnel syndrome, Dupuytren's contracture), *low back* (spinal lumbar scoliosis, chronic




*From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

**FIGURE 1.** Flow diagram showing the study selection process. Abbreviations: MSK, musculoskeletal; RCT, randomized controlled trial; TMJ, temporomandibular joint.



low back pain, lumbar disc herniation, lumbar spinal stenosis, lumbar spondylolisthesis), *pelvis* (sacroiliac joint pain, pudendal neuralgia), *hip* (femoroacetabular impingement syndrome, trochanteric pain syndrome), *knee* (patellofemoral pain syndrome, patellar dislocation, degenerative meniscus tear and OA [arthroscopic surgery], anterior cruciate ligament [ACL] tear and OA [joint replacement surgery], gouty knee arthritis), and *foot* (Achilles tendon rupture, chronic plantar heel pain).

Out of the 100 eligible trials (n = 12 645 patients), 71 had data on pain (n = 9318), 51 on function (n = 7606), 39 on quality of life (n = 5331), and 63 on SAEs (n = 7878). Degenerative meniscus tear and knee OA (arthroscopic surgery, n = 13 trials), lumbar disc herniation (n = 9), Achilles tendon rupture (n = 9), lumbar spinal stenosis (n = 8), and shoulder impingement and pain (n = 8) were the conditions most commonly investigated. Trials were carried out across 20 different countries, with the United States (n = 19), Sweden (n = 14), Finland (n = 10), and Norway (n = 9) being the most common. Out of the 100 trials, 8 included a placebo intervention (6 were placebo surgeries), 91 included a nonsurgical intervention (ranging from passive interventions such as a brace/collar and pain medication to active, supervised interventions including exercise alone or in combination with other nonsurgical interventions), and 2 included no intervention as the comparator. In 24 trials (24%), the surgical intervention group also received the same nonsurgical intervention as the nonsurgical intervention group.

Mean age and the proportion of females in the 100 trials varied between 19.3 and 76.2 years and 0% to 100%, respectively. Characteristics of the included trials and participants as well as risk-of-bias assessment are presented in **TABLE 1**, whereas a list of excluded studies following full-text screening is available in **SUPPLEMENTAL FILE S2**.

As only 1 trial with relevant data was available for SLAP lesions,[106] frozen shoulder,[100] ulnar neuropathy,[96] Dupuytren's contracture,[105] spinal lumbar scoliosis,[49] pudendal neuralgia,[101] trochanteric pain syndrome,[69] patellofemoral pain syndrome,[51] joint replacement surgery,[110] gouty knee arthritis,[119] and chronic plantar heel pain,[72] 17 categories of conditions in 9 body sites were evaluated in meta-analyses.

## Benefits: Synthesis of Results

Results from the meta-analyses for each of the categories of conditions are presented separately in **FIGURE 2** (pain), **FIGURE 3** (function), and **FIGURE 4** (quality of life).

Data from at least 2 trials were available in 13, 11, and 9 categories of conditions for pain, function, and quality of

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions

| Type of Lesion/Injury/ Condition | Author Year Country (Reference) | Participants' n, age (%Female)[a] | Surgical Intervention Group (+/- Nonsurgical Intervention) (Number of Randomized/Number Receiving Surgery) | Nonsurgical Intervention Group (Number of Randomized/Number Receiving Surgery [Crossovers]) | Self-reported Patient Outcomes[b] | Follow-up Period (Months) | Study Reporting Serious Adverse Events Yes/No[c] | Risk-of-Bias Assessment (RoB 2.0 Score) High Risk/Some Concern/Low Risk | Quality of Harm Assessment (McHarm Score) High Risk/Low Risk |
|---|---|---|---|---|---|---|---|---|---|
| Cervical disc herniation | Cesaroni and Nardi[14] 2010 Italy | 120, 46.2 (58) | Plasma disc decompression (62/62) | Multimodal (NSAID, analgesics, TENS, mobilization, collar, posture advice) (58/1) | Pain (VAS) QoL (SF-36) | 12 | Yes | Some concern | High risk |
| Cervical radiculopathy | Engquist et al[23] 2013 Sweden | 68, 46.5 (48) | Decompression + fusion and nonsurgical intervention (35/35) | Structured physiotherapy program (education, neck specific and general + stress management) (33/1) | Pain (VAS) | 12 | Yes | High risk | High risk |
| Cervical radicular pain | Persson et al[92] 1997 Sweden | 81, 47.5 (46) | Anterior decompression (27/27) | Individual physiotherapy program (TENS, heat, cold, massage, stretching, strength, aerobic) (27/1) | Pain (VAS) | 15 | † | High risk | † |
| | | | | Cervical collar (27/5) | | | | | |
| Subacromial shoulder pain | Beard et al[2] 2018 United Kingdom | 313, 53.3 (51) | Arthroscopic decompression (106/89) | Arthroscopy placebo (103/12) | QoL (EQ VAS) | 12 | Yes | Low risk | Low risk |
| | | | | No intervention (104/25) | | | | | |
| Rotator cuff impingement | Brox et al[10] 1993 Norway | 125, 47.5 (46) | Arthroscopic decompression (45/45) | Supervised progressive exercise program (mobility, strength, and scapular stability) (50/1) | Pain (NRS) | 6 | † | Some concern | † |
| | | | | Placebo (detuned laser) (30/2) | | | | Some concern | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Rotator cuff disease | Cederqvist et al[13]<br>2020<br>Finland | 190, 56 (46) | Arthroscopic subacromial decompression<br>(95/59) | Physiotherapist-led rehabilitation program (mobility and strength exercises and manual therapy)<br>(95/12) | Pain (VAS)<br>PF (RAND-36 PF)<br>QoL (RAND-36) | 24 | Yes | Some concern | High risk |
| Subacromial impingement syndrome | Farfaras et al[26]<br>2016<br>Sweden | 87, 47.6 (55) | Open acromioplasty<br>(24/18)<br>Arthroscopic acromioplasty<br>(29/24) | Physiotherapy program (mobility, resistive, and stability exercises)<br>(17/0) | Pain (SF-36 bodily pain)<br>PF (SF-36 PF) | 31 | † | High risk | † |
| Subacromial impingement | Haahr et al[36]<br>2005<br>Denmark | 90, 44.4 (69) | Arthroscopic decompression<br>(45/45) | Multimodal (heat, cold, supervised exercise program [mobility, strength, stability])<br>(45/6) | Pain (NRS)<br>PF (NRS) | 12 | † | Some concern | † |
| Shoulder impingement syndrome | Ketola et al[50]<br>2009<br>Finland | 140, 47.1 (63) | Acromioplasty + nonsurgical intervention<br>(70/58) | Multimodal (information, resistive and stability exercises, ad hoc NSAID and injection)<br>(70/5) | Pain (VAS)<br>PF (shoulder disability VAS) | 12 | Yes | Some concern | High risk |
| Rotator cuff calcification | Maugars et al[66]<br>2009<br>France | 53, 46.2 (77) | Bursoscopy<br>(20/20)<br>Needling fragmentation irrigation<br>(16/16) | NSAID and analgesics on request<br>(17/7) | Pain (VAS)<br>PF (VAS) | 12 | † | High risk | † |
| Shoulder impingement syndrome | Paavola et al[89]<br>2018<br>Finland | 193, 50.4 (68) | Subacromial decompression<br>(59/59) | Supervised progressive exercise program (mobility, strength, and scapular stability)<br>(71/0)<br>Diagnostic arthroscopy<br>(63/0) | Pain (VAS)<br>QoL (15D HR) | 24 | Yes | Some concern<br>Low risk | Low risk |
| Non-traumatic rotator cuff tears | Kukkonen et al[58]<br>2014<br>Finland | 180, 65 (53) | Acromioplasty + nonsurgical intervention<br>(60/60)<br>Acromioplasty + rotator cuff repair + nonsurgical intervention<br>(60/60) | Supervised progressive exercise program (mobility, strength, and scapular stability)<br>(60/4) | Pain (constant pain sub-score)<br>PF (constant ADL sub-score) | 12 | Yes | Some concern | High risk |
| Degenerative rotator cuff tears | Lambers Heerspink et al[59]<br>2015<br>The Netherlands | 56, 60.6 (38) | Rotator cuff repair and partly removal of acromion<br>(25/25) | Multimodal (physiotherapy, steroid injections, and analgesics)<br>(31/3) | Pain (VAS)<br>PF (VAS) | 12 | Yes | High risk | High risk |

*Table continues on page 318.*

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions (continued)

| Type of Lesion/Injury/Condition | Author Year Country (Reference) | Participants' n, age (%Female)[a] | Surgical Intervention Group (+/- Nonsurgical Intervention) (Number of Randomized/Number Receiving Surgery) | Nonsurgical Intervention Group (Number of Randomized/Number Receiving Surgery [Crossovers]) | Self-reported Patient Outcomes[b] | Follow-up Period (Months) | Study Reporting Serious Adverse Events Yes/No[c] | Risk-of-Bias Assessment (RoB 2.0 Score) High Risk/Some Concern/Low Risk | Quality of Harm Assessment (McHarm Score) High Risk/Low Risk |
|---|---|---|---|---|---|---|---|---|---|
| Rotator cuff tears | Moosmayer et al[73] 2010 Norway | 103, 60.0 (29) | Surgical repair (52/51) | Physiotherapy rehabilitation program (posture control, stability, strength exercises) (51/9) | Pain (VAS)<br>PF (SF-36 PF)<br>QoL (SF-36 total) | 12 | Yes | High risk | High risk |
| Small and acute traumatic rotator cuff tears | Ranebo et al[99] 2020 Sweden | 58, 59.7 (45) | Arthroscopic repair (32/32) | Active physiotherapist-led exercises (26/1) | Pain (constant pain sub-score)<br>PF (constant ADL sub-score)<br>QoL (EQ-5D VAS) | 12 | Yes | Some concern | High risk |
| Shoulder lesion (type II SLAP) | Schrøder et al[106] 2017 Norway | 118, 41.0 (40) | Labral repair (40/40)<br>Biceps tenodesis (39/39) | Placebo surgery (40/7) | QoL (EQ-5D VAS) | 12 | Yes | Low risk | Low risk |
| Acute acromioclavicular dislocation | McKee et al[67] 2015 Canada | 83, 37.6 (6) | Surgical reduction and fixation (40/38) | Sling + standard physiotherapy program (mobility, resistive, and strength exercises) (43/1) | No relevant PROM | 12 | Yes | -------- | High risk |
| Acute acromioclavicular dislocation | Murray et al[79] 2018 United Kingdom | 60, 30.5 (6) | Surgical reduction and fixation (29/29) | Sling + physiotherapy program (mobility, resistive, and strength exercises) (31/5) | PF (SF-12 PCS)<br>QoL (SF-12 PCS) | 12 | Yes | Some concern | High risk |
| Traumatic (first) shoulder joint dislocation | Kirkley et al[54] 1999 Canada | 40, 22.4 (13) | Arthroscopic labral repair + nonsurgical intervention (19/19) | Immobilization and rehabilitation (mobility, resistive, stability, and strength exercises) (21/7) | PF (WOSI PF)<br>QoL (WOSI lifestyle) | 34 | † | High risk | † |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Traumatic (first) shoulder joint dislocation | Robinson et al[102] 2008 United Kingdom | 88, 24.8 (7) | Arthroscopic Bankart lesion repair (43/43) | Arthroscopic examination and lavage (45/13) | Not able to extract data | 24 | Yes | -------- | Low risk |
| Shoulder joint dislocation | Zhang et al[126] 2017 China | 60, 33.8 (8) | Arthroscopic anchor implantation (30/not reported) | Manual reposition (30/not reported) | Pain (VAS) | 11 | Yes | High risk | High risk |
| Primary frozen shoulder | Rangan et al[100] 2020 United Kingdom | 302, 54.3 (63) | Arthroscopic capsular release + manipulation under anesthesia + nonsurgical intervention (203/162) | Nonsurgical intervention (99/1) | Pain (NRS)<br>QoL (EQ-5D-5L) | 12 | Yes | Low risk | Low risk |
| Lateral epicondylitis | Kroslak and Murrell[57] 2018 Australia | 26, 52 (73) | Surgical excision of the extensor carpi radialis brevis (13/13) | Placebo surgery (13/0) | No relevant PROM | 6 | Yes | -------- | High risk |
| Lateral epicondylitis | Radwan et al[98] 2008 Egypt | 62, 39.7 (41) | Tenotomy (27/27) | Shockwave therapy (29/0) | Pain (VAS) | 12 | No | Some concern | -------- |
| Ulnar neuropathy | Pompe et al[96] 2020 The Netherlands | 117, 53.3 (44) | Decompression (56/50) | Written instructions (61/7) | Pain (VAS) | 12 | Yes | High risk | High risk |
| Carpal tunnel syndrome | Fernández-de-las Peñas et al[27] 2015 Spain | 120, 46.5 (100) | Open or arthroscopic tunnel decompression and release (60/60) | Manual therapy (mobilization, nerve tension gliding exercises) (60/3) | Pain (NRS)<br>PF (BCTQ) | 12 | Yes | Some concern | High risk |
| Carpal tunnel syndrome | Gerritsen et al[33] 2002 The Netherlands | 176, 49.0 (81) | Open tunnel release (87/14) | Splinting (89/0) | PF (functional status score) | 12 | † | Some concern | † |
| Carpal tunnel syndrome | Hui et al[43] 2005 Hong Kong, China | 50, 49.0 (96) | Open tunnel release (25/25) | Steroid injection (25/0) | No relevant PROM | 5 | Yes | -------- | High risk |
| Carpal tunnel syndrome | Jarvik et al[44] 2009 USA | 116, 50.7 (53) | Decompression (57/42) | Multimodal (NSAID, exercises, education) (59/19) | Pain (NRS)<br>PF (CTSAQ function score)<br>QoL (SF-36) | 12 | No | Some concern | -------- |
| Carpal tunnel syndrome | Ly-Pen et al[62] 2012 Spain | 101, 51.5 (92) | Decompression (54/11) | Local steroid injection (47/1) | Pain (VAS)<br>PF (VAS) | 12 | † | High risk | -------- |
| Carpal tunnel syndrome | Ucan et al[115] 2006 Turkey | 57, 44.5 (93) | Open tunnel release (11/11) | Splinting (23/0)<br>Splinting + steroid injection (23/0) | PF (BQ functional score) | 6 | Yes | High risk | High risk |

*Table continues on page 320.*

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions (continued)

| Type of Lesion/Injury/ Condition | Author Year Country (Reference) | Participants' n, age (%Female)[a] | Surgical Intervention Group (+/- Nonsurgical Intervention) (Number of Randomized/Number Receiving Surgery) | Nonsurgical Intervention Group (Number of Randomized/Number Receiving Surgery [Crossovers]) | Self-reported Patient Outcomes[b] | Follow-up Period (Months) | Study Reporting Serious Adverse Events Yes/No[c] | Risk-of-Bias Assessment (RoB 2.0 Score) High Risk/Some Concern/Low Risk | Quality of Harm Assessment (McHarm Score) High Risk/Low Risk |
|---|---|---|---|---|---|---|---|---|---|
| Dupuytren's contracture | Scherman et al[105] 2016 Sweden | 83, 67 (13) | Needle fasciotomy (45/45) | Collagenase injection followed by manipulation (38/0) | Pain (VAS) | 12 | Yes | High risk | High risk |
| Spinal lumbar scoliosis | Kelly et al[49] 2019 USA | 63, 63 (83) | Spinal fusion (30/23) | Individualized physical therapy (strengthening and aerobic exercises), facet injections, and NSAID (33/15) | No relevant PROM | 12 | Yes | -------- | Low risk |
| Chronic low back pain with disc degeneration | Boody et al[6] 2020 USA | 38 (age and sex not reported) | Lumbar interspinous spacer (23/23) | Pain medication and injections, patient education, and physical therapy (15/12) | No relevant PROM | 24 | Yes | -------- | High risk |
| Chronic low back pain | Brox et al[9] 2003 Norway | 64, 43.4 (61) | Lumbar fusion (37/33) | Multimodal (cognitive + exercise therapy [education, endurance, strength, coordination]) (90/5) (27/1) | Pain (VAS)<br>PF (general function score VAS)<br>QoL (general life satisfaction score) | 12 | † | Some concern | † |
| Chronic low back pain | Fairbank et al[25] 2005 United Kingdom | 349, 40.1 (51) | Lumbar spinal fusion (176/169) | Education + exercise program (173/48) | Pain (SF-36 bodily pain)<br>PF (SF-36 PF)<br>QoL (SF-36 total) | 24 | † | Some concern | † |
| Chronic low back pain | Fritzell et al[30] 2001 Sweden | 294, 43.2 (51) | Lumbar spinal fusion (222/198) | Multimodal (education, exercise, injections, acupuncture, TENS, cognitive therapy) (72/7) | Pain (VAS)<br>PF (general function score VAS) | 24 | † | Some concern | † |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Chronic low back pain with disc degeneration | Hellum et al[38] 2011 Norway | 179, 41.0 (53) | Lumbar disc prosthesis (89/77) | Multimodal (cognitive + exercise therapy [education, endurance, strength, coordination]) (90/5) | Pain (VAS)<br>PF (SF-36 PF)<br>QoL (SF-36 total) | 12 | Yes | Some concern | High risk |
| Chronic discogenic low back pain | Ohtori et al[85] 2011 Japan | 41, 33.9 (43) | Lumbar interbody fusion (15/15)<br>Lumbar posterior lateral fusion (6/6) | Daily walking and stretching exercises (20/0) | Pain (VAS) | 12 | No | High risk | -------- |
| Lumbar disc herniation | Bailey et al[1] 2020 Canada | 128, 37.6 (41) | Microdiscectomy (64/56) | Patient education and injections (64/22) | Pain (VAS)<br>PF (SF-36 PCS)<br>QoL (SF-36 PCS) | 12 | Yes | High risk | High risk |
| Lumbar disc herniation | Buttermann[11] 2004 USA | 100, 40.5 (sex distribution not reported) | Lumbar discectomy (50/2) | Epidural steroid injection (50/27) | Pain (VAS) | 12 | † | High risk | † |
| Lumbar disc herniation | Erginousakis et al[24] 2011 Greece | 62, 37.0 (42) | Percutaneous disc decompression (31/31) | Multimodal (analgesics, NSAID, muscle relaxants, physiotherapy) (31/0) | Pain (NRS) | 12 | Yes | Some concern | High risk |
| Lumbar disc herniation | Gerszten et al[34] 2010 USA | 90, 44.1 (51) | Plasma disc decompression (46/46) | Epidural steroid injection (44/0) | Pain (VAS) | 6 | Yes | High risk | High risk |
| Lumbar disc herniation | McMorland et al[68] 2010 Canada | 40, 41.8 (40) | Lumbar microdiscectomy (20/17) | Spinal manipulative therapy (20/8) | Pain (McGill present pain intensity score)<br>PF (SF-36 PF)<br>QoL (SF-36 total) | 3 | Yes | Some concern | High risk |
| Lumbar disc herniation | Nikoobakht et al[82] 2016 Iran | 177, 37.8 (55) | Percutaneous disc decompression (89/89) | Multimodal (education, NSAID, injections, manual therapy, exercises) (88/0) | Pain (VAS)<br>PF (SF-36 PF)<br>QoL (SF-36 PCS) | 12 | Yes | Some concern | High risk |
| Lumbar disc herniation | Österman et al[87] 2006 Finland | 56, 37.5 (39) | Lumbar microdiscectomy (28/28) | Active exercise program (stretching and strengthening) (28/11) | Pain (VAS)<br>QoL (15D HR) | 12 | † | High risk | † |
| Lumbar disc herniation | Peul et al[94] 2007 The Netherlands | 283, 42.6 (34) | Nerve root decompression using annular fenestration (141/141) | Multimodal (coping strategies, activity advice, analgesics if needed) (142/55) | Pain (VAS)<br>PF (SF-36 PF)<br>QoL (general health VAS) | 12 | Yes | Some concern | High risk |

*Table continues on page 322.*

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions (continued)

| Type of Lesion/Injury/ Condition | Author Year Country (Reference) | Participants' n, age (%Female)[a] | Surgical Intervention Group (+/- Nonsurgical Intervention) (Number of Randomized/Number Receiving Surgery) | Nonsurgical Intervention Group (Number of Randomized/Number Receiving Surgery [Crossovers]) | Self-reported Patient Outcomes[b] | Follow-up Period (Months) | Study Reporting Serious Adverse Events Yes/No[c] | Risk-of-Bias Assessment (RoB 2.0 Score) High Risk/Some Concern/Low Risk | Quality of Harm Assessment (McHarm Score) High Risk/Low Risk |
|---|---|---|---|---|---|---|---|---|---|
| Lumbar disc herniation | Weinstein et al[122] 2006 USA | 501, 42.3 (41) | Open discectomy (245/138) | Active physical therapy, patient education, and NSAID (256/103) | Pain (SF-36 bodily pain) PF (SF-36 PF) | 12 | Yes | Some concern | Low risk |
| Lumbar spinal stenosis | Benyamin and Staats[3] 2016 USA | 302, 75.3 (76) | Interlaminar spinal canal decompression (149/143) | Interlaminar epidural steroid injection (153/18) | Pain (VAS) PF (ZCQ PF) | 12 | Yes | High risk | Low risk |
| Lumbar spinal stenosis | Brown[8] 2012 USA | 38, 76.2 (45) | Interlaminar spinal canal decompression (21/21) | Epidural steroid injection (17/0) | Pain (VAS) | 1.5 | Yes | High risk | High risk |
| Lumbar spinal stenosis | Delitto et al[21] 2015 USA | 169, 68.1 (48) | Lumbar decompression incl. laminectomy (87/2) | Physical therapy program (education, flexion, conditioning and strengthening exercises) (82/45) | PF (SF-36 PF) | 12 | Yes | High risk | High risk |
| Lumbar spinal stenosis | Hsu et al[42] 2006 USA | 191, 69.6 (45) | Lumbar interspinous decompression (100/100) | Multimodal (education, exercises, massage, heat, cold, belts) (91/0) | Pain (SF-36 bodily pain) PF (SF-36 PF) QoL (SF-36 total) | 12 | No | High risk | High risk |
| Lumbar spinal stenosis | Malmivaara et al[63] 2007 Finland | 94, 62.5 (67) | Lumbar interspinous decompression and facetectomy (50/46) | Multimodal individual intervention (NSAID, education, activity advice, exercises, TENS, ultrasound) (44/4) | Pain (VAS walking) | 12 | † | Some concern | † |
| Lumbar spinal stenosis | Puzzilli et al[97] 2014 Italy | 542, 63.6 (47) | Lumbar interspinous decompression (422/422) | Multimodal (NSAID, opioids, epidural injections, orthosis, physiotherapy, SMT) (120/20) | Not able to extract PROM (no SD reported) | 53 | Yes | -------- | High risk |
| Lumbar spinal stenosis | Weinstein et al[123] 2008 USA | 289, 65.5 (38) | Lumbar spinal decompressive laminectomy (138/87) | Multimodal (active physical therapy, NSAID, exercise, education) (151/63) | Pain (SF-36 bodily pain) PF (SF-36 PF) | 12 | Yes | Some concern | Low risk |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Lumbar spinal stenosis | Zucherman et al[127] 2005 USA | 200, 69.6 (45) | Interlaminar spinal canal decompression (100/100) | Multimodal (epidural steroid injection, NSAID, physical therapy) (100/17) | Not able to extract PROM | 12 | Yes | -------- | High risk |
| Lumbar spondylolisthesis | Möller and Hedlund[76] 2000 Sweden | 114, 39.0 (49) | Lumbar posterior lateral fusion (80/80) | Supervised exercise program (strength, posture) (34/3) | Pain (VAS)<br>PF (Disability Rating Index) | 12 | † | High risk | † |
| Lumbar degenerative spondylolisthesis | Weinstein et al[121] 2007 USA | 304, 66.0 (66) | Posterior decompression laminectomy and fusion (159/101) | Multimodal (active physical therapy, exercise, education, counseling, NSAID) (145/71) | Pain (SF-36 bodily pain)<br>PF (SF-36 PF) | 24 | Yes | High risk | High risk |
| Sacroiliac joint pain | Dengler et al[22] 2017 Germany | 109, 48.1 (73) | Sacroiliac joint fusion (54/54) | Multimodal (education, mobility and strength exercises, pain medication, cognitive therapy) (55/21) | Pain (VAS)<br>QoL (EQ-5D VAS) | 12 | Yes | Some concern | High risk |
| Sacroiliac joint pain | Polly et al[95] 2015 USA | 158, 51.3 (70) | Sacroiliac joint fusion (109/109) | Multimodal (physical therapy, exercise, pain medication and NSAID, steroid injection) (49/0) | Pain (VAS)<br>QoL (SF-36 PCS) | 6 | Yes | Some concern | Low risk |
| Pudendal neuralgia | Robert et al[101] 2005 France | 32, 54.1 (72) | Surgical decompression (16/14) | Multimodal (steroid injection, behavioral therapy, antidepressant) (16/0) | Pain (VAS) | 12 | † | High risk | † |
| Femoroacetabular impingement syndrome | Griffin et al[35] 2018 United Kingdom | 348, 35.3 (39) | Hip arthroscopy (171/171) | Multimodal (individual exercise, education, steroid injection) (177/163) | QoL (EQ-5D VAS) | 12 | Yes | Some concern | Low risk |
| Femoroacetabular impingement syndrome | Mansell et al[65] 2018 USA | 80, 30.1 (41) | Hip arthroscopy (40/38) | Physical therapy program (mobilization, motor control, stability and strength exercises) (40/28) | PF (HOS ADL)<br>QoL (iHOT-33) | 12 | Yes | Some concern | High risk |
| Femoroacetabular impingement syndrome | Palmer et al[91] 2019 United Kingdom | 222, 36.2 (66) | Hip arthroscopy (112/99) | Individualized physiotherapy (strengthening and movement control) and activity control (110/6) | Pain (HAGOS pain)<br>PF (HOS ADL)<br>QoL (HAGOS QoL) | 8 | Yes | Some concern | High risk |

*Table continues on page 324.*

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions (continued)

| Type of Lesion/Injury/ Condition | Author Year Country (Reference) | Participants' n, age (%Female)[a] | Surgical Intervention Group (+/- Nonsurgical Intervention) (Number of Randomized/Number Receiving Surgery) | Nonsurgical Intervention Group (Number of Randomized/Number Receiving Surgery [Crossovers]) | Self-reported Patient Outcomes[b] | Follow-up Period (Months) | Study Reporting Serious Adverse Events Yes/No[c] | Risk-of-Bias Assessment (RoB 2.0 Score) High Risk/Some Concern/Low Risk | Quality of Harm Assessment (McHarm Score) High Risk/Low Risk |
|---|---|---|---|---|---|---|---|---|---|
| Trochanteric pain syndrome | Meknas et al[69] 2009 Norway | 12, 47.0 (75) | Surgical release of the internal obturator tendon (6/6) | No intervention (6/0) | Pain (VAS) | 6 | † | High risk | † |
| Patellofemoral pain syndrome | Kettunen et al[51] 2007 Finland | 56, 28.4 (63) | Arthroscopy + nonsurgical intervention (28/28) | Home exercise program (stretching and strengthening exercises) (28/3) | Pain (VAS on activity) | 9 | No | Some concern | -------- |
| Patellar dislocation | Bitar et al[4] 2012 Brazil | 39, 24.0 (48) | MPF ligament reconstruction (21/21) | Brace and physical therapy (range of motion and strengthening exercises) (18/0) | No relevant PROM | 44 | Yes | -------- | High risk |
| Patellar dislocation | Camanho et al[12] 2009 Brazil | 33, 25.7 (61) | MPF ligament repair (17/17) | Splinting and physical therapy (strengthening and stretching exercises) (16/0) | No relevant PROM | 38 | Yes | -------- | High risk |
| Patellar dislocation | Christiansen et al[18] 2008 Denmark | 80, 20.0 (45) | Arthroscopy (reinsertion of MPF ligament) + nonsurgical intervention (43/43) | Bracing (37/0) | Pain (KOOS pain) PF (KOOS ADL) QoL (KOOS QoL) | 24 | † | Some concern | † |
| Patellar dislocation | Ji et al[45] 2017 China | 62, no age (64) | Open relocation and MPF ligament repair (32/32) | Initial immobilization, rehabilitation (mobility and strength exercises) (30/0) | No relevant PROM | 42 | Yes | -------- | High risk |
| Patellar dislocation | Nikku et al[81] 1997 Finland | 125, 19.1 (66) | Surgical realignment (70/70) | Casting and orthosis (55/9) | Pain (VAS activity) | 25 | † | High risk | † |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Patellar dislocation | Petri et al[93] 2013 Germany | 24, 24.6 (35) | Open repair with suturing + nonsurgical intervention (14/14) | DonJoy brace followed by progressive weightbearing (10/0) | No relevant PROM | 24 | Yes | -------- | High risk |
| Knee meniscal symptoms | Gauffin et al[32] 2014 Sweden | 150, 54.0 (27) | Arthroscopy + nonsurgical intervention (75/66) | Structured unsupervised exercise program (muscle strength and postural control) (75/16) | Pain (KOOS pain)<br>PF (KOOS ADL)<br>QoL (KOOS QoL) | 12 | Yes | High risk | High risk |
| Degenerative medial meniscal tears | Herrlin et al[39] 2007 Sweden | 99, 55.4 (39) | Arthroscopy (meniscectomy) (53/53) | Supervised exercise therapy program (flexibility, strength, endurance, balance) (46/3) | Pain (KOOS pain)<br>PF (KOOS ADL)<br>QoL (KOOS QoL) | 6 | No | Some concern | -------- |
| Knee meniscus tear | Katz et al[47] 2013 USA | 351, 58.5 (57) | Arthroscopy (meniscectomy) + nonsurgical intervention (174/174) | Supervised physical therapy program (mobility, strength, cardiovascular, balance) (177/59) | Pain (KOOS pain)<br>PF (WOMAC PF) | 12 | Yes | High risk | Low risk |
| Degenerative knee meniscal tear | Kise et al[55] 2016 Norway | 140, 49.5 (38) | Arthroscopy (meniscectomy) (70/70) | Supervised neuromuscular and strength exercise program (70/13) | Pain (KOOS pain)<br>PF (KOOS ADL)<br>QoL (KOOS QoL) | 12 | Yes | Some concern | Low risk |
| Knee meniscus tear | Roos et al[103] 2018 Denmark | 44, 46.8 (48) | Arthroscopy (partial meniscectomy) (22/22) | Placebo arthroscopy (22/8) | Pain (KOOS pain)<br>PF (KOOS ADL)<br>QoL (KOOS QoL) | 24 | Yes | Some concern | Low risk |
| Degenerative knee meniscal tear | Sihvonen et al[108] 2013 Finland | 146, 52.3 (39) | Arthroscopy (meniscectomy) (70/70) | Placebo arthroscopy (76/4) | Pain (NRS)<br>QoL (WOMET) | 12 | Yes | Low risk | Low risk |
| Knee meniscus tear | van de Graaf et al[117] 2018 The Netherlands | 321, 57.5 (50) | Arthroscopy (partial meniscectomy) (159/42) | Supervised exercise program (cardiovascular, balance, strength) (162/47) | Pain (VAS activity)<br>PF (IKDC score) | 12 | Yes | Some concern | Low risk |
| Degenerative medial meniscal tears | Yim et al[125] 2013 Japan | 108, 56.8 (79) | Arthroscopy (meniscectomy) (54/54) | Supervised exercise program (strength, endurance, flexibility) + analgesics and NSAID (54/1) | Pain (VAS) | 12 | No | Some concern | -------- |
| Degenerative meniscus injury | Østerås et al[88] 2012 Norway | 17, 49.7 (24) | Arthroscopy (meniscectomy) (8/8) | Exercise program (aerobic, weightbearing) (9/0) | Pain (VAS) | 3 | No | Some concern | -------- |

*Table continues on page 326.*

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions (continued)

| Type of Lesion/Injury/ Condition | Author Year Country (Reference) | Participants' n, age (%Female)[a] | Surgical Intervention Group (+/- Nonsurgical Intervention) (Number of Randomized/Number Receiving Surgery) | Nonsurgical Intervention Group (Number of Randomized/Number Receiving Surgery [Crossovers]) | Self-reported Patient Outcomes[b] | Follow-up Period (Months) | Study Reporting Serious Adverse Events Yes/No[c] | Risk-of-Bias Assessment (RoB 2.0 Score) High Risk/Some Concern/Low Risk | Quality of Harm Assessment (McHarm Score) High Risk/Low Risk |
|---|---|---|---|---|---|---|---|---|---|
| Knee OA – arthroscopic | Chang et al[15] 1993 USA | 32, 62.8 (72) | Arthroscopy (18/18) | Needle joint lavage (14/2) | Pain (AIMS VAS) PF (AIMS PF) QoL (overall well-being scale VAS) | 12 | † | Some concern | † |
| Knee OA – arthroscopic | Kirkley et al[53] 2008 Canada | 188, 59.6 (63) | Arthroscopy (debridement and lavage) (94/88) | Multimodal (supervised exercise therapy, advice, NSAID, steroid injections) (94/0) | Pain (WOMAC pain) PF (WOMAC PF) | 12 | † | Some concern | † |
| Knee OA – arthroscopic | Moseley et al[74] 2002 USA | 180, 52.4 (8) | Arthroscopy (debridement) (59/59) | Lavage (arthroscopic) (61/0) Placebo arthroscopy (60/0) | Pain (SF-36 bodily pain) PF (SF-36 PF) | 12 | † | Low risk | † |
| Knee OA – arthroscopic | Moseley et al[75] 1996 USA | 12, 46.4 (0) | Arthroscopy (debridement) (4/4) | Lavage (arthroscopic) (3/0) Placebo arthroscopy (5/0) | Pain (NRS) | 6 | † | Some concern | † |
| Anterior cruciate ligament (ACL) tear | Frobell et al[31] 2010 Sweden | 141, 26.1 (26) | Arthroscopy (ACL reconstruction) + nonsurgical intervention (69/69) | Structured rehabilitation (exercises for range of motion, muscle function, functional performance) (72/23) | Pain (KOOS pain) PF (KOOS ADL) QoL (KOOS QoL) | 25 | Yes | Some concern | Low risk |
| ACL rupture | Meunier et al[71] 2007 Sweden | 100, 21.6 (33) | Open ACL reconstruction + nonsurgical intervention (44/44) | Rehabilitation program (strength and coordination) (56/16) | Pain (KOOS pain) PF (KOOS ADL) QoL (KOOS QoL) | 180 | † | High risk | † |
| ACL rupture | Tsoukas et al[114] 2016 Greece | 32, 31 (0) | Arthroscopic ACL reconstruction + nonsurgical intervention (17/17) | Rehabilitation program (knee brace, proprioception and strength exercises) (15/0) | No relevant PROM | 121 | Yes | -------- | High risk |
| Knee OA – total knee replacement | Skou et al[110] 2015 Denmark | 100, 66.4 (62) | Total knee arthroplasty + nonsurgical intervention (50/49) | Multimodal (neuromuscular exercise program, education, diet, analgesics) (50/13) | Pain (KOOS pain) PF (KOOS ADL) QoL (KOOS QoL) | 12 | Yes | Some concern | Low risk |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Gouty knee arthritis | Wang et al[119]<br>2015<br>China | 60, 42.3 | Arthroscopy (debridement) + nonsurgical intervention<br>(30/30) | Gout suppressant oral medication (colchicine, allopurinol)<br>(30/0) | Pain (NRS) | 11 | Yes | Some concern | High risk |
| Achilles rupture | Keating and Will[48]<br>2011<br>United Kingdom | 80, 40.6 (25) | Surgical repair + nonsurgical intervention<br>(39/59) | Cast<br>(41/1) | No relevant PROM | 12 | Yes | -------- | High risk |
| Achilles rupture | Fischer et al[28]<br>2021<br>Germany | 90, 41.0 (10) | Open surgical repair + nonsurgical intervention<br>(30/30)<br>Minimal invasive surgical repair + nonsurgical intervention<br>(30/28) | Cast, walker, and rehabilitation program<br>(30/1) | PF (SF-36 PCS)<br>QoL (SF-36 PCS) | 24 | Yes | High risk | High risk |
| Achilles rupture | Lantto et al[60]<br>2016<br>Finland | 60, 39.3 (8) | Surgical repair + nonsurgical intervention<br>(32/32) | Cast + orthosis + rehabilitation<br>(28/0) | Pain (RAND-36 pain)<br>PF (RAND-36 PF) | 18 | Yes | Some concern | High risk |
| Achilles rupture | Manent et al[64]<br>2019<br>Spain | 34, 41.1 (9) | Percutaneous repair + nonsurgical intervention<br>(11/11)<br>Open repair + nonsurgical intervention<br>(12/12) | Cast + rehabilitation protocol<br>(11/0) | Pain (NRS) | 12 | Yes | Some concern | High risk |
| Achilles rupture | Metz et al[70]<br>2008<br>The Netherlands | 83, 40.0 (20) | Surgical repair<br>(42/41) | Cast + functional bracing<br>(41/2) | No relevant PROM | 12 | Yes | -------- | High risk |
| Achilles rupture | Möller et al[77]<br>2001<br>Sweden | 112, 39.1 (12) | Surgical repair<br>(59/59) | Plaster cast<br>(53/3) | QoL (VAS) | 2 | † | Some concern | † |
| Achilles rupture | Nilsson-Helander et al[84]<br>2010<br>Sweden | 100, 41.0 (19) | Surgical repair + nonsurgical intervention<br>(50/49) | Cast + adjustable brace<br>(50/2) | PF (ATRS PF) | 12 | Yes | Some concern | High risk |
| Achilles rupture | Olsson et al[86]<br>2013<br>Sweden | 100, 40.0 (14) | Surgical repair + nonsurgical intervention<br>(49/49) | Brace + rehabilitation<br>(51/5) | PF (ATRS PF)<br>QoL (FAOS) | 12 | Yes | Some concern | High risk |
| Achilles rupture | Willits et al[124]<br>2010<br>Canada | 144, 40.4 (18) | Surgical repair + nonsurgical intervention<br>(72/72) | Orthosis + rehabilitation<br>(72/2) | No relevant PROM | 12 | Yes | -------- | High risk |
| Chronic plantar heel pain | Molund et al[72]<br>2018<br>Norway | 40, 45.5 (78) | Gastrocnemius recession + nonsurgical intervention<br>(20/20) | Stretching exercises<br>(20/0) | Pain (VAS)<br>PF (SF-36 PF) | 12 | Yes | Some concern | High risk |

*Table continues on page 328.*

**TABLE 1** Characteristics of Trial Participants, Trial Characteristics, and Risk-of-Bias Assessment of Included Trials of Interventions With and Without Surgery for Musculoskeletal Conditions (continued)

*Abbreviations: ADL, activities of daily living; AIMS, Arthritis Impact Measurement Scale; ATRS, Achilles tendon Total Rupture Score; BCTQ, Boston Carpal Tunnel Questionnaire; BQ, Boston Questionnaire; CTSAQ, Carpal Tunnel Syndrome Assessment Questionnaire; EQ, EuroQual; FAOS, Foot and Ankle Outcome Score; FIS-AP, Foot Impact Scale activity limitation and participation restriction; HR-QoL, health-related quality of life; IKDC, International Knee Documentation Committee; MFPDI, Manchester Foot Pain and Disability Index; NRS, numeric rating scale; PROM, patient-reported outcome measure; SMT, spinal manipulative therapy; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; WOMET, Western Ontario Meniscal Evaluation Tool; WOSI, Western Ontario Shoulder Instability; ZCQ, Zurich Claudication Questionnaire.*
*[a]n = number of participants randomized; age = mean age.*
*[b]Pain score, physical functional score, and/or quality-of-life score.*
*[c]Studies initiating patient recruitment prior to January 2000 are categorized with a "+."*

life, respectively. For 7 categories of conditions, SMDs favored the surgical intervention (+/− nonsurgical intervention) group for at least 1 outcome (ie, statistically significant greater improvements in pain, function, or quality of life); the difference was only clinically relevant for 4 conditions (all on pain). For cervical disc herniation and radiculopathy pain (3 trials[14,23,92]), the SMD (95% CI) was 1.53 (0.90, 2.16) (n = 255 patients, clinically relevant difference) for pain, whereas for lumbar disc herniation (9 trials[1,11,24,34,68,82,87,94,122]), the SMDs (95% CIs) for pain and function were 0.38 (0.13, 0.62) (n = 1269) and 0.36 (0.02, 0.70) (n = 1002), respectively. For lumbar spinal stenosis (6 trials[3,8,21,42,63,123]), the SMDs (95% CIs) for pain and function were 0.57 (0.34, 0.80) (n = 841, clinically relevant difference) and 0.24 (0.08, 0.40) (n = 857), respectively. The SMDs (95% CIs) for chronic low back pain (5 trials,[9,25,30,38,85] 6 comparisons) for pain and function were 0.97 (0.17, 1.77) (n = 784, clinically relevant difference) and 0.29 (0.04, 0.54) (n = 743), respectively. For sacroiliac joint pain (2 trials[22,95]), the SMD (95% CI) for pain was 1.13 (0.63, 1.62) (n = 241, clinically relevant difference), whereas it was 0.35 (0.14, 0.56) (n = 769) for shoulder impingement and pain (7 trials[10,13,26,36,50,66,89]). For degenerative meniscal tears (6 trials[15,32,39,55,103,108]), the SMD (95% CI) for quality of life was 0.29 (0.09, 0.49) (n = 569).

There were no other statistically significant differences between surgery +/− nonsurgical intervention and nonsurgical intervention, placebo surgery, or no-intervention controls for any of the 13 categories of conditions for pain, function, or quality of life.

### Benefits: Risk of Bias

**TABLE 1** presents an overview of risk-of-bias assessment for benefits for the individual trials, whereas **SUPPLEMENTAL FILE S3** presents the detailed description of risk of bias for benefits.

Six trials[2,74,89,100,106,108] were judged as low risk of bias: 2 on shoulder impingement and pain,[2,89] 2 on degenerative meniscus tear and OA,[74,108] 1 on type II SLAP shoulder lesions,[106] and 1 on frozen shoulder.[100] Thirty trials[1,3,8,11,21,23,26,28,32,34,42,47,54,59,62,66,69,71,73,76,81,85,87,92,96,101,105,115,121,126] were at high risk of bias, mainly no blinding of participants, intervention providers, and assessors; large number of crossovers to surgery; and few available statistical analysis plans and/or protocols.

### Harms: Synthesis of Results

The syntheses of the results on harms are presented in **FIGURE 5** (SAEs) and **SUPPLEMENTAL FILE S4** (deaths).

SAEs were analyzed according to the group that the patients were initially randomized to (ie, the intention-to-treat population). Acknowledging that SAEs also happened after crossing over from nonsurgical treatment to surgery during time to follow-up, the risk of SAEs was smaller in patients who were initially randomized to surgery (+/− nonsurgical intervention) for shoulder dislocation (2 trials[102,126]; RR [95% CI], 0.29 [0.11, 0.78]; n = 144), ACL tear (2 trials[31,114]; RR [95% CI], 0.67 [0.53, 0.85]; n = 153), and patellar dislocation (4 trials[4,12,45,93]; RR [95% CI], 0.32 [0.15, 0.70]; n = 150). None of the 16 categories of conditions with available data on deaths from at least 2 trials demonstrated any differences.

### Harms: Risk of Bias

**TABLE 1** presents an overview of risk-of-bias assessment for harms for the individual trials, whereas **SUPPLEMENTAL FILE S5** presents the detailed description of risk of bias for harms.

The risk of bias associated with the assessment and reporting of SAEs and death was moderate. Seventeen trials[2,3,31,35,47,49,55,89,95,100,103,106,108,110,117,122,123] had a score greater than 9, indicating a low risk of bias.

## DISCUSSION

For 9 out of the 13 categories of conditions with available data on pain from at least 2 trials, there were

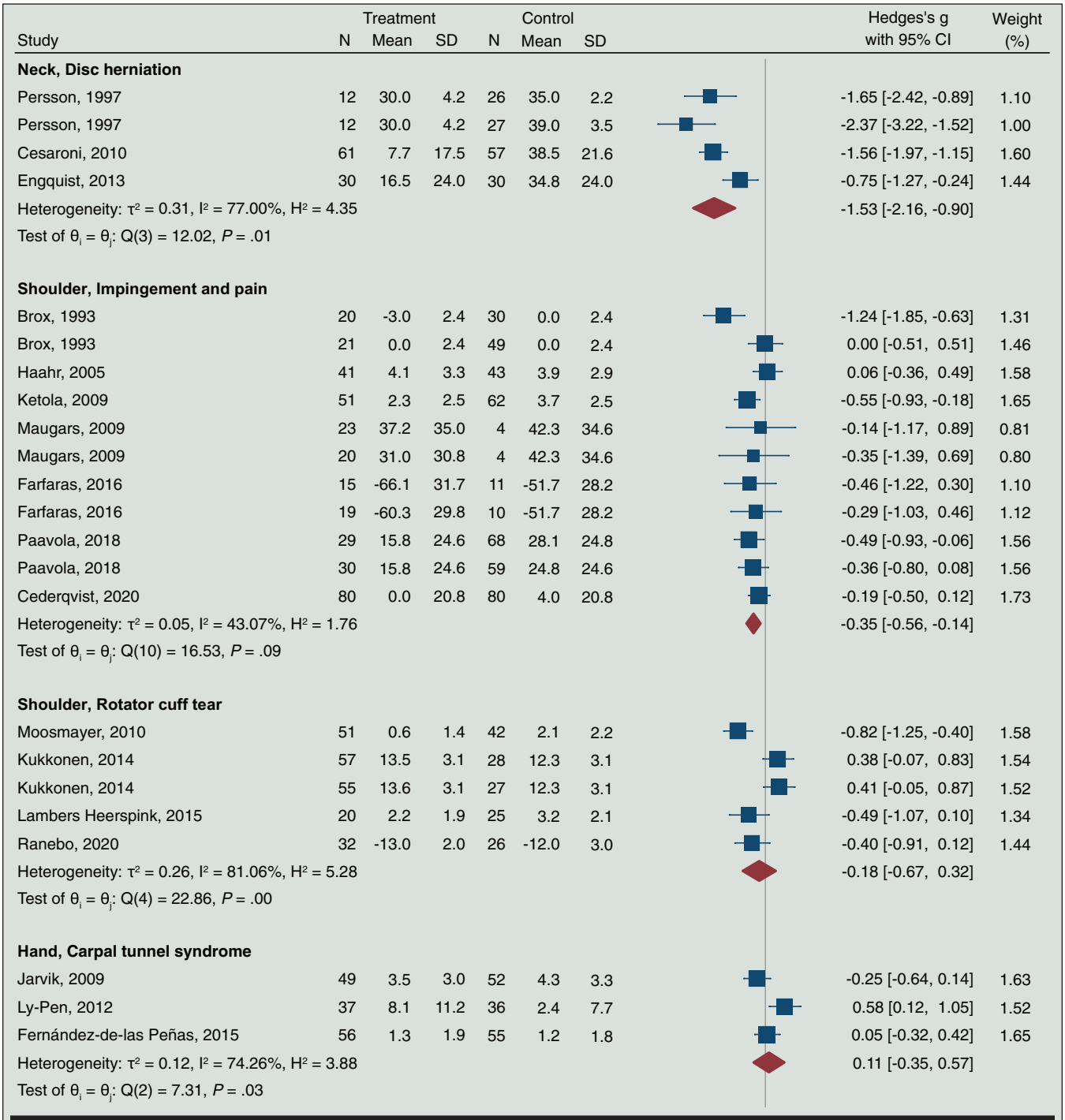



**FIGURE 2.** Effects of interventions with and without surgery on pain. Categories of conditions are ordered after body site going from the neck to the foot. Abbreviations: CI, confidence interval; OA, osteoarthritis; REML, restricted maximum likelihood; SD, standard deviation.



no clinically relevant differences (significant differences with at least a moderate effect size) between interventions with and without surgery. The corresponding number was 11 out of 11 for function and 9 out of 9 for quality of life.

The risk of SAEs was lower in patients who were initially randomized to surgery for shoulder dislocation, ACL tear, and patellar dislocation. However, it is likely that this apparent difference is confounded by SAEs in patients crossing over from

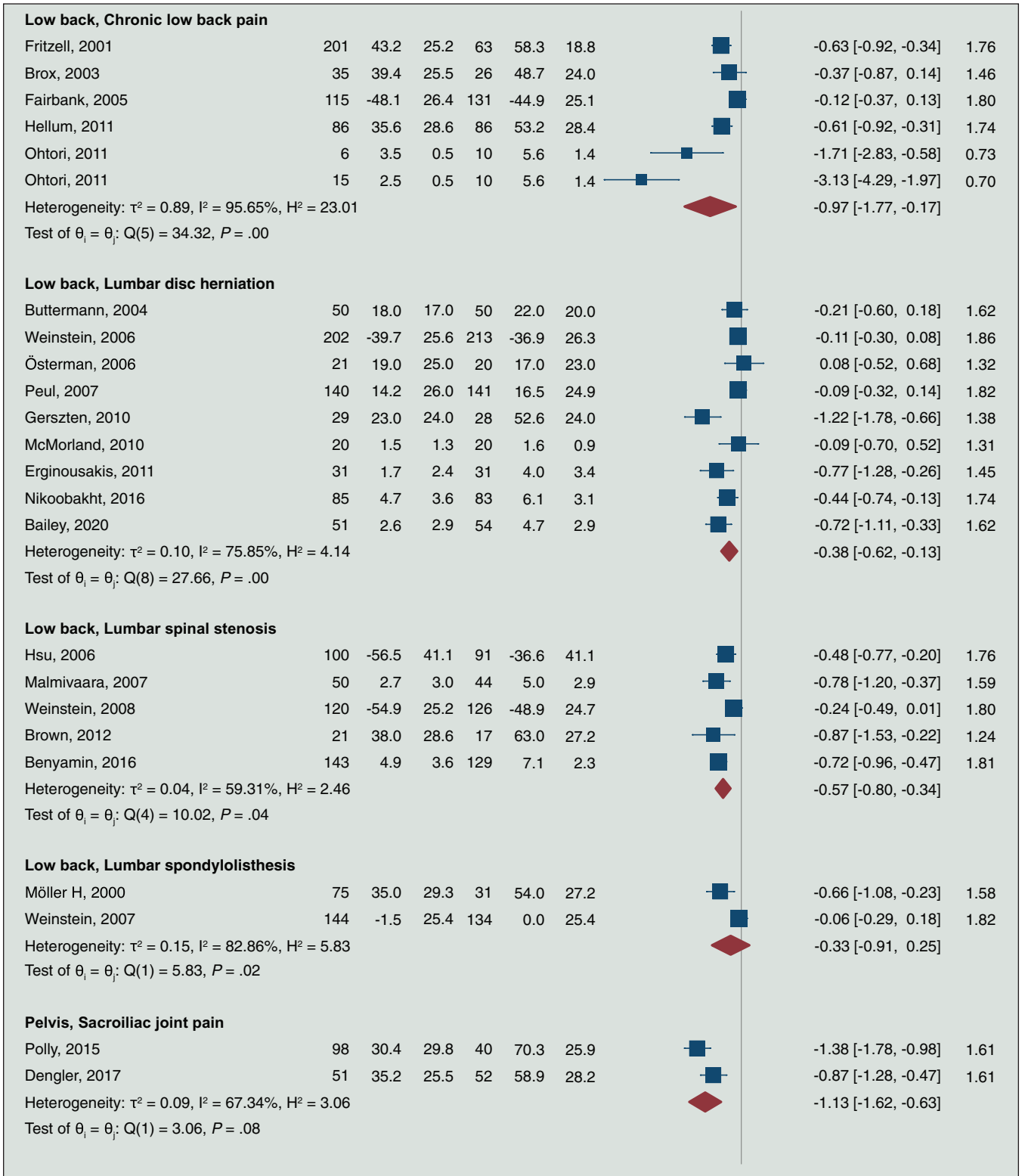



**FIGURE 2.** Continued.

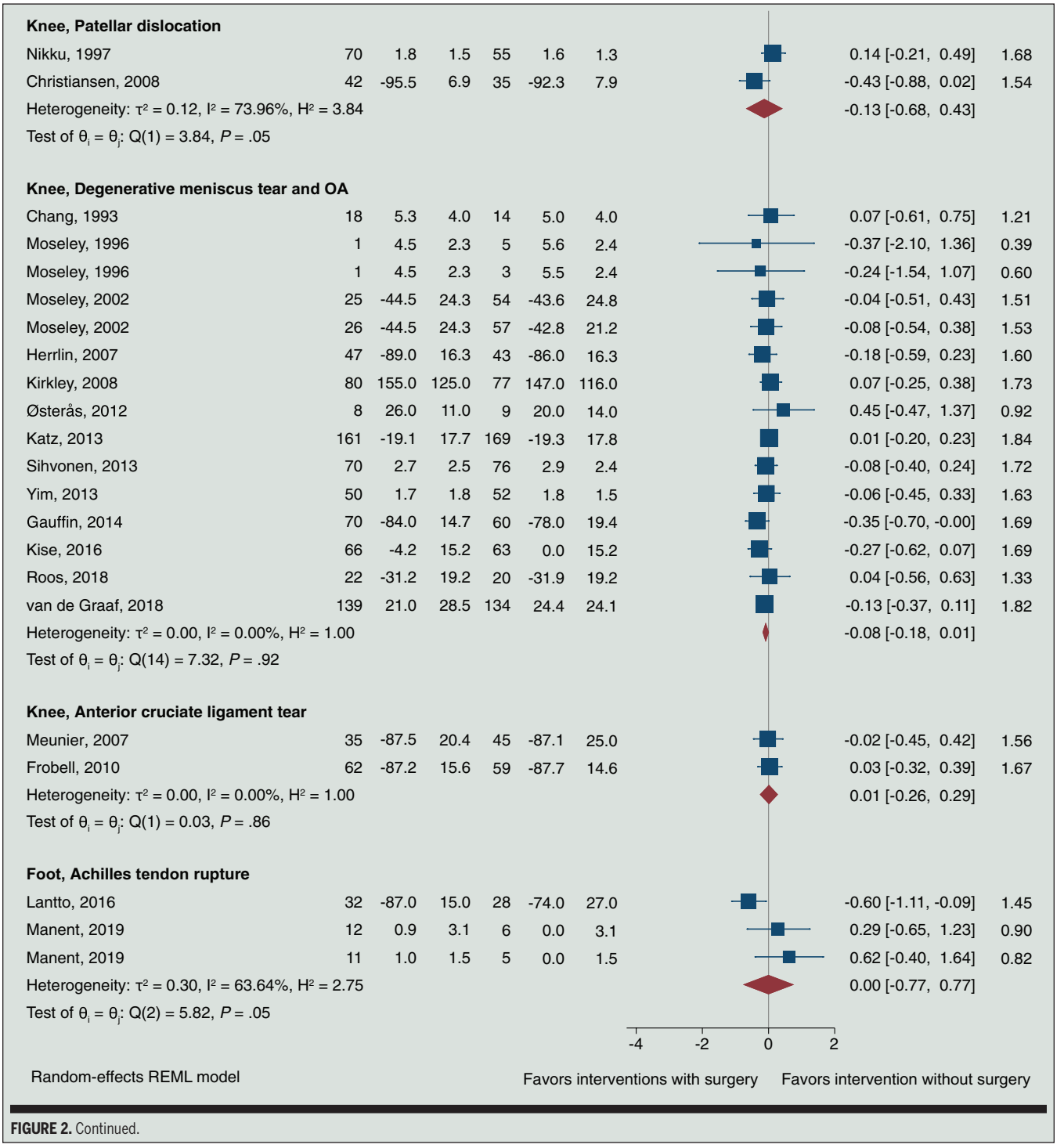



**FIGURE 2.** Continued.



a without-surgery trial arm to surgery and often missing or inconsistent reporting of SAEs.

There is a lack of trials for many MSK conditions, and only 2 conditions (shoulder impingement and pain and degenerative meniscus tear and OA) had at least 2 studies with low risk of bias where there were no clinically relevant differences. The SMDs and RRs were accompanied by large 95% CIs and high statistical heterogeneity, limiting our confidence in these results. High-quality trials are needed for most MSK conditions to guide patients and clinicians in the shared decision mak-

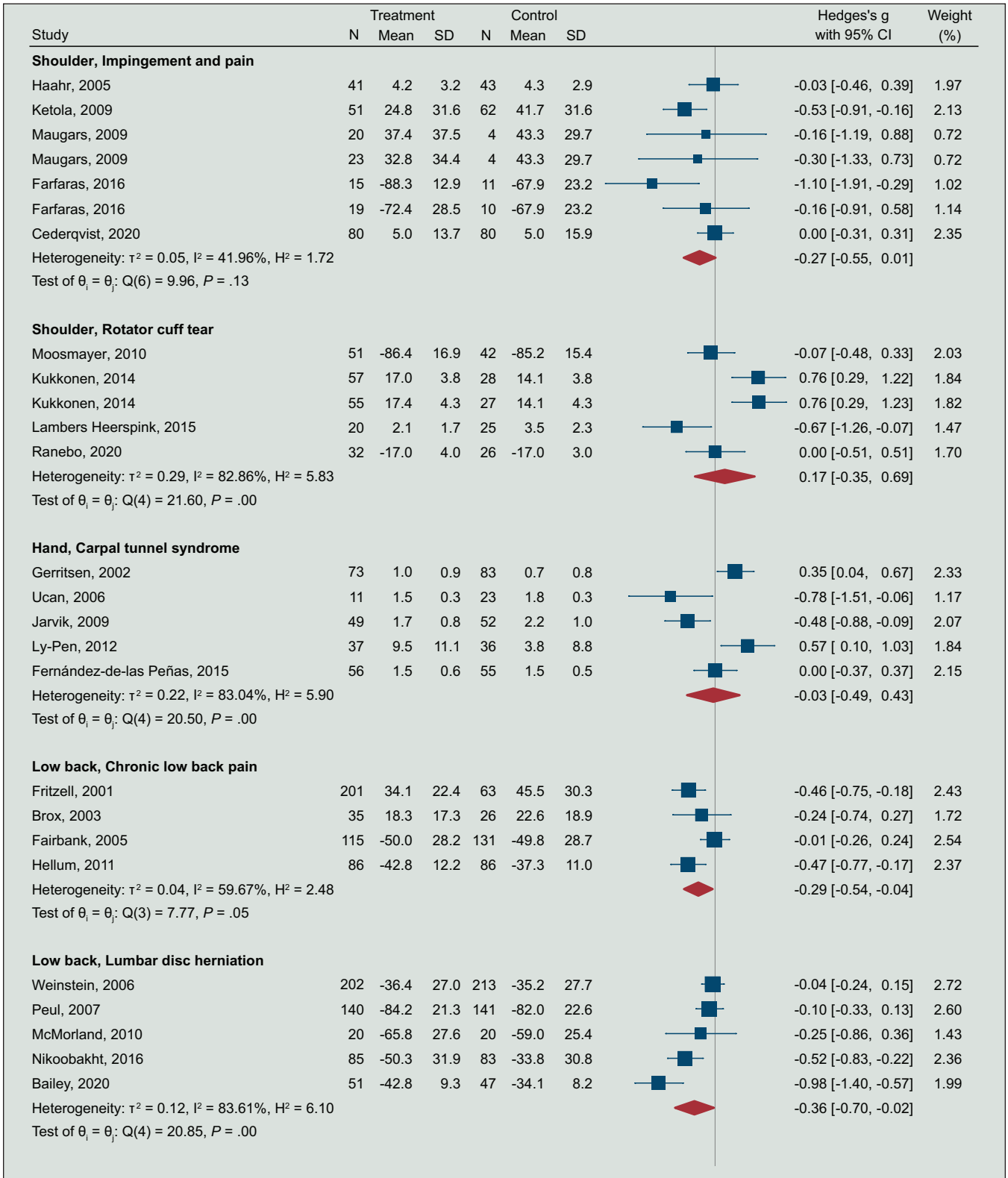



**FIGURE 3.** Effects of interventions with and without surgery on function. Categories of conditions are ordered after body site going from the neck to the foot. Abbreviations: CI, confidence interval; OA, osteoarthritis; REML, restricted maximum likelihood; SD, standard deviation.

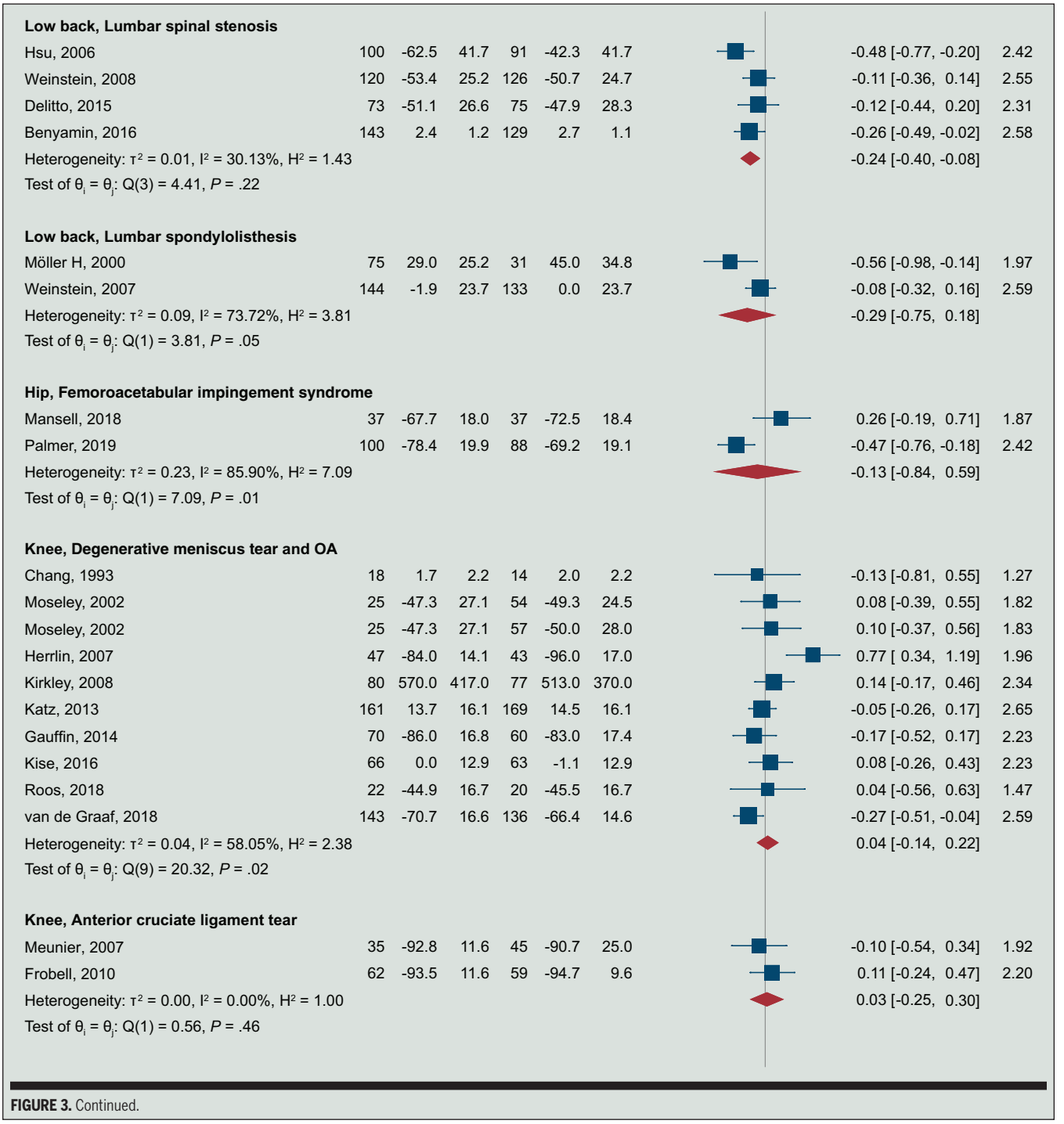



**FIGURE 3.** Continued.



ing process and provide decision makers with relevant information to prioritize treatments in health care.

In our meta-analysis, surgery appeared to lead to a greater improvement of at least moderate effect size on pain for only 4 out of 13 conditions (cervical disc herniation [3 studies], lumbar spinal stenosis [5 studies], sacroiliac joint pain [2 studies], and chronic low back pain [5 studies]), whereas it did not demonstrate greater improvement in function and quality of life for any conditions. The clinically relevant greater effect of surgery for the 4 conditions is interesting as it challenges

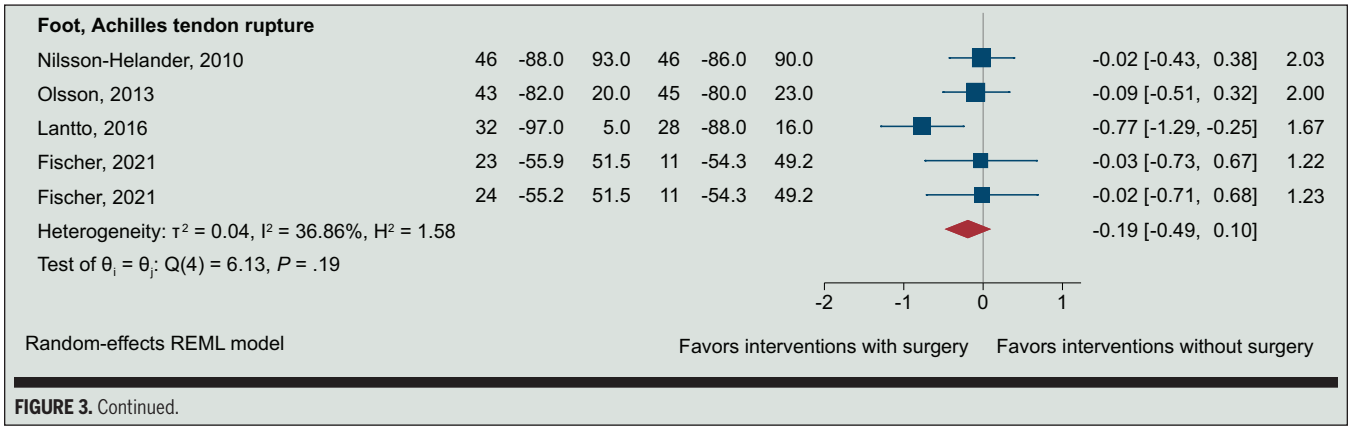



**FIGURE 3.** Continued.

the current understanding that surgery has a very limited role, if any, as treatment for MSK conditions like low back pain.[29]

Although we found statistically significant improvements in favor of surgery for 3 other conditions (quality of life for degenerative meniscal tears, pain for shoulder impingement and pain, and pain and function for lumbar disc herniation), the differences were small and may not be clinically relevant (SMDs of 0.29-0.38). When interpreting our findings, it is important to recognize that neither of the studies with an apparent clinically relevant difference in favor of the surgical group were of low risk of bias; that, for some conditions, pain is not considered the primary indication for intervention (eg, ACL injury, Achilles tendon rupture); and that crossover from nonsurgical to surgical intervention is common, which potentially affects the SMDs and confounds interpretation of results.

A recent umbrella review of meta-analyses of RCTs of 10 common orthopedic procedures compared to nonsurgical intervention, placebo surgery, or no-intervention controls reported contrasting results to our systematic review.[5] The contrasting findings included superiority of surgery over nonsurgical intervention for carpal tunnel syndrome but no difference in effects for lumbar spine decompression and fusion. Potential explanations for the discrepancies with our results include our focus on conditions rather than procedures (eg, for the low back pain conditions), the inclusion of newer trials in our review, the exclusion of trials with insufficient data or outcomes that could not be included in meta-analyses (eg, outcomes combining pain and function in 1 measure), and differences in follow-up times.

## Clinical Implications

Our results with few clinically relevant benefits favoring surgery for MSK conditions confirm findings from previous systematic reviews,[37,46] 1 of which showed that only 14% of trials comparing surgery to nonsurgical intervention, placebo surgery, or no intervention of common MSK conditions demonstrated a clinically relevant benefit from surgical intervention.[37] By quantifying benefits and harms and assessing risk of bias, our study adds weight to previous research and suggests that, for many conditions, best practice nonsurgical interventions are viable alternatives to surgery. Even for patients where nonsurgical treatment is not sufficiently effective, evidence supporting the effects of surgery is missing. For some conditions, surgery is even recommended against by clinical guidelines and does not provide additional benefit to nonsurgical treatment.[107] Interestingly, some studies have demonstrated that even after surgery, the costs[56] and need for further nonsurgical care[52,78] can be high, suggesting that undergoing successful surgery in terms of improved pain and function is not necessarily associated with reduced societal burden of MSK conditions or does not necessarily result in the surgical intervention being more cost effective as an alternative or in addition to nonsurgical interventions in a 2- to 5-year perspective.[52,113]

We found a greater risk of SAEs in patients with shoulder dislocation, ACL tear, and patellar dislocation initially randomized to nonsurgical intervention as compared to surgical intervention and no difference in SAEs for any of the other 12 conditions. Our results challenge the common belief that nonsurgical interventions are safer than surgery and are in contrast to previous systematic reviews, which suggest that surgery is associated with an increased risk of SAEs[46] and that exercise therapy is not.[80] The greater risk of SAEs for the 3 conditions in our study can partially be explained by the fact that a large proportion of patients with shoulder dislocation (30%) and ACL tear (27%) crossed over to surgery during follow-up and that SAEs happened after crossing over to surgery. Our results on SAEs should be evaluated with this in mind and with caution, given the large inconsistency of results in the included studies and often missing reporting of SAEs. The nonexistent consensus in terms and definitions of SAEs calls for the development and validation of a core set of SAEs for different MSK conditions.[7]

MSK conditions are the second most common indication for surgery worldwide, only exceeded by unintentional

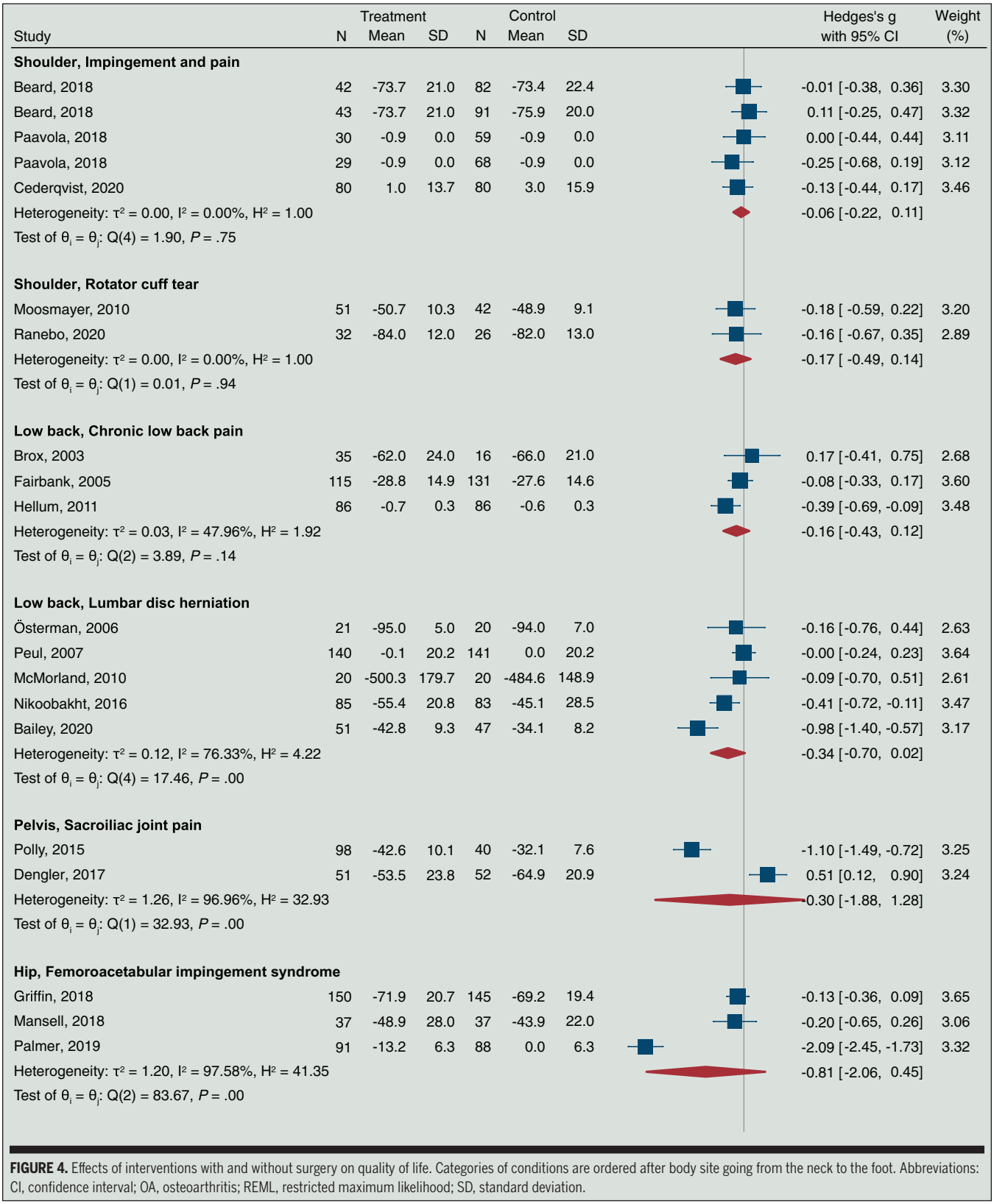



**FIGURE 4.** Effects of interventions with and without surgery on quality of life. Categories of conditions are ordered after body site going from the neck to the foot. Abbreviations: CI, confidence interval; OA, osteoarthritis; REML, restricted maximum likelihood; SD, standard deviation.

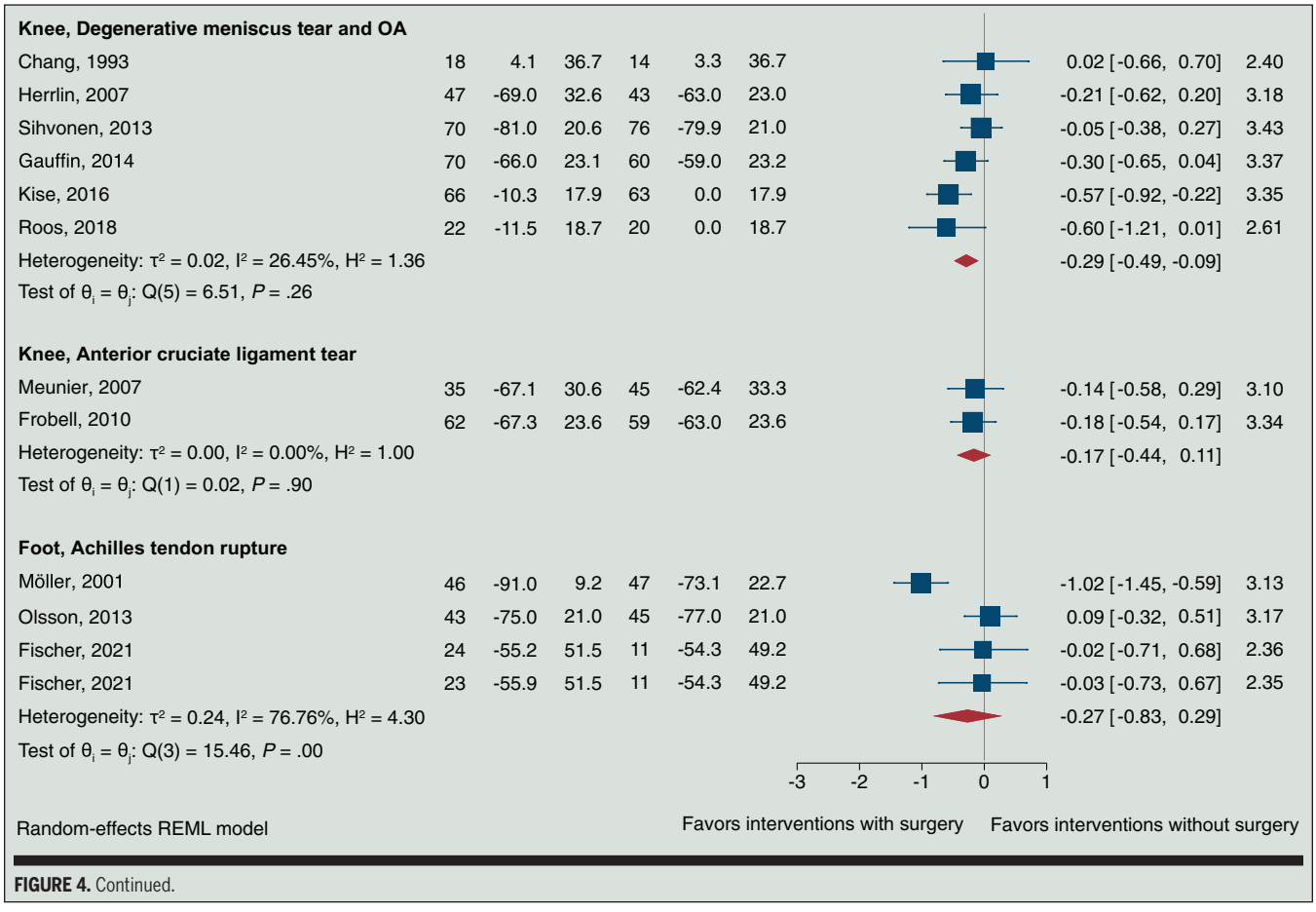



**FIGURE 4.** Continued.



injuries (ie, not caused by self-harm), which often also affect the MSK system.[104] Our study adds to a previous systematic review suggesting that surgical intervention of MSK conditions had less RCT support compared to other surgical procedures and that less than 1% of available RCTs on surgery for MSK conditions had compared surgery to not performing the surgical procedure (eg, by offering nonsurgical intervention).[37] Some of the surgical procedures remain still recommended by national guidelines for specific subgroups and under certain conditions.[5] Comparing surgical and nonsurgical interventions of traumatic skeletal fractures, we found similar results.[109] For fractures and other MSK conditions, there are large variations in indication for and type of surgical and nonsurgical care. Our results cannot be generalized to all MSK conditions, and the absence of available evidence supporting surgical intervention is not proof of the absence of a superior effect of surgery over placebo or nonsurgical intervention, or the converse.

A recent systematic review on the evidence behind orthopedic surgery guidelines found that around 50% of trials were at high risk of bias and underpowered and that the robustness of the trials was largely low, as only minor changes in the results would nullify significant results.[16] In our review, only 6 trials (2 on shoulder impingement and pain,[2,89] 2 on degenerative meniscus tear and OA,[74,108] 1 on type II SLAP shoulder lesions,[106] and 1 on frozen shoulder[100]) were of low risk of bias, precluding any sensitivity analysis of studies with low risk of bias. The lack of possibility to blind patients and intervention providers was 1 of the main reasons for high risk of bias. Blinding patients and intervention providers is challenging in trials comparing surgery and nonsurgical intervention.[20] Given that surgery and, to a lesser extent, nonsurgical interventions have a placebo effect,[120] the specific intervention effects may have been overestimated. Therefore, further placebo-controlled trials are encouraged.

## Limitations

In addition to limitations mentioned above in terms of lack of available data for the specific purpose of our meta-analyses, lack of longer-term follow-ups, and large inconsistency in the reporting of SAEs and death, there are some other important limitations. First, few available trials had low risk of bias, and SMDs and RRs had large 95% CIs and high heterogeneity. Sec-

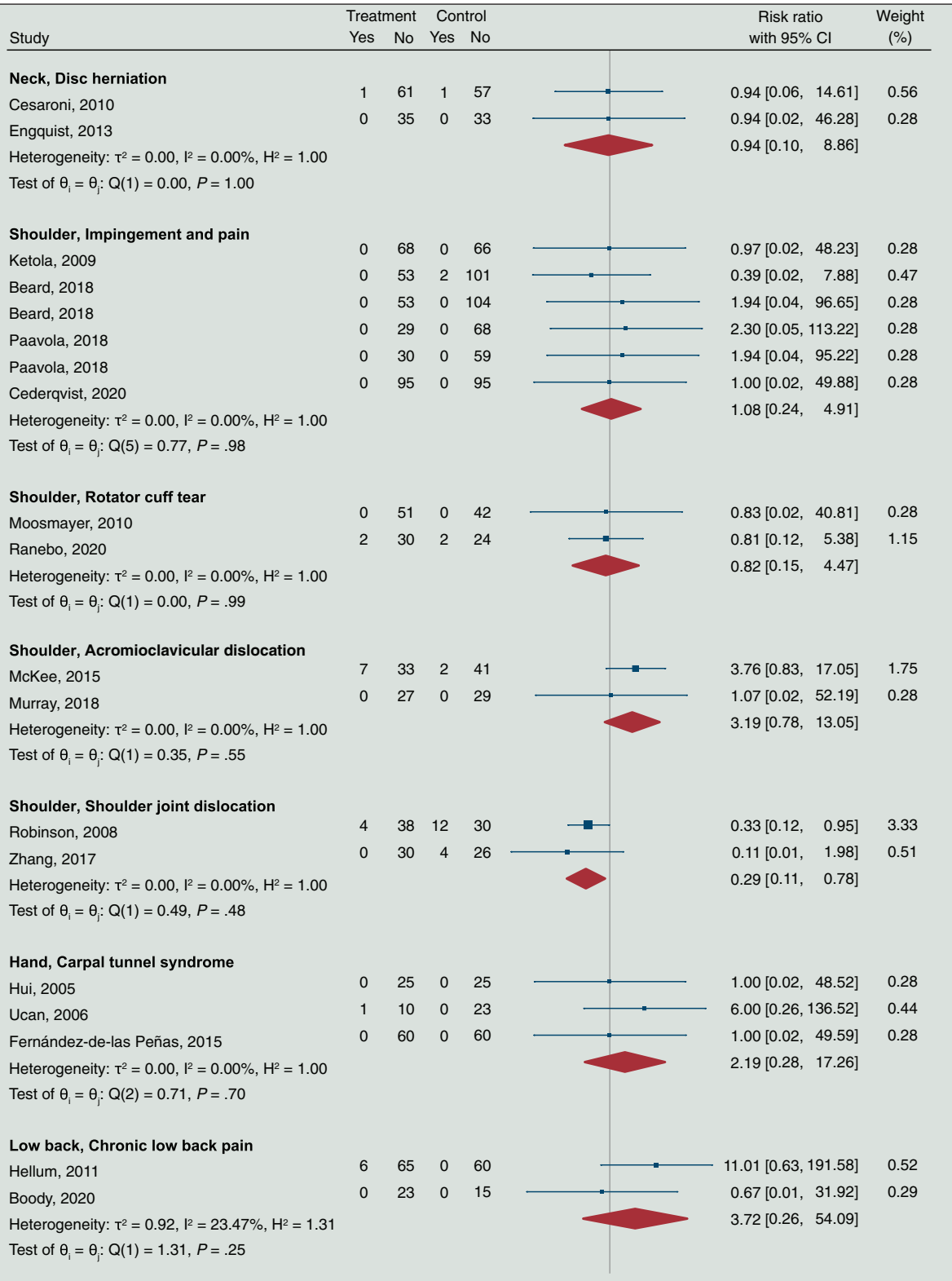



**FIGURE 5.** Effects of interventions with and without surgery on serious adverse events. Categories of conditions are ordered after body site going from the neck to the foot. Abbreviations: CI, confidence interval; OA, osteoarthritis; REML, restricted maximum likelihood.

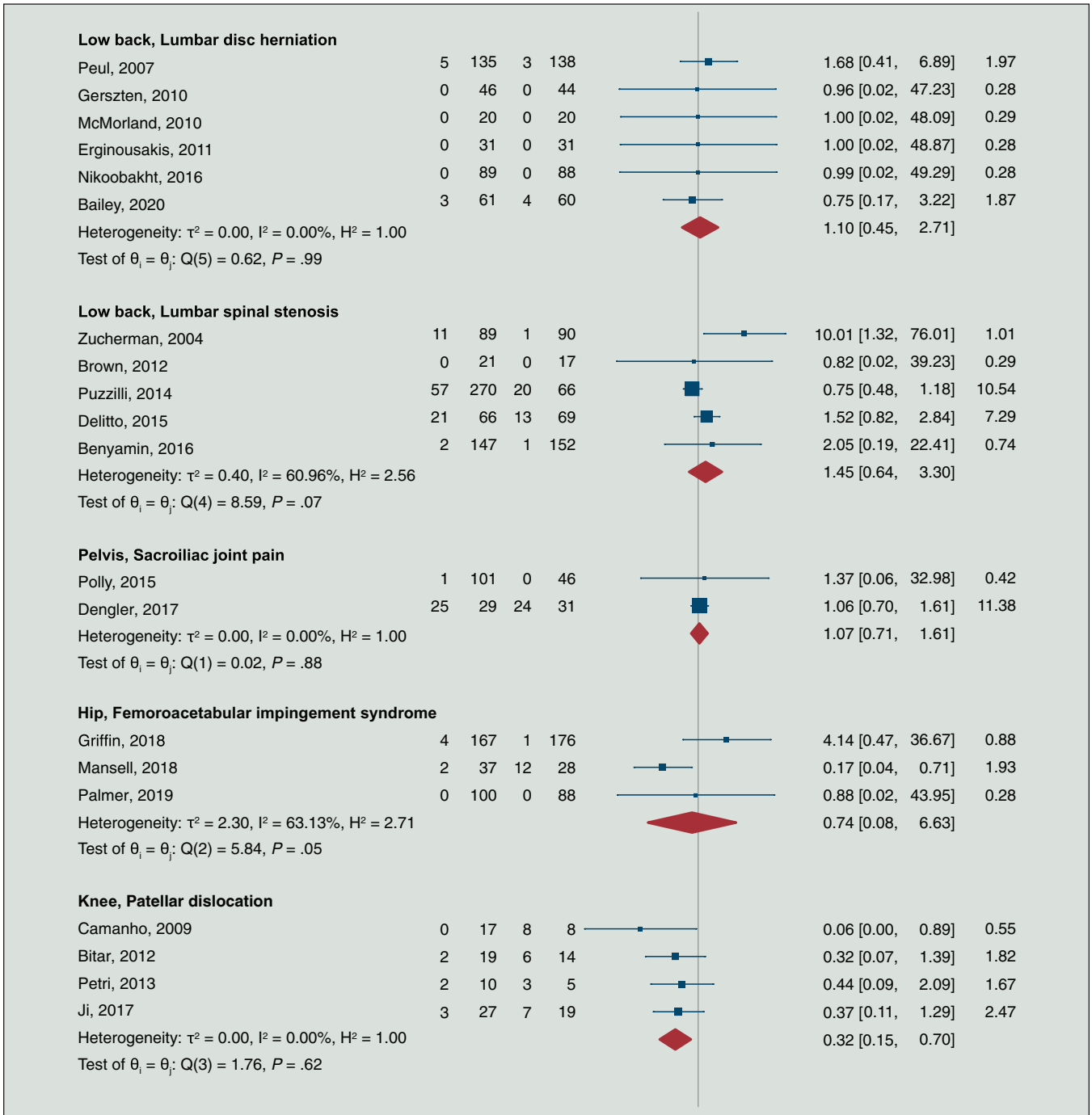



**FIGURE 5.** Continued.



ond, we did not consider the severity of the MSK condition in our analyses, nor did we account for the eligibility criteria in the individual studies. This is important to consider when interpreting and generalizing our results to patients with the individual conditions.

Altogether, our study highlights the need for further high-quality comparisons between surgery and nonsurgical intervention to simulate real-world choices or placebo surgery to study the mechanisms of effect of surgery. Studies should be powered to detect clinically relevant differences in benefits and harms between

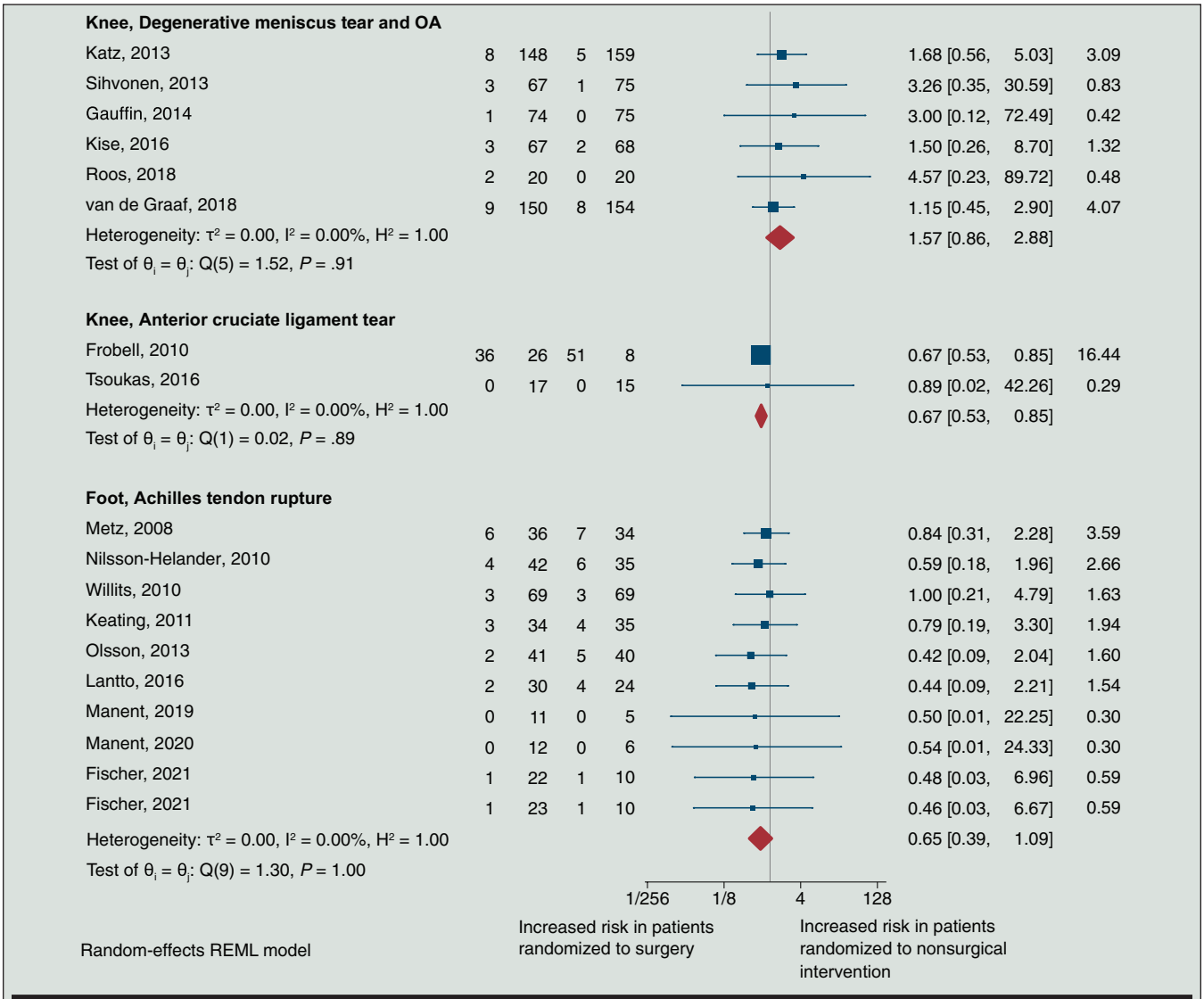



**FIGURE 5.** Continued.



surgical and nonsurgical interventions to help clinicians and patients in the shared decision making process and to provide decision makers with data to prioritize interventions in health care.

## CONCLUSION

For most non-fracture MSK conditions with sufficient available data on pain and SAEs and all conditions with data on function, quality of life, and death, there were no clinically relevant differences between interventions with and without surgery. The low certainty of evidence suggests that best practice nonsurgical interventions are viable alternatives to surgery for many MSK conditions and reveals a need for low–risk of bias trials, which might change the conclusion. ◉

### KEY POINTS

**FINDINGS:** For most conditions with sufficient available data on pain, and all with sufficient data on function and quality of life, there were no clinically relevant differences between interventions with and without surgery for musculoskeletal (MSK) conditions. For most conditions with data on serious adverse events (SAEs), and all with sufficient data on death, there were no differences in the risk of SAEs and death.

**IMPLICATIONS:** Low-certainty evidence suggests that best practice nonsurgical interventions are viable alternatives to surgery for many MSK conditions.

**CAUTION:** Few trials were of low risk of bias, heterogeneity was high, and 95% confidence intervals were large.

## STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** Drs Skou, Juhl, Lohmander, and Roos were involved in study conception and design. Drs Skou, Juhl, Poulsen, and Bricca and Mette Dideriksen were involved in the acquisition of data. All authors were involved in the analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and the final approval of the article. Drs Skou, Poulsen, Bricca, and Juhl had full access to all the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The corresponding author attests that all listed authors meet authorship criteria and that no other authors meeting the criteria have been omitted and that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The authors plan to disseminate the results widely.

**DATA SHARING:** Anything not presented in the manuscript or supplemental appendix is available upon reasonable request to the first author.

**PATIENT AND PUBLIC INVOLVEMENT:** No patients were involved in the design, conduct, interpretation, or translation of the research.



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