International Journal of Technology Assessment in Health Care, 30:2 (2014), 218–225.
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doi:10.1017/S0266462314000129

COST-EFFECTIVENESS AND CLINICAL IMPLICATIONS OF ADVANCED BEARINGS IN TOTAL KNEE ARTHROPLASTY: A LONG-TERM MODELING ANALYSIS

Peter Fennema
Netherlands Institute for Health Sciences, and AMR Advanced Medical Research

Carin A. Uyl-de Groot
Institute for Medical Technology Assessment, Erasmus University

Thomas J. Heyse
Department of Orthopedics and Rheumatology, University Hospital Marburg

Background: Polyethylene (PE) wear is a major contributor to implant loosening following total knee arthroplasty (TKA). Advanced bearings are therefore required in TKA to reduce or eliminate wear-related loosening. A recently introduced bearing that combines oxidized zirconium with highly cross-linked PE has been shown to drastically reduce wear in *in vitro* settings, due to its improved tribological characteristics in both tibial and femoral components. However, there are no data on its cost-effectiveness.
Data and Methods: A Markov model was developed to assess the cost-effectiveness of this low-wear bearing from a German societal perspective. The model population was derived from a registry of 75,000 patients requiring TKA. The model allocated patients to receive either a low-wear or standard articulation, and followed them until death. Revisions and re-revision were included. Input values were derived from registry databases or from published reports in the literature. Threshold analysis and probabilistic sensitivity analysis were conducted to estimate model robustness.
Results: The low-wear articulation prevented 24 (2.4 percent) revisions and 8 (0.8 percent) re-revisions. The total incremental cost-effectiveness ratio (ICER) of the low-wear articulation was EUR 16,474 per quality-adjusted life-year (QALY). For patients aged less than 55 years, an ICER of EUR 653 per QALY was observed. For patients aged over 75 years, this value was EUR 83,300. Threshold and probabilistic sensitivity analysis indicated that these findings were reasonably robust.
Conclusion: Low-wear articulations may be considered cost-effective, although the cost effectiveness is age-dependent, with the cost per QALY being significantly lower for younger people than for older people.

Keywords: Total knee arthroplasty, Advanced bearings, Cost-effectiveness, Markov modeling

Polyethylene (PE) wear is a major cause of implant failure in total knee arthroplasty (TKA). It results from a combination of intra-articular rolling, sliding, and rotation, which may lead to delamination, pitting, and fatigue failure of the PE surface (1). PE wear particles are phagocytized by macrophages, which initiates a cascade of events resulting in the loss of periprosthetic bone (2). PE wear is also related to patient activity levels—as younger and more active patients undergo TKA, the demands placed on implant materials will increase.

As revision knee arthroplasty is both more expensive (3;4) and less successful at producing high-quality outcomes (1), there is a need to improve the longevity of primary prostheses.

Oxidized zirconium (OxZr) alloy (Smith & Nephew Inc., Memphis, TN) was created to address PE wear, and is used as a bearing surface in both TKA and total hip arthroplasty (THA). The material offers a potential solution to the demands placed on prosthetic components, as it combines the surface properties of a ceramic component with the strength and stability of an all-metal implant. The material has superior resistance to surface roughening and lower friction against PE, and offers improved biocompatibility versus traditional cobalt-chromium femoral components (5). *In vitro* simulations have shown that OxZr reduces wear by 55 percent under varus and rotational malalignment (6). One study demonstrated that the benefits of OxZr in TKA are magnified under abrasive conditions (7). To date, no studies linking the use of OxZr with improved survival times have been published so far.

Ultra-high-molecular-weight PE (UHMWPE) has been used in the field of total joint arthroplasty since the 1960s. Highly cross-linked PEs (HXLPEs) were introduced in the late 1990s to reduce wear and prevent revision due to osteolysis. The few available *in vivo* studies reporting clinical outcomes with HXLPLE inserts indicate that they are safe in the short- to mid-term (8;9), although these analyses have insufficient sample sizes and follow-up periods. Nevertheless, *in vitro* testing has confirmed the superior wear characteristics of HXLPE (5).

Verilast (Smith & Nephew Inc., Memphis, TN) is an articulation consisting of HXLPE and OxZr and is used in both THA and TKA. Compared with other articulations tested under similar conditions, this advanced bearing has a relatively low wear rate (5). In a study with a cruciate retaining knee, the mean volumetric wear of this articulation after simulating 3 years of

https://doi.org/10.1017/S0266462314000129 Published online by Cambridge University Press

use (5 million cycles) was approximately 98 percent lower than that for cobalt-chromium (CoCr)/conventional PE couples (2. 7 mm^3 versus 120 mm^3, respectively). After 45 million cycles (equivalent to approximately 30 years of physical activity), the wear was 22.8 mm^3 for the advanced bearing group (10).

The goal of this study was to estimate the clinical and cost effectiveness of this low-wear advanced articular bearing in TKA, from a German societal perspective. A secondary goal was to assess these outcomes across various age groups. Calculations were made based on the assumption that, due to its superior wear characteristics, the use of an advanced bearing would prevent wear-related loosening.

DATA AND METHODS

We developed a state-transition Markov model with the aid of decision analysis software. The model contained yearly cycles to simulate the history of patients undergoing TKA for the treatment of osteoarthritis and compared the cost effectiveness of using the low-wear articulation with that of standard articulation from a German societal perspective. The decision tree was extended by 1-year Markov cycles to simulate long-term follow-up until revision or death, and, therefore, yield survival time estimates for both groups. The model contained states for patient groups aged ≥75 years, between 65 and 75 years, between 55 and 65 years, and <55 years of age, as well as the states "revision" and "death." An initial analysis was undertaken using 1000 microsimulations. The model contained costs associated with the procedure, as well as postoperative utilities, which represent the value that people place on a particular health state. Utilities were expressed as quality-adjusted life-years (QALYs). QALYs were calculated by multiplying the length of time spent in a particular health state by the utility value of that health state.

Revision was defined as explanation of any component and re-implantation using a revision knee. Costs of revision and functional outcomes were equivalent for both study groups. The worst case scenario was defined as two revision procedures, with patients then allocated to the "well with revision" health state until death.

The utility value for primary TKA was set at 0.84, with a range of 0.68 to 0.98 (11–13) (Table 1). Clinical outcome following revision TKA are usually poorer than after primary TKA (11). Therefore, in line with a publication by Slover et al. (12), the associated utility for revision TKA was set at 0.60, with a range from 0.45 to 0.75. We also assumed a disutility (procedure toll) of 0.10 for primary TKA, 0.10 for aseptic revision surgery and 0.20 for septic revision arthroplasty, in accordance with Slover et al. (12). The prerevision utility value was set at 0.40 (13).

In our study, we assessed a scenario in which wear-related TKA loosening does not occur. We first estimated age-specific loosening rates in the total population, and then quantified the proportion of loosening attributable to wear, using data from literature. Data from the Swedish Knee Arthroplasty Register (14;15)(base: 2006), involving 75,000 knees, were used to calculate baseline loosening rates. The incidence rate of revision per 100 component years was 1.26 in those aged <55 years, 1.11 in those aged 55–65 years, 0.77 in those aged 65–75 years, and 0.51 in those aged >75 years. The mean age of the cohort was 71 years, which was equivalent to the mean age of the registry database population.

Ten-year survivorship after revision TKA was 79 percent (16), independent of age. This corresponds to a revision rate of 2.35 per 100 component years. Age-specific mortality probabilities were taken from the Federal Statistical Office of Germany (17).

Next, the literature was systematically assessed for the etiology of primary TKA failure to quantify the proportion related to wear. EMBASE was used for the systematic literature review (search date: 14 November 2011), with the aim of locating papers that specifically examined the failure mode and etiology of loosening, as opposed to individual case series that did not specifically assess the failure mode. Search terms used were: "polyethylene"/exp OR polyethylene AND wear AND revision AND ("total knee arthroplasty"/exp OR "total knee arthroplasty") AND [2000–2012]/py NOT (xlpe OR hxlpe). Papers published before 2000 were excluded to limit the influence of sterilization techniques (i.e., gamma radiation in air) associated with inferior results and that have now largely been abandoned. In addition, we excluded papers in which the failure mode attributable to wear was not assessed, as well as papers on highly cross-linked PE, vitamin E enhanced polyethylene, and unicondylar knee arthroplasty.

In total, the search retrieved 170 abstracts, which were manually assessed for suitability. Failure modes were described in seven papers (18–24). We calculated pooled estimates using the methods described by Deeks et al. (25), which assumes heterogeneity between the populations. Pooled estimates for short-term (≤2 years) and long-term (>2 years) failure caused by wear were 10.5 percent (95 percent confidence interval [CI], 5.2 percent–20.3 percent) and 33.3 percent (95 percent CI, 23.4 percent–44.9 percent), respectively.

Costs were measured in 2011 Euros. The average reimbursement for a primary TKA was based on that for German hospitals for diagnosis-related group for implantation of a bicondylar prosthesis without severe comorbidities (I44B, EUR 7,242), septic revisions implantation of a bicondylar prosthesis with severe comorbidities (I44A, EUR 8,945), and implantation of a hinged prosthesis without severe comorbidities for aseptic revision surgeries (I43B, EUR 9,538). These are average values that include the costs of the implantation of the knee prosthesis, ancillary surgical costs, and hospitalization. The DRG values are adjusted at the level of the hospital for case mix variations at the hospital level. The additional cost of the advanced bearing articulation was set at EUR 960. Rehabilitation costs were based

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Table 1. Most Important Variables in the Markov Model

Variable	Mean	Low range	High range	Source
Wear				
Reduction short-term in loosening[a]	0.105	0	0.203	Berend (21), Bozic (22), Fehring (19), Ghomrawi (23), Gioe (20), Mulhall (24), Sharkey (18)
Reduction long-term in loosening[a]	0.33	0	0.449	Berend (21), Gioe (20), Mulhall (24), Sharkey (18)
Discounting				Smith (33)
Discount rate health	3%	0%	5%	Smith (33)
Discount rate costs	3%	3%	3%	Smith (33)
Costs [EUR]				
Costs primary TKA	7,242	5,000	15,000	
Incremental Costs advanced bearing	960	0	2,500	
Cost revision TKA	9,538	5,000	20,000	
Productivity loss [EUR]:				
< 55	1,668	1,668	1,668	
55 - 65	1,108	1,108	1,108	
65 - 75	205	205	205	
>75	0	0	0	
Utilities				
Utility primary TKA	0.84	0.68	0.98	Heck (11), Slover (12), Slover (13)
Utility revision TKA	0.6	0.45	0.75	Slover (12)
Pre-revision Utility	0.4	0.4	0.4	Slover (12), Slover (13)
Disutility primary TKA and revision TKA	0.1	0.1	0.1	Slover (12)
Disutility septic revision TKA	0.2	0.2	0.2	Slover (12)
Age specific incidence rates:[b]				
< 55	1.26	1.26	1.26	
55 - 65	1.11	1.11	1.11	
65 - 75	0.77	0.77	0.77	
>75	0.51	0.51	0.51	
Revision TKA	2.35	2.35	2.35	Sheng (16)

[a] Expressed as relative risk reduction.
[b] Expressed as number of revision per 100 observed patient year.

on the AOK-proReha concept for rehabilitation after TKA. A flat rate of EUR 1,779 was added to the DRG reimbursement of the knee surgery, and EUR 2,176 was added to all revision surgeries. Costs for preoperative primary care consultations and for co-payments were not included in the model, as these will not be different for the two groups. Costs associated with being in a prerevision state were not included in our model.

Labor participation was taken from the Organization for Economic Co-operation and Development Factbook 2010, at 53.8 percent in the 55–64 age group and 81.0 percent in the 25–54 age group (26). Data on labor participation in the age group over 65–75 years was estimated to be 10 percent (27;28). Based on figures from the Federal Statistical Office of Germany, mean hourly labor costs were set at EUR 29.20, with 253 annual labor days (27).

Productivity loss was calculated as: the mean length of hospital stay (according to the Institution for Hospital Remuneration System) for each surgery (12.3 days for primary TKA, 15.3 days for septic revisions, and 13.4 days for aseptic revisions) plus the length of rehabilitation, multiplied the average daily rate, corrected for labor participation.

Whole patients' out-of-pocket costs represent only a small proportion of the total treatment costs, these costs are substantial from a patient perspective and should be included in the decision-making process. Examples of out-of-pocket costs include transportation to the hospital, over-the-counter medication, and housekeeping. We are unaware of any studies documenting out-of-pocket expenses following TKA in Germany. A study conducted in Australia between 1994 and 1999 found that, on average, the out-of-pocket expenses for patients

https://doi.org/10.1017/S0266462314000129 Published online by Cambridge University Press

receiving unilateral TKA were AUS$ 621 (EUR 465) in the first postoperative year (29). A more recent study on total hip patients published in 2008 found that out-of-pocket expenses were $758 (EUR 559) (30). In absence of any reliable data from Germany, we have taken the Australian estimate and, correcting for inflation in Germany, included a cost of EUR 574 for out-of-pocket expenses in our model.

In our model, we included a slightly increased likelihood of perioperative death for patients undergoing primary TKA (0.5 percent [31]) and for septic or aseptic revision surgery (1.1 percent [32]).

Future costs and utilities were discounted using a constant annual rate of 3 percent in the base case scenario (33).

To assess the robustness of our model, a threshold analysis was performed using different willingness-to-pay (WTP) scenarios. Threshold analyses are performed to calculate the value of a given parameter required to make the ICER equal to a certain WTP. As Germany has not defined any threshold values for new technologies, we have used arbitrary WTPs of EUR 0, 10,000, 25,000, and 50,000, which respectively represent no, low, medium, and high WTP scenarios. Costs for medical interventions were largely unrestricted in the threshold analysis. As productivity loss differed across the different age groups, we included a multiplication factor. This factor ranged from 0 (indicating no productivity losses in any age group) to 4 (indicating four times the productivity losses from the base case scenario).

Next, we performed a probabilistic sensitivity analysis (PSA) using 1,000 × 1,000 simulations. PSA allows the model to simultaneously take into account uncertainty across various parameters. In other words, the PSA allows the analyst to consider the probability that adoption would be regarded as cost effective in the context of a stated willingness to pay. Variables in the PSA were considered mutually independent.

Parameter uncertainty of revision rates for primary TKA were estimated from 200 bootstrap samples of 1,000 subjects sampled from a database from the Swedish Knee Arthroplasty Register (14;15). Similarly, parameter uncertainty of re-revision rates for revision TKA were estimated from a database containing revision survival data from 200 bootstrap samples of 100 subjects. The database was provided by the manufacturer of the low wear articulation. Loosening rates were varied using their 95 percent confidence intervals (CI). Wear reduction associated with the use of the advanced TKA bearing was varied between zero and the upper 95 percent confidence bound of the respective point estimates, the former of which represents the scenario that low wear does not result in any survival advantage.

Markov modeling was performed using TreeAge Pro, 2013, Williamstown, MA. Survival analysis was performed using Stata 12.1 (StataCorp LP, College Station, TX), based on cumulative incidence, accounting for competing risk, as described elsewhere (34).

RESULTS

In total, there were 95 revisions in the low-wear articulation group and 119 in the standard group, indicating that the low-wear articulation prevented 24 revisions (2.4 percent). The cumulative incidence of all-cause loosening at 10 and 25 years was 6.5 percent (95 percent CI, 5.0 percent–8.1 percent) and 9.1 percent (7.4 percent–11.0 percent), respectively, in the low-wear articulation group, and 8.2 percent (6.6 percent–10.0 percent) and 11.4 percent (9.5 percent–13.5 percent), respectively, in the standard group. Due to the lower revision rate in the low-wear articulation group, fewer re-revisions were necessary than in the standard group (27 versus 35).

The mean cost of the low-wear articulation was EUR 12,110 (standard deviation [SD]: EUR 4,070), versus EUR 11,451 (SD: EUR 4,508) for standard TKA. The mean outcome in terms of expected utility was 9.92 QALYs (SD: 4.87 QALYs) for the low-wear articulation and 9.88 QALYs (SD: 4.84 QALYs) for standard TKA; indicating that the incremental cost-effectiveness was EUR 16,475/QALY.

Elderly patient groups were then excluded to assess the effect of age on cost-effectiveness (Table 2). Consistent with our expectations, the ICER decreased with younger population, suggesting that the technique is more cost-effective in these patients.

Among patients aged > 75 years, 65–75 years, and 55–65 years, the ICER was EUR 83,300/QALY, EUR 23,167/QALY, and EUR 5,288/QALY, respectively. As noted in Table 2, those aged <55 years had an ICER of EUR 653.

A threshold analysis was performed to assess the effect of wear rate, discounting health effects, the incremental costs of the low-wear articulation, out-of-pocket costs, revision rates, and productivity loss. The results from the threshold analysis are shown in Table 2. For many of the parameters, no threshold values were noted. Discounting health effects with a higher rate inflates effectiveness and decreases cost-effectiveness. Reducing the discount rate of health effects to zero would decrease the ICER to EUR 8,388/QALY. We also assessed the scenario that the reduction of the *in vitro* wear rate would not be realized completely in clinical practice. With a WTP = 25,000, the value of long-term reduction in loosenings attributable to wear was 27 percent. This suggests that the technology will be cost-effective as long as 100 percent – (33 percent–27 percent)/33 percent∗100 percent = 82 percent of the loosenings attributable to wear can be prevented. With a WTP = 50,000, the values for short- and long-term reductions of loosenings attributable to wear were 3.8 percent and 12 percent, respectively, given a reduction of 100 percent – (33 percent–15 percent)/33 percent∗100 percent = 45 percent.

Parameters for the probabilistic sensitivity analysis were set as indicated in Table 3. A beta distribution was assumed for all probabilities and a gamma distribution for all cost parameters. Results based on WTP thresholds of EUR 0, 10,000,

https://doi.org/10.1017/S0266462314000129 Published online by Cambridge University Press

Table 2. Clinical and Cost-Effectiveness for the Low-Wear and Standard Articulations for the Different Age Groups

	< = 75 years		< = 65 years		< = 55years	
Variable	Low-wear	Standard	Low-wear	Standard	Low-wear	Standard
Costs [EUR] (SD)	12,400 (3,886)	11,866 (4,480)	14,032 (5,124)	13,728 (5,623)	15,231 (5,721)	15,120 (6,174)
Effectiveness [QALY]	11.20 (4.62)	11.15 (4.59)	14.08 (4.55)	13.97 (4.52)	17.07 (4.52)	16.90 (4.24)
ICER [EUR/QALY]	10,680		2,764		653	
10-Year Incidence Revision [%]	6.5 (5.1–8.1)	8.7 (7.1–10.6)	8.8 (7.1–10.7)	11.8 (9.9- 13.9)	11.1 (9.2–13.1)	13.9 (11.8–16.1)
25-Year Incidence Revision [%]	12.0 (10.1–14.1)	15.3 (13.1–17.6)	17.6 (15.3–20.0)	23.1 (20.5–25.8)	20.6 (18.2–23.2)	26.8 (24.1–29.6)
Number of Revisions	127	161	196	255	274	354
Number of Re-Revisions	22	33	63	82	96	125

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; SD = standard deviation.

Table 3. Probabilistic Sensitivity Analysis Variables

Variable	Mean (SD)
Wear	
Reduction in short-term loosening[a]	0.105 (0.0023)
Reduction in long-term loosening[a]	0.33 (0.05)
Age specific loosening rates[b]	
< 55 years	0.012611 (0.001329)
55 – 65 years	0.0111466 (0.001325)
65 – 75 years	0.00773547 (0.00120667)
> 75 years	0.0051332 (0.0010067)
Loosening rates revision TKA	0.0251956 (0.0063114)
Utilities	
Utility primary TKA	0.84 (0.04)
Utility revision TKA	0.60 (0.05)
Costs [EUR]	
Total cost primary TKA	9,021 (2,000)
Total costs revision TKA	11,714 (2,500)

[a]Expressed as relative risk reduction.
[b]Expressed as number of revision per 100 observed patient years.

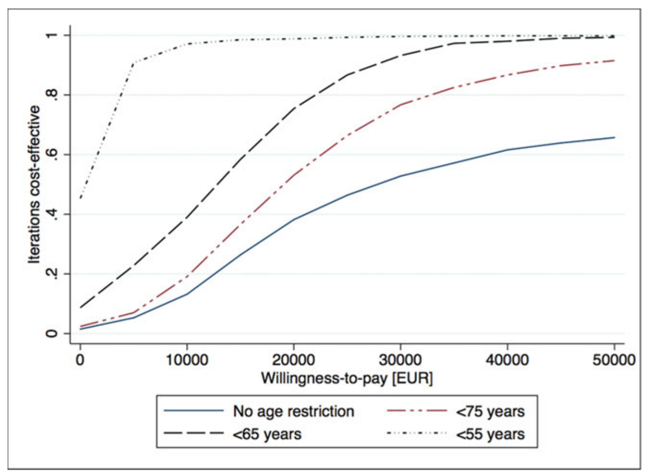

Figure 1. Acceptability curve for the different age groups.

25,000, and 50,000 indicated that the low-wear articulation was cost-effective compared with the standard articulation in 2.2 percent, 4.8 percent, 57.1 percent, and 67.0 percent of cases, respectively (Figure 1). For patients aged < 75, the percentages were 2.4 percent, 19.1 percent, 66.4 percent, and 91.5 percent for WTP thresholds of EUR 0, 10,000, 25,000, and 50,000, respectively. For patients aged <65, the percentages were 8.7 percent, 39.0 percent, 86.7 percent, and 99.3 percent, respectively. For patients aged <55, the percentages were 45.3 percent, 97.1 percent, 99.3 percent, and 100 percent, respectively.

DISCUSSION

Although outcomes following TKA are generally good, an annual revision rate of approximately 1 percent can be expected (35). Revision TKA is more complex and expensive than primary TKA, with generally less favorable outcomes. There is consequently a need to increase implant longevity for primary TKA. Wear reduction through the use of advanced bearing technologies may offer a solution. Using a Markov model analysis, we compared the cost-effectiveness of an advanced TKA bearing with a standard articulation from a German societal perspective.

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There are substantial incremental costs associated with the use of advanced bearings. However, these incremental costs must be considered in the context of the benefit achieved: namely the delay or avoidance of revision surgery—a costly procedure that has a substantial impact on the patient's quality of life. In the base case of our lifetime model, the advanced TKA bearing prevented 24 (2.4 percent) revisions and 8 (0.8 percent) re-revisions, resulting in an ICER of 16,475 EUR/QALY.

As expected, cost-effectiveness decreased substantially with increasing age, due to increased patient mortality. Omitting elderly patient group reduced the ICER to 653 EUR/QALY for the patient aged <55 years. Results from the probabilistic sensitivity analysis confirmed these findings. Conversely, our findings indicate that cost-effectiveness is unlikely to be achieved in the elderly population (at an ICER per 83,300 EUR/QALY for patients aged >75 years), due to their limited life expectancy and the low baseline risk of implant loosening in this cohort.

The acceptance of new technologies does not solely depend on their costs but also upon the willingness of payers to reimburse these products. Given the health-economic burden of revision TKA, all measures that substantially improve the longevity of the primary implant should be carefully appraised. As the application process for a relevant G-DRG code is time consuming, hospitals could instead apply for remuneration of new and innovative diagnosis and treatment methods ("Neue Untersuchungs und Behandlungsmethode, NUB") that have not yet obtained a G-DRG code. We are unaware of data concerning WTP for new medical device technologies in Germany. In the UK, technologies with an incremental costs-effectiveness ratio of £20,000/QALY (approximately EUR 32,000) are likely to receive a positive recommendation from the National Institute for Health and Care Excellence, whereas those with ratios over £30,000/QALY (approximately EUR 48,000) are unlikely to be qualified as cost-effective.

To our knowledge, this is the first health economic analysis of the use of advanced bearings in TKA. There are no available randomized studies showing superiority for advanced bearings in terms of implant survival. While there are *in vivo* studies available investigating the wear characteristics of OxZr and CoCr (36) and XLPE versus standard PE (37), such studies are of limited value as the retrieval techniques (PE particle extraction from synovial fluid) tend to bias toward larger PE particle size. *In vitro* studies show that the vast majority of particles are submicron, which are likely to be more osteolytic (38;39).

Our study has several limitations. We conducted this health economic evaluation using a Markov Chain Monte Carlo Analysis. Such analyses are intrinsically subject to oversimplification of the clinical course that occurs in the real world. In addition, the strength of the conclusions depends on the validity of the values used for the input variables. Whenever possible, German data were taken. However, it was not always possible to use input data collected from one single source, or even data pertaining to the German population. Despite those limitations, Markov chains are valuable tools for simulating the outcome of new technologies and their economic impact. They are more feasible than the alternative approach of conducting a cost-effectiveness analysis by means of a randomized clinical trial, which would require a very large sample size and lengthy study duration. Another limitation is that our inferences on the estimated loosening rates are susceptible to confounding-by-indication. The presence of prognostic differences between the registry population and the population eligible for the current technology cannot be precluded.

The major limitation of this study was the assumption that advanced TKA bearings will completely prevent wear-related loosening, which in practice may not be the case. *In vivo* wear may not be completely related to the mechanical properties of the materials. Threshold analysis has revealed that the model is somewhat sensitive for the scenario that, in clinical practice, loosening attributable to wear occurs in patients who have received an implant with an advanced bearing. For a WTP of 25,000 and 50,000, the proportion of patients who experience loosening attributable to wear will need to be reduced by at least 82 percent and 45 percent, respectively. Even in those scenarios, the use of a low-wear articulation could still be a cost-effective option in younger patients.

We assumed that the proportion of loosenings attributable to wear was constant for all ages, as we were unable to derive any relevant data from the literature. In real life one would expect a steady decline of activity with a corresponding decrease in wear-related loosening, as age is related to activity and activity determines PE wear. If so, cost-effectiveness for the younger patients is likely to be underestimated by our model, as is the ICER of EUR 83,300 for the elderly group. This would support the notion that using an advanced bearing is not cost-effective in the elderly population, which is in line with common sense.

Another limitation is that we did not include direct and indirect costs associated with prerevision morbidity in the model. It is to be expected that patients who are to undergo revision TKA experience forfeits in labor productivity and will make use of healthcare resources, such as radiography, magnetic resonance imaging and scintigraphy, before the actual revision. Costs are also likely to be highly variable between patients. In the absence of specific data from the literature, we did not account for this in our model. This aspect is likely to underestimate the cost-effectiveness of the clinically superior bearing.

The use of HXLPE in TKA is not a settled matter in contemporary orthopedics. It has been shown that modern standard PE inserts sterilized with ethylene oxide and inert gamma effectively eliminated delamination, unlike components sterilized using gamma irradiation in air (40). In addition, influential research investigating the fatigue and fracture behavior of HXLPE has raised questions over the suitability of these materials for knee arthroplasty, given the finding that increasing doses of radiations can result in a loss of mechanical properties (41). Reduced mechanical strength may become especially apparent

https://doi.org/10.1017/S0266462314000129 Published online by Cambridge University Press

in posterior-stabilized designs after long-term follow-up. For these reasons, conventional tibial inserts remain in clinical use today as an additional option alongside HXLPE.

In conclusion, our study indicates that cost-effectiveness of advanced bearings depends crucially on age of the patient population, with the cost per QALY significantly lower for younger than for older patients. In the younger population, the ICER for low-wear articulations falls well below the UK threshold of EUR 32,000, and, we believe, should therefore be considered as treatment option. Our conclusions rely on the scenario that loosening attributable to wear will be substantially reduced in patients who have received a low wear articulation, which requires further clinical investigation.

ACKNOWLEDGMENTS

The authors thank Prof. Dr. Otto Robertsson for providing the anonymized data on implant survival.

CONTACT INFORMATION

Peter Fennema, DSc (p.fennema@amr-cro.com), Netherlands Institute for Health Sciences, Erasmus University Rotterdam, 3000 CA Rotterdam, The Netherlands; AMR Advanced Medical Research, Hofenstrasse 89b, 8708 Männedorf, Switzerland

Thomas J. Heyse, MD, PhD, Department of Orthopedics and Rheumatology, University Hospital Marburg, 35043 Marburg, Germany

Carin A. Uyl-de Groot, PhD, Department of Health Policy & Management, Institute for Medical Technology Assessment, Erasmus University Rotterdam, 3000 DR Rotterdam, The Netherlands

CONFLICTS OF INTEREST

P. Fennema is a former employee of Smith & Nephew and reports no conflicts of interests. T. Heyse is a Consultant for Smith and Nephew, Payment for lectures including service on speakers bureaus to author from Smith & Nephew, and Travel/accommodations/meeting expenses unrelated to activities listed to author from Smith & Nephew. C. Uyl-de Groot has no conflicts of interest.

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