Hip and knee replacement 2

Knee replacement

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This is the second in a **Series** of two papers about hip and knee replacement

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Knee replacement surgery is one of the most commonly done and cost-effective musculoskeletal surgical procedures. The numbers of cases done continue to grow worldwide, with substantial variation in utilisation rates across regions and countries. The main indication for surgery remains painful knee osteoarthritis with reduced function and quality of life. The threshold for intervention is not well defined, and is influenced by many factors including patient and surgeon preference. Most patients have a very good clinical outcome after knee replacement, but multiple studies have reported that 20% or more of patients do not. So despite excellent long-term survivorship, more work is required to enhance this procedure and development is rightly focused on increasing the proportion of patients who have successful pain relief after surgery. Changing implant design has historically been a target for improving outcome, but there is greater recognition that improvements can be achieved by better implantation methods, avoiding complications, and improving perioperative care for patients, such as enhanced recovery programmes. New technologies are likely to advance future knee replacement care further, but their introduction must be regulated and monitored with greater rigour to ensure patient safety.

Introduction

Knee replacement surgery has been routinely done for more than 40 years and usage continues to grow worldwide. Its success is based on improving the quality of life for patients with knee arthritis by reducing pain and improving long-term function. However, 20% of patients are dissatisfied with the outcome of surgery, and research and development in the field focuses on this deficiency. This review concentrates on a number of topical areas in knee replacement, starting with the epidemiology of knee replacement and the variability in intervention rates alongside the indications for surgery. The increasingly important role of patient-reported outcomes and analysis of registry data is considered, together with an overview of the health–economic evidence relating to knee replacement. Enhanced recovery programmes are commonplace and have the potential to positively affect patient outcomes. Development of new implants and supportive technologies is continuously led by the industry, but more robust evidence to support their introduction is still required; we therefore review the regulatory requirements for assessment of new devices and strategies to ensure patient safety in this process.

Search strategy and selection criteria

We searched MEDLINE and PubMed from Jan 1, 1970, to April 30, 2018, using the search term "knee" in combination with "replacement", "joint", "total", "partial", "arthroplasty", "epidemiology", "mortality", "morbidity", "outcomes", "registry", "enhanced-recovery", "indications", "effectiveness", "cost-effectiveness", "survivorship", "follow-up", "innovation", "evaluation", and "regulation". We concentrated on results from randomised trials, registries, and large population cohort studies. We mostly selected publications from 2010 to 2018, but did not exclude commonly referenced and important older publications.

Epidemiology of knee replacement

The use of knee replacement as a treatment for arthritis continues to increase. In the UK, more than 100 000 knee replacements are now done each year and a similar pattern of increased frequency is reported by many worldwide joint registries.[1–5] Total numbers of procedures in the USA have now reached 700 000 per year, and the number is increasing as predicted despite periods of economic downturn (figure 1).[6,7] Projected analyses from

Key messages

- More than 95% of all knee replacements are done for osteoarthritis
- Patients who undergo surgery usually have persistent symptoms of moderate or severe pain, and associated loss of function that has not responded to non-operative measures
- The average age of people undergoing knee replacement is about 65 years, but increasing numbers of knee replacement surgery are done in younger patients
- 80–85% of patients have successful treatment characterised by reduced pain, improved function, and enhanced quality of life
- 15–20% of patients are dissatisfied with their outcome, usually characterised by ongoing pain and poor function
- Following implantation, a 65-year old patient has a 7% lifetime risk of requiring revision surgery, but this risk increases substantially with younger age groups
- The most common reasons for revision surgery are implant loosening, infection, pain, and instability
- 45-day mortality rates following knee replacement have substantially decreased over time

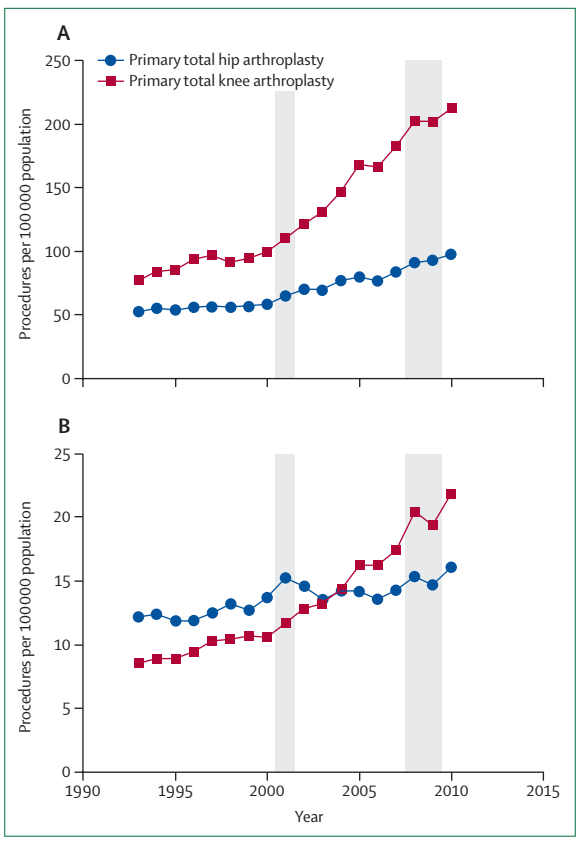

Figure 1: **The incidence of primary (A) and revision (B) total hip and total knee arthroplasties relative to the total US population**
The incidence has increased over time. The years in which the US economy was in recession (2001 and 2008–09) are highlighted. Reproduced from Kurtz et al,[6] by permission of Wolters Kluwer.

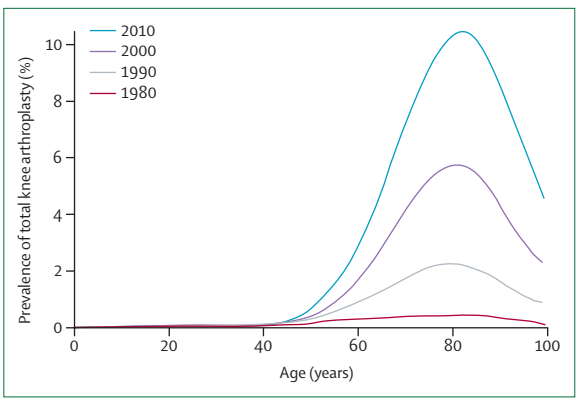

Figure 2: **Secular changes in the prevalence of total knee arthroplasty in the total US population between 1980 and 2010**
Reproduced from Maradit Kremers et al,[10] by permission of Wolters Kluwer.

different counties all suggest that, even with conservative estimates, the increased use of knee replacement will continue.[8,9]

In 2010, the prevalence of knee replacement in the USA reached 1·5% in the general population and 10·4% in patients aged 80 years (figure 2).[10] Data from the UK Clinical Research Practice Datalink database estimates that at the age of 50 years the lifetime risk of undergoing total knee replacement surgery is 10·8% for women and 8·1% for men,[11] with similar findings reported from the New Zealand Joint Registry.[3] In fact, in all registries women undergo knee replacement more commonly than men.[1–5] The most common indication for knee replacement remains primary osteoarthritis, and the increasing numbers of patients with osteoarthritis is one driver for increasing use of knee replacement.[4,12] The numbers of knee replacements done for inflammatory arthropathy, the second most common indication, has not substantially increased in the past 10 years, mainly related to the success of modern disease modifying antirheumatic drugs.[13]

The average age of patients undergoing knee replacement remains in the mid-60s, but with increasing numbers of patients younger than 60 years (figure 2).[14] In all national joint registries, a higher revision is seen in this younger group of patients, who now make up approximately 15% of all patients undergoing knee replacement.[1–4] Recent evidence suggests that in the age group of those younger than 60 years the lifetime risk of revision is approximately 35% for men and 20% for women, with half the rate of revision occurring within the first 5 years of implantation.[15] (figure 3). The increasing trend for knee replacement in the younger patient will inevitably increase the number of revisions done (figure 1).

The reasons for the substantial growth in utilisation rates of knee replacement seen around the world are complex. In the USA, evidence suggests that growth cannot be fully explained by population increase and higher incidence of obesity alone.[16] Health-care reform and greater equity in access to health-care services has been identified as a driver of greater usage.[17] Perhaps most striking is the variation in utilisation seen across different countries. Falbrede and colleagues[18] reported intervention rates of 255–263 per 100 000 inhabitants in Germany and Switzerland, compared with 127 per 100 000 in the USA. Within the Organisation for Economic Co-operation and Development countries, a ten-fold variation in use exists, with strong correlation in frequency of use to gross domestic product, health expenditure, and obesity (figure 4).[14] Differences in knee replacement usage are seen even within closer geographical areas, such as the Nordic countries.[19] The evidence continues to suggest that the interplay of economic variables, health-care system factors, reimbursement, and patient and surgeon preferences all contribute to determining variation in the use of knee arthroplasty surgery. More work is required to reduce this unwarranted variation in practice.[20]

Indications for knee replacement surgery

Total knee replacement has traditionally been offered to older patients with intolerable knee pain, unacceptable activity limitation with the loss of highly valued activities,

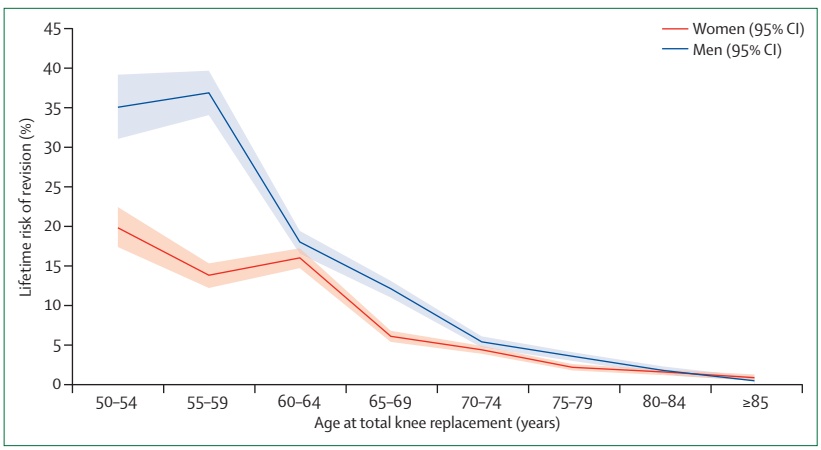

Figure 3: **Lifetime risk of revision after total knee replacement**
The plot shows the estimates of lifetime risk of total knee replacement revision against age at the time of primary total knee replacement surgery in 5-year age bands, and is stratified by sex. Shaded areas are 95% CIs. Results are adjusted for lost and censored population. Reproduced from Bayliss et al,[16] by permission of Elsevier.

and severe end-stage osteoarthritis of the joint.[21] Historically, arthroplasty surgeons have been reluctant to operate on patients with either morbid obesity (because of the higher risk of perioperative complications), and on patients younger than 55 years (because of the increased likelihood of revision in their lifetime).[15,22,23] Surgeons have similarly been cautious about operating on patients with serious medical comorbidities, again for fear of complications but also on those with widespread pain and or catastrophising behaviour, because these problems are associated with higher risk of persistent pain.[24,25] Finally, surgeons have historically set high levels of preoperative pain and functional limitation to justify the risk of surgical intervention.

Recent studies support expanding these traditional indications. For example, although morbid obesity is indeed associated with greater risk of perioperative complications, such as postoperative infection, recent studies show that individuals with a body-mass index (BMI) of more than 35, and even more than 40, experience similar pain relief as patients who are not obese.[22,26] Similarly, studies have shown that patients with worse functional status preoperatively tend to have worse postoperative status, urging caution in permitting functional status to deteriorate while patients await total knee replacement.[27] Despite the higher risk of persistent pain, patients with depression and catastrophising nonetheless have, on average, marked improvements in pain and function following surgery.[24]

An important contributor to the contemporary broadening of indications of knee replacement is the growing importance of the patient's voice in decisions about whether to undertake surgery. Clinical guidance from the UK National Institute for Health and Care Excellence and the American Academy of Orthopaedic Surgeons, together with other authoritative bodies, emphasise the importance of engaging patients in shared decision-making conversations about whether to undertake knee replacement.[28,29] Shared decision making involves patients being appraised of the short-term and long-term risks and benefits of operative and non-operative therapy, to enable a decision that is consistent with their preferences and values. Knee replacement is only one option for patients with advanced knee osteoarthritis, and patients should be informed of alternatives.[29] For example, physical therapy programmes of strengthening and neuromuscular training can give symptomatic improvement in two-thirds of patients with advanced knee osteoarthritis.[30] In this shared decision-making model, the patient and not the physician has the ultimate say over whether to proceed with surgery or not, based on their own individual assessment of the balance of risk versus capacity to benefit.[21]

This process is particularly important to both the older and younger populations with osteoarthritis of the knee. For older individuals, a growing segment of this population are now living long enough to develop functionally limiting knee osteoarthritis in the eighth or ninth decade of their life. Despite their age and comorbidities, this group is increasingly opting for total knee replacement to maintain their quality of life.[2–4] Likewise, younger patients are choosing to undergo knee replacement for quality of life reasons, outweighing the increased risk of revision seen in this patient group. This move toward patient involvement in decision making and research is further epitomised by a recent patient-focused James Lind Alliance Priority Setting Partnership, which was done in the UK, highlighting areas for future research in knee replacement (panel).[31]

Indications for surgery can also be influenced by health-care systems. Preoperative symptom thresholds for knee replacement have recently been applied within the UK National Health System (NHS).[32] So-called pay for performance approaches, in which physicians are financially incentivised to restrict total knee replacement to those likely to have the best outcome (ie, individuals who are not obese or have fewer comorbidities), can potentially create conflict with patient preferences.[33]

Patient-reported outcome after knee replacement surgery

The evaluation of knee replacement has improved over time and the use of patient-reported outcome measures have become more common and influential. A recent systematic review showed 32 different measures that have been used for this purpose, with the Western Ontario and McMaster Universities Osteoarthritis (WOMAC), the Knee Injury and Osteoarthritis Outcome Score, and the Oxford Knee Score (OKS) widely used.[34] These instruments have shown that knee replacement improves quality of life for the majority of patients by substantially reducing pain and improving function.[30,35–37] However, up to 15–20% of patients who have undergone total knee replacement consider themselves to be

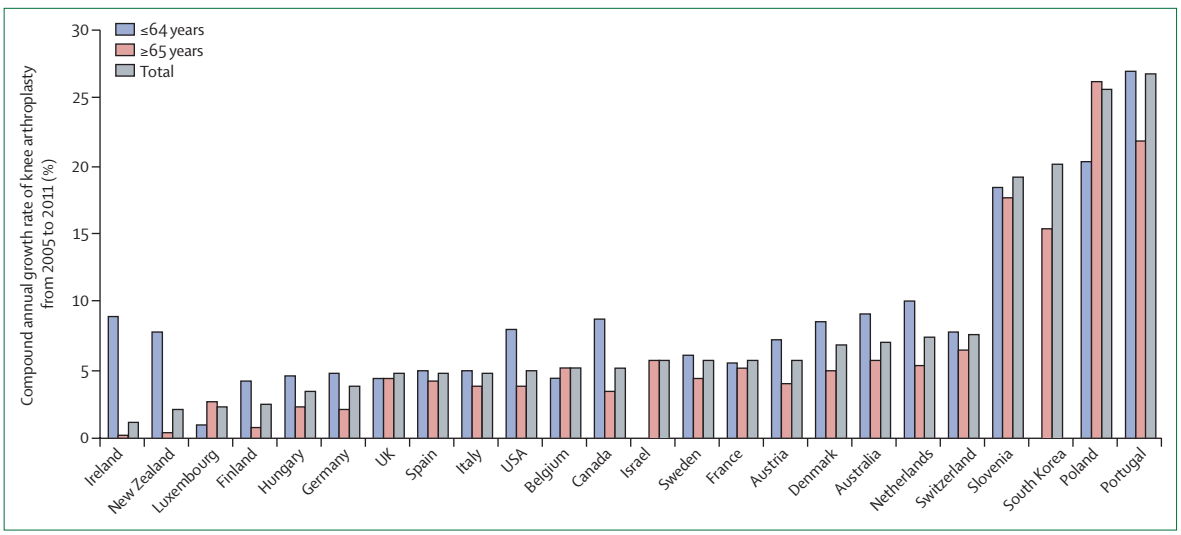

Figure 4: **Growth rates in knee arthroplasty among OECD countries**
Reproduced from Pabinger et al,[14] by permission of Elsevier. OECD=Organisation for Economic Co-operation and Development.

dissatisfied, gaining little benefit or describing a poor outcome following intervention when assessed by patient-reported outcome measures.[38]

For each scoring system, the requirement to establish their measurement properties is increasing, including validity or meaningfulness, repeatability, responsiveness, and usability in the context of knee replacement. The understanding and use of patient-reported outcome measures in this field is increasing and many different instruments are used including condition-specific (eg, WOMAC), joint-specific (eg, OKS), or more general measures of quality of life (eg, EQ-5D).[34] The ability of an instrument to measure change in patient state is important; and for all scores, evidence-based meaningful changes should be calculated.[39] Instruments can be graded according to levels of evidence, and those showing the best suite of measurement properties should be prioritised for use.[34]

To improve the patient's understanding of the results of knee replacement, attempts have been made to translate data of patient-reported outcome measures into categorical outcome (eg, good or poor).[40] However, care is required because no standardised approach exists and different definitions might lead to different interpretations of results.[41] Somewhat abstract numerical scores (such as an Oxford Score or WOMAC),[34] although still valuable research instruments, can be augmented by systems that include direct measures of patient satisfaction and experience of improvement (transition), as seen in the UK national audit of patient-reported outcome measures.[42] The concept of the patient-acceptable symptom state is one approach in determining response to treatment.[43] One possible area of further development is a standardised methodology to combine these patient-reported variables, together with re-operation and complication data, to get a fuller picture of the success or failure of the knee replacement treatment.[40] Some of the major trials of knee replacement are now incorporating such composite measures into their primary and secondary outcome

Panel: **The top ten priority research areas for knee replacement surgery for osteoarthritis**

1 What are the most important patient and clinical outcomes in knee replacement surgery for people with osteoarthritis, and what is the best way to measure them?
2 What is the optimal timing for hip and knee replacement surgery for best postoperative outcomes?
3 What are the preoperative predictors of postoperative success, and what are the risk factors of poor outcomes?
4 What preoperative, intraoperative, and postoperative factors can be modified to influence outcome following knee replacement?
5 What is the best pain control regimen preoperatively, perioperatively, and immediately after surgery?
6 What are the best techniques to control for long-term chronic pain and improve long-term function following knee replacement?
7 What are the long-term outcomes of non-surgical treatments compared with operative treatment for patients with advanced knee osteoarthritis?
8 What is the most effective preoperative and postoperative patient education support and advice for improving outcomes and satisfaction for people following knee replacement?
9 What is an ideal postoperative follow-up period and the best long-term care model for people with osteoarthritis that have had knee replacement?
10 What is the best way to protect patients from the risk of thrombotic events associated with knee replacement?

Adapted from James Lind Alliance Priority Setting Partnership.[31]

assessment.[44] Another approach is the personalisation of outcome measurement, with some scores referencing improvement from an individual's baseline.[45] Such personalisation relies heavily on the complex inter-relationship of patient expectation and satisfaction.[46]

Exploring large datasets of patient-reported outcome measures has led to greater understanding of factors that affect functional outcome after knee replacement: preoperative level of symptoms, expectation, comorbidity, age, and mental state.[38,47] From interrogation of these large datasets, it is possible to calculate an individual's capacity to benefit from knee replacement.[32] These tools that estimate the range of outcome possible are likely to be helpful in shared decision making. However predictive models that attempt to determine final outcome for patients can only explain a modest proportion of the variability in outcome observed and as yet their usefulness is unproven.[38,47]

Cost-effectiveness of knee replacement surgery

As one of the most commonly done elective procedures in the world, total knee replacement has not surprisingly been the subject of a substantial number of cost-effectiveness analyses. Using the health economists' favoured outcome measure—quality-adjusted life-years (QALYs)—these studies have typically estimated the ratio of incremental costs to health gain from total knee replacement to be between approximately £1000 and £12 000 for the average patient in different health-care systems, which is well within the range that most reimbursement and health technology assessment bodies would consider representative of good value for money.[35,36]

These highly favourable results follow from the fact that total knee replacement in most countries is a relatively inexpensive procedure, and has been found by numerous studies to be associated with substantial and sustained improvements from preoperative levels in many domains of both disease-specific and generic health-related quality-of-life measures, which is further explored in a systematic review[48] of 19 studies). In the Knee Arthroplasty Trial, for example—one of the largest and longest randomised trials of different types of total knee replacement—mean quality of life measured using the EQ-5D (1=full health, 0=death) increased from 0·39 immediately before surgery to 0·71 at 1 year and declined only gradually thereafter.[36]

Although most studies have concluded that total knee replacement is in general a highly cost-effective procedure, they have also reported substantial heterogeneity in costs and benefits between patient subgroups. For example, total knee replacement appears to be more cost-effective in younger patients, and in hospitals with higher volumes of procedures.[49] Interest has also focused on BMI, given increasing evidence that higher BMI values are associated with increased health-care costs for total knee replacement.[50] However, several analyses have not reported any clear association between BMI and the cost-effectiveness of total knee replacement, and in general the single best predictor of postoperative costs, outcomes, and cost-effectiveness appears to be preoperative symptom severity.[32,36] This effect might explain why one recent cost-effectiveness study by Ferket and colleagues[51] markedly differed from other analyses in concluding that total knee replacement in a recent US cohort of patients had very small effects on quality of life and correspondingly poor levels of cost-effectiveness: their estimated preoperative quality-of-life scores were very much less severe than those reported in most other cohorts, trials, and registers, with a correspondingly much smaller postoperative improvement. The only strictly randomised comparison of total knee replacement with non-surgical treatment estimated the 1-year effect of surgery on quality of life to be about three times that reported by Ferket and colleagues.[30,51] An economic evaluation based on the trial by Skou and colleagues[30] has not yet been reported.

In addition to the paucity of evidence from randomised studies, a major problem confronting cost-effectiveness analyses of total knee replacement has been how to characterise the comparator—eg, is it usual care, intensified non-surgical care, or delayed surgery? Enhanced recovery programmes for those undergoing total knee replacement are also attracting increasing interest and are being introduced in many NHS hospitals for patients undergoing hip and knee replacement.[52] Robust cost-effectiveness on such programmes is required and an ongoing systematic review will be a useful first step.[53]

As the annual number of total knee replacements done continues to increase globally, it is reasonable to keep the cost-effectiveness of the procedure under review, especially if it is being extended to patients who are much younger or older, or have substantially more co-morbidities or less severe preoperative symptoms. However, it is also important to keep in mind that many patients who could benefit from total knee replacement, and who would meet existing cost-effectiveness criteria, are currently not getting access to this procedure because of overall resource constraints, capacity shortages, or spending restrictions.[32,36]

Enhanced recovery after knee replacement surgery

Enhanced recovery programmes use a multimodal approach aimed at improving the care and subsequent clinical outcome for patients undergoing knee arthroplasty. First proposed in 1997,[54] this approach aims to minimise the physiological and psychological stresses of surgery through the use of specific interventions throughout the care pathway.[55] The principal components of enhanced recovery programmes can be broadly thought of in terms of preoperative optimisation of patients' comorbidities, patient education, perioperative anaesthetic techniques, perioperative surgical techniques, and postoperative rehabilitation. There is now growing evidence that such programmes improve outcomes for knee arthroplasty

patients, with reduction in complications such as stroke, myocardial infarction, acute renal failure, and thromboembolic events potentially leading to reduced mortality after surgery,[56,57] as well as having profound health economic benefits.[52]

A major component of enhanced recovery programmes is the use of standardised anaesthetic protocols that include spinal (ie, neuraxial) and regional anaesthesia. Evidence suggests that using these techniques in knee replacement can reduce perioperative morbidity, reduce length of hospital stay, and encourage faster functional recovery.[58] The use of periarticular local infiltration of anaesthetic around the knee joint as part of a multimodal analgesic programme can also be as effective, if not superior, to regional blockade.[59] The minimisation of blood loss is another important element of enhanced recovery programmes, and this element has resulted in the adoption of tranexamic acid use, a practice that can reduce transfusion requirement following total knee replacement.[60] Additionally, enhanced recovery programmes are adopting new evidence in prevention of venous thromboembolism after knee replacement—for instance, showing that aspirin is a reliable and cost-effective treatment option.[61]

Early mobilisation following surgery is favoured by knee arthroplasty enhanced recovery programmes and is associated with reduced complications, reduced length of stay, and lower costs.[62] The benefits of these programmes are now being applied to facilitate same-day or outpatient knee arthroplasty in carefully selected patient groups.[63]

Joint registries and knee replacement

Patterns of implant use

Analysis of national registry data has become a cornerstone of assessment of knee replacement surgery, reinforced by improvements in data capture, as seen in the UK National Joint Registry (UK NJR).[1] Data from all published registries show expanding usage of knee replacement over time, with women most likely to have surgery, and increasing numbers of patients younger than 60 years having surgery.[1–5] Most implantations are cemented total knee replacements, with far fewer partial (unicompartmental) knee replacements being done. The majority of prostheses implanted are established cruciate retaining or posterior stabilised implants with long-track records, but new implant modifications or new designs continue to be regularly introduced.[1–5] The requirement for close scrutiny of any new implants is highlighted by the introduction of the Beyond Compliance in the UK, which is working closely with the UK NJR and the Orthopaedic Data Evaluation Panel, illustrating the important role for registries to have in this process.

Patterns of revision

In all registries, a revision rate of 3–5% at 10 years is commonly reported for many total knee replacement designs.[1,4] The most common causes for revision reported in national joint registries remains, in order of frequency: implant loosening, infection, pain, and instability, with the overall pattern of reported failure mechanism not changing over the past 10 years.[1–5] The leading cause of early revision following total knee arthroplasty continues to be periprosthetic joint infection.[64] The effect of this devastating complication on patients has been well documented.[65] Recent analysis of the first 15 years of the New Zealand Joint Registry has shown an increase in early revision due to infection, and similar patterns are reported in Sweden and Australia.[2–4] The increasing number of patients with knee periprosthetic joint infection has been partially ascribed to the increase in the number of patients with diabetes or obesity, and young patients undergoing knee arthroplasty.[66,67] Recent work has focused on improving the diagnosis of periprosthetic joint infection and more research is required to improve its treatment.[68] Key to this improvement is the collection of more relevant outcome data, including microbiological profile, antimicrobial therapy, and the patient's general health status, with infection-specific outcomes linked to registry survival results.[69]

New methodologies and roles for registries

Joint replacement registries have been in use for many years to help monitor the outcome following knee replacement surgery. The primary methodology has been identification of failing implants determined by a calculation of device survival, using revision surgery as a hard endpoint. However, new methodologies and roles for registries are being developed. Recently, the International Society of Arthroplasty Registries, an organisation of national registries of 41 members, has included patient-reported outcome measures to enable more patient-specific data to help assess functional outcomes.[70] As stated before, it might be that a more sensitive measure of the success on an implant is a combination of revision and patient-reported outcome measures as endpoints. In support of this concept is emerging evidence that scores of patient-reported outcome measures can predict early failure. The New Zealand Joint Registry, has shown that an Oxford Knee Score less than 27 of 48 at 6 months was associated with a ten-times increased revision risk at 2 years compared with a score of greater than 41.[71] Such early identification of patients at risk enables follow-up of vulnerable patients, providing better overall outcome and reducing health expenditure.

Another substantial advance in the use of registries is the ability to link them to other large national databases. For example in the UK NJR, data have been successfully linked to Hospital Episode Statistics and data of national patient-reported outcome measures to identify a reduction in mortality after knee replacement from 0·37% in 2003 to 0·20% in 2013, and reduced patient morbidity after partial when compared to total knee

For more on the **Orthopaedic Data Evaluation Panel** see http://www.odep.org.uk

arthroplasty.[72,73] A further potential extension of knee replacement registry data is the development of registry-based randomised controlled trials, increasing the power of studies and decreasing cost.[74] The evidence produced from registries can also have a direct role in supporting the delivery of health services, as seen in the UK where the UK NJR reports are routinely used in individual consultant appraisal and hospital level feedback, such as the Getting it Right First Time process.

For more on the **Getting it Right First Time process** see http://gettingitrightfirsttime.co.uk/

Development and new technology in knee replacement surgery

Design of total condylar knee replacement

Posterior cruciate retaining or sacrificing total condylar knee designs remain the two most widely used total knee replacement options.[1–3] Incremental design development continues, such as gender-specific and high-flex components, but evidence that these changes in component shape produce any meaningful improvement in outcome is sparse.[75] Most knee replacements still use a metal on polyethylene-bearing surface and polyethylene wear remains a major cause of implant failure.[1,2,4] Around 20 years ago, highly cross-linked polyethylene, so-called second-generation polyethylene, was introduced and has been successful in minimising polyethylene wear; thereby reducing aseptic loosening and revision.[76] More recently, vitamin-E-infused, highly cross-linked polyethylene, so-called third-generation or antioxidant polyethylene has been developed,[77] but the efficacy of this polyethylene remains to be established.

Alignment in total knee replacement

For more than 30 years, the standard approach to implanting total knee replacements has been to aim for mechanical alignment, where the hip, centre of the reconstructed knee, and the ankle are in alignment.[78] More recently, kinematic alignment has been proposed as an alternative implantation strategy, aiming to mimic the predisease joint surface orientation. This procedure is thought to optimise ligament balance and knee kinematics without the need for ligament releases.[79] The global experience with kinematic alignment in total knee replacement is limited, but a recent literature review[80] reported more favourable outcome after kinematically aligned total knee replacement compared with mechanical alignment; however, the improvement is not universal.[81] The benefit from different alignment methods is possibly influenced by the pattern of osteoarthritis for each individual patient. Mechanical alignment remains the mostly widely used method of implantation and further investigation of the safety of kinematic alignment is needed before the technique can be considered for widespread use.

Partial knee replacement

Most patients receive a total knee replacement implant, but currently approximately 8% of cases receive a partial (unicompartmental) knee replacement in the medial, lateral, or patellofemoral compartment.[1] The proposed benefits of partial knee replacement over total knee replacement include optimised functional outcome, lower postoperative length of stay, fewer medical complications, reduced re-admissions and mortality, and greater cost-effectiveness.[82] Recent evidence from randomised controlled trials has supported these findings, and results from other trials currently in progress are awaited.[44,83,84] The major argument against wider adoption of partial knee replacement as an alternative to total knee replacement is the higher revision rate reported in nearly all national registry reports.[1,2,4] There is increasing evidence that the revision rate for partial knee replacement is related to the number performed or the proportion of partial knee replacement to total knee replacement undertaken by individual surgeons and units.[85] In addition, recent registry evidence has suggested that with improved implantation methods, for instance the introduction of cementless fixation, revision rates for partial knee replacement can be reduced.[3]

Patient-specific instrumentation, computer navigation, and robotics

Patient-specific instrumentation and computer navigation have been introduced in knee arthroplasty surgery to help achieve more precise and accurate alignment.[86] The hope is that potential improvements would lead to improved outcomes and, secondarily, to increased intraoperative and economic efficacy. Literature reports are divergent, but overall there is little to suggest any clinically important difference in implant component positioning, lower limb alignment, or patient outcome is achieved compared with conventional techniques.[87–89] It could be speculated that the main potential of patient-specific instrumentation or computer navigation is to help less experienced, lower volume surgeons to achieve improved precision and accuracy, but this effect remains to be explored. There is some evidence to suggest that computer navigation might reduce revision rates in younger patients with total knee arthroplasty.[90] Robotics in knee arthroplasty surgery has so far had a very limited introduction and high-quality comparative studies showing the potential efficacy over conventional techniques are still required. In conclusion, technology-based assistive techniques are still in the developmental phase and true benefits have yet to be identified.[88]

The regulation and evaluation of innovation in knee replacement surgery

The majority of medical devices and surgical implants, including knee replacements, are used without problem or concern, but in some situations problems have arisen. For example, in the use of metal-on-metal hip replacements in which modifications to design resulted

in the production of excessive metal wear products, in some patients substantial local and sometimes systemic toxic effects were observed.[91] As a result, the regulatory authorities throughout the world have begun to make changes to their processes, and new frameworks for evaluating medical devices have changed.[92] In the past, many surgical implants were introduced in the USA without clinical evidence by the 510(k) route, based on a case of substantial equivalence rather than superiority to a device already on the market.[93] The recent changes to regulation have, in the USA, increased the use of premarket approval, transparency, and justification during the submission process; and have allowed an improvement of the system of device recall, modified the process of new applications to make them more stringent, applied new processes to the review of existing devices, and fortified and reduced the use of the 510(k) system.[92] In Europe, the new rules established in 2017 will continue to use notified bodies to grant CE marks, but with increased oversight by competent authorities, and a new Medical Device Co-ordination Group will provide extra scrutiny for high-risk devices, such as knee replacement.[94] The European Commission will now be responsible for surveillance of implants through Eudamed, and high-risk implants will undergo assessment by the European Medicines Agency.[92]

One specific problem associated with the innovation and introduction of new knee implants into the market is demonstration of safety and benefit over existing technology.[95] It is clear that new innovations need to be introduced in a controlled step-wise manner using multiple study designs in a logical sequence that place the minimum number of patients at risk.[96] Benefit beyond existing technology can only be tested effectively through randomised trials, for which bias and confounding are reduced and allows true determination of efficacy of one type of implant over another.[97] Reliance on randomised trials is also far from ideal, as they are very costly, time consuming, and the validity of the results might be limited to the study population only. There are other barriers to surgical trials, in which the clinical culture makes it difficult for surgeons to express equipoise for different surgical techniques. Despite these issues, high-quality randomised controlled trials in knee replacement surgery are taking place.[30,35,44,84] Registry data are less useful for comparative studies but are capable of establishing temporal relationships of outcomes and adverse events with implantation of the device, and evaluating rare exposures that might occur many years after implantation.[98] Registers are resource intensive, because large cohorts need to be followed up for many years to establish true assessment of risk, and there is the potential for non-representative study populations to arise from loss to follow-up. Ongoing work is required to determine the most cost-effective manner to complete post-market surveillance of implanted devices. Other methodologies, such as roentgen stereophotogrammetric analysis can be effectively used to identify implants with increased risk of late failure.[99] A systematic process that adopts multiple study designs for the safe introduction of implants is being developed but as yet is not fully established.[96]

Improvement of regulatory framework and the quality of evidence for introduction of surgical implants and associated technology is essential.[100] The process should support innovation in knee replacement surgery while protecting patients from the introduction of devices with insufficient evidence of safety or superiority (cost or efficacy) over existing treatments. In the context of an already mature and generally successful technology, such as knee replacement surgery, the process of improved regulation is key to identify technologies that offer true benefit from those that offer no advantage, and at worst those that could cause harm.

Conclusion

Knee replacement surgery is a highly successful established technology, with good evidence of successful treatment outcome and long-term implant survival. A proportion of patients continue to have poor results and addressing this issue is the major challenge for improving care, particularly given the continued increase in worldwide usage and the increasing numbers of younger patients undergoing surgery. Continued incremental changes in implant design do not appear to have achieved any substantial improvement in outcome for patients, and focus could shift towards optimising modifiable patient factors and the use of alternatives to total knee replacement, such as partial knee replacement and perioperative management.

The field's understanding of patient-reported outcome of knee replacement has advanced, but it still needs further refinement. National registries continue to enable our understanding of knee replacement and new analysis methodologies must be harnessed to maximise benefit. As with all medical areas, new technology is being developed at an increasing rate and modernising regulatory change will help assessment of implants and devices to maintain patient safety. Given the existing success of established knee replacement technology, more creative assessment methodologies, including more randomised controlled trials and adaptive designs, must be used when introducing new devices. Greater focus on patient involvement and maintaining patient safety in this process will help to ensure knee replacement continues to be one of the most successful surgical procedures in modern medicine.

Contributors

All authors participated in the literature review. AJP wrote the introduction, conclusion, and the section on the epidemiology of knee replacement. AA wrote the section on enhanced recovery after knee replacement surgery. AT wrote the section on development and new technology in knee replacement surgery. JNK wrote the section on indications for knee replacement surgery. GH wrote the section on joint

registries and knee replacement. AG wrote the section on the cost-effectiveness of knee replacement surgery. AC wrote the section on regulation and evaluation of innovation in knee replacement surgery. DB wrote the section on patient-reported outcomes.

Declaration of interests

AJP has received funding from Zimmer Biomet and De Puy, and personal consultancy fees from Zimmer Biomet, during the conduct of the study. AT has received funding from Zimmer Biomet and De Puy, and personal consultancy fees from Zimmer Biomet, during the conduct of the study. All other authors declare no competing interests.

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