Knee Replacement **Seminar**

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Search strategy and selection criteria

We searched Medline and PubMed from January, 1970, to April, 2018, with 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 2010–18, but did not exclude commonly referenced, and important older publications. Review articles are cited to provide readers with more additional details and references.

Abstract

Knee replacement surgery is one of the most commonly performed and cost-effective musculoskeletal surgical procedures. Worldwide the numbers of cases performed continues to grow with significant 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 influenced by many factors including patient and surgeon preference. The majority of patients have a very good clinical outcome after knee replacement but multiple studies show 20% or more 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 peri-operative 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 performed for over 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 function over the long-term. 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 effect patient outcomes. There is continued industry led development of new implants and supportive technologies but robust evidence to support their introduction is still paramount. We review the regulatory requirements for assessment of new devices and strategies to ensure patient safety in this process.

Epidemiology of knee replacement

The use of knee replacement as a treatment for arthritis continues to grow. In the UK over 100,000 knee replacements are now performed each year and a similar pattern of increased frequency is reported by many worldwide joint registries [1–5]. Total numbers of procedures in the United States have now reached 700,000 per year and the figure is increasing as predicted despite periods of economic downturn (Figure 1) [6,7]. Projected analyses from 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 United States reached 1.5% in the general population and 10.4% in patients 80 years of age [10] (Figure 2). Data from the UK Clinical Research Practice Datalink (CRPD) database estimates that at the age of 50 the life-time risk of undergoing total knee replacement (TKR) surgery is 10.8% for women and 8.1% for men [11] and similar findings are reported from the New Zealand Joint Registry[12]. In fact, in all registries women undergo knee replacement more commonly than males [1,2,4,5,12]. The commonest indication for knee replacement remains primary osteoarthritis (OA) and the increasing numbers of patients with OA is one driver for increasing utilisation [4,13]. The numbers of knee replacements performed for inflammatory arthropathy, the second commonest indication, has not significantly increased over the last 10-years, mainly related to the success of modern disease modifying anti-rheumatic drugs [14].

The average age of patients undergoing knee replacement remains in the mid-sixties, but with increasing numbers of patients under the age of 60 [15] (Figure 2). Interestingly, 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[1,2,4,12] Recent evidence suggests that in the under 60 age group the life-time 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 [16] (See

Figure 3). The increasing trend for knee replacement in the younger patient will inevitably increase the number of revisions performed (Figure 1).

The reasons for the dramatic growth in utilisation rates of knee replacement seen around the world are complex. In the United States evidence suggests that growth cannot be fully explained by population increase and higher incidence of obesity alone [17]. Healthcare reform and greater equity in access to health care services has been identified as a driver of greater usage [18]. Perhaps most striking is the variation in utilisation seen across different countries. Falbrede et al. demonstrated intervention rates of 255-263 per 1000,000 inhabitants in Germany and Switzerland, compared to 127 per 100,000 in the USA [19]. Within OECD (Organisation for Economic Cooperation and Development) countries there is a 10-fold variation in use, with strong correlation in frequency of use to GDP, health expenditure and obesity [15] (See Figure 4). Differences in knee replacement usage are seen even within closer geographical areas, such as the Nordic countries [20]. The evidence continues to suggest that the interplay of economic variables, healthcare system factors, reimbursement, 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 [21]

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, and severe end-stage osteoarthritis of the joint [22] 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 less than 55 years old (because of the increased likelihood of revision in their lifetime [16],[23]. Surgeons have similarly been cautious about operating on patients with serious medical comorbidities, again for fear of complications but also those with widespread pain and or catastrophizing behaviour , because these problems are associated with higher risk of persistent pain [24],[25]. Finally, surgeons have historically

set high levels of pre-operative pain and functional limitation to justify the risk of surgical intervention.

Recent studies support expanding these traditional indications. For example, while morbid obesity is indeed associated with greater risk of perioperative complications, such as post-operative infection, recent studies demonstrate that individuals with BMI > 35, and even > 40, experience similar pain relief as non-obese patients[23],[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 TKR [27]. Despite the higher risk of persistent pain, patients with depression and catastrophizing nonetheless have, on average, dramatic improvements in pain and function following surgery [24].

An important contributor to the contemporary broadening of indications is the growing importance of the patient's voice in decisions about whether to undertake surgery. Clinical guidance from for the UK National Institute for Health and Care Excellence and the American Academy of Orthopaedic Surgeons, together with other authoritative bodies emphasize 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- 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 OA, and patients should be informed of alternatives [29]. For example physical therapy programs of strengthening and neuromuscular training can give symptomatic improvement in two-thirds of patients with advanced knee OA [30]. In this shared decision making paradigm, the patient and not the physician has 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 [22].

This process is particularly important to both the older and younger OA knee populations. For the aged, a growing segment of the population are now living long enough to develop functionally limiting knee OA in the eighth or ninth decade.

Despite their age and comorbidities this group is increasingly opting for TKR to maintain their quality of life [2,4,12]. Likewise, younger patients are choosing to undergo knee replacement for quality of life (QoL) reasons, outweighing the increased risk of revision seen in this patient group [161]. This move toward patient involvement in decision making and research is further epitomised by a recent patient focused James Lind Alliance Priority Setting Partnership, (performed in the UK), which highlighted areas for future research in knee replacement[31] (Table 1).

Indications for surgery can also be influenced by healthcare systems. Pre-operative symptom thresholds for knee replacement have recently been applied within the NHS [32]. "Pay for performance" approaches, where physicians are financially incentivised to restrict TKR to those likely to have the best outcome (non-obese, 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 patient reported outcome measures (PROMs) have become more common and influential. A recent systematic review demonstrates 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 (KOOS) and the Oxford Knee Score (OKS) widely used[34]. These instruments, have clearly demonstrated that knee replacement improves quality of life for the majority of patients by significantly reducing pain and improving function[30,35,36]. However, up to 15-20% of TKR patients consider themselves to be dissatisfied, gaining little benefit or describing a poor outcome following intervention when assessed by PROMs [37].

For each scoring system there is increasing requirement to establish their measurement properties including validity or meaningfulness, repeatability, responsiveness and usability in the context of knee replacement

Our understanding and use of PROMs in this field is evolving and many different instruments are used including condition specific (e.g. WOMAC), joint specific (e.g.

OKS) or more general measures of quality of life (e.g EQ-5D)[34] The ability of an instrument to measure change in patient state is critical and for all scores evidence based meaningful changes should be calculated[38] Instruments can be graded according to levels of evidence and those demonstrating the best suite of measurement properties should be prioritised for use[34].

To improve patient's understanding of the results of knee replacement attempts have been made to translate PROM data into categorical (e.g good or poor) outcome[39]. However, care is required as there is no standardised approach and different definitions may lead to different interpretation of results [40]. Somewhat abstract numerical scores (such as an Oxford Score or WOMAC) [34], whilst 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 PROMs audit [41]. The concept of the patient acceptable symptom state (PASS) is one approach in determining response to treatment [42]. 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 [39]. Some of the major trials of knee replacement are now incorporating such composite measures into their primary and secondary outcome assessment [43]. Another approach is the personalisation of outcome measurement, with some scores referencing improvement from an individual's baseline [44]. Such personalisation relies heavily on the complex interrelationship of patient expectation and satisfaction [45]

Exploring large PROMs datasets has led to greater understanding of factors that affect functional outcome after knee replacement; pre-operative level of symptoms, expectation, co-morbidity, age and mental-state [37,46] From interrogation of large PROM data sets it is possible to calculate an individual's capacity to benefit from knee replacement [32]. Tools like this 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 [37],[46].

Cost-effectiveness of knee replacement surgery

As one of the most commonly performed elective procedures in the world, TKR 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 TKR to be between approximately £1,000 and £12,000 for the average patient in different health care system, well within the range that most reimbursement and HTA bodies would consider represents good value for money[35],[36]

These highly favourable results follow from the fact that TKR in most countries is a relatively inexpensive procedure, and has been found by numerous studies to be associated with substantial and sustained improvements from pre-operative levels in many domains of both disease specific and generic health related quality of life measures (see Shan and colleagues for a systematic review of 19 such studies [47]. In the Knee Arthroplasty Trial (KAT), for example - one of the largest and longest randomised trials of different types of TKR - mean quality of life measured using the EQ-5D (1 = full health, 0 = death) rose from 0.39 immediately preceding surgery to 0.71 at 1 year and declined only gradually thereafter [36].

Although most studies have concluded that TKR is in general a highly cost-effective procedure, they have also reported substantial heterogeneity in costs and benefits between patient subgroups. For example, TKR appears to be more cost-effective in younger patients, and in hospitals with higher volumes of procedures [48]. Interest has also focused on body mass index (BMI), given increasing evidence that BMI is associated with increased health care costs for TKR [49]. However, several analyses have failed to demonstrate any clear association between BMI and the cost-

effectiveness of TKR, and in general the single best predictor of post-operative costs, outcomes and cost-effectiveness appears to be pre-operative symptom severity [3632]. This may explain why one recent cost-effectiveness study by Ferket and colleagues markedly differed from other analyses in concluding that TKR in a recent US cohort of patients had very small effects on quality of life and correspondingly poor levels of cost-effectiveness: their estimated pre-operative quality of life scores were very much less severe than those reported in most other cohorts, trials and registers, with a correspondingly much smaller post-operative improvement [50]. Interestingly, the only strictly randomised comparison of TKR with non-surgical treatment estimated the 1-year impact of TKR on quality of life to be around 3 times that reported by Ferket et al. [5030]. An economic evaluation based on this trial has not yet been reported.

In addition to the very limited evidence from randomised studies, a major problem confronting cost-effectiveness analyses of TKR has been how to characterise the comparator: for example, is it usual care, intensified non-surgical care, or delayed surgery? Enhanced recovery programmes for those undergoing TKR are also attracting increasing interest and are being introduced in many NHS hospitals for patients undergoing hip and knee replacement[51]. Robust cost-effectiveness on such programmes is required and an on-going systematic review will be a useful first step[52].

As the annual number of TKRs performed 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 significantly more comorbidities or less severe pre-operative symptoms. However, it is also important keep in mind that many patients who could benefit from TKR, 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 [3632]. Cost-effectiveness evidence cuts both ways.

Enhanced recovery after knee replacement surgery

Enhanced recovery programmes (ERPs) utilize a multimodal approach aimed at improving the care and subsequent clinical outcome for patients undergoing knee arthroplasty. First proposed in 1997 [53], this approach aims to minimise the physiological and psychological stresses of surgery through the use of specific interventions throughout the care pathway [54]. The principle components of ERPs can be broadly thought of in terms of pre-operative optimization of patients' comorbidities, patient education, peri-operative anaesthetic techniques, peri-operative surgical techniques, as well as post-operative 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 [55],[56] as well as having significant health economic benefits [51]

A major component of ERPs is the use of standardized anaesthetic protocols that include spinal (neuraxial) and regional anaesthesia. Evidence suggests that using these techniques in knee replacement can reduce perioperative morbidity, reduced length of stay and encourage faster functional recovery [57] The use of peri-articular local infiltration of anaesthetic (LIA) around the knee joint as part of a multimodal analgesic programme can also be as effective, if not superior, to regional blockade [58] The minimization of blood loss is another important element of ERPs and this has resulted in the adoption of tranexamic acid use, a practice that can reduce transfusion requirement following total knee replacement[59]. In addition EPRs 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 [60].

Early mobilization following surgery is favoured by knee arthroplasty ERPs and is associated with reduced complications, reduced length of stay and lower costs [61]. The benefits of ERPs are now being applied to facilitate same-day or out-patient knee arthroplasty in carefully selected patient groups [62].

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[1]. Data from all published registries shows expanding usage of knee replacement over time, with women most likely to undergo surgery and increasing numbers of patients under 60 having surgery [1–5]. The vast majority of implantations remain cemented total knee replacements, with far fewer partial (unicompartmental) knee replacements performed. 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 working closely with the UK NJR and ODEP (Orthopaedic Data Evaluation Panel), illustrating the critical role for registries to play in this process [63].

Patterns of revision

In all registries a revision rate of 3-5% at 10-years is commonly reported for many TKR designs [1,4]. The commonest causes for revision reported in National Joint Registries remains (in order of frequency); implant loosening, infection, pain, instability, with the overall pattern of reported failure mechanism not changing over the last 10-years[1–5]. The leading cause of early revision following TKA continues to be periprosthetic joint infection (PJI) [64]. The effect of this devastating complication on patients [65] has been well documented. 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 PJI has been partially ascribed to the rise in the number of diabetic, obese patients and younger undergoing knee arthroplasty [6667]. Recent work has focused on improving the diagnosis of periprosthetic infection and more research is required to improve its treatment [68] Critical to this is the collection of more relevant outcome data including microbiological profile, anti-microbial

therapy 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 (ISAR), an organisation of National registries (41 members), have included PROMs to enable more patient specific data to help assess functional outcomes [70]. As stated before, it may be that a more sensitive measure of the success on an implant is a combination of revision and PROMs as endpoints. In support of this concept is emerging evidence that PROMs scores can predict early failure. The New Zealand Joint Registry, has shown that an Oxford Knee Score less than 27/48 at six months was associated with a 10 times increased revision risk at two years compared to a score of greater than 41/48 [71]. Such early identification of patients at risk, enables follow up of vulnerable patients, providing better overall outcome and reducing health expenditure.

Another significant advance in the use of Registries is the ability to link them to other large national databases. . For example in the UK National Joint Registry data has been successfully linked to Hospital Episode Statistics (HES) and National PROMs data to identify a reduction in mortality after knee replacement from 2003 to 2013 (0.37% to 0.20%) and reduced morbidity after with partial compared to total knee replacement [7273]. 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 to play in supporting the delivery of health services, as seen in the UK where UK NJR reports are routinely used in individual Consultant appraisal and hospital level feedback such as the Getting it Right First Time (GIRFT) process[75].

Development and new technology in knee replacement surgery.

Design of total condylar knee replacement

Posterior cruciate retaining (CR) or sacrificing (PS) total condylar knee designs remain the two most widely used TKR options[1,2,12]. 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 [76]. The vast majority of knee replacements still use a metal on polyethylene bearing surface and polyethylene wear remains a significant cause of implant failure [1,2,4]. Around twenty years ago highly cross-linked polyethylene (PE), so called 2nd generation PE, was introduced and this has been successful in minimizing polyethylene wear and thereby reducing aseptic loosening and revision [77]. More recently Vitamin E infused, highly cross-linked PE, so called 3rd generation or "anti-oxidant" PE has been developed [78] but the efficacy of this remains to be established.

Alignment in TKR

For over 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 [79]. More recently kinematic alignment (KA) has been proposed as an alternative implantation strategy aiming to mimic the pre-disease joint surface orientation. This is thought to optimise ligament balance and knee kinematics without the need for ligament releases [80]. The global experience with KA in TKR is limited but a recent literature review reported more favourable outcome after kinematically aligned TKR [81] compared to mechanical alignment, however, the improvement is not universal [82]. It is possible that the benefit from different alignment methods is influenced by the pattern of OA for each individual patient. Mechanical alignment remains the mostly widely use method of implantation and further investigation of the safety of KA is needed before the technique can be considered for widespread use.

Partial knee replacement (PKR)

The majority of patients receive a TKR implant, but currently approximately 8% of cases a partial (unicompartmental) knee replacement in the medial, lateral or patellofemoral compartment is used [1]. The proposed benefits of PKR over TKR include; optimised functional outcome, lower postoperative length of stay, fewer medical complications, reduced readmissions, mortality and greater cost-effectiveness [83],[84]. Recent evidence from randomized controlled trials has supported these findings and results from other trials currently in progress are awaited [43],[85],[86]. The major argument against wider adoption of PKR as an alternative to TKR is the higher revision rate reported in nearly all national registry reports [1],[2],[4]. There is increasing evidence that the revision rate for PKR is related to the number performed or the proportion of PKR to TKR undertaken by individual surgeons and units [87] In addition, there is recent registry evidence that with improved implantation methods, for instance the introduction of cementless fixation, revision rates for PKR can be reduced [3].

Patient-specific instrumentation, computer navigation and robotics

Patient-specific instrumentation (PSI) and computer navigation have been introduced in knee arthroplasty surgery to help achieve more precise and accurate alignment [88]. The hope is that potential improvements would lead to improved outcomes and secondarily, to increased intra-operative 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 [89],[90] It could be speculated that the main potential of PSI or computer navigation is to help less experienced, lower volume surgeons to achieve improved precision and accuracy, but this remains to be explored. There is some evidence to suggest that computer navigation may reduce revision rates in younger TKA patients [91]. 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 [90]

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 significant problems have arisen. For example, in the use of metal on metal hip replacements where modifications to design resulted in the production of excessive metal wear products with, in some patients, substantial local and sometimes systemic toxic effects [92]. 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 evolved [93]. 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[94]. The recent changes to regulation have, in the USA, increased the use of pre-market approval, increased transparency and justification during the submission process, an improved system of device recall, modified the process of new applications to make them more stringent, applied new processes to the review of existing devices, fortified and reduced the use of the 510(k) system[93]. 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[95]. 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 (EMA)[93].

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 [96]. It is clear is 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 [97]. Benefit beyond existing technology

can only be tested effectively through randomised trial where bias and confounding is reduced and allows true determination of efficacy of one type of implant over another[98]. Reliance on randomised trials is also far from ideal as they are very costly, time consuming and the validity of the results may be limited to the study population only. There are other barriers to surgical trials where 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],[43],[86]. Registry data is 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 may occur many years after implantation [99]. Registers are resource intensive as large cohorts need to be followed 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. On going 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 [100]. An systematic process that adopts multiple study designs for the safe introduction of implants is developing but as yet is not fully established[97].

It is essential that the regulatory framework and the quality of evidence for introduction of surgical implants and associated technology are improved. The process should support innovation in knee replacement surgery whilst 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 critical to identify technologies that offer true benefit, from those that offer no advantage and at worst those that may cause harm.

Summary

Knee replacement surgery is 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 does not appear to have achieved any substantial improvement in outcome for patients and focus could shift towards optimising modifiable patient factors, use of alternatives to TKR such as partial knee replacement and peri-operative management. Our understanding of patient reported outcome of knee replacement has been a significant advance and but 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 modernizing 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 employed 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 conception and writing of the Seminar. Section headings were divided between the authors, and each author did the relevant searches and wrote the assigned sections. AJP collated the sections, and all authors revised and approved the final version of the article.

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Conflict of interest

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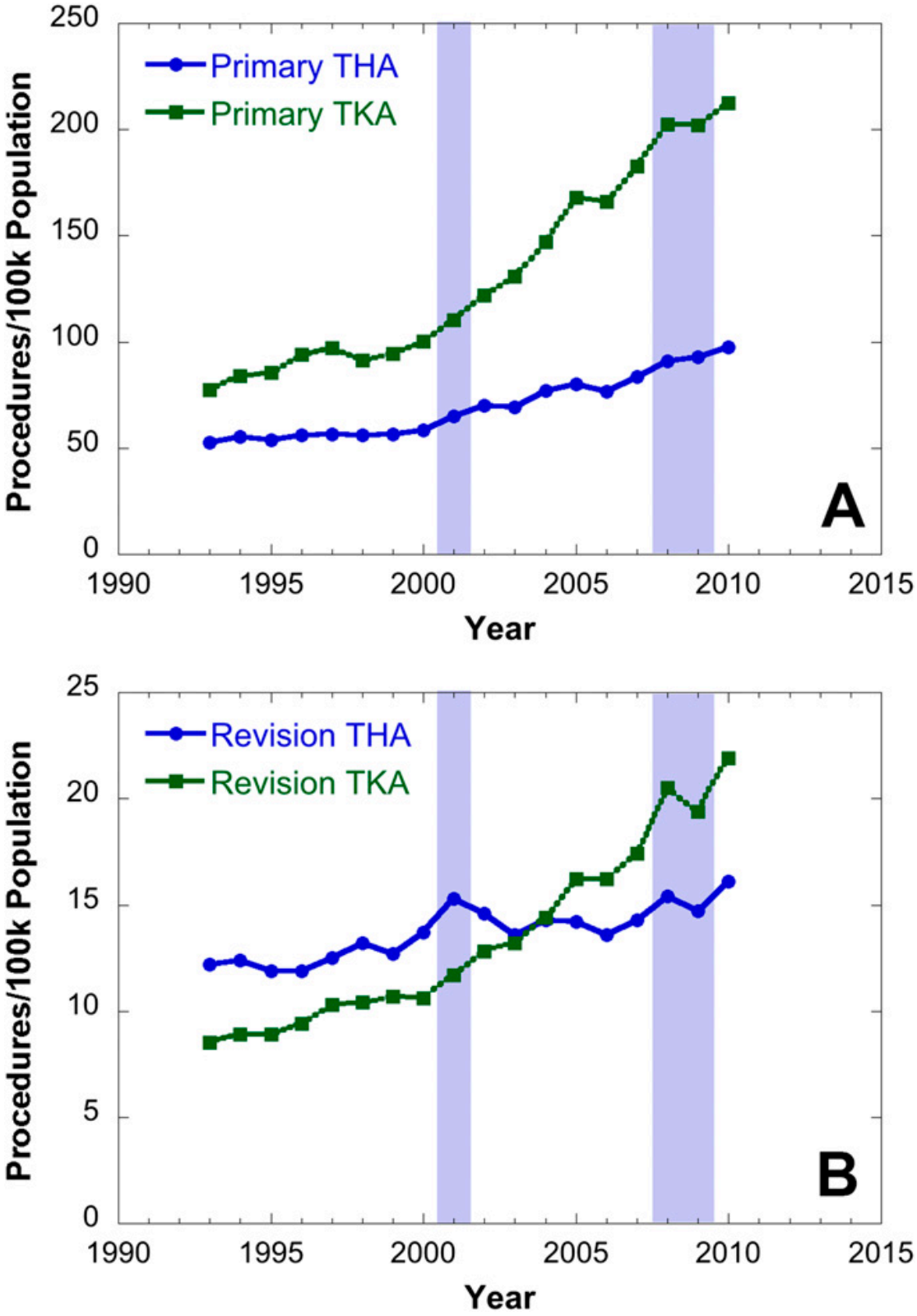

Figure 1:The incidence of primary (A) and revision (B) total hip and total knee arthroplasties relative to the total U.S. population increased over time during the study period. The years in which the U.S. economy was in recession (2001 and 2008 to 2009) are highlighted. (From Kurtz et al.[6]).

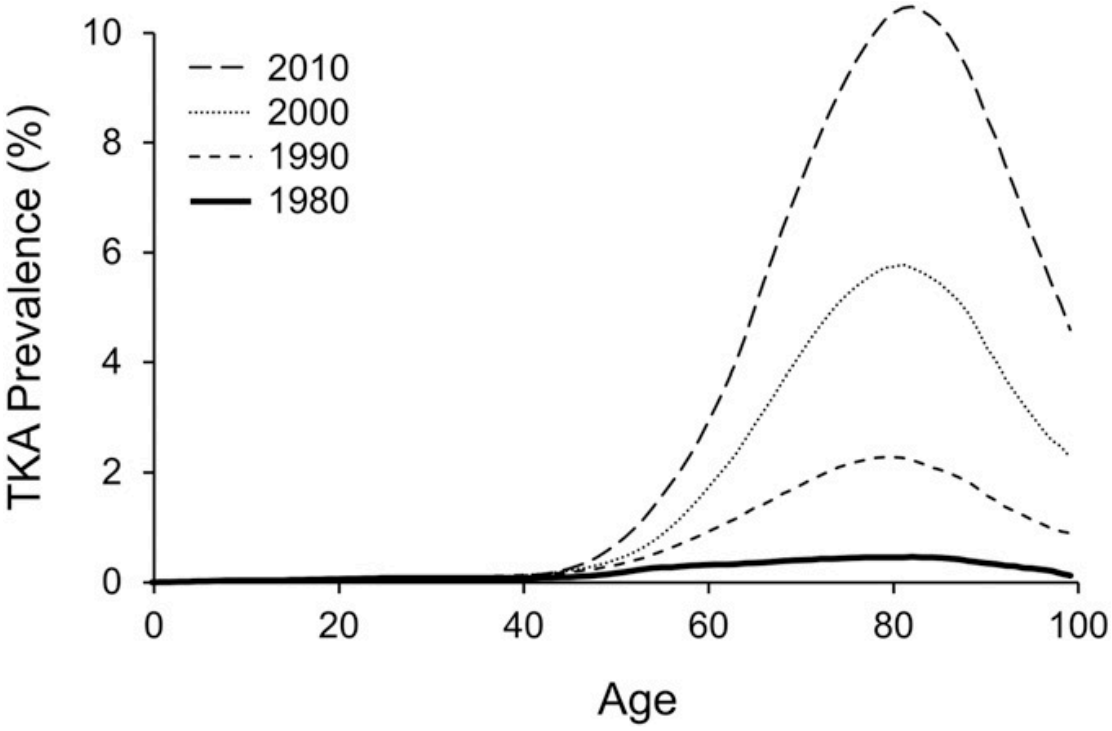

Figure 2: Secular changes in the prevalence of total knee arthroplasty (TKA) in the total U.S. population between1980 and 2010. (From: Kremers et al.[10])

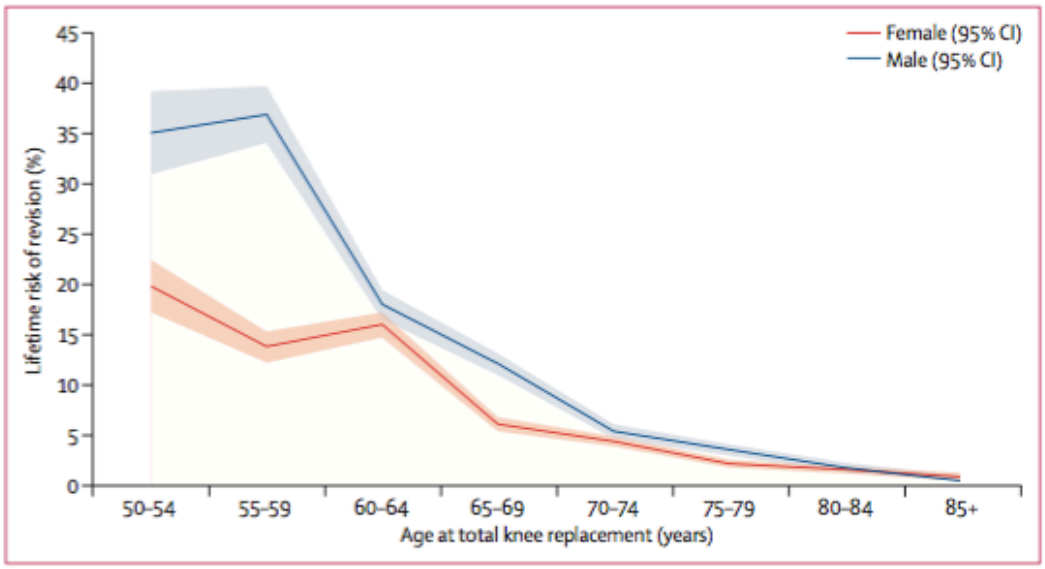

Figure 3: Lifetime risk of revision after total knee replacement.

Plot showing 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 stratified by sex (results adjusted for lost and censored population). (From Bayliss et al.[16])

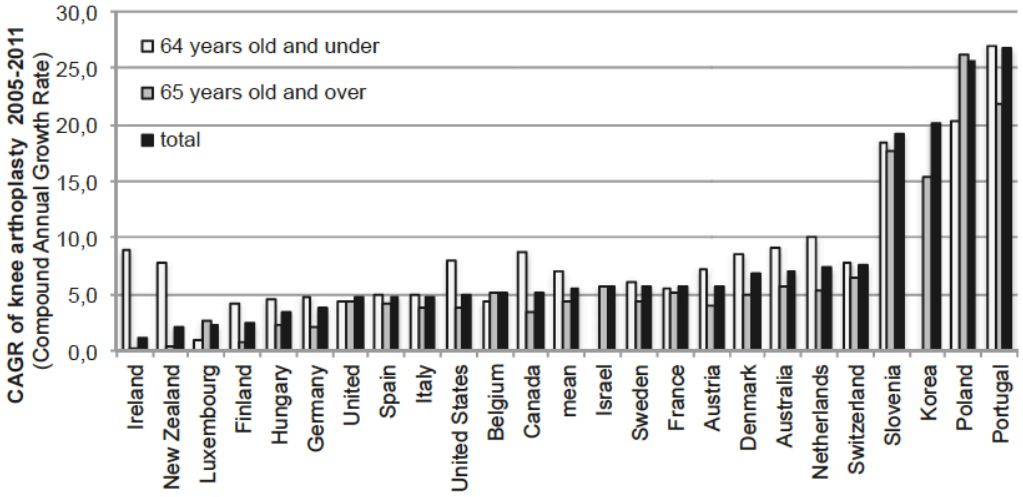

Figure 4: Growth rates in knee arthroplasty among Organisation for Economic Cooperation and Development (OECD) countries.

(From: Pabinger et al.[15])

- Over 95% of all knee replacements are performed 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 around 65 years, but increasing numbers are performed 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 on-going 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 commonest reasons for revision surgery are; implant loosening, infection, pain and instability.
- 45-day mortality rates following knee replacement have substantially fallen over time

Panel 1:

A summary of clinical information regarding knee replacement surgery

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, in people with osteoarthritis, for best post-operative outcomes?
3 In people with osteoarthritis, what are the pre-operative predictors of post-operative success (and risk factors of poor outcomes)?
4 What (health service) pre-operative, intra-operative, and post-operative factors can be modified to influence outcome following knee replacement?
5 What is the best pain control regime pre-operatively, peri-operatively and immediately post-operatively for knee joint replacement surgery for people with osteoarthritis?
6 What are the best techniques to control longer-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 pre and post-operative patient education support and advice for improving outcomes and satisfaction for people following knee replacement?
9 What is an ideal post-operative 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 (blood clots) events associated with knee replacement

Table 1: A table demonstrating the top ten priority research areas for knee replacement to treat osteoarthritis of the knee, generated from a James Lind Alliance Priority Setting Partnership.

(Adapted from: James Lind Alliance Priority Setting Partnership: http://www.jla.nihr.ac.uk/priority-setting-partnerships/hip-and-knee-replacement-for-osteoarthritis/top-10-priorities/)

References

1. Porter M. The National Joint Registry for England, Wales, Northern Ireland and the Isle of Man [Internet]. Annual Report. 2017 [cited 2018 Mar 31]. Available from: http://www.njrreports.org.uk/Portals/0/PDFdownloads/NJR 14th Annual Report 2017.pdf
2. Graves S, de Steiger RN, Lewis P, Harris I. The Australian National Joint Registry 2017 Annual Report [Internet]. 2017. Available from: https://aoanjrr.sahmri.com/annual-reports-2017
3. Rothwell A, Hobbs T, Frampton C, Taylor J, Muir D, Mohammed K. THE NEW ZEALAND JOINT REGISTRY - Annual Report [Internet]. 2017 [cited 2018 Mar 31]. Available from: https://nzoa.org.nz/system/files/DH7827_NZJR_2017_Report_v4_26Oct17.pdf
4. Robertsson O, Sundberg M, Lidgren L, W-Dahl A. The Swedish Knee Arthroplasty Register - Annual Report 2016 [Internet]. 2016 [cited 2018 Mar 31]. Available from: https://www.researchgate.net/publication/311439835_Annual_report_2016_-_The_Swedish_Knee_Arthroplasty_Register
5. Bozic K. American Joint Registry 2017 Annual Report [Internet]. 2017 [cited 2018 Mar 31]. Available from: http://connect.ajrr.net/2017-annual-report-download?hsCtaTracking=211910d3-f75a-440c-8bff-9d3da22c75ad%7C2cb33f5d-6e5a-405d-b3c6-dc5e1914c660
6. Kurtz SM, Ong KL, Lau E, Bozic KJ. Impact of the Economic Downturn on Total Joint Replacement Demand in the United States. J Bone Jt Surgery-American Vol [Internet]. 2014;96(8):624–30. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00004623-201404160-00002
7. Weinstein AM, Rome BN, Reichmann WM, Collins JE, Burbine SA, Thornhill TS, et al. Estimating the burden of total knee replacement in the United States. J Bone Joint Surg Am [Internet]. 2013;95(5):385–92. Available from: http://jbjs.org/content/95/5/385.abstract
8. Inacio MCS, Paxton EW, Graves SE, Namba RS, Nemes S. Projected increase in total knee arthroplasty in the United States - an alternative projection model. Osteoarthr Cartil [Internet]. 2017; Available from: http://dx.doi.org/10.1016/j.joca.2017.07.022
9. Culliford D, Maskell J, Judge A, Cooper C, Prieto-alhambra D, Arden NK, et al. Future projections of total hip and knee arthroplasty in the UK : results from the UK Clinical Practice Research Datalink. Osteoarthr Cartil [Internet]. 2015;23(4):594–600. Available from: http://dx.doi.org/10.1016/j.joca.2014.12.022
10. Maradit Kremers H, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, et al. Prevalence of Total Hip and Knee Replacement in the United States. J Bone Joint Surg Am [Internet]. 2015;97(17):1386–97. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26333733%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4551172
11. Culliford DJ, Maskell J, Kiran A, Judge A, Javaid MK, Cooper C, et al. The

lifetime risk of total hip and knee arthroplasty: Results from the UK general practice research database. Osteoarthr Cartil. 2012;20(6):519–24.
12. Rothwell A. The New Zealand Joint Registry Annual Report 2017 [Internet]. 2017. Available from: https://nzoa.org.nz/system/files/DH7827_NZJR_2017_Report_v4_26Oct17.pdf
13. Turkiewicz A, Petersson IF, Björk J, Hawker G, Dahlberg LE, Lohmander LS, et al. Current and future impact of osteoarthritis on health care: A population-based study with projections to year 2032. Osteoarthr Cartil. 2014;22(11):1826–32.
14. Young BL, Watson SL, Perez JL, McGwin G, Singh JA, Ponce BA. Trends in Joint Replacement Surgery in Patients with Rheumatoid Arthritis. J Rheumatol [Internet]. 2017;45(2):jrheum.170001. Available from: http://www.jrheum.org/lookup/doi/10.3899/jrheum.170001
15. Pabinger C, Lothaller H, Geissler A. Utilization rates of knee-arthroplasty in OECD countries. Osteoarthr Cartil. 2015;23(10):1664–73.
16. Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, et al. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. Lancet [Internet]. 2017;389(10077):1424–30. Available from: http://dx.doi.org/10.1016/S0140-6736(17)30059-4
17. Losina E, Thornhill TS, Rome BN, Wright J, Katz JN. The dramatic increase in total knee replacement utilization rates in the United States cannot be fully explained by growth in population size and the obesity epidemic. J Bone Joint Surg Am [Internet]. 2012;94(3):201–7. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3262184&tool=pmcentrez&rendertype=abstract
18. Hanchate AD, Kapoor A, Katz JN, McCormick D, Lasser KE, Feng C, et al. Massachusetts health reform and disparities in joint replacement use: Difference in differences study. BMJ. 2015;350.
19. Falbrede I, Widmer M, Kurtz S, Schneidmüller D, Dudda M, Röder C. [Utilization rates of lower extremity prostheses in Germany and Switzerland: A comparison of the years 2005-2008]. Orthopade [Internet]. 2011;40(9):793–801. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21681503
20. NiemeläInen MJ, MäKelä KT, Robertsson O, W-Dahl A, Furnes O, Fenstad AM, et al. Different incidences of knee arthroplasty in the Nordic countries: A population-based study from the Nordic Arthroplasty Register Association. Acta Orthop. 2017;88(2):173–8.
21. McCulloch P, Nagendran M, Campbell WB, Price A, Jani A, Birkmeyer JD, et al. Strategies to reduce variation in the use of surgery. Lancet. 2013;382(9898):1130–9.
22. Dieppe P, Lim K, Lohmander S. Who should have knee joint replacement surgery for osteoarthritis? Int J Rheum Dis [Internet]. 2011;14(2):175–80. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&NEWS=N&AN=2011227148
23. Kerkhoffs GMMJ, Servien E, Dunn W, Dahm D, Bramer JAM, Haverkamp D. The

influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. J Bone Joint Surg Am [Internet]. 2012;94(20):1839–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23079875%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3489068

24. Dave AJ, Selzer F, Losina E, Usiskin I, Collins JE, Lee YC, et al. The association of pre-operative body pain diagram scores with pain outcomes following total knee arthroplasty. Osteoarthr Cartil. 2017;25(5):667–75.
25. Burns LC, Ritvo SE, Ferguson MK, Clarke H, Seltzer Z, Katz J. Pain catastrophizing as a risk factor for chronic pain after total knee arthroplasty: A systematic review. Vol. 8, Journal of Pain Research. 2015. p. 21–32.
26. Collins JE, Donnell-Fink LA, Yang HY, Usiskin IM, Lape EC, Wright J, et al. Effect of Obesity on Pain and Functional Recovery Following Total Knee Arthroplasty. J Bone Joint Surg Am. 2017;99(21):1812–8.
27. Fortin PR, Penrod JR, Clarke AE, St-Pierre Y, Joseph L, Bélisle P, et al. Timing of total joint replacement affects clinical outcomes among patients with osteoarthritis of the hip or knee. Arthritis Rheum. 2002;46(12):3327–30.
28. American Academy of Orthopaedic Surgeons. Appropriate Use Criteria: Surgical management of knee osteoarthritis. 2018.
29. NICE. Clinical guideline [CG177]: Osteoarthritis: care and management [Internet]. 2014. Available from: https://www.nice.org.uk/guidance/cg177
30. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. A Randomized, Controlled Trial of Total Knee Replacement. N Engl J Med [Internet]. 2015;373(17):1597–606. Available from: http://www.nejm.org/doi/10.1056/NEJMoa1505467
31. James-Lind-Alliance. Priority setting partnership: Hip and knee replacment for osteoarthritis [Internet]. 2014 [cited 2018 Mar 1]. Available from: http://www.jla.nihr.ac.uk/priority-setting-partnerships/hip-and-knee-replacement-for-osteoarthritis/top-10-priorities/
32. Price AJ, Smith J, Dakin HA, Kang S, Eibich P, Cook J, et al. Introducing Standardized and Evidence Based Thresholds for Hip and Knee Replacement Surgery -The Arthroplasty Candidacy Help Engine (The ACHE tool): A systematic review, clinical and economics analysis. Health Technol Assess. 2018;In press.
33. Giori NJ, Amanatullah DF, Gupta S, Bowe T, Harris AHS. Risk Reduction Compared with Access to Care: Quantifying the Trade-Off of Enforcing a Body Mass Index Eligibility Criterion for Joint Replacement. J Bone Jt Surg [Internet]. 2018;100(7):539–45. Available from: http://insights.ovid.com/crossref?an=00004623-201804040-00001
34. Harris K, Dawson J, Gibbons E, Lim C, Beard D, Fitzpatrick R, et al. Systematic review of measurement properties of patient-reported outcome measures used in patients undergoing hip and knee arthroplasty. Patient Relat Outcome Meas [Internet]. 2016;Volume 7:101–8. Available from: https://www.dovepress.com/systematic-review-of-measurement-properties-of-patient-reported-outcom-peer-reviewed-article-PROM
35. Murray DW, MacLennan GS, Breeman S, Dakin HA, Johnston L, Campbell MK, et al. A randomised controlled trial of the clinical effectiveness and cost-

effectiveness of different knee prostheses: the Knee Arthroplasty Trial (KAT). Health Technol Assess. 2014;18(19).
36. Dakin H, Gray A, Fitzpatrick R, MacLennan G, Murray D. Rationing of total knee replacement: A cost-effectiveness analysis on a large trial data set. BMJ Open. 2012;2(1).
37. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of Prospective studies in unselected patients. Vol. 2, BMJ Open. 2012.
38. Beard DJ, Harris K, Dawson J, Doll H, Murray DW, Carr AJ, et al. Meaningful changes for the Oxford hip and knee scores after joint replacement surgery. J Clin Epidemiol [Internet]. 2015;68(1):73–9. Available from: http://dx.doi.org/10.1016/j.jclinepi.2014.08.009
39. Lange T, Rataj E, Kopkow C, Lützner J, Günther K-P, Schmitt J. Outcome Assessment in Total Knee Arthroplasty: A Systematic Review and Critical Appraisal. J Arthroplasty [Internet]. 2017;32(2):653–665.e1. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0883540316306568
40. Hawker GA, Badley EM, Borkhoff CM, Croxford R, Davis AM, Dunn S, et al. Which patients are most likely to benefit from total joint arthroplasty? Arthritis Rheum. 2013;65(5):1243–52.
41. NHS Digital. Provisional Quarterly Patient Reported Outcome Measures (PROMs) in England, April 2016 to March 2017 [Internet]. 2018 [cited 2018 Mar 31]. Available from: http://digital.nhs.uk/catalogue/PUB30192
42. Escobar A, Gonzalez M, Quintana JM, Vrotsou K, Bilbao A, Herrera-Espiñeira C, et al. Patient acceptable symptom state and OMERACT-OARSI set of responder criteria in joint replacement. Identification of cut-off values. Osteoarthr Cartil [Internet]. 2012;20(2):87–92. Available from: http://dx.doi.org/10.1016/j.joca.2011.11.007
43. Beard D, Price A, Cook J, Fitzpatrick R, Carr A, Campbell M, et al. Total or Partial Knee Arthroplasty Trial - TOPKAT: Study protocol for a randomised controlled trial. Trials. 2013;14(1).
44. Noble PC, Scuderi GR, Brekke AC, Sikorskii A, Benjamin JB, Lonner JH, et al. Development of a new knee society scoring system. In: Clinical Orthopaedics and Related Research. 2012. p. 20–32.
45. Dunbar MJ, Richardson G, Robertsson O. I can't get no satisfaction after my total knee replacement: rhymes and reasons. Vol. 95 B, The bone & joint journal. 2013. p. 148–52.
46. Arden N, Altman D, Beard D, Carr A, Clarke N, Collins G, et al. Lower limb arthroplasty: can we produce a tool to predict outcome and failure, and is it cost-effective? An epidemiological study. Program Grants Appl Res [Internet]. 2017;5(12):1–246. Available from: https://www.journalslibrary.nihr.ac.uk/pgfar/pgfar05120
47. Shan L, Shan B, Suzuki A, Nouh F, Saxena A. Intermediate and Long-Term Quality of Life After Total Knee Replacement.A systematic Review and Meta-Analysis. J Bone Jt Surgery, Am Vol. 2015;97–A(2):156–68.
48. Losina E, Walensky RP, Kessler CL, Emrani PS, Reichmann WM, Wright EA, et al. Cost-effectiveness of total knee arthroplasty in the United States: Patient

risk and hospital volume. Arch Intern Med. 2009;169(12):1113–21.
49. Kent S, Green J, Reeves G, Beral V, Gray A, Jebb SA, et al. Hospital costs in relation to body-mass index in 1·1 million women in England: a prospective cohort study. Lancet Public Heal. 2017;2(5):e214–22.
50. Ferket BS, Feldman Z, Zhou J, Oei EH, Bierma-Zeinstra SMA, Mazumdar M. Impact of total knee replacement practice: cost effectiveness analysis of data from the Osteoarthritis Initiative. Bmj [Internet]. 2017;j1131. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.j1131
51. Duncan CM, Long KH, Warner DO, Pagnano MW, Hebl JR. The economic implications of a multimodal analgesic regimen combined with minimally invasive orthopedic surgery: A comparative cost study. J Anesth Clin Res. 2010;1(1):1–6.
52. Murphy J, Pritchard MG, Cheng LY, Janarthanan R, Leal J. Cost-effectiveness of enhanced recovery in hip and knee replacement: a systematic review protocol. BMJ Open. 2018;8(3):e019740.
53. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78(5):606–17.
54. Soffin EM, Yadeau JT. Enhanced recovery after surgery for primary hip and knee arthroplasty: A review of the evidence. Br J Anaesth. 2016;117(March):iii62-iii72.
55. Savaridas T, Serrano-Pedraza I, Khan SK, Martin K, Malviya A, Reed MR. Reduced medium-term mortality following primary total hip and knee arthroplasty with an enhanced recovery program. Acta Orthop. 2013;84:40–3.
56. Malviya A, Martin K, Harper I, Muller SD, Emmerson KP, Partington PF, et al. Enhanced recovery program for hip and knee replacement reduces death rate: A study of 4,500 consecutive primary hip and knee replacements. Acta Orthop. 2011;82(5):577–81.
57. Johnson RL, Kopp SL, Burkle CM, Duncan CM, Jacob AK, Erwin PJ, et al. Neuraxial vs general anaesthesia for total hip and total knee arthroplasty: A systematic review of comparative-effectiveness research. Br J Anaesth [Internet]. 2016;116(2):163–76. Available from: http://dx.doi.org/10.1093/bja/aev455
58. Hu B, Lin T, Yan S, Tong S-L, Yu J-H, Xu J-J, et al. Local Infiltration Analgesia Versus Regional Blockade for Postoperative Analgesia in Total Knee Arthroplasty: A Meta-analysis of Randomized Controlled Trials. Pain Physician. 2016;19(4):205.
59. Chen T, Chen Y, Jiao J, Wang Y, Qian L, Guo Z, et al. Comparison of the effectiveness and safety of topical versus intravenous tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled trials. J Orthop Surg Res [Internet]. 2017;12(1):11. Available from: http://josr-online.biomedcentral.com/articles/10.1186/s13018-017-0512-4
60. NICE. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. NICE guideline [NG89] [Internet]. 2018 [cited 2018 Aug 8]. Available from: https://www.nice.org.uk/guidance/ng89
61. Guerra ML, Singh PJ, Taylor NF. Early mobilization of patients who have had a hip or knee joint replacement reduces length of stay in hospital: A systematic

review. Clin Rehabil. 2015;29(9):844–54.
62. Kort NP, Bemelmans YFL, van der Kuy PHM, Jansen J, Schotanus MGM. Patient selection criteria for outpatient joint arthroplasty. Knee Surgery, Sport Traumatol Arthrosc [Internet]. 2017;25(9):2668–75. Available from: http://link.springer.com/10.1007/s00167-016-4140-z
63. Tucker K. Beyond Compliance [Internet]. 2011 [cited 2018 Mar 28]. Available from: http://www.odep.org.uk
64. Koh CK, Zeng I, Ravi S, Zhu M, Vince KG, Young SW. Periprosthetic Joint Infection Is the Main Cause of Failure for Modern Knee Arthroplasty: An Analysis of 11,134 Knees. Clin Orthop Relat Res. 2017;475(9):2194–201.
65. Zmistowski B, Karam JA, Durinka JB, Casper DS, Parvizi J. Periprosthetic Joint Infection Increases the Risk of One-Year Mortality. J Bone Jt Surgery-American Vol [Internet]. 2013;95(24):2177–84. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00004623-201312180-00003
66. O'Toole P, Maltenfort MG, Chen AF, Parvizi J. Projected Increase in Periprosthetic Joint Infections Secondary to Rise in Diabetes and Obesity. J Arthroplasty [Internet]. 2016;31(1):7–10. Available from: http://dx.doi.org/10.1016/j.arth.2015.07.034
67. Meehan JP, Danielsen B, Kim SH, Jamali AA, White RH. Younger Age Is Associated with a Higher Risk of Early Periprosthetic Joint Infection and Aseptic Mechanical Failure After Total Knee Arthroplasty. J Bone Jt Surg [Internet]. 2014;96(7):529–35. Available from: http://jbjs.org/cgi/doi/10.2106/JBJS.M.00545
68. Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of Periprosthetic Joint Infection. J Arthroplasty [Internet]. 2014;29(2 SUPPL.):77–83. Available from: http://dx.doi.org/10.1016/j.arth.2013.09.040
69. Haddad FS, George DA. Can National Joint Registries play a role in improving our understanding of periprosthetic infections? Bone and Joint Journal. 2016;98B(3):289–90.
70. Rolfson O, Bohm E, Franklin P, Lyman S, Denissen G, Dawson J, et al. Patient-reported outcome measures in arthroplasty registries: Report of the Patient-Reported Outcome Measures Working Group of the International Society of Arthroplasty RegistriesPart II. Recommendations for selection, administration, and analysis. Acta Orthop. 2016;87:9–23.
71. Rothwell AG, Hooper GJ, Hobbs A, Frampton CM. An analysis of the Oxford hip and knee scores and their relationship to early joint revision in the New Zealand Joint Registry. J Bone Jt Surg - Br Vol [Internet]. 2010;92–B(3):413–8. Available from: http://www.bjj.boneandjoint.org.uk/cgi/doi/10.1302/0301-620X.92B3.22913
72. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101330 matched patients: A study of data from the National Joint Registry for England and Wales. Lancet. 2014;384(9952):1437–45.
73. Hunt LP, Ben-Shlomo Y, Clark EM, Dieppe P, Judge A, Macgregor AJ, et al. 45-day mortality after 467779 knee replacements for osteoarthritis from the National Joint Registry for England and Wales: An observational study. Lancet.

2014;384(9952):1429–36.
74. Lauer MS, D'Agostino RB. The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research? N Engl J Med [Internet]. 2013;369(17):1579–81. Available from: http://www.nejm.org/doi/10.1056/NEJMp1310102
75. NHS. GIRFT - Getting it right first time [Internet]. 2018 [cited 2018 Aug 1]. Available from: http://gettingitrightfirsttime.co.uk
76. Nieuwenhuijse MJ, Nelissen RGHH, Schoones JW, Sedrakyan A. Appraisal of evidence base for introduction of new implants in hip and knee replacement: A Systematic review of five widely used device technologies. BMJ. 2014;349(September):1–12.
77. De Steiger RN, Muratoglu O, Lorimer M, Cuthbert AR, Graves SE. Lower prosthesis-specific 10-year revision rate with crosslinked than with non-crosslinked polyethylene in primary total knee arthroplasty. Acta Orthop. 2015;86(6):721–7.
78. Nebergall AK, Troelsen A, Rubash HE, Malchau H, Rolfson O, Greene ME. Five-Year Experience of Vitamin E-Diffused Highly Cross-Linked Polyethylene Wear in Total Hip Arthroplasty Assessed by Radiostereometric Analysis. J Arthroplasty. 2016;31(6):1251–5.
79. Insall JN, Binazzi R, Soudry M, Mestriner LA. Total knee arthroplasty. Clin Orthop Relat Res [Internet]. 1985;(192):13–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3967412
80. Rivière C, Iranpour F, Auvinet E, Howell S, Pascal.AVendittoli, Cobb J, et al. Alignment Options for Total Knee Arthroplasty: A Systematic Review. Orthop Traumatol Surg Res [Internet]. 2017; Available from: http://www.sciencedirect.com/science/article/pii/S1877056817302281%0A
81. Courtney PM, Lee G-C. Early Outcomes of Kinematic Alignment in Primary Total Knee Arthroplasty: A Meta-Analysis of the Literature. J Arthroplasty [Internet]. 2017;32(6):2028–2032.e1. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0883540317301596
82. Young SW, Walker ML, Bayan A, Briant-Evans T, Pavlou P, Farrington B. The Chitranjan S. Ranawat Award: No Difference in 2-year Functional Outcomes Using Kinematic versus Mechanical Alignment in TKA: A Randomized Controlled Clinical Trial. Clin Orthop Relat Res. 2017;475(1):9–20.
83. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101330 matched patients: A study of data from the National Joint Registry for England and Wales. Lancet [Internet]. 2014;384(9952):1437–45. Available from: http://dx.doi.org/10.1016/S0140-6736(14)60419-0
84. Burn E, Liddle AD, Hamilton TW, Judge A, Pandit HG, Murray DW, et al. Cost-effectiveness of unicompartmental compared with total knee replacement: a population-based study using data from the National Joint Registry for England and Wales. BMJ Open [Internet]. 2018;8(4):e020977. Available from: http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2017-020977
85. Kulshrestha V, Datta B, Kumar S, Mittal G. Outcome of Unicondylar Knee Arthroplasty vs Total Knee Arthroplasty for Early Medial Compartment Arthritis: A Randomized Study. J Arthroplasty. 2017;32(5):1460–9.

86. Odgaard A, Madsen F, Wagner Kristensen P, Kappel A, Fabrin J. The Mark Coventry Award: Patellofemoral Arthroplasty Results in Better Range of Movement and Early Patient-reported Outcomes Than TKA. Clin Orthop Relat Res. 2018;476(1):87–100.
87. Liddle AD, Pandit H, Judge A, Murray DW. Optimal usage of unicompartmental knee arthroplasty: A study of 41 986 cases from the national joint registry for England and Wales. Bone Jt J. 2015;97B(11):1506–11.
88. Gromov K, Korchi M, Thomsen MG, Husted H, Troelsen A. What is the optimal alignment of the tibial and femoral components in knee arthroplasty? An overview of the literature. Acta Orthop. 2014;85(5):480–7.
89. Huijbregts HJTAM, Khan RJK, Sorensen E, Fick DP, Haebich S. Patient-specific instrumentation does not improve radiographic alignment or clinical outcomes after total knee arthroplasty: A meta-analysis. Acta Orthop. 2016;87(4):386–94.
90. van der List JP, Chawla H, Joskowicz L, Pearle AD. Current state of computer navigation and robotics in unicompartmental and total knee arthroplasty: a systematic review with meta-analysis. Vol. 24, Knee Surgery, Sports Traumatology, Arthroscopy. 2016. p. 3482–95.
91. De Steiger RN, Liu YL, Graves SE. Computer navigation for total knee arthroplasty reduces revision rate for patients less than sixty-five years of age. J Bone Jt Surg - Am Vol. 2015;97(8):635–42.
92. Smith AJ, Dieppe P, Howard PW, Blom AW. Failure rates of metal-on-metal hip resurfacings: Analysis of data from the National Joint Registry for England and Wales. Lancet [Internet]. 2012;380(9855):1759–66. Available from: http://dx.doi.org/10.1016/S0140-6736(12)60989-1
93. Sorenson C, Drummond M. Improving medical device regulation: the United States and Europe in perspective. Milbank Q [Internet]. 2014;92(1):114–50. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3955380&tool=pmcentrez&rendertype=abstract
94. Sheth U, Nguyen N, Gaines S, Bhandari M, Mehlman C, Klein G. New orthopedic devices and the FDA. J Long Term Eff Med Implant. 2009;19(3):173–84.
95. MHRA. Notified bodies for medical devices [Internet]. 2017 [cited 2018 Mar 28]. Available from: https://www.gov.uk/government/publications/notified-bodies-for-medical-devices/notified-bodies-for-medical-devices
96. Anand R, Graves SE, de Steiger RN, Davidson DC, Ryan P, Miller LN, et al. What Is the Benefit of Introducing New Hip and Knee Prostheses? J Bone Jt Surg [Internet]. 2011;93(Supplement_3):51–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22262424%5Cnhttp://jbjs.org/cgi/doi/10.2106/JBJS.K.00867
97. Pijls BG, Nelissen RGHH. The era of phased introduction of new implants. Bone Joint Res [Internet]. 2016;5(6):215–7. Available from: http://online.boneandjoint.org.uk/doi/10.1302/2046-3758.56.2000653
98. Faris O, Shuren J. An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials. N Engl J Med [Internet]. 2017;376(14):1350–7. Available from: http://www.nejm.org/doi/10.1056/NEJMra1512592

99. Malchau H, Graves SE, Porter M, Harris WH, Troelsen A. The next critical role of orthopedic registries. Acta Orthop. 2015;86(1):3–4.
100. Nelissen RGHH, Pijls BG, Kärrholm J, Malchau H, Nieuwenhuijse MJ, Valstar ER. RSA and Registries: The Quest for Phased Introduction of New Implants. J Bone Jt Surgery-American Vol [Internet]. 2011;93(Suppl 3):62–5. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00004623-201112213-00010

Appendix 1

Additional references

1. Porter M. The National Joint Registry for England, Wales, Northern Ireland and the Isle of Man [Internet]. Annual Report. 2017 [cited 2018 Mar 31]. Available from: http://www.njrreports.org.uk/Portals/0/PDFdownloads/NJR 14th Annual Report 2017.pdf
2. Graves S, de Steiger RN, Lewis P, Harris I. The Australian National Joint Registry 2017 Annual Report [Internet]. 2017. Available from: https://aoanjrr.sahmri.com/annual-reports-2017
3. Rothwell A, Hobbs T, Frampton C, Taylor J, Muir D, Mohammed K. THE NEW ZEALAND JOINT REGISTRY - Annual Report [Internet]. 2017 [cited 2018 Mar 31]. Available from: https://nzoa.org.nz/system/files/DH7827_NZJR_2017_Report_v4_26Oct17.pdf
4. Robertsson O, Sundberg M, Lidgren L, W-Dahl A. The Swedish Knee Arthroplasty Register - Annual Report 2016 [Internet]. 2016 [cited 2018 Mar 31]. Available from: https://www.researchgate.net/publication/311439835_Annual_report_2016_-_The_Swedish_Knee_Arthroplasty_Register
5. Bozic K. American Joint Registry 2017 Annual Report [Internet]. 2017 [cited 2018 Mar 31]. Available from: http://connect.ajrr.net/2017-annual-report-download?hsCtaTracking=211910d3-f75a-440c-8bff-9d3da22c75ad%7C2cb33f5d-6e5a-405d-b3c6-dc5e1914c660
6. Kurtz SM, Ong KL, Lau E, Bozic KJ. Impact of the Economic Downturn on Total Joint Replacement Demand in the United States. J Bone Jt Surgery-American Vol [Internet]. 2014;96(8):624–30. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00004623-201404160-00002
7. Weinstein AM, Rome BN, Reichmann WM, Collins JE, Burbine SA, Thornhill TS, et al. Estimating the burden of total knee replacement in the United States. J Bone Joint Surg Am [Internet]. 2013;95(5):385–92. Available from: http://jbjs.org/content/95/5/385.abstract
8. Inacio MCS, Paxton EW, Graves SE, Namba RS, Nemes S. Projected increase in total knee arthroplasty in the United States - an alternative projection model. Osteoarthr Cartil [Internet]. 2017; Available from: http://dx.doi.org/10.1016/j.joca.2017.07.022
9. Culliford D, Maskell J, Judge A, Cooper C, Prieto-alhambra D, Arden NK, et al. Future projections of total hip and knee arthroplasty in the UK : results from the UK Clinical Practice Research Datalink. Osteoarthr Cartil [Internet]. 2015;23(4):594–600. Available from: http://dx.doi.org/10.1016/j.joca.2014.12.022
10. Maradit Kremers H, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, et al. Prevalence of Total Hip and Knee Replacement in the United States. J Bone Joint Surg Am [Internet]. 2015;97(17):1386–97. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/26333733%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4551172
11. Culliford DJ, Maskell J, Kiran A, Judge A, Javaid MK, Cooper C, et al. The lifetime risk of total hip and knee arthroplasty: Results from the UK general practice research database. Osteoarthr Cartil. 2012;20(6):519–24.
12. Rothwell A. The New Zealand Joint Registry Annual Report 2017 [Internet]. 2017. Available from: https://nzoa.org.nz/system/files/DH7827_NZJR_2017_Report_v4_26Oct17.pdf
13. Turkiewicz A, Petersson IF, Björk J, Hawker G, Dahlberg LE, Lohmander LS, et al. Current and future impact of osteoarthritis on health care: A population-based study with projections to year 2032. Osteoarthr Cartil. 2014;22(11):1826–32.
14. Young BL, Watson SL, Perez JL, McGwin G, Singh JA, Ponce BA. Trends in Joint Replacement Surgery in Patients with Rheumatoid Arthritis. J Rheumatol [Internet]. 2017;45(2):jrheum.170001. Available from: http://www.jrheum.org/lookup/doi/10.3899/jrheum.170001
15. Pabinger C, Lothaller H, Geissler A. Utilization rates of knee-arthroplasty in OECD countries. Osteoarthr Cartil. 2015;23(10):1664–73.
16. Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, et al. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. Lancet [Internet]. 2017;389(10077):1424–30. Available from: http://dx.doi.org/10.1016/S0140-6736(17)30059-4
17. Losina E, Thornhill TS, Rome BN, Wright J, Katz JN. The dramatic increase in total knee replacement utilization rates in the United States cannot be fully explained by growth in population size and the obesity epidemic. J Bone Joint Surg Am [Internet]. 2012;94(3):201–7. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3262184&tool=pmcentrez&rendertype=abstract
18. Hanchate AD, Kapoor A, Katz JN, McCormick D, Lasser KE, Feng C, et al. Massachusetts health reform and disparities in joint replacement use: Difference in differences study. BMJ. 2015;350.
19. Falbrede I, Widmer M, Kurtz S, Schneidmüller D, Dudda M, Röder C. [Utilization rates of lower extremity prostheses in Germany and Switzerland: A comparison of the years 2005-2008]. Orthopade [Internet]. 2011;40(9):793–801. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21681503
20. NiemeläInen MJ, MäKelä KT, Robertsson O, W-Dahl A, Furnes O, Fenstad AM, et al. Different incidences of knee arthroplasty in the Nordic countries: A population-based study from the Nordic Arthroplasty Register Association. Acta Orthop. 2017;88(2):173–8.
21. McCulloch P, Nagendran M, Campbell WB, Price A, Jani A, Birkmeyer JD, et al. Strategies to reduce variation in the use of surgery. Lancet. 2013;382(9898):1130–9.
22. Dieppe P, Lim K, Lohmander S. Who should have knee joint replacement surgery for osteoarthritis? Int J Rheum Dis [Internet]. 2011;14(2):175–80. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&

NEWS=N&AN=2011227148
23. Kerkhoffs GMMJ, Servien E, Dunn W, Dahm D, Bramer JAM, Haverkamp D. The influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. J Bone Joint Surg Am [Internet]. 2012;94(20):1839–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23079875%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3489068
24. Dave AJ, Selzer F, Losina E, Usiskin I, Collins JE, Lee YC, et al. The association of pre-operative body pain diagram scores with pain outcomes following total knee arthroplasty. Osteoarthr Cartil. 2017;25(5):667–75.
25. Burns LC, Ritvo SE, Ferguson MK, Clarke H, Seltzer Z, Katz J. Pain catastrophizing as a risk factor for chronic pain after total knee arthroplasty: A systematic review. Vol. 8, Journal of Pain Research. 2015. p. 21–32.
26. Collins JE, Donnell-Fink LA, Yang HY, Usiskin IM, Lape EC, Wright J, et al. Effect of Obesity on Pain and Functional Recovery Following Total Knee Arthroplasty. J Bone Joint Surg Am. 2017;99(21):1812–8.
27. Fortin PR, Penrod JR, Clarke AE, St-Pierre Y, Joseph L, Bélisle P, et al. Timing of total joint replacement affects clinical outcomes among patients with osteoarthritis of the hip or knee. Arthritis Rheum. 2002;46(12):3327–30.
28. American Academy of Orthopaedic Surgeons. Appropriate Use Criteria: Surgical management of knee osteoarthritis. 2018.
29. NICE. Clinical guideline [CG177]: Osteoarthritis: care and management [Internet]. 2014. Available from: https://www.nice.org.uk/guidance/cg177
30. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. A Randomized, Controlled Trial of Total Knee Replacement. N Engl J Med [Internet]. 2015;373(17):1597–606. Available from: http://www.nejm.org/doi/10.1056/NEJMoa1505467
31. James-Lind-Alliance. Priority setting partnership: Hip and knee replacment for osteoarthritis [Internet]. 2014 [cited 2018 Mar 1]. Available from: http://www.jla.nihr.ac.uk/priority-setting-partnerships/hip-and-knee-replacement-for-osteoarthritis/top-10-priorities/
32. Price AJ, Smith J, Dakin HA, Kang S, Eibich P, Cook J, et al. Introducing Standardized and Evidence Based Thresholds for Hip and Knee Replacement Surgery -The Arthroplasty Candidacy Help Engine (The ACHE tool): A systematic review, clinical and economics analysis. Health Technol Assess. 2018;In press.
33. Giori NJ, Amanatullah DF, Gupta S, Bowe T, Harris AHS. Risk Reduction Compared with Access to Care: Quantifying the Trade-Off of Enforcing a Body Mass Index Eligibility Criterion for Joint Replacement. J Bone Jt Surg [Internet]. 2018;100(7):539–45. Available from: http://insights.ovid.com/crossref?an=00004623-201804040-00001
34. Harris K, Dawson J, Gibbons E, Lim C, Beard D, Fitzpatrick R, et al. Systematic review of measurement properties of patient-reported outcome measures used in patients undergoing hip and knee arthroplasty. Patient Relat Outcome Meas [Internet]. 2016;Volume 7:101–8. Available

from: https://www.dovepress.com/systematic-review-of-measurement-properties-of-patient-reported-outcom-peer-reviewed-article-PROM
35. Murray DW, MacLennan GS, Breeman S, Dakin HA, Johnston L, Campbell MK, et al. A randomised controlled trial of the clinical effectiveness and cost-effectiveness of different knee prostheses: the Knee Arthroplasty Trial (KAT). Health Technol Assess. 2014;18(19).
36. Dakin H, Gray A, Fitzpatrick R, MacLennan G, Murray D. Rationing of total knee replacement: A cost-effectiveness analysis on a large trial data set. BMJ Open. 2012;2(1).
37. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of Prospective studies in unselected patients. Vol. 2, BMJ Open. 2012.
38. Beard DJ, Harris K, Dawson J, Doll H, Murray DW, Carr AJ, et al. Meaningful changes for the Oxford hip and knee scores after joint replacement surgery. J Clin Epidemiol [Internet]. 2015;68(1):73–9. Available from: http://dx.doi.org/10.1016/j.jclinepi.2014.08.009
39. Lange T, Rataj E, Kopkow C, Lützner J, Günther K-P, Schmitt J. Outcome Assessment in Total Knee Arthroplasty: A Systematic Review and Critical Appraisal. J Arthroplasty [Internet]. 2017;32(2):653–665.e1. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0883540316306568
40. Hawker GA, Badley EM, Borkhoff CM, Croxford R, Davis AM, Dunn S, et al. Which patients are most likely to benefit from total joint arthroplasty? Arthritis Rheum. 2013;65(5):1243–52.
41. NHS Digital. Provisional Quarterly Patient Reported Outcome Measures (PROMs) in England, April 2016 to March 2017 [Internet]. 2018 [cited 2018 Mar 31]. Available from: http://digital.nhs.uk/catalogue/PUB30192
42. Escobar A, Gonzalez M, Quintana JM, Vrotsou K, Bilbao A, Herrera-Espiñeira C, et al. Patient acceptable symptom state and OMERACT-OARSI set of responder criteria in joint replacement. Identification of cut-off values. Osteoarthr Cartil [Internet]. 2012;20(2):87–92. Available from: http://dx.doi.org/10.1016/j.joca.2011.11.007
43. Beard D, Price A, Cook J, Fitzpatrick R, Carr A, Campbell M, et al. Total or Partial Knee Arthroplasty Trial - TOPKAT: Study protocol for a randomised controlled trial. Trials. 2013;14(1).
44. Noble PC, Scuderi GR, Brekke AC, Sikorskii A, Benjamin JB, Lonner JH, et al. Development of a new knee society scoring system. In: Clinical Orthopaedics and Related Research. 2012. p. 20–32.
45. Dunbar MJ, Richardson G, Robertsson O. I can't get no satisfaction after my total knee replacement: rhymes and reasons. Vol. 95 B, The bone & joint journal. 2013. p. 148–52.
46. Arden N, Altman D, Beard D, Carr A, Clarke N, Collins G, et al. Lower limb arthroplasty: can we produce a tool to predict outcome and failure, and is it cost-effective? An epidemiological study. Program Grants Appl Res [Internet]. 2017;5(12):1–246. Available from: https://www.journalslibrary.nihr.ac.uk/pgfar/pgfar05120
47. Shan L, Shan B, Suzuki A, Nouh F, Saxena A. Intermediate and Long-Term Quality of Life After Total Knee Replacement.A systematic Review and Meta-Analysis. J Bone Jt Surgery, Am Vol. 2015;97–A(2):156–68.

48. Losina E, Walensky RP, Kessler CL, Emrani PS, Reichmann WM, Wright EA, et al. Cost-effectiveness of total knee arthroplasty in the United States: Patient risk and hospital volume. Arch Intern Med. 2009;169(12):1113–21.
49. Kent S, Green J, Reeves G, Beral V, Gray A, Jebb SA, et al. Hospital costs in relation to body-mass index in 1·1 million women in England: a prospective cohort study. Lancet Public Heal. 2017;2(5):e214–22.
50. Ferket BS, Feldman Z, Zhou J, Oei EH, Bierma-Zeinstra SMA, Mazumdar M. Impact of total knee replacement practice: cost effectiveness analysis of data from the Osteoarthritis Initiative. Bmj [Internet]. 2017;j1131. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.j1131
51. Duncan CM, Long KH, Warner DO, Pagnano MW, Hebl JR. The economic implications of a multimodal analgesic regimen combined with minimally invasive orthopedic surgery: A comparative cost study. J Anesth Clin Res. 2010;1(1):1–6.
52. Murphy J, Pritchard MG, Cheng LY, Janarthanan R, Leal J. Cost-effectiveness of enhanced recovery in hip and knee replacement: a systematic review protocol. BMJ Open. 2018;8(3):e019740.
53. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78(5):606–17.
54. Soffin EM, Yadeau JT. Enhanced recovery after surgery for primary hip and knee arthroplasty: A review of the evidence. Br J Anaesth. 2016;117(March):iii62-iii72.
55. Savaridas T, Serrano-Pedraza I, Khan SK, Martin K, Malviya A, Reed MR. Reduced medium-term mortality following primary total hip and knee arthroplasty with an enhanced recovery program. Acta Orthop. 2013;84:40–3.
56. Malviya A, Martin K, Harper I, Muller SD, Emmerson KP, Partington PF, et al. Enhanced recovery program for hip and knee replacement reduces death rate: A study of 4,500 consecutive primary hip and knee replacements. Acta Orthop. 2011;82(5):577–81.
57. Johnson RL, Kopp SL, Burkle CM, Duncan CM, Jacob AK, Erwin PJ, et al. Neuraxial vs general anaesthesia for total hip and total knee arthroplasty: A systematic review of comparative-effectiveness research. Br J Anaesth [Internet]. 2016;116(2):163–76. Available from: http://dx.doi.org/10.1093/bja/aev455
58. Hu B, Lin T, Yan S, Tong S-L, Yu J-H, Xu J-J, et al. Local Infiltration Analgesia Versus Regional Blockade for Postoperative Analgesia in Total Knee Arthroplasty: A Meta-analysis of Randomized Controlled Trials. Pain Physician. 2016;19(4):205.
59. Chen T, Chen Y, Jiao J, Wang Y, Qian L, Guo Z, et al. Comparison of the effectiveness and safety of topical versus intravenous tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled trials. J Orthop Surg Res [Internet]. 2017;12(1):11. Available from: http://josr-online.biomedcentral.com/articles/10.1186/s13018-017-0512-4
60. NICE. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. NICE guideline [NG89] [Internet]. 2018 [cited 2018 Aug 8]. Available from:

https://www.nice.org.uk/guidance/ng89
61. Guerra ML, Singh PJ, Taylor NF. Early mobilization of patients who have had a hip or knee joint replacement reduces length of stay in hospital: A systematic review. Clin Rehabil. 2015;29(9):844–54.
62. Kort NP, Bemelmans YFL, van der Kuy PHM, Jansen J, Schotanus MGM. Patient selection criteria for outpatient joint arthroplasty. Knee Surgery, Sport Traumatol Arthrosc [Internet]. 2017;25(9):2668–75. Available from: http://link.springer.com/10.1007/s00167-016-4140-z
63. Tucker K. Beyond Compliance [Internet]. 2011 [cited 2018 Mar 28]. Available from: http://www.odep.org.uk
64. Koh CK, Zeng I, Ravi S, Zhu M, Vince KG, Young SW. Periprosthetic Joint Infection Is the Main Cause of Failure for Modern Knee Arthroplasty: An Analysis of 11,134 Knees. Clin Orthop Relat Res. 2017;475(9):2194–201.
65. Zmistowski B, Karam JA, Durinka JB, Casper DS, Parvizi J. Periprosthetic Joint Infection Increases the Risk of One-Year Mortality. J Bone Jt Surgery-American Vol [Internet]. 2013;95(24):2177–84. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00004623-201312180-00003
66. O'Toole P, Maltenfort MG, Chen AF, Parvizi J. Projected Increase in Periprosthetic Joint Infections Secondary to Rise in Diabetes and Obesity. J Arthroplasty [Internet]. 2016;31(1):7–10. Available from: http://dx.doi.org/10.1016/j.arth.2015.07.034
67. Meehan JP, Danielsen B, Kim SH, Jamali AA, White RH. Younger Age Is Associated with a Higher Risk of Early Periprosthetic Joint Infection and Aseptic Mechanical Failure After Total Knee Arthroplasty. J Bone Jt Surg [Internet]. 2014;96(7):529–35. Available from: http://jbjs.org/cgi/doi/10.2106/JBJS.M.00545
68. Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of Periprosthetic Joint Infection. J Arthroplasty [Internet]. 2014;29(2 SUPPL.):77–83. Available from: http://dx.doi.org/10.1016/j.arth.2013.09.040
69. Haddad FS, George DA. Can National Joint Registries play a role in improving our understanding of periprosthetic infections? Bone and Joint Journal. 2016;98B(3):289–90.
70. Rolfson O, Bohm E, Franklin P, Lyman S, Denissen G, Dawson J, et al. Patient-reported outcome measures in arthroplasty registries: Report of the Patient-Reported Outcome Measures Working Group of the International Society of Arthroplasty RegistriesPart II. Recommendations for selection, administration, and analysis. Acta Orthop. 2016;87:9–23.
71. Rothwell AG, Hooper GJ, Hobbs A, Frampton CM. An analysis of the Oxford hip and knee scores and their relationship to early joint revision in the New Zealand Joint Registry. J Bone Jt Surg - Br Vol [Internet]. 2010;92–B(3):413–8. Available from: http://www.bjj.boneandjoint.org.uk/cgi/doi/10.1302/0301-620X.92B3.22913
72. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101330 matched patients: A study of data from the National Joint Registry for England and Wales. Lancet. 2014;384(9952):1437–45.

73. Hunt LP, Ben-Shlomo Y, Clark EM, Dieppe P, Judge A, Macgregor AJ, et al. 45-day mortality after 467779 knee replacements for osteoarthritis from the National Joint Registry for England and Wales: An observational study. Lancet. 2014;384(9952):1429–36.
74. Lauer MS, D'Agostino RB. The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research? N Engl J Med [Internet]. 2013;369(17):1579–81. Available from: http://www.nejm.org/doi/10.1056/NEJMp1310102
75. NHS. GIRFT - Getting it right first time [Internet]. 2018 [cited 2018 Aug 1]. Available from: http://gettingitrightfirsttime.co.uk
76. Nieuwenhuijse MJ, Nelissen RGHH, Schoones JW, Sedrakyan A. Appraisal of evidence base for introduction of new implants in hip and knee replacement: A Systematic review of five widely used device technologies. BMJ. 2014;349(September):1–12.
77. De Steiger RN, Muratoglu O, Lorimer M, Cuthbert AR, Graves SE. Lower prosthesis-specific 10-year revision rate with crosslinked than with non-crosslinked polyethylene in primary total knee arthroplasty. Acta Orthop. 2015;86(6):721–7.
78. Nebergall AK, Troelsen A, Rubash HE, Malchau H, Rolfson O, Greene ME. Five-Year Experience of Vitamin E-Diffused Highly Cross-Linked Polyethylene Wear in Total Hip Arthroplasty Assessed by Radiostereometric Analysis. J Arthroplasty. 2016;31(6):1251–5.
79. Insall JN, Binazzi R, Soudry M, Mestriner LA. Total knee arthroplasty. Clin Orthop Relat Res [Internet]. 1985;(192):13–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3967412
80. Rivière C, Iranpour F, Auvinet E, Howell S, Pascal.AVendittoli, Cobb J, et al. Alignment Options for Total Knee Arthroplasty: A Systematic Review. Orthop Traumatol Surg Res [Internet]. 2017; Available from: http://www.sciencedirect.com/science/article/pii/S1877056817302281%0A
81. Courtney PM, Lee G-C. Early Outcomes of Kinematic Alignment in Primary Total Knee Arthroplasty: A Meta-Analysis of the Literature. J Arthroplasty [Internet]. 2017;32(6):2028–2032.e1. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0883540317301596
82. Young SW, Walker ML, Bayan A, Briant-Evans T, Pavlou P, Farrington B. The Chitranjan S. Ranawat Award: No Difference in 2-year Functional Outcomes Using Kinematic versus Mechanical Alignment in TKA: A Randomized Controlled Clinical Trial. Clin Orthop Relat Res. 2017;475(1):9–20.
83. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101330 matched patients: A study of data from the National Joint Registry for England and Wales. Lancet [Internet]. 2014;384(9952):1437–45. Available from: http://dx.doi.org/10.1016/S0140-6736(14)60419-0
84. Burn E, Liddle AD, Hamilton TW, Judge A, Pandit HG, Murray DW, et al. Cost-effectiveness of unicompartmental compared with total knee replacement: a population-based study using data from the National Joint Registry for England and Wales. BMJ Open [Internet]. 2018;8(4):e020977. Available from: http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-

2017-020977
85. Kulshrestha V, Datta B, Kumar S, Mittal G. Outcome of Unicondylar Knee Arthroplasty vs Total Knee Arthroplasty for Early Medial Compartment Arthritis: A Randomized Study. J Arthroplasty. 2017;32(5):1460–9.
86. Odgaard A, Madsen F, Wagner Kristensen P, Kappel A, Fabrin J. The Mark Coventry Award: Patellofemoral Arthroplasty Results in Better Range of Movement and Early Patient-reported Outcomes Than TKA. Clin Orthop Relat Res. 2018;476(1):87–100.
87. Liddle AD, Pandit H, Judge A, Murray DW. Optimal usage of unicompartmental knee arthroplasty: A study of 41 986 cases from the national joint registry for England and Wales. Bone Jt J. 2015;97B(11):1506–11.
88. Gromov K, Korchi M, Thomsen MG, Husted H, Troelsen A. What is the optimal alignment of the tibial and femoral components in knee arthroplasty? An overview of the literature. Acta Orthop. 2014;85(5):480–7.
89. Huijbregts HJTAM, Khan RJK, Sorensen E, Fick DP, Haebich S. Patient-specific instrumentation does not improve radiographic alignment or clinical outcomes after total knee arthroplasty: A meta-analysis. Acta Orthop. 2016;87(4):386–94.
90. van der List JP, Chawla H, Joskowicz L, Pearle AD. Current state of computer navigation and robotics in unicompartmental and total knee arthroplasty: a systematic review with meta-analysis. Vol. 24, Knee Surgery, Sports Traumatology, Arthroscopy. 2016. p. 3482–95.
91. De Steiger RN, Liu YL, Graves SE. Computer navigation for total knee arthroplasty reduces revision rate for patients less than sixty-five years of age. J Bone Jt Surg - Am Vol. 2015;97(8):635–42.
92. Smith AJ, Dieppe P, Howard PW, Blom AW. Failure rates of metal-on-metal hip resurfacings: Analysis of data from the National Joint Registry for England and Wales. Lancet [Internet]. 2012;380(9855):1759–66. Available from: http://dx.doi.org/10.1016/S0140-6736(12)60989-1
93. Sorenson C, Drummond M. Improving medical device regulation: the United States and Europe in perspective. Milbank Q [Internet]. 2014;92(1):114–50. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3955380&tool=pmcentrez&rendertype=abstract
94. Sheth U, Nguyen N, Gaines S, Bhandari M, Mehlman C, Klein G. New orthopedic devices and the FDA. J Long Term Eff Med Implant. 2009;19(3):173–84.
95. MHRA. Notified bodies for medical devices [Internet]. 2017 [cited 2018 Mar 28]. Available from: https://www.gov.uk/government/publications/notified-bodies-for-medical-devices/notified-bodies-for-medical-devices
96. Anand R, Graves SE, de Steiger RN, Davidson DC, Ryan P, Miller LN, et al. What Is the Benefit of Introducing New Hip and Knee Prostheses? J Bone Jt Surg [Internet]. 2011;93(Supplement_3):51–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22262424%5Cnhttp://jbjs.org/cgi/doi/10.2106/JBJS.K.00867
97. Pijls BG, Nelissen RGHH. The era of phased introduction of new implants.

Bone Joint Res [Internet]. 2016;5(6):215–7. Available from: http://online.boneandjoint.org.uk/doi/10.1302/2046-3758.56.2000653
98. Faris O, Shuren J. An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials. N Engl J Med [Internet]. 2017;376(14):1350–7. Available from: http://www.nejm.org/doi/10.1056/NEJMra1512592
99. Malchau H, Graves SE, Porter M, Harris WH, Troelsen A. The next critical role of orthopedic registries. Acta Orthop. 2015;86(1):3–4.
100. Nelissen RGHH, Pijls BG, Kärrholm J, Malchau H, Nieuwenhuijse MJ, Valstar ER. RSA and Registries: The Quest for Phased Introduction of New Implants. J Bone Jt Surgery-American Vol [Internet]. 2011;93(Suppl 3):62–5. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00004623-201112213-00010