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What proportion of people have long-term pain after total hip or knee replacement? An update of a systematic review and meta-analysis

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Running title

Prevalence of chronic pain after total hip or knee replacement

Keywords

Chronic pain; Total hip replacement; Total knee replacement; Systematic review; Meta-analysis

Abstract

Objectives

To update our previous systematic review to synthesise latest data on the prevalence of long-term pain in patients who underwent total hip replacement (THR) or total knee replacement (TKR). We aim to describe the prevalence estimates and trends in this review.

Methods

Major electronic databases were searched for prospective cohort studies since January 2011, reporting long-term pain after THR or TKR at 3, 6, 12 and 24 months post-operative. Two reviewers independently identified studies as eligible. One reviewer conducted data extraction, checked by a second reviewer. Bayesian, random-effects meta-analysis was used to synthesise the results. The risk of bias assessment was performed using Hoy's checklist.

Results

For TKR, sixty-eight studies with 89 time points, including 598,498 patients, were included. Multivariate meta-analysis showed a general decrease in pain proportions over time: 21.9% (95% CrI 15.6 to 29.4) at 3 months, 14.1% (10.9 to 17.9) at 6 months, 12.6% (9.9 to 15.9) at 12 months, and 14.6% (9.5 to 22.4) at 24 months. Considerable heterogeneity, unrelated to examined moderators, was indicated by substantial prediction intervals in the univariate models. Substantial loss to follow-up and risk of bias led to low confidence in the results. For THR, only eleven studies were included, so it was not possible to describe the trend. Univariate meta-analysis estimated 13.8% (8.5-20.1) and 13.7% (4.8-31.0) of patients experiencing long-term pain 6 and 12 months after THR, respectively, though concerns in risk of bias results reduced confidence in these findings.

Conclusions

Our review suggests that approximately 22% of patients report unfavourable pain 3 months post-TKR, with 12-15% experiencing long-term pain up to 2 years. At least 14% report unfavourable pain 6-12 months after THR. Given the prevalence of chronic post-surgical pain, developing preventive and management strategies is crucial for optimal patient outcomes.

Study registration

PROSPERO CRD42023475498

Introduction

The primary reason that people with osteoarthritis undergo joint replacement surgery is because of persistent pain that has failed to improve with non-invasive management.[1 2] About 100,000 each of primary total knee and hip replacements were performed in the UK in 2022,[3 4] and in Organisation for Economic Co-operation and Development countries in 2015, over 1.5 million primary knee and nearly 1.7 million primary hip replacements were performed.[5] The number of people with osteoarthritis is projected to increase[6 7] and even in Germany, a country with a declining population, rates of joint replacement are predicted to rise due to the increasing use of knee replacement in younger people and the increasing number of older people requiring hip replacement.[8]

Potential improvements in pain and functionality ability are the primary reasons that patient elect to have a hip or knee replacement, and the most important contributing factors to patient satisfaction with the outcome of surgery.[9 10] However, it is widely recognised that some people experience continuing pain in the months and years following surgery. Our previous systematic review, with searches up to 2011, brought together longitudinal studies in representative populations receiving knee or hip replacement, and found that 10-34% of patients reported unfavourable long-term pain outcomes (moderate-to-severe pain or for whom surgery had not relieved pain) after total knee replacement (TKR) and 7-23% after total hip replacement (THR).[11] Together with qualitative research into patients' experiences,[12 13] our previous review stimulated research into the prediction, prevention, management and treatment of chronic pain after knee and hip replacement.

Twelve years on from publication of our previous review, our aim is to provide updated estimates of the incidence of long-term pain after total knee and hip replacement and explore factors that may influence the rates observed. Findings will support patients, clinicians and researchers as they face the challenge of preventing and treating chronic pain after total knee or hip replacement.

Methods

We updated our previous systematic review from our team,[11] with follow-up intervals between 3 and 24 months post-operative. We limited the follow-up to a maximum of 24 months as pain levels often plateau by this timepoint, and new onset pain beyond this may be related to implant failure.[14] With the more extensive data available for outcomes after TKR in this update, we planned to establish the trend of long-term pain over time up to 24 months post-operative.

The protocol was registered with PROSPERO (CRD42023475498) and conducted in accordance with PRISMA[15] (Supplementary material S1) and relevant contents in MOOSE[16] guidelines and the Cochrane handbook.[17]

Eligibility criteria

We sought prospective cohort studies including patients representative of the general population receiving total knee or hip replacement, predominantly from advanced osteoarthritis as in our previous review.[11] Cohorts were established pre- or peri-operatively in hospital orthopaedic departments and joint replacement centres and followed up prospectively at any defined time between 3 and 24 months. Studies specifically of unicompartmental knee replacement or hip hemiarthroplasty, revision surgery, or exclusively bilateral replacements were excluded.

Outcome

The outcome was the proportion of people with unfavourable pain at 3, 6, 12 and 24 months post-operative. In each study, unfavourable pain was defined using the study authors' definitions or through a consensus between two reviewers with extensive research experience in pain outcome measurement in total knee and hip replacement before commencement of data extraction. To calculate the proportions, we extracted the number of recruited or followed patients as denominators and the number of patients experiencing unfavourable pain as numerators. When a percentage or rate was provided, we rounded the numbers to the nearest whole number.

Searches

We conducted new searches of MEDLINE and Embase databases from January 2011 to 17th February 2024. An example of the search strategy for MEDLINE is included in S2. Web of Science was used to track citations of the original review.[11] Excepting the search strategy, we applied no language restrictions at any stage of the review, with Google Translate used to translate sections of relevant non-English articles. Studies reported only as abstracts were excluded.

Study selection and data collection

Studies identified were imported into EndNote 21 reference management software. After removal of duplicate records, one reviewer screened out clearly off-topic studies. Titles and abstracts of potentially relevant articles were acquired and assessed independently for eligibility by two reviewers. In cases of disagreement, a third reviewer was involved. Eligible articles identified in our previous systematic review were also included.

Data from eligible studies were entered into a Microsoft Excel spreadsheet by one reviewer with checking by a second reviewer. Extracted data were: country; dates of patient recruitment; setting (single or multiple surgeons, single or multiple hospitals, registry, or other; inclusion and exclusion criteria; whether routine "fast-track" surgery; patient characteristics (age, sex); assessment times; number of patients at baseline, number lost to follow up (or died or with revision surgery if reported) and number followed up; and patient reported pain outcome measure.

When more than one pain outcome was reported, we extracted them in order of preference: pain dimension data from osteoarthritis or joint specific outcome scores (Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC); Knee injury and Osteoarthritis Outcome Score (KOOS); Hip injury and Osteoarthritis Outcome Score (HOOS); Oxford Knee Score (OKS); Oxford Hip Score (OHS) and Knee Society Scores if patient generated (KSS, IKSS); Brief Pain Inventory (BPI); pain assessed in EuroQol instruments (EQ-5D or EQ-3D); pain measured on a visual analogue scale (VAS) or Numerical Rating Scale (NRS); and other measures including those developed by study authors.

Risk of bias assessment

Two independent reviewers assessed risk of bias using the non-summative checklist described by Hoy and colleagues.[18] This checklist considers ten aspects of study conduct relating to representation and selection, non-response (>25% of lost to follow-up as high risk), data collection and instrument used, follow up and methods used in calculation of rates. Overall risk of bias was judged to be low, moderate or high depending on whether any of the ten aspects gave concern.

Data synthesis approach

Our primary aim was to describe the proportion of people experiencing unfavourable pain outcomes over time. First, we summarised the characteristics of studies and inspected their clinical heterogeneity before the synthesis using tables and figures. We then meta-analysed proportions with an unfavourable pain outcome, along with accompanying 95% credible intervals (CrIs) and median between-study heterogeneity (τ^2) at 3, 6, 12, and 24 months' time separately when there were more than three studies. We also used prediction intervals

to aid the between-study heterogeneity interpretation.[19] We used Bayesian framework with a random-effects model due to anticipated heterogeneity. Vague prior distributions (e.g. normal with mean 0 and variance 10^5) on model parameters were used. Posterior outcome distributions were based on at least 25,000 simulations after a burn-in of at least 1,000 to ensure convergence.

To account for the multiple time follow-ups reported in certain studies, we adopted a Bayesian, hybrid, multivariate meta-analysis of multiple factors[20] to describe the proportions across time points by borrowing information and accounting for within- and between-study correlations.

All analyses were performed using R version 4.3.1 on RStudio 2023.06.2+561. The *runjags* and *metafor* packages were used to produce pooled estimates, forest plots, meta-regression and subgroup analyses. The *metasens* package was used to generate Doi plots and the LFK index.[21] The *ggplot2* package was used to produce additional figures to explore the clinical heterogeneity in the studies.

Exploration of heterogeneity

For potential sources of heterogeneity, we used meta-regression to explore heterogeneity for continuous factors (mean age of the population, percentage of females, and baseline sample sizes) where more than ten studies were included in the meta-analysis. For categorical factors (geographic region, settings, and pain outcome instruments), we conducted subgroup analyses where more than five studies were included in the meta-analysis.

Sensitivity analysis

In sensitivity analysis, we excluded studies with specific inclusion criteria, those focused on “fast track” surgery, studies where a proportion of people underwent unicompartmental knee replacement, studies with potentially over-inclusive unfavourable pain definitions, and studies with more than 20% lost to follow-up, and studies with an overall high risk of bias. Additionally, we performed worst-best scenario analyses by estimating the proportion of people lost to follow-up who experienced unfavourable pain outcomes, incrementing by tenths from 0% to 100%, to estimate their impact on the meta-analysis results.

Reporting bias and certainty assessment

We assessed publication bias using Doi plots and the LFK index (values between -1 and +1 indicate symmetry; values outside this interval indicate asymmetry) to aid the interpretation in cases where more than ten studies were included in the meta-analysis. We cross-checked the clinical study register and methods section in the report to evaluate non-reporting bias.

The certainty of evidence assessment was not conducted because specific tools for systematic reviews of prevalence were unavailable.

Patient and public involvement

There was no direct patient and public involvement in this systematic review, however, it benefitted from being part of the NIHR-funded STAR programme, which aimed to improve outcomes for patients with chronic pain after knee replacement. [22]Patient and public involvement was integral to STAR, and we worked throughout the programme with an existing patient forum and developed a complementary group focusing exclusively on chronic pain after TKR.

Results

Searches of MEDLINE, Embase, citation tracking in Web of Science and inclusion of potentially relevant articles identified in our previous review yielded a total of 13,807 records. After screening out of clearly irrelevant studies by one reviewer, 979 records were screened in duplicate by two reviewers and ultimately 68 studies with 598,498 TKR participants and 11 studies with 143,101 THR participants were included. Study selection and reasons for exclusion at the full-text stage are summarised in Figure 1. Some articles from our previous review were excluded as the follow up period was longer than 24 months.

Total knee replacement

Individual study characteristics are summarised in S3. The grouped characteristics in Table 1. The baseline dates of data collection ranged from 1993 to 2023. Geographically, most studies were conducted in Europe (n=37) and North America (n=19). More than half of studies (n=39) collected their data at a single hospital, followed by multiple hospitals (n=18). Overall, 598,498 patients were included in the 68 studies with a median sample size per study of 235 (interquartile range 114 to 581). Patients in 52 studies with data had a mean age of 69.6 (SD 9.4) years, and 63% (58 to 69) were women. In terms of primary pain outcome reported, 31 studies reported multi-dimensional pain scales (WOMAC, OKS, KOOS, BPI, or KSS/IKSS), 29 studies reported VAS or NRS pain scores, and 6 studies used researchers' own measures.

After harmonising unfavourable pain outcomes at different time points, there were 15, 28, 36 and 10 studies with data available for 3, 6, 12 and 24 months post-operative. Risk of bias assessments are summarised in Figure 2 (for traffic light plots, see S4). Most studies were judged as overall moderate risk of bias with few overall high risk of bias due to losses to follow up of >25%, or use of scores which are not entirely patient completed or have concerns relating to a low pain cut off.

We synthesised the unfavourable pain outcomes using multivariate meta-analysis (Figure 3), demonstrating a general decrease in pain proportions over time: 21.9% (95% CrI 15.6 to 29.4) at 3 months, 14.1% (10.9 to 17.9) at 6 months, 12.6% (9.9 to 15.9) at 12 months, and 14.6% (9.5 to 22.4) at 24 months. The results of the univariate models were similar due to the limited number of studies with multiple time points (S5), though with slightly wider CrIs (S6). The substantial prediction intervals in the univariate models suggested considerable heterogeneity.

We investigated potential heterogeneity using meta-regression and subgroup analyses in the univariate meta-analysis models. Meta-regression results showed no evidence of age, percentage of women, or sample size contributing to the heterogeneity of the proportion of

individuals with unfavourable pain outcomes (S7). In subgroup analyses (S8), rates of unfavourable pain tended to be lower in studies involving patients from North America compared to other geographic groups. Similarly, studies conducted in single-surgeon series settings showed lower rates of unfavourable pain outcomes. However, these findings should be interpreted with caution due to the limited number of studies in each subgroup. Although we observed small-study effects in the results (S9), potentially attributable to publication bias, it is likely that these resulted from the extremely large variations in sample sizes at the 6-, 12-, and 24-month follow-ups. We did not find evidence of non-reporting bias, as most studies reported long-term pain outcomes in accordance with their reported methods.

In sensitivity analyses, we individually excluded studies with specific criteria to evaluate their impact on the univariate meta-analysis results (S10). The effects of excluding these studies were generally minor, except for studies with a high risk of bias or a high proportion of lost to follow-up. To account for the varying degrees of loss to follow-up, we performed separate scenario analyses by assuming that the same proportion of participants lost to follow-up experienced unfavourable pain outcomes in each study (Table 2). By assuming 10% to 30% of participants lost to follow-up might experience unfavourable pain, this approach could yield more realistic estimates, given that the limited literature available for further imputation.

Total hip replacement

Eleven studies reported unfavourable pain outcomes in individuals who underwent THR. The characteristics of these studies are summarised in S11. Only one study reported unfavourable pain outcomes at the 3-month and 24-month time points (Figure 4), so a trend cannot be established. Meta-analysis of unfavourable pain outcomes at 6 and 12 months provided similar results, with 13.8% (8.5 to 20.1) and 13.7% (4.8 to 31.0), respectively. However, concerns regarding the risk of bias assessment (S12) lead to low confidence in these results.

Discussion

Through our systematic review and meta-analysis, we have synthesised the existing evidence on the proportion of patients who experience long-term pain after knee and hip replacement. By updating our previous review, we have been able to provide estimates of incidence rates at 3, 6, 12 and 24 months post-operative. Our analyses suggest that the proportion of people with an unfavourable level of pain after TKR decreases between three and six months after surgery and then remains stable until at least two years. Our review suggests that approximately 22% of patients will report an unfavourable pain outcome at three months after TKR, with 12-15% of people experiencing an unfavourable longer-term pain outcome up to two years after surgery. For THR, a lack of studies reporting rates of unfavourable pain outcomes in unselected patients limited our analysis. However, our findings suggest that at least 14% of people may report unfavourable pain at 6-12 months after THR.

The strengths and limitations of this review should be considered when interpreting the results**.** Firstly, overall quality of evidence is low due to potential heterogeneity and risk of bias in TKR studies, and we were unable to estimate a trend for THR studies due to a low number of the included studies. The wide range of rates of unfavourable pain across studies suggests that there may be selection that was not apparent in the study methodology. For example, a single surgeon series with lower rates of unfavourable pain may relate to patient selection which is not evident from the cohort inclusion criteria. Secondly, loss to follow-up may have impacted on our estimates of the proportion of patients with chronic pain after TKR and THR. The influence that unfavourable pain and other outcomes have on patient willingness to participate in research follow-up is unclear. Some studies suggest that people with poor outcomes are less likely to participate in follow-up assessments due to dissatisfaction with their care or difficulties completing follow-up.[23-26] However, others report no difference or poorer pain outcomes in those responding to initial invitations or attending follow-up visits compared with those not participating in follow-up visits.[27-29] Our sensitivity analyses in studies of TKR excluding studies with high loss to follow-up rates showed higher rates of unfavourable pain and provide some support for the latter suggestion. Given the uncertainty regarding the impact of loss to follow-up, we conducted separate scenario analyses to provide readers with a range of realistic estimates for their consideration. Thirdly, the scope of our review was broad. We included all different patient-reported measures of pain together, which present a mixture of single and multidimensional measures, and authors' own definitions of unfavourable pain outcome. While this allowed us to take an encompassing approach to the synthesis of existing studies, it was likely an important source of heterogeneity in the results. Despite these limitations, this review is the

most comprehensive attempt to date to collate the existing evidence and provides useful estimates to direct future research and improvements to clinical care.

Chronic pain after total knee or hip replacement has a highly negative impact on people[13 30] to the extent that they may fear pursuing further healthcare and prescribed pain relief.[31] For people who would potentially benefit from further care, how they are identified, assessed and treated varies considerably between centres in the UK.[32] Cost implications for health services are considerable with numerous consultations, investigations and surgical referrals required.[33] Chronic pain after joint replacement is an important research priority, as highlighted by the James Lind Alliance Priority Setting Partnership.[34-36] Acknowledging that an estimated 13-22% of people with TKR and a proportion of people with THR may experience chronic pain after surgery, implementation of evidence-based interventions aimed at the prevention and/or management of chronic pain after joint replacement are required.

Potential pre-operative risk factors for chronic pain after total knee or hip replacement have been studied extensively with the aim of developing interventions and targeting care to those at risk. In a recent systematic review with 54 studies identified, there was no suggestion in meta-analyses that age, sex and body mass index were associated with development of chronic pain after TKR.[37] For a range of further potential risk factors including pre-operative pain, evidence was limited with associations based on small numbers of studies or "vote counting" analysis due to lack of data and methodological heterogeneity. For people receiving THR, consistent associations have been identified between female sex, high pre-operative pain, poorer pre-operative function, and anxiety or depression.[38 39] Systematic reviews have identified that pre-operative pain catastrophizing, psychological distress, and symptoms of anxiety and/or depression are risk factors for long-term pain hip and knee replacement.[40-44] Post-operative risk factors for chronic pain have been studied in TKR and largely relate to length of hospital stay, mechanical complications of the prosthesis, surgical site infection, hospital readmission, reoperation or revision.[45] More generally, acute postoperative pain, caused by surgical methods and influenced by anaesthetic protocols, analgesia and care during the hospital admission, is also acknowledged as a risk factor for chronic postsurgical pain.[46 47]

There is a limited but growing body of evidence evaluating interventions that target risk factors for chronic pain after joint replacement[48-51]. Pre-operatively, general prehabilitation with exercise and education has not shown clear benefit for reduced long-term pain.[48 52 48 53-55] Another focus of efforts has been in removing delays to surgery to avoid possible decline in function and increase in pain while waiting for surgery. However, evidence of associations between longer waiting times for knee or hip replacement and chronic pain is equivocal.[56-58]

In randomised trials evaluating interventions targeting psychological risk factors, cognitive behavioural therapy and pain coping skills programmes have not shown benefit for improved long-term pain.[49 59-64 65-67] However, a mindfulness-based stress-management intervention provided to patients before total hip or knee replacement surgery was associated with reduced long-term pain.[68] During the peri-operative period, the multimodal analgesia regimen provided may influence long-term pain outcomes and there is some support for incorporation of specific treatments, some of which are features of current pain management practice.[50 69] After hospital discharge, care focuses mainly on physiotherapy-based rehabilitation but there is no evidence to support one modality over another in relation to prevention of chronic pain.[51] Exercise-based rehabilitation provided to people considered at risk of a poor outcome after TKR have shown little benefit for primary functional outcomes or long-term pain compared with usual care or less intensive interventions.[70 71]

Systematic reviews have identified a limited evidence-base to guide the treatment and management of chronic pain after joint replacement, and surgery more generally [72 73]. To address this, a programme of research has been conducted focussing on the development and evaluation of an early post-operative intervention to prevent pain chronicity.[22] Recognising the diverse causes of chronic pain, the Support and Treatment After Replacement (STAR) care pathway is a personalised and multifaceted intervention to reduce chronic pain after TKR.[74] The care pathway involves the assessment of people with high levels of pain at 2-3 months after surgery to identify the underlying causes of pain with subsequent provision of referrals for appropriate treatment or management. Evaluation in a randomised controlled trial found the STAR care pathway was cost-effective and associated with a clinically important reduction in pain after one year compared with usual care.[74] Furthermore, there is a suggestion of sustained benefit at up to four years.[75]

Conclusion

The problem of chronic pain after knee and hip replacement is recognised by people who have pain, clinicians and the research community. Our review, bringing together all the published literature to date, suggests that approximately 22% of patients will report an unfavourable pain outcome at three months after TKR, with 12-15% of people experiencing an unfavourable longer-term pain outcome up to two years after surgery. After THR, at least 14% of people may report an unfavourable pain outcome at 12 months after surgery. Throughout the care pathway, there are opportunities for targeted care. There is an urgent need for the implementation of evidence-based interventions to optimise management of chronic pain after joint replacement and evaluation of new preventive strategies that target established risk factors.

Ethical approval

No individual level data are included in this manuscript. All data are aggregated data from published academic articles.

Data sharing

The statistical analysis plan and dataset can be available from the corresponding author on reasonable request.

Sources of funding

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Author's contributions

AB, RGH, MW, and VW conceived the project. AB, VW, WB, and MAS screened studies and collected data for the review. HYC, AB, and VW drafted the manuscript. HYC conducted the analysis. AB and HYC contributed to the interpretation of the results. All authors (AB, MAS, MW, RGH, HYC, VW, and WB) discussed the results and contributed to the writing and editing of the manuscript.

Competing interests

All authors (AB, MAS, MW, RGH, HYC, VW, and WB) have completed the ICMJE uniform disclosure form and declare no competing interests.

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Key messages

What is already known on this topic

- Our previous systematic review of longitudinal studies in representative populations undergoing knee or hip replacement (up to 2011) found that 10-34% of patients reported unfavourable long-term pain outcomes after total knee replacement and 7-23% after total hip replacement.

What this study adds

- Our updated review provides estimates of the prevalence of long-term pain at 3, 6, 12, and 24 months, showing a decrease in the proportion of knee replacement patients experiencing unfavourable pain levels from at least 21% at 3 months to 15% at 24 months.
- At least 14% of people report unfavourable pain at 6-12 months after total hip replacement.

How this study might affect research, practice or policy

- As at least more than one-in-ten people with total knee replacement or total hip replacement may experience long-term pain after surgery. As new approaches to the management of pain after knee replacement show promise, there is now a need to develop and implement evidence-based interventions to prevent long-term pain after knee and hip replacement and to develop approaches to manage pain after hip replacement.

Strengths and limitations of this study

- We updated the review using the latest review methodology, including Bayesian, multivariate meta-analysis and new risk of bias tool, to summarise the prevalence rates reported across studies.
- We included a wide range of patient-reported measures of pain across studies. Despite the heterogeneity identified in the review, this review is the most comprehensive attempt to date to collate the existing evidence in chronic post-surgical pain in populations undergoing knee or hip replacement.
- These prevalence rates are underestimated due to loss of follow-up and the high risk of bias in the included studies. Future research should focus on understanding the reasons for loss to follow-up and their outcomes.

Table 1. Summary of TKR study characteristics

	Overall	3 months	6 months	12 months	24 months
Number of study cohorts	68	15	28	36	10
Total sample sizes	598,498	2503	550,928	36,157	13,953
Median sample size (IQR)	235 (113.5-580.75)	116 (95-184)	197 (111.25-297)	254.5 (115.5-593.75)	396.5 (251.75-692.75)
Baseline time period range	1993-2023	1998-2023	1993-2023	1993-2020	1993-2019
Mean age (SD)	69.6 (9.4) (n = 52*)	68.8 (9.2) (n = 13*)	69.6 (9.4) (n = 24*)	68.1 (9.1) (n = 26*)	70 (9.3) (n = 6*)
Age range	18-98 (n = 24)	18-90 (n = 7)	18-94 (n = 9)	25-98 (n = 14)	28-90 (n = 4)
Median % women (IQR)	63 (58-69.45)	66.1 (62.35-77.55)	65.55 (57.65-72.475)	61.2 (56.95-65.85)	63 (61.03-64.75)
Primary pain outcome reported					
VAS/NRS pain	29	9	16	13	2
WOMAC pain	13	1	4	7	3
OKS pain	7	1	2	5	1
KOOS pain	6	1	1	4	1
BPI	3	1	2	2	0
KSS/IKSS pain	2	0	0	2	1
EQ-5D 5L pain/discomfort	1	0	1	0	0
Pain disturbing sleep	1	1	0	1	0
Author own question	6	1	2	2	2
Setting					
Single hospital	39	8	16	20	9
Multiple hospitals	18	0	6	12	1
Multiple surgeons	4	3	1	1	0
Single surgeon	3	3	2	2	0
National registry	2	0	1	1	0
Health region	1	0	1	0	0
Rehabilitation service	1	1	1	0	0
Country					
Australia	2	0	1	1	1
USA	17	2	8	5	4
UK	9	2	3	7	2
Spain	5	2	3	2	0
Denmark	5	1	0	5	0
France	4	1	3	2	0
Sweden	3	0	0	2	1
China	3	1	1	0	1
Belgium	2	2	1	1	0

Canada	2	0	1	1	0
Finland	2	1	0	0	1
Japan	2	1	2	1	0
Singapore	2	0	2	1	0
South Korea	2	2	0	1	0
The Netherlands	2	0	1	2	0
Hungary	1	0	0	1	0
Italy	1	0	0	1	0
New Zealand	1	0	1	1	0
Norway	1	0	0	1	0
Poland	1	0	1	0	0
Russia	1	0	0	1	0

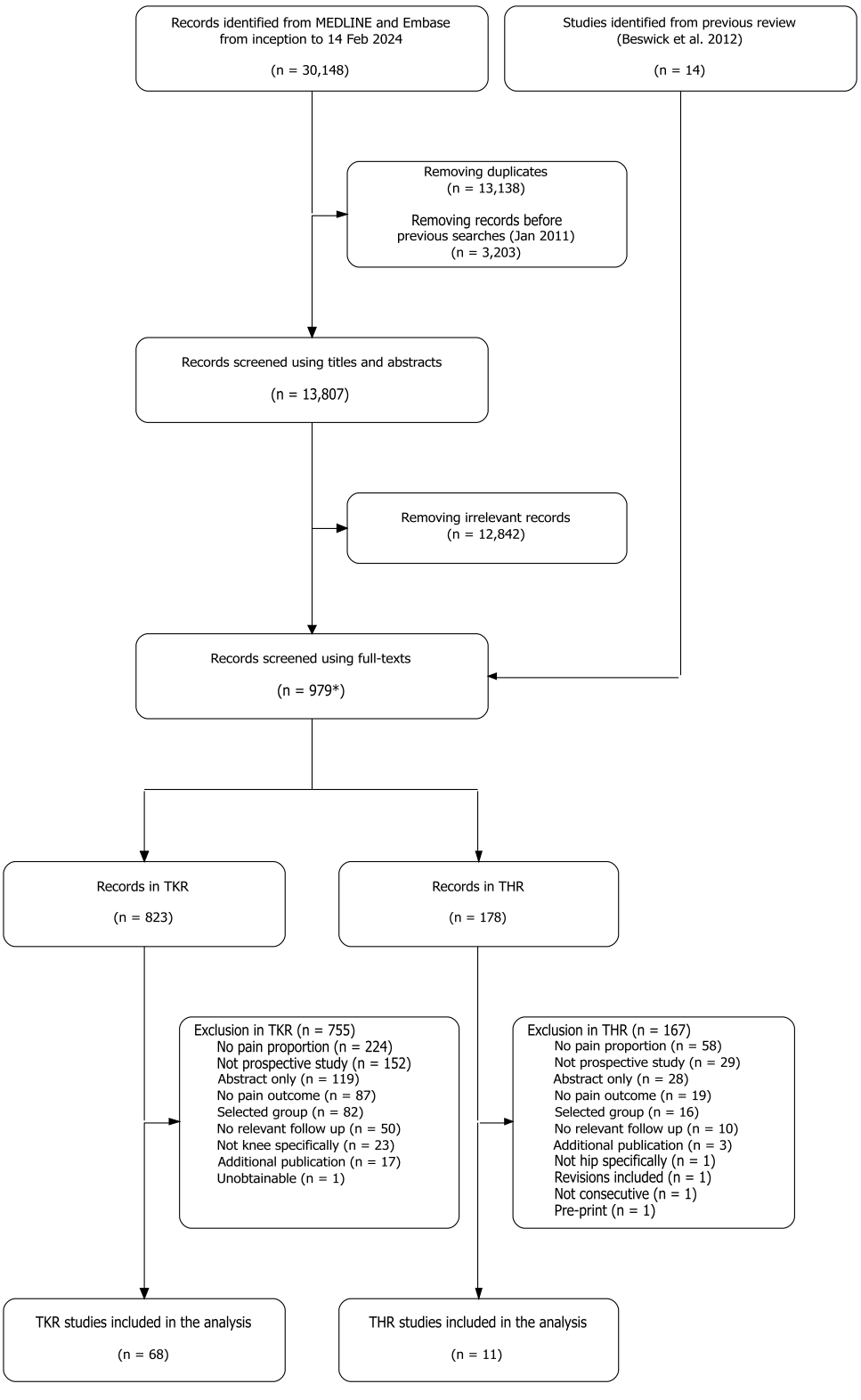
*only studies reported both mean and SD

Table 2. Worst-best case scenario analyses in TKR studies

Proportion* (%)	Median (95% CrI)	τ^2 (95% CrI)
3 month		
0%	21.89 (15.72 - 29.35)	0.5 (0.19 - 1.1)
10%	23.8 (17.38 - 30.4)	0.4 (0.14 - 0.88)
20%	25.61 (19.46 - 32.34)	0.36 (0.12 - 0.78)
30%	27.22 (21 - 33.69)	0.31 (0.11 - 0.69)
40%	28.82 (22.45 - 35.25)	0.3 (0.1 - 0.66)
50%	30.68 (24.49 - 37.25)	0.27 (0.09 - 0.6)
60%	32.07 (25.66 - 38.42)	0.27 (0.09 - 0.6)
70%	33.55 (26.73 - 40.21)	0.28 (0.09 - 0.63)
80%	35.04 (28.15 - 41.98)	0.28 (0.1 - 0.63)
90%	36.71 (29.5 - 43.83)	0.3 (0.11 - 0.68)
100%	38.16 (30.6 - 45.68)	0.31 (0.11 - 0.69)
6 month		
0%	14.06 (10.79 - 17.79)	0.51 (0.26 - 0.88)
10%	16.37 (13.08 - 19.88)	0.37 (0.18 - 0.65)
20%	18.54 (15.24 - 22.09)	0.32 (0.16 - 0.56)
30%	20.5 (17.05 - 24.25)	0.3 (0.15 - 0.53)
40%	22.33 (18.66 - 26.38)	0.3 (0.15 - 0.52)
50%	24.22 (19.94 - 28.43)	0.32 (0.16 - 0.56)
60%	26.03 (21.65 - 30.67)	0.35 (0.18 - 0.6)
70%	27.91 (22.96 - 33.03)	0.39 (0.21 - 0.67)
80%	29.61 (24.15 - 35.12)	0.44 (0.23 - 0.75)
90%	31.39 (25.38 - 37.35)	0.51 (0.27 - 0.87)
100%	33.36 (26.84 - 40.12)	0.58 (0.31 - 1)
12 month		
0%	12.61 (9.88 - 15.84)	0.61 (0.34 - 0.97)
10%	15.22 (12.29 - 18.23)	0.44 (0.25 - 0.72)
20%	17.44 (14.5 - 20.66)	0.37 (0.2 - 0.6)
30%	19.6 (16.46 - 22.97)	0.36 (0.19 - 0.58)
40%	21.6 (18.09 - 25.17)	0.36 (0.2 - 0.58)
50%	23.6 (19.86 - 27.46)	0.37 (0.2 - 0.6)
60%	25.64 (21.74 - 29.89)	0.4 (0.23 - 0.64)
70%	27.57 (23.28 - 32.21)	0.44 (0.25 - 0.7)
80%	29.57 (24.55 - 34.51)	0.49 (0.28 - 0.78)
90%	31.53 (26.01 - 36.95)	0.55 (0.3 - 0.87)
100%	33.62 (27.69 - 39.61)	0.62 (0.37 - 0.99)
24 month		
0%	14.63 (8.83 - 21.5)	0.52 (0.15 - 1.32)
10%	16.67 (10.85 - 23.36)	0.41 (0.13 - 1.07)
20%	18.45 (12.81 - 25.31)	0.35 (0.11 - 0.91)
30%	20.23 (14.19 - 27.13)	0.34 (0.11 - 0.88)
40%	21.89 (15.29 - 29.1)	0.34 (0.11 - 0.88)
50%	23.64 (16.62 - 31.45)	0.35 (0.11 - 0.91)
60%	25.28 (17.78 - 33.83)	0.38 (0.12 - 0.97)
70%	26.89 (18.57 - 35.67)	0.4 (0.12 - 1.02)
80%	28.58 (19.92 - 38.38)	0.43 (0.14 - 1.11)
90%	30.04 (20.59 - 40.22)	0.48 (0.15 - 1.22)
100%	31.76 (21.49 - 42.8)	0.52 (0.15 - 1.32)

*Proportion: The proportion of lost to follow-up patients imputed to experience unfavourable pain outcomes.

Figure 1. Study selection



*Twenty-two studies included both populations

Figure 1. Study selection flowchart.

Figure 2. Summary of risk of bias assessments in TKR studies

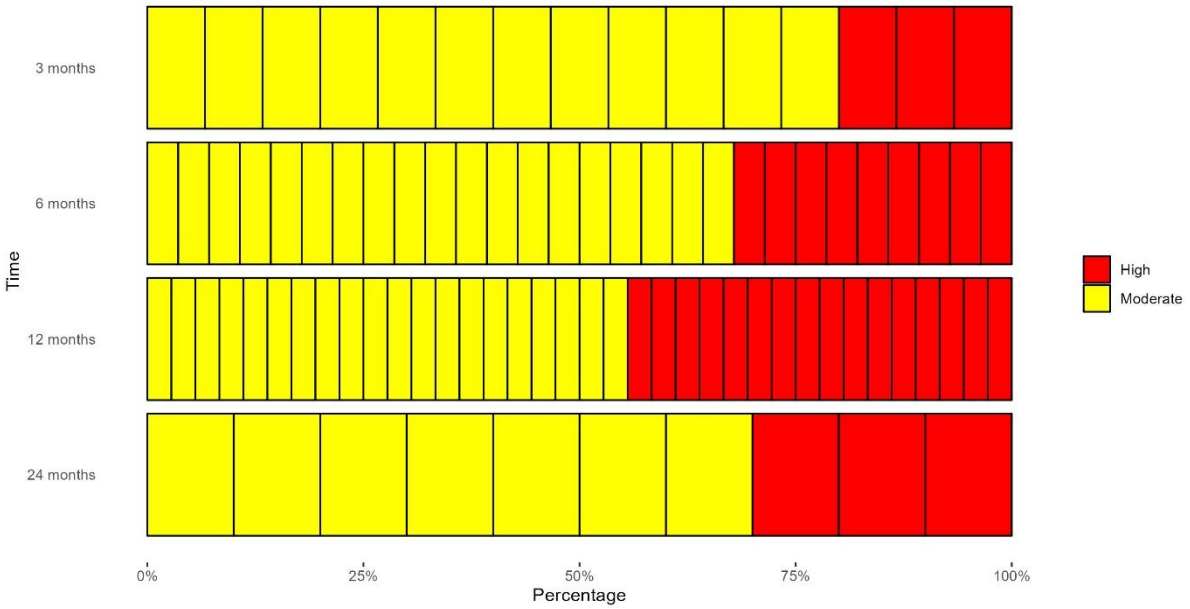


Figure 2. Summary of risk of bias assessments in TKR studies. Each block represents one study.

Figure 3. Multivariate meta-analysis in TKR studies

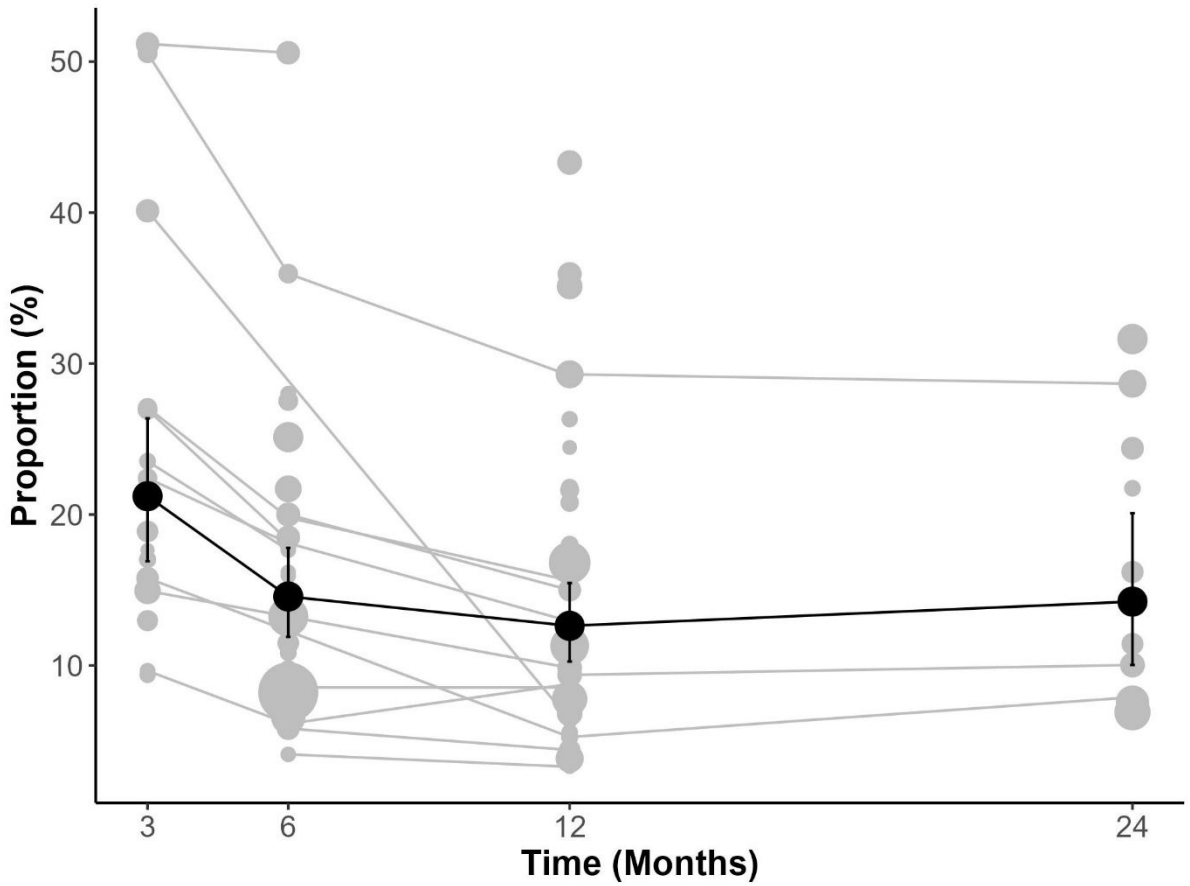


Figure 3. Multivariate meta-analysis of proportions over time in TKR studies plot. Grey dots and lines represent reported proportions across studies and time, while dark dots and lines show the multivariate meta-analysis results. The size of grey dots is proportional to the log of inverse variance.

Figure 4. Forest plot of THR studies

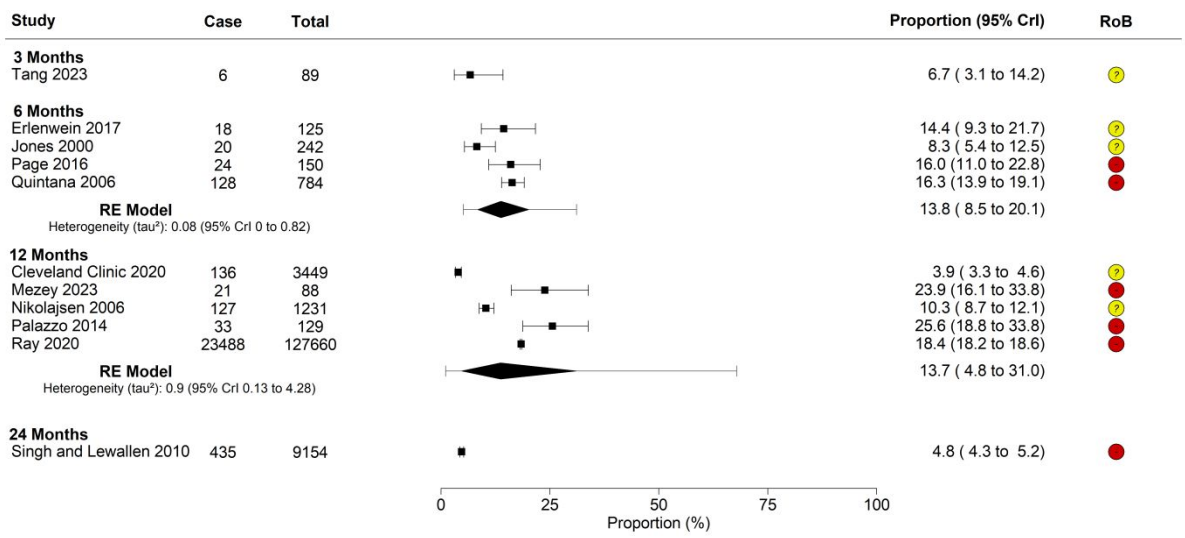


Figure 4. Forest plot of proportions over time in THR studies. Squares and bars represent mean proportion of individual studies. Diamonds represent the point estimate and credible intervals of the meta-analysis results. The bars show the corresponding prediction intervals. Red circles and minus signs represent overall high risk of bias. Yellow circles and question marks represent overall moderate risk of bias. Abbreviations: RoB: Risk of Bias; RE: Random-effects; CrI: Credible intervals.

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Supplementary materials

S1. PRISMA checklist
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S7. Meta-regression analyses in TKR studies
S8. Subgroup analyses in TKR studies
S9. Doi plots and the LFK indexes in TKR studies
S10. Sensitivity analyses in TKR studies
S11. Characteristics of THR studies
S12. Traffic light plot of the risk of bias assessment in THR studies

Prevalence of chronic pain after total hip or knee replacement

Supplementary materials

Prevalence of chronic pain after total hip or knee replacement

Prevalence of chronic pain after total hip or knee replacement

S1. PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 5, 6

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Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 5, 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1, Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7
Study characteristics	17	Cite each included study and present its characteristics.	S3, S11
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Figure 2, S4 and S12
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figure 3, S5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 7 and 8
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figure 3, S5
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 7-8, S7 and S8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 8, S10, Table 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicable
DISCUSSION			

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Section and Topic	Item #	Checklist item	Location where item is reported
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 10
	23b	Discuss any limitations of the evidence included in the review.	Page 10
	23c	Discuss any limitations of the review processes used.	Page 10
	23d	Discuss implications of the results for practice, policy, and future research.	Page11, 12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 2 and 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 2 and 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 4
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 14
Competing interests	26	Declare any competing interests of review authors.	Page 14
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 14

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

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S2. Search Strategy as applied in MEDLINE

S2.1 Total knee replacement

1. survey.mp. or exp Data Collection/
2. prospective study.mp. or exp Prospective Studies/
3. observational study.mp.
4. exp EPIDEMIOLOGY/ or epidemiology.mp.
5. longitudinal study.mp. or exp Longitudinal Studies/
6. follow up study.mp. or exp Follow-Up Studies/
7. exp Arthroplasty, Replacement, Knee/ or exp Knee Prosthesis/ or knee replacement.mp.
8. knee prosthesis.mp. or exp Knee Prosthesis/
9. total knee.tw.
10. (knee adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti, ab.
11. 7 or 8 or 9 or 10
12. pain.tw.
13. 1 or 2 or 3 or 4 or 5 or 6
14. 10 and 12 and 13

S2.2 Total hip replacement

1. survey.mp. or exp Data Collection/
2. prospective study.mp. or exp Prospective Studies/
3. observational study.mp.
4. exp EPIDEMIOLOGY/ or epidemiology.mp.
5. longitudinal study.mp. or exp Longitudinal Studies/
6. follow up study.mp. or exp Follow-Up Studies/
7. exp Arthroplasty, Replacement, Hip/ or exp Hip Prosthesis/ or hip replacement.mp.
8. hip prosthesis.mp. or exp hip Prosthesis/
9. total hip.tw.
10. (hip adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti, ab.
11. 7 or 8 or 9 or 10
12. pain.tw.
13. 1 or 2 or 3 or 4 or 5 or 6
14. 10 and 12 and 13

Prevalence of chronic pain after total hip or knee replacement

S3. Characteristics of TKR studies

Study Country Recruitment dates Setting	Operation Number of patients Age (SD), range % women	Pain measure	Definition of unfavourable pain outcome High risk of bias concern
Alzahrani 2011[1] TWH cohort Canada 1998-2007 2 hospitals	Primary TKR, all 18+ N=482 67.5 (9.6) 62%	WOMAC pain 12 months	No clinically important improvement based on MCID
Aso 2020[2] Japan 2012-2017 1 hospital	Primary TKR, all N=234 75 75.8%	VAS/NRS pain 6, 12 months	Moderate to severe pain (VAS >30 mm), at rest or walking
Attal 2014[3] France 2008-2011 I hospital	Primary TKR, all 18+ N=89 68.7 (8.9) 65.0%	BPI (NRS) 3, 6, 12 months	NRS pain average 3 or greater on 10-point scale
Baker 2007[4] UK 2003 National registry	Primary TKR, all N=9417 70.68 56.8%	OKS pain 12 months	Reported persistent knee pain
Bell 2023[5] USA 2015-2018 7 hospitals	Primary TKR, all 50-89 N=5564 Range 50-89 60.7%	KOOS pain 12 months	MCID not satisfied
Birch 2019[6] Denmark 2011-2013 1 hospital	Primary TKR or UKR, all N=589 67.3 (9.7) 52.0%	OKS pain 4, 12 months	OKS pain moderate/severe High loss to follow up rate at 4 and 12 months
Brander 2003[7] USA 1998-2000 1 surgeon	Primary TKR, all 18+ N=116 66 (10.5), range 36-85 55.2%	VAS/NRS pain 3, 6, 12 months	VAS >40
Buus 2022[8] Denmark 2015-2016 1 hospital	Primary TKR, all 18+ N=217 66.8 (9.3) 52.2%	OKS pain 12 months	Threshold 42.39
Buvanendran 2019[9] USA 2011-2017 1 hospital	Primary TKR, all N=296 65 65.3%	VAS/NRS pain 6 months	NRS pain with movement ≥4

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Chodor and Kruczynski 2022[10] Poland 2016 1 hospital	Primary TKR, all 48+ N=69 67.6 (7.42), range 48-84 76.7%	Author own question 6 months	Pain severely limiting daily life
Clement 2014[11] UK 2010 1 hospital	Primary TKR, all N=578 70 (9.6), range 39-91 58.4%	Author own question "How well did the surgery relieve pain in your affected joint?" 12 months	Fair or poor High loss to follow up rate
Cole 2022[12] UK 2010-2015 2 hospitals	Primary TKR, all N=1025 70 55.8%	OKS pain 12 months	<14 points OKS
Dave 2017[13] USA 2012-2014 3 hospitals	Primary TKR probably, all 40+ N=267 66 (9) 61.0%	WOMAC pain 12 months	WOMAC pain score <MCID
Dowsey 2012[14] Australia 2006-2007 1 hospital	Primary TKR, all N=478 70.8 (8.3), range 45-90 69.2%	IKSS pain 12, 24 months	IKSS pain score <30 moderate to severe pain IKSS may not be entirely patient reported at 12 and 24 months
Dursteler 2021[15] Spain 2014-2017 Spain 1 hospital	Primary TKR, all 18+ N=170 73.1 (7.1) 73.3%	VAS/NRS pain 3, 6 months	NRS 0.3/1 or greater at rest
Edwards 2022[16] USA 2012-2018 2 hospitals	Primary TKR, all 45+ N=248 65.1 (8.2) 59.5%	BPI 6 months	4/10 or greater High loss to follow up rate
Escobar and Riddle 2014[17] Spain 2003-2006 15 hospitals	Primary TKR, all N=1616 71.6 (6.8) 70.0%	WOMAC pain 12 months	Number not attaining PASS High loss to follow up rate
Getachew 2021[18] Norway 2012-2014 1 hospital	Primary TKR, all 18+ N=206 68 (9) 66.0%	BPI 12 months	BPI worst pain score ≥4
Ghomrawi 2017[19] USA 2010-2012 1 hospital	Primary TKR, all N=247 68 (10) 65.0%	WOMAC pain 24 months	Number not achieving MCID

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Grosu 2016[20] Belgium 2009-2010 1 surgeon	Primary TKR probably, all N=114 66 (10) 65.8%	VAS/NRS pain 3, 6, 12 months	Moderate to severe pain High loss to follow up rate at 3, 6 and 12 months
Hardy 2022[21] France 2014-2015 1 hospital	Primary TKR, all >18 N=111 73.3 (9.3) range 29-92 65.0%	VAS/NRS pain 12 months	VAS >30/100
Heath 2021[22] Australia 2018-2020 44 hospitals	Primary and revision TKR, all N=8299 67.5 (8.8) 56.4%	EQ-5D 5L pain/ discomfort 6 months	Moderate/ severe or extreme pain EQ 5D 5L pain/discomfort High loss to follow up rate
Jones 2000[23] Canada 1995-1997 1 health region	Primary TKR, all 40+ N=292 69.2 (9.2) 59.0%	WOMAC pain 6 months	Moderate/ severe pain defined as a gain of <10 points on the WOMAC pain dimension
Khalid 2021[24] UK 2008-2016 National registry	Primary TKR or UKR, all N=531,790 69.7 (9.4) 56.6%	OKS pain 6 months	OKS-pain score of 14 or less at six months after knee replacement can be considered to be in chronic pain
Kim 2015[25] South Korea 2013-2014 1 hospital	Primary TKR, all women N=94 70.18 (5.74), range 20-80 100%	VAS/NRS pain 3 months	>5 points on an 11 point VNRS (verbal numeric rating scale)
Kiran 2015[26] UK 2003-2007 1 hospital	Primary TKR, all N=608 72 61.4%	OKS pain 12, 24 months	Has your knee replacement operation decreased your knee pain? High loss to follow up rate at 12 and 24 months
Kornilov 2018[27] Russia 2014 1 hospital	Primary TKR, all 18+ N=100 63 (8), range 47-81 95.0%	VAS/NRS pain 12 months	Not at least a two-point or approximately 30% (clinically significant) decrease in rating of pain interference with walking from baseline to 1 year (NRS scale 0-10)
Kurien 2018[28] UK Before 2017 1 hospital	Primary TKR probably, all N=50 66.4 (8.3) 60.0%	VAS/NRS pain 6 months	4 or greater
Larsen 2021[29] Denmark 2015-2016 1 hospital	Primary TKR, all 18+ N=185 68.8 (8.9) 55.7%	VAS/NRS pain 12 months	Pain intensity at rest >3 High loss to follow up rate
Latijnhouwers 2022[30]	Primary TKR, all N=282	VAS/NRS pain 12 months	Moderate to severe pain (NRS ≥4)

Prevalence of chronic pain after total hip or knee replacement

The Netherlands 2012-2017 2 hospitals	66 (8.4) 63.0%		High loss to follow up rate
Lavand'homme 2014[31] Belgium 2012 1 surgeon	Primary TKR or UKR, all N=128 68 (10) 66.4%	VAS/NRS pain 3 months	NRS ≥4/10
Lee 2022[32] South Korea 2017-2019 2 surgeons	Primary TKR probably, all N=172 70.7 (4.3) 89.2%	Pain disturbing sleep 3, 12 months	Night pain was defined as pain around the knee experienced at night that could disturb the patient's sleep
Leppanen 2021[33] Finland 2012-2014 1 hospital	Primary TKR, 65 years or younger N=205 60 63.0%	VAS pain exercise 24 months	VAS >30
Leung 2019[34] Singapore 2015 1 hospital	Primary TKR, all N=243 66 (8.3) 78.6%	Author own question 6, 12 months	No change or worsening pain/ slightly better
Lundblad 2008[35] Sweden Before 2006 1 hospital	Primary TKR, all N=69 68 50.7%	VAS/NRS pain 24 months	Pain at rest, VAS >2/10
Lyman 2018[36] USA 2007-2012 1 hospital	Primary TKR, all N=3815 74 (6) 63.0%	KOOS pain 24 months	Number not achieving MCID High loss to follow up rate
Mahdi 2020[37] Sweden 2016-2018 3 hospitals	Primary TKR, all N=615 69.7 52.2%	KOOS pain 12 months	8 cut off High loss to follow up rate
Mekkawy 2023[38] USA 2021 4 surgeons	Primary TKR, all N=112 65.5 (9.2) 69.0%	VAS pain 6 months	Probably NRS score of ≥1 in defined sites Concern over VAS ≥1 being too inclusive and high loss to follow up rate
Mercurio 2020[39] Italy 2015-2017 1 hospital	Primary TKR, all >18 N=45 69.6 (7.8) 65.0%	VAS/NRS pain 12 months	VAS >30 residual pain
Mezey 2023[40] Hungary 2019-2020 2 hospitals	Primary TKR probably, all N=101 69.2 Not reported	WOMAC pain 12 months	Not exceeding MCID High loss to follow up rate
Musbahi 2023[41]	Primary TKR, all 40+	WOMAC pain	WOMAC pain score

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USA 2011-2014 4 hospitals	N=575 66.3 (8.3) 60%	12 months	improvement of <20 High loss to follow up rate
Nishimoto 2023[42] Japan 2021-2023 1 hospital	Primary TKR, all with no complications N=68 75.1 (7.3) 80.9%	KOOS pain 3, 6 months	Not achieving MCID of 10
Noiseux 2014[43] USA Before 2012 2 hospitals	Primary TKR, all 30+ N=215 61.7 (9.8) 58.0%	VAS/NRS pain 6 months	Moderate or severe pain with range of motion, VAS ≥1 Concern over VAS ≥1 being too inclusive
Orr 2022[44] USA 2016-2019 9 hospitals	Primary TKR, all N=7476 67 (9.0) 60.8%	KOOS pain 12 months	Not achieved PASS for KOOS pain High loss to follow up rate
Petersen 2015[45] Denmark Before 2014 1 hospital probably	Primary TKR, all N=78 69 59.0%	VAS/NRS pain 12 months	VAS >3 High loss to follow up rate
Petersen 2018[46] Denmark Before 2017 1 hospital	Primary TKR probably, all N= 200 69 (1.2) 57.0%	VAS/NRS pain 12 months	<30% reduction in pain
Phillips 2014[47] UK 2009-2010 1 hospital	Primary TKR, all N= 96 70.6 56.0%	VAS/NRS pain 3, 6, 12 months	VAS >3
Priol 2023[48] France 2011-2012 1 hospital	Primary TKR, all N=129 74 (10), range 45-94 72.3%	VAS/NRS pain 6 months	Vas 4+ High loss to follow up rate
Pua 2019[49] Singapore 2013-2017 1 hospital	Primary TKR, all 50+ N=5325 68 (7.5) 75.0%	OKS pain 6 months	Moderate or severe pain
Quintana 2006[50] Spain 1999-2000 7 hospitals	Primary TKR, all N=792 71.9 73.0%	WOMAC pain 6 months	No improvement in pain greater than MCID
Rice 2018[51] New Zealand 2012-2015 3 hospitals	Primary TKR, all 18+ N=300 69 (10), range 48-90 48.0%	VAS/NRS pain 6, 12 months	VAS >3
Sideris 2022[52] USA	Primary TKR, all N=179	VAS/NRS pain 6 months	NRS 4+

Prevalence of chronic pain after total hip or knee replacement

2016-2018 1 hospital	67.1 (8.1) 56.2%		
Singh 2014[53] USA 1993-2005 1 hospital	Primary TKR, all N=7229 68 (10) 56.0%	Author own question 24 months	Moderate-severe pain
Solberg 2023[54] USA 2020 22 surgeons	Primary TKR probably, all N=239 66.2 (8.5), range 37-87 60.7%	Author own question 3 months	To what extent have you obtained relief: somewhat, minimal or not at all High loss to follow up rate
Stephens 2002[55] USA Before 2001 1 hospital	Primary TKR, all 50+ N=68 67.4 (8.1), range 50-88 54.0%	WOMAC pain 6 months	No change or increase in pain from pre-operative
Tang 2023[56] China 2020-2021 1 hospital	Primary TKR probably, all 65+ N=196 72 75.1%	VAS/NRS pain 3 months	NRS scores ≥4
Terradas-Monllor 2024[57] Spain 2018-2020 1 home rehabilitation service	Primary TKR or UKR, all 18+ N=115 70.5 (10.7) 66.1%	VAS/NRS pain 3, 6 months	VAS 3+
Thomazeau 2016[58] France 2013 1 hospital	Primary TKR, all N=109 69.2 (9) 71.6%	VAS/NRS pain 6 months	NRS score ≥1/10 for the last 8 days
Tian 2022[59] China 2018-2019 1 hospital	Primary TKR or UKR, all <90 N=271 Not reported 80.8%	Author own question 24 months	Moderate or severe pain on movement
Utrillas-Compaired 2014[60] Spain 2009 1 hospital	Primary TKR, all N=215 73 (6.35) 69.3%	KSS pain 12 months	KSS pain poor KSS may not be entirely patient reported
van der Wees 2017[61] The Netherlands 1993-2014 1 hospital	Primary TKR, all N=704 65 (12) 64.5%	VAS/NRS pain 6, 12 months	30% or less improvement in VAS pain High loss to follow up rate at 6 and 12 months
Vina 2020[62] USA 2005-2015	Primary TKR, all N=315 67.3 (8.6)	WOMAC pain 24 months	Less than MCID

Prevalence of chronic pain after total hip or knee replacement

4 hospitals	60.9%		
Vuorenmaa 2008[63] Finland Before 2007 2 surgeons	Primary TKR, all <80 N=51 70 (5) 80%	VAS/NRS pain 3 months	VAS >30/100
W-Dahl 2014[64] Sweden 2008-2010 2 hospitals	Primary TKR, all N=2736 69.3 (8.7) 58.5%	KOOS pain 12 months	Unchanged or worse pain
Waimann 2014[65] USA 2004-2007 2 hospitals	Primary TKR, all N=236 65.1 (8.9) 66.0%	WOMAC pain 6 months	Less than MCID
Wylde 2013[66] UK 2010-2011 1 hospital	Primary TKR, all N=57 68 58%	WOMAC pain 12 months	WOMAC pain score of >75
Wylde 2019[67] UK 2006-2009 1 hospital	Primary TKR, all eligible for Triathlon prosthesis N=266 70 (9.9), range 41-90 64%	WOMAC pain 3, 12, 24 months	Worse or no change in WOMAC pain High loss to follow up rate
Yan 2023[68] China 2021-2023 1 hospital	Primary TKR, all 45+ N=470 63.4 (7.4) 69.9%	VAS/NRS pain 6 months	NRS score of ≥1 at rest and/or on movement Concern over VAS ≥1 being too inclusive

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S3.1 Mean age and range

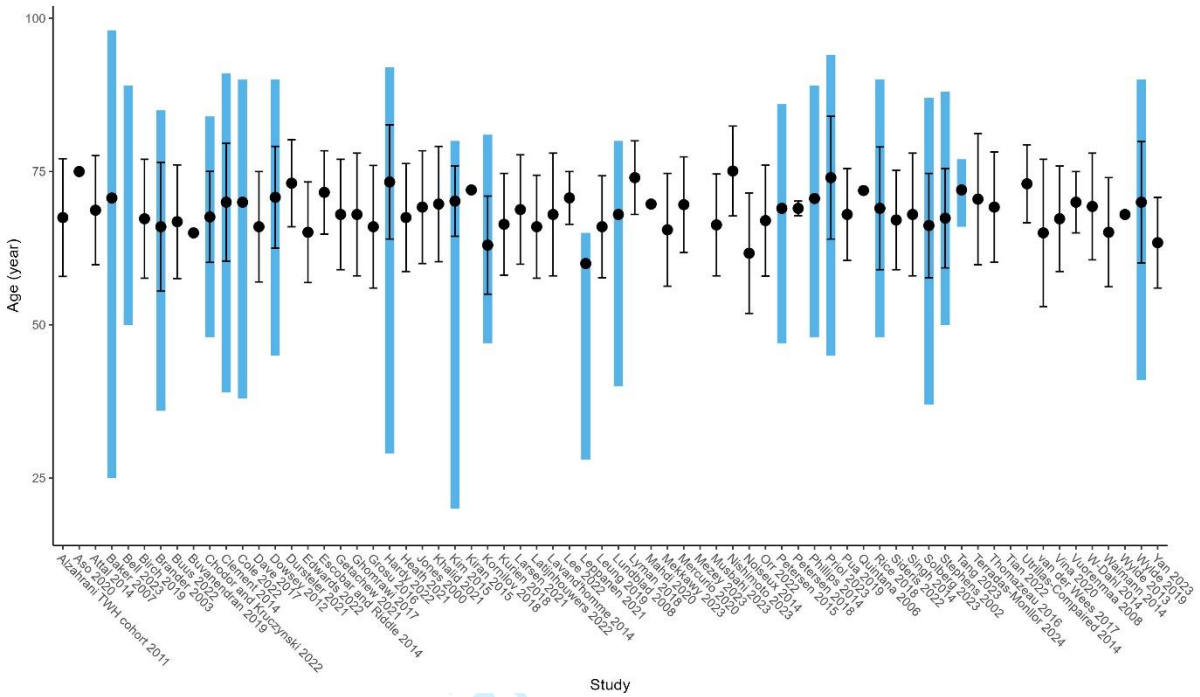


Figure S3.1. Mean age and their standard deviations reported in the individual studies. Range of age was plotted as blue bars.

S3.2 Proportion of females

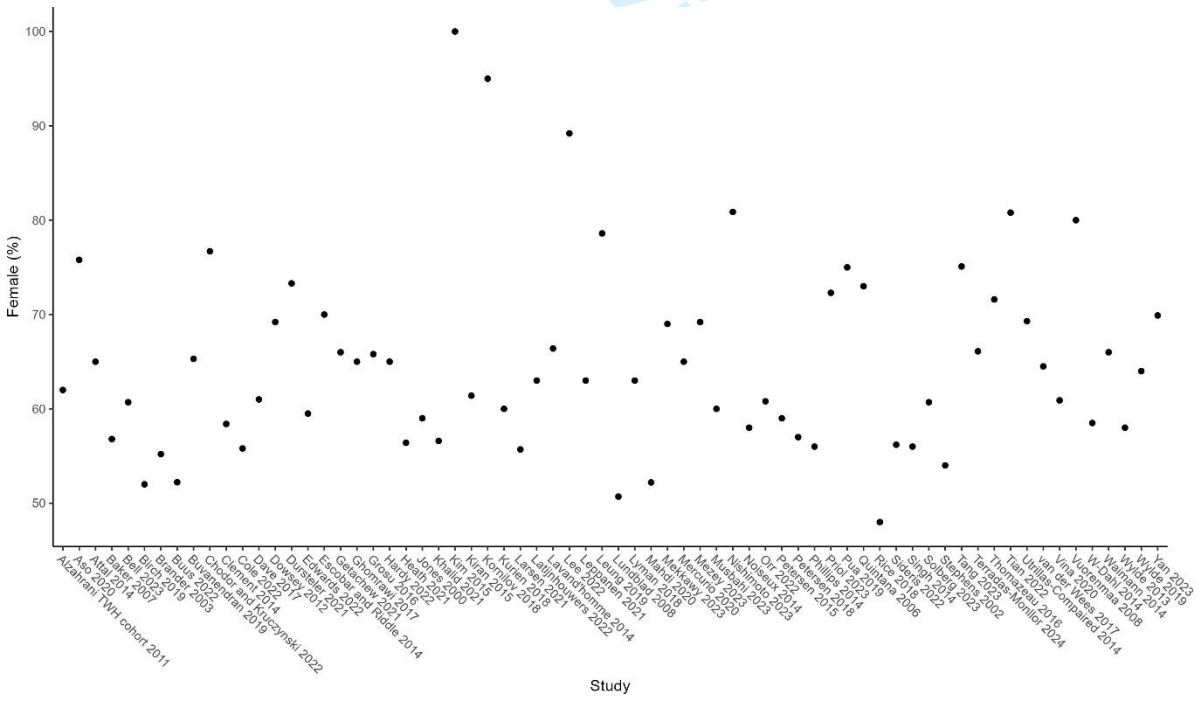


Figure S3.2. Proportion of females reported in the individual studies

S3.3 Data collection timeframe

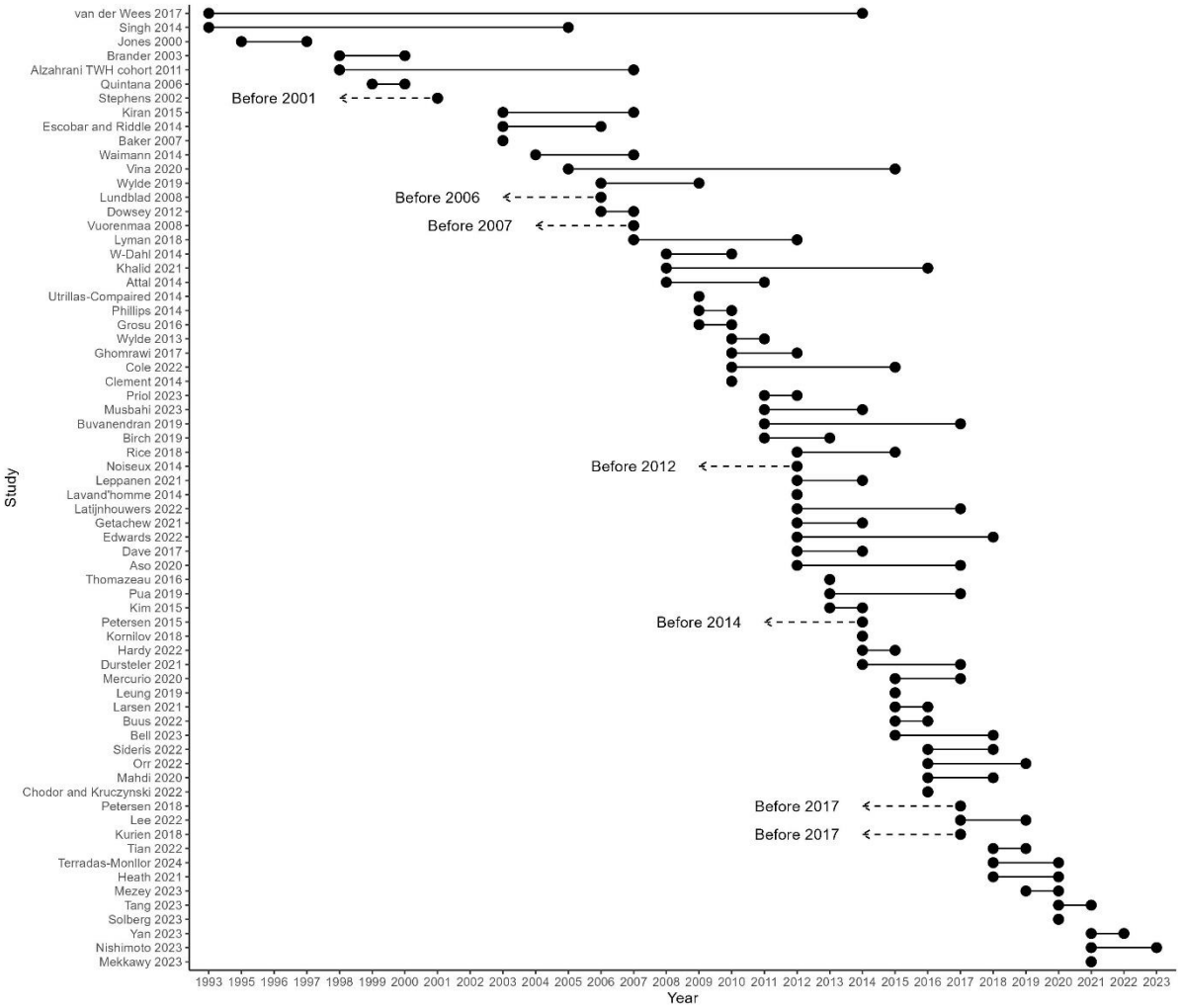


Figure S3.3. Data collection timeframe in the individual studies.

S3.4 Proportions of lost to follow-ups and revisions

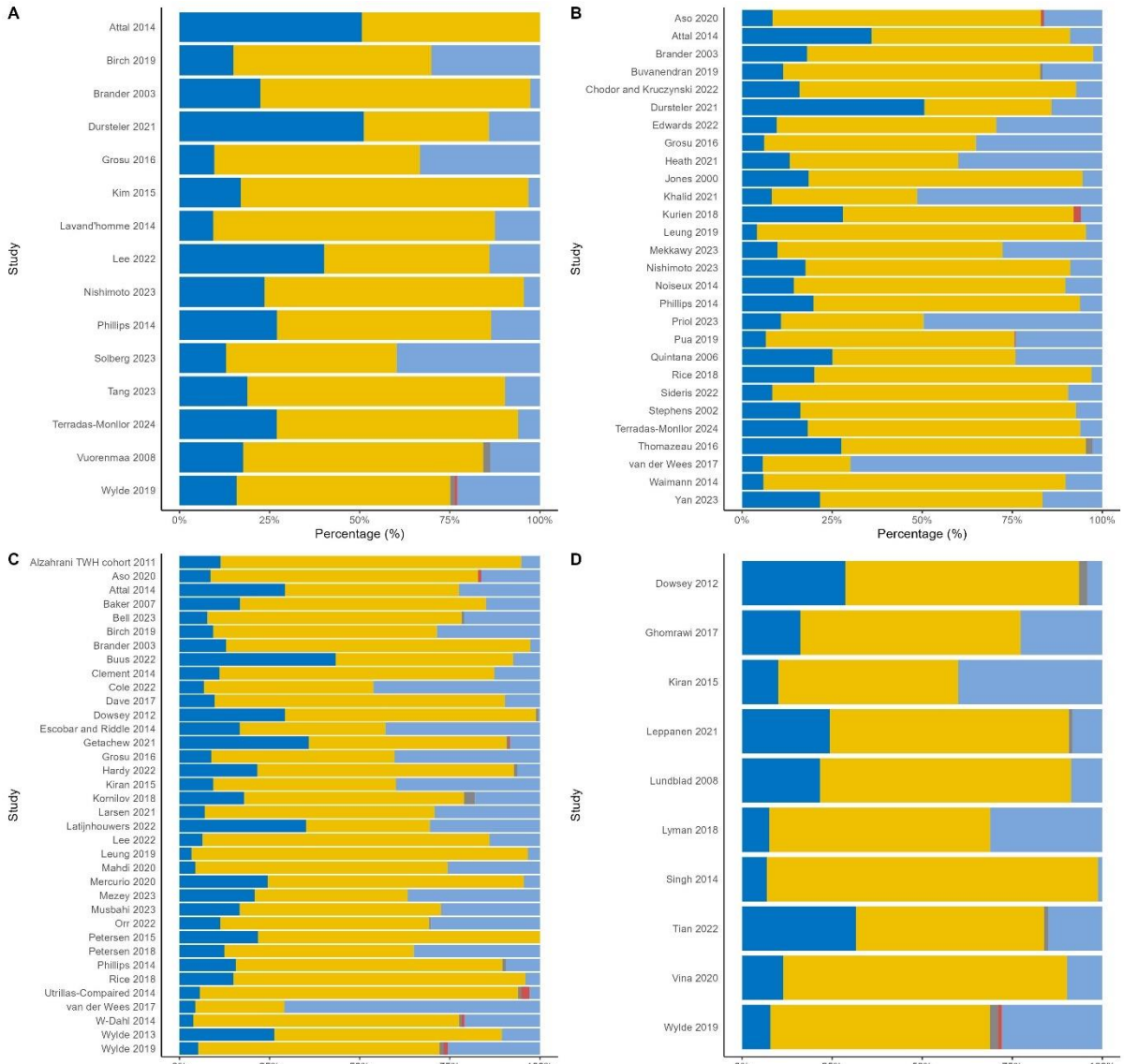


Figure S3.4. Favourable and unfavourable pain outcomes and reasons of missing data reported in 3, 6, 12, and 24 months (represented in sub-plots A, B, C, and D, respectively) in TKR studies.

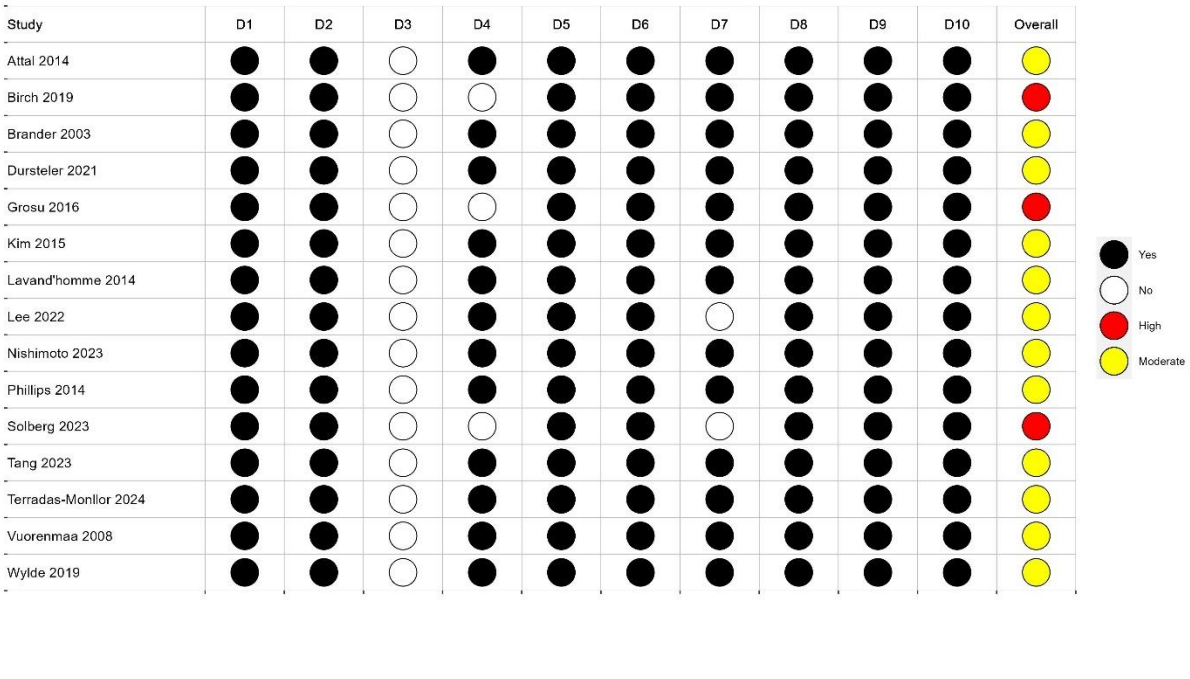
Prevalence of chronic pain after total hip or knee replacement

S4. Traffic light plot of the risk of bias assessments in TKR studies

The corresponding domains in the figures are:

- D1: Was the study's target population a close representation of the national population in relation to relevant variables?
- D2: Was the sampling frame a true or close representation of the target population?
- D3: Was some form of random selection used to select the sample, OR was a census undertaken?
- D4: Was the likelihood of nonresponse bias minimal?
- D5: Were data collected directly from the subjects (as opposed to a proxy)?
- D6: Was an acceptable case definition used in the study?
- D7: Was the study instrument that measured the parameter of interest shown to have validity and reliability?
- D8: Was the same mode of data collection used for all subjects?
- D9: Was the length of the shortest prevalence period for the parameter of interest appropriate?
- D10: Were the numerator(s) and denominator(s) for the parameter of interest appropriate?

S4.1 TKR studies (3 months)



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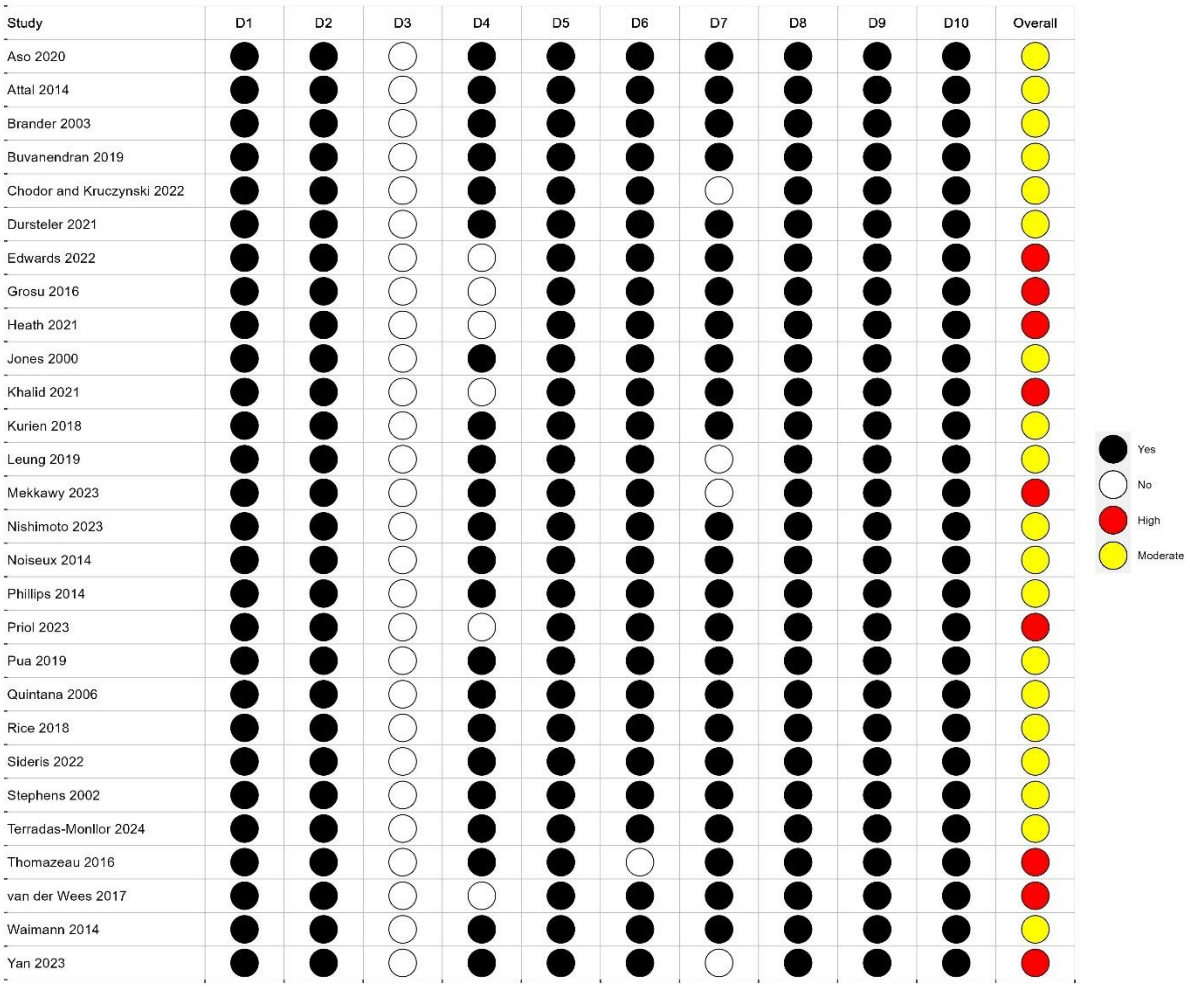
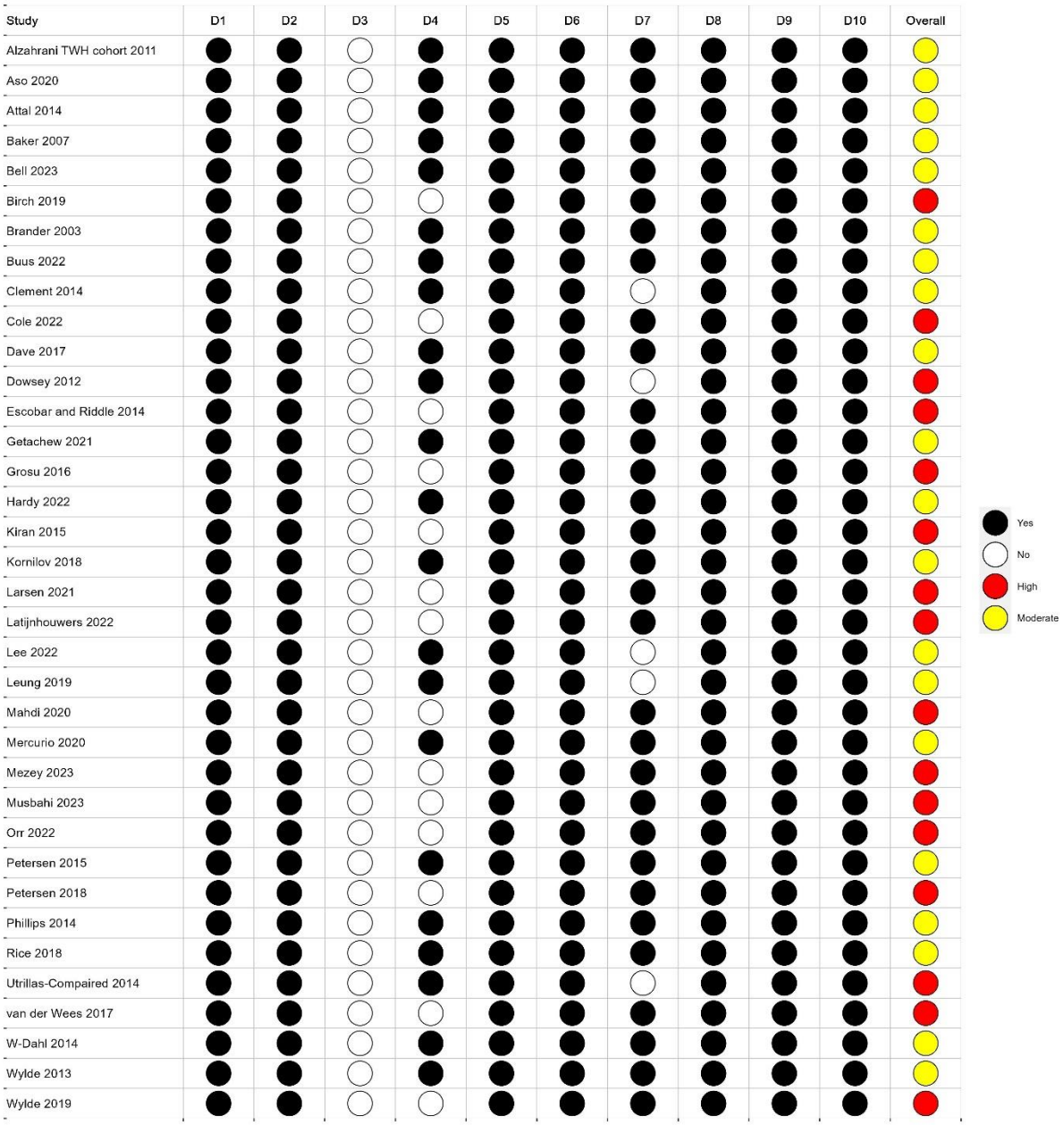
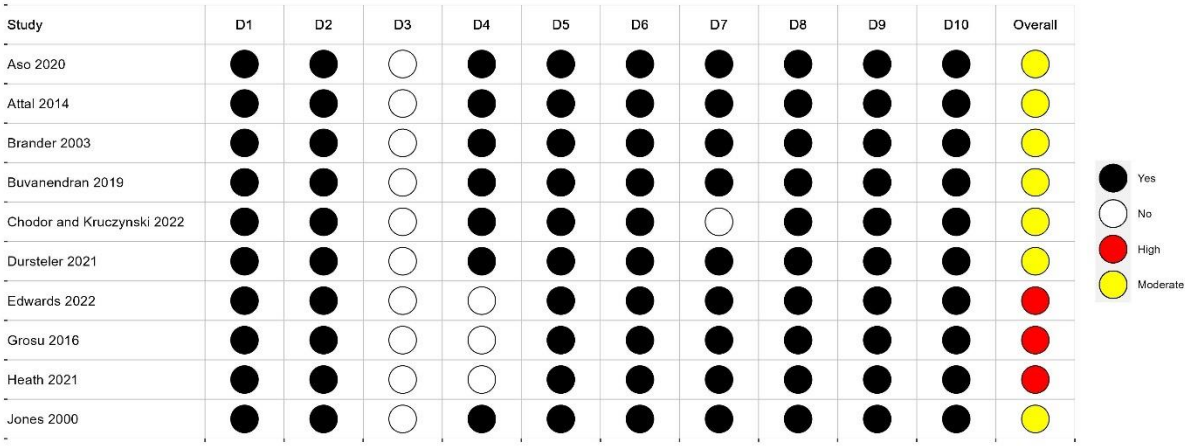
S4.2 TKR studies (6 months)



S4.3 TKR studies (12 months)



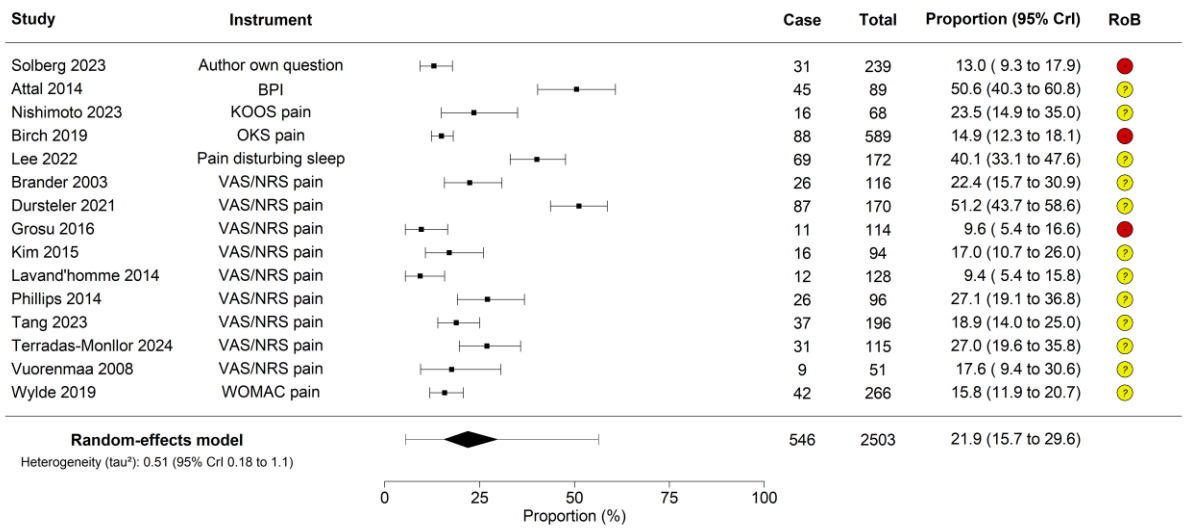
S4.4 TKR studies (24 months)



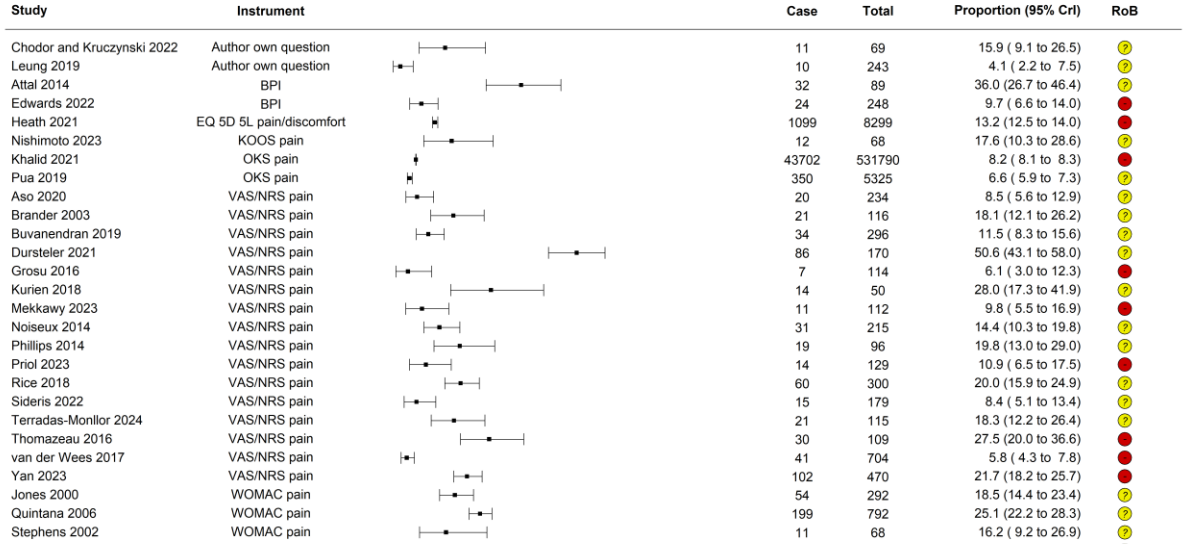
Prevalence of chronic pain after total hip or knee replacement

S5. Forest plots of univariate meta-analyses in TKR studies

S5.1 TKR studies (3 months)

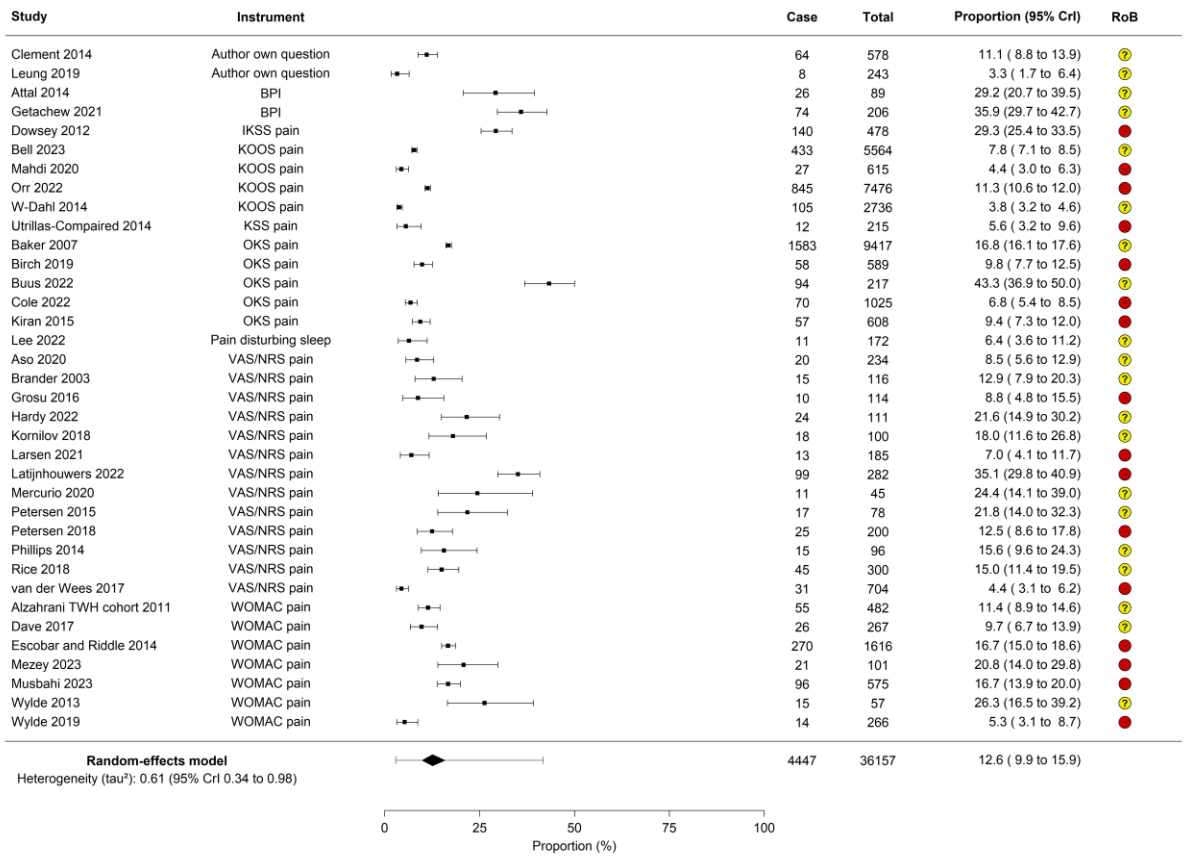


S5.2 TKR studies (6 months)

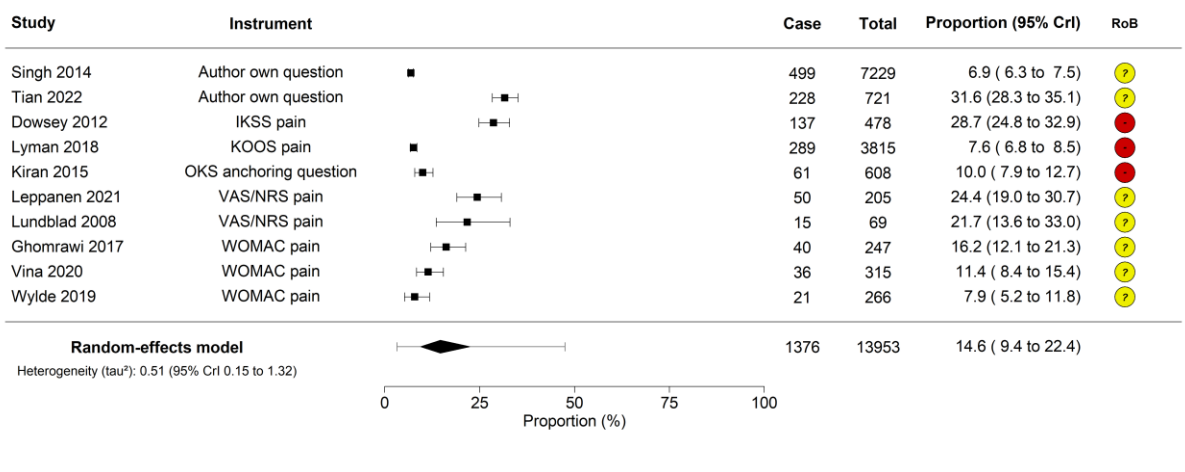


Prevalence of chronic pain after total hip or knee replacement

S5.3 TKR studies (12 months)



S5.4 TKR studies (24 months)



Prevalence of chronic pain after total hip or knee replacement

S6. Table of multivariate and univariate meta-analysis results in TKR studies

	Multivariate meta-analysis		Univariate meta-analysis	
Time	Median (95% CrI)	tau² (95% CrI)	Median (95% CrI)	tau² (95% CrI)
3 months	21.2 (16.9 to 26.4)	0.49 (0.28 to 0.91)	21.9 (15.6 to 29.4)	0.51 (0.18 to 1.1)
6 months	14.6 (11.9 to 17.8)	0.56 (0.34 to 0.91)	14.1 (10.9 to 17.9)	0.51 (0.27 to 0.9)
12 months	12.6 (10.3 to 15.5)	0.63 (0.41 to 0.99)	12.6 (9.9 to 15.9)	0.61 (0.35 to 0.99)
24 months	14.2 (10 to 20.1)	0.58 (0.25 to 1.55)	14.6 (9.5 to 22.4)	0.52 (0.16 to 1.35)

S7. Meta-regression analyses in TKR studies

S7.1 Mean age

Time	No. studies	slope	intercept
3 months	15	0.133	-1.272
6 months	28	0.082	-1.851
12 months	34	-0.029	-1.942
24 months	9	-0.073	-1.886

S7.2 Proportion of females

Time	No. studies	slope	intercept
3 months	15	0.009	-1.273
6 months	28	-0.040	-1.697
12 months	36	-0.006	-1.939
24 months	10	0.045	-1.798

S7.3 Sample sizes

Time	No. studies	slope	intercept
3 months	15	-0.001	-1.269
6 months	28	0.000	-1.785
12 months	36	0.000	-1.936
24 months	10	0.000	-1.750

Prevalence of chronic pain after total hip or knee replacement

S8. Subgroup analyses in TKR studies

- Geographic region (categorical; North America, Asia, Europe, and Australia)
- Data source (categorical; surgeons, single hospital, multi-centre, and national registry
- Pain outcomes instruments (categorical; multidimensional, e.g. WOMAC pain, simple, e.g. VAS/NRS and EQ-5D 5L, and not validated, e.g. author's own questionnaires)

S8.1 Geographical regions

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Asia	4	24.26 (11.85 to 42.3)	0.32 (0 to 2.34)
Europe	9	22.17 (12.42 to 35.18)	0.77 (0.19 to 2.17)
North America	2	16.63 (0.92 to 81.83)	0.21 (0 to 31.7)
6 Months			
Asia	5	9.91 (4.04 to 21.69)	0.64 (0.06 to 3.19)
Australia	2	15.53 (1.23 to 73.87)	0.19 (0 to 23.85)
Europe	12	17.99 (10.88 to 27.3)	0.77 (0.27 to 1.85)
North America	9	11.87 (8.87 to 15.58)	0.13 (0 to 0.45)
12 Months			
Asia	3	5.81 (2.2 to 12.88)	0.12 (0 to 2.76)
Australia	2	21.45 (0.1 to 98.64)	0.73 (0 to 97.26)
Europe	25	13.54 (9.91 to 18.16)	0.72 (0.37 to 1.29)
North America	6	11.15 (8.31 to 14.9)	0.09 (0.01 to 0.4)
24 Months			
Asia	1	31.36 (28.02 to 34.79)	NA
Australia	1	28.29 (24.49 to 32.56)	NA
Europe	4	14.29 (5.86 to 32.4)	0.47 (0.03 to 3.51)
North America	4	9.56 (5.19 to 17.04)	0.2 (0 to 1.45)

S8.2 Setting

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Other	1	26.44 (19.1 to 34.38)	NA
Single hospital	8	25.41 (15.64 to 38.72)	0.55 (0.13 to 1.73)
Surgeon	6	16.89 (8.43 to 29.76)	0.55 (0.07 to 2.2)
6 Months			
Multicentre	6	13.84 (7.93 to 22.5)	0.35 (0.04 to 1.41)
Other	2	18.34 (7.93 to 37.29)	0.02 (0 to 2.68)
Registry	1	8.22 (8.14 to 8.29)	NA
Single hospital	16	15.03 (9.79 to 21.64)	0.73 (0.3 to 1.55)
Surgeon	3	10.82 (3.35 to 30.39)	0.26 (0 to 5.13)
12 Months			
Multicentre	12	11.29 (7.37 to 16.83)	0.56 (0.19 to 1.31)
Registry	1	16.80 (16.07 to 17.57)	NA
Single hospital	20	13.96 (9.77 to 19.93)	0.77 (0.34 to 1.47)
Surgeon	3	8.93 (4.2 to 16.32)	0.05 (0 to 1.6)
24 Months			
Multicentre	1	11.50 (8.14 to 15.03)	NA
Single hospital	9	14.98 (9.11 to 23.7)	0.57 (0.16 to 1.54)

S8.3 Pain outcome instruments

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Multidimensional	5	26.76 (12.16 to 49.19)	0.7 (0.09 to 3.37)
Not validated	1	12.98 (0 to 100)	NA
Simple	9	20.6 (13.08 to 31.41)	0.5 (0.11 to 1.47)
6 Months			
Multidimensional	9	13.68 (8.49 to 22.5)	0.56 (0.14 to 1.57)
Not validated	2	7.65 (0 to 99.79)	1.72 (0 to 219.88)
Simple	17	15.15 (10.99 to 20.57)	0.49 (0.2 to 1.03)
12 Months			
Multidimensional	21	12.67 (8.95 to 17.66)	0.72 (0.33 to 1.34)
Not validated	2	6.51 (0 to 98.5)	1.52 (0 to 166.77)
Simple	13	13.91 (9.63 to 19.73)	0.44 (0.14 to 1.02)
24 Months			
Multidimensional	6	12.39 (6.86 to 20.55)	0.41 (0.07 to 1.58)
Not validated	2	15.65 (0 to 99.99)	3.63 (0.07 to 399.6)
Simple	2	23.53 (8.04 to 48)	0.02 (0 to 4.48)

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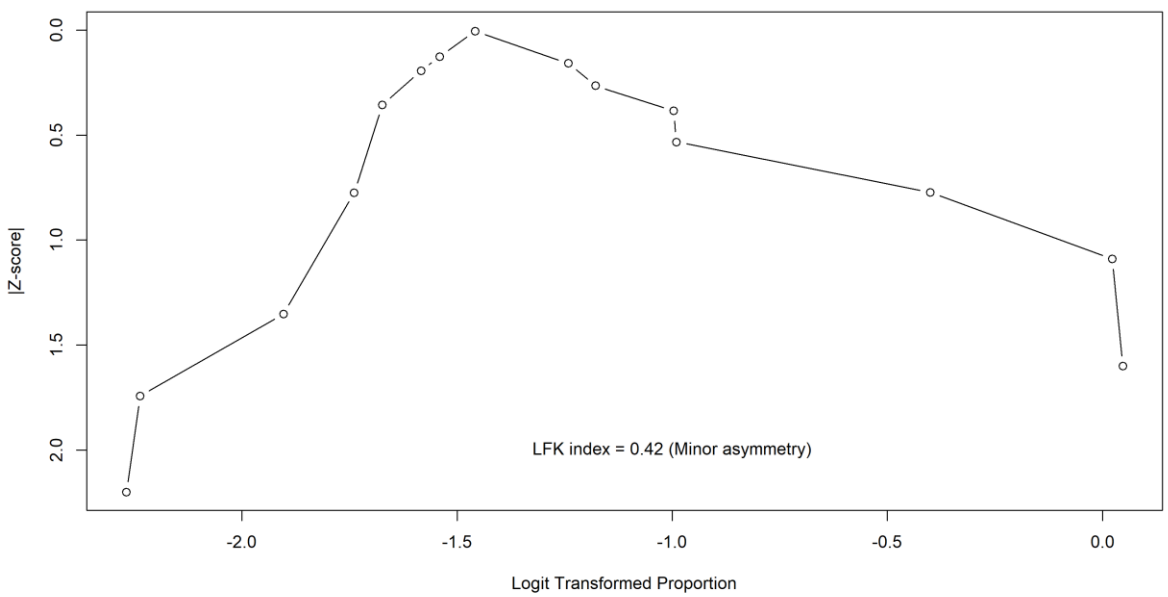
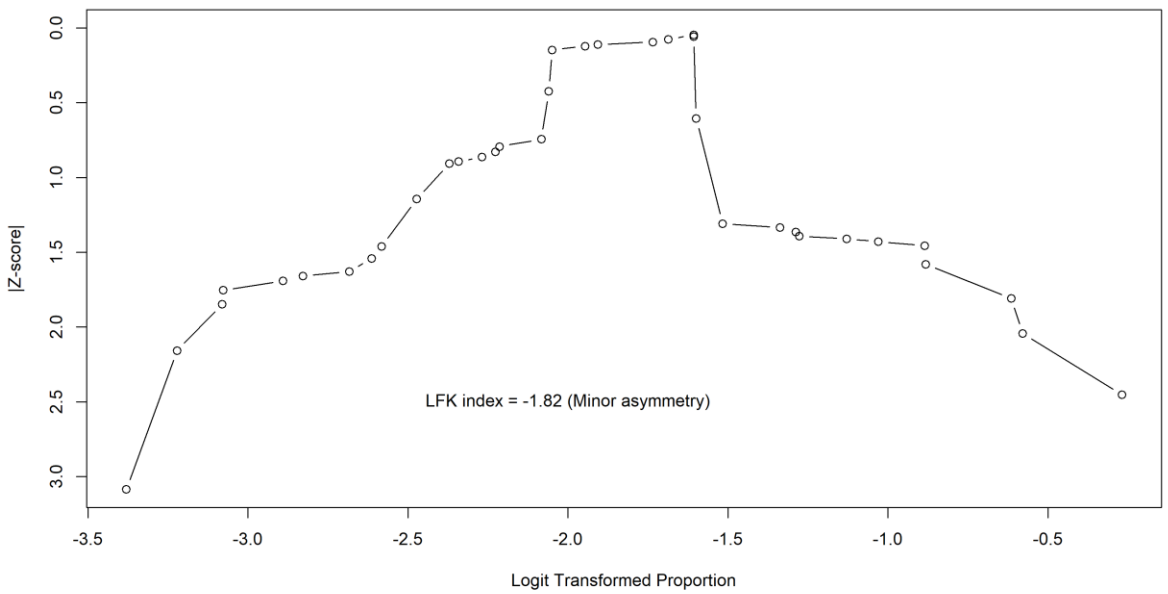
S9. Doi plots and the LFK indexes in TKR studies

S9.1 TKR studies (3 months)

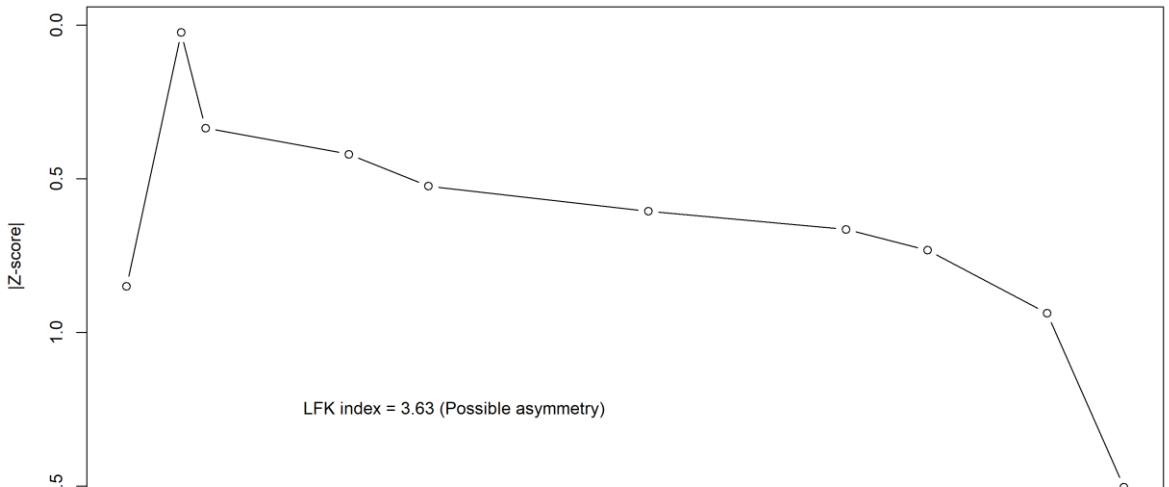


S9.2 TKR studies (6 months)

S9.3 TKR studies (12 months)



S9.4 TKR studies (24 months)



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S10. Sensitivity analyses

In the sensitivity analysis, we excluded the following studies based on their unique clinical characteristics:

- Tang 2023 (impact on 3 months results only)
- Leppanen 2021 (impact on 24 months results only)
- Fast track studies (impact on 3 and 12 months results only)
- Mekkawy 2023 and Yan 2023 (impact on 6 months results only)
- Studies on TKR or UKR operations
- Studies with more than 20% lost to follow-up
- High risk of bias studies

Name	No. studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Excluding Tang 2023	14	22.12 (15.4 to 30.2)	0.55 (0.19 to 1.21)
Excluding Fast track studies	14	22.56 (15.96 to 30.84)	0.53 (0.17 to 1.18)
Excluding TKR or UKR studies	12	23.68 (16.36 to 33.17)	0.53 (0.17 to 1.29)
Excluding studies with > 20% loss to follow-up	11	26.13 (18.08 to 36.46)	0.49 (0.14 to 1.25)
Excluding studies with overall high risk of bias	12	25.01 (17.87 to 34.74)	0.48 (0.16 to 1.17)
6 Months			
Excluding Mekkawy 2023 and Yan 2023	26	13.97 (10.74 to 18.13)	0.54 (0.27 to 0.95)
Excluding TKR or UKR studies	26	14.24 (10.88 to 18.46)	0.54 (0.27 to 0.95)
Excluding studies with > 20% loss to follow-up	19	16.78 (12.37 to 22.52)	0.52 (0.22 to 1.03)
Excluding studies with overall high risk of bias	19	15.63 (11.25 to 21.19)	0.58 (0.24 to 1.12)
12 Months			
Excluding Fast track studies	34	12.15 (9.5 to 15.15)	0.55 (0.3 to 0.91)
Excluding TKR or UKR studies	35	12.72 (9.85 to 16)	0.63 (0.35 to 1.01)
Excluding studies with > 20% loss to follow-up	19	15.3 (11.09 to 21.01)	0.58 (0.23 to 1.16)
Excluding studies with overall high risk of bias	20	14.37 (10.14 to 19.49)	0.65 (0.28 to 1.23)
24 Months			
Excluding Leppanen 2021	9	13.78 (8.33 to 21.28)	0.52 (0.15 to 1.45)
Excluding TKR or UKR studies	9	13.18 (8.59 to 20.26)	0.42 (0.11 to 1.18)
Excluding studies with > 20% loss to follow-up	6	18.74 (9.79 to 33.5)	0.59 (0.11 to 2.29)
Excluding studies with overall high risk of bias	7	15.28 (8.68 to 26.24)	0.53 (0.12 to 1.78)

*Abbreviation: TKR: Total Knee Replacement; UKR: Unicompartmental Knee Replacement

Prevalence of chronic pain after total hip or knee replacement

S11. Characteristics of THR studies

Study Country Recruitment dates Setting	Operation Number of patients Age (SD), range % women	Pain measure	Definition of unfavourable pain outcome High risk of bias concern
Cleveland Clinic OME Arthroplasty Group 2020[1] USA 2015-2018 6 hospitals	Primary THR, all N=3449 Median 65 (IQR 57-72) 57.4%	HOOS pain 12 months	Less than MCID
Erlenwein 2017[2] Germany 2012 1 hospital	Primary THR, all 18+ N=125 63 (12.6) 58%	NRS pain 6 months	Maximum NRS >3 during previous 4 weeks
Jones 2000[3] Canada 1995-1997 1 health region	Primary THR, all 40+ N=242 68.2 (11.1) 60%	WOMAC pain 6 months	Moderate/ severe pain defined as a gain of <10 points on the WOMAC pain dimension
Mezey 2023[4] Hungary 2019-2020 2 hospitals	Primary THR, all N=88 68.7 (THR and TKR patients) 69.2%	WOMAC pain 12 months	Not exceeding MCID High loss to follow up rate
Nikolajsen 2006[5] Denmark 2003 National registry	Primary THR, 18-90 years N=1231 71.6 (8.7) Not reported	Authors' own scale of presence of hip pain and impact on daily life 12-18 months	Pain with moderate, severe or very severe impact on daily life
Page 2016[6] Canada 2009-2012 1 hospital	Primary THR, all 18-75 N=150 60 (9.2) 48%	Authors' own scale 6 months	Chronic pain if pain rated as "discomforting", "distressing", "horrible," or "excruciating" Concern as RCT analysed as cohort study
Palazzo 2014[7] France 2009 3 hospitals	Primary THR, all N=129 63.5 (13.5) 49.6%	Author's own residual pain scale 12 months	"To what extent have you obtained a relief or improvement as a result of THA in the following areas?" (from 0: not at all; to 4: completely)
Quintana 2006[8] Spain 1999-2000 7 hospitals	Primary THR N=784 69.1 48.3%	WOMAC pain 6 months	No improvement in pain greater than MCID Concern for high loss to follow up rate
Ray 2020[9] Sweden 2008-2015 National registry	THR N= 127,660 68 (10) 56%	EQ-5D VAS pain/discomfort 12 months	Worse or no change in pain/discomfort Concern for high loss to follow up rate
Singh and Lewallen 2010[10] USA	Primary THR N=9154 65 (13.3)	Authors' own scale: How much pain do you have in your operated	Moderate or severe pain Concerns for high loss to follow up rate

Prevalence of chronic pain after total hip or knee replacement

1993-2005	51%	hip? None, mild, moderate or severe 24 months	
Tang 2023[11] China 2020-2021 1 hospital	Primary THR probably, all 65+. Osteoarthritis or osteonecrosis (not fracture) N=89 72 (range 63-81) 62.5%	NRS pain 3 months	NRS scores ≥4 Note, n and losses to follow up estimated as proportions because n hips and knees reported together

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S11.1 Proportions of lost to follow-ups and revisions

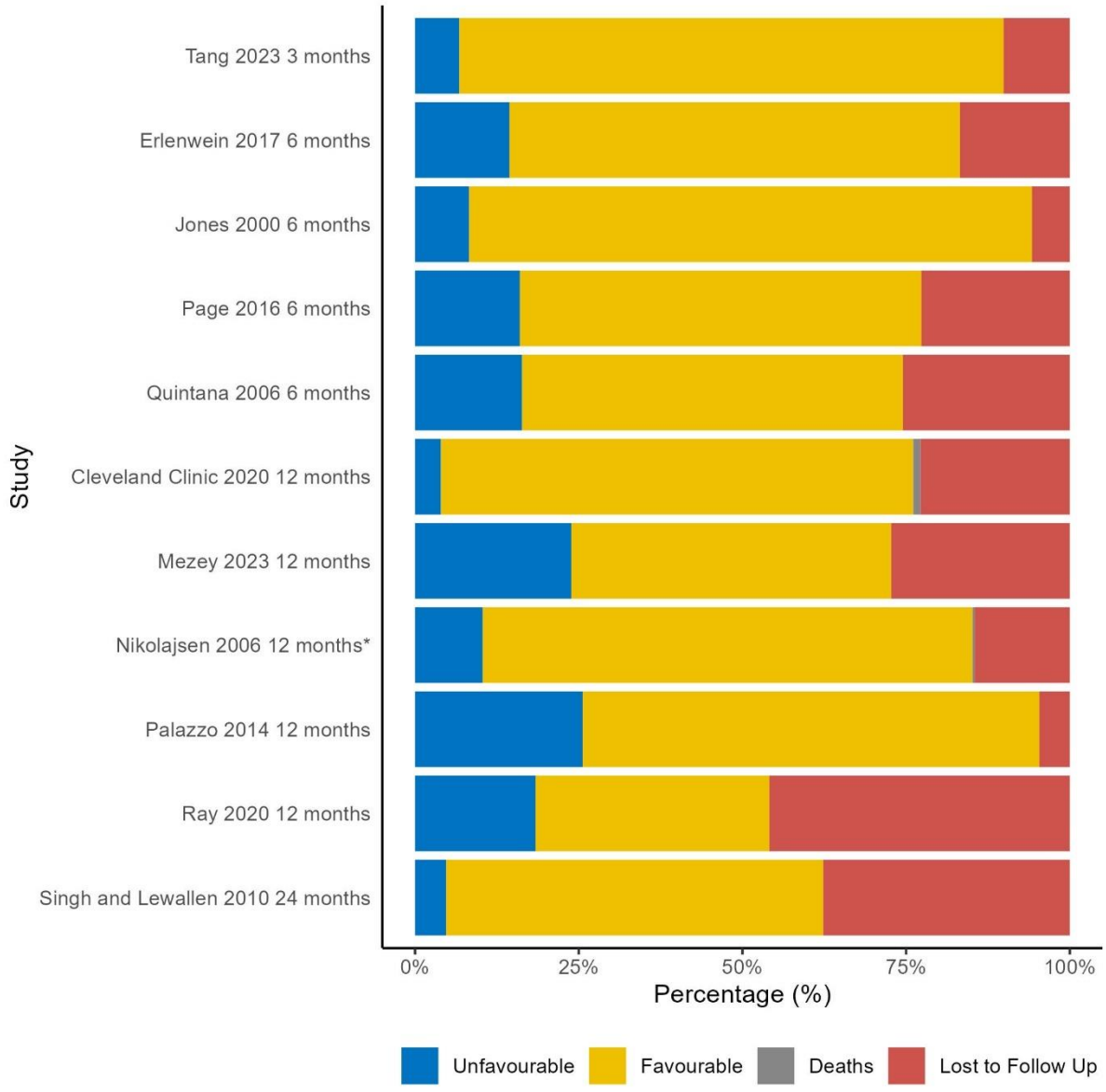
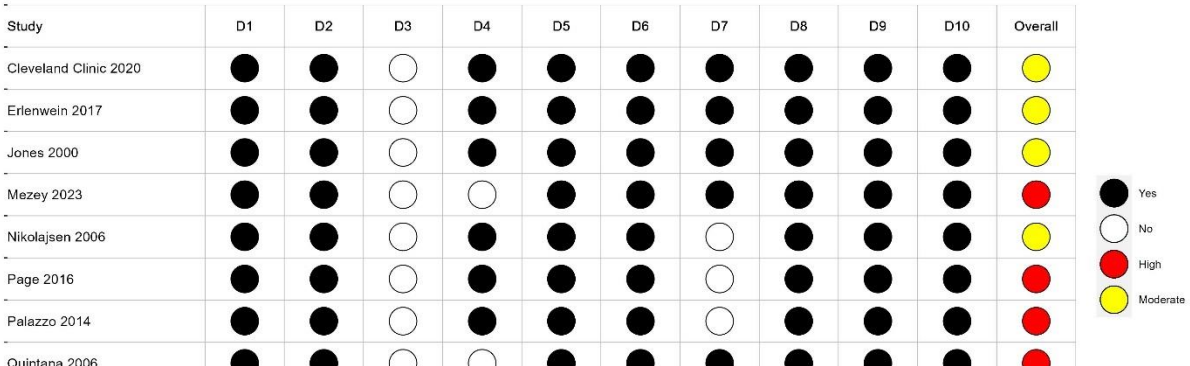


Figure S12.1. Favourable and unfavourable pain outcomes and reasons of missing data in THR studies.

S12. Traffic light plot of the risk of bias assessments in THR studies



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What proportion of people have long-term pain after total hip or knee replacement? An update of a systematic review and meta-analysis

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What proportion of people have long-term pain after total hip or knee replacement? An update of a systematic review and meta-analysis

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Running title

Prevalence of chronic pain after total hip or knee replacement

Keywords

Chronic pain; Total hip replacement; Total knee replacement; Systematic review; Meta-analysis

Abstract

Objectives

To update our previous systematic review to synthesise latest data on the prevalence of long-term pain in patients who underwent total hip replacement (THR) or total knee replacement (TKR). We aim to describe the prevalence estimates and trends in this review.

Design

Systematic review and meta-analysis

Data Sources

Update searches were conducted in MEDLINE and Embase databases from 1st January 2011 to 17th February 2024. Citation tracking was used to identify additional studies.

Eligibility Criteria

We included prospective cohort studies reporting long-term pain after THR or TKR at 3, 6, 12 and 24 months post-operative.

Data Extraction and Synthesis

Two reviewers independently identified studies as eligible. One reviewer conducted data extraction, checked by a second reviewer. The risk of bias assessment was performed using Hoy's checklist. Bayesian, random-effects meta-analysis was used to synthesise the results.

Results

For TKR, sixty-eight studies with 89 time points, including 598,498 patients, were included. Multivariate meta-analysis showed a general decrease in pain proportions over time: 21.9% (95% CrI 15.6 to 29.4) at 3 months, 14.1% (10.9 to 17.9) at 6 months, 12.6% (9.9 to 15.9) at 12 months, and 14.6% (9.5 to 22.4) at 24 months. Considerable heterogeneity, unrelated to examined moderators, was indicated by substantial prediction intervals in the univariate models. Substantial loss to follow-up and risk of bias led to low confidence in the results. For THR, only eleven studies were included, so it was not possible to describe the trend. Univariate meta-analysis estimated 13.8% (8.5-20.1) and 13.7% (4.8-31.0) of patients experiencing long-term pain 6 and 12 months after THR, respectively, though concerns in risk of bias results reduced confidence in these findings.

Conclusions

Our review suggests that approximately 22% of patients report unfavourable pain 3 months post-TKR, with 12-15% experiencing long-term pain up to 2 years. At least 14% report unfavourable pain 6-12 months after THR. Given the prevalence of chronic post-surgical

pain, implementing existing and developing new preventive and management strategies is crucial for optimal patient outcomes.

Study registration

PROSPERO CRD42023475498

Strengths and limitations of this study

- We updated a previous review using the latest review methodology, including Bayesian, multivariate meta-analysis and risk of bias assessment, to summarise the prevalence rates reported across studies of chronic post-surgical pain in patients undergoing total knee or hip replacement.
- We included a wide range of patient-reported measures of pain across studies which resulted in heterogeneity
- These prevalence rates are likely underestimated due to loss to follow-up and the high risk of bias in the included studies.
- Our sensitivity and scenario analyses offer readers plausible and robust prevalence estimates.

Introduction

The primary reason that people with osteoarthritis undergo joint replacement surgery is because of persistent pain that has failed to improve with non-invasive management.[1 2] About 100,000 each of primary total knee and hip replacements were performed in the UK in 2022,[3 4] and in Organisation for Economic Co-operation and Development countries in 2015, over 1.5 million primary knee and nearly 1.7 million primary hip replacements were performed.[5] The number of people with osteoarthritis is projected to increase[6 7] and even in Germany, a country with a declining population, rates of joint replacement are predicted to rise due to the increasing use of knee replacement in younger people and the increasing number of older people requiring hip replacement.[8]

Potential improvements in pain and functionality ability are the primary reasons that patient elect to have a hip or knee replacement, and the most important contributing factors to patient satisfaction with the outcome of surgery.[9 10] It is important to note that pain and patient satisfaction are distinct constructs,[11] as patient satisfaction contains broader aspects of surgical outcomes beyond solely pain relief. In the literature, the terms, such as persistent pain[10 12-14], unchanged pain[15], residual pain[16-18], and worsening pain[19 20], are often used to describe pain that persists despite surgery providing functional improvements and high satisfaction.[11] It is widely recognised that some people experience continuing pain in the months and years following surgery. Our previous systematic review,[21] with searches up to 2011, brought together longitudinal studies in representative populations receiving knee or hip replacement. We found that for a majority of people, their pain outcome was favourable, but for 10-34% of patients the long-term pain outcome could be considered “unfavourable” (moderate-to-severe pain or for whom surgery had not relieved pain) after total knee replacement (TKR) and 7-23% after total hip replacement (THR).[21] Together with qualitative research into patients’ experiences,[22 23] our previous review stimulated research into the prediction, prevention, management and treatment of chronic pain after knee and hip replacement.

Twelve years on from publication of our previous review, our aim is to provide updated estimates of the incidence of long-term pain after total knee and hip replacement and explore factors that may influence the rates observed. Findings will support patients, clinicians and researchers as they face the challenge of preventing and treating chronic pain after total knee or hip replacement.

Methods

We updated our previous systematic review from our team,[21] with follow-up intervals between 3 and 24 months post-operative. We limited the follow-up to a maximum of 24 months as pain levels often plateau by this timepoint, and new onset pain beyond this may be related to implant failure.[24] With the more extensive data available for outcomes after TKR in this update, we planned to establish the trend of long-term pain over time up to 24 months post-operative.

The protocol was registered with PROSPERO (CRD42023475498) and this review was reported in accordance with MOOSE[25] (Supplementary material S1) and relevant contents in PRISMA[26] guidelines and the Cochrane handbook.[27]

Eligibility criteria

We sought prospective cohort studies including patients representative of the general population receiving total knee or hip replacement, predominantly from advanced osteoarthritis as in our previous review.[21] Cohorts were established pre- or peri-operatively in hospital orthopaedic departments and joint replacement centres and followed up prospectively at any defined time between 3 and 24 months. Studies specifically of unicompartmental knee replacement or hip hemiarthroplasty, revision surgery, or exclusively bilateral replacements were excluded.

Outcome

The outcome was the proportion of people with unfavourable pain in the operated joint at 3, 6, 12 and 24 months post-operative. We adopted the term 'unfavourable pain' from the previous review, which serves as a collective label to include the various descriptions used by study authors–such as persistent pain, worsening pain, or residual pain--rather than as an indicator of dissatisfaction.[21 28] In each study, unfavourable pain was defined using the study authors' definitions or through a consensus between two reviewers with extensive research experience in pain outcome measurement in total knee and hip replacement before commencement of data extraction. Most studies used a single cut-off value, often based on a pre-specified post-operative visual analogue scale (VAS) or numerical rating scale (NRS) score. For the few studies that provided multiple cut-off values, such as Musbahi and colleagues,[18] we selected the cut-off values that the authors concluded were the best balance between sensitivity and specificity. For studies that used general tools, such as the VAS or NRS, we only included those that reported VAS or NRS scores specific to the operated joint, rather than general VAS pain scores. To calculate the proportions, we extracted the number of recruited or followed patients as denominators and the number of

patients experiencing unfavourable pain as numerators. When a percentage or rate was provided, we rounded the numbers to the nearest whole number.

Searches

We conducted new searches of MEDLINE and Embase databases from January 2011 to 17th February 2024. The search strategies for MEDLINE and Embase are included in S2. Web of Science was used to track citations of the original review.[21] Excepting the search strategy, we applied no language restrictions at any stage of the review, with Google Translate used to translate sections of relevant non-English articles. We did not contact authors as we only focused on published studies. Studies reported only as abstracts were excluded.

Study selection and data collection

Studies identified were imported into EndNote 21 reference management software. After removal of duplicate records, one reviewer screened out clearly off-topic studies. Titles and abstracts of potentially relevant articles were acquired and assessed independently for eligibility by two reviewers. In cases of disagreement, a third reviewer was involved. Eligible articles identified in our previous systematic review were also included.

Data from eligible studies were entered into a Microsoft Excel spreadsheet by one reviewer with checking by a second reviewer. Extracted data were: country; dates of patient recruitment; setting (single or multiple surgeons, single or multiple hospitals, registry, or other; inclusion and exclusion criteria; whether routine “fast-track” surgery; patient characteristics (age, sex); assessment times; number of patients at baseline, number lost to follow up (or died or with revision surgery if reported) and number followed up; and patient reported pain outcome measure.

When more than one pain outcome was reported, we extracted them in order of preference: pain dimension data from osteoarthritis or joint specific outcome scores (Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC); Knee injury and Osteoarthritis Outcome Score (KOOS); Hip injury and Osteoarthritis Outcome Score (HOOS); Oxford Knee Score (OKS); Oxford Hip Score (OHS) and Knee Society Scores if patient generated (KSS, IKSS); Brief Pain Inventory (BPI); pain assessed in EuroQol instruments (EQ-5D or EQ-3D); joint pain after surgery, measured on a VAS or NRS; and other measures including those developed by study authors.

Risk of bias assessment

Two independent reviewers assessed risk of bias using the non-summative checklist described by Hoy and colleagues.[29] This checklist considers ten aspects of study conduct

relating to representation and selection, non-response (>25% of lost to follow-up as high risk), data collection and instrument used, follow up and methods used in calculation of rates. Overall risk of bias was judged to be low, moderate or high depending on whether any of the ten aspects gave concern.

Data synthesis approach

Our primary aim was to describe the proportion of people experiencing unfavourable pain outcomes over time. First, we summarised the characteristics of studies and inspected their clinical heterogeneity before the synthesis using tables and figures. We then meta-analysed proportions with an unfavourable pain outcome, along with accompanying 95% credible intervals (CrIs) and median between-study heterogeneity (τ^2) at 3, 6, 12, and 24 months' time separately when there were more than three studies. We also used prediction intervals to aid the between-study heterogeneity interpretation.[30] We used Bayesian framework with a random-effects model due to anticipated heterogeneity. Vague prior distributions (e.g. normal with mean 0 and variance 10^5) on model parameters were used. Posterior outcome distributions were based on at least 25,000 simulations after a burn-in of at least 1,000 to ensure convergence.

To account for the multiple time follow-ups reported in certain studies, we adopted a Bayesian, hybrid, multivariate meta-analysis of multiple factors[31] to describe the proportions across time points by borrowing information and accounting for within- and between-study correlations.

All analyses were performed using R version 4.3.1 on RStudio 2023.06.2+561. The *runjags* and *metafor* packages were used to produce pooled estimates, forest plots, meta-regression and subgroup analyses. The *metasens* package was used to generate Doi plots and the LFK index.[32] The *ggplot2* package was used to produce additional figures to explore the clinical heterogeneity in the studies.

Exploration of heterogeneity

For potential sources of heterogeneity, we used meta-regression to explore heterogeneity for continuous factors (mean age of the population, percentage of females, and baseline sample sizes) where more than ten studies were included in the meta-analysis. For categorical factors (geographic region, settings, and pain outcome instruments), we conducted subgroup analyses where more than five studies were included in the meta-analysis.

Sensitivity analysis

In sensitivity analysis, we excluded studies with specific inclusion criteria, those focused on "fast track" surgery, studies where a proportion of people underwent unicompartmental knee

replacement, studies with potentially over-inclusive unfavourable pain definitions, and studies with more than 20% lost to follow-up, and studies with an overall high risk of bias. Additionally, we performed worst-best scenario analyses by estimating the proportion of people lost to follow-up who experienced unfavourable pain outcomes, incrementing by tenths from 0% to 100%, to estimate their impact on the meta-analysis results.

Reporting bias and certainty assessment

We assessed publication bias using Doi plots and the LFK index (values between -1 and +1 indicate symmetry; values outside this interval indicate asymmetry) to aid the interpretation in cases where more than ten studies were included in the meta-analysis. We cross-checked the clinical study register and methods section in the report to evaluate non-reporting bias. The certainty of evidence assessment was not conducted because specific tools for systematic reviews of prevalence were unavailable.

Patient and public involvement

There was no direct patient and public involvement in this systematic review, however, it benefitted from being part of the NIHR-funded STAR programme, which aimed to improve outcomes for patients with chronic pain after knee replacement. [33]Patient and public involvement was integral to STAR, and we worked throughout the programme with an existing patient forum and developed a complementary group focusing exclusively on chronic pain after TKR.

Results

Searches of MEDLINE, Embase, citation tracking in Web of Science and inclusion of potentially relevant articles identified in our previous review yielded a total of 13,807 records. After screening out of clearly irrelevant studies by one reviewer, 979 records were screened in duplicate by two reviewers and ultimately 68 studies with 598,498 TKR participants and 11 studies with 143,101 THR participants were included. Study selection and reasons for exclusion at the full-text stage are summarised in Figure 1. Some articles from our previous review were excluded as the follow up period was longer than 24 months.

Total knee replacement

Individual study characteristics are summarised in S3. The grouped characteristics in Table 1. The baseline dates of data collection ranged from 1993 to 2023. Geographically, most studies were conducted in Europe (n=37) and North America (n=19). More than half of studies (n=39) collected their data at a single hospital, followed by multiple hospitals (n=18). Overall, 598,498 patients were included in the 68 studies with a median sample size per study of 235 (interquartile range 114 to 581). Patients in 52 studies with data had a mean age of 69.6 (SD 9.4) years, and 63% (58 to 69) were women. In terms of primary pain outcome reported, 31 studies reported multi-dimensional pain scales (WOMAC, OKS, KOOS, BPI, or KSS/IKSS), 29 studies reported VAS or NRS pain scores, and 6 studies used researchers' own measures.

After harmonising unfavourable pain outcomes at different time points, there were 15, 28, 36 and 10 studies with data available for 3, 6, 12 and 24 months post-operative. Risk of bias assessments are summarised in Figure 2 (for traffic light plots, see S4). Most studies were judged as overall moderate risk of bias with few overall high risk of bias due to losses to follow up of >25%, or use of scores which are not entirely patient completed or have concerns relating to a low pain cut off.

As noted in the previous review, the proportions of people with unfavourable pain varied widely across studies. Studies reported ranges of people with unfavourable pain at 3 months of 9.4 to 51.2%, at 6 months of 4.1 to 50.6%, at 12 months of 3.3 to 43.3%, and at 24 months of 6.9 to 31.6% (S5). We synthesised the unfavourable pain outcomes using multivariate meta-analysis (Figure 3), demonstrating a general decrease in pain proportions over time: 21.9% (95% CrI 15.6 to 29.4) at 3 months, 14.1% (10.9 to 17.9) at 6 months, 12.6% (9.9 to 15.9) at 12 months, and 14.6% (9.5 to 22.4) at 24 months. The results of the univariate models were similar due to the limited number of studies with multiple time points (S5), though with slightly wider CrIs (S6). The substantial prediction intervals in the univariate models suggested considerable heterogeneity.

We investigated potential heterogeneity using meta-regression and subgroup analyses in the univariate meta-analysis models. Meta-regression results showed no evidence of age, percentage of women, or sample size contributing to the heterogeneity of the proportion of individuals with unfavourable pain outcomes (S7).

Subgroup findings should be interpreted with caution due to the limited number of studies in some subgroups. In subgroup analyses, rates of unfavourable pain tended to be lower in studies involving patients from North America compared to other geographic groups (S8.1). Similarly, studies conducted in single-surgeon series settings showed lower rates of unfavourable pain outcomes (S8.2).

Outcome instruments that were not validated, frequently suggested low levels of unfavourable pain, while multidimensional measures were consistent with overall meta-analysis at 3, 6, 12 and 24 months (S8.3). Results were also consistent for simple pain measures at 3, 6 and 12 months, but data was limited at 24 months. Cut-offs which defined an unfavourable pain outcome were based on pain intensity, symptom improvement, the functional impact of pain, and minimally important clinical differences or patient acceptable symptom states calculated within each dataset. Excepting at 24 months when data was sparse, cut-offs relying on a simple dichotomisation by levels of pain intensity were reasonably consistent with meta-analyses (S8.4). In 3 and 5 studies respectively, cut-offs based on minimally important clinical differences in WOMAC or KOOS outcomes at 6 and 12 months provided similar estimates of unfavourable pain to the meta-analyses. At 24 months, in 3 studies the estimate of 10.88 (4.18 to 25.04) was lower than that in the overall meta-analysis, 14.6% (9.5 to 22.4). Two studies reported the proportion of people not achieving a patient acceptable symptom state at 12 months. Results were similar to those in the overall meta-analysis. In the studies with cut-offs based on symptom improvement, the proportions of people with unfavourable pain were lower than seen in the overall meta-analyses.

Although we observed small-study effects in the results (S9), potentially attributable to publication bias, it is likely that these resulted from the extremely large variations in sample sizes at the 6-, 12-, and 24-month follow-ups. We did not find evidence of non-reporting bias, as most studies reported long-term pain outcomes in accordance with their reported methods.

In sensitivity analyses, we individually excluded studies with specific criteria to evaluate their impact on the univariate meta-analysis results (S10). The effects of excluding these studies were generally minor, except for studies with a high risk of bias or a high proportion of lost to follow-up. To account for the varying degrees of loss to follow-up, we performed separate scenario analyses by assuming that the same proportion of participants lost to follow-up

experienced unfavourable pain outcomes in each study (Table 2). By assuming 10% to 30% of participants lost to follow-up might experience unfavourable pain, this approach could yield more realistic estimates, given the limited literature available for further imputation.

Total hip replacement

Eleven studies reported unfavourable pain outcomes in individuals who underwent THR. The characteristics of these studies are summarised in S11. Only one study reported unfavourable pain outcomes at the 3-month and 24-month time points, so a trend cannot be established. Studies reported ranges of people with unfavourable pain at 6 months of 8.3 to 16.3%, and at 12 months of 3.9 to 25.6% (Figure 4).

Meta-analysis of unfavourable pain outcomes provided similar results at 6 and 12 months, with 13.8% (8.5 to 20.1) and 13.7% (4.8 to 31.0), respectively. However, concerns regarding the risk of bias assessment (S12) lead to low confidence in these results.

Discussion

Through our systematic review and meta-analysis, we have synthesised the existing evidence on the proportion of patients who experience long-term pain after knee and hip replacement. By updating our previous review, we have been able to provide estimates of incidence rates at 3, 6, 12 and 24 months post-operative. As noted previously,[21] studies report widely varying estimates of unfavourable pain outcome, and these may depend on the methods and analyses used. For example, at 12 months after TKR when patients should have recovered from surgery and be largely unaffected by issues relating to implant failure, the range of unfavourable pain across studies was 3.3 to 43.3%. After THR at 12 months the range was 3.9 to 25.6%. With the large number of studies now available, meta-analyses have permitted us to provide point estimates with 95% credible intervals to describe uncertainty, and to explore patient and study level factors that may explain the variation in unfavourable pain observed.

Our meta-analyses suggest that the proportion of people with an unfavourable level of pain after TKR decreases between three and six months after surgery and then remains stable until at least two years. While recognising the associated wide credible intervals, approximately 22% of patients will report an unfavourable pain outcome at three months after TKR, with 12-15% of people experiencing an unfavourable longer-term pain outcome up to two years after surgery. For THR, a lack of studies reporting rates of unfavourable pain outcomes in unselected patients limited our analysis. However, our findings suggest that at least 14% of people may report unfavourable pain at 6-12 months after THR.

The strengths and limitations of this review should be considered when interpreting the results**.** Firstly, overall quality of evidence is low due to potential heterogeneity and risk of bias in TKR studies, and we were unable to estimate trends for THR studies due to a low number of included studies. Data from good quality registry studies was limited as estimates of proportions of people with chronic pain are seldom reported. The wide range of rates of unfavourable pain across studies may reflect the different definitions used by the study authors, however, we were unable to investigate conclusively the relationships between the definition used and prevalence estimates within this review as we did not have access to individual patient data. Studies in specific cohorts have reported proportions of people with different definitions of unfavourable pain outcomes.[18] For example, in the study by Musbahi and colleagues, thresholds based on combinations of different minimal clinically important differences and patient acceptable symptom states for WOMAC pain ranged from 5% to 52%.[18] The authors note that a WOMAC pain score improvement of <20/100 as reported by 23% of people had sensitivity and specificity for predicting a patient's dissatisfaction with pain relief and overall outcome of TKR. We believe that studies reporting on different

outcome assessments and those exploring the patient experience of pain after TKR and THR complement our research. The varying rates of unfavourable pain outcomes may also suggest that there is selection that was not apparent in the study methodology. For example, a single surgeon series with lower rates of unfavourable pain may relate to patient selection which is not evident from the cohort inclusion criteria. Secondly, loss to follow-up may have impacted on our estimates of the proportion of patients with chronic pain after TKR and THR. The influence that unfavourable pain and other outcomes have on patient willingness to participate in research follow-up is unclear. Some studies suggest that people with poor outcomes are less likely to participate in follow-up assessments due to dissatisfaction with their care or difficulties completing follow-up.[34-37] However, others report no difference or poorer pain outcomes in those responding to initial invitations or attending follow-up visits compared with those not participating in follow-up visits.[38-40] Our sensitivity analyses in studies of TKR excluding studies with high loss to follow-up rates showed higher rates of unfavourable pain and provide some support for the latter suggestion. Given the uncertainty regarding the impact of loss to follow-up, we conducted separate scenario analyses to provide readers with a range of realistic estimates for their consideration. Thirdly, the scope of our review was broad. We included all different patient-reported measures of pain together, which present a mixture of single and multidimensional measures, and authors' own definitions of unfavourable pain outcome. While this allowed us to take an encompassing approach to the synthesis of existing studies, it was likely an important source of heterogeneity in the results. It should also be noted that unfavourable pain does not necessarily equate with failure or dissatisfaction.[11] Additionally, there were very few studies that provided multiple cut-off points for further analyses to elucidate the relationship between pain and satisfaction since the majority of studies only used a single post-operative VAS or NRS point. Despite these limitations, this review is the most comprehensive attempt to date to collate the existing evidence and provides useful estimates to direct future research and improvements to clinical care.

Chronic pain after total knee or hip replacement has a highly negative impact on people[23 41] to the extent that they may fear pursuing further healthcare and prescribed pain relief.[42] For people who would potentially benefit from further care, how they are identified, assessed and treated varies considerably between centres in the UK.[43] Cost implications for health services are considerable with numerous consultations, investigations and surgical referrals required.[44] Chronic pain after joint replacement is an important research priority, as highlighted by the James Lind Alliance Priority Setting Partnership.[45-47] Acknowledging that an estimated 13-22% of people with TKR and a proportion of people with THR may experience chronic pain after surgery, implementation of evidence-based interventions

aimed at the prevention and/or management of chronic pain after joint replacement are required.

Potential pre-operative risk factors for chronic pain after total knee or hip replacement have been studied extensively with the aim of developing interventions and targeting care to those at risk. In a recent systematic review with 54 studies identified, there was no suggestion in meta-analyses that age, sex and body mass index were associated with development of chronic pain after TKR.[48] For a range of further potential risk factors including pre-operative pain, evidence was limited with associations based on small numbers of studies or "vote counting" analysis due to lack of data and methodological heterogeneity. For people receiving THR, consistent associations have been identified between female sex, high pre-operative pain, poorer pre-operative function, and anxiety or depression.[49 50] Systematic reviews have identified that pre-operative pain catastrophizing, psychological distress, and symptoms of anxiety and/or depression are risk factors for long-term pain hip and knee replacement.[51-55] Post-operative risk factors for chronic pain have been studied in TKR and largely relate to length of hospital stay, mechanical complications of the prosthesis, surgical site infection, hospital readmission, reoperation or revision[56] and patients with chronic pain are likely to undergo revision at a later time period.[57] More generally, acute postoperative pain, caused by surgical methods and influenced by anaesthetic protocols, analgesia and care during the hospital admission, is also acknowledged as a risk factor for chronic postsurgical pain.[58 59]

There is a limited but growing body of evidence evaluating interventions that target risk factors for chronic pain after joint replacement[60-63]. Pre-operatively, general prehabilitation with exercise and education has not shown clear benefit for reduced long-term pain.[60 64 60 65-67] Another focus of efforts has been in removing delays to surgery to avoid possible decline in function and increase in pain while waiting for surgery. However, evidence of associations between longer waiting times for knee or hip replacement and chronic pain is equivocal.[68-70] In randomised trials evaluating interventions targeting psychological risk factors, cognitive behavioural therapy and pain coping skills programmes have not shown benefit for improved long-term pain.[61 71-76 77-79] However, a mindfulness-based stress-management intervention provided to patients before total hip or knee replacement surgery was associated with reduced long-term pain.[80] During the peri-operative period, the multimodal analgesia regimen provided may influence long-term pain outcomes and there is some support for incorporation of specific treatments, some of which are features of current pain management practice.[62 81] After hospital discharge, care focuses mainly on physiotherapy-based rehabilitation but there is no evidence to support one modality over another in relation to prevention of chronic pain.[63] Exercise-based rehabilitation provided to people considered at

risk of a poor outcome after TKR have shown little benefit for primary functional outcomes or long-term pain compared with usual care or less intensive interventions.[82 83]

Systematic reviews have identified a limited evidence-base to guide the treatment and management of chronic pain after joint replacement, and surgery more generally [84 85]. To address this, a programme of research has been conducted focussing on the development and evaluation of an early post-operative intervention to prevent pain chronicity.[33] Recognising the diverse causes of chronic pain, the Support and Treatment After Replacement (STAR) care pathway is a personalised and multifaceted intervention to reduce chronic pain after TKR.[86] The care pathway involves the assessment of people with high levels of pain at 2-3 months after surgery to identify the underlying causes of pain with subsequent provision of referrals for appropriate treatment or management. Evaluation in a randomised controlled trial found the STAR care pathway was cost-effective and associated with a clinically important reduction in pain after one year compared with usual care.[86] Furthermore, there is a suggestion of sustained benefit at up to four years.[87]

Conclusion

The problem of chronic pain after knee and hip replacement is recognised by people who have pain, clinicians and the research community. Our review, bringing together all the published literature to date, suggests that approximately 22% of patients will report an unfavourable pain outcome at three months after TKR, with 12-15% of people experiencing an unfavourable longer-term pain outcome up to two years after surgery. After THR, at least 14% of people may report an unfavourable pain outcome at 12 months after surgery. Registry studies are a potentially rich and largely untapped source of data from representative populations for the exploration of patient and healthcare factors in relation to chronic pain. Throughout the care pathway, there are opportunities for targeted care. There is an urgent need for the implementation of evidence-based interventions to optimise management of chronic pain after joint replacement and evaluation of new preventive strategies that target established risk factors.

Ethical approval

No individual level data are included in this manuscript. All data are aggregated data from published academic articles.

Data sharing

The statistical analysis plan and dataset can be available from the corresponding author on reasonable request.

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Author's contributions

AB, RGH, MW, and VW conceived the project. AB, VW, WB, and MAS screened studies and collected data for the review. HYC, AB, and VW drafted the manuscript. HYC conducted the analysis. AB and HYC contributed to the interpretation of the results. All authors (AB, MAS, MW, RGH, HYC, VW, and WB) discussed the results and contributed to the writing and editing of the manuscript.

VW is the guarantor.

Competing interests

All authors (AB, MAS, MW, RGH, HYC, VW, and WB) have completed the ICMJE uniform disclosure form and declare no competing interests.

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Table 1. Summary of TKR study characteristics

	Overall	3 months	6 months	12 months	24 months
Number of study cohorts	68	15	28	36	10
Total sample sizes	598,498	2503	550,928	36,157	13,953
Median sample size (IQR)	235 (113.5-580.75)	116 (95-184)	197 (111.25-297)	254.5 (115.5-593.75)	396.5 (251.75-692.75)
Baseline time period range	1993-2023	1998-2023	1993-2023	1993-2020	1993-2019
Mean age (SD)	69.6 (9.4) (n = 52*)	68.8 (9.2) (n = 13*)	69.6 (9.4) (n = 24*)	68.1 (9.1) (n = 26*)	70 (9.3) (n = 6*)
Age range	18-98 (n = 24)	18-90 (n = 7)	18-94 (n = 9)	25-98 (n = 14)	28-90 (n = 4)
Median % women (IQR)	63 (58-69.45)	66.1 (62.35-77.55)	65.55 (57.65-72.475)	61.2 (56.95-65.85)	63 (61.03-64.75)
Primary pain outcome reported					
VAS/NRS pain	29	9	16	13	2
WOMAC pain	13	1	4	7	3
OKS pain	7	1	2	5	1
KOOS pain	6	1	1	4	1
BPI	3	1	2	2	0
KSS/IKSS pain	2	0	0	2	1
EQ-5D 5L pain/discomfort	1	0	1	0	0
Pain disturbing sleep	1	1	0	1	0
Author own question	6	1	2	2	2
Setting					
Single hospital	39	8	16	20	9
Multiple hospitals	18	0	6	12	1
Multiple surgeons	4	3	1	1	0
Single surgeon	3	3	2	2	0
National registry	2	0	1	1	0
Health region	1	0	1	0	0
Rehabilitation service	1	1	1	0	0
Country					
Australia	2	0	1	1	1
USA	17	2	8	5	4
UK	9	2	3	7	2
Spain	5	2	3	2	0
Denmark	5	1	0	5	0
France	4	1	3	2	0
Sweden	3	0	0	2	1
China	3	1	1	0	1
Belgium	2	2	1	1	0

Canada	2	0	1	1	0
Finland	2	1	0	0	1
Japan	2	1	2	1	0
Singapore	2	0	2	1	0
South Korea	2	2	0	1	0
The Netherlands	2	0	1	2	0
Hungary	1	0	0	1	0
Italy	1	0	0	1	0
New Zealand	1	0	1	1	0
Norway	1	0	0	1	0
Poland	1	0	1	0	0
Russia	1	0	0	1	0

*only studies reported both mean and SD

Table 2. Worst-best case scenario analyses in TKR studies

Proportion* (%)	Median (95% CrI)	τ^2 (95% CrI)
3 month		
0%	21.89 (15.72 - 29.35)	0.5 (0.19 - 1.1)
10%	23.8 (17.38 - 30.4)	0.4 (0.14 - 0.88)
20%	25.61 (19.46 - 32.34)	0.36 (0.12 - 0.78)
30%	27.22 (21 - 33.69)	0.31 (0.11 - 0.69)
40%	28.82 (22.45 - 35.25)	0.3 (0.1 - 0.66)
50%	30.68 (24.49 - 37.25)	0.27 (0.09 - 0.6)
60%	32.07 (25.66 - 38.42)	0.27 (0.09 - 0.6)
70%	33.55 (26.73 - 40.21)	0.28 (0.09 - 0.63)
80%	35.04 (28.15 - 41.98)	0.28 (0.1 - 0.63)
90%	36.71 (29.5 - 43.83)	0.3 (0.11 - 0.68)
100%	38.16 (30.6 - 45.68)	0.31 (0.11 - 0.69)
6 month		
0%	14.06 (10.79 - 17.79)	0.51 (0.26 - 0.88)
10%	16.37 (13.08 - 19.88)	0.37 (0.18 - 0.65)
20%	18.54 (15.24 - 22.09)	0.32 (0.16 - 0.56)
30%	20.5 (17.05 - 24.25)	0.3 (0.15 - 0.53)
40%	22.33 (18.66 - 26.38)	0.3 (0.15 - 0.52)
50%	24.22 (19.94 - 28.43)	0.32 (0.16 - 0.56)
60%	26.03 (21.65 - 30.67)	0.35 (0.18 - 0.6)
70%	27.91 (22.96 - 33.03)	0.39 (0.21 - 0.67)
80%	29.61 (24.15 - 35.12)	0.44 (0.23 - 0.75)
90%	31.39 (25.38 - 37.35)	0.51 (0.27 - 0.87)
100%	33.36 (26.84 - 40.12)	0.58 (0.31 - 1)
12 month		
0%	12.61 (9.88 - 15.84)	0.61 (0.34 - 0.97)
10%	15.22 (12.29 - 18.23)	0.44 (0.25 - 0.72)
20%	17.44 (14.5 - 20.66)	0.37 (0.2 - 0.6)
30%	19.6 (16.46 - 22.97)	0.36 (0.19 - 0.58)
40%	21.6 (18.09 - 25.17)	0.36 (0.2 - 0.58)
50%	23.6 (19.86 - 27.46)	0.37 (0.2 - 0.6)
60%	25.64 (21.74 - 29.89)	0.4 (0.23 - 0.64)
70%	27.57 (23.28 - 32.21)	0.44 (0.25 - 0.7)
80%	29.57 (24.55 - 34.51)	0.49 (0.28 - 0.78)
90%	31.53 (26.01 - 36.95)	0.55 (0.3 - 0.87)
100%	33.62 (27.69 - 39.61)	0.62 (0.37 - 0.99)
24 month		
0%	14.63 (8.83 - 21.5)	0.52 (0.15 - 1.32)
10%	16.67 (10.85 - 23.36)	0.41 (0.13 - 1.07)
20%	18.45 (12.81 - 25.31)	0.35 (0.11 - 0.91)
30%	20.23 (14.19 - 27.13)	0.34 (0.11 - 0.88)
40%	21.89 (15.29 - 29.1)	0.34 (0.11 - 0.88)
50%	23.64 (16.62 - 31.45)	0.35 (0.11 - 0.91)
60%	25.28 (17.78 - 33.83)	0.38 (0.12 - 0.97)
70%	26.89 (18.57 - 35.67)	0.4 (0.12 - 1.02)
80%	28.58 (19.92 - 38.38)	0.43 (0.14 - 1.11)
90%	30.04 (20.59 - 40.22)	0.48 (0.15 - 1.22)
100%	31.76 (21.49 - 42.8)	0.52 (0.15 - 1.32)

*Proportion: The proportion of lost to follow-up patients imputed to experience unfavourable pain outcomes.

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Figure legends

Figure 1. Study selection flowchart.

Figure 2. Summary of risk of bias assessments in TKR studies. Each block represents one study. Red represents an overall high risk of bias in a study; yellow represents an overall moderate risk of bias.

Figure 3. Multivariate meta-analysis of proportions over time in TKR studies plot. Grey dots and lines represent reported proportions across studies and time, while dark dots and lines show the multivariate meta-analysis results. The size of grey dots is proportional to the log of inverse variance.

Figure 4. Forest plot of proportions over time in THR studies. Squares and bars represent the mean proportion of individual studies. Diamonds represent the point estimate and credible intervals of the meta-analysis results. The bars show the corresponding prediction intervals. Red circles and minus signs represent overall high risk of bias. Yellow circles and question marks represent overall moderate risk of bias. Abbreviations: RoB: Risk of Bias; RE: Random-effects; CrI: Credible intervals.

Supplementary materials

S1. PRISMA checklist
S2. Search strategy as applied in MEDLINE and Embase
S3. Characteristics of TKR studies
S4. Traffic light plot of the risk of bias assessment in TKR studies
S5. Forest plots of univariate meta-analyses in TKR studies
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S7. Meta-regression analyses in TKR studies
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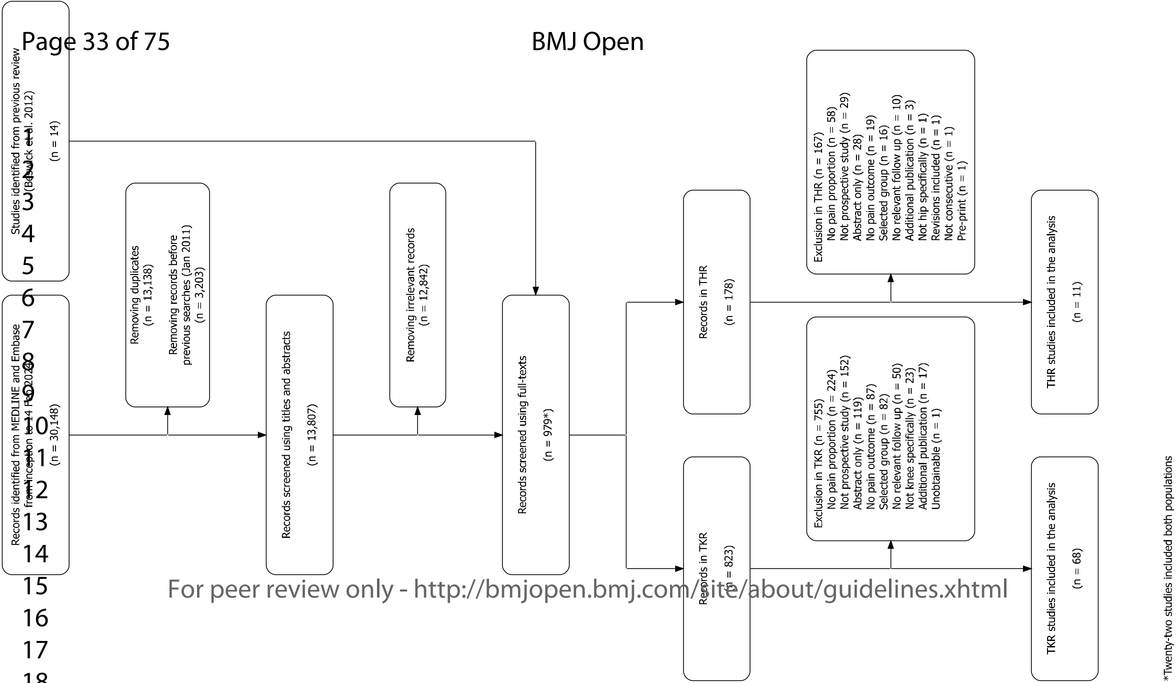
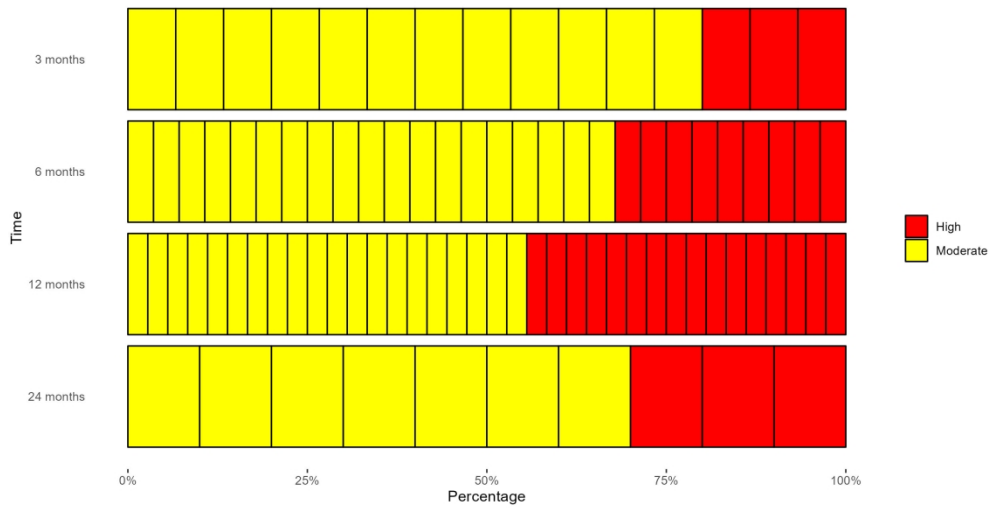
S9. Doi plots and the LFK indexes in TKR studies
S10. Sensitivity analyses in TKR studies
S11. Characteristics of THR studies
S12. Traffic light plot of the risk of bias assessment in THR studies





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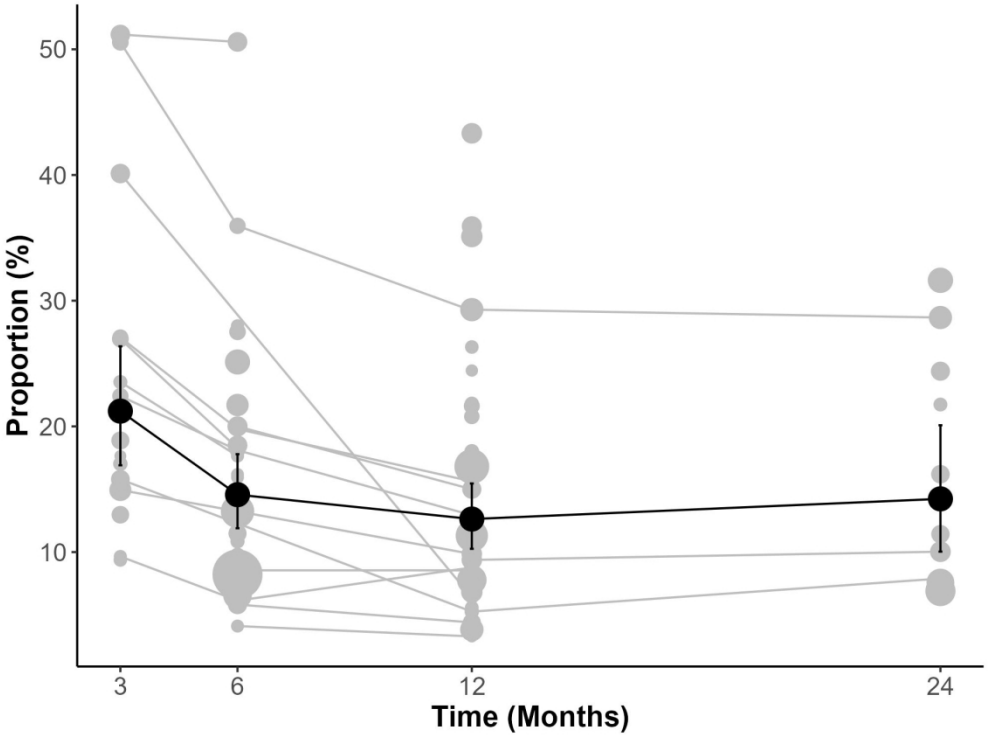

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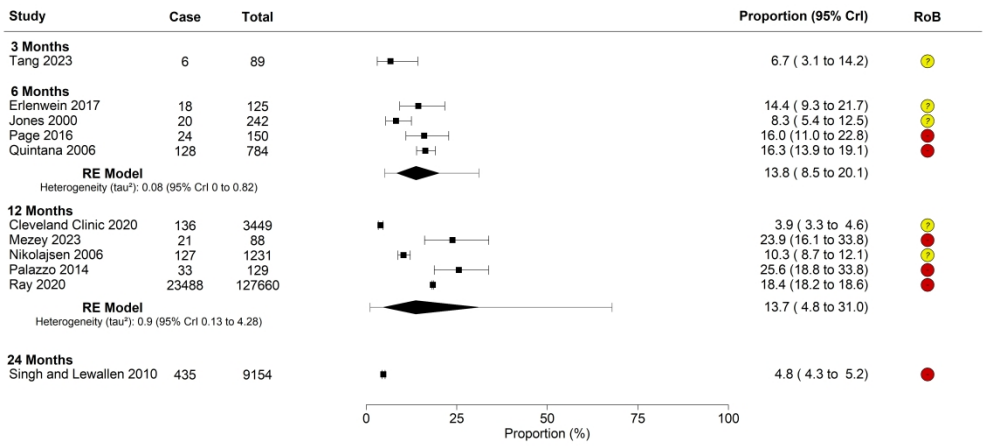

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Prevalence of chronic pain after total hip or knee replacement

Supplementary materials

Prevalence of chronic pain after total hip or knee replacement

Prevalence of chronic pain after total hip or knee replacement

S1. MOOSE checklist

Item No	Recommendation	Reported on Page Number	Reported on Section/Paragraph
Reporting of background			
1	Problem definition	Page 4	Introduction
2	Hypothesis statement	Page 4	Introduction
3	Description of Study Outcome(s)	Page 5	Outcome, Methods
4	Type of exposure or intervention used	Page 5	Eligibility Criteria, Methods
5	Type of study design used	Page 5	Eligibility Criteria, Methods
6	Study population	Page 5	Eligibility Criteria, Methods
Reporting on search strategy			
7	Qualifications of searchers (e.g., librarians and investigators)	Using existing search strategies	
8	Search strategy, including time period included in the synthesis and keywords		Supplementary S2
9	Effort to include all available studies, including contact with authors	Page 5-6	Searches, Methods
10	Databases and registries searched	Page 5	Searches, Methods
11	Search software used, name and version, including special features used (e.g., explosion)	Page 6	Study selection and data collection, Methods
12	Use of hand searching (e.g., reference lists of obtained articles)	Page 5	Searches, Methods
13	List of citations located and those excluded, including justification		Figure 1 (PRISMA flowchart)
14	Method for addressing articles published in languages other than English	Page 5	Searches, Methods
15	Method of handling abstracts and unpublished studies	Page 5	Searches, Methods
16	Description of any contact with authors	Page 5-6	Searches, Methods
Reporting of methods			
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested		Table 1
18	Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Page 6	Study selection and data collection, Methods

Prevalence of chronic pain after total hip or knee replacement

19	Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Page 6	Study selection and data collection, Methods
20	Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)		Tables 1, S3 and S11
21	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Page 6	Risk of bias assessment/ Methods
22	Assessment of heterogeneity	Page 7	Exploration of heterogeneity, Methods
23	Description of statistical methods (e.g., complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Page 6-7	Data synthesis approach, Methods
24	Provision of appropriate tables and graphics		Results
Reporting of results			
25	Graphic summarizing individual study estimates and overall estimate		Figures 3, 4, and S5
26	Table giving descriptive information for each study included		Tables S3 and S11
27	Results of sensitivity testing (e.g., subgroup analysis)		Tables S7, S8, and S10
28	Indication of statistical uncertainty of findings		Table 2 and S6
Reporting of discussion			
29	Quantitative assessment of bias (e.g., publication bias)		Figures S9
30	Justification for exclusion (e.g., exclusion of non–English-language citations)		Not applicable
31	Assessment of quality of included studies		Figures 2 and 4
Reporting of conclusions			
32	Consideration of alternative explanations for observed results		Conclusion
33	Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review)		Conclusion
34	Guidelines for future research		Conclusion
35	Disclosure of funding source		Sources of funding

From: Brooke BS, Schwartz TA, Pawlik TM. MOOSE Reporting Guidelines for Meta-analyses of Observational Studies. JAMA Surg. 2021;156(8):787–788. doi:10.1001/jamasurg.2021.0522

Prevalence of chronic pain after total hip or knee replacement

S2. Search Strategy as applied in MEDLINE and Embase

S2.1 Total knee replacement

Medline

1. survey.mp. or exp Data Collection/
2. prospective study.mp. or exp Prospective Studies/
3. observational study.mp.
4. exp EPIDEMIOLOGY/ or epidemiology.mp.
5. longitudinal study.mp. or exp Longitudinal Studies/
6. follow up study.mp. or exp Follow-Up Studies/
7. exp Arthroplasty, Replacement, Knee/ or exp Knee Prosthesis/ or knee replacement.mp.
8. knee prosthesis.mp. or exp Knee Prosthesis/
9. total knee.tw.
10. (knee adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti, ab.
11. 7 or 8 or 9 or 10
12. pain.tw.
13. 1 or 2 or 3 or 4 or 5 or 6
14. 10 and 12 and 13

Embase

1. Clinical study/
2. Longitudinal study/
3. Prospective study/
4. Cohort analysis/
5. (Cohort adj (study or studies)).mp.
6. (follow up adj (study or studies)).tw.
7. (observational adj (study or studies)).tw.
8. (epidemiologic$ adj (study or studies)).tw.
9. exp Arthroplasty, Replacement, Knee/ or exp Knee Prosthesis/ or knee replacement.mp.
10. knee prosthesis.mp. or exp Knee Prosthesis/
11. total knee.tw.
12. (knee adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti,ab.
13. pain.tw.
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
15. 9 or 10 or 11 or 12
16. 13 and 14 and 15

S2.2 Total hip replacement

Medline

1. survey.mp. or exp Data Collection/
2. prospective study.mp. or exp Prospective Studies/
3. observational study.mp.
4. exp EPIDEMIOLOGY/ or epidemiology.mp.
5. longitudinal study.mp. or exp Longitudinal Studies/
6. follow up study.mp. or exp Follow-Up Studies/
7. exp Arthroplasty, Replacement, Hip/ or exp Hip Prosthesis/ or hip replacement.mp.
8. hip prosthesis.mp. or exp hip Prosthesis/
9. total hip.tw.
10. (hip adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti, ab.

Prevalence of chronic pain after total hip or knee replacement

11. 7 or 8 or 9 or 10
12. pain.tw.
13. 1 or 2 or 3 or 4 or 5 or 6
14. 10 and 12 and 13

Embase

1. Clinical study/
2. Longitudinal study/
3. Prospective study/
4. Cohort analysis/
5. (Cohort adj (study or studies)).mp.
6. (follow up adj (study or studies)).tw.
7. (observational adj (study or studies)).tw.
8. (epidemiologic$ adj (study or studies)).tw.
9. exp Arthroplasty, Replacement, hip/ or exp hip Prosthesis/ or hip replacement.mp.
10. hip prosthesis.mp. or exp hip Prosthesis/
11. total hip.tw.
12. (hip adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti,ab.
13. pain.tw.
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
15. 9 or 10 or 11 or 12
16. 13 and 14 and 15

Prevalence of chronic pain after total hip or knee replacement

S3. Characteristics of TKR studies

Study Country Recruitment dates Setting	Operation Number of patients Age (SD), range % women	Pain measure	Definition of unfavourable pain outcome High risk of bias concern
Alzahrani 2011[1] TWH cohort Canada 1998-2007 2 hospitals	Primary TKR, all 18+ N=482 67.5 (9.6) 62%	WOMAC pain 12 months	No clinically important improvement based on MCID (WOMAC index of 7.5)
Aso 2020[2] Japan 2012-2017 1 hospital	Primary TKR, all N=234 75 75.8%	VAS/NRS pain 6, 12 months	Moderate to severe pain (VAS >30 mm), at rest or walking
Attal 2014[3] France 2008-2011 I hospital	Primary TKR, all 18+ N=89 68.7 (8.9) 65.0%	BPI (NRS) 3, 6, 12 months	NRS pain average 3 or greater on 10-point scale
Baker 2007[4] UK 2003 National registry	Primary TKR, all N=9417 70.68 56.8%	OKS pain 12 months	Reported persistent knee pain
Bell 2023[5] USA 2015-2018 7 hospitals	Primary TKR, all 50-89 N=5564 Range 50-89 60.7%	KOOS pain 12 months	MCID not satisfied (15 points)
Birch 2019[6] Denmark 2011-2013 1 hospital	Primary TKR or UKR, all N=589 67.3 (9.7) 52.0%	OKS pain 4, 12 months	OKS pain moderate/severe High loss to follow up rate at 4 and 12 months
Brander 2003[7] USA 1998-2000 1 surgeon	Primary TKR, all 18+ N=116 66 (10.5), range 36-85 55.2%	VAS/NRS pain 3, 6, 12 months	VAS >40
Buus 2022[8] Denmark 2015-2016 1 hospital	Primary TKR, all 18+ N=217 66.8 (9.3) 52.2%	OKS pain 12 months	Threshold 42.39[69]
Buvanendran 2019[9] USA 2011-2017 1 hospital	Primary TKR, all N=296 65 65.3%	VAS/NRS pain 6 months	NRS pain with movement ≥4

Prevalence of chronic pain after total hip or knee replacement

Chodor and Kruczynski 2022[10] Poland 2016 1 hospital	Primary TKR, all 48+ N=69 67.6 (7.42), range 48-84 76.7%	Author own question 6 months	Pain severely limiting daily life
Clement 2014[11] UK 2010 1 hospital	Primary TKR, all N=578 70 (9.6), range 39-91 58.4%	Author's own question "How well did the surgery relieve pain in your affected joint?" 12 months	Fair or poor High loss to follow up rate
Cole 2022[12] UK 2010-2015 2 hospitals	Primary TKR, all N=1025 70 55.8%	OKS pain 12 months	<14 points OKS
Dave 2017[13] USA 2012-2014 3 hospitals	Primary TKR probably, all 40+ N=267 66 (9) 61.0%	WOMAC pain 12 months	WOMAC pain score < MCID (WOMAC pain of 15)
Dowsey 2012[14] Australia 2006-2007 1 hospital	Primary TKR, all N=478 70.8 (8.3), range 45-90 69.2%	IKSS pain 12, 24 months	IKSS pain score <30 moderate to severe pain IKSS may not be entirely patient reported at 12 and 24 months
Dursteler 2021[15] Spain 2014-2017 Spain 1 hospital	Primary TKR, all 18+ N=170 73.1 (7.1) 73.3%	VAS/NRS pain 3, 6 months	NRS 0.3/1 or greater at rest
Edwards 2022[16] USA 2012-2018 2 hospitals	Primary TKR, all 45+ N=248 65.1 (8.2) 59.5%	BPI 6 months	4/10 or greater High loss to follow up rate
Escobar and Riddle 2014[17] Spain 2003-2006 15 hospitals	Primary TKR, all N=1616 71.6 (6.8) 70.0%	WOMAC pain 12 months	Number not attaining PASS (i.e. "No" in the question, "*If you had to be the rest of your life with the symptoms you have now, how would you feel?*") as the twenty-fifth percentile of the final score at 1 year instead of the seventy-fifth percentile (reverse option for WOMAC scores). High loss to follow up rate
Getachew 2021[18]	Primary TKR, all 18+	BPI	BPI worst pain score ≥4

Prevalence of chronic pain after total hip or knee replacement

Norway 2012-2014 1 hospital	N=206 68 (9) 66.0%	12 months	
Ghomrawi 2017[19] USA 2010-2012 1 hospital	Primary TKR, all N=247 68 (10) 65.0%	WOMAC pain 24 months	Number not achieving MCID (baseline-adjusted MCIDs, as described by Escobar et al.[70])
Grosu 2016[20] Belgium 2009-2010 1 surgeon	Primary TKR probably, all N=114 66 (10) 65.8%	VAS/NRS pain 3, 6, 12 months	Moderate to severe pain High loss to follow up rate at 3, 6 and 12 months
Hardy 2022[21] France 2014-2015 1 hospital	Primary TKR, all >18 N=111 73.3 (9.3) range 29-92 65.0%	VAS/NRS pain 12 months	VAS >30/100
Heath 2021[22] Australia 2018-2020 44 hospitals	Primary and revision TKR, all N=8299 67.5 (8.8) 56.4%	EQ-5D 5L pain/ discomfort 6 months	Moderate/ severe or extreme pain EQ 5D 5L pain/discomfort High loss to follow up rate
Jones 2000[23] Canada 1995-1997 1 health region	Primary TKR, all 40+ N=292 69.2 (9.2) 59.0%	WOMAC pain 6 months	Moderate/ severe pain defined as a gain of <10 points on the WOMAC pain dimension
Khalid 2021[24] UK 2008-2016 National registry	Primary TKR or UKR, all N=531,790 69.7 (9.4) 56.6%	OKS pain 6 months	OKS-pain score of 14 or less at six months after knee replacement can be considered to be in chronic pain
Kim 2015[25] South Korea 2013-2014 1 hospital	Primary TKR, all women N=94 70.18 (5.74), range 20-80 100%	VAS/NRS pain 3 months	>5 points on an 11 point VAS/NRS (verbal numeric rating scale)
Kiran 2015[26] UK 2003-2007 1 hospital	Primary TKR, all N=608 72 61.4%	OKS pain 12, 24 months	Has your knee replacement operation decreased your knee pain? High loss to follow up rate at 12 and 24 months
Kornilov 2018[27] Russia 2014 1 hospital	Primary TKR, all 18+ N=100 63 (8), range 47-81 95.0%	VAS/NRS pain 12 months	Not at least a two-point or approximately 30% (clinically significant) decrease in rating of pain interference with walking from baseline to 1 year (NRS scale 0-10)
Kurien 2018[28] UK Before 2017	Primary TKR probably, all N=50	VAS/NRS pain 6 months	4 or greater

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1 hospital	66.4 (8.3) 60.0%		
Larsen 2021[29] Denmark 2015-2016 1 hospital	Primary TKR, all 18+ N=185 68.8 (8.9) 55.7%	VAS/NRS pain 12 months	Pain intensity at rest >3 High loss to follow up rate
Latijnhouwers 2022[30] The Netherlands 2012-2017 2 hospitals	Primary TKR, all N=282 66 (8.4) 63.0%	VAS/NRS pain 12 months	Moderate to severe pain (NRS ≥4) High loss to follow up rate
Lavand'homme 2014[31] Belgium 2012 1 surgeon	Primary TKR or UKR, all N=128 68 (10) 66.4%	VAS/NRS pain 3 months	NRS ≥4/10
Lee 2022[32] South Korea 2017-2019 2 surgeons	Primary TKR probably, all N=172 70.7 (4.3) 89.2%	Pain disturbing sleep 3, 12 months	Night pain was defined as pain around the knee experienced at night that could disturb the patient's sleep
Leppanen 2021[33] Finland 2012-2014 1 hospital	Primary TKR, 65 years or younger N=205 60 63.0%	VAS pain exercise 24 months	VAS >30
Leung 2019[34] Singapore 2015 1 hospital	Primary TKR, all N=243 66 (8.3) 78.6%	Author own question 6, 12 months	No change or worsening pain/ slightly better
Lundblad 2008[35] Sweden Before 2006 1 hospital	Primary TKR, all N=69 68 50.7%	VAS/NRS pain 24 months	Pain at rest, VAS >2/10
Lyman 2018[36] USA 2007-2012 1 hospital	Primary TKR, all N=3815 74 (6) 63.0%	KOOS pain 24 months	Number not achieving MCID (8 by distribution-based method [71]) High loss to follow up rate
Mahdi 2020[37] Sweden 2016-2018 3 hospitals	Primary TKR, all N=615 69.7 52.2%	KOOS pain 12 months	8 cut off High loss to follow up rate
Mekkawy 2023[38] USA 2021 4 surgeons	Primary TKR, all N=112 65.5 (9.2) 69.0%	VAS pain 6 months	Probably NRS score of ≥1 in defined sites Concern over VAS ≥1 being too inclusive and high loss to follow up rate

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Mercurio 2020[39] Italy 2015-2017 1 hospital	Primary TKR, all >18 N=45 69.6 (7.8) 65.0%	VAS/NRS pain 12 months	VAS >30 residual pain
Mezey 2023[40] Hungary 2019-2020 2 hospitals	Primary TKR probably, all N=101 69.2 Not reported	WOMAC pain 12 months	Not exceeding MCID (WOMAC pain of 13.3) High loss to follow up rate
Musbahi 2023[41] USA 2011-2014 4 hospitals	Primary TKR, all 40+ N=575 66.3 (8.3) 60%	WOMAC pain 12 months	WOMAC pain score (converted to a 0-to-100 scale) improvement of <20 High loss to follow up rate
Nishimoto 2023[42] Japan 2021-2023 1 hospital	Primary TKR, all with no complications N=68 75.1 (7.3) 80.9%	KOOS pain 3, 6 months	Not achieving MCID of 10 (3 months) and 13 (6 months). MCID was calculated using the anchor method.[72]
Noiseux 2014[43] USA Before 2012 2 hospitals	Primary TKR, all 30+ N=215 61.7 (9.8) 58.0%	VAS/NRS pain 6 months	Moderate or severe pain with range of motion, VAS ≥1 Concern over VAS ≥1 being too inclusive
Orr 2022[44] USA 2016-2019 9 hospitals	Primary TKR, all N=7476 67 (9.0) 60.8%	KOOS pain 12 months	Not achieved PASS (i.e. "No" in the question, "*Taking into account all the activity you have during your daily life, your level of pain and also your activity limitations and participation restrictions, do you onsider the current state of your knee satisfactory?*") for KOOS pain High loss to follow up rate
Petersen 2015[45] Denmark Before 2014 1 hospital probably	Primary TKR, all N=78 69 59.0%	VAS/NRS pain 12 months	VAS >3 High loss to follow up rate
Petersen 2018[46] Denmark Before 2017 1 hospital	Primary TKR probably, all N= 200 69 (1.2) 57.0%	VAS/NRS pain 12 months	<30% reduction in pain
Phillips 2014[47] UK 2009-2010 1 hospital	Primary TKR, all N= 96 70.6 56.0%	VAS/NRS pain 3, 6, 12 months	VAS >3

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Priol 2023[48] France 2011-2012 1 hospital	Primary TKR, all N=129 74 (10), range 45-94 72.3%	VAS/NRS pain 6 months	VAS 4+ High loss to follow up rate
Pua 2019[49] Singapore 2013-2017 1 hospital	Primary TKR, all 50+ N=5325 68 (7.5) 75.0%	OKS pain 6 months	Moderate or severe pain
Quintana 2006[50] Spain 1999-2000 7 hospitals	Primary TKR, all N=792 71.9 73.0%	WOMAC pain 6 months	No improvement in pain greater than MCID (22.60 of 100) using an anchor-based method.
Rice 2018[51] New Zealand 2012-2015 3 hospitals	Primary TKR, all 18+ N=300 69 (10), range 48-90 48.0%	VAS/NRS pain 6, 12 months	VAS >3
Sideris 2022[52] USA 2016-2018 1 hospital	Primary TKR, all N=179 67.1 (8.1) 56.2%	VAS/NRS pain 6 months	NRS 4+
Singh 2014[53] USA 1993-2005 1 hospital	Primary TKR, all N=7229 68 (10) 56.0%	Author own question 24 months	Moderate-severe pain
Solberg 2023[54] USA 2020 22 surgeons	Primary TKR probably, all N=239 66.2 (8.5), range 37-87 60.7%	Author own question 3 months	To what extent have you obtained relief: somewhat, minimal or not at all High loss to follow up rate
Stephens 2002[55] USA Before 2001 1 hospital	Primary TKR, all 50+ N=68 67.4 (8.1), range 50-88 54.0%	WOMAC pain 6 months	No change or increase in pain from pre-operative
Tang 2023[56] China 2020-2021 1 hospital	Primary TKR probably, all 65+ N=196 72 75.1%	VAS/NRS pain 3 months	NRS scores ≥4
Terradas-Monllor 2024[57] Spain 2018-2020 1 home rehabilitation service	Primary TKR or UKR, all 18+ N=115 70.5 (10.7) 66.1%	VAS/NRS pain 3, 6 months	VAS 3+
Thomazeau 2016[58] France 2013 1 hospital	Primary TKR, all N=109 69.2 (9) 71.6%	VAS/NRS pain 6 months	NRS score ≥1/10 for the last 8 days

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Tian 2022[59] China 2018-2019 1 hospital	Primary TKR or UKR, all <90 N=271 Not reported 80.8%	Author own question 24 months	Moderate or severe pain on movement
Utrillas-Compaired 2014[60] Spain 2009 1 hospital	Primary TKR, all N=215 73 (6.35) 69.3%	KSS pain 12 months	KSS pain poor (less than 60 points) KSS may not be entirely patient reported
van der Wees 2017[61] The Netherlands 1993-2014 1 hospital	Primary TKR, all N=704 65 (12) 64.5%	VAS/NRS pain 6, 12 months	30% or less improvement in VAS pain High loss to follow up rate at 6 and 12 months
Vina 2020[62] USA 2005-2015 4 hospitals	Primary TKR, all N=315 67.3 (8.6) 60.9%	WOMAC pain 24 months	Less than MCID of 1.5
Vuorenmaa 2008[63] Finland Before 2007 2 surgeons	Primary TKR, all <80 N=51 70 (5) 80%	VAS/NRS pain 3 months	VAS >30/100
W-Dahl 2014[64] Sweden 2008-2010 2 hospitals	Primary TKR, all N=2736 69.3 (8.7) 58.5%	KOOS pain 12 months	Unchanged or worse pain
Waimann 2014[65] USA 2004-2007 2 hospitals	Primary TKR, all N=236 65.1 (8.9) 66.0%	WOMAC pain 6 months	Less than MCID of ≥20 in both the WOMAC pain and function scores (scaled to 100)
Wylde 2013[66] UK 2010-2011 1 hospital	Primary TKR, all N=57 68 58%	WOMAC pain 12 months	WOMAC pain score of >75
Wylde 2019[67] UK 2006-2009 1 hospital	Primary TKR, all eligible for Triathlon prosthesis N=266 70 (9.9), range 41-90 64%	WOMAC pain 3, 12, 24 months	Worse or no change in WOMAC pain of 14 point (based on MCID) High loss to follow up rate
Yan 2023[68] China 2021-2023 1 hospital	Primary TKR, all 45+ N=470 63.4 (7.4) 69.9%	VAS/NRS pain 6 months	NRS score of ≥1 at rest and/or on movement Concern over VAS ≥1 being too inclusive

*Abbreviations: PASS (Patient Acceptable Symptom State), MCID (Minimal Clinically Important Difference)

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S3.1 Mean age and range

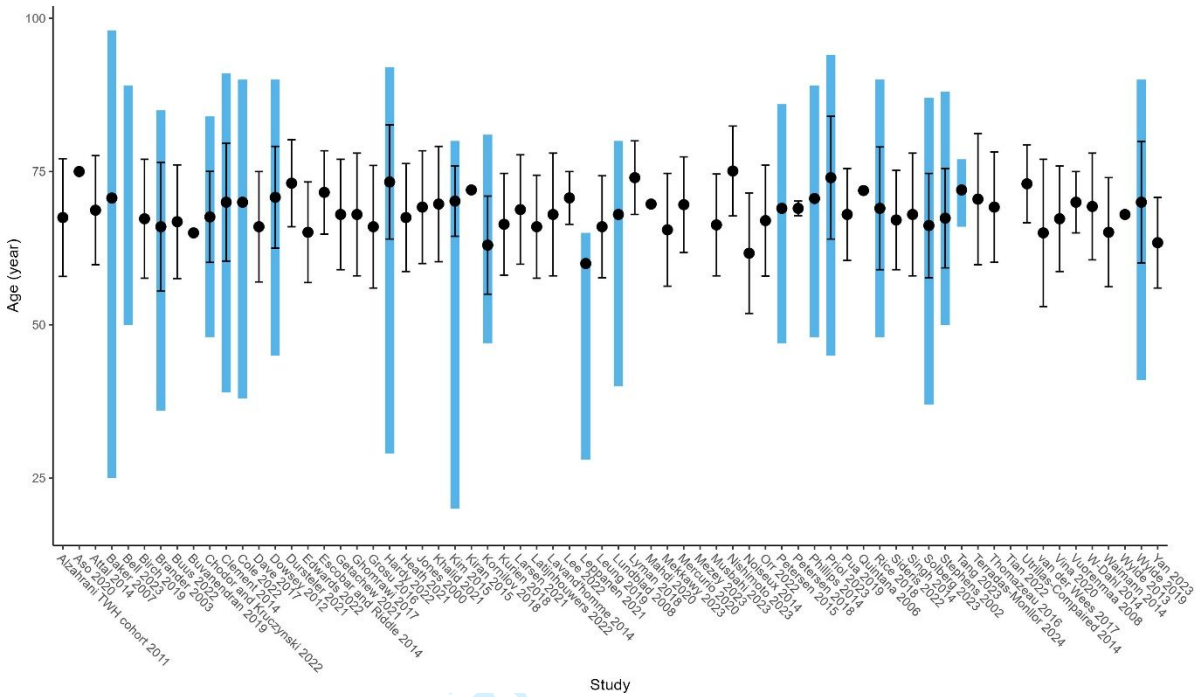


Figure S3.1. Mean age and their standard deviations reported in the individual studies. Range of age was plotted as blue bars.

S3.2 Proportion of females

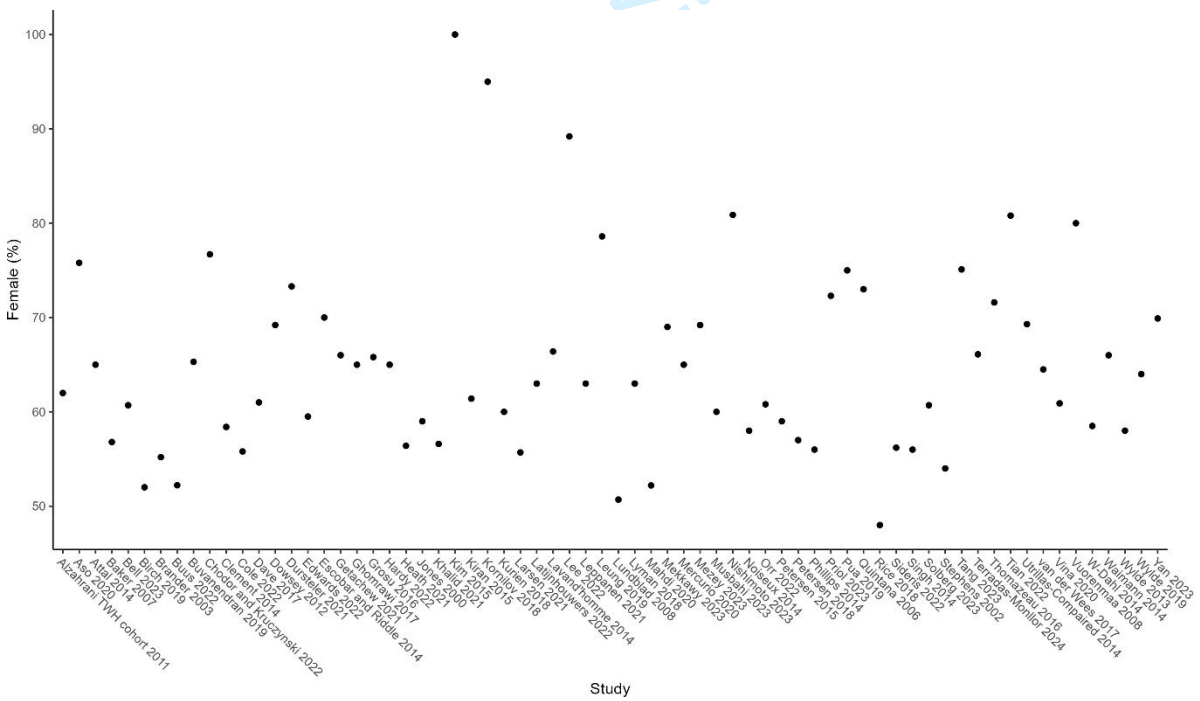


Figure S3.2. Proportion of females reported in the individual studies

S3.3 Data collection timeframe

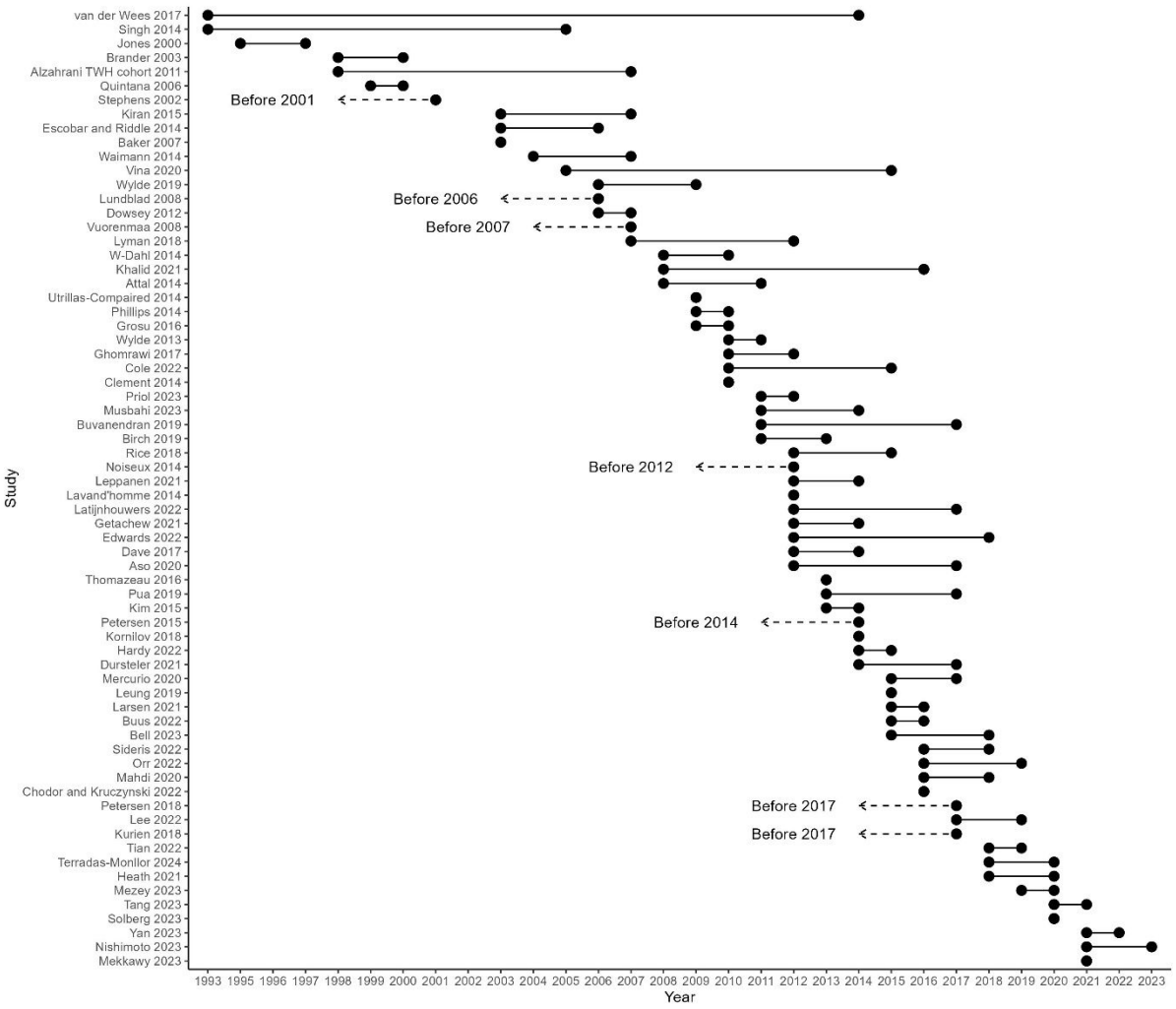


Figure S3.3. Data collection timeframe in the individual studies.

S3.4 Proportions of lost to follow-ups and revisions

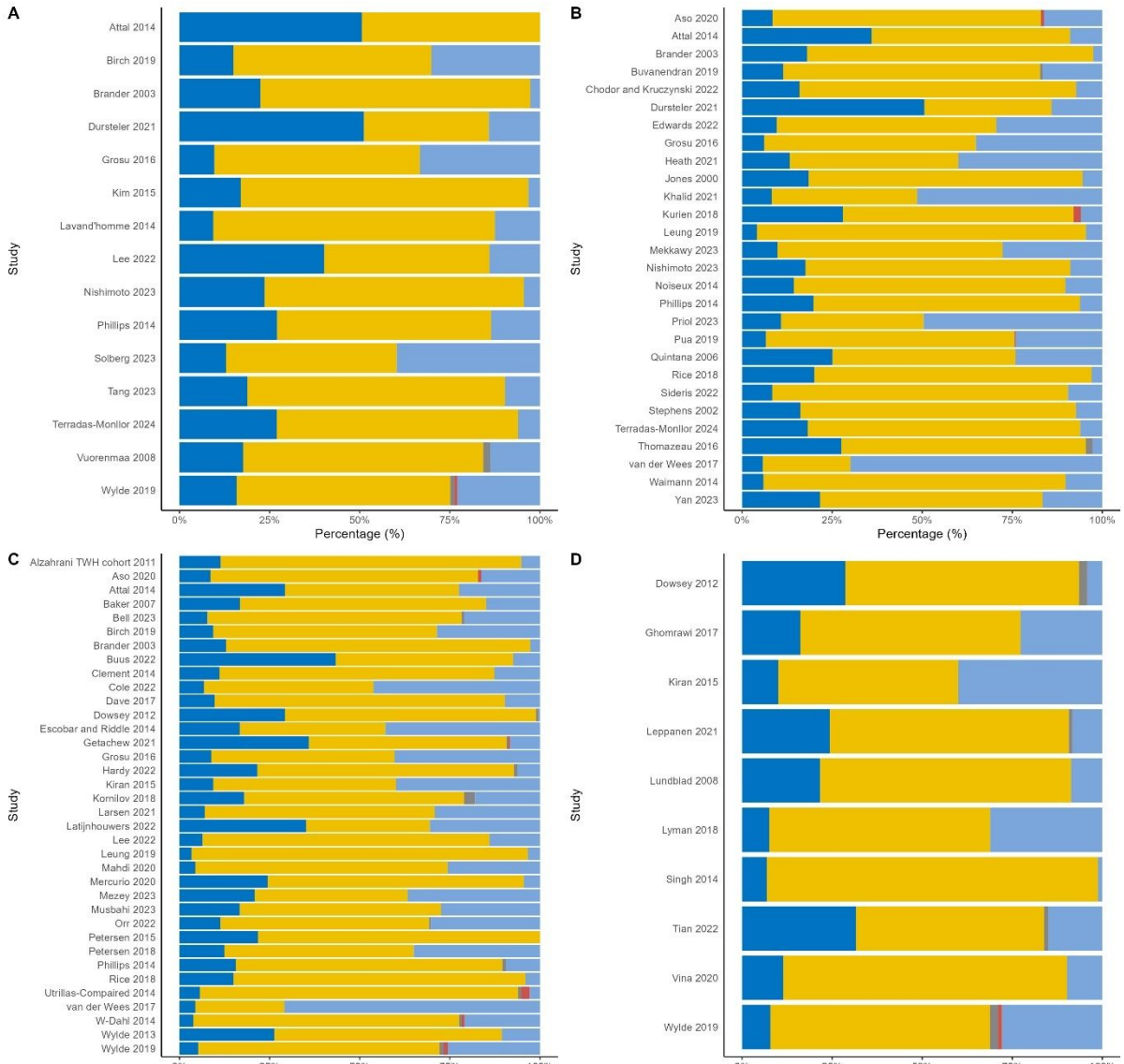


Figure S3.4. Favourable and unfavourable pain outcomes and reasons of missing data reported in 3, 6, 12, and 24 months (represented in sub-plots A, B, C, and D, respectively) in TKR studies.

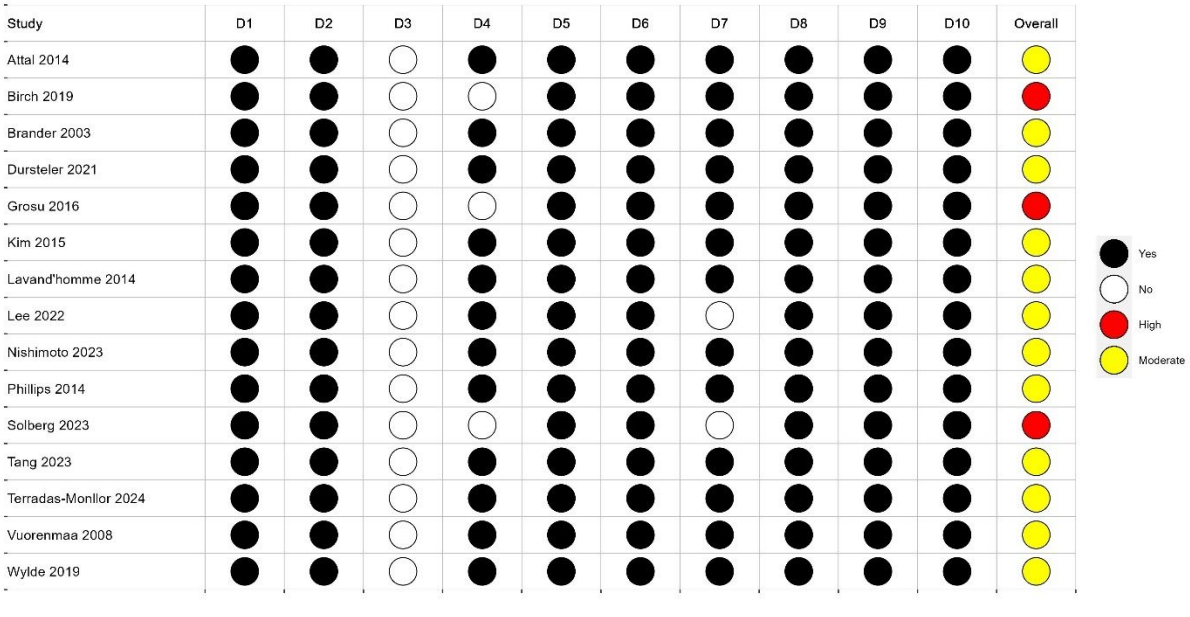
Prevalence of chronic pain after total hip or knee replacement

S4. Traffic light plot of the risk of bias assessments in TKR studies

The corresponding domains in the figures are:

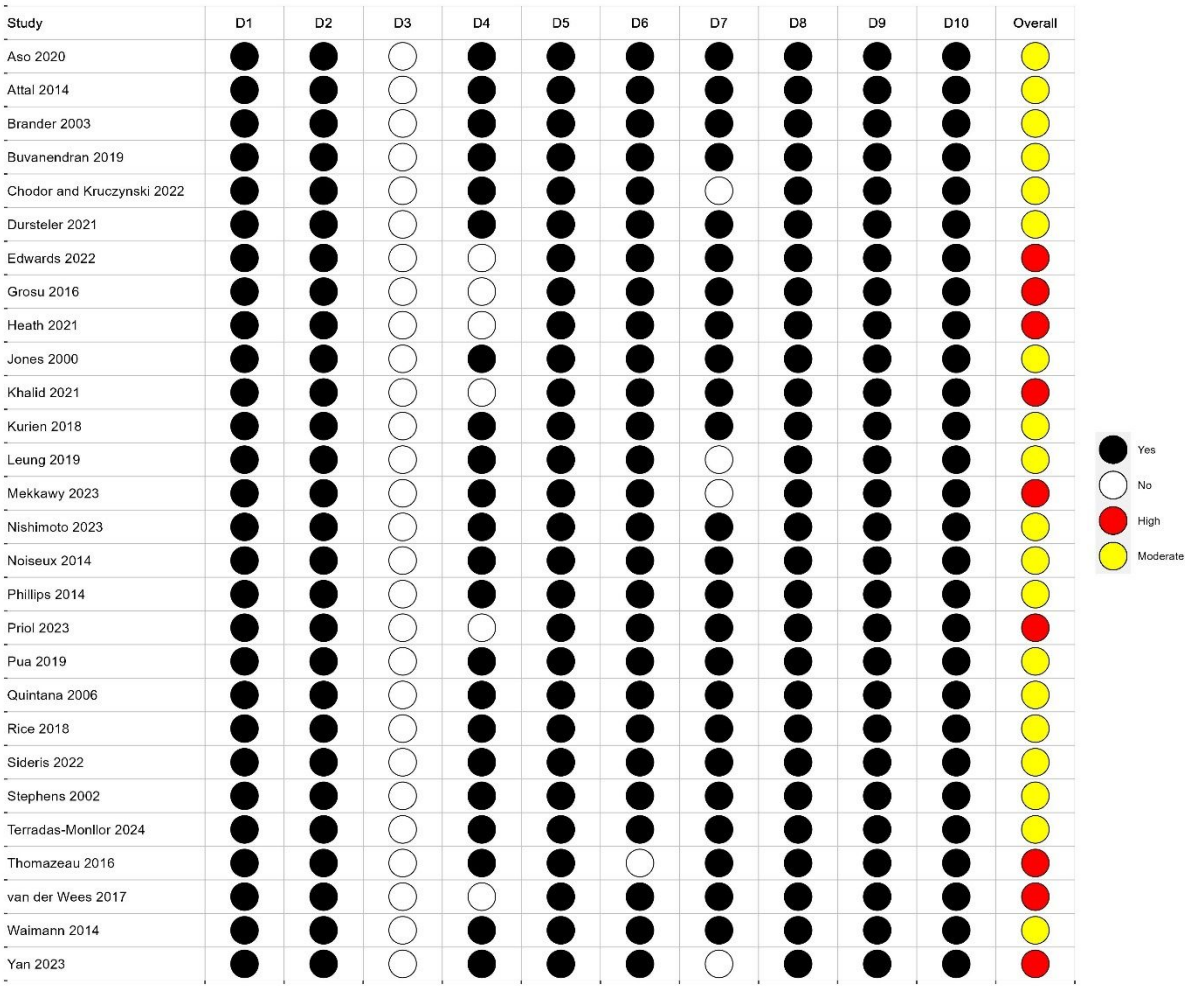
- D1: Was the study's target population a close representation of the national population in relation to relevant variables?
- D2: Was the sampling frame a true or close representation of the target population?
- D3: Was some form of random selection used to select the sample, OR was a census undertaken?
- D4: Was the likelihood of nonresponse bias minimal?
- D5: Were data collected directly from the subjects (as opposed to a proxy)?
- D6: Was an acceptable case definition used in the study?
- D7: Was the study instrument that measured the parameter of interest shown to have validity and reliability?
- D8: Was the same mode of data collection used for all subjects?
- D9: Was the length of the shortest prevalence period for the parameter of interest appropriate?
- D10: Were the numerator(s) and denominator(s) for the parameter of interest appropriate?

S4.1 TKR studies (3 months)

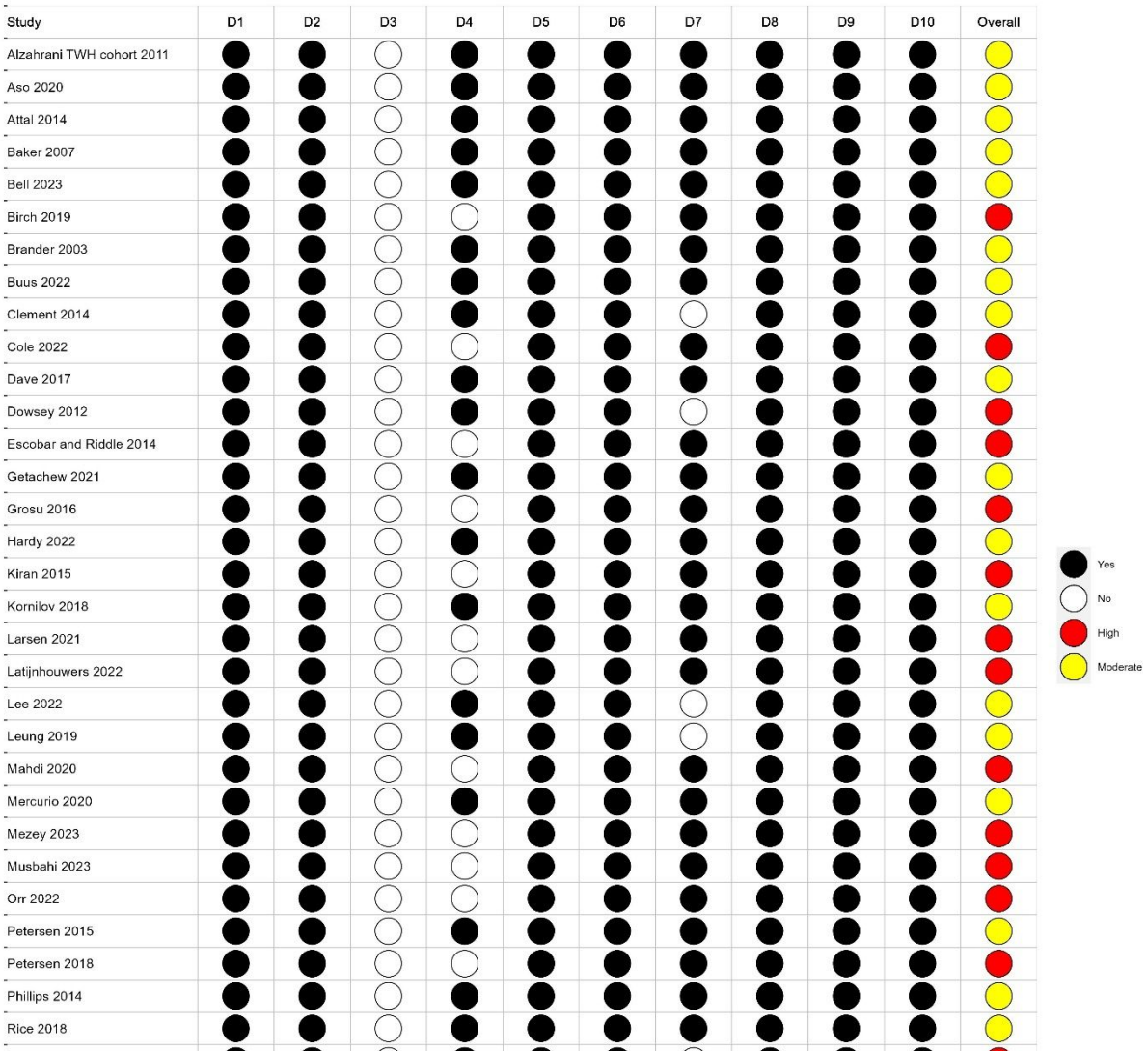


Prevalence of chronic pain after total hip or knee replacement

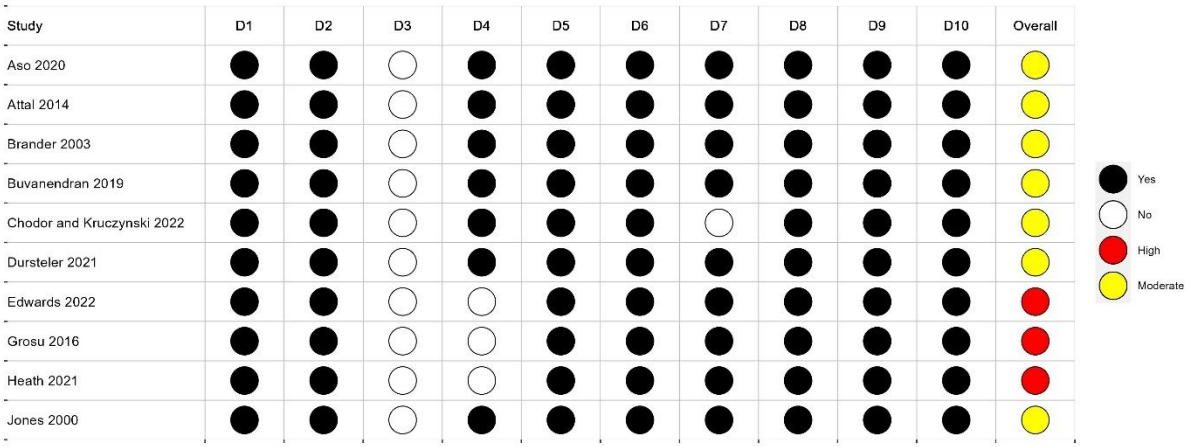
S4.2 TKR studies (6 months)



S4.3 TKR studies (12 months)



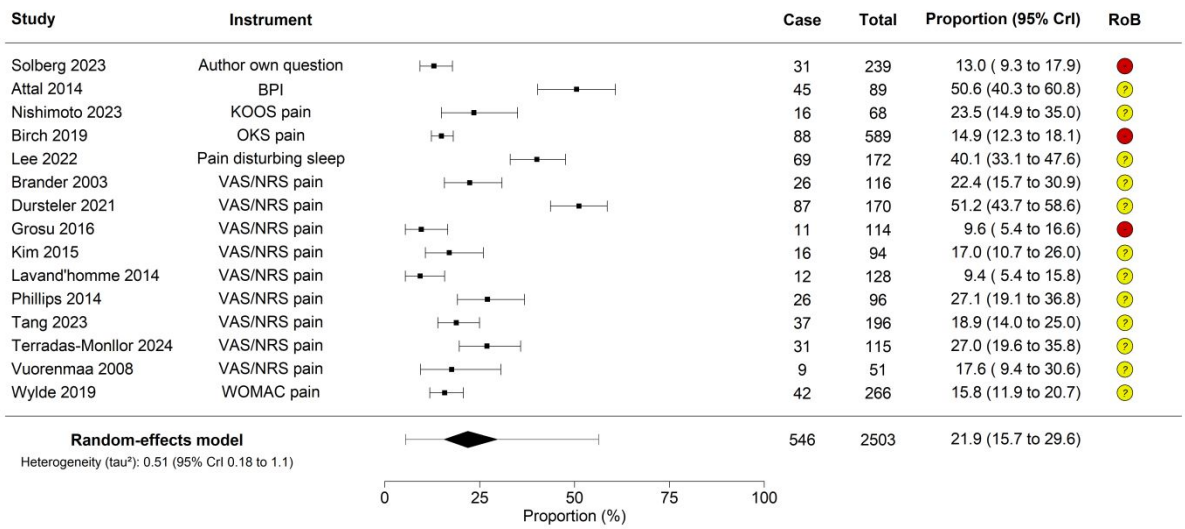
S4.4 TKR studies (24 months)



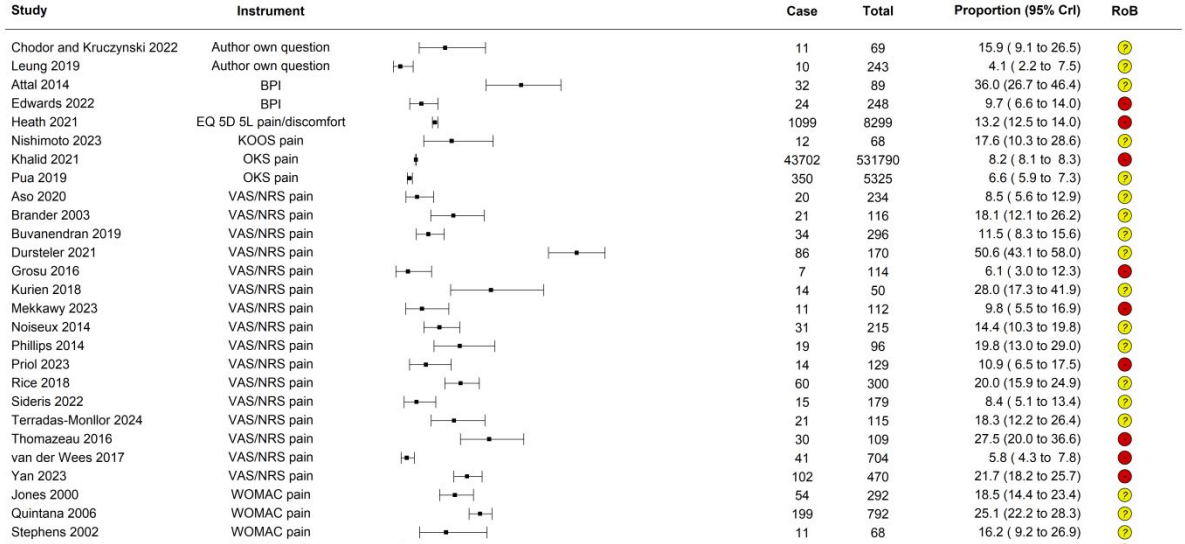
Prevalence of chronic pain after total hip or knee replacement

S5. Forest plots of univariate meta-analyses in TKR studies

S5.1 TKR studies (3 months)

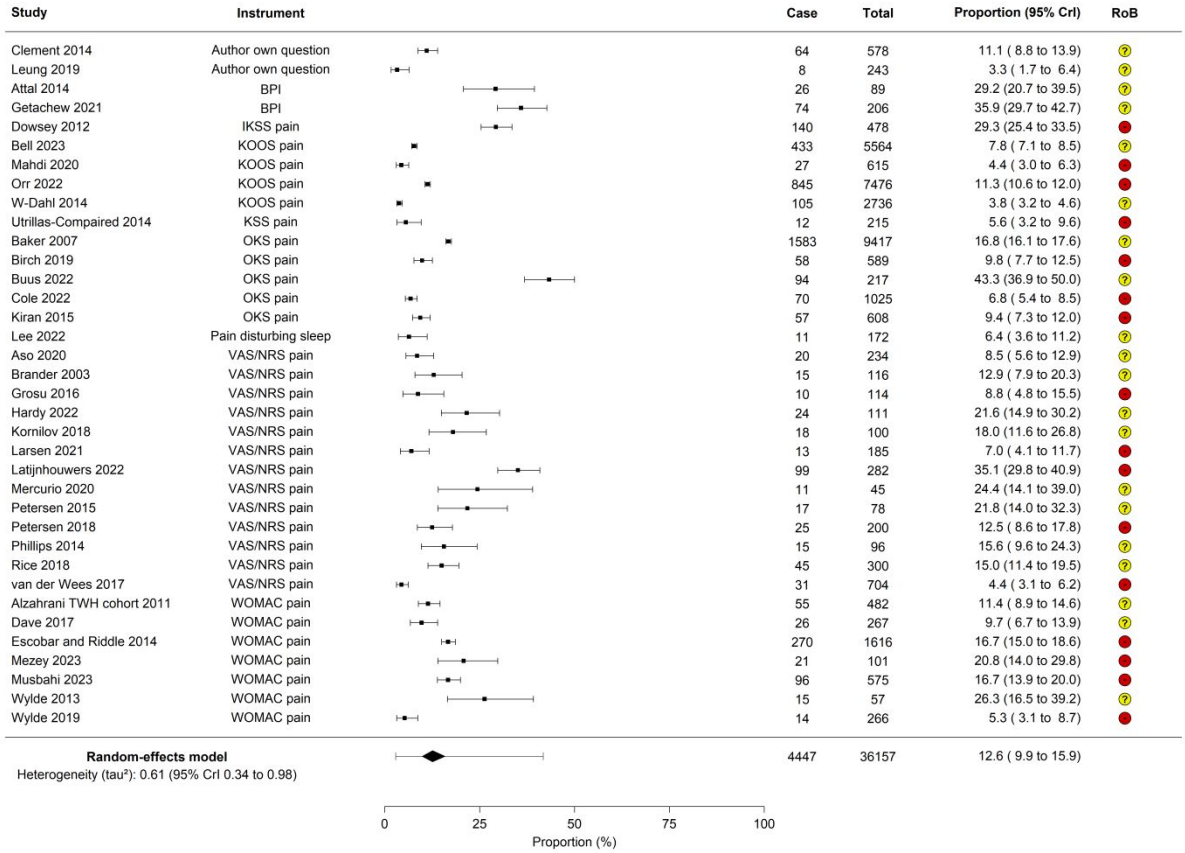


S5.2 TKR studies (6 months)

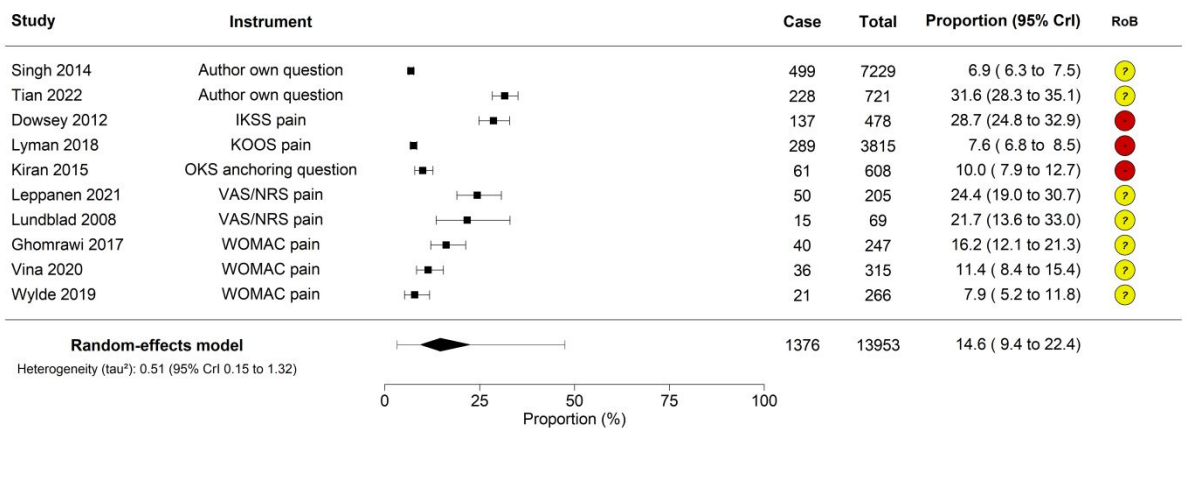


Prevalence of chronic pain after total hip or knee replacement

S5.3 TKR studies (12 months)



S5.4 TKR studies (24 months)



S6. Table of multivariate and univariate meta-analysis results in TKR studies

	Multivariate meta-analysis		Univariate meta-analysis	
Time	Median (95% CrI)	tau² (95% CrI)	Median (95% CrI)	tau² (95% CrI)
3 months	21.2 (16.9 to 26.4)	0.49 (0.28 to 0.91)	21.9 (15.6 to 29.4)	0.51 (0.18 to 1.1)
6 months	14.6 (11.9 to 17.8)	0.56 (0.34 to 0.91)	14.1 (10.9 to 17.9)	0.51 (0.27 to 0.9)
12 months	12.6 (10.3 to 15.5)	0.63 (0.41 to 0.99)	12.6 (9.9 to 15.9)	0.61 (0.35 to 0.99)
24 months	14.2 (10 to 20.1)	0.58 (0.25 to 1.55)	14.6 (9.5 to 22.4)	0.52 (0.16 to 1.35)

S7. Meta-regression analyses in TKR studies

S7.1 Mean age

Time	No. studies	slope	intercept
3 months	15	0.133	-1.272
6 months	28	0.082	-1.851
12 months	34	-0.029	-1.942
24 months	9	-0.073	-1.886

S7.2 Proportion of females

Time	No. studies	slope	intercept
3 months	15	0.009	-1.273
6 months	28	-0.040	-1.697
12 months	36	-0.006	-1.939
24 months	10	0.045	-1.798

S7.3 Sample sizes

Time	No. studies	slope	intercept
3 months	15	-0.001	-1.269
6 months	28	0.000	-1.785
12 months	36	0.000	-1.936
24 months	10	0.000	-1.750

Prevalence of chronic pain after total hip or knee replacement

S8. Subgroup analyses in TKR studies

- Geographic region (categorical; North America, Asia, Europe, and Australia)
- Data source (categorical; surgeons, single hospital, multi-centre, and national registry
- Pain outcomes instruments (categorical; multidimensional, e.g. WOMAC pain, simple, e.g. VAS/NRS and EQ-5D 5L, and not validated, e.g. author's own questionnaires)
- Cut-off definitions (categorical; based on MCID, based on PASS, based on pain intensity, e.g. specific post-operative VAS values, based on functional impact, e.g. night pain, pain on movement, or limiting daily life, based on symptom improvement, e.g. no change or increase in pain from pre-operative)

S8.1 Geographical regions

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Asia	4	24.26 (11.85 to 42.3)	0.32 (0 to 2.34)
Europe	9	22.17 (12.42 to 35.18)	0.77 (0.19 to 2.17)
North America	2	16.63 (0.92 to 81.83)	0.21 (0 to 31.7)
6 Months			
Asia	5	9.91 (4.04 to 21.69)	0.64 (0.06 to 3.19)
Australia	2	15.53 (1.23 to 73.87)	0.19 (0 to 23.85)
Europe	12	17.99 (10.88 to 27.3)	0.77 (0.27 to 1.85)
North America	9	11.87 (8.87 to 15.58)	0.13 (0 to 0.45)
12 Months			
Asia	3	5.81 (2.2 to 12.88)	0.12 (0 to 2.76)
Australia	2	21.45 (0.1 to 98.64)	0.73 (0 to 97.26)
Europe	25	13.54 (9.91 to 18.16)	0.72 (0.37 to 1.29)
North America	6	11.15 (8.31 to 14.9)	0.09 (0.01 to 0.4)
24 Months			
Asia	1	31.36 (28.02 to 34.79)	NA
Australia	1	28.29 (24.49 to 32.56)	NA
Europe	4	14.29 (5.86 to 32.4)	0.47 (0.03 to 3.51)
North America	4	9.56 (5.19 to 17.04)	0.2 (0 to 1.45)

S8.2 Setting

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Other	1	26.44 (19.1 to 34.38)	NA
Single hospital	8	25.41 (15.64 to 38.72)	0.55 (0.13 to 1.73)
Surgeon	6	16.89 (8.43 to 29.76)	0.55 (0.07 to 2.2)
6 Months			
Multicentre	6	13.84 (7.93 to 22.5)	0.35 (0.04 to 1.41)
Other	2	18.34 (7.93 to 37.29)	0.02 (0 to 2.68)
Registry	1	8.22 (8.14 to 8.29)	NA
Single hospital	16	15.03 (9.79 to 21.64)	0.73 (0.3 to 1.55)
Surgeon	3	10.82 (3.35 to 30.39)	0.26 (0 to 5.13)
12 Months			
Multicentre	12	11.29 (7.37 to 16.83)	0.56 (0.19 to 1.31)
Registry	1	16.80 (16.07 to 17.57)	NA

Single hospital	20	13.96 (9.77 to 19.93)	0.77 (0.34 to 1.47)
Surgeon	3	8.93 (4.2 to 16.32)	0.05 (0 to 1.6)
24 Months			
Multicentre	1	11.50 (8.14 to 15.03)	NA
Single hospital	9	14.98 (9.11 to 23.7)	0.57 (0.16 to 1.54)

S8.3 Pain outcome instruments

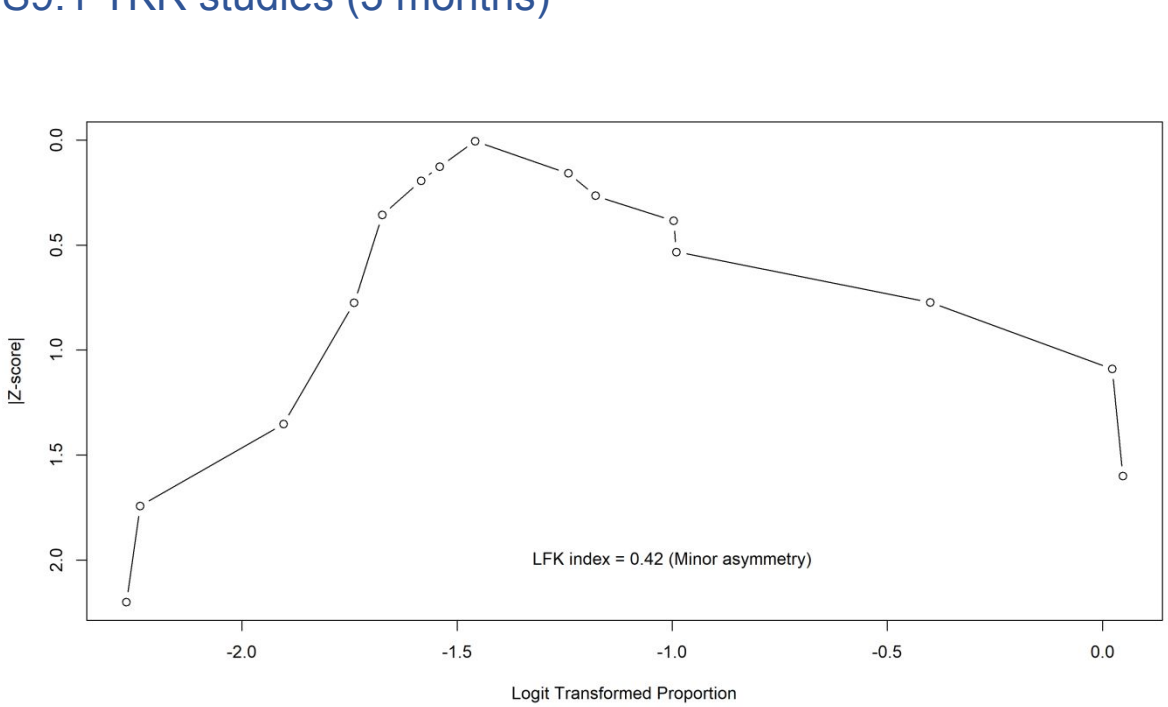
Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Multidimensional	5	26.76 (12.16 to 49.19)	0.7 (0.09 to 3.37)
Not validated	1	12.98 (9.3 to 17.9)	NA
Simple	9	20.6 (13.08 to 31.41)	0.5 (0.11 to 1.47)
6 Months			
Multidimensional	9	13.68 (8.49 to 22.5)	0.56 (0.14 to 1.57)
Not validated	2	7.65 (0 to 99.79)	1.72 (0 to 219.88)
Simple	17	15.15 (10.99 to 20.57)	0.49 (0.2 to 1.03)
12 Months			
Multidimensional	21	12.67 (8.95 to 17.66)	0.72 (0.33 to 1.34)
Not validated	2	6.51 (0 to 98.5)	1.52 (0 to 166.77)
Simple	13	13.91 (9.63 to 19.73)	0.44 (0.14 to 1.02)
24 Months			
Multidimensional	6	12.39 (6.86 to 20.55)	0.41 (0.07 to 1.58)
Not validated	2	15.65 (0 to 99.99)	3.63 (0.07 to 399.6)
Simple	2	23.53 (8.04 to 48)	0.02 (0 to 4.48)

S8.4 Cut-off definitions

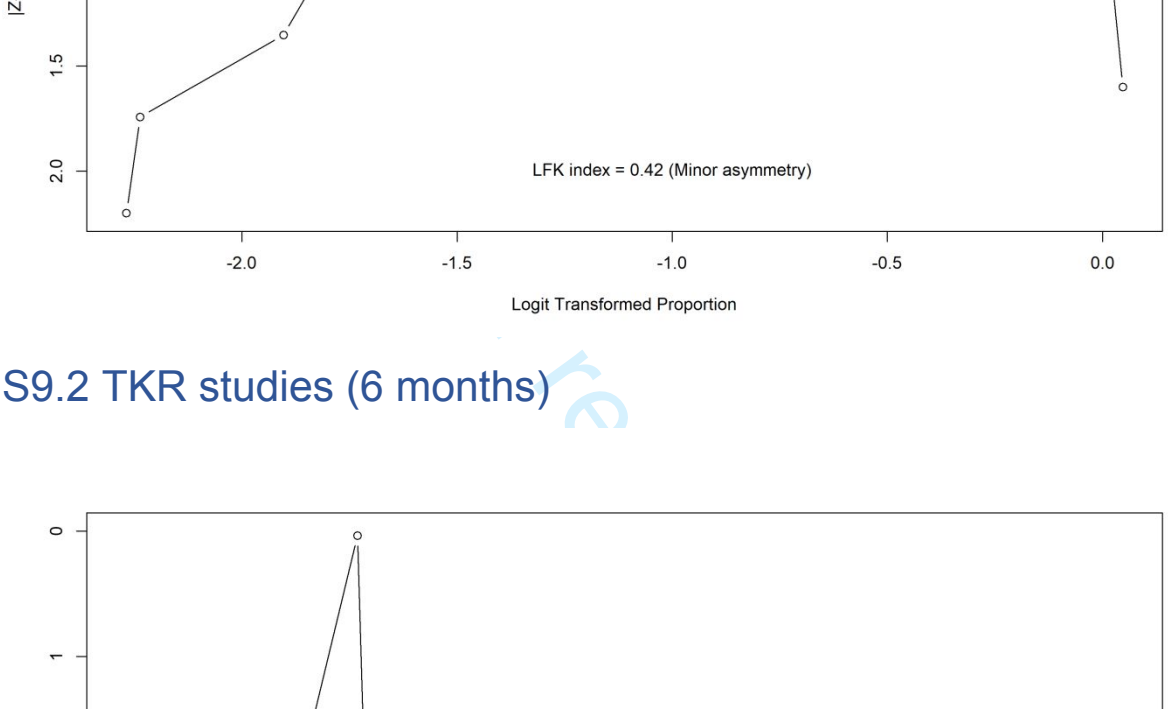
Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Based on functional impact	1	40.1 (33.1 to 47.6)	NA
Based on MCID	2	17.91 (4.01 to 63.34)	NA
Based on pain intensity	10	21.61 (13.37 to 33.15)	0.66 (0.18 to 1.74)
Based on symptom improvement	2	18.26 (0.26 to 95.83)	NA
6 Months			
Based on functional impact	1	15.9 (9.1 to 26.5)	NA
Based on MCID	3	14.38 (1.88 to 56.47)	1 (0.05 to 13.77)
Based on pain intensity	21	15.26 (11.63 to 19.96)	0.48 (0.23 to 0.92)
Based on symptom improvement	3	6.75 (1.68 to 26.53)	0.44 (0 to 7.44)
12 Months			
Based on functional impact	1	6.4 (3.6 to 11.2)	NA
Based on MCID	5	15.77 (5.83 to 36.93)	0.92 (0.13 to 4.38)
Based on pain intensity	19	14.34 (10.16 to 19.75)	0.61 (0.26 to 1.19)
Based on PASS	2	13.7 (1.08 to 66.8)	NA
Based on symptom improvement	9	8.86 (5.08 to 15.27)	0.63 (0.15 to 1.81)
24 Months			
Based on functional impact	1	31.6 (28.3 to 35.1)	NA
Based on MCID	3	10.88 (4.18 to 25.04)	0.22 (0 to 3.32)
Based on pain intensity	4	18.24 (6.02 to 43.02)	0.75 (0.08 to 5.12)
Based on symptom improvement	2	9.15 (2.73 to 24.14)	NA

S9. Doi plots and the LFK indexes in TKR studies

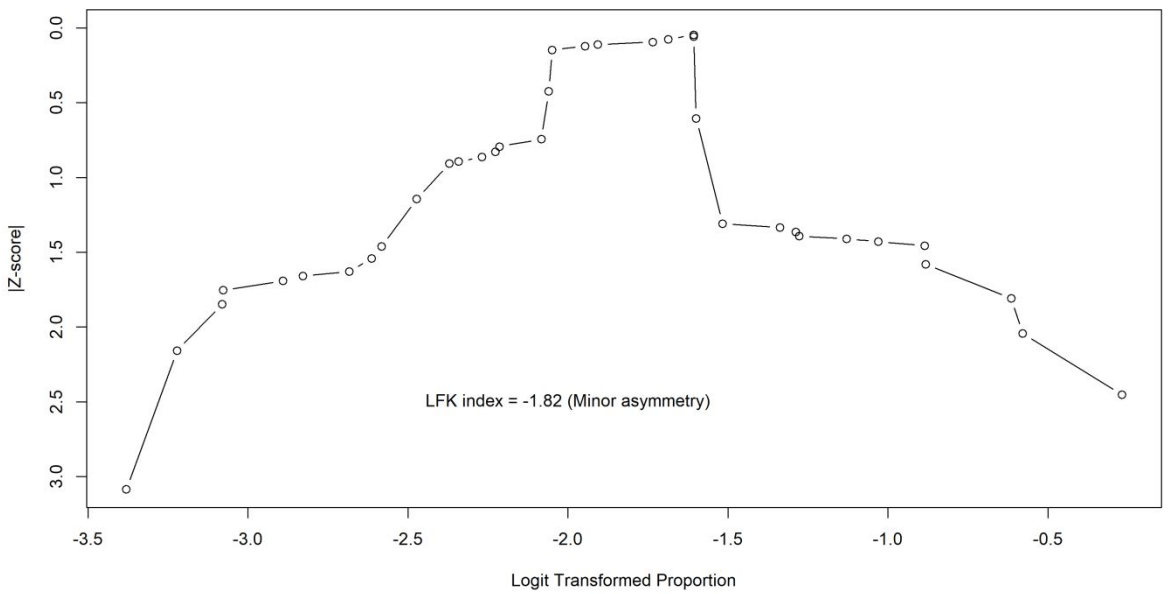
S9.1 TKR studies (3 months)



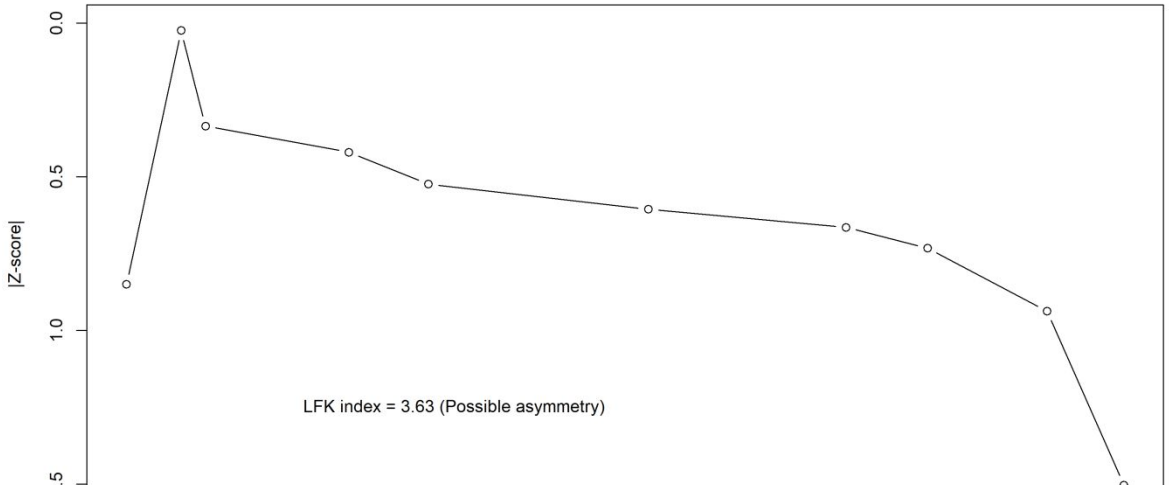
S9.2 TKR studies (6 months)



S9.3 TKR studies (12 months)



S9.4 TKR studies (24 months)



S10. Sensitivity analyses

In the sensitivity analysis, we excluded the following studies based on their unique clinical characteristics:

- Tang 2023 (impact on 3 months results only)
- Leppanen 2021 (impact on 24 months results only)
- Fast track studies (impact on 3 and 12 months results only)
- Mekkawy 2023 and Yan 2023 (impact on 6 months results only)
- Studies on TKR or UKR operations
- Studies with more than 20% lost to follow-up
- High risk of bias studies

Name	No. studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Excluding Tang 2023	14	22.12 (15.4 to 30.2)	0.55 (0.19 to 1.21)
Excluding Fast track studies	14	22.56 (15.96 to 30.84)	0.53 (0.17 to 1.18)
Excluding TKR or UKR studies	12	23.68 (16.36 to 33.17)	0.53 (0.17 to 1.29)
Excluding studies with > 20% loss to follow-up	11	26.13 (18.08 to 36.46)	0.49 (0.14 to 1.25)
Excluding studies with overall high risk of bias	12	25.01 (17.87 to 34.74)	0.48 (0.16 to 1.17)
6 Months			
Excluding Mekkawy 2023 and Yan 2023	26	13.97 (10.74 to 18.13)	0.54 (0.27 to 0.95)
Excluding TKR or UKR studies	26	14.24 (10.88 to 18.46)	0.54 (0.27 to 0.95)
Excluding studies with > 20% loss to follow-up	19	16.78 (12.37 to 22.52)	0.52 (0.22 to 1.03)
Excluding studies with overall high risk of bias	19	15.63 (11.25 to 21.19)	0.58 (0.24 to 1.12)
12 Months			
Excluding Fast track studies	34	12.15 (9.5 to 15.15)	0.55 (0.3 to 0.91)
Excluding TKR or UKR studies	35	12.72 (9.85 to 16)	0.63 (0.35 to 1.01)
Excluding studies with > 20% loss to follow-up	19	15.3 (11.09 to 21.01)	0.58 (0.23 to 1.16)
Excluding studies with overall high risk of bias	20	14.37 (10.14 to 19.49)	0.65 (0.28 to 1.23)
24 Months			
Excluding Leppanen 2021	9	13.78 (8.33 to 21.28)	0.52 (0.15 to 1.45)
Excluding TKR or UKR studies	9	13.18 (8.59 to 20.26)	0.42 (0.11 to 1.18)
Excluding studies with > 20% loss to follow-up	6	18.74 (9.79 to 33.5)	0.59 (0.11 to 2.29)
Excluding studies with overall high risk of bias	7	15.28 (8.68 to 26.24)	0.53 (0.12 to 1.78)

*Abbreviation: TKR: Total Knee Replacement; UKR: Unicompartmental Knee Replacement

Prevalence of chronic pain after total hip or knee replacement

S11. Characteristics of THR studies

Study Country Recruitment dates Setting	Operation Number of patients Age (SD), range % women	Pain measure	Definition of unfavourable pain outcome High risk of bias concern
Cleveland Clinic OME Arthroplasty Group 2020[1] USA 2015-2018 6 hospitals	Primary THR, all N=3449 Median 65 (IQR 57-72) 57.4%	HOOS pain 12 months	Less than MCID (15 points)
Erlenwein 2017[2] Germany 2012 1 hospital	Primary THR, all 18+ N=125 63 (12.6) 58%	NRS pain 6 months	Maximum NRS >3 during previous 4 weeks
Jones 2000[3] Canada 1995-1997 1 health region	Primary THR, all 40+ N=242 68.2 (11.1) 60%	WOMAC pain 6 months	Moderate/ severe pain defined as a gain of <10 points on the WOMAC pain dimension
Mezey 2023[4] Hungary 2019-2020 2 hospitals	Primary THR, all N=88 68.7 (THR and TKR patients) 69.2%	WOMAC pain 12 months	Not exceeding MCID (8.3) High loss to follow up rate
Nikolajsen 2006[5] Denmark 2003 National registry	Primary THR, 18-90 years N=1231 71.6 (8.7) Not reported	Authors' own scale of presence of hip pain and impact on daily life 12-18 months	Pain with moderate, severe or very severe impact on daily life
Page 2016[6] Canada 2009-2012 1 hospital	Primary THR, all 18-75 N=150 60 (9.2) 48%	Authors' own scale 6 months	Chronic pain if pain rated as "discomforting", "distressing", "horrible," or "excruciating" Concern as RCT analysed as cohort study
Palazzo 2014[7] France 2009 3 hospitals	Primary THR, all N=129 63.5 (13.5) 49.6%	Author's own residual pain scale 12 months	"To what extent have you obtained a relief or improvement as a result of THA in the following areas?" (from 0: not at all; to 4: completely)
Quintana 2006[8] Spain 1999-2000 7 hospitals	Primary THR N=784 69.1 48.3%	WOMAC pain 6 months	No improvement in pain greater than MCID (24.55 of 100) using an anchor-based method. Concern for high loss to follow up rate
Ray 2020[9] Sweden 2008-2015 National registry	THR N= 127,660 68 (10) 56%	EQ-5D VAS pain/discomfort 12 months	Worse or no change in pain/discomfort Concern for high loss to follow up rate

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Singh and Lewallen 2010[10] USA 1993-2005	Primary THR N=9154 65 (13.3) 51%	Authors' own scale: How much pain do you have in your operated hip? None, mild, moderate or severe 24 months	Moderate or severe pain Concerns for high loss to follow up rate
Tang 2023[11] China 2020-2021 1 hospital	Primary THR probably, all 65+. Osteoarthritis or osteonecrosis (not fracture) N=89 72 (range 63-81) 62.5%	NRS pain 3 months	NRS scores ≥4 Note, n and losses to follow up estimated as proportions because n hips and knees reported together

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S11.1 Proportions of lost to follow-ups and revisions

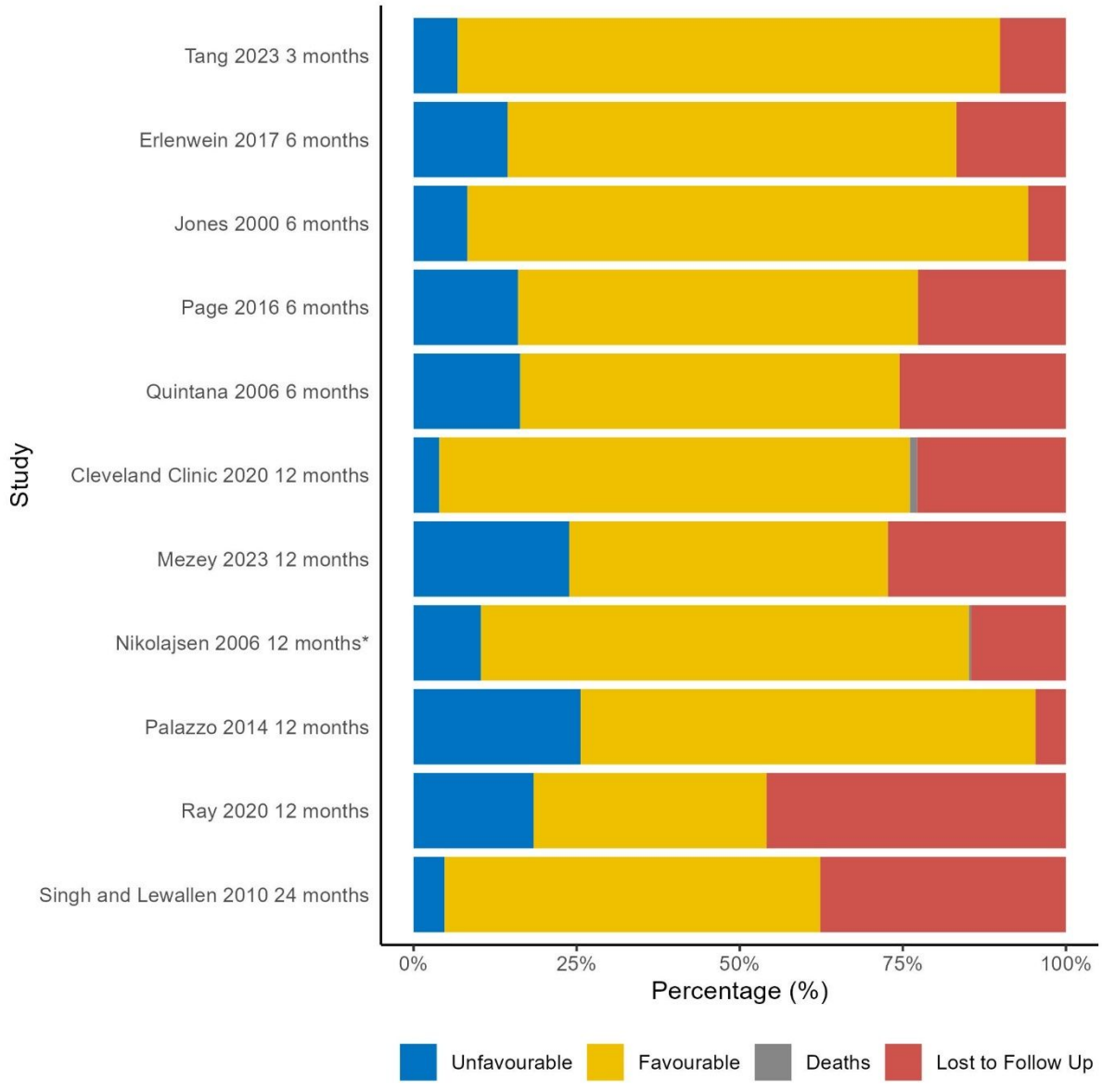
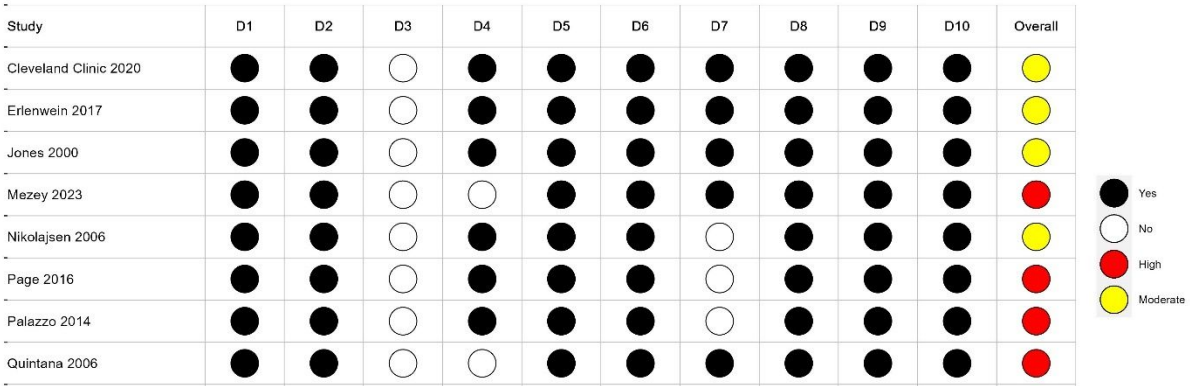


Figure S12.1. Favourable and unfavourable pain outcomes and reasons of missing data in THR studies.

Prevalence of chronic pain after total hip or knee replacement

S12. Traffic light plot of the risk of bias assessments in THR studies



BMJ Open

What proportion of people have long-term pain after total hip or knee replacement? An update of a systematic review and meta-analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-088975.R2
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What proportion of people have long-term pain after total hip or knee replacement? An update of a systematic review and meta-analysis

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Running title

Prevalence of chronic pain after total hip or knee replacement

Keywords

Chronic pain; Total hip replacement; Total knee replacement; Systematic review; Meta-analysis

Abstract

Objectives

To update our previous systematic review to synthesise latest data on the prevalence of long-term pain in patients who underwent total hip replacement (THR) or total knee replacement (TKR). We aim to describe the prevalence estimates and trends in this review.

Design

Systematic review and meta-analysis

Data Sources

Update searches were conducted in MEDLINE and Embase databases from 1st January 2011 to 17th February 2024. Citation tracking was used to identify additional studies.

Eligibility Criteria

We included prospective cohort studies reporting long-term pain after THR or TKR at 3, 6, 12 and 24 months post-operative.

Data Extraction and Synthesis

Two reviewers independently identified studies as eligible. One reviewer conducted data extraction, checked by a second reviewer. The risk of bias assessment was performed using Hoy's checklist. Bayesian, random-effects meta-analysis was used to synthesise the results.

Results

For TKR, sixty-eight studies with 89 time points, including 598,498 patients, were included. Multivariate meta-analysis showed a general decrease in pain proportions over time: 21.9% (95% CrI 15.6 to 29.4) at 3 months, 14.1% (10.9 to 17.9) at 6 months, 12.6% (9.9 to 15.9) at 12 months, and 14.6% (9.5 to 22.4) at 24 months. Considerable heterogeneity, unrelated to examined moderators, was indicated by substantial prediction intervals in the univariate models. Substantial loss to follow-up and risk of bias led to low confidence in the results. For THR, only eleven studies were included, so it was not possible to describe the trend. Univariate meta-analysis estimated 13.8% (8.5-20.1) and 13.7% (4.8-31.0) of patients experiencing long-term pain 6 and 12 months after THR, respectively, though concerns in risk of bias results reduced confidence in these findings.

Conclusions

Our review suggests that approximately 22% of patients report pain 3 months post-TKR, with 12-15% experiencing long-term pain up to 2 years. At least 14% report pain 6-12 months after THR. Given the prevalence of chronic post-surgical pain, implementing existing and

developing new preventive and management strategies is crucial for optimal patient outcomes.

Study registration

PROSPERO CRD42023475498

Strengths and limitations of this study

- We updated a previous review using the latest review methodology, including Bayesian, multivariate meta-analysis and risk of bias assessment, to summarise the prevalence rates reported across studies of chronic post-surgical pain in patients undergoing total knee or hip replacement.
- We included a wide range of patient-reported measures of pain across studies which resulted in heterogeneity
- These prevalence rates are likely underestimated due to loss to follow-up and the high risk of bias in the included studies.
- Our sensitivity and scenario analyses offer readers plausible and robust prevalence estimates.

Introduction

The primary reason that people with osteoarthritis undergo joint replacement surgery is because of persistent pain that has failed to improve with non-invasive management.[1 2] About 100,000 each of primary total knee and hip replacements were performed in the UK in 2022,[3 4] and in Organisation for Economic Co-operation and Development countries in 2015, over 1.5 million primary knee and nearly 1.7 million primary hip replacements were performed.[5] The number of people with osteoarthritis is projected to increase[6 7] and even in Germany, a country with a declining population, rates of joint replacement are predicted to rise due to the increasing use of knee replacement in younger people and the increasing number of older people requiring hip replacement.[8]

Potential improvements in pain and functionality ability are the primary reasons that patient elect to have a hip or knee replacement, and the most important contributing factors to patient satisfaction with the outcome of surgery.[9 10] It is important to note that pain and patient satisfaction are distinct constructs,[11] as patient satisfaction contains broader aspects of surgical outcomes beyond solely pain relief. In the literature, the terms, such as persistent pain[10 12-14], unchanged pain[15], residual pain[16-18], and worsening pain[19 20], are often used to describe pain that persists despite surgery providing functional improvements and high satisfaction.[11] It is widely recognised that some people experience continuing pain in the months and years following surgery. Our previous systematic review,[21] with searches up to 2011, brought together longitudinal studies in representative populations receiving knee or hip replacement. We found that for a majority of people, their pain outcome was favourable, but for 10-34% of patients the long-term pain outcome could be considered “unfavourable” (moderate-to-severe pain or for whom surgery had not relieved pain) after total knee replacement (TKR) and 7-23% after total hip replacement (THR).[21] Together with qualitative research into patients’ experiences,[22 23] our previous review stimulated research into the prediction, prevention, management and treatment of chronic pain after knee and hip replacement.

Thirteen years on from publication of our previous review, our aim is to provide updated estimates of the incidence of long-term pain after total knee and hip replacement and explore factors that may influence the rates observed. Findings will support patients, clinicians and researchers as they face the challenge of preventing and treating chronic pain after total knee or hip replacement.

Methods

We updated our previous systematic review from our team,[21] with follow-up intervals between 3 and 24 months post-operative. We limited the follow-up to a maximum of 24 months as pain levels often plateau by this timepoint, and new onset pain beyond this may be related to implant failure.[24] With the more extensive data available for outcomes after TKR in this update, we planned to establish the trend of long-term pain over time up to 24 months post-operative.

The protocol was registered with PROSPERO (CRD42023475498) and this review was reported in accordance with MOOSE[25] (Supplementary material S1) and relevant contents in PRISMA[26] guidelines and the Cochrane handbook.[27]

Eligibility criteria

We sought prospective cohort studies including patients representative of the general population receiving total knee or hip replacement, predominantly from advanced osteoarthritis as in our previous review.[21] Cohorts were established pre- or peri-operatively in hospital orthopaedic departments and joint replacement centres and followed up prospectively at any defined time between 3 and 24 months. Studies specifically of unicompartmental knee replacement or hip hemiarthroplasty, revision surgery, or exclusively bilateral replacements were excluded.

Outcome

The outcome was the proportion of people with unfavourable pain in the operated joint at 3, 6, 12 and 24 months post-operative. We adopted the term 'unfavourable pain' from the previous review, which serves as a collective label to include the various descriptions used by study authors–such as persistent pain, worsening pain, or residual pain--rather than as an indicator of dissatisfaction.[21 28] In each study, unfavourable pain was defined using the study authors' definitions or through a consensus between two reviewers with extensive research experience in pain outcome measurement in total knee and hip replacement before commencement of data extraction. Most studies used a single cut-off value, often based on a pre-specified post-operative visual analogue scale (VAS) or numerical rating scale (NRS) score. For the few studies that provided multiple cut-off values, such as Musbahi and colleagues,[18] we selected the cut-off values that the authors concluded were the best balance between sensitivity and specificity. For studies that used general tools, such as the VAS or NRS, we only included those that reported VAS or NRS scores specific to the operated joint, rather than general VAS pain scores. To calculate the proportions, we extracted the number of recruited or followed patients as denominators and the number of

patients experiencing unfavourable pain as numerators. When a percentage or rate was provided, we rounded the numbers to the nearest whole number.

Searches

We conducted new searches of MEDLINE and Embase databases from January 2011 to 17th February 2024. The search strategies for MEDLINE and Embase are included in S2. Web of Science was used to track citations of the original review.[21] Excepting the search strategy, we applied no language restrictions at any stage of the review, with Google Translate used to translate sections of relevant non-English articles. We did not contact authors as we only focused on published studies. Studies reported only as abstracts were excluded.

Study selection and data collection

Studies identified were imported into EndNote 21 reference management software. After removal of duplicate records, one reviewer screened out clearly off-topic studies. Titles and abstracts of potentially relevant articles were acquired and assessed independently for eligibility by two reviewers. In cases of disagreement, a third reviewer was involved. Eligible articles identified in our previous systematic review were also included.

Data from eligible studies were entered into a Microsoft Excel spreadsheet by one reviewer with checking by a second reviewer. Extracted data were: country; dates of patient recruitment; setting (single or multiple surgeons, single or multiple hospitals, registry, or other; inclusion and exclusion criteria; whether routine “fast-track” surgery; patient characteristics (age, sex); assessment times; number of patients at baseline, number lost to follow up (or died or with revision surgery if reported) and number followed up; and patient reported pain outcome measure.

When more than one pain outcome was reported, we extracted them in order of preference: pain dimension data from osteoarthritis or joint specific outcome scores (Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC); Knee injury and Osteoarthritis Outcome Score (KOOS); Hip injury and Osteoarthritis Outcome Score (HOOS); Oxford Knee Score (OKS); Oxford Hip Score (OHS) and Knee Society Scores if patient generated (KSS, IKSS); Brief Pain Inventory (BPI); pain assessed in EuroQol instruments (EQ-5D or EQ-3D); joint pain after surgery, measured on a VAS or NRS; and other measures including those developed by study authors.

Risk of bias assessment

Two independent reviewers assessed risk of bias using the non-summative checklist described by Hoy and colleagues.[29] This checklist considers ten aspects of study conduct

relating to representation and selection, non-response (>25% of lost to follow-up as high risk), data collection and instrument used, follow up and methods used in calculation of rates. Overall risk of bias was judged to be low, moderate or high depending on whether any of the ten aspects gave concern.

Data synthesis approach

Our primary aim was to describe the proportion of people experiencing unfavourable pain outcomes over time. First, we summarised the characteristics of studies and inspected their clinical heterogeneity before the synthesis using tables and figures. We then meta-analysed proportions with an unfavourable pain outcome, along with accompanying 95% credible intervals (CrIs) and median between-study heterogeneity (τ^2) at 3, 6, 12, and 24 months' time separately when there were more than three studies. We also used prediction intervals to aid the between-study heterogeneity interpretation.[30] We used Bayesian framework with a random-effects model due to anticipated heterogeneity. Vague prior distributions (e.g. normal with mean 0 and variance 10^5) on model parameters were used. Posterior outcome distributions were based on at least 25,000 simulations after a burn-in of at least 1,000 to ensure convergence.

To account for the multiple time follow-ups reported in certain studies, we adopted a Bayesian, hybrid, multivariate meta-analysis of multiple factors[31] to describe the proportions across time points by borrowing information and accounting for within- and between-study correlations.

All analyses were performed using R version 4.3.1 on RStudio 2023.06.2+561. The *runjags* and *metafor* packages were used to produce pooled estimates, forest plots, meta-regression and subgroup analyses. The *metasens* package was used to generate Doi plots and the LFK index.[32] The *ggplot2* package was used to produce additional figures to explore the clinical heterogeneity in the studies.

Exploration of heterogeneity

For potential sources of heterogeneity, we used meta-regression to explore heterogeneity for continuous factors (mean age of the population, percentage of females, and baseline sample sizes) where more than ten studies were included in the meta-analysis. For categorical factors (geographic region, settings, and pain outcome instruments), we conducted subgroup analyses where more than five studies were included in the meta-analysis.

Sensitivity analysis

In sensitivity analysis, we excluded studies with specific inclusion criteria, those focused on "fast track" surgery, studies where a proportion of people underwent unicompartmental knee

replacement, studies with potentially over-inclusive unfavourable pain definitions, and studies with more than 20% lost to follow-up, and studies with an overall high risk of bias. Additionally, we performed worst-best scenario analyses by estimating the proportion of people lost to follow-up who experienced unfavourable pain outcomes, incrementing by tenths from 0% to 100%, to estimate their impact on the meta-analysis results.

Reporting bias and certainty assessment

We assessed publication bias using Doi plots and the LFK index (values between -1 and +1 indicate symmetry; values outside this interval indicate asymmetry) to aid the interpretation in cases where more than ten studies were included in the meta-analysis. We cross-checked the clinical study register and methods section in the report to evaluate non-reporting bias. The certainty of evidence assessment was not conducted because specific tools for systematic reviews of prevalence were unavailable.

Patient and public involvement

There was no direct patient and public involvement in this systematic review, however, it benefitted from being part of the NIHR-funded STAR programme, which aimed to improve outcomes for patients with chronic pain after knee replacement. [33]Patient and public involvement was integral to STAR, and we worked throughout the programme with an existing patient forum and developed a complementary group focusing exclusively on chronic pain after TKR.

Results

Searches of MEDLINE, Embase, citation tracking in Web of Science and inclusion of potentially relevant articles identified in our previous review yielded a total of 13,807 records. After screening out of clearly irrelevant studies by one reviewer, 979 records were screened in duplicate by two reviewers and ultimately 68 studies with 598,498 TKR participants and 11 studies with 143,101 THR participants were included. Study selection and reasons for exclusion at the full-text stage are summarised in Figure 1. Some articles from our previous review were excluded as the follow up period was longer than 24 months.

Total knee replacement

Individual study characteristics are summarised in S3. The grouped characteristics in Table 1. The baseline dates of data collection ranged from 1993 to 2023. Geographically, most studies were conducted in Europe (n=37) and North America (n=19). More than half of studies (n=39) collected their data at a single hospital, followed by multiple hospitals (n=18). Overall, 598,498 patients were included in the 68 studies with a median sample size per study of 235 (interquartile range 114 to 581). Patients in 52 studies with data had a mean age of 69.6 (SD 9.4) years, and 63% (58 to 69) were women. In terms of primary pain outcome reported, 31 studies reported multi-dimensional pain scales (WOMAC, OKS, KOOS, BPI, or KSS/IKSS), 29 studies reported VAS or NRS pain scores, and 6 studies used researchers' own measures.

After harmonising unfavourable pain outcomes at different time points, there were 15, 28, 36 and 10 studies with data available for 3, 6, 12 and 24 months post-operative. Risk of bias assessments are summarised in Figure 2 (for traffic light plots, see S4). Most studies were judged as overall moderate risk of bias with few overall high risk of bias due to losses to follow up of >25%, or use of scores which are not entirely patient completed or have concerns relating to a low pain cut off.

As noted in the previous review, the proportions of people with unfavourable pain varied widely across studies. Studies reported ranges of people with unfavourable pain at 3 months of 9.4 to 51.2%, at 6 months of 4.1 to 50.6%, at 12 months of 3.3 to 43.3%, and at 24 months of 6.9 to 31.6% (S5). We synthesised the unfavourable pain outcomes using multivariate meta-analysis (Figure 3), demonstrating a general decrease in pain proportions over time: 21.9% (95% CrI 15.6 to 29.4) at 3 months, 14.1% (10.9 to 17.9) at 6 months, 12.6% (9.9 to 15.9) at 12 months, and 14.6% (9.5 to 22.4) at 24 months. The results of the univariate models were similar due to the limited number of studies with multiple time points (S5), though with slightly wider CrIs (S6). The substantial prediction intervals in the univariate models suggested considerable heterogeneity.

We investigated potential heterogeneity using meta-regression and subgroup analyses in the univariate meta-analysis models. Meta-regression results showed no evidence of age, percentage of women, or sample size contributing to the heterogeneity of the proportion of individuals with unfavourable pain outcomes (S7).

Subgroup findings should be interpreted with caution due to the limited number of studies in some subgroups. In subgroup analyses, rates of unfavourable pain tended to be lower in studies involving patients from North America compared to other geographic groups (S8.1). Similarly, studies conducted in single-surgeon series settings showed lower rates of unfavourable pain outcomes (S8.2).

Outcome instruments that were not validated, frequently suggested low levels of unfavourable pain, while multidimensional measures were consistent with overall meta-analysis at 3, 6, 12 and 24 months (S8.3). Results were also consistent for simple pain measures at 3, 6 and 12 months, but data was limited at 24 months. Cut-offs which defined an unfavourable pain outcome were based on pain intensity, symptom improvement, the functional impact of pain, and minimally important clinical differences or patient acceptable symptom states calculated within each dataset. Excepting at 24 months when data was sparse, cut-offs relying on a simple dichotomisation by levels of pain intensity were reasonably consistent with meta-analyses (S8.4). In 3 and 5 studies respectively, cut-offs based on minimally important clinical differences in WOMAC or KOOS outcomes at 6 and 12 months provided similar estimates of unfavourable pain to the meta-analyses. At 24 months, in 3 studies the estimate of 10.88 (4.18 to 25.04) was lower than that in the overall meta-analysis, 14.6% (9.5 to 22.4). Two studies reported the proportion of people not achieving a patient acceptable symptom state at 12 months. Results were similar to those in the overall meta-analysis. In the studies with cut-offs based on symptom improvement, the proportions of people with unfavourable pain were lower than seen in the overall meta-analyses.

Although we observed small-study effects in the results (S9), potentially attributable to publication bias, it is likely that these resulted from the extremely large variations in sample sizes at the 6-, 12-, and 24-month follow-ups. We did not find evidence of non-reporting bias, as most studies reported long-term pain outcomes in accordance with their reported methods.

In sensitivity analyses, we individually excluded studies with specific criteria to evaluate their impact on the univariate meta-analysis results (S10). The effects of excluding these studies were generally minor, except for studies with a high risk of bias or a high proportion of lost to follow-up. To account for the varying degrees of loss to follow-up, we performed separate scenario analyses by assuming that the same proportion of participants lost to follow-up

experienced unfavourable pain outcomes in each study (Table 2). By assuming 10% to 30% of participants lost to follow-up might experience unfavourable pain, this approach could yield more realistic estimates, given the limited literature available for further imputation.

Total hip replacement

Eleven studies reported unfavourable pain outcomes in individuals who underwent THR. The characteristics of these studies are summarised in S11. Only one study reported unfavourable pain outcomes at the 3-month and 24-month time points, so a trend cannot be established. Studies reported ranges of people with unfavourable pain at 6 months of 8.3 to 16.3%, and at 12 months of 3.9 to 25.6% (Figure 4).

Meta-analysis of unfavourable pain outcomes provided similar results at 6 and 12 months, with 13.8% (8.5 to 20.1) and 13.7% (4.8 to 31.0), respectively. However, concerns regarding the risk of bias assessment (S12) lead to low confidence in these results.

Discussion

Through our systematic review and meta-analysis, we have synthesised the existing evidence on the proportion of patients who experience long-term pain after knee and hip replacement. By updating our previous review, we have been able to provide estimates of incidence rates at 3, 6, 12 and 24 months post-operative. As noted previously,[21] studies report widely varying estimates of unfavourable pain outcome, and these may depend on the methods and analyses used. For example, at 12 months after TKR when patients should have recovered from surgery and be largely unaffected by issues relating to implant failure, the range of unfavourable pain across studies was 3.3 to 43.3%. After THR at 12 months the range was 3.9 to 25.6%. With the large number of studies now available, meta-analyses have permitted us to provide point estimates with 95% credible intervals to describe uncertainty, and to explore patient and study level factors that may explain the variation in unfavourable pain observed.

Our meta-analyses suggest that the proportion of people with an unfavourable level of pain after TKR decreases between three and six months after surgery and then remains stable until at least two years. While recognising the associated wide credible intervals, approximately 22% of patients will report an unfavourable pain outcome at three months after TKR, with 12-15% of people experiencing an unfavourable longer-term pain outcome up to two years after surgery. For THR, a lack of studies reporting rates of unfavourable pain outcomes in unselected patients limited our analysis. However, our findings suggest that at least 14% of people may report unfavourable pain at 6-12 months after THR.

The strengths and limitations of this review should be considered when interpreting the results**.** Firstly, overall quality of evidence is low due to potential heterogeneity and risk of bias in TKR studies, and we were unable to estimate trends for THR studies due to a low number of included studies. Data from good quality registry studies was limited as estimates of proportions of people with chronic pain are seldom reported. The wide range of rates of unfavourable pain across studies may reflect the different definitions used by the study authors, however, we were unable to investigate conclusively the relationships between the definition used and prevalence estimates within this review as we did not have access to individual patient data. Studies in specific cohorts have reported proportions of people with different definitions of unfavourable pain outcomes.[18] For example, in the study by Musbahi and colleagues, thresholds based on combinations of different minimal clinically important differences and patient acceptable symptom states for WOMAC pain ranged from 5% to 52%.[18] The authors note that a WOMAC pain score improvement of <20/100 as reported by 23% of people had sensitivity and specificity for predicting a patient's dissatisfaction with pain relief and overall outcome of TKR. We believe that studies reporting on different

outcome assessments and those exploring the patient experience of pain after TKR and THR complement our research. The varying rates of unfavourable pain outcomes may also suggest that there is selection that was not apparent in the study methodology. For example, a single surgeon series with lower rates of unfavourable pain may relate to patient selection which is not evident from the cohort inclusion criteria. Secondly, loss to follow-up may have impacted on our estimates of the proportion of patients with chronic pain after TKR and THR. The influence that unfavourable pain and other outcomes have on patient willingness to participate in research follow-up is unclear. Some studies suggest that people with poor outcomes are less likely to participate in follow-up assessments due to dissatisfaction with their care or difficulties completing follow-up.[34-37] However, others report no difference or poorer pain outcomes in those responding to initial invitations or attending follow-up visits compared with those not participating in follow-up visits.[38-40] Our sensitivity analyses in studies of TKR excluding studies with high loss to follow-up rates showed higher rates of unfavourable pain and provide some support for the latter suggestion. Given the uncertainty regarding the impact of loss to follow-up, we conducted separate scenario analyses to provide readers with a range of realistic estimates for their consideration. Thirdly, the scope of our review was broad. We included all different patient-reported measures of pain together, which present a mixture of single and multidimensional measures, and authors' own definitions of unfavourable pain outcome. While this allowed us to take an encompassing approach to the synthesis of existing studies, it was likely an important source of heterogeneity in the results. It should also be noted that unfavourable pain does not necessarily equate with failure or dissatisfaction.[11] Additionally, there were very few studies that provided multiple cut-off points for further analyses to elucidate the relationship between pain and satisfaction since the majority of studies only used a single post-operative VAS or NRS point. Additionally, it is also important to acknowledge that the included studies span over three decades, during which clinical practice and post-operative care may have evolved significantly. However, due to limited reporting and heterogeneity in study settings, designs, and data collection periods, we were unable to formally explore the impact of temporal changes on the outcomes. Despite these limitations, this review is the most comprehensive attempt to date to collate the existing evidence and provides useful estimates to direct future research and improvements to clinical care.

Chronic pain after total knee or hip replacement has a highly negative impact on people[23 41] to the extent that they may fear pursuing further healthcare and prescribed pain relief.[42] For people who would potentially benefit from further care, how they are identified, assessed and treated varies considerably between centres in the UK.[43] Cost implications for health services are considerable with numerous consultations, investigations and surgical referrals

required.[44] Chronic pain after joint replacement is an important research priority, as highlighted by the James Lind Alliance Priority Setting Partnership.[45-47] Acknowledging that an estimated 13-22% of people with TKR and a proportion of people with THR may experience chronic pain after surgery, implementation of evidence-based interventions aimed at the prevention and/or management of chronic pain after joint replacement are required.

Potential pre-operative risk factors for chronic pain after total knee or hip replacement have been studied extensively with the aim of developing interventions and targeting care to those at risk. In a recent systematic review with 54 studies identified, there was no suggestion in meta-analyses that age, sex and body mass index were associated with development of chronic pain after TKR.[48] For a range of further potential risk factors including pre-operative pain, evidence was limited with associations based on small numbers of studies or "vote counting" analysis due to lack of data and methodological heterogeneity. For people receiving THR, consistent associations have been identified between female sex, high pre-operative pain, poorer pre-operative function, and anxiety or depression.[49 50] Systematic reviews have identified that pre-operative pain catastrophizing, psychological distress, and symptoms of anxiety and/or depression are risk factors for long-term pain hip and knee replacement.[51-55] Post-operative risk factors for chronic pain have been studied in TKR and largely relate to length of hospital stay, mechanical complications of the prosthesis, surgical site infection, hospital readmission, reoperation or revision[56] and patients with chronic pain are likely to undergo revision at a later time period.[57] More generally, acute postoperative pain, caused by surgical methods and influenced by anaesthetic protocols, analgesia and care during the hospital admission, is also acknowledged as a risk factor for chronic postsurgical pain.[58 59]

There is a limited but growing body of evidence evaluating interventions that target risk factors for chronic pain after joint replacement[60-63]. Pre-operatively, general prehabilitation with exercise and education has not shown clear benefit for reduced long-term pain.[60 64 60 65-67] Another focus of efforts has been in removing delays to surgery to avoid possible decline in function and increase in pain while waiting for surgery. However, evidence of associations between longer waiting times for knee or hip replacement and chronic pain is equivocal.[68-70] In randomised trials evaluating interventions targeting psychological risk factors, cognitive behavioural therapy and pain coping skills programmes have not shown benefit for improved long-term pain.[61 71-76 77-79] However, a mindfulness-based stress-management intervention provided to patients before total hip or knee replacement surgery was associated with reduced long-term pain.[80] During the peri-operative period, the multimodal analgesia regimen provided may influence long-term pain outcomes and there is some support for

incorporation of specific treatments, some of which are features of current pain management practice.[62 81] After hospital discharge, care focuses mainly on physiotherapy-based rehabilitation but there is no evidence to support one modality over another in relation to prevention of chronic pain.[63] Exercise-based rehabilitation provided to people considered at risk of a poor outcome after TKR have shown little benefit for primary functional outcomes or long-term pain compared with usual care or less intensive interventions.[82 83]

Systematic reviews have identified a limited evidence-base to guide the treatment and management of chronic pain after joint replacement, and surgery more generally [84 85]. To address this, a programme of research has been conducted focussing on the development and evaluation of an early post-operative intervention to prevent pain chronicity.[33] Recognising the diverse causes of chronic pain, the Support and Treatment After Replacement (STAR) care pathway is a personalised and multifaceted intervention to reduce chronic pain after TKR.[86] The care pathway involves the assessment of people with high levels of pain at 2-3 months after surgery to identify the underlying causes of pain with subsequent provision of referrals for appropriate treatment or management. Evaluation in a randomised controlled trial found the STAR care pathway was cost-effective and associated with a clinically important reduction in pain after one year compared with usual care.[86] Furthermore, there is a suggestion of sustained benefit at up to four years.[87]

Conclusion

The problem of chronic pain after knee and hip replacement is recognised by people who have pain, clinicians and the research community. Our review, bringing together all the published literature to date, suggests that a substantial proportion of patients continue to experience an unfavourable longer-term pain outcome up to two years after surgery. These findings highlight the need to improve pain management across the care pathway. There is an urgent need for the implementation of evidence-based interventions to optimise the management of chronic pain after joint replacement and evaluation of new preventive strategies that target established risk factors after joint replacement.

Ethical approval

No individual level data are included in this manuscript. All data are aggregated data from published academic articles.

Data sharing

The statistical analysis plan and dataset can be available from the corresponding author on reasonable request.

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Author's contributions

AB, RGH, MW, and VW conceived the project. AB, VW, WB, and MAS screened studies and collected data for the review. HYC, AB, and VW drafted the manuscript. HYC conducted the analysis. AB and HYC contributed to the interpretation of the results. All authors (AB, MAS, MW, RGH, HYC, VW, and WB) discussed the results and contributed to the writing and editing of the manuscript.

VW is the guarantor.

Competing interests

All authors (AB, MAS, MW, RGH, HYC, VW, and WB) have completed the ICMJE uniform disclosure form and declare no competing interests.

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Table 1. Summary of TKR study characteristics

	Overall	3 months	6 months	12 months	24 months
Number of study cohorts	68	15	28	36	10
Total sample sizes	598,498	2503	550,928	36,157	13,953
Median sample size (IQR)	235 (113.5-580.75)	116 (95-184)	197 (111.25-297)	254.5 (115.5-593.75)	396.5 (251.75-692.75)
Baseline time period range	1993-2023	1998-2023	1993-2023	1993-2020	1993-2019
Mean age (SD)	69.6 (9.4) (n = 52*)	68.8 (9.2) (n = 13*)	69.6 (9.4) (n = 24*)	68.1 (9.1) (n = 26*)	70 (9.3) (n = 6*)
Age range	18-98 (n = 24)	18-90 (n = 7)	18-94 (n = 9)	25-98 (n = 14)	28-90 (n = 4)
Median % women (IQR)	63 (58-69.45)	66.1 (62.35-77.55)	65.55 (57.65-72.475)	61.2 (56.95-65.85)	63 (61.03-64.75)
Primary pain outcome reported					
VAS/NRS pain	29	9	16	13	2
WOMAC pain	13	1	4	7	3
OKS pain	7	1	2	5	1
KOOS pain	6	1	1	4	1
BPI	3	1	2	2	0
KSS/IKSS pain	2	0	0	2	1
EQ-5D 5L pain/discomfort	1	0	1	0	0
Pain disturbing sleep	1	1	0	1	0
Author own question	6	1	2	2	2
Setting					
Single hospital	39	8	16	20	9
Multiple hospitals	18	0	6	12	1
Multiple surgeons	4	3	1	1	0
Single surgeon	3	3	2	2	0
National registry	2	0	1	1	0
Health region	1	0	1	0	0
Rehabilitation service	1	1	1	0	0
Country					
Australia	2	0	1	1	1
USA	17	2	8	5	4
UK	9	2	3	7	2
Spain	5	2	3	2	0
Denmark	5	1	0	5	0
France	4	1	3	2	0
Sweden	3	0	0	2	1
China	3	1	1	0	1
Belgium	2	2	1	1	0

Canada	2	0	1	1	0
Finland	2	1	0	0	1
Japan	2	1	2	1	0
Singapore	2	0	2	1	0
South Korea	2	2	0	1	0
The Netherlands	2	0	1	2	0
Hungary	1	0	0	1	0
Italy	1	0	0	1	0
New Zealand	1	0	1	1	0
Norway	1	0	0	1	0
Poland	1	0	1	0	0
Russia	1	0	0	1	0

*only studies reported both mean and SD

Table 2. Worst-best case scenario analyses in TKR studies

Proportion* (%)	Median (95% CrI)	τ^2 (95% CrI)
3 month		
0%	21.89 (15.72 - 29.35)	0.5 (0.19 - 1.1)
10%	23.8 (17.38 - 30.4)	0.4 (0.14 - 0.88)
20%	25.61 (19.46 - 32.34)	0.36 (0.12 - 0.78)
30%	27.22 (21 - 33.69)	0.31 (0.11 - 0.69)
40%	28.82 (22.45 - 35.25)	0.3 (0.1 - 0.66)
50%	30.68 (24.49 - 37.25)	0.27 (0.09 - 0.6)
60%	32.07 (25.66 - 38.42)	0.27 (0.09 - 0.6)
70%	33.55 (26.73 - 40.21)	0.28 (0.09 - 0.63)
80%	35.04 (28.15 - 41.98)	0.28 (0.1 - 0.63)
90%	36.71 (29.5 - 43.83)	0.3 (0.11 - 0.68)
100%	38.16 (30.6 - 45.68)	0.31 (0.11 - 0.69)
6 month		
0%	14.06 (10.79 - 17.79)	0.51 (0.26 - 0.88)
10%	16.37 (13.08 - 19.88)	0.37 (0.18 - 0.65)
20%	18.54 (15.24 - 22.09)	0.32 (0.16 - 0.56)
30%	20.5 (17.05 - 24.25)	0.3 (0.15 - 0.53)
40%	22.33 (18.66 - 26.38)	0.3 (0.15 - 0.52)
50%	24.22 (19.94 - 28.43)	0.32 (0.16 - 0.56)
60%	26.03 (21.65 - 30.67)	0.35 (0.18 - 0.6)
70%	27.91 (22.96 - 33.03)	0.39 (0.21 - 0.67)
80%	29.61 (24.15 - 35.12)	0.44 (0.23 - 0.75)
90%	31.39 (25.38 - 37.35)	0.51 (0.27 - 0.87)
100%	33.36 (26.84 - 40.12)	0.58 (0.31 - 1)
12 month		
0%	12.61 (9.88 - 15.84)	0.61 (0.34 - 0.97)
10%	15.22 (12.29 - 18.23)	0.44 (0.25 - 0.72)
20%	17.44 (14.5 - 20.66)	0.37 (0.2 - 0.6)
30%	19.6 (16.46 - 22.97)	0.36 (0.19 - 0.58)
40%	21.6 (18.09 - 25.17)	0.36 (0.2 - 0.58)
50%	23.6 (19.86 - 27.46)	0.37 (0.2 - 0.6)
60%	25.64 (21.74 - 29.89)	0.4 (0.23 - 0.64)
70%	27.57 (23.28 - 32.21)	0.44 (0.25 - 0.7)
80%	29.57 (24.55 - 34.51)	0.49 (0.28 - 0.78)
90%	31.53 (26.01 - 36.95)	0.55 (0.3 - 0.87)
100%	33.62 (27.69 - 39.61)	0.62 (0.37 - 0.99)
24 month		
0%	14.63 (8.83 - 21.5)	0.52 (0.15 - 1.32)
10%	16.67 (10.85 - 23.36)	0.41 (0.13 - 1.07)
20%	18.45 (12.81 - 25.31)	0.35 (0.11 - 0.91)
30%	20.23 (14.19 - 27.13)	0.34 (0.11 - 0.88)
40%	21.89 (15.29 - 29.1)	0.34 (0.11 - 0.88)
50%	23.64 (16.62 - 31.45)	0.35 (0.11 - 0.91)
60%	25.28 (17.78 - 33.83)	0.38 (0.12 - 0.97)
70%	26.89 (18.57 - 35.67)	0.4 (0.12 - 1.02)
80%	28.58 (19.92 - 38.38)	0.43 (0.14 - 1.11)
90%	30.04 (20.59 - 40.22)	0.48 (0.15 - 1.22)
100%	31.76 (21.49 - 42.8)	0.52 (0.15 - 1.32)

*Proportion: The proportion of lost to follow-up patients imputed to experience unfavourable pain outcomes.

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Figure legends

Figure 1. Study selection flowchart.

Figure 2. Summary of risk of bias assessments in TKR studies. Each block represents one study. Red represents an overall high risk of bias in a study; yellow represents an overall moderate risk of bias.

Figure 3. Multivariate meta-analysis of proportions over time in TKR studies plot. Grey dots and lines represent reported proportions across studies and time, while dark dots and lines show the multivariate meta-analysis results. The size of grey dots is proportional to the log of inverse variance.

Figure 4. Forest plot of proportions over time in THR studies. Squares and bars represent the mean proportion of individual studies. Diamonds represent the point estimate and credible intervals of the meta-analysis results. The bars show the corresponding prediction intervals. Red circles and minus signs represent overall high risk of bias. Yellow circles and question marks represent overall moderate risk of bias. Abbreviations: RoB: Risk of Bias; RE: Random-effects; CrI: Credible intervals.

Supplementary materials

S1. PRISMA checklist
S2. Search strategy as applied in MEDLINE and Embase
S3. Characteristics of TKR studies
S4. Traffic light plot of the risk of bias assessment in TKR studies
S5. Forest plots of univariate meta-analyses in TKR studies
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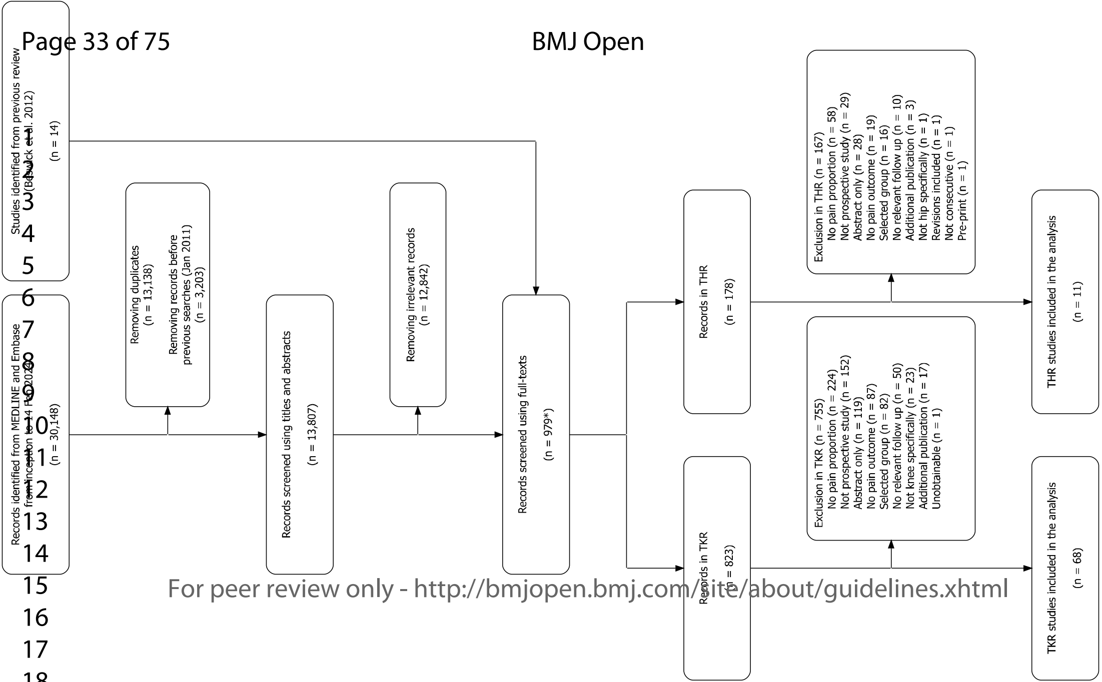
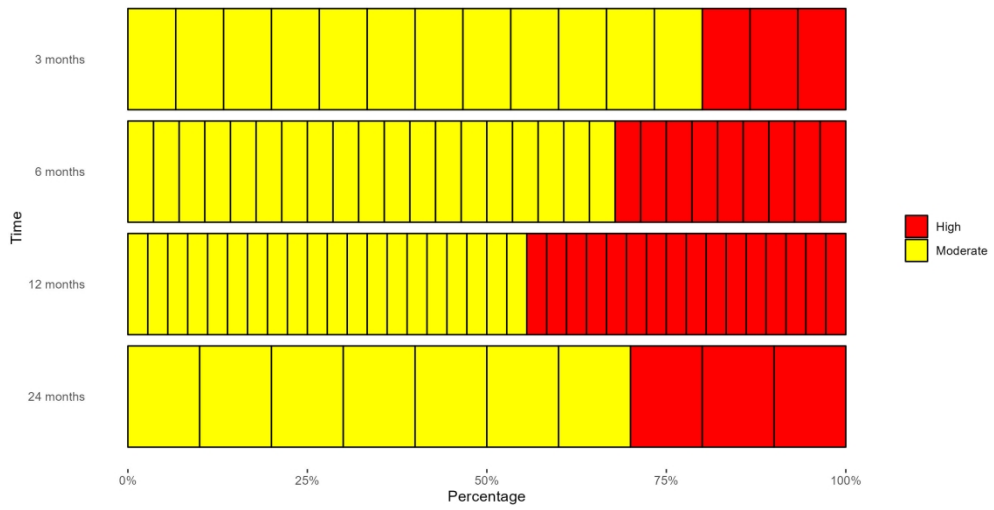
S7. Meta-regression analyses in TKR studies
S8. Subgroup analyses in TKR studies
S9. Doi plots and the LFK indexes in TKR studies
S10. Sensitivity analyses in TKR studies
S11. Characteristics of THR studies
S12. Traffic light plot of the risk of bias assessment in THR studies



*Twenty-two studies included both populations



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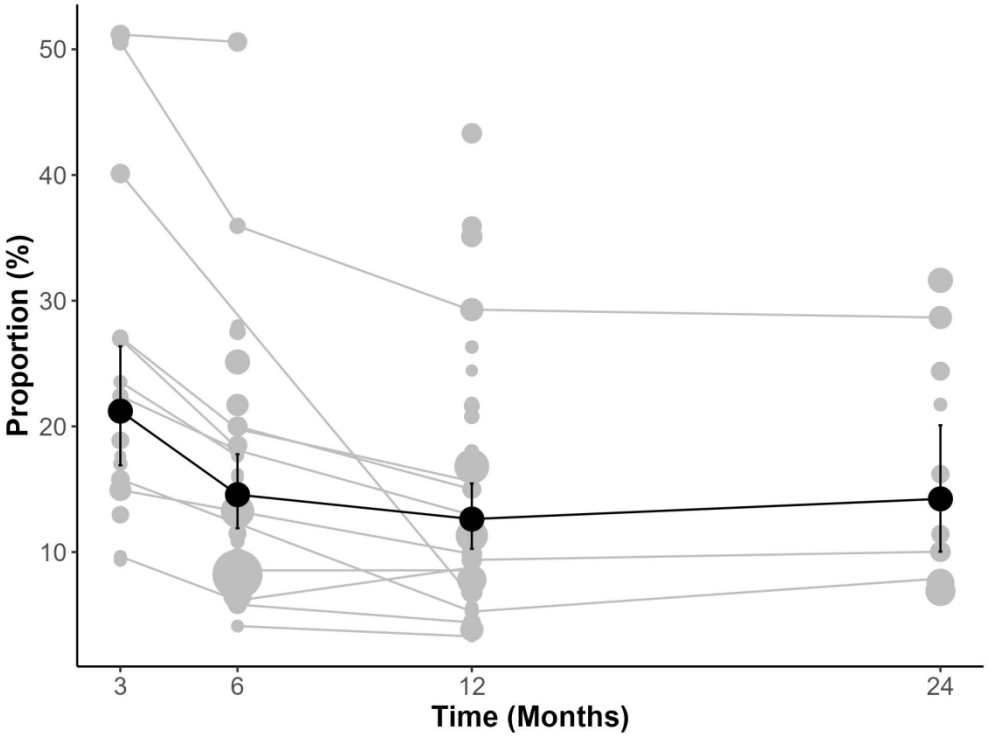

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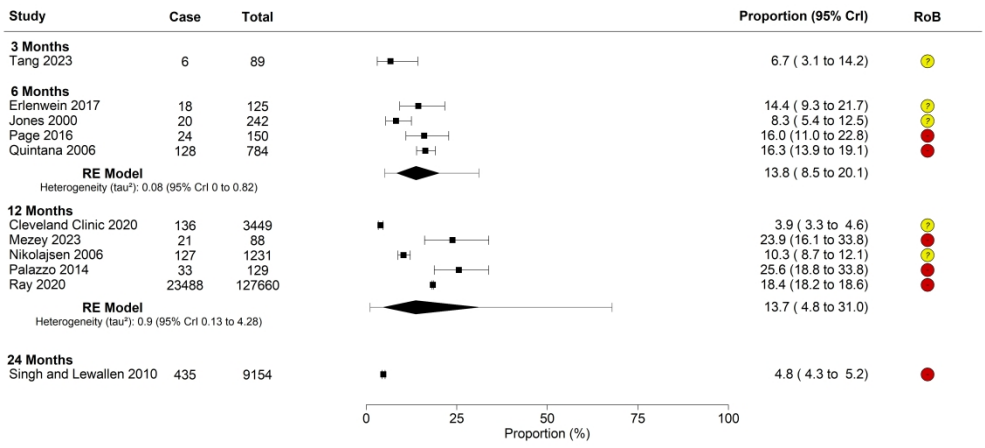

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Prevalence of chronic pain after total hip or knee replacement

Supplementary materials

Prevalence of chronic pain after total hip or knee replacement

Prevalence of chronic pain after total hip or knee replacement

S1. MOOSE checklist

Item No	Recommendation	Reported on Page Number	Reported on Section/Paragraph
Reporting of background			
1	Problem definition	Page 4	Introduction
2	Hypothesis statement	Page 4	Introduction
3	Description of Study Outcome(s)	Page 5	Outcome, Methods
4	Type of exposure or intervention used	Page 5	Eligibility Criteria, Methods
5	Type of study design used	Page 5	Eligibility Criteria, Methods
6	Study population	Page 5	Eligibility Criteria, Methods
Reporting on search strategy			
7	Qualifications of searchers (e.g., librarians and investigators)	Using existing search strategies	
8	Search strategy, including time period included in the synthesis and keywords		Supplementary S2
9	Effort to include all available studies, including contact with authors	Page 5-6	Searches, Methods
10	Databases and registries searched	Page 5	Searches, Methods
11	Search software used, name and version, including special features used (e.g., explosion)	Page 6	Study selection and data collection, Methods
12	Use of hand searching (e.g., reference lists of obtained articles)	Page 5	Searches, Methods
13	List of citations located and those excluded, including justification		Figure 1 (PRISMA flowchart)
14	Method for addressing articles published in languages other than English	Page 5	Searches, Methods
15	Method of handling abstracts and unpublished studies	Page 5	Searches, Methods
16	Description of any contact with authors	Page 5-6	Searches, Methods
Reporting of methods			
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested		Table 1
18	Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Page 6	Study selection and data collection, Methods

Prevalence of chronic pain after total hip or knee replacement

19	Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Page 6	Study selection and data collection, Methods
20	Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)		Tables 1, S3 and S11
21	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Page 6	Risk of bias assessment/ Methods
22	Assessment of heterogeneity	Page 7	Exploration of heterogeneity, Methods
23	Description of statistical methods (e.g., complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Page 6-7	Data synthesis approach, Methods
24	Provision of appropriate tables and graphics		Results
Reporting of results			
25	Graphic summarizing individual study estimates and overall estimate		Figures 3, 4, and S5
26	Table giving descriptive information for each study included		Tables S3 and S11
27	Results of sensitivity testing (e.g., subgroup analysis)		Tables S7, S8, and S10
28	Indication of statistical uncertainty of findings		Table 2 and S6
Reporting of discussion			
29	Quantitative assessment of bias (e.g., publication bias)		Figures S9
30	Justification for exclusion (e.g., exclusion of non–English-language citations)		Not applicable
31	Assessment of quality of included studies		Figures 2 and 4
Reporting of conclusions			
32	Consideration of alternative explanations for observed results		Conclusion
33	Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review)		Conclusion
34	Guidelines for future research		Conclusion
35	Disclosure of funding source		Sources of funding

From: Brooke BS, Schwartz TA, Pawlik TM. MOOSE Reporting Guidelines for Meta-analyses of Observational Studies. JAMA Surg. 2021;156(8):787–788. doi:10.1001/jamasurg.2021.0522

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S2. Search Strategy as applied in MEDLINE and Embase

S2.1 Total knee replacement

Medline

1. survey.mp. or exp Data Collection/
2. prospective study.mp. or exp Prospective Studies/
3. observational study.mp.
4. exp EPIDEMIOLOGY/ or epidemiology.mp.
5. longitudinal study.mp. or exp Longitudinal Studies/
6. follow up study.mp. or exp Follow-Up Studies/
7. exp Arthroplasty, Replacement, Knee/ or exp Knee Prosthesis/ or knee replacement.mp.
8. knee prosthesis.mp. or exp Knee Prosthesis/
9. total knee.tw.
10. (knee adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti, ab.
11. 7 or 8 or 9 or 10
12. pain.tw.
13. 1 or 2 or 3 or 4 or 5 or 6
14. 10 and 12 and 13

Embase

1. Clinical study/
2. Longitudinal study/
3. Prospective study/
4. Cohort analysis/
5. (Cohort adj (study or studies)).mp.
6. (follow up adj (study or studies)).tw.
7. (observational adj (study or studies)).tw.
8. (epidemiologic$ adj (study or studies)).tw.
9. exp Arthroplasty, Replacement, Knee/ or exp Knee Prosthesis/ or knee replacement.mp.
10. knee prosthesis.mp. or exp Knee Prosthesis/
11. total knee.tw.
12. (knee adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti,ab.
13. pain.tw.
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
15. 9 or 10 or 11 or 12
16. 13 and 14 and 15

S2.2 Total hip replacement

Medline

1. survey.mp. or exp Data Collection/
2. prospective study.mp. or exp Prospective Studies/
3. observational study.mp.
4. exp EPIDEMIOLOGY/ or epidemiology.mp.
5. longitudinal study.mp. or exp Longitudinal Studies/
6. follow up study.mp. or exp Follow-Up Studies/
7. exp Arthroplasty, Replacement, Hip/ or exp Hip Prosthesis/ or hip replacement.mp.
8. hip prosthesis.mp. or exp hip Prosthesis/
9. total hip.tw.
10. (hip adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti, ab.

Prevalence of chronic pain after total hip or knee replacement

11. 7 or 8 or 9 or 10
12. pain.tw.
13. 1 or 2 or 3 or 4 or 5 or 6
14. 10 and 12 and 13

Embase

1. Clinical study/
2. Longitudinal study/
3. Prospective study/
4. Cohort analysis/
5. (Cohort adj (study or studies)).mp.
6. (follow up adj (study or studies)).tw.
7. (observational adj (study or studies)).tw.
8. (epidemiologic$ adj (study or studies)).tw.
9. exp Arthroplasty, Replacement, hip/ or exp hip Prosthesis/ or hip replacement.mp.
10. hip prosthesis.mp. or exp hip Prosthesis/
11. total hip.tw.
12. (hip adj10 (replace$ or arthroplast$ or prosthe$ or implant$)).ti,ab.
13. pain.tw.
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
15. 9 or 10 or 11 or 12
16. 13 and 14 and 15

Prevalence of chronic pain after total hip or knee replacement

S3. Characteristics of TKR studies

Study Country Recruitment dates Setting	Operation Number of patients Age (SD), range % women	Pain measure	Definition of unfavourable pain outcome High risk of bias concern
Alzahrani 2011[1] TWH cohort Canada 1998-2007 2 hospitals	Primary TKR, all 18+ N=482 67.5 (9.6) 62%	WOMAC pain 12 months	No clinically important improvement based on MCID (WOMAC index of 7.5)
Aso 2020[2] Japan 2012-2017 1 hospital	Primary TKR, all N=234 75 75.8%	VAS/NRS pain 6, 12 months	Moderate to severe pain (VAS >30 mm), at rest or walking
Attal 2014[3] France 2008-2011 I hospital	Primary TKR, all 18+ N=89 68.7 (8.9) 65.0%	BPI (NRS) 3, 6, 12 months	NRS pain average 3 or greater on 10-point scale
Baker 2007[4] UK 2003 National registry	Primary TKR, all N=9417 70.68 56.8%	OKS pain 12 months	Reported persistent knee pain
Bell 2023[5] USA 2015-2018 7 hospitals	Primary TKR, all 50-89 N=5564 Range 50-89 60.7%	KOOS pain 12 months	MCID not satisfied (15 points)
Birch 2019[6] Denmark 2011-2013 1 hospital	Primary TKR or UKR, all N=589 67.3 (9.7) 52.0%	OKS pain 4, 12 months	OKS pain moderate/severe High loss to follow up rate at 4 and 12 months
Brander 2003[7] USA 1998-2000 1 surgeon	Primary TKR, all 18+ N=116 66 (10.5), range 36-85 55.2%	VAS/NRS pain 3, 6, 12 months	VAS >40
Buus 2022[8] Denmark 2015-2016 1 hospital	Primary TKR, all 18+ N=217 66.8 (9.3) 52.2%	OKS pain 12 months	Threshold 42.39[69]
Buvanendran 2019[9] USA 2011-2017 1 hospital	Primary TKR, all N=296 65 65.3%	VAS/NRS pain 6 months	NRS pain with movement ≥4

Prevalence of chronic pain after total hip or knee replacement

Chodor and Kruczynski 2022[10] Poland 2016 1 hospital	Primary TKR, all 48+ N=69 67.6 (7.42), range 48-84 76.7%	Author own question 6 months	Pain severely limiting daily life
Clement 2014[11] UK 2010 1 hospital	Primary TKR, all N=578 70 (9.6), range 39-91 58.4%	Author's own question "How well did the surgery relieve pain in your affected joint?" 12 months	Fair or poor High loss to follow up rate
Cole 2022[12] UK 2010-2015 2 hospitals	Primary TKR, all N=1025 70 55.8%	OKS pain 12 months	<14 points OKS
Dave 2017[13] USA 2012-2014 3 hospitals	Primary TKR probably, all 40+ N=267 66 (9) 61.0%	WOMAC pain 12 months	WOMAC pain score < MCID (WOMAC pain of 15)
Dowsey 2012[14] Australia 2006-2007 1 hospital	Primary TKR, all N=478 70.8 (8.3), range 45-90 69.2%	IKSS pain 12, 24 months	IKSS pain score <30 moderate to severe pain IKSS may not be entirely patient reported at 12 and 24 months
Dursteler 2021[15] Spain 2014-2017 Spain 1 hospital	Primary TKR, all 18+ N=170 73.1 (7.1) 73.3%	VAS/NRS pain 3, 6 months	NRS 0.3/1 or greater at rest
Edwards 2022[16] USA 2012-2018 2 hospitals	Primary TKR, all 45+ N=248 65.1 (8.2) 59.5%	BPI 6 months	4/10 or greater High loss to follow up rate
Escobar and Riddle 2014[17] Spain 2003-2006 15 hospitals	Primary TKR, all N=1616 71.6 (6.8) 70.0%	WOMAC pain 12 months	Number not attaining PASS (i.e. "No" in the question, "*If you had to be the rest of your life with the symptoms you have now, how would you feel?*") as the twenty-fifth percentile of the final score at 1 year instead of the seventy-fifth percentile (reverse option for WOMAC scores). High loss to follow up rate
Getachew 2021[18]	Primary TKR, all 18+	BPI	BPI worst pain score ≥4

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Norway 2012-2014 1 hospital	N=206 68 (9) 66.0%	12 months	
Ghomrawi 2017[19] USA 2010-2012 1 hospital	Primary TKR, all N=247 68 (10) 65.0%	WOMAC pain 24 months	Number not achieving MCID (baseline-adjusted MCIDs, as described by Escobar et al.[70])
Grosu 2016[20] Belgium 2009-2010 1 surgeon	Primary TKR probably, all N=114 66 (10) 65.8%	VAS/NRS pain 3, 6, 12 months	Moderate to severe pain High loss to follow up rate at 3, 6 and 12 months
Hardy 2022[21] France 2014-2015 1 hospital	Primary TKR, all >18 N=111 73.3 (9.3) range 29-92 65.0%	VAS/NRS pain 12 months	VAS >30/100
Heath 2021[22] Australia 2018-2020 44 hospitals	Primary and revision TKR, all N=8299 67.5 (8.8) 56.4%	EQ-5D 5L pain/ discomfort 6 months	Moderate/ severe or extreme pain EQ 5D 5L pain/discomfort High loss to follow up rate
Jones 2000[23] Canada 1995-1997 1 health region	Primary TKR, all 40+ N=292 69.2 (9.2) 59.0%	WOMAC pain 6 months	Moderate/ severe pain defined as a gain of <10 points on the WOMAC pain dimension
Khalid 2021[24] UK 2008-2016 National registry	Primary TKR or UKR, all N=531,790 69.7 (9.4) 56.6%	OKS pain 6 months	OKS-pain score of 14 or less at six months after knee replacement can be considered to be in chronic pain
Kim 2015[25] South Korea 2013-2014 1 hospital	Primary TKR, all women N=94 70.18 (5.74), range 20-80 100%	VAS/NRS pain 3 months	>5 points on an 11 point VAS/NRS (verbal numeric rating scale)
Kiran 2015[26] UK 2003-2007 1 hospital	Primary TKR, all N=608 72 61.4%	OKS pain 12, 24 months	Has your knee replacement operation decreased your knee pain? High loss to follow up rate at 12 and 24 months
Kornilov 2018[27] Russia 2014 1 hospital	Primary TKR, all 18+ N=100 63 (8), range 47-81 95.0%	VAS/NRS pain 12 months	Not at least a two-point or approximately 30% (clinically significant) decrease in rating of pain interference with walking from baseline to 1 year (NRS scale 0-10)
Kurien 2018[28] UK Before 2017	Primary TKR probably, all N=50	VAS/NRS pain 6 months	4 or greater

Prevalence of chronic pain after total hip or knee replacement

1 hospital	66.4 (8.3) 60.0%		
Larsen 2021[29] Denmark 2015-2016 1 hospital	Primary TKR, all 18+ N=185 68.8 (8.9) 55.7%	VAS/NRS pain 12 months	Pain intensity at rest >3 High loss to follow up rate
Latijnhouwers 2022[30] The Netherlands 2012-2017 2 hospitals	Primary TKR, all N=282 66 (8.4) 63.0%	VAS/NRS pain 12 months	Moderate to severe pain (NRS ≥4) High loss to follow up rate
Lavand'homme 2014[31] Belgium 2012 1 surgeon	Primary TKR or UKR, all N=128 68 (10) 66.4%	VAS/NRS pain 3 months	NRS ≥4/10
Lee 2022[32] South Korea 2017-2019 2 surgeons	Primary TKR probably, all N=172 70.7 (4.3) 89.2%	Pain disturbing sleep 3, 12 months	Night pain was defined as pain around the knee experienced at night that could disturb the patient's sleep
Leppanen 2021[33] Finland 2012-2014 1 hospital	Primary TKR, 65 years or younger N=205 60 63.0%	VAS pain exercise 24 months	VAS >30
Leung 2019[34] Singapore 2015 1 hospital	Primary TKR, all N=243 66 (8.3) 78.6%	Author own question 6, 12 months	No change or worsening pain/ slightly better
Lundblad 2008[35] Sweden Before 2006 1 hospital	Primary TKR, all N=69 68 50.7%	VAS/NRS pain 24 months	Pain at rest, VAS >2/10
Lyman 2018[36] USA 2007-2012 1 hospital	Primary TKR, all N=3815 74 (6) 63.0%	KOOS pain 24 months	Number not achieving MCID (8 by distribution-based method [71]) High loss to follow up rate
Mahdi 2020[37] Sweden 2016-2018 3 hospitals	Primary TKR, all N=615 69.7 52.2%	KOOS pain 12 months	8 cut off High loss to follow up rate
Mekkawy 2023[38] USA 2021 4 surgeons	Primary TKR, all N=112 65.5 (9.2) 69.0%	VAS pain 6 months	Probably NRS score of ≥1 in defined sites Concern over VAS ≥1 being too inclusive and high loss to follow up rate

Prevalence of chronic pain after total hip or knee replacement

Mercurio 2020[39] Italy 2015-2017 1 hospital	Primary TKR, all >18 N=45 69.6 (7.8) 65.0%	VAS/NRS pain 12 months	VAS >30 residual pain
Mezey 2023[40] Hungary 2019-2020 2 hospitals	Primary TKR probably, all N=101 69.2 Not reported	WOMAC pain 12 months	Not exceeding MCID (WOMAC pain of 13.3) High loss to follow up rate
Musbahi 2023[41] USA 2011-2014 4 hospitals	Primary TKR, all 40+ N=575 66.3 (8.3) 60%	WOMAC pain 12 months	WOMAC pain score (converted to a 0-to-100 scale) improvement of <20 High loss to follow up rate
Nishimoto 2023[42] Japan 2021-2023 1 hospital	Primary TKR, all with no complications N=68 75.1 (7.3) 80.9%	KOOS pain 3, 6 months	Not achieving MCID of 10 (3 months) and 13 (6 months). MCID was calculated using the anchor method.[72]
Noiseux 2014[43] USA Before 2012 2 hospitals	Primary TKR, all 30+ N=215 61.7 (9.8) 58.0%	VAS/NRS pain 6 months	Moderate or severe pain with range of motion, VAS ≥1 Concern over VAS ≥1 being too inclusive
Orr 2022[44] USA 2016-2019 9 hospitals	Primary TKR, all N=7476 67 (9.0) 60.8%	KOOS pain 12 months	Not achieved PASS (i.e. "No" in the question, "*Taking into account all the activity you have during your daily life, your level of pain and also your activity limitations and participation restrictions, do you onsider the current state of your knee satisfactory?*") for KOOS pain High loss to follow up rate
Petersen 2015[45] Denmark Before 2014 1 hospital probably	Primary TKR, all N=78 69 59.0%	VAS/NRS pain 12 months	VAS >3 High loss to follow up rate
Petersen 2018[46] Denmark Before 2017 1 hospital	Primary TKR probably, all N= 200 69 (1.2) 57.0%	VAS/NRS pain 12 months	<30% reduction in pain
Phillips 2014[47] UK 2009-2010 1 hospital	Primary TKR, all N= 96 70.6 56.0%	VAS/NRS pain 3, 6, 12 months	VAS >3

Prevalence of chronic pain after total hip or knee replacement

Priol 2023[48] France 2011-2012 1 hospital	Primary TKR, all N=129 74 (10), range 45-94 72.3%	VAS/NRS pain 6 months	VAS 4+ High loss to follow up rate
Pua 2019[49] Singapore 2013-2017 1 hospital	Primary TKR, all 50+ N=5325 68 (7.5) 75.0%	OKS pain 6 months	Moderate or severe pain
Quintana 2006[50] Spain 1999-2000 7 hospitals	Primary TKR, all N=792 71.9 73.0%	WOMAC pain 6 months	No improvement in pain greater than MCID (22.60 of 100) using an anchor-based method.
Rice 2018[51] New Zealand 2012-2015 3 hospitals	Primary TKR, all 18+ N=300 69 (10), range 48-90 48.0%	VAS/NRS pain 6, 12 months	VAS >3
Sideris 2022[52] USA 2016-2018 1 hospital	Primary TKR, all N=179 67.1 (8.1) 56.2%	VAS/NRS pain 6 months	NRS 4+
Singh 2014[53] USA 1993-2005 1 hospital	Primary TKR, all N=7229 68 (10) 56.0%	Author own question 24 months	Moderate-severe pain
Solberg 2023[54] USA 2020 22 surgeons	Primary TKR probably, all N=239 66.2 (8.5), range 37-87 60.7%	Author own question 3 months	To what extent have you obtained relief: somewhat, minimal or not at all High loss to follow up rate
Stephens 2002[55] USA Before 2001 1 hospital	Primary TKR, all 50+ N=68 67.4 (8.1), range 50-88 54.0%	WOMAC pain 6 months	No change or increase in pain from pre-operative
Tang 2023[56] China 2020-2021 1 hospital	Primary TKR probably, all 65+ N=196 72 75.1%	VAS/NRS pain 3 months	NRS scores ≥4
Terradas-Monllor 2024[57] Spain 2018-2020 1 home rehabilitation service	Primary TKR or UKR, all 18+ N=115 70.5 (10.7) 66.1%	VAS/NRS pain 3, 6 months	VAS 3+
Thomazeau 2016[58] France 2013 1 hospital	Primary TKR, all N=109 69.2 (9) 71.6%	VAS/NRS pain 6 months	NRS score ≥1/10 for the last 8 days

Prevalence of chronic pain after total hip or knee replacement

Tian 2022[59] China 2018-2019 1 hospital	Primary TKR or UKR, all <90 N=271 Not reported 80.8%	Author own question 24 months	Moderate or severe pain on movement
Utrillas-Compaired 2014[60] Spain 2009 1 hospital	Primary TKR, all N=215 73 (6.35) 69.3%	KSS pain 12 months	KSS pain poor (less than 60 points) KSS may not be entirely patient reported
van der Wees 2017[61] The Netherlands 1993-2014 1 hospital	Primary TKR, all N=704 65 (12) 64.5%	VAS/NRS pain 6, 12 months	30% or less improvement in VAS pain High loss to follow up rate at 6 and 12 months
Vina 2020[62] USA 2005-2015 4 hospitals	Primary TKR, all N=315 67.3 (8.6) 60.9%	WOMAC pain 24 months	Less than MCID of 1.5
Vuorenmaa 2008[63] Finland Before 2007 2 surgeons	Primary TKR, all <80 N=51 70 (5) 80%	VAS/NRS pain 3 months	VAS >30/100
W-Dahl 2014[64] Sweden 2008-2010 2 hospitals	Primary TKR, all N=2736 69.3 (8.7) 58.5%	KOOS pain 12 months	Unchanged or worse pain
Waimann 2014[65] USA 2004-2007 2 hospitals	Primary TKR, all N=236 65.1 (8.9) 66.0%	WOMAC pain 6 months	Less than MCID of ≥20 in both the WOMAC pain and function scores (scaled to 100)
Wylde 2013[66] UK 2010-2011 1 hospital	Primary TKR, all N=57 68 58%	WOMAC pain 12 months	WOMAC pain score of >75
Wylde 2019[67] UK 2006-2009 1 hospital	Primary TKR, all eligible for Triathlon prosthesis N=266 70 (9.9), range 41-90 64%	WOMAC pain 3, 12, 24 months	Worse or no change in WOMAC pain of 14 point (based on MCID) High loss to follow up rate
Yan 2023[68] China 2021-2023 1 hospital	Primary TKR, all 45+ N=470 63.4 (7.4) 69.9%	VAS/NRS pain 6 months	NRS score of ≥1 at rest and/or on movement Concern over VAS ≥1 being too inclusive

*Abbreviations: PASS (Patient Acceptable Symptom State), MCID (Minimal Clinically Important Difference)

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S3.1 Mean age and range

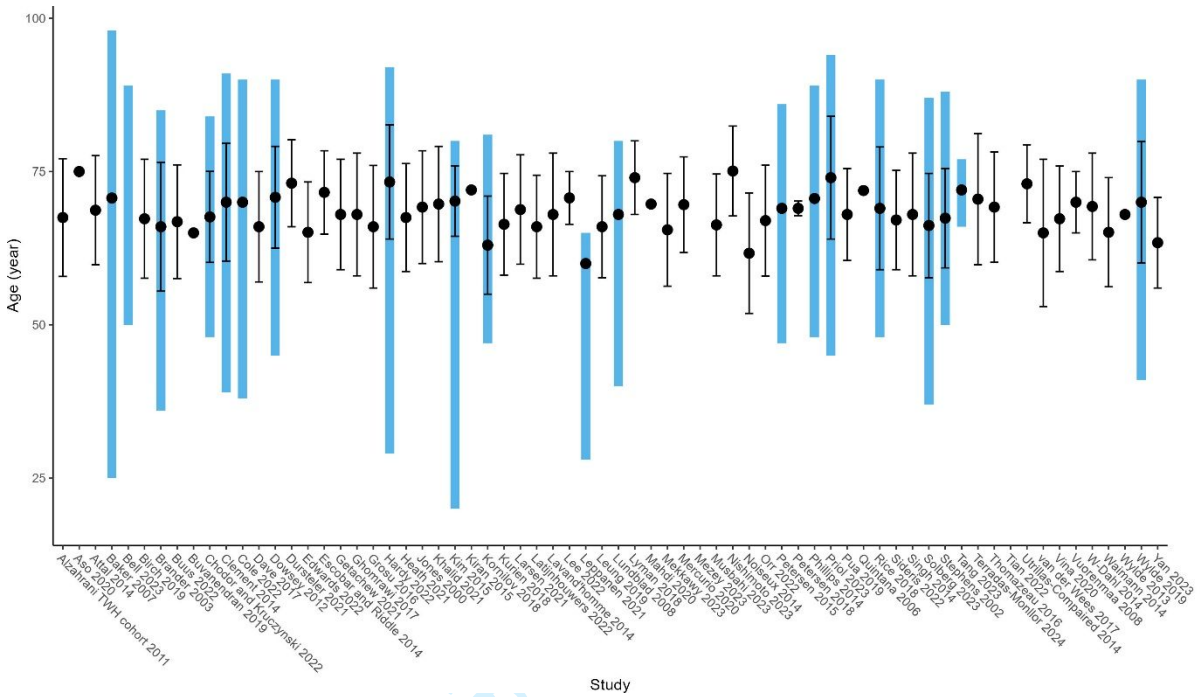

Figure S3.1. Mean age and their standard deviations reported in the individual studies. Range of age was plotted as blue bars.

S3.2 Proportion of females

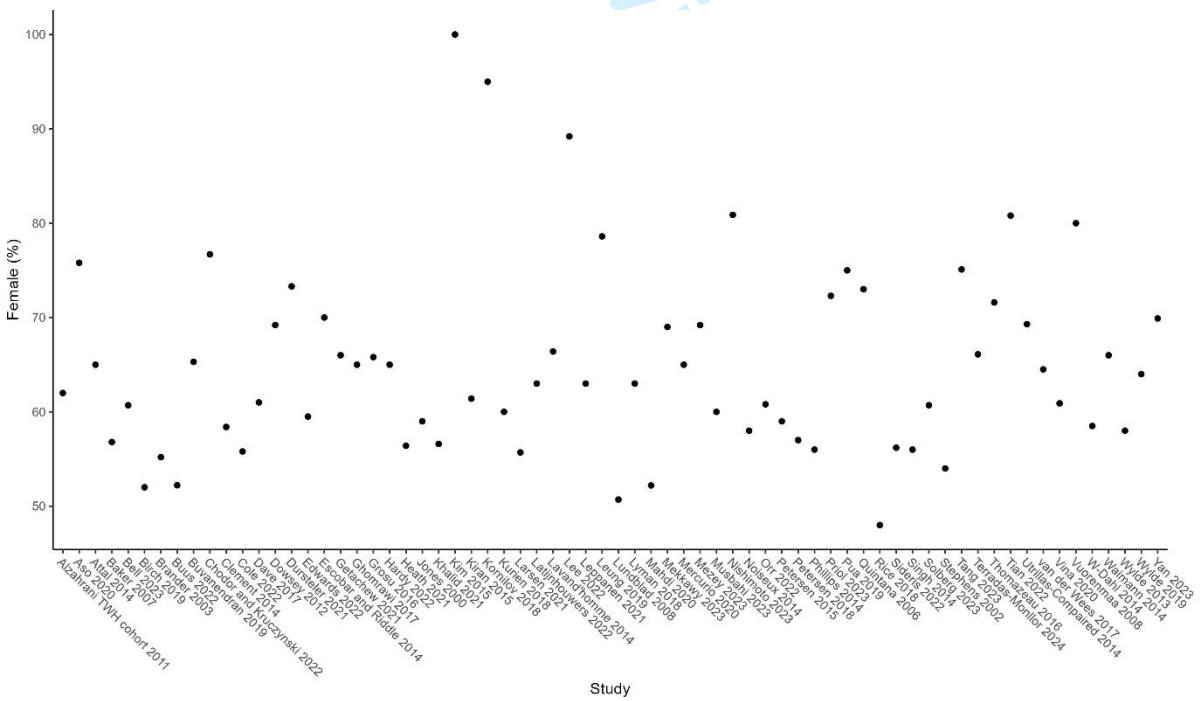

Figure S3.2. Proportion of females reported in the individual studies

S3.3 Data collection timeframe

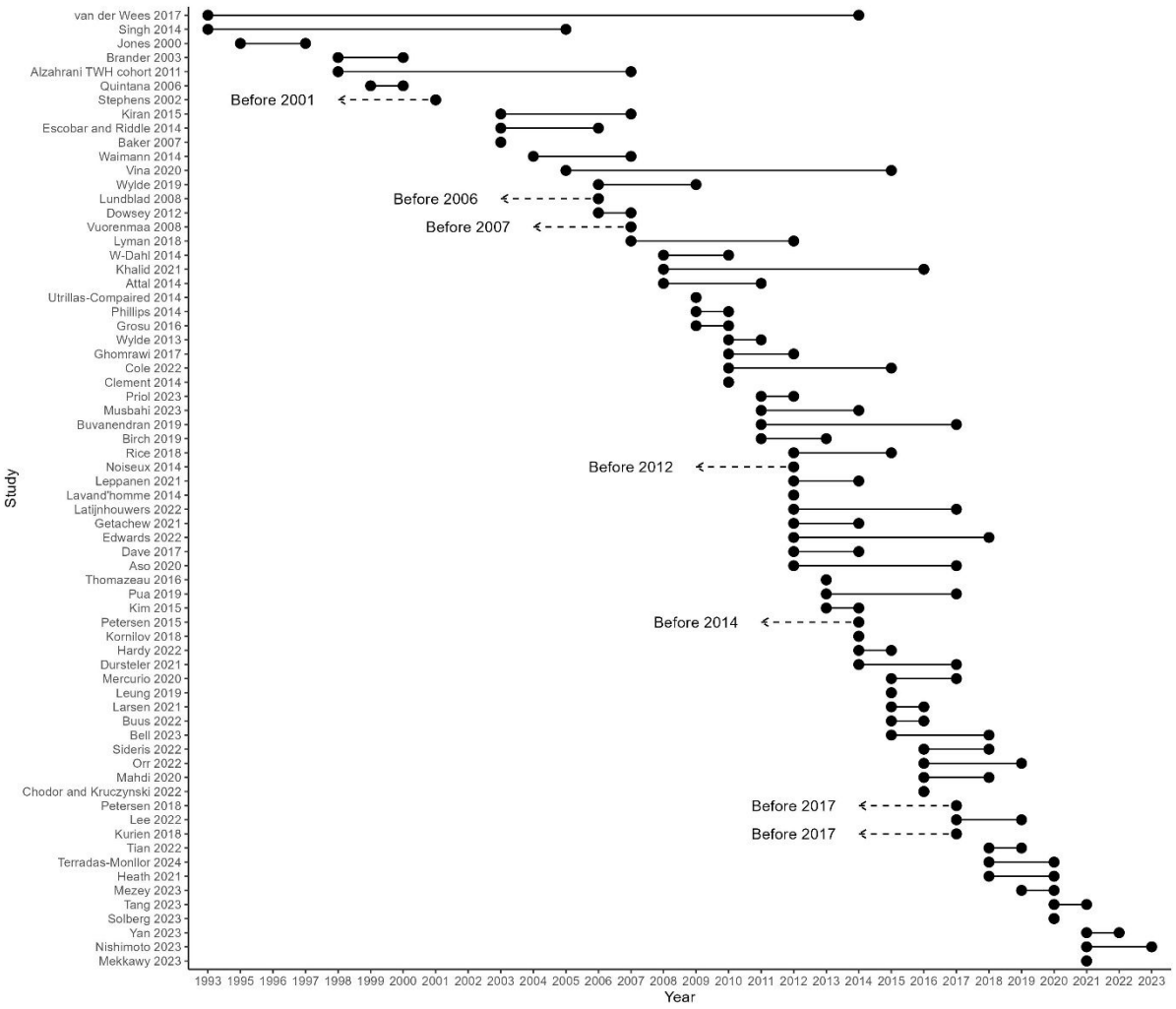

Figure S3.3. Data collection timeframe in the individual studies.

S3.4 Proportions of lost to follow-ups and revisions

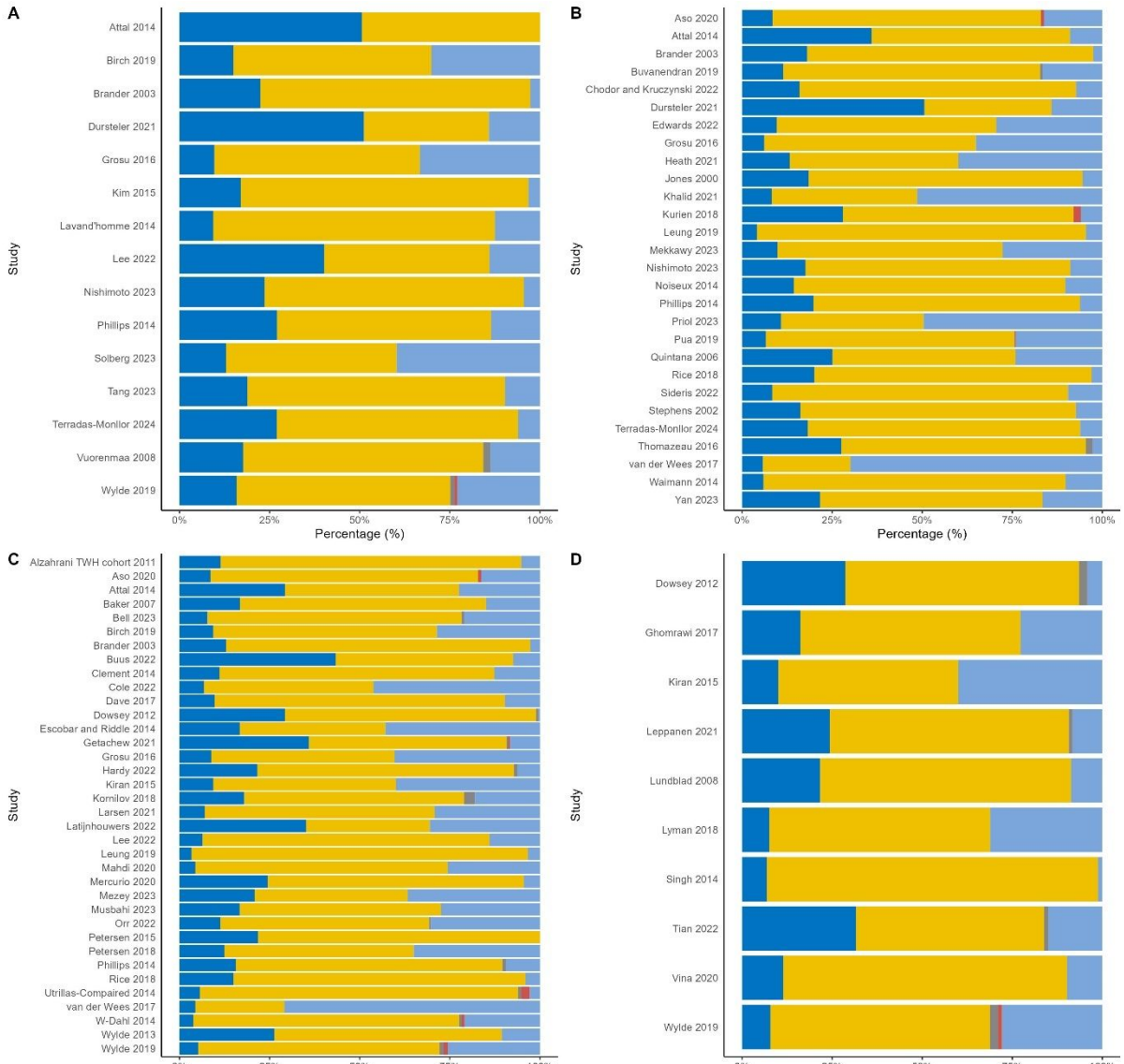

Figure S3.4. Favourable and unfavourable pain outcomes and reasons of missing data reported in 3, 6, 12, and 24 months (represented in sub-plots A, B, C, and D, respectively) in TKR studies.

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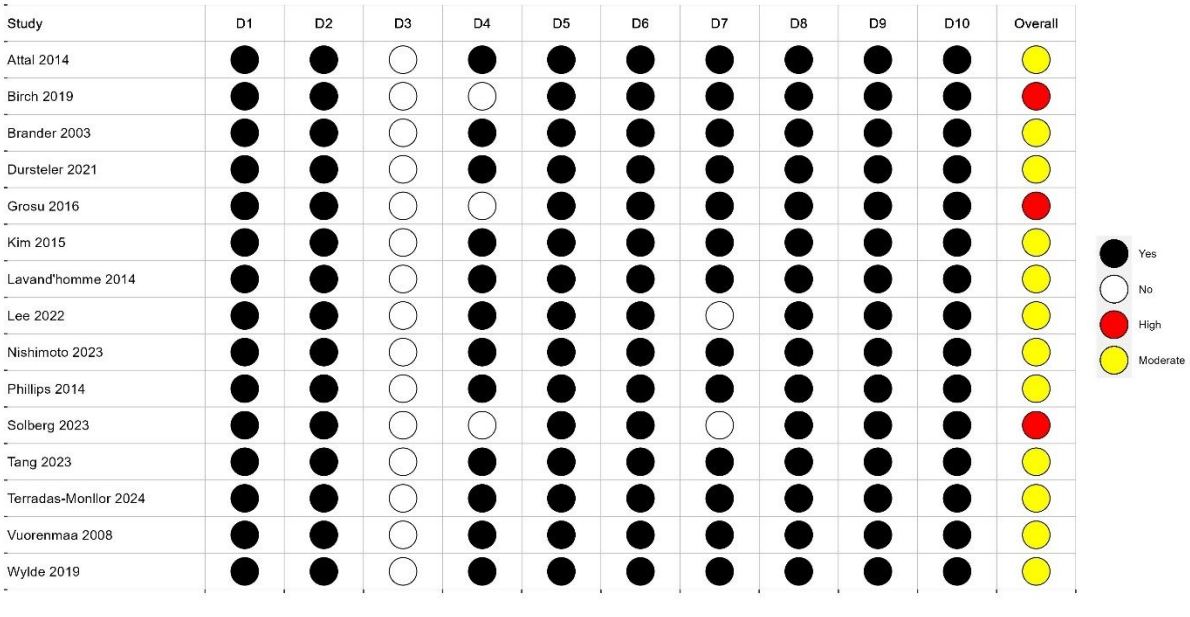
S4. Traffic light plot of the risk of bias assessments in TKR studies

The corresponding domains in the figures are:

- D1: Was the study's target population a close representation of the national population in relation to relevant variables?
- D2: Was the sampling frame a true or close representation of the target population?
- D3: Was some form of random selection used to select the sample, OR was a census undertaken?
- D4: Was the likelihood of nonresponse bias minimal?
- D5: Were data collected directly from the subjects (as opposed to a proxy)?
- D6: Was an acceptable case definition used in the study?
- D7: Was the study instrument that measured the parameter of interest shown to have validity and reliability?
- D8: Was the same mode of data collection used for all subjects?
- D9: Was the length of the shortest prevalence period for the parameter of interest appropriate?
- D10: Were the numerator(s) and denominator(s) for the parameter of interest appropriate?

S4.1 TKR studies (3 months)



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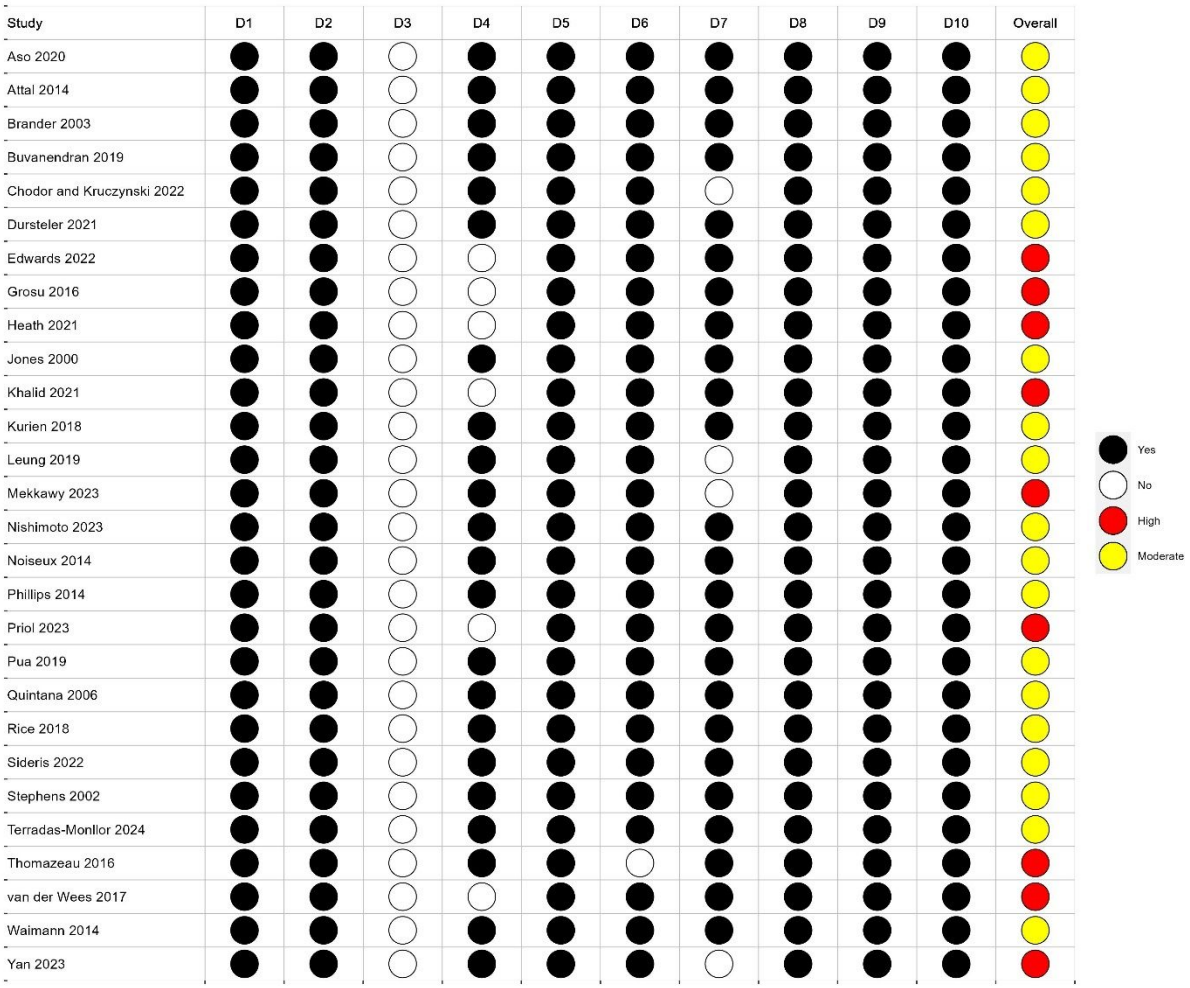
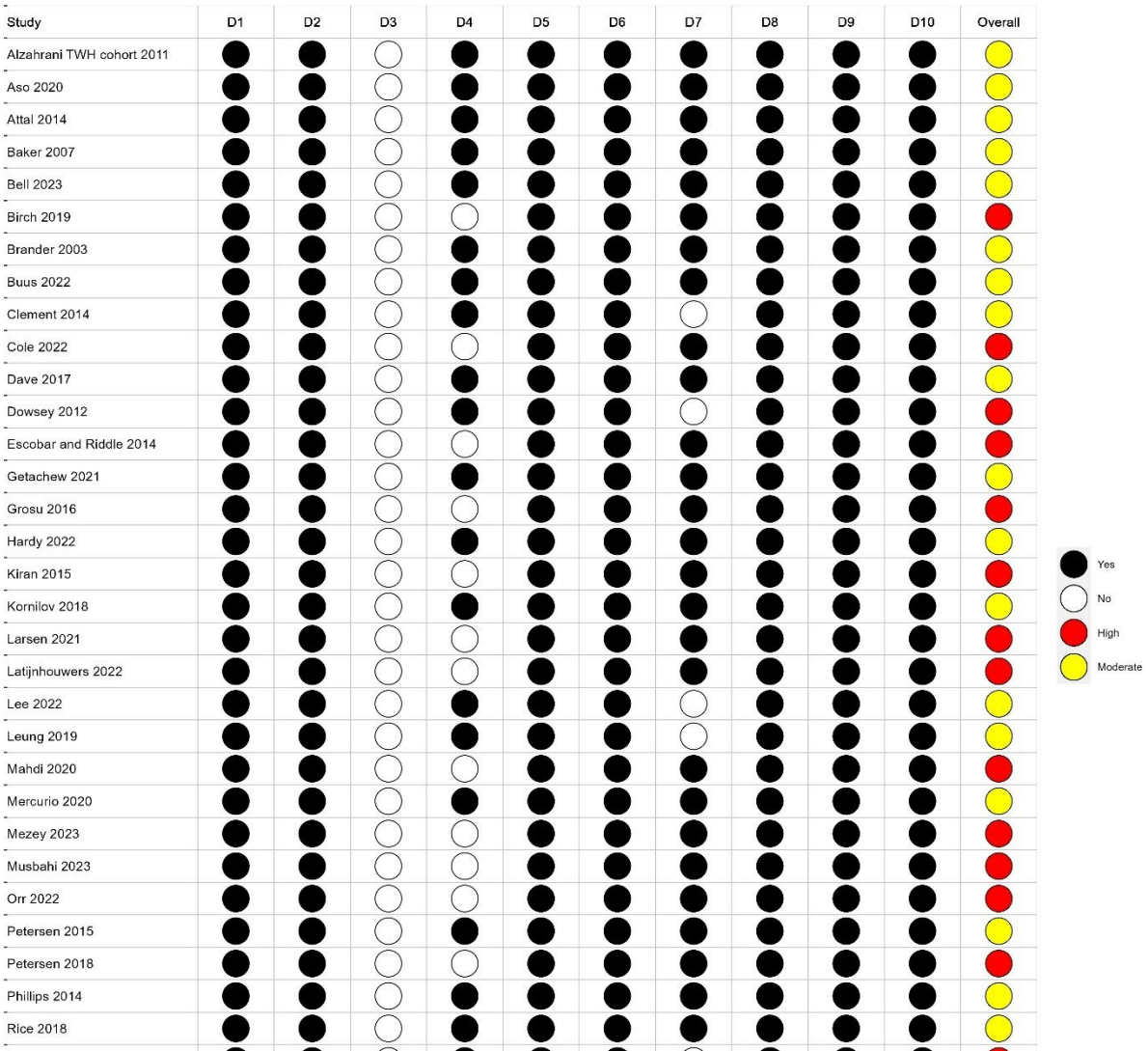
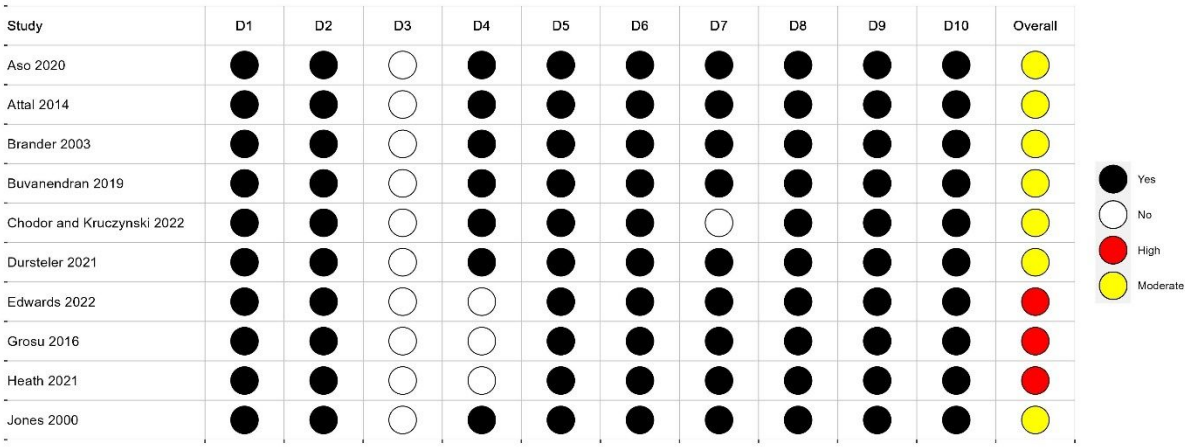
S4.2 TKR studies (6 months)



S4.3 TKR studies (12 months)



S4.4 TKR studies (24 months)



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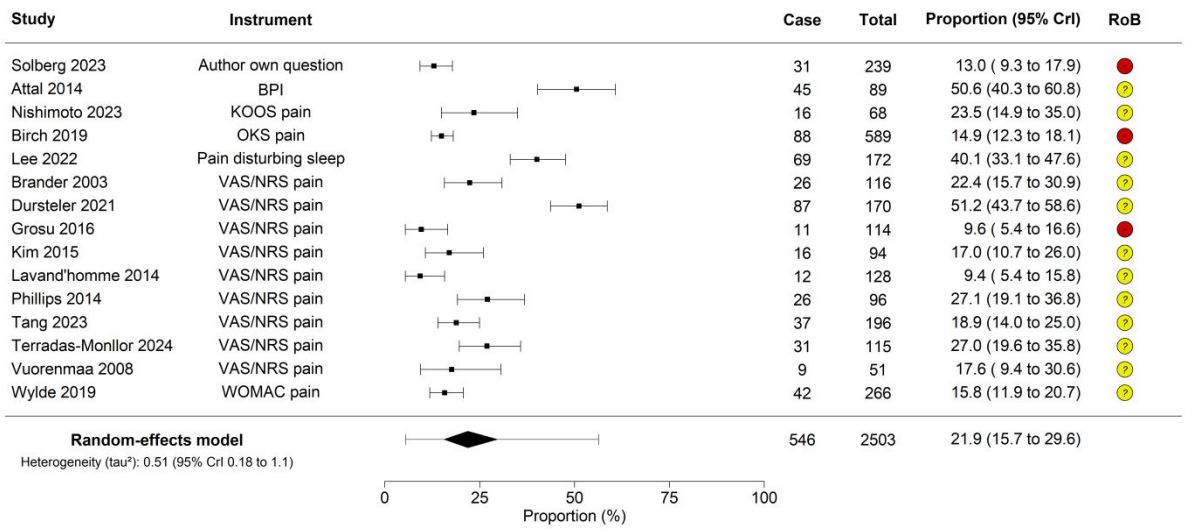
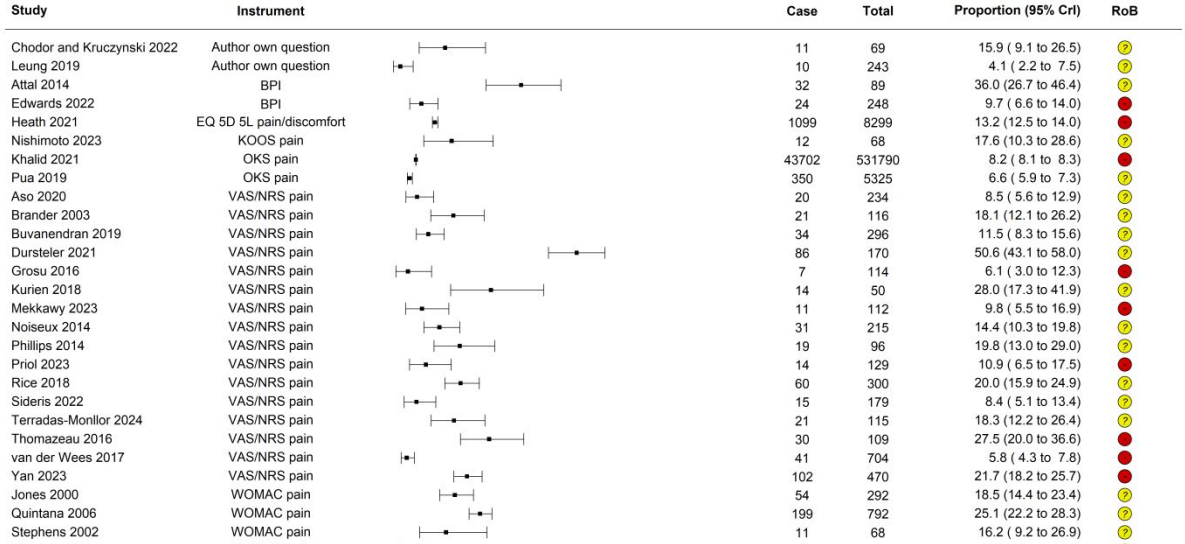
S5. Forest plots of univariate meta-analyses in TKR studies

S5.1 TKR studies (3 months)



S5.2 TKR studies (6 months)



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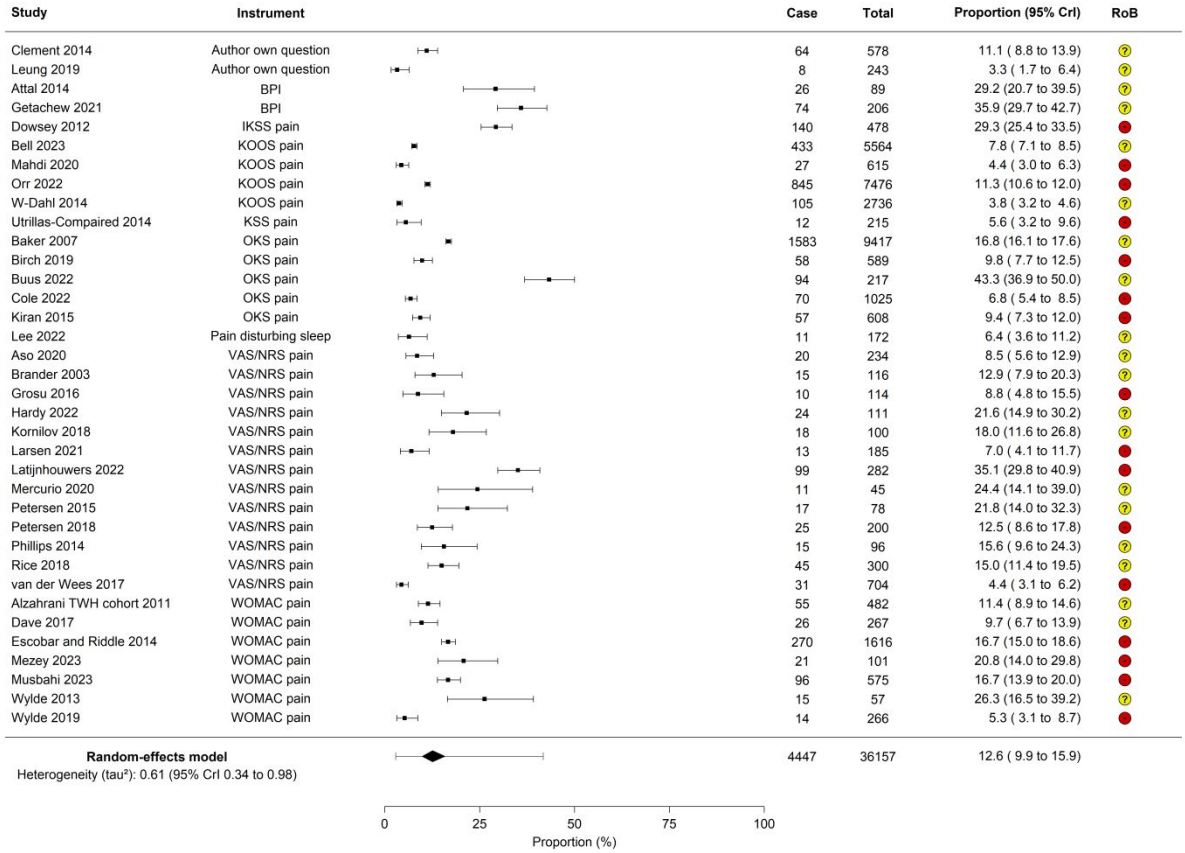
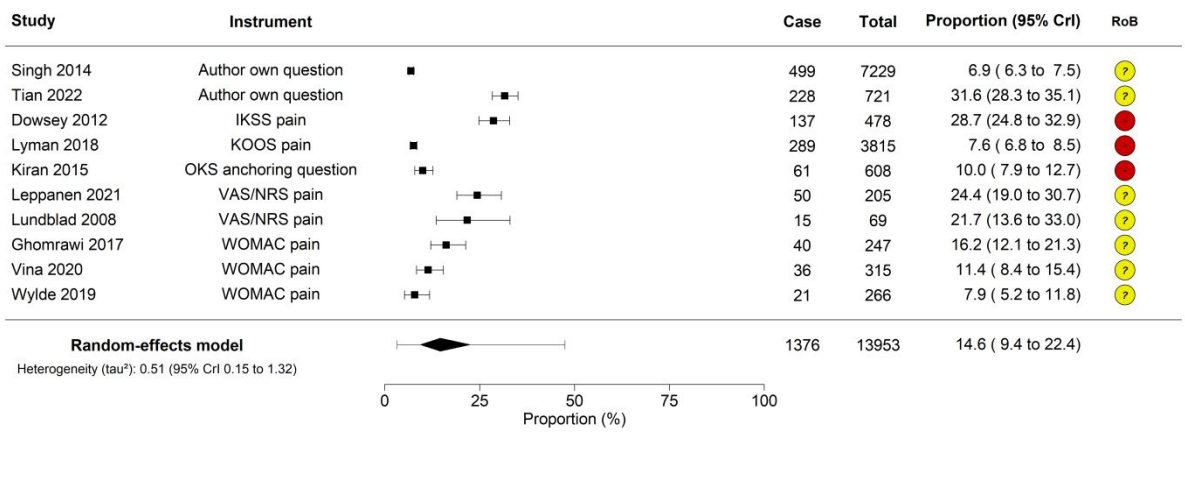
S5.3 TKR studies (12 months)



S5.4 TKR studies (24 months)



S6. Table of multivariate and univariate meta-analysis results in TKR studies

	Multivariate meta-analysis		Univariate meta-analysis	
Time	Median (95% CrI)	tau² (95% CrI)	Median (95% CrI)	tau² (95% CrI)
3 months	21.2 (16.9 to 26.4)	0.49 (0.28 to 0.91)	21.9 (15.6 to 29.4)	0.51 (0.18 to 1.1)
6 months	14.6 (11.9 to 17.8)	0.56 (0.34 to 0.91)	14.1 (10.9 to 17.9)	0.51 (0.27 to 0.9)
12 months	12.6 (10.3 to 15.5)	0.63 (0.41 to 0.99)	12.6 (9.9 to 15.9)	0.61 (0.35 to 0.99)
24 months	14.2 (10 to 20.1)	0.58 (0.25 to 1.55)	14.6 (9.5 to 22.4)	0.52 (0.16 to 1.35)

S7. Meta-regression analyses in TKR studies

S7.1 Mean age

Time	No. studies	slope	intercept
3 months	15	0.133	-1.272
6 months	28	0.082	-1.851
12 months	34	-0.029	-1.942
24 months	9	-0.073	-1.886

S7.2 Proportion of females

Time	No. studies	slope	intercept
3 months	15	0.009	-1.273
6 months	28	-0.040	-1.697
12 months	36	-0.006	-1.939
24 months	10	0.045	-1.798

S7.3 Sample sizes

Time	No. studies	slope	intercept
3 months	15	-0.001	-1.269
6 months	28	0.000	-1.785
12 months	36	0.000	-1.936
24 months	10	0.000	-1.750

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S8. Subgroup analyses in TKR studies

- Geographic region (categorical; North America, Asia, Europe, and Australia)
- Data source (categorical; surgeons, single hospital, multi-centre, and national registry
- Pain outcomes instruments (categorical; multidimensional, e.g. WOMAC pain, simple, e.g. VAS/NRS and EQ-5D 5L, and not validated, e.g. author's own questionnaires)
- Cut-off definitions (categorical; based on MCID, based on PASS, based on pain intensity, e.g. specific post-operative VAS values, based on functional impact, e.g. night pain, pain on movement, or limiting daily life, based on symptom improvement, e.g. no change or increase in pain from pre-operative)

S8.1 Geographical regions

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Asia	4	24.26 (11.85 to 42.3)	0.32 (0 to 2.34)
Europe	9	22.17 (12.42 to 35.18)	0.77 (0.19 to 2.17)
North America	2	16.63 (0.92 to 81.83)	0.21 (0 to 31.7)
6 Months			
Asia	5	9.91 (4.04 to 21.69)	0.64 (0.06 to 3.19)
Australia	2	15.53 (1.23 to 73.87)	0.19 (0 to 23.85)
Europe	12	17.99 (10.88 to 27.3)	0.77 (0.27 to 1.85)
North America	9	11.87 (8.87 to 15.58)	0.13 (0 to 0.45)
12 Months			
Asia	3	5.81 (2.2 to 12.88)	0.12 (0 to 2.76)
Australia	2	21.45 (0.1 to 98.64)	0.73 (0 to 97.26)
Europe	25	13.54 (9.91 to 18.16)	0.72 (0.37 to 1.29)
North America	6	11.15 (8.31 to 14.9)	0.09 (0.01 to 0.4)
24 Months			
Asia	1	31.36 (28.02 to 34.79)	NA
Australia	1	28.29 (24.49 to 32.56)	NA
Europe	4	14.29 (5.86 to 32.4)	0.47 (0.03 to 3.51)
North America	4	9.56 (5.19 to 17.04)	0.2 (0 to 1.45)

S8.2 Setting

Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Other	1	26.44 (19.1 to 34.38)	NA
Single hospital	8	25.41 (15.64 to 38.72)	0.55 (0.13 to 1.73)
Surgeon	6	16.89 (8.43 to 29.76)	0.55 (0.07 to 2.2)
6 Months			
Multicentre	6	13.84 (7.93 to 22.5)	0.35 (0.04 to 1.41)
Other	2	18.34 (7.93 to 37.29)	0.02 (0 to 2.68)
Registry	1	8.22 (8.14 to 8.29)	NA
Single hospital	16	15.03 (9.79 to 21.64)	0.73 (0.3 to 1.55)
Surgeon	3	10.82 (3.35 to 30.39)	0.26 (0 to 5.13)
12 Months			
Multicentre	12	11.29 (7.37 to 16.83)	0.56 (0.19 to 1.31)
Registry	1	16.80 (16.07 to 17.57)	NA

Single hospital	20	13.96 (9.77 to 19.93)	0.77 (0.34 to 1.47)
Surgeon	3	8.93 (4.2 to 16.32)	0.05 (0 to 1.6)
24 Months			
Multicentre	1	11.50 (8.14 to 15.03)	NA
Single hospital	9	14.98 (9.11 to 23.7)	0.57 (0.16 to 1.54)

S8.3 Pain outcome instruments

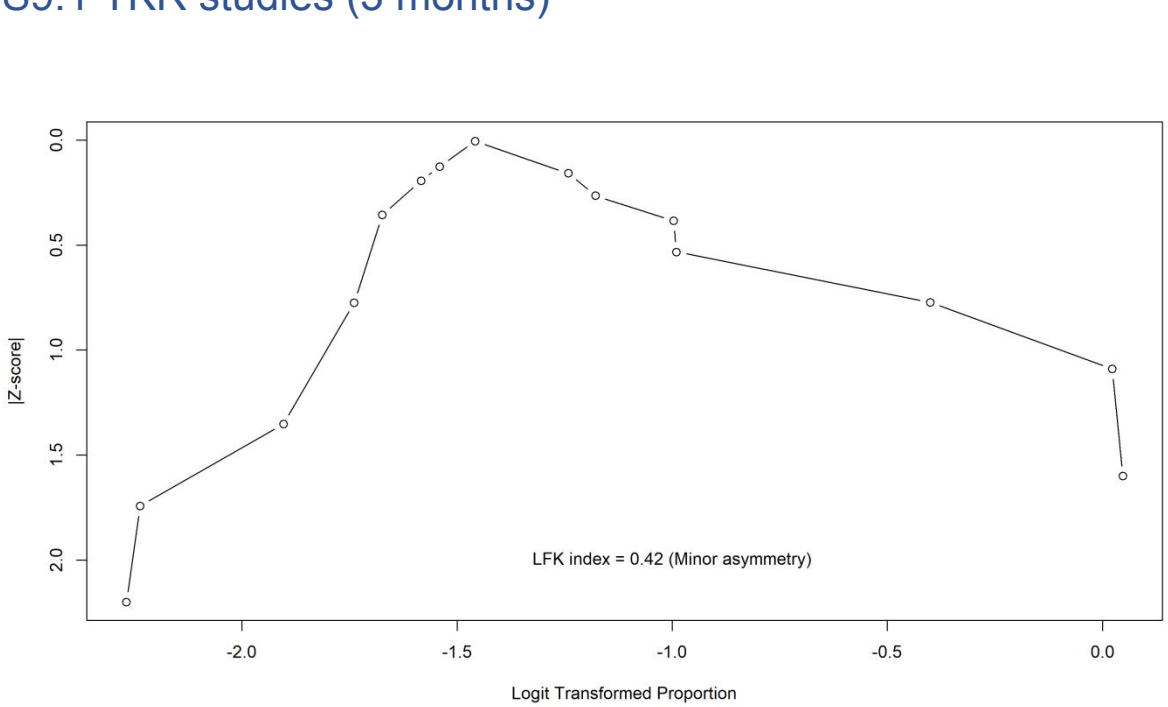
Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Multidimensional	5	26.76 (12.16 to 49.19)	0.7 (0.09 to 3.37)
Not validated	1	12.98 (9.3 to 17.9)	NA
Simple	9	20.6 (13.08 to 31.41)	0.5 (0.11 to 1.47)
6 Months			
Multidimensional	9	13.68 (8.49 to 22.5)	0.56 (0.14 to 1.57)
Not validated	2	7.65 (0 to 99.79)	1.72 (0 to 219.88)
Simple	17	15.15 (10.99 to 20.57)	0.49 (0.2 to 1.03)
12 Months			
Multidimensional	21	12.67 (8.95 to 17.66)	0.72 (0.33 to 1.34)
Not validated	2	6.51 (0 to 98.5)	1.52 (0 to 166.77)
Simple	13	13.91 (9.63 to 19.73)	0.44 (0.14 to 1.02)
24 Months			
Multidimensional	6	12.39 (6.86 to 20.55)	0.41 (0.07 to 1.58)
Not validated	2	15.65 (0 to 99.99)	3.63 (0.07 to 399.6)
Simple	2	23.53 (8.04 to 48)	0.02 (0 to 4.48)

S8.4 Cut-off definitions

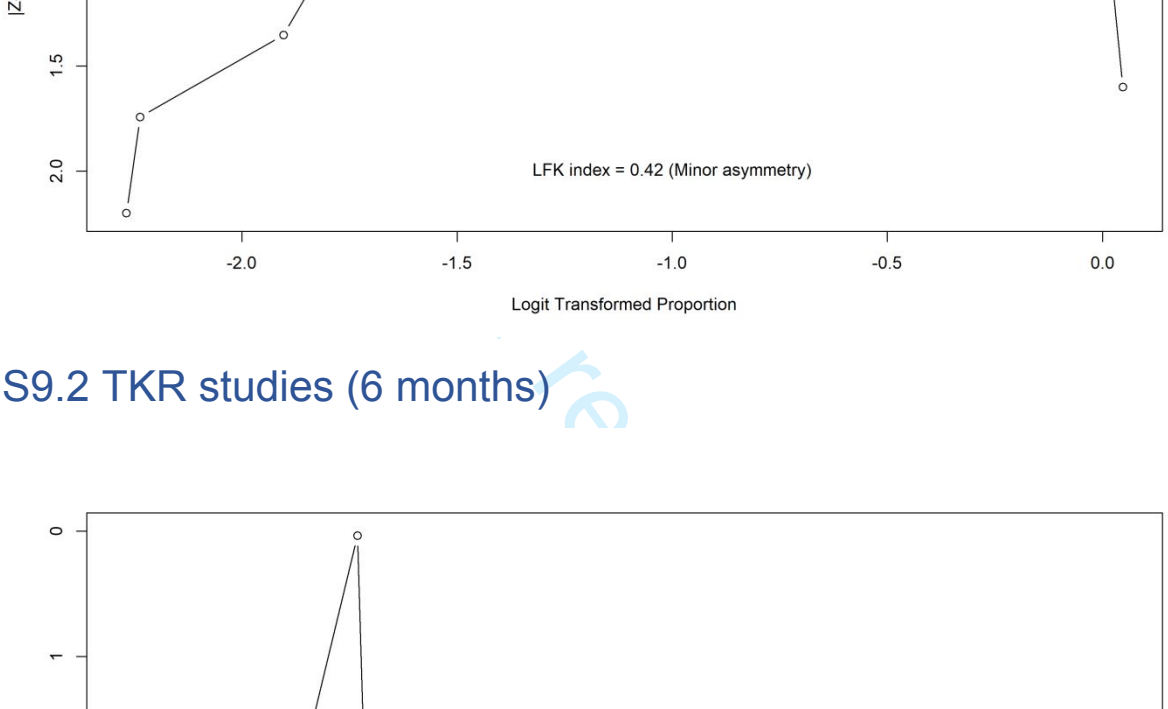
Subgroup	No. Studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Based on functional impact	1	40.1 (33.1 to 47.6)	NA
Based on MCID	2	17.91 (4.01 to 63.34)	NA
Based on pain intensity	10	21.61 (13.37 to 33.15)	0.66 (0.18 to 1.74)
Based on symptom improvement	2	18.26 (0.26 to 95.83)	NA
6 Months			
Based on functional impact	1	15.9 (9.1 to 26.5)	NA
Based on MCID	3	14.38 (1.88 to 56.47)	1 (0.05 to 13.77)
Based on pain intensity	21	15.26 (11.63 to 19.96)	0.48 (0.23 to 0.92)
Based on symptom improvement	3	6.75 (1.68 to 26.53)	0.44 (0 to 7.44)
12 Months			
Based on functional impact	1	6.4 (3.6 to 11.2)	NA
Based on MCID	5	15.77 (5.83 to 36.93)	0.92 (0.13 to 4.38)
Based on pain intensity	19	14.34 (10.16 to 19.75)	0.61 (0.26 to 1.19)
Based on PASS	2	13.7 (1.08 to 66.8)	NA
Based on symptom improvement	9	8.86 (5.08 to 15.27)	0.63 (0.15 to 1.81)
24 Months			
Based on functional impact	1	31.6 (28.3 to 35.1)	NA
Based on MCID	3	10.88 (4.18 to 25.04)	0.22 (0 to 3.32)
Based on pain intensity	4	18.24 (6.02 to 43.02)	0.75 (0.08 to 5.12)
Based on symptom improvement	2	9.15 (2.73 to 24.14)	NA

S9. Doi plots and the LFK indexes in TKR studies

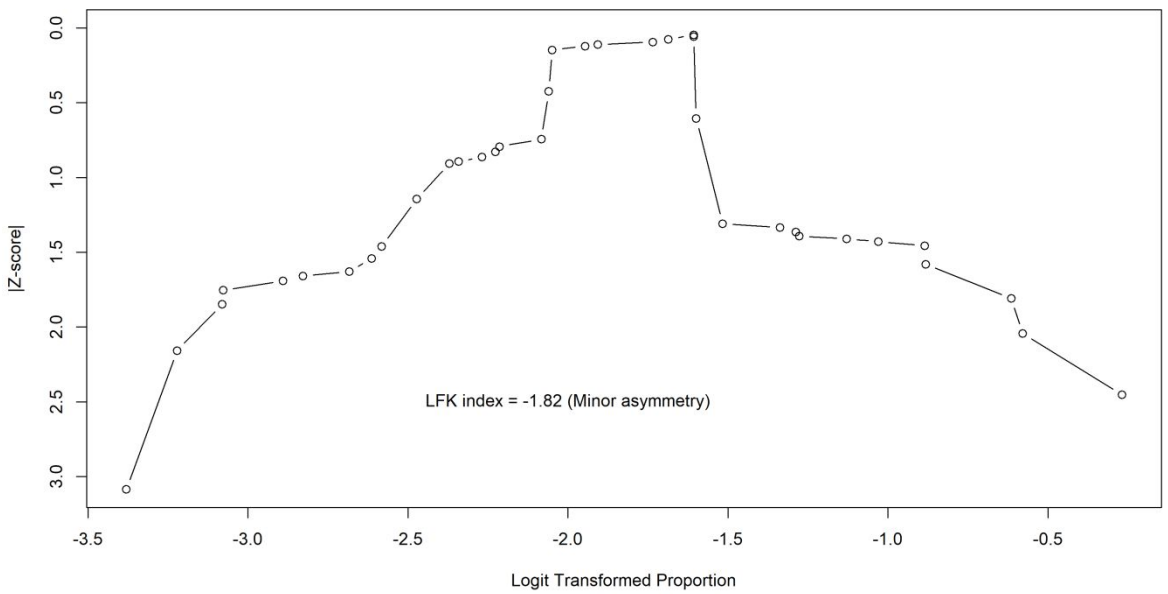
S9.1 TKR studies (3 months)



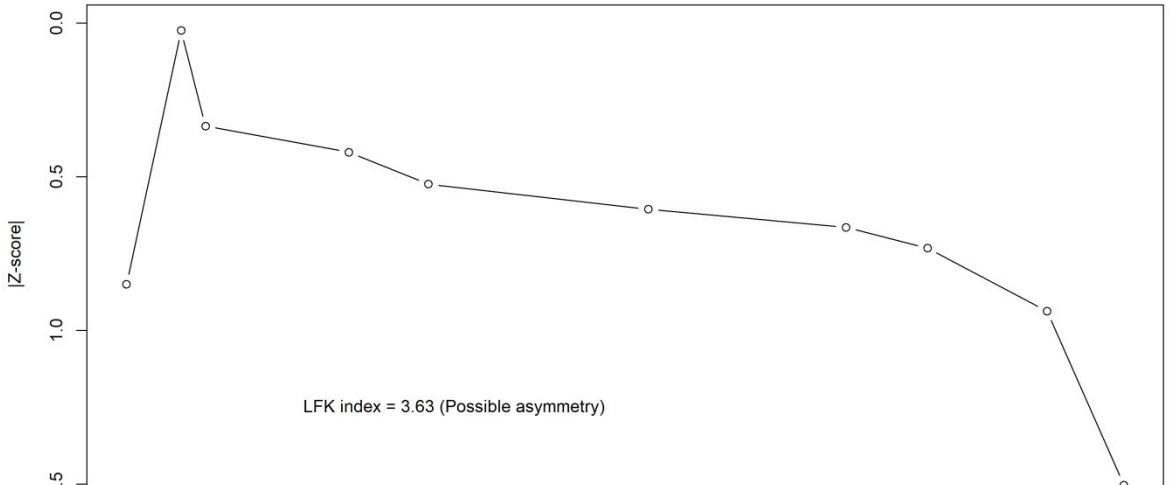
S9.2 TKR studies (6 months)



S9.3 TKR studies (12 months)



S9.4 TKR studies (24 months)



S10. Sensitivity analyses

In the sensitivity analysis, we excluded the following studies based on their unique clinical characteristics:

- Tang 2023 (impact on 3 months results only)
- Leppanen 2021 (impact on 24 months results only)
- Fast track studies (impact on 3 and 12 months results only)
- Mekkawy 2023 and Yan 2023 (impact on 6 months results only)
- Studies on TKR or UKR operations
- Studies with more than 20% lost to follow-up
- High risk of bias studies

Name	No. studies	Median (95% CrI)	tau² (95% CrI)
3 Months			
Excluding Tang 2023	14	22.12 (15.4 to 30.2)	0.55 (0.19 to 1.21)
Excluding Fast track studies	14	22.56 (15.96 to 30.84)	0.53 (0.17 to 1.18)
Excluding TKR or UKR studies	12	23.68 (16.36 to 33.17)	0.53 (0.17 to 1.29)
Excluding studies with > 20% loss to follow-up	11	26.13 (18.08 to 36.46)	0.49 (0.14 to 1.25)
Excluding studies with overall high risk of bias	12	25.01 (17.87 to 34.74)	0.48 (0.16 to 1.17)
6 Months			
Excluding Mekkawy 2023 and Yan 2023	26	13.97 (10.74 to 18.13)	0.54 (0.27 to 0.95)
Excluding TKR or UKR studies	26	14.24 (10.88 to 18.46)	0.54 (0.27 to 0.95)
Excluding studies with > 20% loss to follow-up	19	16.78 (12.37 to 22.52)	0.52 (0.22 to 1.03)
Excluding studies with overall high risk of bias	19	15.63 (11.25 to 21.19)	0.58 (0.24 to 1.12)
12 Months			
Excluding Fast track studies	34	12.15 (9.5 to 15.15)	0.55 (0.3 to 0.91)
Excluding TKR or UKR studies	35	12.72 (9.85 to 16)	0.63 (0.35 to 1.01)
Excluding studies with > 20% loss to follow-up	19	15.3 (11.09 to 21.01)	0.58 (0.23 to 1.16)
Excluding studies with overall high risk of bias	20	14.37 (10.14 to 19.49)	0.65 (0.28 to 1.23)
24 Months			
Excluding Leppanen 2021	9	13.78 (8.33 to 21.28)	0.52 (0.15 to 1.45)
Excluding TKR or UKR studies	9	13.18 (8.59 to 20.26)	0.42 (0.11 to 1.18)
Excluding studies with > 20% loss to follow-up	6	18.74 (9.79 to 33.5)	0.59 (0.11 to 2.29)
Excluding studies with overall high risk of bias	7	15.28 (8.68 to 26.24)	0.53 (0.12 to 1.78)

*Abbreviation: TKR: Total Knee Replacement; UKR: Unicompartmental Knee Replacement

Prevalence of chronic pain after total hip or knee replacement

S11. Characteristics of THR studies

Study Country Recruitment dates Setting	Operation Number of patients Age (SD), range % women	Pain measure	Definition of unfavourable pain outcome High risk of bias concern
Cleveland Clinic OME Arthroplasty Group 2020[1] USA 2015-2018 6 hospitals	Primary THR, all N=3449 Median 65 (IQR 57-72) 57.4%	HOOS pain 12 months	Less than MCID (15 points)
Erlenwein 2017[2] Germany 2012 1 hospital	Primary THR, all 18+ N=125 63 (12.6) 58%	NRS pain 6 months	Maximum NRS >3 during previous 4 weeks
Jones 2000[3] Canada 1995-1997 1 health region	Primary THR, all 40+ N=242 68.2 (11.1) 60%	WOMAC pain 6 months	Moderate/ severe pain defined as a gain of <10 points on the WOMAC pain dimension
Mezey 2023[4] Hungary 2019-2020 2 hospitals	Primary THR, all N=88 68.7 (THR and TKR patients) 69.2%	WOMAC pain 12 months	Not exceeding MCID (8.3) High loss to follow up rate
Nikolajsen 2006[5] Denmark 2003 National registry	Primary THR, 18-90 years N=1231 71.6 (8.7) Not reported	Authors' own scale of presence of hip pain and impact on daily life 12-18 months	Pain with moderate, severe or very severe impact on daily life
Page 2016[6] Canada 2009-2012 1 hospital	Primary THR, all 18-75 N=150 60 (9.2) 48%	Authors' own scale 6 months	Chronic pain if pain rated as "discomforting", "distressing", "horrible," or "excruciating" Concern as RCT analysed as cohort study
Palazzo 2014[7] France 2009 3 hospitals	Primary THR, all N=129 63.5 (13.5) 49.6%	Author's own residual pain scale 12 months	"To what extent have you obtained a relief or improvement as a result of THA in the following areas?" (from 0: not at all; to 4: completely)
Quintana 2006[8] Spain 1999-2000 7 hospitals	Primary THR N=784 69.1 48.3%	WOMAC pain 6 months	No improvement in pain greater than MCID (24.55 of 100) using an anchor-based method. Concern for high loss to follow up rate
Ray 2020[9] Sweden 2008-2015 National registry	THR N= 127,660 68 (10) 56%	EQ-5D VAS pain/discomfort 12 months	Worse or no change in pain/discomfort Concern for high loss to follow up rate

Prevalence of chronic pain after total hip or knee replacement

Singh and Lewallen 2010[10] USA 1993-2005	Primary THR N=9154 65 (13.3) 51%	Authors' own scale: How much pain do you have in your operated hip? None, mild, moderate or severe 24 months	Moderate or severe pain Concerns for high loss to follow up rate
Tang 2023[11] China 2020-2021 1 hospital	Primary THR probably, all 65+. Osteoarthritis or osteonecrosis (not fracture) N=89 72 (range 63-81) 62.5%	NRS pain 3 months	NRS scores ≥4 Note, n and losses to follow up estimated as proportions because n hips and knees reported together

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S11.1 Proportions of lost to follow-ups and revisions

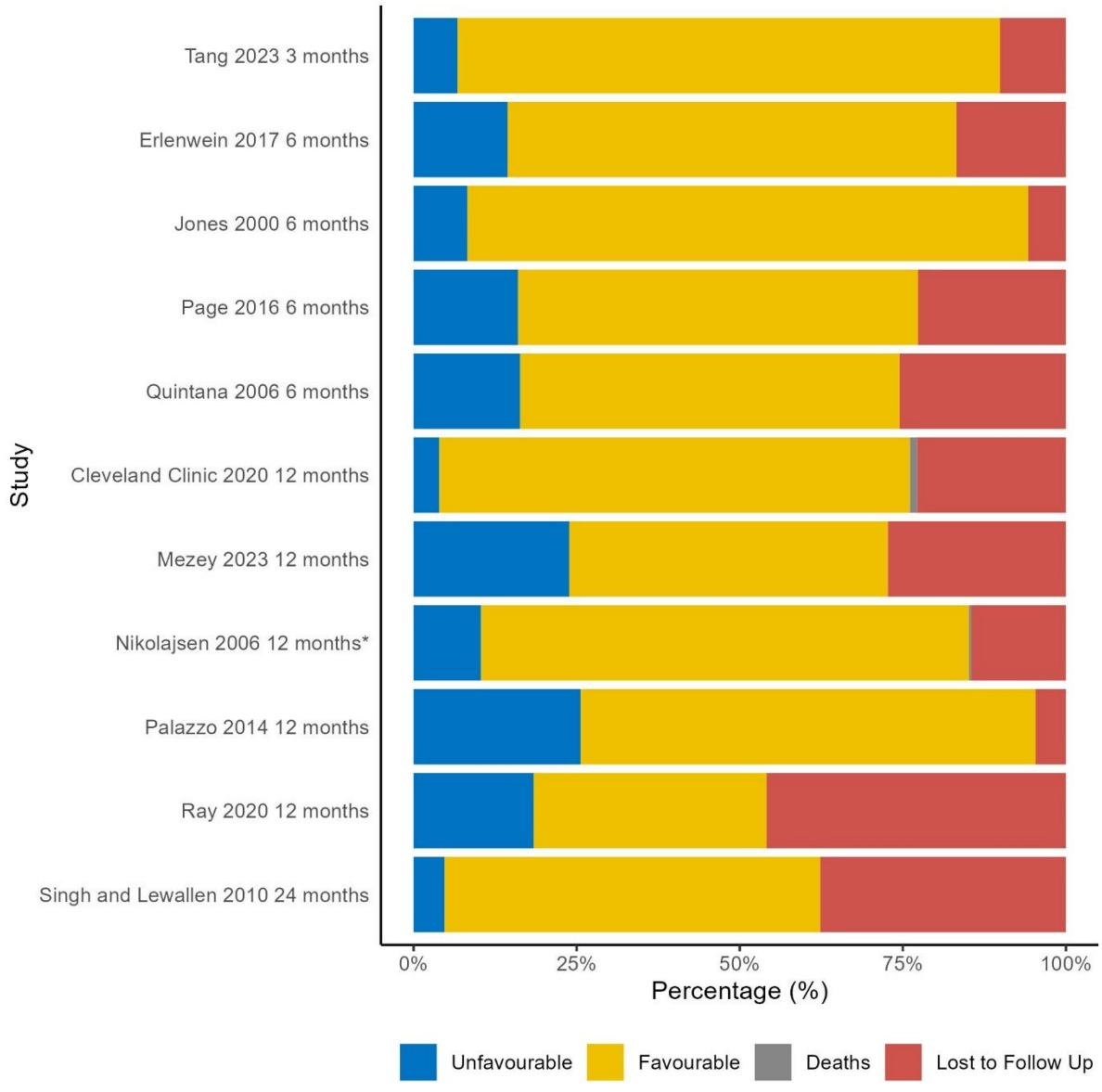

Figure S12.1. Favourable and unfavourable pain outcomes and reasons of missing data in THR studies.

Prevalence of chronic pain after total hip or knee replacement

S12. Traffic light plot of the risk of bias assessments in THR studies