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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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Complete List of Authors:	Cheng, Hung-Yuan; University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences; University of Bristol, Bristol Medical School Beswick, Andrew; University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences; University Hospitals Bristol and Weston NHS Foundation Trust, National Institute for Health and Care Research Applied Research Collaboration West Bertram, Wendy; University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences; University Hospitals Bristol and Weston NHS Foundation Trust, National Institute for Health and Care Research Applied Research Collaboration West Bertram, Wendy; University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences; University Hospitals Bristol and Weston NHS Foundation Trust, National Institute for Health and Care Research Applied Research Collaboration West Siddiqui, Mohammad Ammar; University of Bristol, Bristol Medical School Gooberman-Hill, Rachael; University of Bristol, Bristol Medical School Whitehouse, Michael; University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences; University Hospitals Bristol and Weston NHS Foundation Trust, National Institute for Health and Care Research Applied Research Collaboration West Wylde, Vikki; University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences; University Hospitals Bristol and Weston NHS Foundation Trust, National Institute for Health and Care Research Applied Research Collaboration West
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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

Authors and affiliations

Hung-Yuan Cheng ^{1, 2*}, Andrew Beswick ^{1,3*}, Wendy Bertram ^{1,3}, Mohammad Ammar Siddiqui ¹, Rachael Gooberman-Hill ^{1,2}, Michael R Whitehouse ^{1,3}, Vikki Wylde ^{1,3}

1 Musculoskeletal Research Unit, Bristol Medical School, University of Bristol, Bristol, BS10 5NB, United Kingdom

2 Bristol Medical School, University of Bristol, Bristol, BS8 2PN, United Kingdom

3 National Institute for Health and Care Research Applied Research Collaboration West at University Hospitals Bristol and Weston NHS Foundation Trust, United Kingdom

reliez

*equal contribution

Corresponding author:

Professor Vikki Wylde: V.Wylde@bristol.ac.uk

Address: Musculoskeletal Research Unit, Translational Health Sciences, Bristol Medical School, Learning and Research Building, Level 1, Southmead Hospital, University of Bristol, BS10 5NB, UK

Running title

Prevalence of chronic pain after total hip or knee replacement

Keywords

Chronic pain; Total hip replacement; Total knee replacement; Systematic review; Metaanalysis

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% Crl 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.¹² About 100,000 each of primary total knee and hip replacements were performed in the UK in 2022,³⁴ 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 increase⁶⁷ 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 PRISMA¹⁵ (Supplementary material S1) and relevant contents in MOOSE¹⁶ 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.

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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 10⁵) 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 factors²⁰ 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.

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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. ²²Patient 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. to beet teries only

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 <u>Figure 1</u>. 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 <u>Table</u> <u>1</u>. 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

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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

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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 preoperative 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 replacement⁴⁸⁻⁵¹. 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

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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

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 postsurgical 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

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	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 outc	ome reporte	d			
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

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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
For peer texiew only					

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

Proportion* (%)	Median (95% Crl)	т² (95% Crl)		
	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 2. Summary of risk of bias assessments 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.

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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; Crl: Credible intervals.

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Supplementary materials

- S1. **PRISMA checklist**
- S2. Search strategy as applied in MEDLINE
- S3. Characteristics of TKR studies
- Traffic light plot of the risk of bias assessment in TKR studies S4.
- S5. Forest plots of univariate meta-analyses in TKR studies
- S6. Table of multivariate and univariate meta-analysis results in TKR studies
- Meta-regression analyses in TKR studies S7.
- S8. Subgroup analyses in TKR studies
- Doi plots and the LFK indexes in TKR studies S9.
- S10. Sensitivity analyses in TKR studies
- S11. Characteristics of THR studies
- i R s. ndexes TKR studies ne risk of bias as. S12. Traffic light plot of the risk of bias assessment in THR studies

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Prevalence of chronic pain after total hip or knee replacement

Supplementary materials

S1. PRISMA checklist	3
S2. Search Strategy as applied in MEDLINE	6
S2.1 Total knee replacement	6
S2.2 Total hip replacement	6
S3. Characteristics of TKR studies	7
References	
S3.1 Mean age and range	
S3.2 Proportion of females	
S3.3 Data collection timeframe	19
S3.4 Proportions of lost to follow-ups and revisions	
S4. Traffic light plot of the risk of bias assessments in TKR studies	21
S4.1 TKR studies (3 months)	21
S4.2 TKR studies (6 months)	
S4.3 TKR studies (12 months)	23
S4.4 TKR studies (24 months)	24
S5. Forest plots of univariate meta-analyses in TKR studies	25
S5.1 TKR studies (3 months)	25
S5.2 TKR studies (6 months)	25
S5.3 TKR studies (12 months)	
S5.4 TKR studies (24 months)	
S6. Table of multivariate and univariate meta-analysis results in TKR studies	s27
S7. Meta-regression analyses in TKR studies	
S7.1 Mean age	
S7.2 Proportion of females	
S7.3 Sample sizes	
S8. Subgroup analyses in TKR studies	
S8.1 Geographical regions	
S8.2 Setting	
S8.3 Pain outcome instruments	
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	
S11. Characteristics of THR studies	
--	----
References	35
S11.1 Proportions of lost to follow-ups and revisions	
S12. Traffic light plot of the risk of bias assessments in THR studies	

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		BMJ Open 5 3. 8 9	Page 36 of
Prevalence of cl	hronic	pain after total hip or knee replacement	
S1. PRISM	A ch	necklist	
Section and Topic	ltem #	Checklist item	Location where item is reported
TITLE	n	es	
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT	1		
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION	1		
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	1		
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the symptoms.	Page 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searche 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 interview 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 to be 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 applied 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 deside 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 tools, 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 🕏 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 messing 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

Page 36 of 69

Prevalence of c	nronic		
Section and Topic	ltem #	Checklist item	Location where ite is reporte
	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. and to explore possible causes of heterogeneity among study results (e.g. and to explore 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 the perting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome of a local sector of the se	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 above a scluded.	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 and S12
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriated and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figure 3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 7 a 8
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the stammary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, descript the direction of the effect.	Figure 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 7-8 S7 and 9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results of all sensitivity analyses conducted to assess the robustness of the synthesized results of all sensitivity analyses conducted to assess the robustness of the synthesized results of all sensitivity analyses conducted to assess the robustness of the synthesized results of all sensitivity analyses conducted to assess the robustness of the synthesized results of all sensitivity analyses conducted to assess the robustness of the synthesized results of all sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to assess the robustness of the synthesized results of a sensitivity analyses conducted to a sensitivity analyses conducted to a sensitivity analyses of the synthesized results of a sensitivity analyses of a sensitity analyses of a sensitivity analyses of a sen	Page 8, S10, Tab 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicab
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicab
DISCUSSION			

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Prevalence of chronic pain after total hip or knee replacement

Discussion	Item	Checklist item	Location where ite
Discussion	#	ng	is report
	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,
OTHER INFORMA	TION		
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or States hat the review was not registered.	Page 2 a 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 2 a 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 approximations 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
		on June 14, 2025 at Age imilar technologies.	
		5	

Prevalence of chronic pain after total hip or knee replacement

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.

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- 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

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	Primary TKR, all 18+ N=482 67.5 (9.6)	WOMAC pain 12 months	No clinically important improvement based on MCID
1998-2007	62%		
2 hospitals			
Aso 2020[2]	Primary TKR, all	VAS/NRS pain	Moderate to severe pain
Japan	N=234	6, 12 months	(VAS >30 mm), at rest or walking
2012-2017	75		Walking
1 hospital	75.8%		
Attal 2014[3]	Primary TKR, all 18+	BPI (NRS)	NRS pain average 3 or
France	N=89	3, 6, 12 months	greater on 10-point scale
2008-2011	68.7 (8.9)		
l hospital	65.0%		
Baker 2007[4]	Primary TKR, all	OKS pain	Reported persistent knee
UK	N=9417	12 months	pain
2003	70.68		
National registry	56.8%		
Bell 2023[5]	Primary TKR, all 50-89	KOOS pain	MCID not satisfied
USA	N=5564	12 months	
2015-2018	Range 50-89		
7 hospitals	60.7%		
Birch 2019[6]	Primary TKR or UKR, all	OKS pain	OKS pain moderate/severe
Denmark	N=589	4, 12 months	High loss to follow up rate
2011-2013	67.3 (9.7)		at 4 and 12 months
1 hospital	52.0%		
Brander 2003[7]	Primary TKR, all 18+	VAS/NRS pain	VAS >40
USA	N=116	3, 6, 12 months	
1998-2000	66 (10.5), range 36-85	-, -,	
1 surgeon	55.2%		
Buus 2022[8]	Primary TKR all 18+	OKS pain	Threshold 42 39
Denmark	N=217	12 months	
2015-2016	66.8 (9.3)		
1 hospital	52.2%		
Buvanendran 2019[9]	Primary TKR, all	VAS/NRS pain	NRS pain with movement
USA	N=296	6 months	≥4
2011-2017	65		
1 hospital	65.3%		

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Chodor and	Primary TKR, all 48+	Author own	Pain severely limiting o
Kruczynski 2022[10]	N=69	question	life
Poland	67.6 (7.42), range 48-84	6 months	
	76.7%		
		Authoriouria	
	Primary TKK, all	Author own question "How	Fair or poor
UK 2010	N=378	well did the	High loss to follow up
	70 (9.6), range 39-91	surgery relieve	
i nospital	30.4%	pain in your	
		12 months	
Cole 2022[12]	Primary TKR all	OKS nain	<14 points OKS
	N=1025	12 months	
2010-2015	70	12 11011113	
2010-2015 2 hospitals	70 55 9%		
2 1005pilais	Drimony TKD probably		
	all 40+		wowac pain score <
USA 2012 2014	N=267	r∠ months	
2012-2014	66 (9)		
3 nospitais	61 0%		
	01.070		
Dowcov 2012[1/]	Drimony TKP oll	IKSS pain	IKSS pain score <20
		12 24 months	moderate to severe pa
	N=470 70.9 (9.2) rongo 45.00	12, 24 11011015	IKSS may not be entir
2000-2007	70.0 (0.3), Tange 45-90		patient reported at 12
Thospital	09.2%		24 months
Dursteler 2021[15]	Primary TKR, all 18+	VAS/NRS pain	NRS 0.3/1 or greater a
Spain	N=170	3, 6 months	
2014-2017	73.1 (7.1)		
Spain	73.3%		
1 hospital			
Edwards 2022[16]	Primary TKR, all 45+	BPI	4/10 or greater
USA	N=248	6 months	 High loss to follow up r
2012-2018	65.1 (8.2)		
2 hospitals	59.5%		
Escobar and Riddle	Primary TKR, all	WOMAC pain	Number not attaining F
2014[17]	N=1616	12 months	High loss to follow up
Spain	71.6 (6.8)		
2003-2006	70.0%		
15 hospitals			
Getachew 2021[18]	Primary TKR, all 18+	BPI	BPI worst pain score ≥
Norway	N=206	12 months	
2012-2014	68 (9)		
1 hospital	66.0%		
Ghomrawi 2017[19]	Primary TKR, all	WOMAC pain	Number not achieving
USA	N=247	24 months	MCID
2010-2012	68 (10)		

Grosu 2016[20]	Primary TKR probably,	VAS/NRS pain	Moderate to severe pain
Belgium	all	3, 6, 12 months	High loss to follow up rate
2009-2010	N=114		at 3, 6 and 12 months
1 surgeon	66 (10)		
	65.8%		
Hardy 2022[21]	Primary TKR, all >18	VAS/NRS pain	VAS >30/100
France	N=111	12 months	
2014-2015	73.3 (9.3) range 29-92		
1 hospital	65.0%		
Heath 2021[22]	Primary and revision	EQ-5D 5L pain/	Moderate/ severe or
Australia	I KR, all	discomfort	extreme pain EQ 5D 5L
2018-2020	N=8299	6 months	High loss to follow up rate
44 hospitals	67.5 (8.8)		Figh loss to follow up rate
	56.4%		
Jones 2000[23]	Primary TKR, all 40+	WOMAC pain	Moderate/ severe pain
Canada	N=292	6 months	defined as a gain of <10
1995-1997	69.2 (9.2)		dimension
1 health region	59.0%		
Khalid 2021[24]	Primary TKR or UKR, all	OKS pain	OKS-pain score of 14 or
UK	N=531,790	6 months	less at six months after
2008-2016	69.7 (9.4)		knee replacement can be
National registry	56.6%		considered to be in chronic
Kim 2015[25]	Primary TKR all women	VAS/NRS nain	>5 points on an 11 point
South Korea	N=94	3 months	VNRS (verbal numeric
2012 2014	N=94 70.18 (5.74) range 20	3 11011015	rating scale)
2013-2014 1 hoopital	80		
i nospital	100%		
Kiran 2015[26]	Primary TKR, all	OKS pain	Has your knee replacement
UK	N=608	12 24 months	operation decreased your
2003-2007	72	12, 21 Monario	knee pain?
1 hospital	61.4%		High loss to follow up rate
Поэрна	01.478		at 12 and 24 months
Kornilov 2018[27]	Primary TKR, all 18+	VAS/NRS pain	Not at least a two-point or
Russia	N=100	12 months	approximately 30%
2014	63 (8), range 47-81		decrease in rating of pain
1 hospital	95.0%		interference with walking
			from baseline to 1 year
			(NRS scale 0-10)
Kurien 2018[28]	Primary TKR probably,	VAS/NRS pain	4 or greater
UK	all	6 months	
Before 2017	N=50		
1 hospital	66.4 (8.3)		
	60.0%		
Larsen 2021[29]	Primary TKR, all 18+	VAS/NRS pain	Pain intensity at rest >3
Denmark	N=185	12 months	High loss to follow up rate
2015-2016	68.8 (8.9)		
1 hospital	55.7%		
Latijnhouwers	Primary TKR, all	VAS/NRS pain	Moderate to severe pain
2022[30]	N=282	12 months	(NRS ≥4)

Prevalence of chronic pain after total hip or knee replacement

2				
3	The Netherlands	66 (8.4)		High loss to follow up rate
4	2012-2017	63.0%		
5	2 hospitals			
7	Lavand'homme	Primary TKR or UKR, all	VAS/NRS pain	NRS ≥4/10
8	2014[31]	N=128	3 months	
9	Belgium	68 (10)		
10	2012	66 <u>/</u> %		
11	1 surgeon	00.470		
12	l ee 2022[32]	Primary TKR probably	Pain disturbing	Night pain was defined as
13	South Korea	all	sleep	pain around the knee
15	2017-2010	N=172	3. 12 months	experienced at night that
16	2017-2019	70.7 (4.3)	-,	could disturb the patient's
17	z surgeons	89.2%		sleep
18	Lennanen 2021[33]	Primary TKR 65 years	VAS nain	VAS >30
19	Eeppanen 2021[00]	or vounger	exercise	VA3 >30
20		N=205	24 months	
21	2012-2014	60		
22	1 nospital	63.0%		
24	Loung 2010[24]		Authorown	No change of worsening
25		Philliary TKR, all	Author Own	no change of worsening
26	Singapore	N=243	6 12 months	pair signity better
27	2015	66 (8.3)	0, 12 11011115	
28	1 hospital	78.6%		
29	Lundblad 2008[35]	Primary TKR, all	VAS/NRS pain	Pain at rest, VAS >2/10
31	Sweden	N=69	24 months	
32	Before 2006	68		
33	1 hospital	50.7%		
34	Lyman 2018[36]	Primary TKR, all	KOOS pain	Number not achieving
35	USA	N=3815	24 months	MCID
36	2007-2012	74 (6)		High loss to follow up rate
37	1 hospital	63.0%		
39	Mahdi 2020[37]	Primary TKR all	KOOS pain	8 cut off
40	Sweden	N-615	12 months	High loss to follow up rate
41	2016-2018	60.7		
42	2010-2010	52.2%		
43	Makkowa 2022[20]			Drahably NDC assess of >1
44		Philliary IKR, all		in defined sites Concern
45	USA	N=112	6 months	over VAS ≥1 being too
47	2021	65.5 (9.2)		inclusive and high loss to
48	4 surgeons	69.0%		follow up rate
49	Mercurio 2020[39]	Primary TKR, all >18	VAS/NRS pain	VAS >30 residual pain
50	Italy	N=45	12 months	
51	2015-2017	69.6 (7.8)		
52 53	1 hospital	65.0%		
55	Mezey 2023[40]	Primary TKR probably.	WOMAC pain	Not exceeding MCID
55	Hungary	all	12 months	High loss to follow up rate
56	2019-2020	N=101		
57	2 hospitals	69.2		
58		Not reported		
59	Mushahi 2023[41]	Primary TKR all 40+	WOMAC nain	WOMAC pain score
60				

USA	N=575	12 months	improvement of <20
2011-2014	66.3 (8.3)		High loss to follow up rate
4 hospitals	60%		
Nishimoto 2023[42]	Primary TKR, all with no	KOOS pain	Not achieving MCID of 1
Japan	complications	3, 6 months	
2021-2023	N=68		
1 hospital	75.1 (7.3)		
	80.9%		
Noiseux 2014[43]	Primary TKR, all 30+	VAS/NRS pain	Moderate or severe pain
USA	N=215	6 months	with range of motion, VA
Before 2012	61.7 (9.8)		≥1
2 hospitals	58.0%		Concern over VAS ≥1 being too inclusive
Orr 2022[44]	Primary TKR, all	KOOS pain	Not achieved PASS for
USA	N=7476	12 months	KOOS pain
2016-2019	67 (9.0)		High loss to follow up rate
9 hospitals	60.8%		
Petersen 2015[45]	Primary TKR, all	VAS/NRS pain	VAS >3
Denmark	N=78	12 months	High loss to follow up rat
Before 2014	69		. 1 *
1 hospital probably	59.0%		
Petersen 2018[46]	Primary TKR probably.	VAS/NRS pain	<30% reduction in pain
Denmark	all	12 months	·····
Before 2017	N= 200		
1 hospital	69 (1.2)		
Поэрна	57.0%		
Phillips 2014[47]	Primary TKR, all	VAS/NRS pain	VAS >3
UK	N= 96	3, 6, 12 months	
2009-2010	70.6		
1 hospital	56.0%		
Priol 2023[48]	Primary TKR, all	VAS/NRS pain	Vas 4+
France	N=129	6 months	High loss to follow up rat
2011-2012	74 (10) range 45-94		ingritoco to follow up fu
1 hospital	72 3%		
Pua 2010[/0]	Primary TKR all 50+	OKS nain	Moderate or severe pain
Singanore	N=5325	6 months	moderate of severe pair
0112 2017	N-JJ2J 69 (7 5)		
2013-2017 1 hoganital	00 (7.3) 75 0%		
			No improvement in a sta
	Minary IKK, all		areater than MCID
Spain Agoa goog	IN=/92	o montns	grouter that word
1999-2000	/1.9		
/ hospitals	/3.0%		
Rice 2018[51]	Primary TKR, all 18+	VAS/NRS pain	VAS >3
New Zealand	N=300	6, 12 months	
2012-2015	69 (10), range 48-90		
2012-2015 3 hospitals	69 (10), range 48-90 48.0%		
2012-2015 3 hospitals Sideris 2022[52]	69 (10), range 48-90 48.0% Primary TKR, all	VAS/NRS pain	NRS 4+

Page 45 of 69

1

BMJ Open

Prevalence of chronic pain after total hip or knee replacement

2				
3	2016-2018	67.1 (8.1)		
4	1 hospital	56.2%		
5	Singh 2014[53]	Primary TKR, all	Author own	Moderate-severe pain
7	USA	N=7229	question	
8	1993-2005	68 (10)	24 months	
9	1 hospital	56.0%		
10	Solborg 2022[54]	Brimony TKB probably	Authorown	To what extent have you
11		all	question	obtained relief: somewhat
12	USA	N-239	3 months	minimal or not at all
13 14	2020	66.2(8.5) range $37-87$	o montilo	High loss to follow up rate
14	22 surgeons	60.2 (0.0), range 37-07		5
16	Stanbana 2002[55]			No change aginerades in
17	Stephens 2002[55]	Primary TKR, all 50+		no change of increase in
18	USA	N=68	6 months	pair nom pre operative
19	Before 2001	67.4 (8.1), range 50-88		
20	1 hospital	54.0%		
21	Tang 2023[56]	Primary TKR probably,	VAS/NRS pain	NRS scores ≥4
23	China	all 65+	3 months	
24	2020-2021	N=196		
25	1 hospital	72		
26		75.1%		
27	Terradas-Monllor	Primary TKR or UKR, all	VAS/NRS pain	VAS 3+
28	2024[57]	18+	3, 6 months	
30	Spain	N=115		
31	2018-2020	70.5 (10.7)		
32 33	1 home rehabilitation service	66.1%		
34	Thomazeau 2016[58]	Primary TKR, all	VAS/NRS pain	NRS score ≥1/10 for the
35	France	N=109	6 months	last 8 days
36	2013	69.2 (9)		
37	1 hospital	71.6%		
30	Tian 2022[59]	Primary TKR or UKR, all	Author own	Moderate or severe pain on
40	China	<90	question	movement
41	2018-2019	N=271	24 months	
42	1 hospital	Not reported		
43		80.8%		
44	Utrillas-Compaired	Primary TKR, all	KSS pain 🔷	KSS pain poor
45 46	2014[60]	N=215	12 months	KSS may not be entirely
47	Spain	73 (6.35)		patient reported
48	2009	69.3%		
49	1 hospital			
50	van der Wees	Primary TKR all	VAS/NRS nain	30% or less improvement in
51	2017[61]	N=704	6 12 months	VAS pain
52 53	The Netherlands	65 (12)	0, 12 11011110	High loss to follow up rate
54	1993-2014	64 59/		at 6 and 12 months
55	1 hospital	04.070		
56	Vina 2020[62]	Primary TKR all	WOMAC nain	Less than MCID
57		N–315	24 months	
58 50	2005-2015	67 3 (8 6)		
53	2003-2013	0.0)		

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

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Prevalence of chronic pain after total hip or knee replacement



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



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

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Prevalence of chronic pain after total hip or knee replacement



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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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)

Judy	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall		
Aso 2020			\bigcirc								\bigcirc		
Attal 2014	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Brander 2003	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Buvanendran 2019	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Chodor and Kruczynski 2022	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ		
Dursteler 2021	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Edwards 2022	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Grosu 2016	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Heath 2021	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
lones 2000	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Õ		
Khalid 2021	Ŏ	Ŏ	Õ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Kurien 2018	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
_eung 2019	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Yes	
Mekkawy 2023	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	◯ No	
Nishimoto 2023	ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	ŏ	Ŏ	High	
Noiseux 2014	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Mode	rate
Phillips 2014	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Priol 2023	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Pua 2019	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Quintana 2006	ŏ	Ŏ	Ŏ	Ŏ	Ŏ	ŏ	Ŏ	ŏ	Ŏ	ŏ	Ŏ		
Rice 2018	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Sideris 2022	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Stephens 2002	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Ferradas-Monllor 2024	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
Thomazeau 2016	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
van der Wees 2017	Ŏ	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	ĕ		
Vaimann 2014	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ		
ran 2023	ě	ě	Ŏ	ě	ě	ě	Õ	ě	ě	ě	ĕ		

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	
Alzahrani TWH cohort 2011			\bigcirc								\bigcirc	
Aso 2020			Õ		۲	•			۲		0	
Attal 2014			Ō	•							$\overline{\bigcirc}$	
Baker 2007			Õ						•		\bigcirc	
Bell 2023		Ó	Ō	Ő		•	•	۲	Ŏ	•	Ō	
Birch 2019	•	•	Õ	Õ	•	۲		•	•	•		
Brander 2003			0								\bigcirc	
Buus 2022			\bigcirc								\bigcirc	
Clement 2014			\bigcirc				\bigcirc				\bigcirc	
Cole 2022			0	\bigcirc								
Dave 2017			\bigcirc								\bigcirc	
Dowsey 2012			\bigcirc				\bigcirc					
Escobar and Riddle 2014			\bigcirc	0								
Getachew 2021			\bigcirc								\bigcirc	
Grosu 2016			\bigcirc	\bigcirc								
Hardy 2022			\bigcirc								\bigcirc	
Kiran 2015			\bigcirc	\bigcirc								
Kornilov 2018			\bigcirc								\bigcirc	
Larsen 2021			\bigcirc	\bigcirc								
Latijnhouwers 2022			\bigcirc	\bigcirc								
Lee 2022			\bigcirc				\bigcirc				\bigcirc	
Leung 2019			\bigcirc				\bigcirc				\bigcirc	
Mahdi 2020			\bigcirc	0								
Mercurio 2020			\bigcirc								\bigcirc	
Mezey 2023			\bigcirc	\bigcirc			•					
Musbahi 2023			\bigcirc	\bigcirc								
Orr 2022			\bigcirc	\bigcirc		\bullet						
Petersen 2015			\bigcirc								\bigcirc	
Petersen 2018			\bigcirc	0								
Phillips 2014			\bigcirc								\bigcirc	
Rice 2018			\bigcirc								\bigcirc	
Utrillas-Compaired 2014			\bigcirc				\bigcirc					
van der Wees 2017			Ō	Ō		•						
W-Dahl 2014		Ó	Ó	Ó		Ó	Ó	Ó	Ó	Ŏ	Ó	
Wylde 2013			Ō			Ó					$\overline{\bigcirc}$	
Wylde 2019	Ā	é	Ó	Ō	é	é	Á	Ó	é	Ă		

Yes

No

High

Moderate

Prevalence of chronic pain after total hip or knee replacement

S4.4 TKR studies (24 months)

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall
Aso 2020			\bigcirc								\bigcirc
Attal 2014			0								\bigcirc
Brander 2003	•		0							۲	\bigcirc
Buvanendran 2019			0								\bigcirc
Chodor and Kruczynski 2022			0				\bigcirc			٠	\bigcirc
Dursteler 2021			\bigcirc								\bigcirc
Edwards 2022			0	0							
Grosu 2016			0	0							
Heath 2021			0	0							
Jones 2000			\bigcirc								

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Prevalence of chronic pain after total hip or knee replacement

S5. Forest plots of univariate meta-analyses in TKR studiesS5.1 TKR studies (3 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Solberg 2023	Author own question	⊢∙−⊣	31	239	13.0 (9.3 to 17.9)	•
Attal 2014	BPI	⊢	45	89	50.6 (40.3 to 60.8)	?
Nishimoto 2023	KOOS pain		16	68	23.5 (14.9 to 35.0)	?
Birch 2019	OKS pain	⊢∎⊣	88	589	14.9 (12.3 to 18.1)	•
Lee 2022	Pain disturbing sleep	⊢	69	172	40.1 (33.1 to 47.6)	?
Brander 2003	VAS/NRS pain	⊢ − − −1	26	116	22.4 (15.7 to 30.9)	?
Dursteler 2021	VAS/NRS pain	⊢ •−-	87	170	51.2 (43.7 to 58.6)	?
Grosu 2016	VAS/NRS pain	-■	11	114	9.6 (5.4 to 16.6)	•
Kim 2015	VAS/NRS pain	⊢ ∎−−−	16	94	17.0 (10.7 to 26.0)	?
Lavand'homme 2014	VAS/NRS pain	⊢•	12	128	9.4 (5.4 to 15.8)	?
Phillips 2014	VAS/NRS pain		26	96	27.1 (19.1 to 36.8)	?
Tang 2023	VAS/NRS pain	⊢	37	196	18.9 (14.0 to 25.0)	?
Terradas-Monllor 2024	VAS/NRS pain		31	115	27.0 (19.6 to 35.8)	?
Vuorenmaa 2008	VAS/NRS pain	⊢	9	51	17.6 (9.4 to 30.6)	?
Wylde 2019	WOMAC pain	⊢ •−-1	42	266	15.8 (11.9 to 20.7)	?
Random-effect Heterogeneity (tau ²): 0.51 (9	t s model 95% Crl 0.18 to 1.1)		546	2503	21.9 (15.7 to 29.6)	
- / / /	,	0 25 50 75 Proportion (%)	100			



Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Chodor and Kruczynski 2022	Author own question	⊢ − • −−−	11	69	15.9 (9.1 to 26.5)	?
Leung 2019	Author own question	┝┻─┤	10	243	4.1 (2.2 to 7.5)	?
Attal 2014	BPI		32	89	36.0 (26.7 to 46.4)	2
Edwards 2022	BPI	-∎	24	248	9.7 (6.6 to 14.0)	
Heath 2021	EQ 5D 5L pain/discomfort	H	1099	8299	13.2 (12.5 to 14.0)	•
Nishimoto 2023	KOOS pain	— •———————————————————————————————————	12	68	17.6 (10.3 to 28.6)	2
Khalid 2021	OKS pain	+	43702	531790	8.2 (8.1 to 8.3)	
Pua 2019	OKS pain	н	350	5325	6.6 (5.9 to 7.3)	2
Aso 2020	VAS/NRS pain	⊢ ∙	20	234	8.5 (5.6 to 12.9)	0
Brander 2003	VAS/NRS pain		21	116	18.1 (12.1 to 26.2)	2
Buvanendran 2019	VAS/NRS pain	⊢•	34	296	11.5 (8.3 to 15.6)	2
Dursteler 2021	VAS/NRS pain	⊢ •−−1	86	170	50.6 (43.1 to 58.0)	2
Grosu 2016	VAS/NRS pain	⊢ ∎]	7	114	6.1 (3.0 to 12.3)	ĕ
Kurien 2018	VAS/NRS pain	· · · · · · · · · · · · · · · · · · ·	14	50	28.0 (17.3 to 41.9)	2
Mekkawy 2023	VAS/NRS pain	⊢ •−−−1	11	112	9.8 (5.5 to 16.9)	ĕ
Noiseux 2014	VAS/NRS pain		31	215	14.4 (10.3 to 19.8)	0
Phillips 2014	VAS/NRS pain	⊢ •−−−	19	96	19.8 (13.0 to 29.0)	2
Priol 2023	VAS/NRS pain	⊢ •−−1	14	129	10.9 (6.5 to 17.5)	ĕ
Rice 2018	VAS/NRS pain		60	300	20.0 (15.9 to 24.9)	2
Sideris 2022	VAS/NRS pain	⊢ •−−1	15	179	8.4 (5.1 to 13.4)	õ
Terradas-Monllor 2024	VAS/NRS pain	↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓	21	115	18.3 (12.2 to 26.4)	õ
Thomazeau 2016	VAS/NRS pain	· · · ·	30	109	27.5 (20.0 to 36.6)	ĕ
van der Wees 2017	VAS/NRS pain	 ■-	41	704	5.8 (4.3 to 7.8)	ě
Yan 2023	VAS/NRS pain		102	470	21.7 (18.2 to 25.7)	ĕ
Jones 2000	WOMAC pain		54	292	18.5 (14.4 to 23.4)	õ
Quintana 2006	WOMAC pain	· · · · · · · · · · · · · · · · · · ·	199	792	25.1 (22.2 to 28.3)	õ
Stephens 2002	WOMAC pain	⊢−− −−−−−	11	68	16.2 (9.2 to 26.9)	2
Waimann 2014	WOMAC pain	┝┻┥┤	14	236	5.9 (3.5 to 9.8)	0
Random-effects	model		46044	550928	14.1 (10.9 to 17.9)	
meterogeneity (tau*): 0.	51 (95% CH 0.26 to 0.88)					
		0 25 50 75	100			
		Proportion (%)				

Prevalence of chronic pain after total hip or knee replacement

S5.3 TKR studies (12 months)

		Case	Total	Proportion (95% Crl)	Ro
Author own question		64	578	11.1 (8.8 to 13.9)	?
Author own question	H∎i	8	243	3.3 (1.7 to 6.4)	?
BPI		26	89	29.2 (20.7 to 39.5)	?
BPI	⊢	74	206	35.9 (29.7 to 42.7)	?
IKSS pain	⊢ ∎i	140	478	29.3 (25.4 to 33.5)	
KOOS pain	•	433	5564	7.8 (7.1 to 8.5)	?
KOOS pain	H=H	27	615	4.4 (3.0 to 6.3)	
KOOS pain	*	845	7476	11.3 (10.6 to 12.0)	
KOOS pain		105	2736	3.8 (3.2 to 4.6)	?
KSS pain	⊢ ∎—-i	12	215	5.6 (3.2 to 9.6)	
OKS pain		1583	9417	16.8 (16.1 to 17.6)	?
OKS pain	⊢ ∎	58	589	9.8 (7.7 to 12.5)	ē
OKS pain		94	217	43.3 (36.9 to 50.0)	?
OKS pain	H a -I	70	1025	6.8 (5.4 to 8.5)	ē
OKS pain		57	608	9.4 (7.3 to 12.0)	ē
Pain disturbing sleep		11	172	6.4 (3.6 to 11.2)	2
VAS/NRS pain	⊢∎1	20	234	8.5 (5.6 to 12.9)	· · ·
VAS/NRS pain		15	116	12.9 (7.9 to 20.3)	?
VAS/NRS pain	⊢ ∎	10	114	8.8 (4.8 to 15.5)	ĕ
VAS/NRS pain	—	24	111	21.6 (14.9 to 30.2)	2
VAS/NRS pain	—	18	100	18.0 (11.6 to 26.8)	2
VAS/NRS pain	H 	13	185	7.0 (4.1 to 11.7)	ĕ
VAS/NRS pain	— •—1	99	282	35.1 (29.8 to 40.9)	ē
VAS/NRS pain		11	45	24.4 (14.1 to 39.0)	2
VAS/NRS pain		17	78	21.8 (14.0 to 32.3)	?
VAS/NRS pain	⊢ ∎]	25	200	12.5 (8.6 to 17.8)	ĕ
VAS/NRS pain	—	15	96	15.6 (9.6 to 24.3)	0
VAS/NRS pain		45	300	15.0 (11.4 to 19.5)	0
VAS/NRS pain	H H	31	704	4.4 (3.1 to 6.2)	ĕ
WOMAC pain	H H -1	55	482	114 (89 to 146)	0
WOMAC pain		26	267	97 (67 to 13.9)	0
WOMAC pain	H=-1	270	1616	16.7 (15.0 to 18.6)	ĕ
WOMAC pain		210	1010	20.8 (14.0 to 29.8)	
WOMAC pain		96	575	16.7 (13.9 to 20.0)	
WOMAC pain		15	57	26.3 (16.5 to 39.2)	
riona io punt		15	07	20.0 (10.0 (0 00.2)	<u>u</u>
	Author own question BPI BPI IKSS pain KOOS pain KOOS pain KOOS pain KOOS pain KSS pain OKS pain OKS pain OKS pain OKS pain OKS pain OKS pain OKS pain VAS/NRS pain	Author own question	Author own questionImage: Constraint of the second se	Author own question + 8 243 BPI - 26 89 BPI - 74 206 IKSS pain + 433 5564 KOOS pain + 433 5564 KOOS pain + 433 5564 KOOS pain + 27 615 KOOS pain + 105 2736 KSS pain + 105 2736 KSS pain + 1583 9417 OKS pain + 1583 9417 OKS pain + 70 1025 OKS pain + 70 1025 OKS pain + 70 1025 OKS pain + 11 172 VAS/NRS pain + 13 185 VAS/NRS pain + 13 185 VAS/NRS pain + 17 78 VAS/NRS pain + 17 78 VAS/NRS pain + 17 78 VAS/NRS pain +	Author own question → 8 243 3.3 (1.7 to 6.4) BPI → 26 89 29.2 (20.7 to 39.5) BPI → 74 206 35.9 (29.7 to 42.7) IKSS pain → 433 5564 7.8 (7.1 to 8.5) KOOS pain + 433 5564 7.8 (7.1 to 8.5) KOOS pain + 433 5564 7.8 (7.1 to 8.5) KOOS pain + 105 2736 3.8 (3.2 to 4.6) KSS pain + 12 215 5.6 (3.2 to 9.6) OKS pain + 1583 9417 16.8 (16.1 to 17.6) OKS pain + 70 1025 6.8 (5.4 to 8.5) OKS pain + 70 1025 6.8 (5.4 to 8.5) OKS pain + 70 1025 6.8 (5.4 to 8.5) OKS pain + 11 172 6.4 (3.6 to 11.2) Pain districting sleep + 11 172 6.4 (3.6 to 11.2) VASINRS pain + 20 234 8.5 (5.6 to 12.9) VASINRS pain + 10 114 8.4 (8.10 to 52.3) VASINRS pain + 13 106 18.0 (11.6 to 26.8) VASINRS pain<

S5.4 TKR studies (24 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Singh 2014	Author own question	•	499	7229	6.9 (6.3 to 7.5)	?
Tian 2022	Author own question	⊢∎⊣	228	721	31.6 (28.3 to 35.1)	?
Dowsey 2012	IKSS pain	⊨∎⊣	137	478	28.7 (24.8 to 32.9)	ĕ
Lyman 2018	KOOS pain	•	289	3815	7.6 (6.8 to 8.5)	ĕ
Kiran 2015	OKS anchoring question	⊦∎⊣	61	608	10.0 (7.9 to 12.7)	ĕ
Leppanen 2021	VAS/NRS pain	⊢-■	50	205	24.4 (19.0 to 30.7)	2
Lundblad 2008	VAS/NRS pain		15	69	21.7 (13.6 to 33.0)	?
Ghomrawi 2017	WOMAC pain		40	247	16.2 (12.1 to 21.3)	?
Vina 2020	WOMAC pain	⊢∎−−↓	36	315	11.4 (8.4 to 15.4)	?
Wylde 2019	WOMAC pain	⊦∎⊣	21	266	7.9 (5.2 to 11.8)	?
Random-effects model			1376	13953	14.6 (9.4 to 22.4)	
Heterogeneity (tau ²): 0.	51 (95% Crl 0.15 to 1.32)					
		0 25 50 75 Proportion (%)	100			



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

	Multivariate n	neta-analysis	Univariate m	eta-analysis
Time	Median (95% Crl)	tau ² (95% Crl)	Median (95% Crl)	tau ² (95% CrI)
3 months	21.2	0.49	21.9	0.51
	(16.9 to 26.4)	(0.28 to 0.91)	(15.6 to 29.4)	(0.18 to 1.1)
6 months	14.6	0.56	14.1	0.51
	(11.9 to 17.8)	(0.34 to 0.91)	(10.9 to 17.9)	(0.27 to 0.9)
12 months	12.6	0.63	12.6	0.61
	(10.3 to 15.5)	(0.41 to 0.99)	(9.9 to 15.9)	(0.35 to 0.99)
24 months	14.2	0.58	14.6	0.52
	(10 to 20.1)	(0.25 to 1.55)	(9.5 to 22.4)	(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)

S8.1 Geographical regions

Subgroup	No. Studies	Median (95% Crl)	tau ² (95% Crl)					
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)					
CO O Cotting								
So.2 Setting								

S8.2 Setting

Subgroup	No. Studies	Median (95% Crl)	tau ² (95% Crl)				
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) 20.55 (0.07 to					
		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	3 10.82 (3.35 to 30.39) 0.26 (0 to					
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	3 8.93 (4.2 to 16.32) 0.05 (0 to 1.					
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)				

Prevalence of chronic pain after total hip or knee replacement

S8.3 Pain outcome instruments

Multidimensional Not validated Simple Multidimensional Not validated Simple	5 1 9 9	3 Months 26.76 (12.16 to 49.19) 12.98 (0 to 100) 20.6 (13.08 to 31.41) 6 Months	0.7 (0.09 to 3.37) NA 0.5 (0.11 to 1.47)
Multidimensional Not validated Simple Multidimensional Not validated Simple	5 1 9 9	26.76 (12.16 to 49.19) 12.98 (0 to 100) 20.6 (13.08 to 31.41) 6 Months	0.7 (0.09 to 3.37) NA 0.5 (0.11 to 1.47)
Not validated Simple Multidimensional Not validated Simple	1 9 9	12.98 (0 to 100) 20.6 (13.08 to 31.41) 6 Months	NA 0.5 (0.11 to 1.47)
Simple Multidimensional Not validated Simple	9	20.6 (13.08 to 31.41) 6 Months	0.5 (0.11 to 1.47)
Multidimensional Not validated Simple	9	6 Months	
Multidimensional Not validated Simple	9		
Not validated Simple	•	13.68 (8.49 to 22.5)	0.56 (0.14 to 1.57)
Simple	2	7.65 (0 to 99.79)	1.72 (0 to 219.88)
	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)

S9. Doi plots and the LFK indexes in TKR studies S9.1 TKR studies (3 months)







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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% Crl)	tau ² (95% Crl)						
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 Mor	nths							
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 Mo	nths							
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)						
*Abbroviation: TKD: Total Knoo	Poploomont:	IIKP: Unicomportmontal	Knog Bonloggmont						

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

Prevalence of chronic pain after total hip or knee replacement

S11. Characteristics of THR studies

5 6 7 8	Study Country Recruitment dates	Operation Number of patients Age (SD), range	Pain measure	Definition of unfavourable pain outcome High risk of bias concern			
9 10 11 12 13 14 15	Cleveland Clinic OMEPrimary THR, allArthroplasty GroupN=34492020[1]Median 65 (IQR 57USA57.4%2015-20186 hospitals		HOOS pain 12 months	Less than MCID			
16 17 18 19 20	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			
21 22 23 24 25	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			
26 27 28 29 30	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			
31 32 33 34 35 36	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			
37 38 39 40 41 42	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			
43 44 45 46 47 48	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)			
49 50 51 52	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			
53 54 55 56	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			
57 58 59 60	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			

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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 scores ≥4 Note, n and losses to follow up estimated as proportions because n hips and knees reported together		

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Prevalence of chronic pain after total hip or knee replacement



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

D2	D1	D2 D3	D4	D5	D6	D7	D8	D9	D10	Overall	
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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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Secondary Subject Heading:	Epidemiology, Rehabilitation medicine
Keywords:	Chronic Pain, Systematic Review, Meta-Analysis, Hip < ORTHOPAEDIC & TRAUMA SURGERY, Knee < ORTHOPAEDIC & TRAUMA SURGERY, ORTHOPAEDIC & TRAUMA SURGERY





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

Authors and affiliations 5

- 6 Hung-Yuan Cheng^{1*}, Andrew D Beswick^{1,2*}, Wendy Bertram^{1,2}, Mohammad Ammar
- 7 Siddiqui¹, Rachael Gooberman-Hill¹, Michael R Whitehouse^{1,2}, Vikki Wylde^{1,2}
- 8 1 Bristol Medical School, University of Bristol, Bristol, BS8 2PN, United Kingdom
- 9 2 NIHR Bristol Biomedical Research Centre, University Hospitals Bristol and Weston NHS
- 10 Foundation Trust and University of Bristol, United Kingdom

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- 12 *equal contribution
- 13

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Corresponding author: 17

- set terier 18 Professor Vikki Wylde: V.Wylde@bristol.ac.uk
- 19 Address: Musculoskeletal Research Unit, Translational Health Sciences, Bristol Medical
- 20 School, Learning and Research Building, Level 1, Southmead Hospital, University of Bristol,
- 21 BS10 5NB, UK

Running title 22

23 Prevalence of chronic pain after total hip or knee replacement

Keywords 24

25 Chronic pain; Total hip replacement; Total knee replacement; Systematic review; Meta-26 analysis

1 2						
2 3 4	28	Abstract				
5 6	29	Objectives				
7 8	30	To update our previous systematic review to synthesise latest data on the prevalence of				
9	31	long-term pain in patients who underwent total hip replacement (THR) or total knee				
10 11	32	replacement (TKR). We aim to describe the prevalence estimates and trends in this review.				
12 13	33	Design				
14 15	34	Systematic review and meta-analysis				
15 16	0.5					
17 18	35	Data Sources				
19	36	Update searches were conducted in MEDLINE and Embase databases from 1st January				
20 21	37	2011 to 17th February 2024. Citation tracking was used to identify additional studies.				
22 23	38	Eligibility Criteria				
24	39	We included prospective cohort studies reporting long-term pain after THR or TKR at 3, 6,				
25 26	40	12 and 24 months post-operative.				
27 28	41	Data Extraction and Synthesis				
29 30 31 32 33 34 35 36 37 38 39	42	Two reviewers independently identified studies as eligible. One reviewer conducted data				
	43	extraction, checked by a second reviewer. The risk of bias assessment was performed using				
	44	Hoy's checklist Bayesian random-effects meta-analysis was used to synthesise the results				
	••					
	45	Results				
	46	For TKR, sixty-eight studies with 89 time points, including 598,498 patients, were included.				
	47	Multivariate meta-analysis showed a general decrease in pain proportions over time: 21.9%				
40 41	48	(95% Crl 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				
42	49	12 months, and 14.6% (9.5 to 22.4) at 24 months. Considerable heterogeneity, unrelated to				
43 44	50	examined moderators, was indicated by substantial prediction intervals in the univariate				
45	51	models. Substantial loss to follow-up and risk of bias led to low confidence in the results. For				
46 47	52	THR, only eleven studies were included, so it was not possible to describe the trend.				
48	53	Univariate meta-analysis estimated 13.8% (8.5-20.1) and 13.7% (4.8-31.0) of patients				
49 50	54	experiencing long-term pain 6 and 12 months after THR, respectively, though concerns in				
51 52	55	risk of bias results reduced confidence in these findings.				
52 53	56	Conclusions				
55	57	Our review suggests that approximately 22% of patients report unfavourable pain 3 months				
56 57	58	post-TKR, with 12-15% experiencing long-term pain up to 2 years. At least 14% report				
58 59 60	59	unfavourable pain 6-12 months after THR. Given the prevalence of chronic post-surgical				

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60 pain, implementing existing and developing new preventive and management strategies is

61 crucial for optimal patient outcomes.

- 62 Study registration
- 63 PROSPERO CRD42023475498

66 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.

77 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.¹² About 100,000 each of primary total knee and hip replacements were performed in the UK in 2022,³⁴ 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 increase⁶⁷ 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.⁹¹⁰ 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 pain¹⁰ ¹²⁻¹⁴, unchanged pain¹⁵, residual pain¹⁶⁻¹⁸, and worsening pain¹⁹ 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.

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

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110 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 MOOSE²⁵ (Supplementary material S1) and relevant contents in
 PRISMA²⁶ guidelines and the Cochrane handbook.²⁷

1 120 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.

¹ 128 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

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

146 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.

²⁰ 154 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.

⁵⁵ 175 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.

¹⁰ 182 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 (Crls) 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 10⁵) 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.

194 To account for the multiple time follow-ups reported in certain studies, we adopted a
 195 Bayesian, hybrid, multivariate meta-analysis of multiple factors³¹ to describe the proportions
 196 across time points by borrowing information and accounting for within- and between-study
 197 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.

⁴⁵ 203 Exploration of heterogeneity ⁴⁶

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.

56 209 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

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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

Patient and public involvement

chronic pain after TKR.

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- 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. 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. ³³Patient 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

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

exclusion at the full-text stage are summarised in Figure 1. Some articles from our previous

Individual study characteristics are summarised in S3. The grouped characteristics in Table

studies (n=39) collected their data at a single hospital, followed by multiple hospitals (n=18).

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

Overall, 598,498 patients were included in the 68 studies with a median sample size per

Searches of MEDLINE, Embase, citation tracking in Web of Science and inclusion of

studies with 143.101 THR participants were included. Study selection and reasons for

review were excluded as the follow up period was longer than 24 months.

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Results

Total knee replacement

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% Crl 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 Crls (S6). The substantial prediction intervals in the univariate models suggested considerable heterogeneity.

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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

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3 4	302	experienced unfavourable pain outcomes in each study (<u>Table 2</u>). By assuming 10% to 30%
5	303	of participants lost to follow-up might experience unfavourable pain, this approach could
0 7	304	yield more realistic estimates, given the limited literature available for further imputation.
8 9	305	Total hip replacement
10 11	306	Eleven studies reported unfavourable pain outcomes in individuals who underwent THR. The
12	307	characteristics of these studies are summarised in S11. Only one study reported
13 14	308	unfavourable pain outcomes at the 3-month and 24-month time points, so a trend cannot be
15	309	established. Studies reported ranges of people with unfavourable pain at 6 months of 8.3 to
16 17	310	16.3%, and at 12 months of 3.9 to 25.6% (<u>Figure 4</u>).
18 19	311	Meta-analysis of unfavourable pain outcomes provided similar results at 6 and 12 months.
20	312	with 13.8% (8.5 to 20.1) and 13.7% (4.8 to 31.0), respectively. However, concerns regarding
21 22	313	the risk of bias assessment (S12) lead to low confidence in these results.
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316 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.

329 Our meta-analyses suggest that the proportion of people with an unfavourable level of pain
 330 after TKR decreases between three and six months after surgery and then remains stable
 331 until at least two years. While recognising the associated wide credible intervals,
 332 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

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3 388 aimed at the prevention and/or management of chronic pain after joint replacement are
 5 389 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 revision⁵⁶ 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 replacement⁶⁰⁻⁶³. 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.8283 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

447 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 optimisemanagement of chronic pain after joint replacement and evaluation of new preventive
- 449 management of chronic pain after joint replacement and evaluation of new preventive450 strategies that target established risk factors.
- ⁴⁹₅₀ 451 Ethical approval

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

55 454 Data sharing

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

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480 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 outc	ome reporte	d			
VAS/NRS pain	29	9	16	13	2
WOMAC pain	13		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	1	1			
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	1	1			1
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

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4		Canada	2	0	1	1	0
5		Finland	2	1	0	0	1
6		Japan	2	1	2	1	0
7		Singapore	2	0	2	1	0
8		South Korea	2	2	0	1	0
9		The Netherlands	2	0	1	2	0
10		Hungary	1	0	0	1	0
11		Italy	1	0	0	1	0
12		New Zealand	1	0	1	1	0
13		Norway	1	0	0	1	0
14		Poland	1	0	1	0	0
15		Russia	1	0	0	1	0
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483 Table 2. Worst-best case scenario analyses in TKR studies

Proportion* (%)	Median (95% Crl)	τ² (95% Crl)
	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)	0.51(0.27 - 0.07)
100 /0	12 month	0.30 (0.31 - 1)
0%	12 61 (9 88 - 15 84)	0.61(0.34 - 0.97)
10%	15 22 (12 20 18 23)	0.01(0.34 - 0.37)
20%	17.44 (14.5, 20.66)	0.44(0.23-0.72)
20%	10.6 (16.46 22.07)	0.37(0.2-0.0)
J0 /6	21.6 (18.00, 25.17)	0.36 (0.2 0.58)
40 /0 50%	21.0(10.09 - 25.17)	0.30(0.2 - 0.30)
50% 60%	25.0(19.00 - 27.40)	0.37(0.2 - 0.0)
60% 70%	23.04(21.74-29.09)	0.4(0.23 - 0.04)
70%	27.57 (23.20 - 32.21)	0.44(0.25-0.7)
00%	29.57 (24.55 - 54.51)	0.49(0.26-0.76)
90%	31.53 (20.01 - 30.95)	0.55(0.3-0.87)
100%	33.02 (27.09 - 39.01)	0.62 (0.37 - 0.99)
00/		0.50 (0.45 4.00)
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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792 Figure legends

793 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.

⁴ 808 Supplementary materials

- 6 809 S1. PRISMA checklist
- 87 810 S2. Search strategy as applied in MEDLINE and Embase
 - 811 S3. Characteristics of TKR studies
 - 812 S4. Traffic light plot of the risk of bias assessment in TKR studies
 - 813 S5. Forest plots of univariate meta-analyses in TKR studies
- 814 S6. Table of multivariate and univariate meta-analysis results in TKR studies
- ² 815 S7. Meta-regression analyses in TKR studies
- 816 S8. Subgroup analyses in TKR studies
- ⁴ 817 S9. Doi plots and the LFK indexes in TKR studies
- 5 818 S10. Sensitivity analyses in TKR studies
- 6 819 S11. Characteristics of THR studies
- $^{+7}_{48}$ 820 S12. Traffic light plot of the risk of bias assessment in THR studies





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Study Case Total Proportion (95% Crl) RoB 3 Months Tang 2023 6.7 (3.1 to 14.2) 6 Months Erlenwein 2017 20 24 128 242 150 784 14.4 (9.3 to 21.7) 8.3 (5.4 to 12.5) 16.0 (11.0 to 22.8) 16.3 (13.9 to 19.1) ? ? • Jones 2000 Page 2016 Quintana 2006 RE Model Heterogeneity (tau²): 0.08 (95% Crl 0 to 0.82) 13.8 (8.5 to 20.1) 12 Months Cleveland Clinic 2020 Mezey 2023 Nikolajsen 2006 Palazzo 2014 Ray 2020 3.9 (3.3 to 4.6) 23.9 (16.1 to 33.8) 10.3 (8.7 to 12.1) 25.6 (18.8 to 33.8) 18.4 (18.2 to 18.6) 127 33 23488 1231 129 127660 ž RE Model Heterogeneity (tau²): 0.9 (95% Crl 0.13 to 4.28) 13.7 (4.8 to 31.0) 24 Months Singh and Lewallen 2010 435 4.8 (4.3 to 5.2) Proportion (%) 1291x645mm (118 x 118 DPI) For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Prevalence of chronic pain after total hip or knee replacement

Supplementary materials

S1. MOOSE checklist	3
S2. Search Strategy as applied in MEDLINE and Embase	5
S2.1 Total knee replacement	5
S2.2 Total hip replacement	5
S3. Characteristics of TKR studies	7
References	14
S3.1 Mean age and range	19
S3.2 Proportion of females	19
S3.3 Data collection timeframe	20
S3.4 Proportions of lost to follow-ups and revisions	21
S4. Traffic light plot of the risk of bias assessments in TKR studies	22
S4.1 TKR studies (3 months)	22
S4.2 TKR studies (6 months)	23
S4.3 TKR studies (12 months)	24
S4.4 TKR studies (24 months)	25
S5. Forest plots of univariate meta-analyses in TKR studies	26
S5.1 TKR studies (3 months)	26
S5.2 TKR studies (6 months)	26
S5.3 TKR studies (12 months)	27
S5.4 TKR studies (24 months)	27
S6. Table of multivariate and univariate meta-analysis results in TKR studies	28
S7. Meta-regression analyses in TKR studies	29
S7.1 Mean age	29
S7.2 Proportion of females	29
S7.3 Sample sizes	29
S8. Subgroup analyses in TKR studies	30
S8.1 Geographical regions	30
S8.2 Setting	30
S8.3 Pain outcome instruments	31
S8.4 Cut-off definitions	31
S9. Doi plots and the LFK indexes in TKR studies	33
S9.1 TKR studies (3 months)	33
S9.2 TKR studies (6 months)	33
S9.3 TKR studies (12 months)	34
S9.4 TKR studies (24 months)	34

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S10. Sensitivity analyses	35
S11. Characteristics of THR studies	36
References	37
S11.1 Proportions of lost to follow-ups and revisions	39
S12. Traffic light plot of the risk of bias assessments in THR studies	40

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P	revalence of chronic pain after total hip or knee replacement	en-2024- ppyright,	
S	1. MOOSE checklist	088975 includir	
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R	eporting of background	use Se	
1	Problem definition		Introduction
2	Hypothesis statement	Page 4 ap 25	Introduction
3	Description of Study Outcome(s)	Page 5 8 3 0	Outcome, Methods
4	Type of exposure or intervention used	Page 5 to text	Eligibility Criteria, Methods
5	Type of study design used	Page 5 and d	Eligibility Criteria, Methods
6	Study population	Page 5 ata m BEE	Eligibility Criteria, Methods
R	eporting on search strategy	inir S)	
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	trai	Supplementary S2
9	Effort to include all available studies, including contact with authors	Page 5-🗗 🔓	Searches, Methods
1(D Databases and registries searched	Page 5 👷 🛃	Searches, Methods
1'	Search software used, name and version, including special features used (e.g., explosion)	Page 6 and siin c	Study selection and dat collection, Methods
12	2 Use of hand searching (e.g., reference lists of obtained articles)	Page 5 ni	Searches, Methods
13	3 List of citations located and those excluded, including justification	une 1. ar tech	Figure 1 (PRISMA flowchart)
14	4 Method for addressing articles published in languages other than English	Page 5 0	Searches, Methods
1	5 Method of handling abstracts and unpublished studies	Page 5 8 8	Searches, Methods
16	5 Description of any contact with authors	Page 5-	Searches, Methods
R	eporting of methods	Ag	
17	7 Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	ence	Table 1
18	8 Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Page 6 Bi	Study selection and dat collection, Methods

	BMJ Open	omjope by cop	
Preva	alence of chronic pain after total hip or knee replacement	:n-2024-(>yright, i	
19	Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Page 6 udin	Study selection and dat collection, Methods
20	Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	on 21 Ig for u	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 es r	Risk of bias assessmer Methods
22	Assessment of heterogeneity	Page 7 elated	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-text and t	Data synthesis approac Methods
24	Provision of appropriate tables and graphics	dat:	Results
Repo	orting of results		
25	Graphic summarizing individual study estimates and overall estimate	inii	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)	A jo	Tables S7, S8, and S1
28	Indication of statistical uncertainty of findings	trai	Table 2 and S6
Repo	orting of discussion	nin n.b	
29	Quantitative assessment of bias (e.g., publication bias)	<u> </u>	Figures S9
30	Justification for exclusion (e.g., exclusion of non–English-language citations)	and	Not applicable
31	Assessment of quality of included studies	l sir	Figures 2 and 4
Repo	orting of conclusions	nila J	
32	Consideration of alternative explanations for observed results	ar t	Conclusion
33	Generalization of the conclusions (i.e., appropriate for the data presented and within	e 1. ech	Conclusion
	the domain of the literature review)	4, 2 nol	
34	Guidelines for future research	025 log	Conclusion
35	Disclosure of funding source	5 at	Sources of funding

From: Brooke BS, Schwartz TA, Pawlik TM. MOOSE Reporting Guidelines for Meta-analyses of Observational Studies. JAMA Surg. 2021;156(8):789 Bijographic Provide Provide

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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.

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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.
- or 8 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 concerr
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/severed 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

Chodor and	Primary TKR, all 48+	Author own	Pain severely limiting daily
Kruczynski 2022[10]	N=69	question	life
Poland	67.6 (7.42), range 48-84	6 months	
2016	76.7%		
1 hospital			
Clement 2014[11]	Primary TKR, all	Author's own	Fair or poor
UK	N=578	question "How	High loss to follow up rate
2010	70 (9.6), range 39-91	surgery relieve	
1 hospital	58.4%	pain in your	
		affected joint?"	
		12 months	
Cole 2022[12]	Primary TKR, all	OKS pain	<14 points OKS
UK	N=1025	12 months	
2010-2015	70		
2 hospitals	55.8%		
Dave 2017[13]	Primary TKR probably,	WOMAC pain	WOMAC pain score <
USA	all 40+	12 months	MCID (WOMAC pain of 15)
2012-2014	N=267		
3 hospitals	66 (9)		
	61.0%		
Dowsey 2012[14]	Primary TKR, all	IKSS pain	IKSS pain score <30
Australia	N=478	12, 24 months	
2006-2007	70.8 (8.3), range 45-90		IKSS may not be optically
1 hospital	69.2%		patient reported at 12 and
			24 months
Dursteler 2021[15]	Primary TKR, all 18+	VAS/NRS pain	NRS 0.3/1 or greater at rest
Spain	N=170	3, 6 months	
2014-2017	73.1 (7.1)		
Spain	73.3%		
1 hospital			
Edwards 2022[16]	Primary TKR, all 45+	BPI	4/10 or greater
USA	N=248	6 months	
2012-2018	65.1 (8.2)		High loss to follow up rate
2 hospitals	59.5%		
Escobar and Riddle	Primary TKR, all	WOMAC pain	Number not attaining PASS
2014[17]	N=1616	12 months	(i.e. "No" in the question, "If
Spain	71.6 (6.8)		you had to be the rest of
2003-2006	70.0%		your life with the symptoms
15 hospitals	10.070		you have now, now would you feel?") as the twenty-
			fifth percentile of the final
			score at 1 year instead of
			the seventy-fifth percentile
			(reverse option for vvOMAC 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

Ξ				
3	Norway	N=206	12 months	
4	2012-2014	68 (9)		
5	1 hospital	66.0%		
6 7	Chamrowi 2017[10]	Drimony TKP oll	WOMAC nain	Number pet appioving
/	Giloiniawi 2017[19]			MCID (baseline-adjusted
0	USA	N=247	24 months	MCIDs as described by
9 10	2010-2012	68 (10)		Escobar et al.[70])
10	1 hospital	65.0%		
12	Grosu 2016[20]	Primary TKR probably,	VAS/NRS pain	Moderate to severe pain
13	Belaium	all	3. 6. 12 months	
14	2009-2010	N=114		High loss to follow up rate
15		66 (10)		at 3. 6 and 12 months
16	i suigeon	65.8%		,
17	Hardy 2022[21]	Primary TKP all >18		VAS >30/100
18				VA3 -30/100
19	France	N=111	12 months	
20	2014-2015	73.3 (9.3) range 29-92		
21	1 hospital	65.0%		
2Z ·	Heath 2021[22]	Primary and revision	EQ-5D 5L pain/	Moderate/ severe or
25	Australia	TKR, all	discomfort	extreme pain EQ 5D 5L
24	2018-2020	N=8299	6 months	pain/discomfort
26	14 hospitals	67.5 (8.8)		
27	44 Hospitals	56.4%		High loss to follow up rate
28	lones 2000[23]	Primary TKP all 10+		Moderate/ severe pain
29	Canada		6 months	defined as a gain of <10
30		N=292	6 monuns	points on the WOMAC pain
31	1995-1997	69.2 (9.2)		dimension
32	1 health region	59.0%		
33	Khalid 2021[24]	Primary TKR or UKR, all	OKS pain	OKS-pain score of 14 or
34	UK	N=531,790	6 months	less at six months after
35	2008-2016	69.7 (9.4)		knee replacement can be
30 27	National registry	56.6%		considered to be in chronic
38			N (4 Q (9) D Q)	
39	Kim 2015[25]	Primary IKR, all women	VAS/NRS pain	>5 points on an 11 point
40	South Korea	N=94	3 months	vAS/NRS (verbal numeric
41	2013-2014	70.18 (5.74), range 20-		rating scale)
42	1 hospital	80		
43		100%		
44	Kiran 2015[26]	Primary TKR, all	OKS pain	Has your knee replacement
45	UK	N=608	12. 24 months	operation decreased your
46	2003-2007	72	,	knee pain?
47	1 hospital	61 4%		
48	i nospital	01.478		High loss to follow up rate
49				at 12 and 24 months
50 -	Kornilov 2018[27]	Primary TKR, all 18+	VAS/NRS pain	Not at least a two-point or
52	Russia	N=100	12 months	approximately 30%
53	2014	63 (8) range 47-81	-	(clinically significant)
54	1 hospital	95.0%		decrease in rating of pain
55	поэрна	00.070		Interference with walking
56				(NRS scale 0.10)
57	Kurion 2019[20]	Drimony TVD probably		4 or groater
58		all		4 UI YIEALEI
59	UK	N-50	6 months	
60	Before 2017	N-30		

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1 hospital	66.4 (8.3)		
	60.0%		
Larsen 2021[29]	Primary TKR, all 18+	VAS/NRS pain	Pain intensity at rest >3
Denmark	N=185	12 months	Liberto La casta da da Una como casta
2015-2016	68.8 (8.9)		High loss to follow up rate
1 hospital	55.7%		
Latijnhouwers	Primary TKR, all	VAS/NRS pain	Moderate to severe pain
ZUZZ[JU] The Netherlands	N=282	12 months	(NR3 24)
	66 (8.4)		High loss to follow up rate
2 hospitals	63.0%		
z nospilais	Drimony TKD or LIKD oll		NDC >1/10
2014[31]		2 months	NR3 24/10
Belaium	68 (10)	5 11011115	
2012	66 4%		
1 surgeon	00.47		
Lee 2022[32]	Primary TKR probably	Pain disturbing	Night pain was defined as
South Korea	all	sleep	pain around the knee
2017-2019	N=172	3, 12 months	experienced at night that
2 surgeons	70.7 (4.3)		could disturb the patient's
2 ourgoono	89.2%		sleep
Leppanen 2021[33]	Primary TKR, 65 years	VAS pain	VAS >30
Finland	or younger	exercise	
2012-2014	N=205	24 months	
1 hospital	60		
	63.0%		
Leung 2019[34]	Primary TKR, all	Author own	No change or worsening
Singapore	N=243	question	pain/ slightly better
2015	66 (8.3)	6, 12 months	
1 hospital	78.6%		
Lundblad 2008[35]	Primary TKR, all	VAS/NRS pain	Pain at rest, VAS >2/10
Sweden	N=69	24 months	
Before 2006	68		
1 hospital	50.7%		
Lyman 2018[36]	Primary TKR, all	KOOS pain	Number not achieving
USA	N=3815	24 months	MCID (8 by distribution-
2007-2012	74 (6)		
1 hospital	63.0%		High loss to follow up rate
Mahdi 2020[37]	Primary TKR, all	KOOS pain	8 cut off
Sweden	N=615	12 months	
2016-2018	69.7		High loss to follow up rate
3 hospitals	52.2%		J
Mekkawv 2023[38]	Primary TKR. all	VAS pain	Probably NRS score of ≥1
USA	N=112	6 months	in defined sites
2021	65.5 (9.2)		
4 surgeons	69.0%		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]	Primary TKR, all >18	VAS/NRS pain	VAS >30 residual pain
Italy	N=45	12 months	
2015-2017	69.6 (7.8)		
1 hospital	65.0%		
Mezey 2023[40]	Primary TKR probably,	WOMAC pain	Not exceeding MCID
Hungary	all	12 months	(WOMAC pain of 13.3)
2019-2020	N=101		
2 hospitals	69.2		High loss to follow up rate
	Not reported		
Musbahi 2023[41]	Primary TKR, all 40+	WOMAC pain	WOMAC pain score
USA	N=575	12 months	(converted to a 0-to-100
2011-2014	66.3 (8.3)		scale) improvement of <20
4 hospitals	60%		High loss to follow up rate
Nishimoto 2023[42]	Primary TKR, all with no	KOOS pain	Not achieving MCID of 10
.lanan	complications	3 6 months	(3 months) and 13 (6
2021-2023	N=68	o, o montrio	months). MCID was
1 hospital	75.1 (7.3)		calculated using the ancho
Ποοριαί	80.9%		method.[/2]
Noiseux 2014[43]	Primary TKR, all 30+	VAS/NRS pain	Moderate or severe pain
USA	N=215	6 months	with range of motion, VAS
Before 2012	61.7 (9.8)		≥1
2 hospitals	58.0%		
	6		Concern over VAS ≥1 being too inclusive
Orr 2022[44]	Primary TKR, all	KOOS pain	Not achieved PASS (i.e.
USA	N=7476	12 months	"No" in the question,
2016-2019	67 (9.0)		activity you have during
9 hospitals	60.8%		your daily life, your level of
			pain and also your activity
			limitations and participation
			the current state of your
			knee satisfactory?") for
			KOOS pain
			High loss to follow up rate
Petersen 2015[45]	Primary TKR, all	VAS/NRS pain	VAS >3
Denmark	N=78	12 months	
Before 2014	69		High loss to follow up rate
1 hospital probably	59.0%		
Petersen 2018[46]	Primary TKR probably,	VAS/NRS pain	<30% reduction in pain
Denmark		12 months	
	all		
Before 2017	all N= 200		
Before 2017 1 hospital	all N= 200 69 (1.2)		
Before 2017 1 hospital	all N= 200 69 (1.2) 57.0%	V/404/22	N40-0
Before 2017 1 hospital Phillips 2014[47]	all N= 200 69 (1.2) 57.0% Primary TKR, all	VAS/NRS pain	VAS >3
Before 2017 1 hospital Phillips 2014[47] UK	all N= 200 69 (1.2) 57.0% Primary TKR, all N= 96	VAS/NRS pain 3, 6, 12 months	VAS >3
Before 2017 1 hospital Phillips 2014[47] UK 2009-2010	all N= 200 69 (1.2) 57.0% Primary TKR, all N= 96 70.6	VAS/NRS pain 3, 6, 12 months	VAS >3

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Prevalence of chronic pain after total hip or knee replacement

Priol 2023[48]	Primary TKR, all	VAS/NRS pain	VAS 4+
France	N=129	6 months	
2011-2012	74 (10), range 45-94		High loss to follow up rate
1 hospital	72.3%		
Pua 2019[49]	Primary TKR, all 50+	OKS pain	Moderate or severe pain
Singapore	N=5325	6 months	
2013-2017	68 (7.5)		
1 hospital	75.0%		
Quintana 2006[50]	Primary TKR, all	WOMAC pain	No improvement in pain
Spain	N=792	6 months	greater than MCID (22.60
1999-2000	71.9		of 100) using an anchor-
7 hospitals	73.0%		based method.
Rice 2018[51]	Primary TKR, all 18+	VAS/NRS pain	VAS >3
New Zealand	N=300	6 12 months	
2012-2015	69 (10) range 48-90	0, 12 1101110	
3 hospitals	48.0%		
Siderie 2022[52]			
	H_{111}	6 months	NK3 4+
03A 2016 2019	N = 179	0 monuns	
2010-2018 1 haanital	67.1 (8.1) 50.00(
	56.2%	A (1	
Singh 2014[53]	Primary TKR, all	Author own	Moderate-severe pain
USA	N=7229	question 24 months	
1993-2005	68 (10)	24 11011015	
1 hospital	56.0%		
Solberg 2023[54]	Primary TKR probably,	Author own	To what extent have you
USA		question	minimal or not at all
2020	N=239	3 months	High loss to follow up rate
22 surgeons	66.2 (8.5), range 37-87		
	60.7%		
Stephens 2002[55]	Primary TKR, all 50+	WOMAC pain	No change or increase in
USA	N=68	6 months	pain nom pre-operative
Before 2001	67.4 (8.1), range 50-88		
1 hospital	54.0%		
Tang 2023[56]	Primary TKR probably,	VAS/NRS pain 🏹	NRS scores ≥4
China	all 65+	3 months	
2020-2021	N=196		
1 hospital	72		
	75.1%		
Terradas-Monllor	Primary TKR or UKR, all	VAS/NRS pain	VAS 3+
2024[57]	18+	3, 6 months	
Spain	N=115		
2018-2020	70.5 (10.7)		
1 home rehabilitation	66.1%		
I homazeau 2016[58]	Primary TKR, all	VAS/NRS pain	NRS score ≥1/10 for the
France	N=109	6 months	iast o uays
2013	69.2 (9)		
1 hospital	71.6%		

Prevalence of chronic pain after total hip or knee replacement

Tian 2022[59]	Primary TKR or UKR, all <90	Author own question	Moderate or severe pain or movement
2019 2010	N=271	24 months	
1 hospital	Not reported		
Поэрна	80.8%		
Utrillas-Compaired	Primary TKR, all	KSS pain	KSS pain poor (less than
2014[60]	N=215	12 months	60 points)
Spain	73 (6.35)		
2009	69.3%		KSS may not be entirely
1 hospital			patient reported
van der Wees	Primary TKR, all	VAS/NRS pain	30% or less improvement i
2017[61]	N=704	6, 12 months	VAS pain
The Netherlands	65 (12)		
1993-2014	64.5%		High loss to follow up rate
1 hospital			at 6 and 12 months
Vina 2020[62]	Primary TKR, all	WOMAC pain	Less than MCID of 1.5
USA	N=315	24 months	
2005-2015	67.3 (8.6)		
4 hospitals	60.9%		
Vuorenmaa 2008[63]	Primary TKR, all <80	VAS/NRS pain	VAS >30/100
Finland	N=51	3 months	
Before 2007	70 (5)		
2 surgeons	80%		
W Dabl 2014[64]	Drimony TKD all	KOOS pain	Linchanged or worse pain
Swodon		12 months	Unchanged of worse pain
	IN-2/30	12 montins	
2008-2010 2 haanitala	09.3 (8.7) 59.50/		
			Less then MOID of S00 in
vvaimann 2014[65]			both the WOMAC pain and
USA	N=236	6 months	function scores (scaled to
2004-2007	65.1 (8.9)		100) `
2 hospitals	66.0%		
Wylde 2013[66]	Primary TKR, all	WOMAC pain	WOMAC pain score of >75
UK	N=57	12 months	
2010-2011	68		
1 hospital	58%		
Wylde 2019[67]	Primary TKR, all eligible for Triathlon prosthesis	WOMAC pain	Worse or no change in WOMAC pain of 14 point
	N=266	5, 12, 24 monuns	(based on MCID)
2006-2009	$70(0.0)$ range 41_00		
1 hospital	64%		High loss to follow up rate
Yan 2023[68]	Primary TKR, all 45+	VAS/NRS pain	NRS score of ≥1 at rest
China	N=470	6 months	and/or on movement
2021-2023	63.4 (7.4)		
1 hospital	69.9%		Concern over VAS ≥1

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Prevalence of chronic pain after total hip or knee replacement

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Prevalence of chronic pain after total hip or knee replacement



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



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

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Prevalence of chronic pain after total hip or knee replacement



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)

Prevalence of chronic pain after total hip or knee replacement

S4.2 TKR studies (6 months)

	-	02	D3	04		1000		-	03	010	Overall	
Aso 2020			0								\bigcirc	
Attal 2014			0								\bigcirc	
Brander 2003			0								\bigcirc	
Buvanendran 2019			\bigcirc								\bigcirc	
Chodor and Kruczynski 2022			\bigcirc				\bigcirc				\bigcirc	
Dursteler 2021			\bigcirc								\bigcirc	
Edwards 2022			\bigcirc	\bigcirc								
Grosu 2016			\bigcirc	\bigcirc								
Heath 2021			\bigcirc	\bigcirc								
Jones 2000			0								\bigcirc	
Khalid 2021			0	\bigcirc								
Kurien 2018			\bigcirc								\bigcirc	•
Leung 2019			Ó	•	۲	۲	Ó	•			\bigcirc	Yes
Mekkawy 2023			0				\bigcirc					O №
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Noiseux 2014	Ó		Õ	Ó	•	۲		•	•		\bigcirc	Moder
Phillips 2014			Ō					•			\bigcirc	
Priol 2023	Ó		Õ	Õ		Ó		•	۲			
Pua 2019	Ŏ	Ŏ	Õ	Ŏ	۲	۲	Ŏ	Ŏ	۲	Ŏ	Õ	
Quintana 2006	Ó	Ó	Õ	Ŏ	Ó	Ó	Ŏ	Ŏ	۲	Ó	Õ	
Rice 2018	Ó		Õ	Ó	•	۲		•	•		0	
Sideris 2022	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	
Stephens 2002	Ŏ		Õ	Ŏ		Ó	Ó	•	۲		Õ	
Terradas-Monllor 2024	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ó	Ŏ	Ŏ	
Thomazeau 2016	Ó	Ó	Õ	Ŏ	Ó	Õ	Ó	Ŏ	Ó	Ó	Ó	
van der Wees 2017	•		Ō	Ō				•				
Waimann 2014	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Õ	
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Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	
Alzahrani TWH cohort 2011			0								\bigcirc	
Aso 2020			\bigcirc								\bigcirc	
Attal 2014			\bigcirc								\bigcirc	
Baker 2007			\bigcirc								\bigcirc	
Bell 2023			\bigcirc								\bigcirc	
Birch 2019	۲	•	\bigcirc	Ō								
Brander 2003			\bigcirc								\bigcirc	
Buus 2022			\bigcirc								\bigcirc	
Clement 2014			\bigcirc				0				\bigcirc	
Cole 2022			\bigcirc	\bigcirc								
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Dowsey 2012			\bigcirc				\bigcirc					
Escobar and Riddle 2014			\bigcirc	\bigcirc								
Getachew 2021			\bigcirc								\bigcirc	
Grosu 2016			\bigcirc	\bigcirc								
Hardy 2022			\bigcirc								\bigcirc	
Kiran 2015			\bigcirc	\bigcirc								Yes
Kornilov 2018			\bigcirc								\bigcirc	O No
Larsen 2021			\bigcirc	\bigcirc								High
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Lee 2022			\bigcirc				\bigcirc				\bigcirc	
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Musbahi 2023			\bigcirc	\bigcirc								
Orr 2022			\bigcirc	\bigcirc								
Petersen 2015			\bigcirc								\bigcirc	
Petersen 2018			\bigcirc	\bigcirc								
Phillips 2014			\bigcirc								\bigcirc	
Rice 2018			\bigcirc								\bigcirc	
Utrillas-Compaired 2014			\bigcirc				\bigcirc					
van der Wees 2017			\bigcirc	\bigcirc								
W-Dahl 2014			\bigcirc								\bigcirc	
Wylde 2013			\bigcirc								\bigcirc	
Wylde 2019			\bigcirc	\bigcirc								

Page 60 of 75

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Prevalence of chronic pain after total hip or knee replacement

S4.4 TKR studies (24 months)

cardy C1 C2 C3 C4	Study	DI	02	05	04	05	00	07	00	119		(N/OFO	
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twonendran 2019 Image: Control of the control of t	Brander 2003			\bigcirc									
Deduct and Kuczynski 2022 	Juvanendran 2019			\bigcirc									Yes
Juriteir 2021	Shodor and Kruczynski 2022			\bigcirc				\bigcirc					High
idwards 2022 idwards 2024 idwards 2021 idwards 2021 idwards 2020 idwards 202 idwards 2020 <td>Jursteler 2021</td> <td></td> <td></td> <td>\bigcirc</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>•</td> <td></td> <td></td> <td>Mode</td>	Jursteler 2021			\bigcirc						•			Mode
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	irosu 2016	•		\bigcirc	0		•			•	•		
	leath 2021	•	•	\bigcirc	\bigcirc	•		•		•	•	•	
	Jones 2000			\bigcirc		\bullet	\bullet		\bullet	•		\bigcirc	

S5. Forest plots of univariate meta-analyses in TKR studiesS5.1 TKR studies (3 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Solberg 2023	Author own question	⊢ - 1	31	239	13.0 (9.3 to 17.9)	
Attal 2014	BPI	⊢	45	89	50.6 (40.3 to 60.8)	2
Nishimoto 2023	KOOS pain	→	16	68	23.5 (14.9 to 35.0)	0
Birch 2019	OKS pain	H=H	88	589	14.9 (12.3 to 18.1)	•
Lee 2022	Pain disturbing sleep	⊢ •−−1	69	172	40.1 (33.1 to 47.6)	0
Brander 2003	VAS/NRS pain	⊢ •−−1	26	116	22.4 (15.7 to 30.9)	0
Dursteler 2021	VAS/NRS pain	⊢_ ■	87	170	51.2 (43.7 to 58.6)	(?)
Grosu 2016	VAS/NRS pain	⊢■ →	11	114	9.6 (5.4 to 16.6)	•
Kim 2015	VAS/NRS pain	⊢ •−−−	16	94	17.0 (10.7 to 26.0)	0
Lavand'homme 2014	VAS/NRS pain	⊢∎	12	128	9.4 (5.4 to 15.8)	(?)
Phillips 2014	VAS/NRS pain	⊢	26	96	27.1 (19.1 to 36.8)	0
Tang 2023	VAS/NRS pain	⊢	37	196	18.9 (14.0 to 25.0)	0
Terradas-Monllor 2024	VAS/NRS pain	⊢ ∎−−−	31	115	27.0 (19.6 to 35.8)	0
Vuorenmaa 2008	VAS/NRS pain	⊢ −−−−−	9	51	17.6 (9.4 to 30.6)	0
Wylde 2019	WOMAC pain	+•	42	266	15.8 (11.9 to 20.7)	2
Random-effects model			546	2503	21.9 (15.7 to 29.6)	
Heterogeneity (tau ²): 0.51 (9	95% Cri 0.18 to 1.1)					
		0 25 50 75 Proportion (%)	100			

S5.2 TKR studies (6 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Chodor and Kruczynski 2022	Author own question	⊢	11	69	15.9 (9.1 to 26.5)	0
Leung 2019	Author own question	⊢ •	10	243	4.1 (2.2 to 7.5)	0
Attal 2014	BPI		32	89	36.0 (26.7 to 46.4)	2
Edwards 2022	BPI	⊢ •	24	248	9.7 (6.6 to 14.0)	
Heath 2021	EQ 5D 5L pain/discomfort	н	1099	8299	13.2 (12.5 to 14.0)	•
Nishimoto 2023	KOOS pain	—	12	68	17.6 (10.3 to 28.6)	0
Khalid 2021	OKS pain	•	4370	2 531790	8.2 (8.1 to 8.3)	
Pua 2019	OKS pain	H	350	5325	6.6 (5.9 to 7.3)	2
Aso 2020	VAS/NRS pain	⊢ •−−	20	234	8.5 (5.6 to 12.9)	0
Brander 2003	VAS/NRS pain	⊢ •−−1	21	116	18.1 (12.1 to 26.2)	2
Buvanendran 2019	VAS/NRS pain	H•	34	296	11.5 (8.3 to 15.6)	(?)
Dursteler 2021	VAS/NRS pain	⊢ •−−1	86	170	50.6 (43.1 to 58.0)	2
Grosu 2016	VAS/NRS pain	⊢ •−−1	7	114	6.1 (3.0 to 12.3)	
Kurien 2018	VAS/NRS pain	—	14	50	28.0 (17.3 to 41.9)	(?)
Mekkawy 2023	VAS/NRS pain	⊢ •−−1	11	112	9.8 (5.5 to 16.9)	
Noiseux 2014	VAS/NRS pain	⊢ •−−1	31	215	14.4 (10.3 to 19.8)	0
Phillips 2014	VAS/NRS pain	——————————————————————————————————————	19	96	19.8 (13.0 to 29.0)	(?)
Priol 2023	VAS/NRS pain	—	14	129	10.9 (6.5 to 17.5)	
Rice 2018	VAS/NRS pain	⊢	60	300	20.0 (15.9 to 24.9)	2
Sideris 2022	VAS/NRS pain	⊢ ⊷⊣	15	179	8.4 (5.1 to 13.4)	2
Terradas-Monllor 2024	VAS/NRS pain		21	115	18.3 (12.2 to 26.4)	0
Thomazeau 2016	VAS/NRS pain	⊢ −•−−1	30	109	27.5 (20.0 to 36.6)	
van der Wees 2017	VAS/NRS pain	⊢ -	41	704	5.8 (4.3 to 7.8)	
Yan 2023	VAS/NRS pain	⊢ •−1	102	470	21.7 (18.2 to 25.7)	ē
Jones 2000	WOMAC pain	⊢ •−−1	54	292	18.5 (14.4 to 23.4)	0
Quintana 2006	WOMAC pain	H	199	792	25.1 (22.2 to 28.3)	2
Stephens 2002	WOMAC pain	—	11	68	16.2 (9.2 to 26.9)	0
Waimann 2014	WOMAC pain	⊢⊷⊣	14	236	5.9 (3.5 to 9.8)	0
Random-effects	model	⊢ →	4604	4 550928	14.1 (10.9 to 17.9)	
Heterogeneity (tau ²): 0.	51 (95% Crl 0.26 to 0.88)					
		0 25 50 7	5 100			
		Proportion (%)				

Prevalence of chronic pain after total hip or knee replacement

S5.3 TKR studies (12 months)

Clement 2014 .eung 2019 Attal 2014 Setachew 2021	Author own question	H H H	64			1.12.1
eung 2019 Attal 2014 Setachew 2021	Author own question		04	578	11.1 (8.8 to 13.9)	?
Attal 2014 Setachew 2021	Autor own question	H H -1	8	243	3.3 (1.7 to 6.4)	?
Setachew 2021	BPI		26	89	29.2 (20.7 to 39.5)	?
	BPI	→	74	206	35.9 (29.7 to 42.7)	?
Dowsey 2012	IKSS pain	⊢ •→	140	478	29.3 (25.4 to 33.5)	
Bell 2023	KOOS pain		433	5564	7.8 (7.1 to 8.5)	?
/ahdi 2020	KOOS pain	Hel	27	615	4.4 (3.0 to 6.3)	
Drr 2022	KOOS pain	H	845	7476	11.3 (10.6 to 12.0)	
V-Dahl 2014	KOOS pain		105	2736	3.8 (3.2 to 4.6)	?
Jtrillas-Compaired 2014	KSS pain		12	215	5.6 (3.2 to 9.6)	
Baker 2007	OKS pain		1583	9417	16.8 (16.1 to 17.6)	?
Birch 2019	OKS pain	H=	58	589	9.8 (7.7 to 12.5)	
Buus 2022	OKS pain	⊢	94	217	43.3 (36.9 to 50.0)	?
Cole 2022	OKS pain	i=4	70	1025	6.8 (5.4 to 8.5)	
Kiran 2015	OKS pain	H=	57	608	9.4 (7.3 to 12.0)	
ee 2022	Pain disturbing sleep	H=	11	172	6.4 (3.6 to 11.2)	0
so 2020	VAS/NRS pain		20	234	8.5 (5.6 to 12.9)	0
Brander 2003	VAS/NRS pain	⊢ ∎−−−+	15	116	12.9 (7.9 to 20.3)	?
Grosu 2016	VAS/NRS pain	⊢ •−−−1	10	114	8.8 (4.8 to 15.5)	
Hardy 2022	VAS/NRS pain		24	111	21.6 (14.9 to 30.2)	0
Kornilov 2018	VAS/NRS pain	⊢	18	100	18.0 (11.6 to 26.8)	?
arsen 2021	VAS/NRS pain	⊢ ∎	13	185	7.0 (4.1 to 11.7)	
atijnhouwers 2022	VAS/NRS pain	⊢	99	282	35.1 (29.8 to 40.9)	
Aercurio 2020	VAS/NRS pain	·	11	45	24.4 (14.1 to 39.0)	0
Petersen 2015	VAS/NRS pain		17	78	21.8 (14.0 to 32.3)	?
Petersen 2018	VAS/NRS pain	⊢ ∎−−1	25	200	12.5 (8.6 to 17.8)	
hillips 2014	VAS/NRS pain	H	15	96	15.6 (9.6 to 24.3)	0
Rice 2018	VAS/NRS pain	⊢∎ −−−1	45	300	15.0 (11.4 to 19.5)	?
an der Wees 2017	VAS/NRS pain	H=1	31	704	4.4 (3.1 to 6.2)	
Alzahrani TWH cohort 2011	WOMAC pain	H -	55	482	11.4 (8.9 to 14.6)	0
Dave 2017	WOMAC pain	⊢ •−-1	26	267	9.7 (6.7 to 13.9)	0
scobar and Riddle 2014	WOMAC pain	Heri	270	1616	16.7 (15.0 to 18.6)	
Aezey 2023	WOMAC pain		21	101	20.8 (14.0 to 29.8)	
Ausbahi 2023	WOMAC pain	H=	96	575	16.7 (13.9 to 20.0)	
Vylde 2013	WOMAC pain		15	57	26.3 (16.5 to 39.2)	(?)
Vylde 2019	WOMAC pain	H•	14	266	5.3 (3.1 to 8.7)	
Random-effects n Heterogeneity (tau ²): 0.61 (95%	nodel 6 Crl 0.34 to 0.98)	⊢ →	4447	36157	12.6 (9.9 to 15.9)	

S5.4 TKR studies (24 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Singh 2014	Author own question	•	499	7229	6.9 (6.3 to 7.5)	?
Tian 2022	Author own question	+=-1	228	721	31.6 (28.3 to 35.1)	?
Dowsey 2012	IKSS pain	⊢∎ −1	137	478	28.7 (24.8 to 32.9)	
Lyman 2018	KOOS pain	•	289	3815	7.6 (6.8 to 8.5)	ĕ
Kiran 2015	OKS anchoring question	H∎-I	61	608	10.0 (7.9 to 12.7)	ĕ
Leppanen 2021	VAS/NRS pain	⊢-■	50	205	24.4 (19.0 to 30.7)	?
Lundblad 2008	VAS/NRS pain	⊢	15	69	21.7 (13.6 to 33.0)	?
Ghomrawi 2017	WOMAC pain	H 	40	247	16.2 (12.1 to 21.3)	?
Vina 2020	WOMAC pain	⊢∎→	36	315	11.4 (8.4 to 15.4)	?
Wylde 2019	WOMAC pain	H ∎ →I	21	266	7.9 (5.2 to 11.8)	?
Random-effects model			1376	13953	14.6 (9.4 to 22.4)	
Heterogeneity (tau ²): 0.8	51 (95% Crl 0.15 to 1.32)	0 25 50 75	100			
		Proportion (%)	100			

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

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

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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% Crl)	tau ² (95% Crl)					
		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								

S8.2 Setting

Subgroup	No. Studies	Median (95% Crl)	tau ² (95% Crl)	
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	

Prevalence of chronic pain after total hip or knee replacement

Single hospital 20 13.96 (9.77 to 19.93) 0.77 (0.34 to 1.4				
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% Crl)	tau ² (95% Crl)	
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% Crl) 	tau² (95% Crl)	
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 Mont	hs 🦳		
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 Mon	ths		
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	

Prevalence of chronic pain after total hip or knee replacement

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% Crl)	tau² (95% Crl)		
	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 Mor	nths			
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 Mo	nths			
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

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

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

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	
- Cleveland Clinic 2020		•	0		•	•	•			•	\bigcirc	
- Erlenwein 2017	•	•	Õ	•	•	٠	•	•	•		0	
Jones 2000		•	0		•				•		0	
Mezey 2023			0	0								Yes
Nikolajsen 2006		٠	\bigcirc		•	٠	\bigcirc				\bigcirc	No No
Page 2016		٠	\bigcirc		•		\bigcirc		۲			High
Palazzo 2014		۲	\bigcirc				\bigcirc					Moderate
Quintana 2006		۲	\bigcirc	\bigcirc		٠			۲			
Ray 2020			\bigcirc	\bigcirc				\bullet				
Singh and Lewallen 2010		•	0	\bigcirc			\bigcirc					

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

Authors and affiliations 5

- 6 Hung-Yuan Cheng^{1*}, Andrew D Beswick^{1,2*}, Wendy Bertram^{1,2}, Mohammad Ammar
- 7 Siddiqui¹, Rachael Gooberman-Hill¹, Michael R Whitehouse^{1,2}, Vikki Wylde^{1,2}
- 8 1 Bristol Medical School, University of Bristol, Bristol, BS8 2PN, United Kingdom
- 9 2 NIHR Bristol Biomedical Research Centre, University Hospitals Bristol and Weston NHS
- 10 Foundation Trust and University of Bristol, United Kingdom

1 2

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3 4

- 12 *equal contribution
- 13

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- 14
- 15
- 16

Corresponding author: 17

- set terier 18 Professor Vikki Wylde: V.Wylde@bristol.ac.uk
- 19 Address: Musculoskeletal Research Unit, Translational Health Sciences, Bristol Medical
- 20 School, Learning and Research Building, Level 1, Southmead Hospital, University of Bristol,
- 21 BS10 5NB, UK

Running title 22

23 Prevalence of chronic pain after total hip or knee replacement

Keywords 24

25 Chronic pain; Total hip replacement; Total knee replacement; Systematic review; Meta-26 analysis

1 2		
3	28	Abstract
5 6	29	Objectives
7 8	30	To update our previous systematic review to synthesise latest data on the prevalence of
9	31	long-term pain in patients who underwent total hip replacement (THR) or total knee
10 11	32	replacement (TKR). We aim to describe the prevalence estimates and trends in this review.
12 13	33	Design
14 15	34	Systematic review and meta-analysis
16 17	35	Data Sources
18 19	36	Update searches were conducted in MEDLINE and Embase databases from 1st January
20 21	37	2011 to 17th February 2024. Citation tracking was used to identify additional studies.
22 23	38	Eligibility Criteria
23 24	39	We included prospective cohort studies reporting long-term pain after THR or TKR at 3, 6,
25 26	40	12 and 24 months post-operative.
27 28	41	Data Extraction and Synthesis
29 30	42	Two reviewers independently identified studies as eligible. One reviewer conducted data
31	43	extraction, checked by a second reviewer. The risk of bias assessment was performed using
32 33 24	44	Hoy's checklist. Bayesian, random-effects meta-analysis was used to synthesise the results.
34 35	45	Results
36 37	46	For TKR, sixty-eight studies with 89 time points, including 598,498 patients, were included.
38 30	47	Multivariate meta-analysis showed a general decrease in pain proportions over time: 21.9%
40	48	(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
41 42	49	12 months, and 14.6% (9.5 to 22.4) at 24 months. Considerable heterogeneity, unrelated to
43	50	examined moderators, was indicated by substantial prediction intervals in the univariate
44 45	51	models. Substantial loss to follow-up and risk of bias led to low confidence in the results. For
46 47	52	THR, only eleven studies were included, so it was not possible to describe the trend.
47 48	53	Univariate meta-analysis estimated 13.8% (8.5-20.1) and 13.7% (4.8-31.0) of patients
49 50	54	experiencing long-term pain 6 and 12 months after THR, respectively, though concerns in
50 51 52	55	risk of bias results reduced confidence in these findings.
52 53 54	56	Conclusions
55	57	Our review suggests that approximately 22% of patients report pain 3 months post-TKR, with
56 57	58	12-15% experiencing long-term pain up to 2 years. At least 14% report pain 6-12 months
58 59 60	59	after THR. Given the prevalence of chronic post-surgical pain, implementing existing and

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> 60 developing new preventive and management strategies is crucial for optimal patient 61 outcomes.

- 62 Study registration
- 63 PROSPERO CRD42023475498

66 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.

77 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.¹² About 100,000 each of primary total knee and hip replacements were performed in the UK in 2022,³⁴ 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 increase⁶⁷ 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.⁹¹⁰ 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 pain¹⁰ ¹²⁻¹⁴, unchanged pain¹⁵, residual pain¹⁶⁻¹⁸, and worsening pain¹⁹ 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.

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

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110 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 MOOSE²⁵ (Supplementary material S1) and relevant contents in
 PRISMA²⁶ guidelines and the Cochrane handbook.²⁷

1 120 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.

128 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

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

146 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.

²⁰ 154 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.

⁵⁵ 175 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

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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.

¹⁰ 182 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 (Crls) 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 10⁵) 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.

194 To account for the multiple time follow-ups reported in certain studies, we adopted a
 195 Bayesian, hybrid, multivariate meta-analysis of multiple factors³¹ to describe the proportions
 196 across time points by borrowing information and accounting for within- and between-study
 197 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.

⁴⁵ 203 Exploration of heterogeneity ⁴⁶

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.

56 209 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

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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

Patient and public involvement

chronic pain after TKR.

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- 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. 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. ³³Patient 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

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

exclusion at the full-text stage are summarised in Figure 1. Some articles from our previous

Individual study characteristics are summarised in S3. The grouped characteristics in Table

studies (n=39) collected their data at a single hospital, followed by multiple hospitals (n=18).

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

Overall, 598,498 patients were included in the 68 studies with a median sample size per

Searches of MEDLINE, Embase, citation tracking in Web of Science and inclusion of

studies with 143.101 THR participants were included. Study selection and reasons for

review were excluded as the follow up period was longer than 24 months.

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Results

Total knee replacement

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% Crl 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 Crls (S6). The substantial prediction intervals in the univariate models suggested considerable heterogeneity.

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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

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3 4	302	experienced unfavourable pain outcomes in each study (<u>Table 2</u>). By assuming 10% to 30%
5	303	of participants lost to follow-up might experience unfavourable pain, this approach could
0 7	304	yield more realistic estimates, given the limited literature available for further imputation.
8 9	305	Total hip replacement
10 11	306	Eleven studies reported unfavourable pain outcomes in individuals who underwent THR. The
12	307	characteristics of these studies are summarised in S11. Only one study reported
13 14	308	unfavourable pain outcomes at the 3-month and 24-month time points, so a trend cannot be
15	309	established. Studies reported ranges of people with unfavourable pain at 6 months of 8.3 to
16 17	310	16.3%, and at 12 months of 3.9 to 25.6% (<u>Figure 4</u>).
18 19	311	Meta-analysis of unfavourable pain outcomes provided similar results at 6 and 12 months.
20	312	with 13.8% (8.5 to 20.1) and 13.7% (4.8 to 31.0), respectively. However, concerns regarding
21 22	313	the risk of bias assessment (S12) lead to low confidence in these results.
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316 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.

329 Our meta-analyses suggest that the proportion of people with an unfavourable level of pain
 330 after TKR decreases between three and six months after surgery and then remains stable
 331 until at least two years. While recognising the associated wide credible intervals,
 332 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

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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

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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 revision⁵⁶ 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 replacement⁶⁰⁻⁶³. 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.8283 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

³³₃₄ 442 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.

⁴⁹₅₀ 451 Ethical approval

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

56 454 Data sharing

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

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480 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 outc	ome reporte	d			
VAS/NRS pain	29	9	16	13	2
WOMAC pain	13		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	1	1			
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	1	1			1
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

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4		Canada	2	0	1	1	0
5		Finland	2	1	0	0	1
6		Japan	2	1	2	1	0
7		Singapore	2	0	2	1	0
8		South Korea	2	2	0	1	0
9		The Netherlands	2	0	1	2	0
10		Hungary	1	0	0	1	0
11		Italy	1	0	0	1	0
12		New Zealand	1	0	1	1	0
13		Norway	1	0	0	1	0
14		Poland	1	0	1	0	0
15		Russia	1	0	0	1	0
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483 Table 2. Worst-best case scenario analyses in TKR studies

Proportion* (%)	Median (95% Crl)	τ² (95% Crl)
	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)	0.51(0.27 - 0.07)
100 /0	12 month	0.30 (0.31 - 1)
0%	12 61 (9 88 - 15 84)	0.61(0.34 - 0.97)
10%	15 22 (12 20 18 23)	0.01(0.34 - 0.37)
20%	17.44 (14.5, 20.66)	0.44(0.23-0.72)
20%	10.6 (16.46 22.07)	0.37(0.2-0.0)
J0 /6	21.6 (18.00, 25.17)	0.36 (0.2 0.58)
40 /0 50%	21.0(10.09 - 25.17)	0.30(0.2 - 0.30)
50% 60%	25.0(19.00 - 27.40)	0.37(0.2 - 0.0)
60% 70%	23.04(21.74-29.09)	0.4(0.23 - 0.04)
70%	27.57 (23.20 - 32.21)	0.44(0.25-0.7)
00%	29.57 (24.55 - 54.51)	0.49(0.26-0.76)
90%	31.53 (20.01 - 30.95)	0.55(0.3-0.87)
100%	33.02 (27.09 - 39.01)	0.62 (0.37 - 0.99)
00/		0.50 (0.45 4.00)
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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792 Figure legends

793 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.

⁴ 808 Supplementary materials

- 6 809 S1. PRISMA checklist
- 87 810 S2. Search strategy as applied in MEDLINE and Embase
 - 811 S3. Characteristics of TKR studies
 - 812 S4. Traffic light plot of the risk of bias assessment in TKR studies
 - 813 S5. Forest plots of univariate meta-analyses in TKR studies
- 814 S6. Table of multivariate and univariate meta-analysis results in TKR studies
- ² 815 S7. Meta-regression analyses in TKR studies
- 816 S8. Subgroup analyses in TKR studies
- ⁴ 817 S9. Doi plots and the LFK indexes in TKR studies
- 5 818 S10. Sensitivity analyses in TKR studies
- 6 819 S11. Characteristics of THR studies
- $^{+7}_{48}$ 820 S12. Traffic light plot of the risk of bias assessment in THR studies


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Study Case Total Proportion (95% Crl) RoB 3 Months Tang 2023 6.7 (3.1 to 14.2) 6 Months Erlenwein 2017 20 24 128 242 150 784 14.4 (9.3 to 21.7) 8.3 (5.4 to 12.5) 16.0 (11.0 to 22.8) 16.3 (13.9 to 19.1) ? ? • Jones 2000 Page 2016 Quintana 2006 RE Model Heterogeneity (tau²): 0.08 (95% Crl 0 to 0.82) 13.8 (8.5 to 20.1) 12 Months Cleveland Clinic 2020 Mezey 2023 Nikolajsen 2006 Palazzo 2014 Ray 2020 3.9 (3.3 to 4.6) 23.9 (16.1 to 33.8) 10.3 (8.7 to 12.1) 25.6 (18.8 to 33.8) 18.4 (18.2 to 18.6) 127 33 23488 1231 129 127660 ž RE Model Heterogeneity (tau²): 0.9 (95% Crl 0.13 to 4.28) 13.7 (4.8 to 31.0) 24 Months Singh and Lewallen 2010 435 4.8 (4.3 to 5.2) Proportion (%) 1291x645mm (118 x 118 DPI) For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Prevalence of chronic pain after total hip or knee replacement

Supplementary materials

S1. MOOSE checklist	3
S2. Search Strategy as applied in MEDLINE and Embase	5
S2.1 Total knee replacement	5
S2.2 Total hip replacement	5
S3. Characteristics of TKR studies	7
References	14
S3.1 Mean age and range	19
S3.2 Proportion of females	19
S3.3 Data collection timeframe	20
S3.4 Proportions of lost to follow-ups and revisions	21
S4. Traffic light plot of the risk of bias assessments in TKR studies	22
S4.1 TKR studies (3 months)	22
S4.2 TKR studies (6 months)	23
S4.3 TKR studies (12 months)	24
S4.4 TKR studies (24 months)	25
S5. Forest plots of univariate meta-analyses in TKR studies	26
S5.1 TKR studies (3 months)	26
S5.2 TKR studies (6 months)	26
S5.3 TKR studies (12 months)	27
S5.4 TKR studies (24 months)	27
S6. Table of multivariate and univariate meta-analysis results in TKR studies	28
S7. Meta-regression analyses in TKR studies	29
S7.1 Mean age	29
S7.2 Proportion of females	29
S7.3 Sample sizes	29
S8. Subgroup analyses in TKR studies	30
S8.1 Geographical regions	30
S8.2 Setting	30
S8.3 Pain outcome instruments	31
S8.4 Cut-off definitions	31
S9. Doi plots and the LFK indexes in TKR studies	33
S9.1 TKR studies (3 months)	33
S9.2 TKR studies (6 months)	33
S9.3 TKR studies (12 months)	34
S9.4 TKR studies (24 months)	34

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S10. Sensitivity analyses	35
S11. Characteristics of THR studies	36
References	37
S11.1 Proportions of lost to follow-ups and revisions	39
S12. Traffic light plot of the risk of bias assessments in THR studies	40

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P	revalence of chronic pain after total hip or knee replacement	en-2024- ppyright,	
S	1. MOOSE checklist	088975 includir	
lte N	em Recommendation	Reportếd တို Page Number 🎽	Reported on Section/Paragraph
R	eporting of background	use Se	
1	Problem definition	Page 4 s s v	Introduction
2	Hypothesis statement	Page 4 ap 25	Introduction
3	Description of Study Outcome(s)	Page 5 8 3 0	Outcome, Methods
4	Type of exposure or intervention used	Page 5 to text	Eligibility Criteria, Methods
5	Type of study design used	Page 5 and d	Eligibility Criteria, Methods
6	Study population	Page 5 ata m BEE	Eligibility Criteria, Methods
R	eporting on search strategy	inir S)	
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	trai	Supplementary S2
9	Effort to include all available studies, including contact with authors	Page 5-🗗 🔓	Searches, Methods
1(D Databases and registries searched	Page 5 👷 🛃	Searches, Methods
1'	Search software used, name and version, including special features used (e.g., explosion)	Page 6 and siin c	Study selection and dat collection, Methods
12	2 Use of hand searching (e.g., reference lists of obtained articles)	Page 5 ni	Searches, Methods
13	3 List of citations located and those excluded, including justification	une 1. ar tech	Figure 1 (PRISMA flowchart)
14	4 Method for addressing articles published in languages other than English	Page 5 0	Searches, Methods
1	5 Method of handling abstracts and unpublished studies	Page 5 8 8	Searches, Methods
16	5 Description of any contact with authors	Page 5-	Searches, Methods
R	eporting of methods	Ag	
17	7 Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	ence	Table 1
18	8 Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Page 6 Bi	Study selection and dat collection, Methods

	BMJ Open	omjope by cop	
Preva	alence of chronic pain after total hip or knee replacement	:n-2024-(>yright, i	
19	Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Page 6 udin	Study selection and dat collection, Methods
20	Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	on 21 Ig for u	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 es r	Risk of bias assessmer Methods
22	Assessment of heterogeneity	Page 7 elated	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-text and t	Data synthesis approac Methods
24	Provision of appropriate tables and graphics	dat:	Results
Repo	orting of results		
25	Graphic summarizing individual study estimates and overall estimate	inii	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)	A jo	Tables S7, S8, and S1
28	Indication of statistical uncertainty of findings	trai	Table 2 and S6
Repo	orting of discussion	nin n.b	
29	Quantitative assessment of bias (e.g., publication bias)	<u> </u>	Figures S9
30	Justification for exclusion (e.g., exclusion of non–English-language citations)	and	Not applicable
31	Assessment of quality of included studies	l sir	Figures 2 and 4
Repo	orting of conclusions	nila J	
32	Consideration of alternative explanations for observed results	ar t	Conclusion
33	Generalization of the conclusions (i.e., appropriate for the data presented and within	e 1. ech	Conclusion
	the domain of the literature review)	4, 2 nol	
34	Guidelines for future research	025 log	Conclusion
35	Disclosure of funding source	5 at	Sources of funding

From: Brooke BS, Schwartz TA, Pawlik TM. MOOSE Reporting Guidelines for Meta-analyses of Observational Studies. JAMA Surg. 2021;156(8):789 Bijographic Provide Provide

59

60

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.

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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.
- or 8 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 concerr
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/severed 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

Chodor and	Primary TKR, all 48+	Author own	Pain severely limiting daily
Kruczynski 2022[10]	N=69	question	life
Poland	67.6 (7.42), range 48-84	6 months	
2016	76.7%		
1 hospital			
Clement 2014[11]	Primary TKR, all	Author's own	Fair or poor
UK	N=578	question "How	High loss to follow up rate
2010	70 (9.6), range 39-91	surgery relieve	
1 hospital	58.4%	pain in your	
		affected joint?"	
		12 months	
Cole 2022[12]	Primary TKR, all	OKS pain	<14 points OKS
UK	N=1025	12 months	
2010-2015	70		
2 hospitals	55.8%		
Dave 2017[13]	Primary TKR probably,	WOMAC pain	WOMAC pain score <
USA	all 40+	12 months	MCID (WOMAC pain of 15)
2012-2014	N=267		
3 hospitals	66 (9)		
	61.0%		
Dowsey 2012[14]	Primary TKR, all	IKSS pain	IKSS pain score <30
Australia	N=478	12, 24 months	
2006-2007	70.8 (8.3), range 45-90		IKSS may not be optically
1 hospital	69.2%		patient reported at 12 and
			24 months
Dursteler 2021[15]	Primary TKR, all 18+	VAS/NRS pain	NRS 0.3/1 or greater at rest
Spain	N=170	3, 6 months	
2014-2017	73.1 (7.1)		
Spain	73.3%		
1 hospital			
Edwards 2022[16]	Primary TKR, all 45+	BPI	4/10 or greater
USA	N=248	6 months	
2012-2018	65.1 (8.2)		High loss to follow up rate
2 hospitals	59.5%		
Escobar and Riddle	Primary TKR, all	WOMAC pain	Number not attaining PASS
2014[17]	N=1616	12 months	(i.e. "No" in the question, "If
Spain	71.6 (6.8)		you had to be the rest of
2003-2006	70.0%		your life with the symptoms
15 hospitals	10.070		you have now, now would you feel?") as the twenty-
			fifth percentile of the final
			score at 1 year instead of
			the seventy-fifth percentile
			(reverse option for vvOMAC 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

Ξ				
3	Norway	N=206	12 months	
4	2012-2014	68 (9)		
5	1 hospital	66.0%		
6 7	Chamrowi 2017[10]	Drimony TKP oll	WOMAC nain	Number pet appioving
/	Giloiniawi 2017[19]			MCID (baseline-adjusted
0	USA	N=247	24 months	MCIDs as described by
9 10	2010-2012	68 (10)		Escobar et al.[70])
10	1 hospital	65.0%		
12	Grosu 2016[20]	Primary TKR probably,	VAS/NRS pain	Moderate to severe pain
13	Belaium	all	3. 6. 12 months	
14	2009-2010	N=114		High loss to follow up rate
15		66 (10)		at 3. 6 and 12 months
16	i suigeon	65.8%		,
17	Hardy 2022[21]	Primary TKP all >18		VAS >30/100
18				VA3 -30/100
19	France	N=111	12 months	
20	2014-2015	73.3 (9.3) range 29-92		
21	1 hospital	65.0%		
2Z ·	Heath 2021[22]	Primary and revision	EQ-5D 5L pain/	Moderate/ severe or
25	Australia	TKR, all	discomfort	extreme pain EQ 5D 5L
24	2018-2020	N=8299	6 months	pain/discomfort
26	14 hospitals	67.5 (8.8)		
27	44 Hospitals	56.4%		High loss to follow up rate
28	lones 2000[23]	Primary TKP all 10+		Moderate/ severe pain
29	Canada		6 months	defined as a gain of <10
30		N=292	6 monuns	points on the WOMAC pain
31	1995-1997	69.2 (9.2)		dimension
32	1 health region	59.0%		
33	Khalid 2021[24]	Primary TKR or UKR, all	OKS pain	OKS-pain score of 14 or
34	UK	N=531,790	6 months	less at six months after
35	2008-2016	69.7 (9.4)		knee replacement can be
30 27	National registry	56.6%		considered to be in chronic
38			N (4 Q (9) D Q)	
39	Kim 2015[25]	Primary IKR, all women	VAS/NRS pain	>5 points on an 11 point
40	South Korea	N=94	3 months	vAS/NRS (verbal numeric
41	2013-2014	70.18 (5.74), range 20-		rating scale)
42	1 hospital	80		
43		100%		
44	Kiran 2015[26]	Primary TKR, all	OKS pain	Has your knee replacement
45	UK	N=608	12. 24 months	operation decreased your
46	2003-2007	72	,	knee pain?
47	1 hospital	61 4%		
48	i nospital	01.478		High loss to follow up rate
49				at 12 and 24 months
50 -	Kornilov 2018[27]	Primary TKR, all 18+	VAS/NRS pain	Not at least a two-point or
52	Russia	N=100	12 months	approximately 30%
53	2014	63 (8) range 47-81	-	(clinically significant)
54	1 hospital	95.0%		decrease in rating of pain
55	поэрна	00.070		Interference with walking
56				(NRS scale 0.10)
57	Kurion 2019[20]	Drimony TVD probably		4 or groater
58		all		4 UI YIEALEI
59	UK	N-50	6 months	
60	Before 2017	N-30		

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1 hospital	66.4 (8.3)		
	60.0%		
Larsen 2021[29]	Primary TKR, all 18+	VAS/NRS pain	Pain intensity at rest >3
Denmark	N=185	12 months	Liberto La casta da da Una como casta
2015-2016	68.8 (8.9)		High loss to follow up rate
1 hospital	55.7%		
Latijnhouwers	Primary TKR, all	VAS/NRS pain	Moderate to severe pain
ZUZZ[JU] The Netherlands	N=282	12 months	(NR3 24)
	66 (8.4)		High loss to follow up rate
2 hospitals	63.0%		
z nospilais	Drimony TKD or LIKD oll		NDC >1/10
2014[31]		2 months	NR3 24/10
Belaium	68 (10)	5 11011115	
2012	66 4%		
1 surgeon	00.47		
Lee 2022[32]	Primary TKR probably	Pain disturbing	Night pain was defined as
South Korea	all	sleep	pain around the knee
2017-2019	N=172	3, 12 months	experienced at night that
2 surgeons	70.7 (4.3)		could disturb the patient's
2 ourgoono	89.2%		sleep
Leppanen 2021[33]	Primary TKR, 65 years	VAS pain	VAS >30
Finland	or younger	exercise	
2012-2014	N=205	24 months	
1 hospital	60		
	63.0%		
Leung 2019[34]	Primary TKR, all	Author own	No change or worsening
Singapore	N=243	question	pain/ slightly better
2015	66 (8.3)	6, 12 months	
1 hospital	78.6%		
Lundblad 2008[35]	Primary TKR, all	VAS/NRS pain	Pain at rest, VAS >2/10
Sweden	N=69	24 months	
Before 2006	68		
1 hospital	50.7%		
Lyman 2018[36]	Primary TKR, all	KOOS pain	Number not achieving
USA	N=3815	24 months	MCID (8 by distribution-
2007-2012	74 (6)		
1 hospital	63.0%		High loss to follow up rate
Mahdi 2020[37]	Primary TKR, all	KOOS pain	8 cut off
Sweden	N=615	12 months	
2016-2018	69.7		High loss to follow up rate
3 hospitals	52.2%		J
Mekkawv 2023[38]	Primary TKR. all	VAS pain	Probably NRS score of ≥1
USA	N=112	6 months	in defined sites
2021	65.5 (9.2)		
4 surgeons	69.0%		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]	Primary TKR, all >18	VAS/NRS pain	VAS >30 residual pain
Italy	N=45	12 months	
2015-2017	69.6 (7.8)		
1 hospital	65.0%		
Mezey 2023[40]	Primary TKR probably,	WOMAC pain	Not exceeding MCID
Hungary	all	12 months	(WOMAC pain of 13.3)
2019-2020	N=101		
2 hospitals	69.2		High loss to follow up rate
	Not reported		
Musbahi 2023[41]	Primary TKR, all 40+	WOMAC pain	WOMAC pain score
USA	N=575	12 months	(converted to a 0-to-100
2011-2014	66.3 (8.3)		scale) improvement of <20
4 hospitals	60%		High loss to follow up rate
Nishimoto 2023[42]	Primary TKR, all with no	KOOS pain	Not achieving MCID of 10
.lanan	complications	3 6 months	(3 months) and 13 (6
2021-2023	N=68	o, o montrio	months). MCID was
1 hospital	75.1 (7.3)		calculated using the ancho
Ποοριαί	80.9%		method.[/2]
Noiseux 2014[43]	Primary TKR, all 30+	VAS/NRS pain	Moderate or severe pain
USA	N=215	6 months	with range of motion, VAS
Before 2012	61.7 (9.8)		≥1
2 hospitals	58.0%		
·	6		Concern over VAS ≥1 being too inclusive
Orr 2022[44]	Primary TKR, all	KOOS pain	Not achieved PASS (i.e.
USA	N=7476	12 months	"No" in the question,
2016-2019	67 (9.0)		activity you have during
9 hospitals	60.8%		your daily life, your level of
			pain and also your activity
			limitations and participation
			the current state of your
			knee satisfactory?") for
			KOOS pain
			High loss to follow up rate
Petersen 2015[45]	Primary TKR, all	VAS/NRS pain	VAS >3
Denmark	N=78	12 months	
Before 2014	69		High loss to follow up rate
1 hospital probably	59.0%		
Petersen 2018[46]	Primary TKR probably,	VAS/NRS pain	<30% reduction in pain
Denmark		12 months	
	all		
Before 2017	all N= 200		
Before 2017 1 hospital	all N= 200 69 (1.2)		
Before 2017 1 hospital	all N= 200 69 (1.2) 57.0%	V/404/22	N40-0
Before 2017 1 hospital Phillips 2014[47]	all N= 200 69 (1.2) 57.0% Primary TKR, all	VAS/NRS pain	VAS >3
Before 2017 1 hospital Phillips 2014[47] UK	all N= 200 69 (1.2) 57.0% Primary TKR, all N= 96	VAS/NRS pain 3, 6, 12 months	VAS >3
Before 2017 1 hospital Phillips 2014[47] UK 2009-2010	all N= 200 69 (1.2) 57.0% Primary TKR, all N= 96 70.6	VAS/NRS pain 3, 6, 12 months	VAS >3

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Prevalence of chronic pain after total hip or knee replacement

Priol 2023[48]	Primary TKR, all	VAS/NRS pain	VAS 4+
France	N=129	6 months	
2011-2012	74 (10), range 45-94		High loss to follow up rate
1 hospital	72.3%		
Pua 2019[49]	Primary TKR, all 50+	OKS pain	Moderate or severe pain
Singapore	N=5325	6 months	
2013-2017	68 (7.5)		
1 hospital	75.0%		
Quintana 2006[50]	Primary TKR, all	WOMAC pain	No improvement in pain
Spain	N=792	6 months	greater than MCID (22.60
1999-2000	71.9		of 100) using an anchor-
7 hospitals	73.0%		based method.
Rice 2018[51]	Primary TKR, all 18+	VAS/NRS pain	VAS >3
New Zealand	N=300	6 12 months	
2012-2015	69 (10) range 48-90	0, 12 1101110	
3 hospitals	48.0%		
Siderie 2022[52]			
	H_{111}	6 months	NK3 4+
03A 2016 2019	N = 179	0 monuns	
2010-2018 1 haanital	67.1 (8.1) 50.00(
	56.2%	A (1	
Singh 2014[53]	Primary TKR, all	Author own	Moderate-severe pain
USA	N=7229	question 24 months	
1993-2005	68 (10)	24 11011115	
1 hospital	56.0%		
Solberg 2023[54]	Primary TKR probably,	Author own	To what extent have you
USA		question	minimal or not at all
2020	N=239	3 months	High loss to follow up rate
22 surgeons	66.2 (8.5), range 37-87		
	60.7%		
Stephens 2002[55]	Primary TKR, all 50+	WOMAC pain	No change or increase in
USA	N=68	6 months	pain nom pre-operative
Before 2001	67.4 (8.1), range 50-88		
1 hospital	54.0%		
Tang 2023[56]	Primary TKR probably,	VAS/NRS pain 🏹	NRS scores ≥4
China	all 65+	3 months	
2020-2021	N=196		
1 hospital	72		
	75.1%		
Terradas-Monllor	Primary TKR or UKR, all	VAS/NRS pain	VAS 3+
2024[57]	18+	3, 6 months	
Spain	N=115		
2018-2020	70.5 (10.7)		
1 home rehabilitation	66.1%		
I homazeau 2016[58]	Primary TKR, all	VAS/NRS pain	NRS score ≥1/10 for the
France	N=109	6 months	iast o uays
2013	69.2 (9)		
1 hospital	71.6%		

Prevalence of chronic pain after total hip or knee replacement

Tian 2022[59]	Primary TKR or UKR, all <90	Author own question	Moderate or severe pain or movement
2019 2010	N=271	24 months	
1 hospital	Not reported		
Поэрна	80.8%		
Utrillas-Compaired	Primary TKR, all	KSS pain	KSS pain poor (less than
2014[60]	N=215	12 months	60 points)
Spain	73 (6.35)		
2009	69.3%		KSS may not be entirely
1 hospital			patient reported
van der Wees	Primary TKR, all	VAS/NRS pain	30% or less improvement i
2017[61]	N=704	6, 12 months	VAS pain
The Netherlands	65 (12)		
1993-2014	64.5%		High loss to follow up rate
1 hospital			at 6 and 12 months
Vina 2020[62]	Primary TKR, all	WOMAC pain	Less than MCID of 1.5
USA	N=315	24 months	
2005-2015	67.3 (8.6)		
4 hospitals	60.9%		
Vuorenmaa 2008[63]	Primary TKR, all <80	VAS/NRS pain	VAS >30/100
Finland	N=51	3 months	
Before 2007	70 (5)		
2 surgeons	80%		
W Dabl 2014[64]	Drimony TKD all	KOOS pain	Linchanged or worse pain
Swodon		12 months	Unchanged of worse pain
	IN-2/30	12 months	
2008-2010 2 haanitala	09.3 (8.7) 59.50/		
			Less then MOID of S00 in
vvaimann 2014[65]			both the WOMAC pain and
USA	N=236	6 months	function scores (scaled to
2004-2007	65.1 (8.9)		100) `
2 hospitals	66.0%		
Wylde 2013[66]	Primary TKR, all	WOMAC pain	WOMAC pain score of >7
UK	N=57	12 months	
2010-2011	68		
1 hospital	58%		
Wylde 2019[67]	Primary TKR, all eligible for Triathlon prosthesis	WOMAC pain	Worse or no change in WOMAC pain of 14 point
	N=266	5, 12, 24 monuns	(based on MCID)
2006-2009	$70(0.0)$ range 41_00		
1 hospital	64%		High loss to follow up rate
Yan 2023[68]	Primary TKR, all 45+	VAS/NRS pain	NRS score of ≥1 at rest
China	N=470	6 months	and/or on movement
2021-2023	63.4 (7.4)		
1 hospital	69.9%		Concern over VAS ≥1

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Prevalence of chronic pain after total hip or knee replacement



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



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

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Prevalence of chronic pain after total hip or knee replacement



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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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)

	-	02	D3	04		1000		-	03	010	Overall	
Aso 2020			0								\bigcirc	
Attal 2014			0								\bigcirc	
Brander 2003			0								\bigcirc	
Buvanendran 2019			\bigcirc								\bigcirc	
Chodor and Kruczynski 2022			\bigcirc				\bigcirc				\bigcirc	
Dursteler 2021			\bigcirc								\bigcirc	
Edwards 2022			\bigcirc	\bigcirc								
Grosu 2016			\bigcirc	\bigcirc								
Heath 2021			\bigcirc	\bigcirc								
Jones 2000			0								\bigcirc	
Khalid 2021			0	\bigcirc								
Kurien 2018			\bigcirc								\bigcirc	•
Leung 2019			Ó	•	۲	۲	Ó	•			\bigcirc	Yes
Mekkawy 2023			0				\bigcirc					O №
Nishimoto 2023	Ŏ	Ó	Ō	Ó	Ó	۲		Ŏ		Ó	0	High
Noiseux 2014	Ó		Õ	Ó	•	۲		•	•		\bigcirc	Moder
Phillips 2014			Ō					•			\bigcirc	
Priol 2023	Ó		Õ	Õ		Ó		•	۲			
Pua 2019	Ŏ	Ŏ	Õ	Ŏ	۲	۲	Ŏ	Ŏ	۲	Ŏ	Õ	
Quintana 2006	Ó	Ó	Õ	Ŏ	Ó	Ó	Ŏ	Ŏ	۲	Ó	Õ	
Rice 2018	Ó		Õ	Ó	•	۲		•	•		0	
Sideris 2022	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	
Stephens 2002	Ŏ		Õ	Ŏ		Ó	Ó	•	۲		Õ	
Terradas-Monllor 2024	Ŏ	Ŏ	Õ	Ŏ	Ŏ	Ŏ	Ŏ	Ŏ	Ó	Ŏ	Ŏ	
Thomazeau 2016	Ó	Ó	Õ	Ŏ	Ó	Õ	Ó	Ŏ	Ó	Ó	Ó	
van der Wees 2017	•		Ō	Ō				•				
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Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	
Alzahrani TWH cohort 2011			0								\bigcirc	
Aso 2020			\bigcirc								\bigcirc	
Attal 2014			\bigcirc								\bigcirc	
Baker 2007			\bigcirc								\bigcirc	
Bell 2023			\bigcirc								\bigcirc	
Birch 2019	۲	•	\bigcirc	0								
Brander 2003			\bigcirc								\bigcirc	
Buus 2022			\bigcirc								\bigcirc	
Clement 2014			\bigcirc				0				\bigcirc	
Cole 2022			\bigcirc	\bigcirc								
Dave 2017			\bigcirc								\bigcirc	
Dowsey 2012			\bigcirc				\bigcirc					
Escobar and Riddle 2014			\bigcirc	\bigcirc								
Getachew 2021			\bigcirc								\bigcirc	
Grosu 2016			\bigcirc	\bigcirc								
Hardy 2022			\bigcirc								\bigcirc	
Kiran 2015			\bigcirc	\bigcirc								Yes
Kornilov 2018			\bigcirc								\bigcirc	O No
Larsen 2021			\bigcirc	\bigcirc								High
Latijnhouwers 2022			\bigcirc	\bigcirc								Moderat
Lee 2022			\bigcirc				\bigcirc				\bigcirc	
Leung 2019			\bigcirc				\bigcirc				\bigcirc	
Mahdi 2020			\bigcirc	\bigcirc								
Mercurio 2020			\bigcirc								\bigcirc	
Mezey 2023			\bigcirc	\bigcirc								
Musbahi 2023			\bigcirc	\bigcirc								
Orr 2022			\bigcirc	\bigcirc								
Petersen 2015			\bigcirc								\bigcirc	
Petersen 2018			\bigcirc	\bigcirc								
Phillips 2014			\bigcirc								\bigcirc	
Rice 2018			\bigcirc								\bigcirc	
Utrillas-Compaired 2014			\bigcirc				\bigcirc					
van der Wees 2017			\bigcirc	\bigcirc								
W-Dahl 2014			\bigcirc								\bigcirc	
Wylde 2013			\bigcirc								\bigcirc	
Wylde 2019			\bigcirc	\bigcirc								

Page 60 of 75

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Prevalence of chronic pain after total hip or knee replacement

S4.4 TKR studies (24 months)

cardy C1 C2 C3 C4	Study	DI	02	05	04	05	Do	07	00	119		(N/OFO	
As 12 (24) At 12 (21 (At 12 (21 (21 (21 (At 12 (21 (21 (21 (21 (21 (21 (21 (21 (21		-	-	\bigcirc				-				Overall	
Alli (2014 •	4so 2020			\bigcirc									
Itender 2003 Image:	Attal 2014			\bigcirc									
twonendran 2019 Image: Control of the control of t	Brander 2003			\bigcirc									
Deduct and Kuczynski 2022 	Juvanendran 2019			\bigcirc									Yes
Juriteir 2021	Shodor and Kruczynski 2022			\bigcirc				\bigcirc					High
idwards 2022 idwards 2024 idwards 2021 idwards 2021 idwards 2020 idwards 202 idwards 2020 <td>Jursteler 2021</td> <td></td> <td></td> <td>\bigcirc</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>•</td> <td></td> <td></td> <td>Mode</td>	Jursteler 2021			\bigcirc						•			Mode
Jones 2000 Jones 2000 <td>dwards 2022</td> <td></td> <td></td> <td>\bigcirc</td> <td>\bigcirc</td> <td></td> <td></td> <td></td> <td></td> <td>•</td> <td></td> <td></td> <td></td>	dwards 2022			\bigcirc	\bigcirc					•			
	irosu 2016	•		\bigcirc	0		•			•	•		
	leath 2021	•	•	\bigcirc	\bigcirc	•		•		•	•	•	
	Jones 2000			\bigcirc		\bullet	\bullet		\bullet	•		\bigcirc	

S5. Forest plots of univariate meta-analyses in TKR studiesS5.1 TKR studies (3 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Solberg 2023	Author own question	⊢ - 1	31	239	13.0 (9.3 to 17.9)	
Attal 2014	BPI	⊢	45	89	50.6 (40.3 to 60.8)	2
Nishimoto 2023	KOOS pain	→	16	68	23.5 (14.9 to 35.0)	0
Birch 2019	OKS pain	H=H	88	589	14.9 (12.3 to 18.1)	•
Lee 2022	Pain disturbing sleep	⊢ •−−1	69	172	40.1 (33.1 to 47.6)	0
Brander 2003	VAS/NRS pain	⊢ •−−1	26	116	22.4 (15.7 to 30.9)	0
Dursteler 2021	VAS/NRS pain	⊢_ ■	87	170	51.2 (43.7 to 58.6)	(?)
Grosu 2016	VAS/NRS pain	⊢■ →	11	114	9.6 (5.4 to 16.6)	•
Kim 2015	VAS/NRS pain	⊢ •−−−	16	94	17.0 (10.7 to 26.0)	0
Lavand'homme 2014	VAS/NRS pain	⊢∎	12	128	9.4 (5.4 to 15.8)	(?)
Phillips 2014	VAS/NRS pain	⊢	26	96	27.1 (19.1 to 36.8)	0
Tang 2023	VAS/NRS pain	⊢	37	196	18.9 (14.0 to 25.0)	0
Terradas-Monllor 2024	VAS/NRS pain	⊢ ∎−−−	31	115	27.0 (19.6 to 35.8)	0
Vuorenmaa 2008	VAS/NRS pain	⊢ −−−−−	9	51	17.6 (9.4 to 30.6)	0
Wylde 2019	WOMAC pain	+•	42	266	15.8 (11.9 to 20.7)	2
Random-effects model			546	2503	21.9 (15.7 to 29.6)	
Heterogeneity (tau ²): 0.51 (9	95% Cri 0.18 to 1.1)					
		0 25 50 75 Proportion (%)	100			

S5.2 TKR studies (6 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Chodor and Kruczynski 2022	Author own question	⊢	11	69	15.9 (9.1 to 26.5)	0
Leung 2019	Author own question	⊢ •	10	243	4.1 (2.2 to 7.5)	0
Attal 2014	BPI		32	89	36.0 (26.7 to 46.4)	2
Edwards 2022	BPI	⊢ •	24	248	9.7 (6.6 to 14.0)	
Heath 2021	EQ 5D 5L pain/discomfort	н	1099	8299	13.2 (12.5 to 14.0)	•
Nishimoto 2023	KOOS pain	—	12	68	17.6 (10.3 to 28.6)	0
Khalid 2021	OKS pain	•	4370	2 531790	8.2 (8.1 to 8.3)	
Pua 2019	OKS pain	Η	350	5325	6.6 (5.9 to 7.3)	2
Aso 2020	VAS/NRS pain	⊢ •	20	234	8.5 (5.6 to 12.9)	0
Brander 2003	VAS/NRS pain	⊢ •−−1	21	116	18.1 (12.1 to 26.2)	2
Buvanendran 2019	VAS/NRS pain	H•	34	296	11.5 (8.3 to 15.6)	(?)
Dursteler 2021	VAS/NRS pain	⊢ •−−1	86	170	50.6 (43.1 to 58.0)	2
Grosu 2016	VAS/NRS pain	H	7	114	6.1 (3.0 to 12.3)	
Kurien 2018	VAS/NRS pain	—	14	50	28.0 (17.3 to 41.9)	(?)
Mekkawy 2023	VAS/NRS pain	⊢ •−−1	11	112	9.8 (5.5 to 16.9)	
Noiseux 2014	VAS/NRS pain	⊢ •−−1	31	215	14.4 (10.3 to 19.8)	0
Phillips 2014	VAS/NRS pain	——————————————————————————————————————	19	96	19.8 (13.0 to 29.0)	(?)
Priol 2023	VAS/NRS pain	—	14	129	10.9 (6.5 to 17.5)	
Rice 2018	VAS/NRS pain	⊢	60	300	20.0 (15.9 to 24.9)	2
Sideris 2022	VAS/NRS pain	⊢ ⊷⊣	15	179	8.4 (5.1 to 13.4)	2
Terradas-Monllor 2024	VAS/NRS pain		21	115	18.3 (12.2 to 26.4)	0
Thomazeau 2016	VAS/NRS pain	⊢ −•−−1	30	109	27.5 (20.0 to 36.6)	
van der Wees 2017	VAS/NRS pain	⊢ -	41	704	5.8 (4.3 to 7.8)	
Yan 2023	VAS/NRS pain	⊢ •−1	102	470	21.7 (18.2 to 25.7)	ē
Jones 2000	WOMAC pain	⊢ •−−1	54	292	18.5 (14.4 to 23.4)	0
Quintana 2006	WOMAC pain	H	199	792	25.1 (22.2 to 28.3)	2
Stephens 2002	WOMAC pain	—	11	68	16.2 (9.2 to 26.9)	0
Waimann 2014	WOMAC pain	⊢⊷⊣	14	236	5.9 (3.5 to 9.8)	0
Random-effects	model	⊢ →	4604	4 550928	14.1 (10.9 to 17.9)	
Heterogeneity (tau ²): 0.	51 (95% Crl 0.26 to 0.88)					
		0 25 50 7	5 100			
		Proportion (%)				

Prevalence of chronic pain after total hip or knee replacement

S5.3 TKR studies (12 months)

Clement 2014 .eung 2019 Attal 2014 Setachew 2021	Author own question	H H H	64			1.12.1
eung 2019 Attal 2014 Setachew 2021	Author own question		04	578	11.1 (8.8 to 13.9)	?
Attal 2014 Setachew 2021	Autor own question	H H -1	8	243	3.3 (1.7 to 6.4)	?
Setachew 2021	BPI		26	89	29.2 (20.7 to 39.5)	?
	BPI	→	74	206	35.9 (29.7 to 42.7)	?
Dowsey 2012	IKSS pain	⊢ •→	140	478	29.3 (25.4 to 33.5)	
Bell 2023	KOOS pain		433	5564	7.8 (7.1 to 8.5)	?
/ahdi 2020	KOOS pain	Hei	27	615	4.4 (3.0 to 6.3)	
Drr 2022	KOOS pain	H	845	7476	11.3 (10.6 to 12.0)	
V-Dahl 2014	KOOS pain		105	2736	3.8 (3.2 to 4.6)	?
Jtrillas-Compaired 2014	KSS pain		12	215	5.6 (3.2 to 9.6)	
Baker 2007	OKS pain		1583	9417	16.8 (16.1 to 17.6)	?
Birch 2019	OKS pain	H=	58	589	9.8 (7.7 to 12.5)	
Buus 2022	OKS pain	⊢	94	217	43.3 (36.9 to 50.0)	?
Cole 2022	OKS pain	i=4	70	1025	6.8 (5.4 to 8.5)	
Kiran 2015	OKS pain	H=	57	608	9.4 (7.3 to 12.0)	
ee 2022	Pain disturbing sleep	H=	11	172	6.4 (3.6 to 11.2)	0
so 2020	VAS/NRS pain		20	234	8.5 (5.6 to 12.9)	0
Brander 2003	VAS/NRS pain	⊢ ∎−−−+	15	116	12.9 (7.9 to 20.3)	?
Grosu 2016	VAS/NRS pain	⊢ •−−−1	10	114	8.8 (4.8 to 15.5)	
Hardy 2022	VAS/NRS pain		24	111	21.6 (14.9 to 30.2)	0
Kornilov 2018	VAS/NRS pain	⊢	18	100	18.0 (11.6 to 26.8)	?
arsen 2021	VAS/NRS pain	⊢ ∎	13	185	7.0 (4.1 to 11.7)	
atijnhouwers 2022	VAS/NRS pain	⊢	99	282	35.1 (29.8 to 40.9)	
Aercurio 2020	VAS/NRS pain	·	11	45	24.4 (14.1 to 39.0)	0
Petersen 2015	VAS/NRS pain		17	78	21.8 (14.0 to 32.3)	?
Petersen 2018	VAS/NRS pain	⊢ ∎−−1	25	200	12.5 (8.6 to 17.8)	
hillips 2014	VAS/NRS pain	H	15	96	15.6 (9.6 to 24.3)	0
Rice 2018	VAS/NRS pain	⊢∎ −−−1	45	300	15.0 (11.4 to 19.5)	?
an der Wees 2017	VAS/NRS pain	H=1	31	704	4.4 (3.1 to 6.2)	
Alzahrani TWH cohort 2011	WOMAC pain	H -	55	482	11.4 (8.9 to 14.6)	0
Dave 2017	WOMAC pain	⊢ •−-1	26	267	9.7 (6.7 to 13.9)	0
scobar and Riddle 2014	WOMAC pain	Heri	270	1616	16.7 (15.0 to 18.6)	
Aezey 2023	WOMAC pain		21	101	20.8 (14.0 to 29.8)	
Ausbahi 2023	WOMAC pain	H=	96	575	16.7 (13.9 to 20.0)	
Vylde 2013	WOMAC pain		15	57	26.3 (16.5 to 39.2)	(?)
Vylde 2019	WOMAC pain	H•	14	266	5.3 (3.1 to 8.7)	
Random-effects n Heterogeneity (tau ²): 0.61 (95%	nodel 6 Crl 0.34 to 0.98)	⊢ →	4447	36157	12.6 (9.9 to 15.9)	

S5.4 TKR studies (24 months)

Study	Instrument		Case	Total	Proportion (95% Crl)	RoB
Singh 2014	Author own question	•	499	7229	6.9 (6.3 to 7.5)	?
Tian 2022	Author own question	+=-1	228	721	31.6 (28.3 to 35.1)	?
Dowsey 2012	IKSS pain	⊢∎ −1	137	478	28.7 (24.8 to 32.9)	
Lyman 2018	KOOS pain	•	289	3815	7.6 (6.8 to 8.5)	ĕ
Kiran 2015	OKS anchoring question	H∎-I	61	608	10.0 (7.9 to 12.7)	ĕ
Leppanen 2021	VAS/NRS pain	⊢-■	50	205	24.4 (19.0 to 30.7)	?
Lundblad 2008	VAS/NRS pain	⊢	15	69	21.7 (13.6 to 33.0)	?
Ghomrawi 2017	WOMAC pain	H 	40	247	16.2 (12.1 to 21.3)	?
Vina 2020	WOMAC pain	⊢∎→	36	315	11.4 (8.4 to 15.4)	?
Wylde 2019	WOMAC pain	H ∎ →I	21	266	7.9 (5.2 to 11.8)	?
Random-effects model			1376	13953	14.6 (9.4 to 22.4)	
Heterogeneity (tau ²): 0.8	51 (95% Crl 0.15 to 1.32)	0 25 50 75	100			
		Proportion (%)	100			

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

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

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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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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% Crl)	tau ² (95% Crl)					
		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								

S8.2 Setting

Subgroup	No. Studies	Median (95% Crl)	tau ² (95% Crl)			
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			

Prevalence of chronic pain after total hip or knee replacement

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% Crl)	tau ² (95% Crl)				
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% Crl) 	tau² (95% Crl)			
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			

Prevalence of chronic pain after total hip or knee replacement

S9. Doi plots and the LFK indexes in TKR studies S9.1 TKR studies (3 months)

S9.2 TKR studies (6 months)

Prevalence of chronic pain after total hip or knee replacement

S9.3 TKR studies (12 months)



S9.4 TKR studies (24 months)



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Prevalence of chronic pain after total hip or knee replacement

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% Crl)	tau² (95% Crl)							
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 Mo	nths								
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

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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

ingh and Lewallen Primary THR D10[10] N=9154 SA 65 (13.3) 993-2005 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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Prevalence of chronic pain after total hip or knee replacement



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

Study	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall	
- Cleveland Clinic 2020		•	0			•					\bigcirc	
- Erlenwein 2017	•	•	Õ	•	•	•		•	•	•	\bigcirc	
Jones 2000		•	0		•	•		•	•		\bigcirc	
Mezey 2023		٠	0	\bigcirc								Yes
Nikolajsen 2006		٠	0			•	\bigcirc				\bigcirc	No No
Page 2016		۲	\bigcirc		٠		\bigcirc		٠			High
Palazzo 2014		۲	\bigcirc		٠		\bigcirc					Moderate
Quintana 2006		۲	\bigcirc	\bigcirc					۲			
Ray 2020			\bigcirc	\bigcirc								
Singh and Lewallen 2010		•	\bigcirc	\bigcirc			\bigcirc		•			