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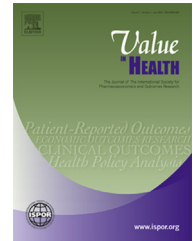
Economic Evaluation

Choice of Prosthetic Implant Combinations in Total Hip Replacement: Cost-Effectiveness Analysis Using UK and Swedish Hip Joint Registries Data

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A B S T R A C T

Background: Prosthetic implants used in total hip replacements (THR) have a range of bearing surface combinations (metal-on-polyethylene, ceramic-on-polyethylene, ceramic-on-ceramic, and metal-on-metal), head sizes (small [<36 mm in diameter] and large [≥36 mm in diameter]), and fixation techniques (cemented, uncemented, hybrid, and reverse hybrid). These can influence prosthesis survival, patients' quality of life, and healthcare costs. **Objectives:** To compare the lifetime cost-effectiveness of implants for patients of different age and sex profiles. **Methods:** We developed a Markov model to compare the cost-effectiveness of various implants against small-head cemented metal-on-polyethylene implants. The probability that patients required 1 or more revision surgeries was estimated from analyses of more than 1 million patients in the UK and Swedish hip joint registries, for men and women younger than 55, 55 to 64, 65 to 74, 75 to 84, and 85 years and older. Implant and healthcare costs were estimated from local procurement prices, national tariffs, and the literature. Quality-adjusted life-years were calculated using published utility estimates for patients undergoing THR in the United Kingdom.

Results: Small-head cemented metal-on-polyethylene implants were the most cost-effective for men and women older than 65 years. These findings were robust to sensitivity analyses. Small-head cemented ceramic-on-polyethylene implants were most cost-effective in men and women younger than 65 years, but these results were more uncertain. **Conclusions:** The older the patient group, the more likely that the cheapest implants, small-head cemented metal-on-polyethylene implants, were cost-effective. We found no evidence that uncemented, hybrid, or reverse hybrid implants were the most cost-effective option for any patient group. Our findings can influence clinical practice and procurement decisions for healthcare payers worldwide.

Keywords: combinations, cost-effectiveness, prosthetic hip implant, total hip replacement.

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Introduction

Total hip replacement (THR) is one of the most successful surgeries performed worldwide,[1] with 87 733 primary THRs performed in England and Wales in 2016.[2] In Sweden, there were 16 609 surgeries performed in 2015, which was 329 per 100 000 inhabitants aged 40 years and older,[3] and a further 8 402 in Norway and 44 710 in Australia.[4] In the United States, an estimated 2.5 million people are living with a hip replacement.[5] The first

effective hip implants were developed in the 1950s, with a small metal head that articulates with a polyethylene cup fixed with cement. They are the cheapest and most prevalent type of hip implant, with a long track record of use worldwide.[2-4,6] The polyethylene component wears with increased physical activity and load, resulting in loosening and bone loss over time, which is of more consequence in younger and more active patients because implant failure requires further surgery to revise and replace the prosthetic hip implant.[1] Newer polyethylenes,

alternative bearing surface combinations, larger head sizes, and different fixation methods have been developed to improve long-term patient outcomes,[1] but at potentially much higher costs.

Recent observational evidence found that newer metal-on-metal implants failed more often than traditional metal-on-polyethylene implants, which caused much concern to patients and clinicians.[7] Some studies suggested that ceramic-on-ceramic or ceramic-on-polyethylene prostheses, which can cost 4 times more than metal-on-polyethylene implants, performed better in young and active patients, and so their use is increasing in many countries.[2-4,8] Given the range of implant combinations currently available at widely different prices, and the rising volume of THR procedures performed worldwide, it is important to consider the cost-effectiveness of prosthetic implants for different patient groups undergoing THR surgery.

In this article, we compared the lifetime cost-effectiveness of hip implant combinations for men and women of different age profiles in the United Kingdom. Previous models have examined the cost-effectiveness of prosthetic implants, but may have used simpler assumptions, such as assuming constant risks of revision after surgery,[9] without reliable long-term estimates,[9-11] or were too narrow in scope, comparing few or just 2 implants[9-12] or only 1 or more implant material.[13-15] Previous models either grouped patients[13,16,17] or examined a small subset of different age and sex profiles.[10,11] Our work exceeds previous analyses by (1) assessing complete implant combinations that form the constructs currently in clinical use, (2) incorporating high-quality real-world evidence on implant survival and allowing the risk of revision to vary over time, and (3) focusing on a wide array of patient subgroups. Our findings provide evidence to inform the decisions of patients, surgeons, and healthcare commissioners worldwide.

Methods

Prosthetic Implant Combinations for Analysis

There were 24 implant combinations compared in this analysis, defined by bearing surface combination, fixation technique, and femoral head size (see Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013).[18] Bearing surface combinations included metal-on-polyethylene, metal-on-metal, ceramic-on-polyethylene, and ceramic-on-ceramic implants; surgical fixation techniques

were cemented, uncemented, hybrid, and reverse hybrid; and femoral heads were considered small if less than 36 mm in diameter and large if 36 mm or more in diameter. We considered only implants in current regular clinical practice; implants rarely used, namely, ceramic-on-metal and cemented ceramic-on-ceramic and metal-on-metal, were excluded. The "reference implant" combination for analysis was the small-head (<36 mm) cemented metal-on-polyethylene implant, the most commonly used implant combination in the United Kingdom,[2] as elsewhere.[3,8]

Model Development and Structure

To develop our model, we consulted with hip surgeons and patients to make realistic assumptions about the risk of revision over time and to identify outcomes that might be relevant for analysis. We searched the MEDLINE and Embase databases on OvidSP, and the National Health Service (NHS) economic evaluation database for models used in previous economic evaluations, as detailed in Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013; an overview of these studies is also provided in this appendix.

We developed a Markov model with a lifetime time horizon and a 1-year cycle length (Fig. 1), as in previous economic models.[13,15,19] Unlike previous models, the hazard of first revision was assumed to vary between 3 time periods after primary THR surgery ("early," up to 2 years; "middle," 2-10 years; and "late," 10 years or more) but remain constant within each period. This assumption was based on clinical opinion and observation of implant survivorship data from successive annual reports of the National Joint Registry (NJR) for England, Wales, Northern Ireland, and the Isle of Man,[20] which showed that the hazard of first revision after primary THR was high within the initial period after surgery, low in the medium term, and rising in the longer term. Failure in the early period is predominantly from dislocation, fracture (from intraoperative events), and infection; the middle period from a wide range of causes; and the late period predominantly from aseptic loosening and wear. Fixation and bearing surface materials have an effect on which implants fail in each of these time periods. For example, uncemented implants are at a higher risk of both early postoperative fracture and subsidence. After consultation with a range of clinicians and methodologists and analysis of the NJR and the Swedish Hip Arthroplasty Register (SHAR), we set our cutoffs at 0 to 2 years for early first revision, 2 to 10 years for middle first revision, and 10 or more years for late first
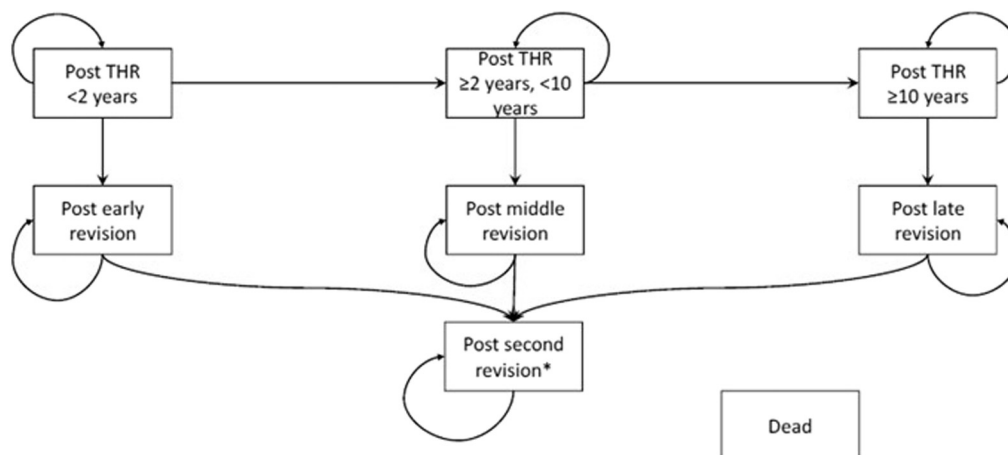

Figure 1 – Markov model structure—base-case analysis. *Patients in post–second revision state can experience further revisions but return to the same state thereafter. THR indicates total hip replacement.

revision (and considered sensitivity around these cutoffs, as further detailed). Clinical opinion also suggested that hazard of a second revision was higher for patients who had a first revision sooner after primary THR, which was also confirmed by NJR data.[2,21] We separately tracked cohorts with early, middle, and late first revisions using Markov tunnel states. Patients who had 2 or more revisions were tracked in a single "post–second revision" health state. Patients could die at any stage, because of postoperative mortality or all-cause mortality.

Data

Evidence sources for the model inputs are presented in Table 1 and described herein.

Estimating the hazard of revision surgery

We conducted a network meta-analysis of randomized controlled trials (RCTs) comparing revision rates between implant combinations, but because of the small size of most studies, limited follow-up periods, and poor reporting, there was insufficient evidence on the hazard of revision to inform our model.[22] We instead used individual-patient observational data from the NJR, the largest national joint replacement cohort with 796 636 records of primary THR surgeries since 2003/2004.[2] The number of primary and revision surgeries and length of follow-up provided by the NJR are presented in Table 2. For longer term estimates (beyond NJR follow-up), we analyzed data from the SHAR, which has up to 25 years of follow-up on 359 579 primary THRs.[3]

In both registries, we defined revision surgery as the removal of failing implants and/or insertion of new components (see Appendix 3a in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013). The registries provided information on time to first revision, by age bracket (younger than 55, 55-64, 65-74, 75-84, and 85 years and older) and sex. To reflect the assumption that risk of revision varies with time from primary surgery, we estimated the hazard of first revision for 3 different time periods (early, middle, and late). We used a piecewise constant hazard model to estimate the baseline hazard of revision for patients using the reference implant for each period, and estimated hazard ratios of revision for all other implants, stratified by age and sex (see Appendix 3b in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013). This involved fitting separate functions to each of the 10 age and sex subgroups, with hazard ratios estimated for each of the 23 implants relative to the reference implant (small-head cemented metal-on-polythene implant). By assuming a piecewise constant hazard model with constant hazard ratios over the 3 time periods, it allowed certain implants, such as ceramic-on-polyethylene, to have a greater impact on late rather than early revisions (further details are provided in Appendix 3b in Supplemental Materials). Because our focus was on UK policy, we used the NJR data for the short- and medium-term periods (early and middle), where reliable estimates were observed. We calibrated estimates from SHAR to the NJR population where sufficient evidence was available from both (see Appendix 3c in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013). We then used these calibrated SHAR estimates to predict the longer term NJR estimates, and the shorter term estimates where NJR estimates were unreliable. The estimated probabilities are presented in Appendix 3d in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013.

We estimated the baseline hazard of second revision using NJR data for patients who had an early revision, and hazard ratios for patients who had middle and late revisions. Because of limited data on the hazard of second revision, we assumed the same rate across implant types and over time. A common hazard of subsequent revision (third or higher) was also estimated (Table 1).

Mortality

We assumed postoperative mortality (within 90 days of surgery). We assumed mortality rates were constant between implant combinations, but varied by age and sex, as per clinical advice. The NJR data were used to estimate 90-day mortality for primary THR, by age and sex (Table 1). The data on mortality after revision surgeries by age and sex were limited. To estimate postoperative mortality after revision surgery, we used a Bayesian multiparameter evidence synthesis model using aggregated data on revision surgery and information on primary THR (see Appendix 4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013).

We also applied all-cause mortality rates, stratified by age and sex, to all patients using UK data from the Office for National Statistics.[23]

Cost estimates

The model considered costs from the health and social care payer perspectives. We included the cost of the implant used in primary THR, but excluded the cost of primary THR surgery because we assumed these costs were common across implants; this assumption was tested in sensitivity analysis because surgery costs may vary by fixation method, for example. We excluded the cost of adverse events, such as stroke or heart attack, because there is no good-quality evidence to suggest that the risk of these medical complications vary significantly by implant, and mortality from these complications does not relate to implant choice.[24] Implant prices were obtained from the North Bristol NHS Trust and were comparable with average prices paid nationally.[25]

We included the cost of revision surgery and follow-up care after revision surgery. On the basis of clinical opinion, we weighted the published Department of Health national reference costs for revision surgery to estimate the average cost of revision surgery, which reflected complications and comorbidities, average length of stay, and average cost per excess bed day.[26] We assumed the same cost of revision for first and subsequent revision surgeries. We included published ambulatory care costs for the first 12 months postsurgery,[27] inflated to 2015/2016 prices using the Hospital and Community Health Services index (Table 1).[28]

All unit costs were expressed in sterling (£) and valued at 2015/2016 prices.

Quality-of-life estimates

We obtained quality-of-life data, or health utilities, from the UK Patient-Reported Outcome Measures (PROMs) data set for patients who had a THR in 2010/2011.[29] The PROMs data set recorded 3-level EuroQol 5-dimensional questionnaire data at 6 months after primary and revision surgeries for 32 577 patients older than 40 years, with complete data. We assumed the same utilities after first and subsequent revisions. Utilities were not stratified by implant type because improvements in patients' outcomes at 6 months postsurgery are comparable across implant types.[30] Utilities were stratified by age and sex for primary THR, and sex only for revision surgery (Table 1). The health utilities were combined with survival to estimate quality-adjusted life-years (QALYs).

Cost-Effectiveness Analysis

Base-case analysis

The base-case analysis compared the lifetime cost-effectiveness of 24 implant combinations for men and women younger than 55, 55 to 64, 65 to 74, 75 to 84, and 85 years and older in the United Kingdom. Estimated costs and QALYs were discounted at 3.5% per annum, as per the National Institute for Health and Care Excellence guidelines.[31] We calculated expected costs and QALYs per 1000 patients using a probabilistic analysis, which reflected parameter uncertainty

Table 1 – Model input parameters.

	Estimate	SE	Distribution	Source
Revision risks				
Probability of first revision	Appendix 3d	Appendix 3d	Normal	NJR/SHAR
Log hazard rates of second revision from				
Early first revision	−3.446	0.031	Normal	NJR
Middle first revision	−0.181	0.045	Normal	NJR
Late first revision	0.256	0.290	Normal	NJR
Log hazard rates of third revision				
3 or more revisions	−2.849	0.053	Normal	NJR
Mortality				
Log hazard rates of 90-d mortality after primary THR				
Men				
<55 y	−5.019	0.115	Normal	NJR
55-64 y	−4.691	0.075	Normal	NJR
65-74 y	−4.069	0.047	Normal	NJR
75-84 y	−3.156	0.037	Normal	NJR
>85 y	−2.041	0.056	Normal	NJR
Women				
<55 y	−4.922	0.110	Normal	NJR
55-64 y	−4.983	0.079	Normal	NJR
65-74 y	−4.559	0.049	Normal	NJR
75-84 y	−3.664	0.035	Normal	NJR
>85 y	−2.596	0.046	Normal	NJR
Log hazard rates of 90-d mortality after first revision*				
Men				
<55 y	−4.296	0.135	Normal	NJR
55-64 y	−3.967	0.103	Normal	NJR
65-74 y	−3.346	0.084	Normal	NJR
75-84 y	−2.433	0.079	Normal	NJR
>85 y	−1.317	0.089	Normal	NJR
Women				
<55 y	−4.199	0.129	Normal	NJR
55-64 y	−4.259	0.106	Normal	NJR
65-74 y	−3.835	0.086	Normal	NJR
75-84 y	−2.940	0.079	Normal	NJR
>85 y	−1.872	0.085	Normal	NJR
Log hazard rates of 90-d mortality after second or subsequent revision*				
Men				
<55 y	−4.306	0.252	Normal	NJR
55-64 y	−3.977	0.236	Normal	NJR
65-74 y	−3.356	0.228	Normal	NJR
75-84 y	−2.443	0.226	Normal	NJR
>85 y	−1.327	0.231	Normal	NJR
Women				
<55 y	−4.209	0.250	Normal	NJR
55-64 y	−4.269	0.237	Normal	NJR
65-74 y	−3.846	0.229	Normal	NJR
75-84 y	−2.950	0.227	Normal	NJR
>85 y	−1.882	0.229	Normal	NJR
Costs				
Implant costs†				
MoP cemented	£756.00	NA	Fixed	North Bristol Trust
MoP uncemented	£2047.00	NA	Fixed	North Bristol Trust
MoP hybrid	£1315.00	NA	Fixed	North Bristol Trust
MoP reverse hybrid	£1107.00	NA	Fixed	North Bristol Trust
MoM uncemented	£1924.00	NA	Fixed	North Bristol Trust
MoM hybrid	£1662.00	NA	Fixed	North Bristol Trust
CoP cemented	£1038.00	NA	Fixed	North Bristol Trust
CoP uncemented	£2386.00	NA	Fixed	North Bristol Trust
CoP hybrid	£1597.00	NA	Fixed	North Bristol Trust

Table 1 – continued

	Estimate	SE	Distribution	Source
CoP reverse hybrid	£1446.00	NA	Fixed	North Bristol Trust
CoC uncemented	£2262.00	NA	Fixed	North Bristol Trust
CoC hybrid	£1848.00	NA	Fixed	North Bristol Trust
Revision costs				
Revision THR[‡]	£8595.83	£1524.29	Normal	Department of Health[26]
12-mo ambulatory care costs after revision surgery[§]				
Outpatient	£305.18	£29.03	Normal	Edlin et al[27]
Primary/community	£54.18	£9.26	Normal	Edlin et al[27]
Aids and adaptations	£23.22	£5.53	Normal	Edlin et al[27]
Medication	£26.54	£5.67	Normal	Edlin et al[27]
Total resource use costs	£409.12			
Quality of life				
Utilities—PROMs[‖]				
Primary THR				
Men				
<55 y	0.736	0.018	Normal	UK Patient-Reported Outcome Measures[29]
55-64 y	0.767	0.007	Normal	UK Patient-Reported Outcome Measures[29]
65-74 y	0.762	0.004	Normal	UK Patient-Reported Outcome Measures[29]
75-84 y	0.790	0.003	Normal	UK Patient-Reported Outcome Measures[29]
>85 y	0.790	0.007	Normal	UK Patient-Reported Outcome Measures[29]
Women				
<55 y	0.720	0.013	Normal	UK Patient-Reported Outcome Measures[29]
55-64 y	0.742	0.006	Normal	UK Patient-Reported Outcome Measures[29]
65-74 y	0.769	0.003	Normal	UK Patient-Reported Outcome Measures[29]
75-84 y	0.747	0.003	Normal	UK Patient-Reported Outcome Measures[29]
85 y	0.710	0.005	Normal	UK Patient-Reported Outcome Measures[29]
Revision surgery				
Men	0.575	0.009	Normal	UK Patient-Reported Outcome Measures[29]
Women	0.553	0.007	Normal	UK Patient-Reported Outcome Measures[29]

CC, complications and comorbidities; CoC indicates ceramic-on-ceramic; CoP, ceramic-on-polyethylene; HRG, Healthcare Resource Group; MoM, metal-on-metal; MoP, metal-on-polyethylene; NA, not applicable; NJR, National Joint Registry; PROMs, patient-reported outcome measures; SE, standard error.

[*] Bayesian estimate (see Appendix 4 in Supplemental Materials).

[†] Implant prices did not vary by femoral head size.

[‡] The current HRG v.4 2014-2015 reference costs in the United Kingdom were used to estimate the cost of revision surgery, which reflects the average length of stay and average cost per excess bed day. HRGs describe varying levels of complications and comorbidities, which allowed us to model complete costs using a weighted average cost. We followed clinical opinion to assign a representative HRG code to revision surgery: HN81A-HN81E (complex, hip or knee procedures for nontrauma, with complications and comorbidities score 0-9+). We used information on the interquartile range to estimate the SE, assuming a normal distribution.

[§] We inflated the estimates to current prices (2015/2016) using the Hospital and Community Health Services index.

[‖] Assuming studied age bands.

in the sampled distributions (Table 1). Using Microsoft Excel software,[32] we simulated 10 000 iterations. We estimated cost-effectiveness using the mean incremental net monetary benefit (INMB) statistic for each implant compared with the reference implant, at National Institute for Health and Care Excellence's lower willingness-to-pay threshold of £20 000 per QALY gained.[31] The implant with the highest mean INMB reflected the most cost-effective implant in each subgroup. We illustrated the probability that implants were most cost-effective at varying willingness-to-pay thresholds using cost-effectiveness acceptability curves.

Sensitivity analyses
Our sensitivity analyses assessed the robustness of the results to changes in key parameters and assumptions.

In a sensitivity analysis scenario, we harmonized implant prices by setting them as equal (£0) to assess the extent that cost-effectiveness findings might be influenced by implant prices alone. Uncemented implants typically cost £1300 more than their cemented counterparts (Table 1), and clinical opinion suggests that

surgery time is shorter, saving approximately 20 minutes of theater time. Theater time has been valued at £15 per minute in a previous study.[33] Setting cemented and uncemented implant costs as equal is equivalent to saving, on average, 90 minutes of theater time at £15 per minute,[33] or 20 minutes at a higher cost of £65 per minute.

There is no strong evidence for our choice of time periods to define early, middle, and late periods for revision risks. We therefore assessed sensitivity to this key structural assumption by adjusting the time periods. In this scenario, we assumed 0 to 5 years for early first revision, 5 to 10 years for middle first revision, and 10 or more years for late first revision.

Results

Base-Case Findings
Table 3 ranks the top implant combinations by their expected mean INMB for each age and sex subgroup. Complete base-case

Table 2 – Number of primary and revision surgeries and length of follow-up provided by the National Joint Registry.					
Implant	Number of primaries	Number of revisions	Date of earliest primary	Date of latest primary	Length of follow-up (y)
MoP Cem S	243 292	3 951	April 1, 2003	December 1, 2015	12.7
MoP Cem L	3 742	52	December 2, 2003	December 1, 2015	12.0
CoP Cem S	27 747	324	April 1, 2003	December 1, 2015	12.7
CoP Cem L	797	15	January 12, 2005	December 1, 2015	10.9
MoP Uncem S	94 709	2 135	April 1, 2003	December 1, 2015	12.7
MoP Uncem L	23 954	487	September 18, 2003	December 1, 2015	12.2
MoM Uncem S	2 075	159	April 1, 2003	January 11, 2013	9.8
MoM Uncem L	26 542	3 687	April 8, 2003	November 7, 2013	10.6
CoP Uncem S	39 936	746	April 1, 2003	December 1, 2015	12.7
CoP Uncem L	13 147	198	March 14, 2005	December 1, 2015	10.7
CoC Uncem S	39 822	1 007	April 2, 2003	December 1, 2015	12.7
CoC Uncem L	64 021	1 221	April 9, 2003	December 1, 2015	12.7
MoP Hyb S	70 002	1 254	April 1, 2003	December 1, 2015	12.7
MoP Hyb L	21 046	303	April 7, 2003	December 1, 2015	12.7
MoM Hyb S	509	42	April 2, 2003	February 27, 2012	8.9
MoM Hyb L	1 637	227	April 8, 2003	August 28, 2012	9.4
CoP Hyb S	17 419	192	April 2, 2003	December 1, 2015	12.7
CoP Hyb L	10 105	97	January 22, 2005	December 1, 2015	10.9
CoC Hyb S	15 908	244	April 3, 2003	December 1, 2015	12.7
CoC Hyb L	5 547	94	June 20, 2003	December 1, 2015	12.5
MoP RevHyb S	13 174	223	April 2, 2003	December 1, 2015	12.7
MoP RevHyb L	239	7	January 13, 2005	December 1, 2015	10.9
CoP RevHyb S	6 086	98	April 1, 2003	December 1, 2015	12.7
CoP RevHyb L	201	5	September 21, 2007	December 1, 2015	8.2

Source: National Joint Registry (unpublished data, 2016).
Cem indicates cemented; CoC, ceramic-on-ceramic; CoP, ceramic-on-polyethylene; Hyb, hybrid; L, large; MoM, metal-on-metal; MoP, metal-on-polyethylene; RevHyb, reverse hybrid; S, small; Uncem, uncemented.

findings are provided in Appendix 5, and the cost-effectiveness acceptability curves are presented in Appendix 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.013. Small-head cemented ceramic-on-polyethylene implant had the highest expected mean INMB for men and women younger than 65 years (Table 3). This result was uncertain and driven by imprecise revision rate estimates, with low likelihood of being the most cost-effective implant. For adults aged 55 to 64 years, for example, the mean INMB was £514 (95% confidence interval [CI] −£313 to £1807) for men and £104 (95% CI −£729 to £625) for women; the probability that small-head cemented ceramic-on-polyethylene implant was the most cost-effective choice in these subgroups was less than 50%. Despite higher implant prices, the lower risk of revision in these patient groups (see Appendix 3d in Supplemental Materials) led to lower average lifetime costs and higher QALY gains compared with the reference implant. Uncemented, hybrid, reverse hybrid, and other bearing surface combinations performed poorly in these age groups, partly because of higher implant costs, but also because of poorer revision rates.

In older age categories, the small-head cemented metal-on-polyethylene implant combination (reference implant) consistently displayed lower implant and lifetime costs, low revision rates, and the same or higher QALY gains than all other implant combinations. The probability that the reference implant was the most cost-effective implant combination was high, with more than 80% probability of being the most cost-effective choice for adults older than 75 years. All alternative implant combinations, including implants with large head sizes, performed poorly, with negative mean INMBs (due to higher implant costs) or higher revision rates. Across all subgroups, large-head implant combinations were not cost-effective.

Sensitivity Analysis Findings

When implant prices were harmonized, allowing us to assess the effect of implant prices and surgery costs on cost-effectiveness findings, differences in lifetime costs between first- and second-best implants were often minor. As such, all findings were more uncertain, and the probability that any implant was the most cost-effective implant was much lower than the base-case analysis (Table 4; see Appendix 5 in Supplemental Materials). Hybrid and uncemented ceramic implants became more cost-effective, rising to the top 3 positions compared with the base-case analysis. Nevertheless, harmonizing implant prices did not affect the base-case findings for men, although in women aged 55 to 64 years, small-head hybrid ceramic-on-ceramic implant combination was now preferred to small-head cemented ceramic-on-polyethylene implant combination (mean INMB = £478 [95% CI −£1006 to £1131]). The uncertainty observed in the newer implant types suggested that even though they were designed to reduce revision rates,[34] this has not been evidenced in registry data.

The base-case findings were robust to the change in the time periods for revision risks after primary THR (see Appendix 5 in Supplemental Materials).

Discussion

In the context of previous cost-effectiveness evidence, our findings are novel. Pulikottil-Jacob et al[11] used a previous economic model[9] to compare 5 commonly used implant combinations in the United Kingdom. They used NJR data to estimate the risk of revision and did not account for timing of first and subsequent revisions from primary THR. The authors also found that cemented metal-on-polyethylene implant was cost-effective with increased

Sex	Age (y)	Top implants	Cost (95% CI)	QALYs (95% CI)	Mean INMB (95% CI)*	Probability most cost-effective*
Table 3 – Top implant combinations by age and sex, ranked by mean INMB (base case).						
Men	<55	CoP Cem S	£2528 (£1588 to £4797)	14.10 (13.84 to 14.35)	£1163 (−£1147 to £3356)	0.222
		MoP Cem S	£3284 (£2140 to £4983)	14.08 (13.82 to 14.33)	£0	0.002
		CoC Uncem S	£4226 (£3150 to £6339)	14.08 (13.83 to 14.34)	−£754 (−£2701 to £1111)	0.000
	55-64	CoP Cem S	£1576 (£1221 to £2374)	10.73 (10.66 to 10.80)	£514 (−£313 to £1807)	0.477
		MoP Cem S	£1826 (£1247 to £3144)	10.72 (10.64 to 10.79)	£0	0.033
		MoP Hyb S	£2409 (£1814 to £3567)	10.72 (10.64 to 10.79)	−£577 (−£1102 to −£33)	0.000
	65-74	MoP Cem S	£1300 (£1112 to £1510)	7.99 (7.94 to 8.04)	£0	0.399
		CoP Cem S	£1648 (£1286 to £2423)	7.99 (7.93 to 8.04)	−£358 (−£1385 to £117)	0.054
		MoP Hyb S	£1941 (£1686 to £2324)	7.98 (7.93 to 8.04)	−£673 (−£1079 to −£438)	0.000
	75-84	MoP Cem S	£986 (£907 to £1071)	5.09 (5.05 to 5.14)	£0	0.882
		CoP Cem S	£1333 (£1151 to £1842)	5.09 (5.04 to 5.14)	−£370 (−£1103 to −£115)	0.000
		MoP Hyb S	£1676 (£1518 to £1954)	5.09 (5.04 to 5.13)	−£755 (−£1087 to −£604)	0.000
	>85	MoP Cem S	£867 (£826 to £916)	2.43 (2.37 to 2.50)	£0	0.901
		CoP Cem S	£1197 (£1064 to £1630)	2.43 (2.37 to 2.50)	−£365 (−£1111 to −£133)	0.000
		MoP Hyb S	£1440 (£1370 to £1562)	2.43 (2.37 to 2.50)	−£575 (−£734 to −£475)	0.000
Women	<55	CoP Cem S	£1822 (£1427 to £2596)	14.48 (14.29 to 14.67)	£823 (£10 to £2140)	0.499
		MoP Cem S	£2374 (£1635 to £3623)	14.47 (14.28 to 14.66)	£0	0.006
		MoP Hyb S	£2749 (£2058 to £3928)	14.47 (14.28 to 14.66)	−£351 (−£1150 to £520)	0.000
	55-64	CoP Cem S	£1673 (£1324 to £2513)	11.43 (11.36 to 11.49)	£104 (−£729 to £625)	0.281
		MoP Cem S	£1692 (£1344 to £2118)	11.42 (11.36 to 11.49)	£0	0.085
		MoP Hyb S	£2033 (£1734 to £2455)	11.43 (11.36 to 11.49)	−£296 (−£582 to £30)	0.001
	65-74	MoP Cem S	£1210 (£1052 to £1380)	8.66 (8.61 to 8.70)	£0	0.838
		CoP Cem S	£1452 (£1233 to £1982)	8.66 (8.61 to 8.70)	−£218 (−£746 to £14)	0.031
		MoP Hyb S	£1973 (£1704 to £2361)	8.66 (8.61 to 8.70)	−£778 (−£1103 to −£596)	0.000
	75-84	MoP Cem S	£940 (£877 to £1007)	5.51 (5.47 to 5.55)	£0	0.935
		CoP Cem S	£1319 (£1148 to £1870)	5.51 (5.47 to 5.55)	−£369 (−£879 to −£211)	0.000
		MoP Hyb S	£1594 (£1478 to £1804)	5.51 (5.47 to 5.55)	−£660 (−£831 to −£587)	0.000
	>85	MoP Cem S	£840 (£810 to £874)	2.75 (2.70 to 2.79)	£0	0.990
		CoP Cem S	£1191 (£1067 to £1530)	2.75 (2.71 to 2.79)	−£344 (−£687 to −£220)	0.000
		MoP Cem L	£1433 (£900 to £2200)	2.75 (2.71 to 2.80)	−£498 (−£1219 to −£66)	0.002

Cem indicates cemented; CI, confidence interval; CoC, ceramic-on-ceramic; CoP, ceramic-on-polyethylene; Hyb, hybrid; INMB, incremental net monetary benefit; L, large; MoP, metal-on-polyethylene; QALY, quality-adjusted life-year; RevHyb, reverse hybrid; S, small; Uncem, uncemented.

* At £20 000 willingness-to-pay threshold.

age, whereas cemented ceramic-on-polyethylene was favorable in younger adults, aged 60 years. Clarke et al[10] found that cemented ceramic-on-polyethylene was favorable in young adults when comparing 5 similar implant combinations with hip resurfacing in adults aged 40, 50, and 60 years in the United Kingdom. Although both studies are consistent with our findings, they were limited in the number of implants compared. They used only NJR data to estimate the risk of revision and extrapolated these data to provide longer term estimates. Our study exceeded these analyses by incorporating reliable long-term estimates of revision risk from SHAR. We also examined implant head size and found evidence in favor of small-head implant sizes.

Our results differed from those reported by Pennington et al[15] who found that hybrid prostheses were most likely to be cost-effective in adults aged 60, 70, and 80 years in the United Kingdom, with the exception of women aged 80 years for whom cemented prostheses were cost-effective. Although this model[15] used NJR and Hospital Episode Statistics data to estimate the hazard of first revision, it did not distinguish between bearing surface combination or implant head size. Pennington et al[15] also used prosthesis-specific utility estimates, which returned higher utility gains for hybrid prostheses than did cemented and uncemented prostheses. We used the same utility estimates for primary THR, irrespective of the implant combination, because we did not consider implant type to affect

quality of life beyond the first 6 months of surgery, as evidenced elsewhere.[30]

Previous models for the Italian population also focused on identifying the most cost-effective fixation technique. Di Tanna et al[13] showed that uncemented implants were cost-effective compared with hybrid prostheses, whereas Marinelli et al[14] found that cemented prostheses were less costly than uncemented prostheses, but also less effective. These studies were limited by their use of regional registry data in Italy, which had fewer than 10 years follow-up on less than 50 000 patients. We found that cemented prostheses were at least as effective as uncemented prostheses, and it is their much lower price that renders them cost-effective options. In US[35] and Canadian[36] studies, THR implants were compared with hip resurfacing, with conflicting results. We did not consider hip resurfacing in our analysis because the method is declining in clinical use in the United Kingdom (now <1% of hip replacements)[2] and is not recommended in women and men who do not have very large native femoral heads.[37]

We acknowledge that there are limitations associated with this work. We used a piecewise constant hazard model to estimate the hazard of revision, which was often uncertain. We considered alternative parametric functions including a Weibull model and structured model that combined information on bearing surface, fixation technique, and head size. Ultimately, the

Sex	Age (y)	Top implants	Base-case INMB ranking	Cost (95% CI)	QALYs (95% CI)	Mean INMB (95% CI)*	Probability most cost-effective*
Table 4 – Top implant combinations by age and sex, ranked by mean INMB (sensitivity analysis).							
Men	<55	CoP Cem S	1	£1487 (£548 to £3661)	14.10 (13.85 to 14.35)	£1419 (−£877 to £3542)	0.039
		CoC Uncem S	3	£1966 (£893 to £4111)	14.08 (13.83 to 14.34)	£718 (−£1273 to £2570)	0.000
		MoP Cem S	2	£2505 (£1358 to £4203)	14.08 (13.83 to 14.33)	£0	0.000
	55-64†	CoP Cem S	1	£536 (£185 to £1349)	10.73 (10.66 to 10.8)	£794 (−£53 to £2058)	0.142
		CoC Hyb S	4	£792 (£213 to £2422)	10.73 (10.65 to 10.80)	£445 (−£1547 to £1853)	0.066
		CoP Uncem S	8	£1047 (£453 to £2149)	10.72 (10.64 to 10.79)	£64 (−£756 to £886)	0.000
	65-74	MoP Cem S	1	£543 (£352 to £749)	7.99 (7.94 to 8.04)	£0	0.000
		CoP Cem S	2	£609 (£249 to £1372)	7.99 (7.93 to 8.04)	−£75 (−£1074 to £399)	0.009
		CoC Uncem S	6	£603 (£328 to £1159)	7.99 (7.93 to 8.03)	−£75 (−£778 to £245)	0.000
	75-84	MoP Cem S	1	£229 (£151 to £313)	5.09 (5.05 to 5.14)	£0	0.031
		CoP Cem S	2	£294 (£110 to £807)	5.09 (5.04 to 5.14)	−£88 (−£811 to £164)	0.112
		MoP Hyb S	3	£360 (£203 to £632)	5.09 (5.04 to 5.13)	−£196 (−£535 to −£42)	0.000
	>85	MoP Cem S	1	£111 (£69 to £161)	2.43 (2.37 to 2.5)	£0	0.035
		MoP Hyb S	3	£127 (£55 to £250)	2.43 (2.37 to 2.5)	−£19 (−£187 to £84)	0.051
		CoP Cem S	2	£159 (£27 to £610)	2.43 (2.36 to 2.5)	−£83 (−£881 to £148)	0.115
Women	<55‡	CoP Cem S	1	£785 (£381 to £1584)	14.48 (14.30 to 14.67)	£1109 (£293 to £2457)	0.127
		CoC Hyb S	4	£1269 (£371 to £3914)	14.48 (14.29 to 14.67)	£576 (−£2201 to £2056)	0.107
		CoP Uncem L	7	£1478 (£459 to £3835)	14.48 (14.28 to 14.66)	£256 (−£2145 to £1690)	0.038
	55-64§	CoC Hyb S	4	£561 (£209 to £1962)	11.43 (11.36 to 11.49)	£478 (−£1006 to £1131)	0.175
		CoP Cem S	1	£635 (£285 to £1481)	11.43 (11.36 to 11.49)	£381 (−£449 to £896)	0.036
		MoP Hyb S	3	£715 (£416 to £1139)	11.43 (11.36 to 11.49)	£262 (−£25 to £590)	0.001
	65-74	CoP Cem S	2	£413 (£194 to £926)	8.66 (8.61 to 8.70)	£65 (−£438 to £292)	0.086
		MoP Cem S	1	£453 (£291 to £621)	8.66 (8.61 to 8.70)	£0	0.000
		CoP Uncem S	6	£522 (£301 to £886)	8.66 (8.61 to 8.70)	−£96 (−£414 to £76)	0.000
	75-84	MoP Cem S	1	£184 (£122 to £251)	5.51 (5.47 to 5.55)	£0	0.058
		CoP Cem S	2	£276 (£110 to £798)	5.51 (5.47 to 5.55)	−£82 (−£567 to £74)	0.049
		MoP Hyb S	3	£279 (£163 to £491)	5.51 (5.47 to 5.55)	−£100 (−£274 to −£27)	0.000
	>85	MoP Cem S	1	£85 (£54 to £119)	2.75 (2.71 to 2.79)	£0	0.184
		MoP Hyb S	5	£115 (£63 to £191)	2.75 (2.71 to 2.79)	−£35 (−£98 to £8)	0.015
		CoP Cem S	2	£156 (£28 to £513)	2.75 (2.71 to 2.79)	−£65 (−£422 to £63)	0.126

Cem indicates cemented; CI, confidence interval; CoC, ceramic-on-ceramic; CoP, ceramic-on-polyethylene; Hyb, hybrid; INMB, incremental net monetary benefit; L, large; MoP, metal-on-polyethylene; QALY, quality-adjusted life-year; RevHyb, reverse hybrid; S, small; Uncem, uncemented.

* At £20 000 willingness-to-pay threshold.

† Men 55-64 y: reference implant cost, £1067 (£481-£2407); QALYs, 10.72 (10.64-10.79).

‡ Women <55 y: reference implant cost, £1621 (£866-£2864); QALYs, 14.47 (14.28-14.66).

§ Women 55-64 y: reference implant cost, £933 (£582-£1369); QALYs, 11.42 (11.36-11.49).

piecewise constant hazard model was either the best fit for the data or yielded a similar level of precision of revision risk. Established in 2002, with data collection commencing 2003/2004, the NJR had limited follow-up data to predict lifetime hazards of revision, particularly for newer implants. SHAR collects information on polyethylene implants, whereas the NJR does not classify polyethylene types. It is possible that different types of polyethylene, for example, newer highly cross-linked (HCL) polyethylene, would lead to different implant survival profiles. In previous work, we performed a systematic review and synthesis of RCT evidence, which included comparisons between HCL and non-HCL implants, and did not find an effect for newer polyethylene types.[22] In the absence of reliable or precise estimates from RCTs, we were required to rely on joint registries. Such real-world evidence[22] has the advantage of large sample sizes, external validity, and longer term follow-up. A general difficulty with using observational data is selection bias. To attempt to mitigate bias and obtain as robust estimates as possible, we stratified our analyses by known predictors of revision risk, such as implant combination, patients' age and sex, and time from first revision. Nevertheless, it is possible that surgeons select patients to receive

different implant combinations on the basis of other factors, such as their surgical training or skills, preferences for implant types or bands, patients' bone anatomy or comorbidities, or hospital procurement decisions and costs. These factors are not routinely captured in joint registries, and we were therefore unable to adjust for these factors in our analyses. Although SHAR provided long-term evidence on implant survival, a limitation associated with using SHAR data was that 90% of prostheses were fixed with cement,[38] leaving little information on hybrid/reverse hybrid and uncemented prostheses. As would be expected, this uncertainty propagated into the cost-effectiveness results. We estimated the risk of first revision stratified by implant type, patients' age and sex, and time from primary surgery. There were insufficient data in both registries to stratify the risk of subsequent revisions by all these factors, and it was necessary to assume the same risk across all implants, ages, and sexes for subsequent revisions. Limited availability of data for more recent or less common implant types led to imprecise hazard ratios for some implant combinations (as presented in Table 2). These account for the uncertainty in our results, particularly for younger patients. Although we aimed to provide a comprehensive analysis of all possible implant

combinations using the most up-to-date data available, there might not be enough evidence yet to fully assess these implant combinations. Future research should assess the longer term benefits associated with newer implant combinations. Implant costs were assumed fixed, but likely vary between healthcare providers because of locally negotiated contracts with manufacturers. Finally, although we assumed the same utility scores across implant combinations, as in the studies by Pulikottil-Jacob et al[11] and Clarke et al,[10] it is possible some differences exist. Pennington et al,[15] using observational PROMs data, found a modest association between quality-of-life scores at 6 months postsurgery and fixation techniques. Nevertheless, when comparing across fixation techniques with optimal and suboptimal bearing surface combinations and femoral head sizes, Jameson et al[30] found no difference in utility scores at 6 months postsurgery using the same data set. Their analysis more closely resembled ours (i.e., by comparing bearing surface combination, fixation technique, and head size), and so we assumed no difference in utility scores by implant types and instead stratified utility estimates by age and sex. Further research is needed to determine whether utility scores differ by implant combinations because potential differences may have an impact on cost-effectiveness findings.

Our findings suggest that for older patients, the small-head cemented metal-on-polyethylene implant is the most likely cost-effective choice in primary THR. This is the cheapest and most common implant combination used in the United Kingdom, used in 30% of patients with THR since 2003/2004.[2] Metal-on-polyethylene implants also remain the most commonly used bearing surface material in Sweden, Norway, Australia, and the United States, although in some countries, such as the United States and Australia, they are more commonly fixed without cement.[3,4,39] Ceramic and uncemented or hybrid combinations are increasingly used in younger adults worldwide.[2-4] Our findings indicate that cemented hip implants would be the cost-effective fixation option, regardless of bearing size and surface combination.

Our study can influence clinical practice and commissioning of services. We, however, highlight the need for rigorous RCTs with long-term follow-up before costly new implants are widely adopted in practice.

Conclusions

We found that the older the patient group, the more likely that the small-head cemented metal-on-polyethylene implant is the cost-effective choice. This implant has more than 80% probability of being the most cost-effective choice for men and women aged 65 years and older. The small-head cemented metal-on-polyethylene implant is the cheapest implant combination available, at about £750, and displays some of the lowest risks of revision surgery for older men and women. For patients younger than 65 years, the small-head cemented ceramic-on-polyethylene implant is cost-effective, but these results are more uncertain, mainly because of more imprecise estimates of revision risks. The key drivers of the analysis were revision costs and revision risks. In younger adults, the lower risk of revision after small-head cemented ceramic-on-polyethylene hip replacements led to lower average lifetime costs and higher QALY gains compared with the most commonly used implant. Similarly, in older adults, small-head cemented metal-on-polyethylene hip replacements consistently displayed lower lifetime costs and the same or higher QALY gains because of lower implant costs and more favorable revision rates.

Our findings are based on the best available current evidence. We analyzed more than 1 million individual-patient records across 2 national joint registries in the United Kingdom and Sweden. We developed a tunnel-state Markov model, informed by a team of hip surgeons, patients, and previous economic models. Our model's structure was flexible enough to capture the impact of age, sex, and time since initial THR on the hazards and hazard ratios of revision, as well as the clinical reality that patients who were revised soon after primary THR were at an increased risk of having second and subsequent revisions.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2018.08.013.

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