Incidence, temporal trends and potential risk factors for aseptic loosening following primary unicompartmental knee arthroplasty: a meta-analysis of 96,294 knees

Matthew C. Barrett[1], Florence O. Wilkinson[1], Ashley W. Blom[2,3], Michael R. Whitehouse[2,3], Setor K. Kunutsor[2,3]

[1]Barts and The London School of Medicine and Dentistry, 4 Newark St, Whitechapel, London E1 2AT

[2]National Institute for Health Research Bristol Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, UK

[3]Translational Health Sciences, Bristol Medical School, Musculoskeletal Research Unit, University of Bristol, Learning & Research Building (Level 1), Southmead Hospital, Bristol, BS10 5NB, UK

Corresponding Author

Matthew C. Barrett, Barts and The London School of Medicine & Dentistry, Queen Mary University London, Garrod Building, 4 Newark St, Whitechapel, London E1 2AT, UK.

Email: ha16662@qmul.ac.uk

Abstract

Background: Aseptic loosening (AL) is among the major reasons for revision of failed primary unicompartmental knee arthroplasty (UKA). There is an ongoing temporal increase in the use of UKA with a resultant increase in the revision burden. We aimed to evaluate the incidence of, temporal trends and risk factors for AL.

Methods: Longitudinal studies reporting the incidence of AL following primary UKA were sought from MEDLINE, Embase, Web of Science and Cochrane Library up to 6th April 2020. Incidence and relative risks (RR) (with 95% confidence intervals) were calculated.

Results: We identified 62 studies for inclusion. Overall, 96,294 primary UKA procedures accounting for 1,752 AL cases were included. AL incidence ranged from 0.00% to 22.70% over a 7.7 year weighted mean follow-up. The pooled random effects incidence (95% CI) was 1.77% (1.34-2.25) in the same follow-up period. The annual rate of AL was 0.10% (0.02-0.22). AL incidence increased with length of follow-up, but there was a temporal decrease from the 1970s onwards. Tibial loosening was more common than femoral component loosening: incidence (95% CI) of 1.63% (0.96-2.44) and 0.58% (0.20-1.09) respectively over a weighted follow-up of 6.6 years. Fixed bearing implant design and cemented fixation were both associated with increased AL risk, whereas robotic-assisted surgery was associated with decreased risk.

Conclusion: The overall incidence of AL following primary UKA is primarily driven by tibial component loosening and there is a temporal decline in rates. The use of mobile bearing, uncemented implants inserted with robotic assisted surgery may reduce the risk of AL.

Keywords:

UKA; aseptic loosening; UKR; unicondylar knee arthroplasty; unicondylar knee replacement; metaanalysis

Incidence, temporal trends and potential risk factors for aseptic loosening following primary unicompartmental knee arthroplasty: a meta-analysis of 96,294 knees

Abstract

Background: Aseptic loosening (AL) is among the major reasons for revision of failed primary unicompartmental knee arthroplasty (UKA). There is an ongoing temporal increase in the use of UKA with a resultant increase in the revision burden. We aimed to evaluate the incidence of, temporal trends and risk factors for AL.

Methods: Longitudinal studies reporting the incidence of AL following primary UKA were sought from MEDLINE, Embase, Web of Science and Cochrane Library up to 6th April 2020. Incidence and relative risks (RR) (with 95% confidence intervals) were calculated.

Results: We identified 62 studies for inclusion. Overall, 96,294 primary UKA procedures accounting for 1,752 AL cases were included. AL incidence ranged from 0.00% to 22.70% over a 7.7 year weighted mean follow-up. The pooled random effects incidence (95% CI) was 1.77% (1.34-2.25) in the same follow-up period. The annual rate of AL was 0.10% (0.02-0.22). AL incidence increased with length of follow-up, but there was a temporal decrease from the 1970s onwards. Tibial loosening was more common than femoral component loosening: incidence (95% CI) of 1.63% (0.96-2.44) and 0.58% (0.20-1.09) respectively over a weighted follow-up of 6.6 years. Fixed bearing implant design and cemented fixation were both associated with increased AL risk, whereas robotic-assisted surgery was associated with decreased risk.

Conclusion: The overall incidence of AL following primary UKA is primarily driven by tibial component loosening and there is a temporal decline in rates. The use of mobile bearing, uncemented implants inserted with robotic assisted surgery may reduce the risk of AL.

Keywords: aseptic loosening, UKA, unicondylar, unicompartmental, incidence, knee

1. Introduction

Unicompartmental knee arthroplasty (UKA) is an effective means to treat degenerative knee conditions. It is an alternative to total knee arthroplasty (TKA) for select circumstances where disease processes are restricted to a single compartment of the tibiofemoral joint. Though there has been a general increase in the use of UKA as a result of recent innovations in implant design and minimally invasive surgical techniques,(1-3) some select countries including Australia and Sweden have reported a declining trend in the use of UKA compared to TKA. (4, 5)

Despite the growing utility of UKA in treating limited degenerative disorders of the knee, national joint registry data of England, Australia and New Zealand continue to highlight concerns with respect to high rates of failure, necessitating revision UKA or conversion to TKR (1, 10, 11). In a recent analysis, Hansen *et al*. demonstrated survivorship of 80.9% *vs*. 95.7% for UKA *vs*. TKA respectively, at 7 years of follow-up (8). Aseptic loosening (AL) is one of the main causes of UKA failure (12, 13). AL is also cited as the commonest cause of failure following TKA. The resulting economic impact on health systems has resulted in significant efforts to understand the pathogenesis of AL (14). However, there is currently limited evidence on the risk factors for AL in the population of patients undergoing UKA.

To date, no systematic reviews and/or meta-analyses have attempted to evaluate the temporal incidence of AL in UKA. With a temporal increase in the use of UKA internationally, and a projected increase in revision procedures consequent thereof, a better understanding of the incidence and temporal trends of AL following primary UKA would be valuable to patients, clinicians and policy makers. A number of host, surgical and implant-related factors are known to influence the risk of developing AL, but the nature and magnitude of their associations with AL are not well described. Previous studies have not been able to adequately quantify the magnitude of the associations because of their small sample sizes. A greater understanding of the risk factors could aid in stratifying those at greater risk of AL-mediated UKA failure and inform both decision making on choice of implant class and preventive strategies. In this context, we aimed to utilize a systematic meta-analytic approach to aggregate the existing literature to describe the incidence of AL following primary UKA and the temporal trends thereof, and quantify the nature and magnitude of the associations of host, surgical and implant-related factors with the risk of AL.

2. Methods

2.1 Data Sources and Search Strategy

This review was conducted in accordance with PRISMA and MOOSE guidelines (15, 16), (**Supplementary Materials 1-2**) using a pre-defined protocol which was registered with the prospective register of systematic reviews, PROSPERO (CRD42019150836). We systematically searched MEDLINE, EMBASE, Web of Science and Cochrane databases for studies reporting on AL following primary UKA. The search strategy included MeSH search terms to describe the target population (e.g. “unicompartmental knee replacement”, “unicondylar knee arthroplasty”, “partial knee replacement”), in combination with search terms related to outcome (“aseptic loosening”, “polyethylene wear”, “mechanical wear”). The search was not limited to the English language and included those published from inception of each database to 6th April 2020. Full details of the search strategy can be found in **Supplementary Material 3.** Titles and abstracts of all potentially relevant studies were initially screened. Full-text articles were acquired for relevant studies to determine whether they fulfilled our eligibility criteria. In an attempt to identify any studies that were not identified by our original search, reference lists of the full-text articles were manually assessed.

2.2 Eligibility Criteria

Our eligibility criteria were agreed by all authors prior to performing the search. Eligible study designs were longitudinal studies (prospective or retrospective cohort, case-cohort, nested-case control, or clinical trials) that reported the incidence of AL following primary UKA. There were no restrictions on the follow-up duration. We excluded studies which: (i) were only restricted to patients with prevalent diseases (e.g. diabetes, renal disease, etc.) without a control group; (ii) involved surgical interventions other than primary UKA, such as in the setting of fracture fixation, infection, revision arthroplasty, or patellofemoral replacement arthroplasty; or, in the context of identifying AL risk factors (iii) failed to report AL risk in a non-exposed control group. Controversy on whether a study should be included were discussed by two reviewers before approaching a third reviewer for consensus.

2.3 Data extraction and Quality Assessment

Three independent authors performed data extraction and quality assessments, using a pre-designed, standardized, data collection spreadsheet. Where available, data was extracted for study design, publication date, geographical location, mean age, percentage of males, duration of follow-up, sample size, type of prosthesis, number of AL cases, potential risk factors, risk estimates (relative risks or hazard ratios for cohort studies and odds ratios for case-control studies) and degree of adjustment for potential confounders (univariate or multivariate). In the scenario where the same cohort had been described in multiple publications, the study with the most up-to-date or comprehensive information was included. The quality of each study was assessed using the nine-star Newcastle-Ottawa Scale (NOS), a validated tool for assessing the quality of non-randomised studies included in systematic or meta-analytic reviews. NOS measures the quality of evidence from a score of zero to nine, based on three pre-defined domains including: (i) selection of participants; (ii) comparability; and (iii) ascertainment of outcomes of interest (17).

2.4 Data synthesis and analyses

The incidence of AL with 95% confidence intervals (CIs) was estimated from the number of cases of revision due to AL within period of follow-up/total number of participants or procedures as reported. Given that the data was binary with low rates, the Freeman-Tukey variance stabilising double arcsine transformation (18) was used in calculating the rates as done in previous reports (19-21). On the assumption that AL can occur anytime following surgery, annual rates of AL were derived using the length of follow-up of each study. Temporal trends in incidence were evaluated using the median year of data collection/surgery, as previously reported (22-24). The measures of association were presented as RRs with 95% CIs. No studies reported multivariable-adjusted risk estimates, hence crude RRs were calculated from the raw counts provided. Random-effects models by DerSimonian and Laird which takes into account heterogeneity, both within and between studies, were used to combine RRs and account for the effect of heterogeneity (25). In the absence of substantial heterogeneity, fixed-effect models were employed. We estimated 95% prediction intervals to determine the degree of heterogeneity, as they provide a range in which the underlying true effects of future studies will lie with 95% certainty (26, 27). All statistical analyses were conducted using STATA MP 16 (Stata Corp, College Station, Texas, USA).

3. Results

3.1 Study identification and selection

The study selection process is summarised in **Figure 1**. A total of 1,785 potential citations were identified by the literature search and manual screening of relevant articles. Of these, 100 satisfied the review inclusion criteria based on titles and abstracts. Following detailed evaluation of full texts, 51 citations were excluded due to the following reasons: (i) population was not relevant (n=16); (ii) duplicate of another study included in review (n=1); (iii) the outcome was not relevant (n=18); (iv) study design was not relevant (n=6); and (v) full text not accessible (n=11). An additional 12 studies were identified and included after review of the reference lists of eligible studies. The remaining 62 articles which comprised of 63 unique studies were found to be eligible (**Figure 1; Supplementary Material 4**).

3.2 Study characteristics and study quality

Table 1 is a summary table of relevant study characteristics for the 62 studies. Publication dates of included studies ranged from 1993 to 2020. **Table 2** provides details of the key characteristics and quality assessment scores of the individual studies. Studies were all observational cohort studies. Overall, there were 96,294 primary UKRs and 1,752 cases of AL. Twenty-six studies provided data on whether AL was tibial (n=16,019) or femoral (n= 16,019). Patient populations were recruited from Europe (Belgium, Denmark, Finland, France, Germany, Italy, Norway, Poland, Sweden, Switzerland and UK); North America (Canada and USA); Asia (China and Korea); the Pacific (Australia) and Africa (Egypt). The weighted mean age and mean follow-up duration was 66.0 and 7.7 years respectively. Methodological quality of all included studies ranged from 5 to 9.

3.3 Incidence of aseptic loosening following primary UKR

Across 62 studies with relevant data, the incidence of AL over a weighted mean follow-up duration of 7.7 years ranged from 0.00% to 22.70%. The pooled random effects incidence (95% CI) over this follow-up duration was 1.77% (1.34-2.25) (**Figure 2**). The 95% prediction interval for the summary incidence was 0.01 to 5.40%, suggesting that the true incidence for any single new study will usually fall within this range. The annual rate of AL was 0.10% (0.02-0.22) (**Supplementary Material 5**). In pooled analysis of 26 studies comprising of 32,038 primary UKRs, the pooled incidence of tibial loosening and femoral loosening over a weighted mean follow-up duration of 6.6 years was 1.63% (0.96-2.44) and 0.58% (0.20-1.09) respectively (**Supplementary Materials 6-7**). The pooled incidence of AL for fixed and mobile bearings over a weighted mean follow-up duration of 5.9 years was 2.76% (1.63-4.12) and 1.15% (0.61-1.82) respectively (**Supplementary Material 8**).

The pooled incidence of AL at specific average follow-up periods reported by studies was 1.30% (1.03-1.59) at 2 years, 1.69% (0.82-2.82) at 3 years, 1.64% (0.69-2.88) at 5 years, 2.80% (1.84-3.94) at 10 years, and 2.90% (1.41-4.78) at 15 years (**Figure 3**). Based on the median year of data collection/surgery, the pooled incidence of AL was 4.57% (2.67-6.89) in 1970-1980s, 1.51% (0.73-2.50) in the 1990s, 1.55% (0.97-2.24) in 2000-2009 and 1.05% (0.39-1.96) in 2010 and beyond (**Figure 4A**). In meta-regression analysis, there was a significant association between incidence of AL and median year of data collection/surgery (p=0.022) and therefore independent of length of follow-up (**Figure 4B**).

3.4 Potential risk factors for aseptic loosening following primary UKR

A total of 11 of the included studies reported data that could be used in estimating the associations of potential risk factors with the risk of AL. The results are summarised in **Supplementary Materials 9**. Comparing males with females in pooled analysis of six studies (n=138), the RR (95% CI) for AL was 1.68 (0.85-3.32). Comparing a medial with a lateral UKR in pooled analysis of three studies (n=47,759), there was no significant evidence of an association with AL RR (95% CI) of 1.18 (0.91-1.52). Results of single reports showed bearing type (fixed *vs.* mobile; n=32,847)(28), implant fixation (cemented *vs*. non-cemented; n=14,814)(29) and non-robotically-assisted surgery (non-robotic *vs*. robotic-assisted; n=7,091)(30), to be associated with an increased risk of AL.

4. Discussion

4.1 Key findings

UKA involves the replacement of the articular surfaces in the affected compartment, with preservation of the cruciate ligaments and other compartments. The less invasive nature of this technique and retention of more normal knee kinematics have been shown to result in faster recovery, improved PROMs and reduced rates of infection, morbidity and mortality when compared to TKA. (6-9) Given limited data on incidence trends of AL and its potential risk factors, we carried out a systematic review and meta-analysis to evaluate the existing evidence. Over a weighted average follow-up period of about 8 years, the incidence of AL following primary UKA ranged from 0.00 to 22.70% across individual studies and averaged approximately 1.77% in pooled analysis. The incidence of tibial loosening was higher than that of femoral loosening. AL incidence increased with increasing follow-up during the post-operative period and reached a peak 10 years post-operatively. There was a temporal decline in incidence of AL from the 1970s to 2010 and beyond. Our analysis of potential risk factors for AL after primary UKA found no statistically significant association with sex (male *vs*. female), laterality (right *vs*. left), or affected compartment (medial *vs*. lateral). Results of single reports found an increased risk of AL associated with fixed-implant design and cemented implant fixation, whereas robotic-assisted UKA was associated with decreased risk of AL.

4.2 Comparison with previous work

Although several other meta-analyses identify AL as the chief cause of revision following UKA (31, 32), we did not identify any previous reviews that have attempted to summarise evidence on the incidence trends of AL following primary UKA. Furthermore, no other meta-analyses have attempted to comprehensively evaluate multiple risk factors in this setting. Our findings are in keeping with several other reviews that report AL incidence rates, restricted to specific groups. The largest was of Mohammad *et al*. (33). Their assessment of long-term outcomes of 8,658 medial Oxford phase III knees, aggregated from 15 studies, reported an AL incidence of 1.25%. Ernstbrunner *et al*. (31) reported 74 cases of AL in a meta-analysis of 4,573 patients, equating to an incidence of 1.62%; only lateral UKAs were included. Yoon et al. (34) reported an AL incidence of 0.94% (6 out of 637 UKAs) when comparing UKAs performed due to underlying spontaneous osteonecrosis of the knee *vs*. medial osteoarthritis. Other than being restricted to specific subpopulations, a major limitation in these previous approaches was that incidence rates were estimated from the number of AL cases divided by the total number of UKA procedures and expressed as a percentage; hence, such findings do not account for time. By employing relevant statistical approaches and taking into account the period of follow-up (weighted means), our review represents the first attempt at evaluating and synthesising AL incidence and its temporal trends in more detail than ever before.

Furthermore, as our secondary outcome measure, this is the first aggregate analysis to evaluate the associations of patient- and surgery-related factors with AL risk following UKA. We have identified no association with sex, laterality or specific tibio-femoral compartment, and only individual reports show an association of fixed implant design and cemented implant fixation with an increased risk of AL. Our results are in contrast to a recent meta-analysis by Huang *et al*. (35) which found no significant differences in the rate of AL between fixed and mobile bearing UKA. Their report included eight studies totaling 1,996 knees; far less than the 32,847 knees included in the single study captured in our search strategy, suggesting a lack of statistical power to measure this association.

4.3 Possible explanation for findings

AL following UKA has been reported in the literature to be influenced by a number of intra-operative factors, including component malalignment, under-correction of the pre-degeneration deformity, deficiency of the anterior cruciate ligament and excessive tibial slope (3). In our study, AL more commonly affected the tibial component; other studies have varied on whether tibial or femoral components are more susceptible (36-38). Tibial loosening tends to be associated with component malalignment. Chatellard *et al*. demonstrated that a difference of >2 mm between medial and lateral joint spaces was associated with tibial AL (39). Femoral loosening on the other hand is thought to result from poor fixation (40). Improvements in prosthetic design and fixation techniques over time may have led to less femoral loosening and hence a higher proportion of tibial loosening as reported in our study.

We report a temporal decline in AL since the 1970s. This may reflect improvements in prosthetic design and surgical technique (41). Over this period all-cause revision has similarly declined. Although early studies of UKA reported revision rates as high as 32% within seven years of follow-up (42, 43), more recent studies and registry data report failure rates of <10% at ten years in certain prosthetic designs (1, 44). Modern designs are now thought to produce better outcomes even in young, active patients, who are otherwise thought to be at a greater risk of early failure (45).

Fixed-bearing and cemented UKAs each had an increased risk of AL compared to mobile-bearing and non-cemented UKAs, respectively, but these were based on single reports (28, 29). It is thought that fixed-bearing UKA results in greater contact stress on the polyethylene insert of the tibial component compared to mobile-bearing implants. Furthermore, the constraint of the bearing leads to increased transmission of force to the implant/bone interface. Thus, poor conformity and subsequent micro-motion in fixed implants may accelerate the development of AL (12). However, a recent meta-analysis by Abu Al-Rub et al. which compared fixed with mobile bearing unicompartmental knee replacement did not find any difference between implant survivorship (46). A direct comparison of AL rates in cemented *vs*. uncemented UKAs were reported by Mohammad *et al* (33). The group reported AL rates of 1.0% vs. 0.42% at a 10-year follow-up ($p<0.001$) for cemented *vs*. uncemented groups in 14,814 UKAs. The lower risk of AL in uncemented implants may in part by explained by radiographic evidence from a randomized controlled trial, demonstrating fewer radiolucent tibial lines surrounding uncemented implants and thus better fixation than cemented UKAs (47). We identified a single study through our search criteria that investigated AL following robotic-assisted surgery comparing the Mako Robotic-Arm Assisted System vs. non-robotic UKA in 7,091 patients (30). The group reported a reduced incidence of AL in the robotic group (10 *vs*. 114; $p=0.001$). It is of note that the authors of this study do acknowledge funding from a related commercial party and is thus at risk of reporting bias. Reliable data independent from industry funding is currently ongoing (48).

4.4 Implications of our findings

It is pleasing that the incidence of AL following UKA is decreasing, but as UKA is becoming more common (49), the overall revision burden due to AL is still likely to increase. Despite the growing number of surgeons performing UKA for localized tibio-femoral compartment degenerative disease, UKAs have high rates of revision compared to total knee arthroplasty at 16.4% by 14 years. Registry data for England, Wales and Northern Island have reported that the main causes of revision are coded as aseptic loosening, ‘other’ reasons (including progressive arthritis), instability and pain. According to their 16th Annual Report, AL accounted for revision rates (95%CI) of 3.32 (3.18-3.47) per 1,000 prosthesis-years following primary UKA (1).

Our findings on the incidence and temporal trends of AL will inform decision making and resource planning. Our findings suggest AL is uncommon at <2% at 8 years, with a decreasing temporal trend. Considering this low incidence and the high failure rates in recent registry data, our findings also highlight the important question: what is driving UKAs to fail at such a high rate? It is the opinion of the authors that we should shift attention to appropriate decision making and patient selection, rather than implant and surgical-factors such as AL, as this may be driving the high burden of UKA revision.

4.5 Study strength and limitations

To our knowledge, this is the first aggregate analysis attempting to assess the temporal incidence trends in AL following primary UKA, combined with the evaluation of a number of patient-, implant- and surgery-related risk factors in a single comprehensive investigation. Our inclusion of 96,294 patients across many continents makes our results generalizable with enhanced power to assess AL associations in greater detail than previous reviews. Appropriate meta-analytic approaches were utilised in all analyses, which included accounting for heterogeneity between studies, using meta-regression techniques, and ensuring that studies with zero rates were not excluded from the pooled analysis. There are some limitations to our analysis, such as (i) though observational study designs are valuable tools for assessing associations between a risk factor and outcome, they do not prove causation and are limited by biases such as selection bias, residual confounding, and regression dilution bias; (ii) the majority of studies did not adjust for confounding; (iii) temporal trends in AL rates were based on the reported median year of data collection, which may not accurately capture specific periods of surgery and follow-up; (iv) only two studies specifically reported the use of onlay and inlay tibial components, which precluded the estimation of the incidence of AL in these subgroups; (v) due to lack of data, our analyses were unable to identify the contribution of sociodemographic factors such as age or BMI; (vi) the annual event rate for AL was estimated on the assumption that AL can occur anytime following surgery; hence, the results may be biased and (vii) several of the association findings were based on single study evaluations, and hence require interpretation with caution and replication in further studies.

5. Conclusions

The overall incidence of AL following primary UKA is variable; the average incidence is less than 2% over an average follow-up period of 8 years and appears to be driven by tibial component loosening. There is a temporal decline in incidence. Surgical measures that reduce AL risk such as use of mobile-bearings, non-cemented fixations, or robotic-assisted surgery may be employed by surgeons when performing primary UKA.

6. Funding

This study was funded by the NIHR Biomedical Research Centre at University Hospitals Bristol and Weston NHS Foundation Trust and the University of Bristol (BRC-1215-20011). The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

7. References

1. National Joint Registry of England WNI. National Joint Registry 15th Annual Report. 2018.
2. Foran JR, Brown NM, Della Valle CJ, Berger RA, Galante JO. Long-term survivorship and failure modes of unicompartmental knee arthroplasty. Clin Orthop Relat Res. 2013;471(1):102-8.
3. Vasso M, Corona K, D'Apolito R, Mazzitelli G, Panni AS. Unicompartmental Knee Arthroplasty: Modes of Failure and Conversion to Total Knee Arthroplasty. Joints. 2017;5(1):44-50.
4. NiemeläInen MJ, MäKelä KT, Robertsson O, W-Dahl A, Furnes O, Fenstad AM, et al. Different incidences of knee arthroplasty in the Nordic countries. Acta Orthop. 2017;88(2):173-8.
5. Australian Orthopaedic Association. Australian Orthopaedic Association National joint replacement registry: Hip, knee and shoulder arthroplasty. Australia. 2020.
6. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101,330 matched patients: a study of data from the National Joint Registry for England and Wales. Lancet. 2014;384(9952):1437-45.
7. Liddle AD, Pandit H, Judge A, Murray DW. Patient-reported outcomes after total and unicompartmental knee arthroplasty: a study of 14,076 matched patients from the National Joint Registry for England and Wales. Bone Joint J. 2015;97-B(6):793-801.
8. Hansen EN, Ong KL, Lau E, Kurtz SM, Lonner JH. Unicondylar Knee Arthroplasty Has Fewer Complications but Higher Revision Rates Than Total Knee Arthroplasty in a Study of Large United States Databases. J Arthroplasty. 2019;34(8):1617-25.
9. Price AJ, Waite JC, Svard U. Long-term clinical results of the medial Oxford unicompartmental knee arthroplasty. Clin Orthop Relat Res. 2005(435):171-80.
10. Association AO. Australian Orthopaedic Association Annual Report. 2018.
11. Zealand N, Association O. New Zealand
Orthopaedic Association
Annual Report 2017 – 2018. 2018.
12. Kim KT, Lee S, Lee JI, Kim JW. Analysis and Treatment of Complications after Unicompartmental Knee Arthroplasty. Knee Surg Relat Res. 2016;28(1):46-54.
13. Clark M, Campbell DG, Kiss G, Dobson PJ, Lewis PL. Reintervention after mobile-bearing Oxford unicompartmental knee arthroplasty. Clin Orthop Relat Res. 2010;468(2):576-80.
14. Gallo J, Goodman SB, Konttinen YT, Wimmer MA, Holinka M. Osteolysis around total knee arthroplasty: a review of pathogenetic mechanisms. Acta Biomater. 2013;9(9):8046-58.
15. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of Observational Studies in Epidemiology. JAMA: The Journal of the American Medical Association. 2000;283(15):2008-12.
16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.
17. Wells GS, B. O'Connell, D. Peterson, J. Welch, V. Losos, M. Tugwell, P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2011.
18. Freeman MF, Tukey JW. Transformations Related to the Angular and the Square Root. Ann Math Statist. 1950:607-11.

19. Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, Inform Team. Re-infection outcomes following one- and two-stage surgical revision of infected hip prosthesis: A systematic review and meta-analysis. PloS one. 2015;10(9):e0139166.
20. Kunutsor SK, Whitehouse MR, Lenguerrand E, Blom AW, Beswick AD, Inform Team. Re-infection outcomes following one- and two-stage surgical revision of infected knee prosthesis: A systematic review and meta-analysis. PloS one. 2016;11(3):e0151537.
21. Kunutsor SK, Beswick AD, Whitehouse MR, Wylde V, Blom AW. Debridement, antibiotics and implant retention for periprosthetic joint infections: A systematic review and meta-analysis of treatment outcomes. J Infect. 2018;77(6):479-88.
22. Kunutsor SK, Barrett MC, Beswick AD, Judge A, Blom AW, Wylde V, et al. Risk factors for dislocation after primary total hip replacement: a systematic review and meta-analysis of 125 studies involving approximately five million hip replacements. The Lancet Rheumatology. 2019;1(2):e111-e21.
23. Kunutsor SK, Barrett MC, Whitehouse MR, Blom AW. Venous thromboembolism following 672,495 primary total shoulder and elbow replacements: Meta-analyses of incidence, temporal trends and potential risk factors. Thromb Res. 2020;189:13-23.
24. Kunutsor SK, Barrett MC, Whitehouse MR, Craig RS, Lenguerrand E, Beswick AD, et al. Incidence, temporal trends and potential risk factors for prosthetic joint infection after primary total shoulder and elbow replacement: Systematic review and meta-analysis. J Infect. 2020;80(4):426-36.
25. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-88.
26. Riley RD, Higgins JP, Deeks JJ. Interpretation of random effects meta-analyses. BMJ. 2011;342:d549.
27. Higgins JP, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. J R Stat Soc Ser A Stat Soc. 2009;172(1):137-59.
28. Baker PN, Jameson SS, Deehan DJ, Gregg PJ, Porter M, Tucker K. Mid-term equivalent survival of medial and lateral unicondylar knee replacement: an analysis of data from a National Joint Registry. J Bone Joint Surg Br. 2012;94(12):1641-8.
29. Mohammad HRM, G.S. Judge E, A. Murray, D.W. Comparison of the 10-year outcomes of cemented and cementlessunicompartmental knee replacements: data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. Acta Orthopaedica; 2020. p. 76-81.
30. St Mart JP, de Steiger RN, Cuthbert A, Donnelly W. The three-year survivorship of robotically assisted versus non-robotically assisted unicompartmental knee arthroplasty. Bone Joint J. 2020;102-B(3):319-28.
31. Ernstbrunner L, Imam MA, Andronic O, Perz T, Wieser K, Fucentese SF. Lateral unicompartmental knee replacement: a systematic review of reasons for failure. Int Orthop. 2018;42(8):1827-33.
32. Peersman G, Stuyts B, Vandenlangenbergh T, Cartier P, Fennema P. Fixed- versus mobile-bearing UKA: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2015;23(11):3296-305.
33. Mohammad HR, Strickland L, Hamilton TW, Murray DW. Long-term outcomes of over 8,000 medial Oxford Phase 3 Unicompartmental Knees-a systematic review. Acta Orthop. 2018;89(1):101-7.
34. Yoon C, Chang MJ, Chang CB, Choi JH, Lee SA, Kang SB. Does unicompartmental knee arthroplasty have worse outcomes in spontaneous osteonecrosis of the knee than in medial compartment osteoarthritis? A systematic review and meta-analysis. Arch Orthop Trauma Surg. 2019;139(3):393-403.

35. Huang F, Wu D, Chang J, Zhang C, Qin K, Liao F, et al. A Comparison of Mobile- and Fixed-Bearing Unicompartmental Knee Arthroplasties in the Treatment of Medial Knee Osteoarthritis: A Systematic Review and Meta-analysis of 1,861 Patients. J Knee Surg. 2019.
36. Monk AP, Keys GW, Murray DW. Loosening of the femoral component after unicompartmental knee replacement. J Bone Joint Surg Br. 2009;91(3):405-7.
37. Murray DW, Goodfellow JW, O'Connor JJ. The Oxford medial unicompartmental arthroplasty: a ten-year survival study. J Bone Joint Surg Br. 1998;80(6):983-9.
38. Bordini B, Stea S, Falcioni S, Ancarani C, Toni A. Unicompartmental knee arthroplasty: 11-year experience from 3929 implants in RIPO register. Knee. 2014;21(6):1275-9.
39. Chatellard R, Sauleau V, Colmar M, Robert H, Raynaud G, Brilhault J, et al. Medial unicompartmental knee arthroplasty: does tibial component position influence clinical outcomes and arthroplasty survival? Orthop Traumatol Surg Res. 2013;99(4 Suppl):S219-25.
40. Crawford DA, Berend KR, Lombardi AV. Management of the Failed Medial Unicompartmental Knee Arthroplasty. J Am Acad Orthop Surg. 2018;26(20):e426-e33.
41. Campi S, Tibrewal S, Cuthbert R, Tibrewal SB. Unicompartmental knee replacement - Current perspectives. J Clin Orthop Trauma. 2018;9(1):17-23.
42. Insall J, Aglietti P. A five to seven-year follow-up of unicondylar arthroplasty. J Bone Joint Surg Am. 1980;62(8):1329-37.
43. Lindstrand A, Stenström A, Lewold S. Multicenter study of unicompartmental knee revision. PCA, Marmor, and St Georg compared in 3,777 cases of arthrosis. Acta Orthop Scand. 1992;63(3):256-9.
44. Citak M, Dersch K, Kamath AF, Haasper C, Gehrke T, Kendoff D. Common causes of failed unicompartmental knee arthroplasty: a single-centre analysis of four hundred and seventy one cases. Int Orthop. 2014;38(5):961-5.
45. Thompson SA, Liabaud B, Nellans KW, Geller JA. Factors associated with poor outcomes following unicompartmental knee arthroplasty: redefining the "classic" indications for surgery. J Arthroplasty. 2013;28(9):1561-4.
46. Z Abu Al-Rub JNL, R M West , X Yang , Y Hu , H G Pandit. Survivorship of fixed vs mobile bearing unicompartmental knee replacement: A systematic review and meta-analysis of sixty-four studies and National Joint Registries. The Knee. 2020;27(5):1635-44.
47. Kendrick BJ, Kaptein BL, Valstar ER, Gill HS, Jackson WF, Dodd CA, et al. Cemented versus cementless Oxford unicompartmental knee arthroplasty using radiostereometric analysis: a randomised controlled trial. Bone Joint J. 2015;97-B(2):185-91.
48. Metcalfe A. https://www.fundingawards.nihr.ac.uk/award/NIHR128768.
49. Murray DW, Liddle AD, Liddle A, Dodd CA, Pandit H. Unicompartmental knee arthroplasty: is the glass half full or half empty? Bone Joint J. 2015;97-B(10 Suppl A):3-8.