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Title

WHAT IS THE PATIENT EXPERIENCE FOLLOWING REVISION KNEE REPLACEMENT: A systematic review and meta-analysis of the medium term patient reported outcomes

Abstract

Aims
Revision knee replacement is an increasingly common procedure, however, information on patient-focused outcomes is limited. This systematic review and meta-analysis aimed to investigate the medium-term patient reported outcomes following a revision knee replacement.

Methods

We performed a systematic review of MEDLINE and EMBASE (from inception to 1st March 2021) for articles reporting five year or greater patient reported outcome measures (PROMs) following revision knee replacement. A meta-analysis of PROMs data was undertaken using the Standardised Mean Difference (SMD). Quality of methodology was assessed using Wylde’s non-summative four-point system. The study was registered with PROPSERO (CRD42021199289).

Results
A total of 23 studies met the inclusion criteria containing 2414 patients at a mean minimum follow-up of 74 months (60-122). The reporting of PROMs were poorly standardised with several PROMs being used. The most commonly reported patient reported outcome was the Knee Society Score reported in 65% of studies (15/23). A meta-analysis of 629 eligible patients undergoing revision knee replacement revealed a significant improvement in pre-operative state with a SMD 2.05 95% CI 0.87, 3.23.

Conclusion
This systematic review has found a significant and sustained improvement in patient-reported outcomes following a revision knee arthroplasty beyond five years. We found a variation in the usage and administration of PROMs which hinders a clear synthesis of results. Furthermore, the PROMs have not been robustly tested for validity in the context of a revision knee replacement.

[231]
**Introduction**

The number of revision total knee replacements performed in the UK has increased year on year as predicted.\(^1\) A total of 6,708 revision knee replacements were performed in the UK between 2019-2020. Since 2004 the number of revision knee replacements has increased more than five-fold.\(^2\) With the increasing frequency of surgery, an appraisal of patient-focused outcomes is vital to inform treatment decisions and as an adjunct to patient-clinician communication. In 2018 the James Lind Alliance (JLA) in association with the UK British Association for Surgery of the Knee (BASK) leveraged a patient, carer and healthcare professional collaborative to formulate the top ten research questions in revision knee arthroplasty. This Priority Setting Partnership (PSP) identified a lack of knowledge surrounding the long-term functional efficacy of the intervention, and consequently made this one of their research priorities.\(^3\)

Patient reported outcome measures (PROMs) capture patients’ own evaluation of their health status.\(^4\) They are a key approach in measuring the biopsychosocial perspective by being responsive to the needs and preferences of the individuals themselves.\(^5\) As such, there are region specific PROMs such as the Oxford Knee Score and generic standardised PROMs such as the EuroQuol, a multi-attribute health related quality of life measure. Generic instruments can also be used for economic evaluations through estimation of quality adjusted life years (QALYs).\(^6\) PROMs are currently used throughout the healthcare spectrum from individual patient monitoring to national organisations such as the NHS England National
PROMs programme\textsuperscript{7} and also internationally as part of the Patient-Reported Indicator Surveys (PaRIS) initiative. \textsuperscript{8}

Currently PROMs following revision knee replacement are reported predominantly in case series and cohort studies and a clear synthesis of the data has not yet been established. Furthermore, the reporting of PROMs alongside registry data in this context is suboptimal. The previously mentioned NHS PROMs programme is limited to six months follow up data and the data attrition has been reported to be very high with 50% of respondents lost to follow up.\textsuperscript{9} Similarly the New Zealand registry provided the only registry published PROMs. Despite 4,982 revision knee questionnaire responses with 54% achieving a good to excellent Oxford Knee Score, the follow up duration was limited to 6 months.\textsuperscript{10}

In an effort to explore the lived experience of revision knee replacement, a formal appraisal and synthesis of PROMs from extended follow-up studies is required. The primary aims of this study are to investigate the medium-term usage of PROMs following revision knee replacement and estimate the patient orientated treatment effect.

**Methods**

*Search Strategy and selection criteria*
We conducted a systematic review and meta-analysis assessing PROMs of revision knee replacements following a pre-defined protocol registered with PROSPERO (CRD42021199289) and complying with PRISMA guidelines.\textsuperscript{11,12}

A search strategy using keywords and MeSH terms relating to revision knee replacement and PROMs (appendix 1) was used in the databases MEDLINE and EMBASE accessed through OVID Silver Platter. The databases were searched from their commencement to 1\textsuperscript{st} March 2021.\textsuperscript{13} The strategy development was guided by previously published search strategies exploring PROMS in arthroplasty.\textsuperscript{14} Backward and forward reference searching was manually performed to identify additional articles.

Studies were included if they assessed patients who had undergone the following types of revision knee replacement: Cruciate retaining (CR), hinged type (HK), constrained condylar device (CCK) or posterior cruciate substituting prosthesis (PS). Patients undergoing patella resurfacing procedures were excluded. There was no restriction on indication for surgery yet this data was extracted for analysis. For inclusion the case-series had to report the PROMs of revision knee implants with a minimum follow-up of greater than 5 years. Initial scoping review identified that inclusion of studies with a minimum follow up of 5 years would yield an appropriate volume of data. Only studies reporting both mean pre and post intervention PROMs with 95\% confidence intervals or standard deviation were included in the meta-analysis. A manual search of the national joint registries was also conducted through a review of relevant websites and most recent published annual reports.
Studies were excluded if they reported the outcome following re-revision knee replacement as this is often more complex surgery and it is likely that this cohort will have poorer functional outcomes. Conference abstracts were excluded due to the limited data available from these reports.

Article screening and data extraction

Screening of articles was undertaken in a stepwise manner using a dual reviewer structure (AM, TM) and arbitration of conflict by a third reviewer (JE). Screening was conducted using the web application Rayyan. A full-text review and data extraction was performed using a standardised data collection form for study characteristics and outcome data. This form was hosted on the Research Electronic Data Capture (REDCap) data management platform. For each study data extracted were the name of PROM used, its administration intervals and methodology as outlined in the Cochrane’s guide on conducting systematic reviews.

Data synthesis

Of the series where two or more groups were compared separately within the same study; these were included as separate series in the meta-analysis. A descriptive analysis was performed by categorising each study’s results into four subgroups including methods, participants, interventions and outcomes. For the meta-analysis The Standardised Mean Difference (SMD) which considers the effect size in each study relative to the variability in the study was calculated. SMD was chosen as a
method for the synthesis of PROMs from studies reporting different instruments, a methodology that has been previously applied in orthopaedic research. Where 95% confidence intervals (CIs) were reported, the standard deviation was calculated using the Cochrane group recommendations. The SMD of the PROM reported in each study was pooled in the meta-analysis using a random effects model as a more conservative estimate of treatment effect. This model aims to minimize the expected high levels of heterogeneity. SMD serves as an easy way to judge the magnitude of the effect. Cohen’s criteria of magnitude of effect was used where an SMD of 0.2 represents a “small” effect, an SMD of 0.5 represents a “medium” effect, and an SMD of 0.8 represents a “large” effect. To correct for differences in the scale direction between outcome measures each measure was linearly transformed to the scoring direction of the most frequently applied PROM. Sensitivity analysis was conducted to assess the impact of surgical indication and, in the presence of positive or negative outlier data, the associated impact of its removal.

All statistical analysis was conducted in Stata 15 (*Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC*)

*Risk of bias*

Study quality was assessed using the non-summative four-point checklist developed by Wylde et al. This checklist consists of four items to assess selection bias (inclusion of consecutive patients and representativeness), bias due to missing data (follow up rates) and bias due to inadequate consideration of confounding. Each item is reported as adequate, not adequate or not reported. This checklist has been used previously in systematic reviews investigating outcomes in joint replacement.
surgery. A risk of bias visualisation tool will be used to format the results using a traffic-light plot.

**Results**

The initial search identified 682 potentially relevant articles. Following detailed assessment and recording of exclusion reasons, 23 articles met the inclusion criteria and underwent full-text extraction. Nine articles were included in the final PROMs synthesis. The New Zealand registry provided the only registry published PROMs favoring the Oxford Knee Score. However, the short follow-up duration precluded this data from our results. The results of the search are shown in the PRISMA flow diagram in figure 1.

The mean minimum follow-up was 74 months (60–122) reporting on 2414 patients after their revision knee replacement. The proportion of revision knee replacement performed for aseptic loosening was 56% (1360 patients). All of the 23 studies reported the outcome of knee-specific PROMs. The most frequently reported PROMs were the Knee Society Score (65% or 15/23) and the Oxford Knee Score (26% or 6/23). Study and participant level characteristics are summarised in table 1.

Pooled PROMs data was possible from nine studies which reported both pre and post intervention data. Of the nine studies 629 patients were included in the meta-analysis. The minimum follow-up was 88 months (60–122). The pooled SMD from reported PROMs (KSS, OKS and Western Ontario and McMaster Universities Arthritis Index WOMAC) are shown in the forest plot in figure 2.
The SMD was calculated to be 2.05 (95% CI 0.87, 3.23). According to Cohens criteria this showed a significant improvement compared with the pre-operative state. A sensitivity analysis (figure 3) removing the extreme outlier by Watts et al owing to the very narrow reported standard deviation and confirming maintenance in large effect size of 1.48 (95% CI 0.99, 1.96). Within our analysis we were able to compare results by indication displayed in figure 4. We observed no difference in the magnitude of effect in PROM result between a revision knee replacement for aseptic loosening and those for prosthetic joint infection.

The assessment of study methodological quality for these studies is presented in figure 4. As with most orthopaedic systematic reviews we were limited by the quality of the studies. Quality assessment was performed for the final PROMs synthesis. This revealed that eight (89%) series were consecutive, none were multicenter, six (67%) had >80% follow-up and only one (11%) undertook multivariable analysis. These proportions are in keeping with the fact that the quality of published case-series is low.

**Discussion**

This is the first systematic review and meta-analysis to study the medium-term PROMs following a revision knee replacement. At a minimum follow up of 5 years patients can expect a large and sustained improvement in their patient reported outcome measures (SMD 2.05 95% CI 0.87, 3.23). As registries may not provide this PROMs data for some time to come, we are reliant on the synthesis of data from extended case-series data, we anticipate this will be reassuring for patients, health professionals and commissioners of health services.
It is encouraging that where results were grouped by indication there were no statistical differences between the large effect sizes observed for each group.

However, the indications for the majority of these revisions included in this analysis were largely for elective procedures and may not be generalisable to urgent cases such as those for periprosthetic fractures. There was a variation in the type of the implant used and it was unclear what implant philosophy was definitively employed. As such we could not draw meaningful observations on surgical technique and encourage the transparent reporting of these aspects in future studies.

The methodology used in this paper is one that has been previously applied successfully to arthroplasty with the production of simple and generalisable results. However, within our pooled meta-analysis of PROMs we did observe an outlier result presented in the study by Watts et al. The SMD showed a significantly large effect size of 11.37 (95% CI 10.04, 12.71). Although the difference between pre and post-operative mean score for this population was of a representative magnitude to the other reported studies, the SMD was inflated as a consequence of a very narrow standard deviation. As such, sensitivity analysis was conducted which reduced though reducing the magnitude of effect, remained large. In an effort to not inflate and misrepresent the effect within the subgroup analysis, data from this study were removed.

We acknowledge some heterogeneity in the method of fixation and degree of bone loss reported between the studies. Many papers have praised the virtues of hybrid fixation reporting good to excellent results compared with cemented fixation alone. We were unable to synthesise this data due to poor reporting of fixation method.
Furthermore large bone defects and compromised bone stock can make reconstruction and fixation challenging, however comparison was hindered through poor reporting of technical notes within the studies.\textsuperscript{45} We anticipate that registry data will assist in the analysis of how these factors influence outcomes however our focus was to produce a simple and generalisable result.

We noticed that all studies reported knee-specific PROMs without the inclusion of a generic health-related quality of life measure. A recent paper by Sabah et al\textsuperscript{46} identified that despite 65.6% of patients achieving a clinically meaningful improvement in Oxford Knee Score after elective revision knee arthroplasty only half of all patients achieved a ‘better’ EQ5D. It is recommended that both a condition specific and a generic PROM is used in the collection of PROMs.\textsuperscript{47} The condition specific PROM provides a detailed picture of a patient’s assessment of their own health. Whereas the generic PROM provides the vital common currency that allows for aggregation and comparison across different patient groups. It is also often the most relevant PROM in making an economic assessment utilising quality-adjusted life year analysis.

We observed some consistency in the PROM reported with the majority of studies using the Knee Society Score or the Oxford Knee Score. However other PROMs included WOMAC, Visual Analogue Pain Scale (VAS-Pain), Forgotten Joint Score, Short Form 36, Knee Injury and Osteoarthritis Outcome Score (KOOS), Tegner Lysholm Knee Scoring Scale (TLKSS) and the Mayo Knee Questionnaire. While the authors of this paper recognise the concern regarding the validity and responsiveness of using arthritis indices in the context of a revision knee
replacement, we echo calls for consensus in outcome choice to facilitate synthesis of the data.\textsuperscript{44} The are currently no guidelines on PROM selection for revision knee surgery. A recent study by Sabah et al (2021)\textsuperscript{48} suggested the OKS was a useful and valid instrument in revision knee replacements. However, this evaluation was retrospective without a patient focus. The construct validity of the OKS was compared only with EQ5D only. In addition to obvious construct difference between the two measures, EQ5D did not emerge as a reported outcome instrument in our systematic review. There was also no test-retest reliability and no assessment of OKS domain structure in revision knee surgery via an exploratory factor analysis. We have identified the need for a core outcome set in this group of patients. A standardised evaluation is needed using EMPRO\textsuperscript{49} (evaluating measures of patient reported outcomes) or COSMIN\textsuperscript{49} (COnsensus-based Standards for the selection of health Measurement Instruments) to define the metric properties of these commonly used outcomes and their useability in the context of revision knee arthroplasty.

This analysis identified shortcomings in the utilisation of PROMs within national joint registries. Within the UK, the national PROMs program\textsuperscript{51} records information from PROM questionnaires but this data is only limited to 6-month follow up. The inclusion of PROMs in registry data has the potential to dramatically improve the assessment of patient-focused outcomes. We argue that there is a need for continued longitudinal assessment of PROMs within such registry data to dramatically improve the assessment of patient orientated outcomes.

There are limitations of this work. The data did not allow stratification or adjustment for patient factors such as age and obesity that may have affected outcomes in the
pooled analysis. Many of the series are derived from single-surgeon or single centre series. Therefore, surgeon or centre-specific preferences may alter the resultant weighted synthesis of outcomes. As previously alluded to we recognise that emergent techniques and implants may demonstrate superior function that is yet to be demonstrated with medium-term follow-up. We acknowledge that we concentrated on patient reported measures in this analysis rather than other outcome measures which are also important such as survival and complications.

**Conclusion**

This systematic review and meta-analysis provides patient level evidence for sustained improvements in outcomes at more than five years following a revision knee replacement. These results can be generalised to those undergoing revision knee surgery for elective procedures to include aseptic loosening and infection. Currently there is a lack of consensus on the most appropriate PROM to use in this patient group. This is evidenced by the observed variation in the PROM collected and the lack of robust reliability and validity evidence in the literature. We advocate the need for further research with a patient focus to test the value of using such PROMs following revision knee replacement.

**Take Home Message**

- This review has identified favorable medium-term patient reported outcomes following revision knee replacement beyond 5 years.
- A wide variation in PROMs are collected for revision knee replacement particularly joint specific PROMs designed for primary joint replacement. As such we
recommend further work to assess their validity and responsiveness in the context of revision knee replacement.

References


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Association for Surgery of the Knee and the James Lind Alliance. The bone and joint journal 2020; 102-B (9): 1176-1182


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34. van Rensch PJH, Hannink G, Heesterbeek PJC, Wymenga AB, van Hellemontd GG. Long-Term Outcome Following Revision Total Knee


47. Devlin NJ, Appleby J. Getting the most out of PROMS. Putting health outcomes at the heart of NHS decision making. London: King’s Fund; 2010.


Tables and figures

Figure 1 – PRISMA Flowchart representing systematic review processes for this study

Records identified through database (Medline and Embase) searching (n=681)

Additional records identified through other sources (n=1)

Records after duplicates removed (n = 418)

Records screened (n=418)

Records excluded (n =380)

Full text articles assessed for eligibility (n=38)

• Follow up <5 years (n=11)
• Contains patients from same database as another included study (n=1)
• Not reporting PROMs (n=3)

Studies included in descriptive analysis (n=23)
Studies included in PROMs synthesis qualitative synthesis (n=9)
Table 1 – Study level and participant level characteristics of contributing data sources (n=23). KSS, Knee Society Score; OKS, Oxford Knee Score, WOMAC, Western Ontario and McMaster Universities Arthritis Index; VAS-Pain, Visual Analogue Pain Scale; FJS, Forgotten Joint Score; SF-36, Short Form 36; KOOS, Knee Injury and Osteoarthritis Outcome Score; TLKSS, Tegner Lysholm Knee Scoring Scale; MKQ, Mayo Knee Questionnaire; PJI, Prosthetic Joint Infection.

<table>
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<th>Minimum follow up (months)</th>
<th>Number of Patients</th>
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<td>Abdelazi z et al 21</td>
<td>Case Series</td>
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<td>Endo-Model Waldemar-Link rotating hinge prosthesis (Waldemar Link Spain, Barcelona)</td>
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Revision Total Knee Arthroplasty (Smith & Nephew, Memphis, TN, USA) OKS

Not stated KSS

The Advantim (Wright Medical Technology, Arlington) KSS
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Figure 2 – Forest plot showing pooled patient-reported outcome measures using a random effects model. CI, confidence interval; ES, effect size; N, number of participants in study; SD, standard deviation; SMD, standardized mean difference; PROM, patient reported outcome measure.

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Overall Heterogeneity: $I^2 = 6.00$, $I^2 = 98.66$, $H^2 = 74.88$
Test of $I = I$: $Q(16) = 382.51$, $p = 0.00$
Test of $\theta = 0$: $t = 3.40$, $p = 0.00$

Random-effects REML model
Figure 3 – Forest plot showing pooled patient-reported outcome measures with extreme outlier removed using a random effects model. CI, confidence interval; ES, effect size; N, number of participants in study; SD, standard deviation; SMD, standardized mean difference; PROM, patient reported outcome measure.
Figure 4 – Pooled patient reported outcome measure with sensitivity analysis performed by indication for revision total knee replacement with outlier result removed using a random effects model.
Figure 5 – A traffic light plot showing the methodological quality of the studies included in the PROMs synthesis described by Wylde et al.\textsuperscript{11}

<table>
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<th>D3</th>
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</table>

D1: Consecutive Patients  
D2: Multicentre Adequate  
D3: >80% adequate  
D4: Multi-variable analysis  

Judgement:  
- Red: High  
- Green: Low  
- Grey: Not applicable
Appendix 1 Search Strategy

Database: Ovid MEDLINE(R) ALL <1946 to January 19, 2021>, Embase <1974 to 2021 January 19>

Search Strategy:

--------------------------------------------------------------------------------
1 revision knee replacement.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (104)
2 (revision adj2 knee).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (3905)
3 (revision adj2 knee adj2 replacement?).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (401)
4 (revision knee adj2 replacement?).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (130)
5 (revision adj2 TKR).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (180)
6 outcome.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (4680173)
7 pain.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (2059660)
8 (pain adj2 improvement).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (15271)
9 (pain adj2 scor*).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (94765)
10 function.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (5849665)
11 (function* adj2 outcome?).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (129648)
12 (function* adj2 scor*).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (50475)
13 PROMs.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (5992)
14 (patient adj reported adj outcome adj measur*).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (21815)
15 (Quality adj of adj life).mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (992057)
16 follow?up.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (69164)
17 series.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (1491439)
18 cohort.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (1832404)
19 registr*.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (691294)
20  long?term.mp. [mp=ti, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, an, sy, tn, dm, mf, dv, kw, dq] (33889)

21  1 or 2 or 3 or 4 or 5 (4013)

22  6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (12056586)

23  16 or 17 or 18 or 19 (3874551)

24  21 and 22 and 23 (681)