

Original citation:

Pulikottil-Jacob, Ruth, Connock, Martin, Kandala, Ngianga-Bakwin, Mistry, Hema, Grove, Amy L., Freeman, Karoline, Costa, Matthew L., Sutcliffe, Paul and Clarke, Aileen. (2016) Has metal-on-metal resurfacing been a cost-effective intervention for health care providers? - a registry based study. PLoS One, 11 (11). e0165021.

Permanent WRAP URL:

http://wrap.warwick.ac.uk/82135

Copyright and reuse:

The Warwick Research Archive Portal (WRAP) makes this work of researchers of the University of Warwick available open access under the following conditions.

This article is made available under the Creative Commons Attribution 4.0 International license (CC BY 4.0) and may be reused according to the conditions of the license. For more details see: <u>http://creativecommons.org/licenses/by/4.0/</u>

A note on versions:

The version presented in WRAP is the published version, or, version of record, and may be cited as it appears here.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk



Citation: Pulikottil-Jacob R, Connock M, Kandala N-B, Mistry H, Grove A, Freeman K, et al. (2016) Has Metal-On-Metal Resurfacing Been a Cost-Effective Intervention for Health Care Providers?— A Registry Based Study. PLoS ONE 11(11): e0165021. doi:10.1371/journal.pone.0165021

Editor: Ara Nazarian, Harvard Medical School/ BIDMC, UNITED STATES

Received: May 13, 2016

Accepted: October 5, 2016

Published: November 1, 2016

Copyright: © 2016 Pulikottil-Jacob et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: This project was funded by the Health Technology Assessment programme (project number 11/118). Further information available at: http://www.nets.nihr.ac.uk/programmes/hta. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. **RESEARCH ARTICLE**

Has Metal-On-Metal Resurfacing Been a Cost-Effective Intervention for Health Care Providers?—A Registry Based Study

Ruth Pulikottil-Jacob¹, Martin Connock¹, Ngianga-Bakwin Kandala^{1,2}, Hema Mistry¹, Amy Grove¹, Karoline Freeman¹, Matthew Costa¹, Paul Sutcliffe¹, Aileen Clarke¹*

1 Warwick Evidence, Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, United Kingdom, 2 Northumbria University, Department of Mathematics, Physics and Electrical Engineering, Faculty of Engineering and Environment, Newcastle upon Tyne, United Kingdom

* Aileen.Clarke@warwick.ac.uk

Abstract

Background

Total hip replacement for end stage arthritis of the hip is currently the most common elective surgical procedure. In 2007 about 7.5% of UK implants were metal-on-metal joint resurfacing (MoM RS) procedures. Due to poor revision performance and concerns about metal debris, the use of RS had declined by 2012 to about a 1% share of UK hip procedures. This study estimated the lifetime cost-effectiveness of metal-on-metal resurfacing (RS) procedures versus commonly employed total hip replacement (THR) methods.

Methodology/Principal Findings

We performed a cost-utility analysis using a well-established multi-state semi-Markov model from an NHS and personal and social services perspective. We used individual patient data (IPD) from the National Joint Registry (NJR) for England and Wales on RS and THR surgery for osteoarthritis recorded from April 2003 to December 2012. We used flexible parametric modelling of NJR RS data to guide identification of patient subgroups and RS devices which delivered revision rates within the NICE 5% revision rate benchmark at 10 years. RS procedures overall have an estimated revision rate of 13% at 10 years, compared to <4% for most THR devices. New NICE guidance now recommends a revision rate benchmark of <5% at 10 years. 60% of RS implants in men and 2% in women were predicted to be within the revision benchmark. RS devices satisfying the 5% benchmark were unlikely to be cost-effective compared to THR at a standard UK willingness to pay of £20,000 per quality-adjusted life-year. However, the probability of cost effectiveness was sensitive to small changes in the costs of devices or in quality of life or revision rate estimates.

Conclusion/Significance

Our results imply that in most cases RS has not been a cost-effective resource and should probably not be adopted by decision makers concerned with the cost effectiveness of hip



Competing Interests: The authors have declared that no competing interests exist.

replacement, or by patients concerned about the likelihood of revision, regardless of patient age or gender.

Introduction

Hip replacement is a common elective surgical procedure. If an estimated 80,000 replacements are conducted annually at an average cost of £8,500 per procedure, this would cost the UK NHS approximately £680 million per annum [1, 2]. The overall post-operative costs are approximately five times greater than this due to hospital stay and post-operative support [3]. Approximately 80,000 procedures are performed each year and, assuming lifetime revision rates are about 5% and the average cost of revision surgery is approximately £17,000, prosthesis failure adds a further £68 million over subsequent years [4]. Total hip replacement is currently the most commonly used surgical intervention for end stage arthritis of the hip. In 2007 about 7.5% of UK implants were metal-on-metal joint resurfacing (MoM RS) procedures [5], but due to high revision rates and concerns about metal debris, the use of RS declined to about 1% of UK hip procedures in 2012. The DePuy Articular Surface Replacement (ASR) device (representing about 9% of UK RS) was recently withdrawn after unacceptably high revision rates were observed, and in 2015 Smith and Nephew voluntarily withdrew some Birmingham Hip devices (the most widely used RS device in the UK) on the grounds that in certain populations (e.g. women) devices with a relatively small head size failed to reach the NICE benchmark for revision. Similar concerns have led to the near abandonment of metal-on-metal THRs [6–9]. However some people still advocate for RS in the young and active, whose primary implant is expected to need replacement over their lifetime [1,10]. In particular, it has been argued that there may be a role for the best RS devices in highly selected patients such as active young men with a large femoral head size [1,11].

Updated NICE guidance for hip replacement recommends a 10 year revision rate benchmark of <5% [12]. The 11th National Joint Registry (NJR) report (2014) estimated that in the past the RS 10 year revision rate has been about 13% [5]. This compares unfavourably with 10-year revision rates for frequently used THR devices, which are less than 4% and indicates that, as a class, RS is unlikely to have been cost-effective relative to THR [12–14]. RS devices produced by at least sixteen different manufacturers have been used in the UK and they differ with respect to revision rate [5]. It remains an open question whether implantation of any RS devices or the best RS devices in highly selected patients such as active young men with a large femoral head size can be cost-effective.

We use data from the National Joint Registry for England and Wales to identify RS devicepatient combinations likely to satisfy the NICE benchmark, and to address the question of whether past use of any RS devices, even those within the 5% revision rate at 10 years, has represented a cost-effective use of NHS resources.

Methods

Prosthesis categories

The National Joint Registry (NJR) for England and Wales supplied individual patient data (IPD) for RS and THR surgery for osteoarthritis, recorded from April 2003 to December 2012. Following the approach of others [5,12,13], we used flexible parametric modelling (Lambert and Royston 2009) [15] of NJR RS data to guide identification of patient subgroups and RS devices which delivered revision rates within the NICE 5% revision rate benchmark at 10 years.

Variables investigated included the following: device manufacturer, RS head size, age at primary intervention, American Society of Anaesthetologists (ASA) grade, and sex Patients were coded in the NJR as: ASA grade 1 ("*normal healthy individuals*"); ASA 2 ("*mild systemic disease that does not limit activity*"); or ASA grades 3 to 5 ("*severe systemic disease that limits activity but is not incapacitating*", "*incapacitating systemic disease which is constantly life threatening*", and "*moribund, not expected to survive 24 hours with or without surgery*"). Patients who had a primary indication for surgery other than osteoarthritis were excluded along with those graded ASA 3, ASA4 and ASA5 (who represented only 3% of RS recipients), and those receving the DePuy RS device and data were then stratified according to sex. . .Devices produced by six of the sixteen manufaturers which contributed 96% of relevant implants were included, comprising Birmingham Hip, Biomet, Centerpulse, Corin, Finsbury and Wright UK. Where modelling indicated that patients and devices had satisfied the NICE benchmark, we pooled device and patient subgroups by manufacturer with the aim of estimating cost-effectiveness relative to THRs that satisfy the NICE benchmark.

Multiple manufacturers providing about 150 different THR components are listed in the NJR. The most commonly used THR devices (covering 62% of all THRs) were selected for potential comparison with RS on the basis of frequency of use of components (cup component group; cup component type; cup composition; cup fixation; cup implant type; head component type; head component type; liner composition; stem component type; stem fixation; stem implant type) [12,16]. S1 Table summarises the characteristics of five frequently used THR devices which differ according to bearing surfaces, and/or mode of fixation. We have previously reported that all these devices have shown revision rates within the NICE benchmark [12].

Economic model

We used the well-established simple multi-state semi-Markov model developed by Fitzpatrick *et al.* (Fig 1) [17]; this model has been used repeatedly by others [14,18,19]. In the model, patients occupy one of four mutually exclusive health states: (1) successful primary THR or RS surgery (2) revision THR surgery (patients can move into this state more than once but stay in this health state for one annual cycle only); (3) successful revision THR surgery; (4) dead (patients may enter this state both due to operative mortality or due to death from other causes). We assumed that if the initial RS or THR required revision, the patient would be revised with a THR prosthesis.

Model inputs included the following: annual transition probabilities for time to revision and death, costs, and utilities of health states. The model cycle length was one year. We explored multiple parametric distributions to model lifetime revision rates using individual patient data from the NJR. The transition probability to death after cycle one was based on data from the Office for National Statistics for appropriately aged men and women [20]. An NHS and Social Services perspective was chosen for costs and a 3.5% annual discount rate was applied to both costs and health outcomes [21] All costs are reported in 2014 British Pounds. Table 1 summarises the model input parameters and sources [4,22–26].

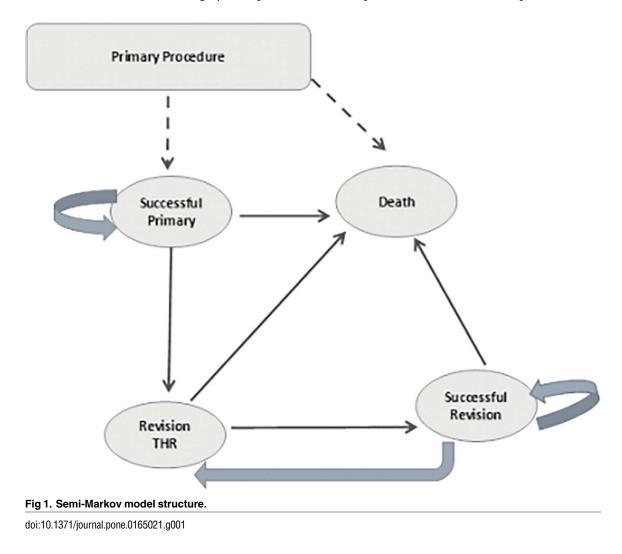
The model was run probabilistically, with 1,000 iterations using standard distributions for input parameters in order to capture uncertainties [27]. Time horizons were 10 years and lifetime (to 100 years of age). Model outputs were mean quality-adjusted life years gained (QALYs), mean costs accumulated, the estimated probability that a particular prosthesis is cost-effective at a willingness to pay threshold of £20,000/QALY, and the incremental cost-effectiveness ratio (ICER in terms of cost/QALY) in scenarios where RS accumulated more QALYs at greater cost than THR.

Health outcomes

Health outcomes were measured in QALYs [27]. Quality of life data were obtained from the patient reported outcome measures (PROMS) database for patients who had received a hip replacement between January 2009 and December 2012 [24]. EQ-5D scores for successful primary health and revision health states were adjusted for age and sex differences. The age-related utilities were assumed to be the same for the comparison of RS with THR (see previous publication for further information on PROMS analysis) [16]. In a sensitivity analysis we used the utility difference of RS versus THR reported by Edlin *et al.* (2012), and applied this for the first two years post-surgery [26]. (see S2 Table).

Resource use and cost estimates

The NHS Supply Chain provided June 2013 costs for components of each prosthesis type and the total cost of each prosthesis (see previous publication for further information on THR prosthesis cost [16] and <u>S3 Table</u> for cost of RS prosthesis). We assumed the costs to be the same for the Birmingham Hip, Biomet and Finsbury prostheses due to lack of cost data for each individual prosthesis. The costs of a successful primary THR, RS, revision procedure and successful revision procedure were taken from the literature [4,25,26]. Costs of primary and revision THRs included surgery costs, prosthesis costs, hospital ward costs, and follow-up costs



[4,25,26]. The cost of a successful revision procedure (£16,517) and cost of post-revision follow up (£394) were assumed to be the same for both RS and THR. The projected Health Services Cost Index (HSCI) was used to inflate costs to current prices (2014) [28].

Sensitivity analyses

The base case utilized probabilistic sensitivity analysis to assess uncertainty in the model. Scenario analyses included the following: (a) changing the parametric distribution used to model

| Table 1. | Model inputs | for the base case a | analysis of cos | t-effectiveness. |
|----------|--------------|---------------------|-----------------|------------------|
|----------|--------------|---------------------|-----------------|------------------|

| Transition probabilities | | | | | |
|--------------------------------------|--------------|--------|---------------------------------------|--------------------------------------|---------------------------------------|
| Health state | Mean value | SE | | | Source |
| Surgical mortality* | 0.0050 | 0.001 | | | NJR annual report ²² |
| Risk of re-revision | 0.0518 | N/A | | | Pennington <i>et al</i> ³⁰ |
| Utility inputs | | | | | |
| Utilities—Male | Mean value | SE | Beta distribution Parameter α | Beta distribution Parameter β | Source |
| Age 40–50 | 0.736 | 0.0179 | 443 | 159 | PROMS ²⁴ |
| Age 50–60 | 0.767 | 0.0066 | 3133 | 952 | |
| Age 60–70 | 0.762 | 0.0038 | 9112 | 2393 | |
| Revision surgery | 0.575 | 0.009 | 1496 | 1106 | - |
| Utilities—Female | | | | | |
| Age 40–50 | 0.720 | 0.0129 | 872 | 339 | PROMS ²⁴ |
| Age 50–60 | 0.742 | 0.0058 | 4287 | 1491 | - |
| Age 60–70 | 0.769 | 0.0032 | 13128 | 3944 | - |
| Revision surgery | 0.553 | 0.007 | 2201 | 1779 | - |
| Cost inputs | | | | | |
| RS versus THR | | | | | |
| Cost | Mean value £ | SE | Gamma distribution Parameter α | Gamma distribution Parameter β | Source |
| RS comparison | | | | | |
| Prosthesis cost | 2,808 | N/A | N/A | N/A | NHS Supply Chain |
| Surgery costs (excluding prosthesis) | 1,738 | N/A | N/A | N/A | Vale <i>et al</i> . ²⁵ |
| Hospital inpatient stay | 1,628 | N/A | N/A | N/A | Edlin et al.26 |
| Follow-up cost post- RS | 509 | 44 | 130 | 4 | |
| Revision surgery | 16,794 | 443 | 1435 | 12 | Vanhegan <i>et al.</i> 4 |
| Post revision follow-up | 400 | 30 | 169 | 2 | Edlin <i>et al.</i> ²⁶ |
| THR comparison | | | | | |
| Prosthesis cost (CeMoP) | 1,575 | N/A | N/A | N/A | NHS Supply Chain |
| Prosthesis cost (CeLCoC) | 3,911 | N/A | N/A | N/A | NHS Supply Chain |
| Prosthesis cost (CeCoP) | 2,018 | N/A | N/A | N/A | NHS Supply Chain |
| Surgery costs (excluding prosthesis) | 1,738 | N/A | N/A | N/A | Vale <i>et al</i> . ²⁵ |
| Hospital inpatient stay | 1,687 | N/A | N/A | N/A | Edlin <i>et al</i> . ²⁶ |
| Follow-up cost post- THR | 400 | 30 | 169 | 2 |] |
| Revision surgery | 16,794 | 443 | 1435 | 12 | Vanhegan <i>et al.</i> 4 |
| | | | | | |

*surgical mortality was the same for THR/RS and revision

doi:10.1371/journal.pone.0165021.t001

lifetime revision rates (b) using device costs supplied by manufacturers to the National Institute for Health and Care Excellence for technology appraisal TA304 [29]; (c) using alternative quality of life utility values [26]. Additional scenarios investigated included the following: comparing the Birmingham Hip, Biomet and Finsbury male patient-device combinations that satisfy the NICE benchmark versus cemented metal on polythene device (CeMoP), cemented THR with ceramic on polythene bearing surface (CeCoP) and/or cementless ceramic on ceramic bearing surface (CeLCoC) THRs.

Results

Six manufacturers of RS components accounted for almost all (96%) of RS interventions (S1 Fig). The Birmingham Hip contributed more than half of all RS use. Patient ASA grade and age distributions were similar between manufacturers (S2 Fig and S3 Fig). Usage of various head sizes was idiosyncratic and differed between the 6 manufacturers (S4 Fig).

Kaplan-Meier analyses indicated that for all six manufacturers, men experienced lower revision rates than women. However, even for men, the revision rate was poor for most manufacturers and flexible parametric models predicted a low probability of satisfying the 10 year NICE benchmark (Fig 2). The only device which delivered an overall revision rate within or near the 10 year benchmark was the Birmingham Hip. For women, no manufacturer's device delivered a revision rate within the benchmark. All exceeded 5% revision within only 5 years, and by 10 years, predicted rates in women were all greater than 10% (S5 Fig).

In addition to RS device manufacturer and sex, the requirement for revision is likely to be influenced by the size of the head component and patient age [13]. We therefore estimated the predicted ten year revision rate for different head sizes using flexible parametric models with age as a covariate. Graphical examples are shown in S6-S9 Figs.

These flexible parametric models predicted poor 10 year performance for almost all female RS recipients irrespective of device head size, patient age at intervention or device manufacturer. Of the 6,646 women provided with RS, only about 2% were in head size-age-manufacturer categories likely to satisfy the NICE benchmark for revision. Of 18,720 male RS recipients, around 60% were estimated to be in such categories. Of these, 87% were Birmingham Hip recipients in head size categories of 50 mm or greater, and the rest were mostly recipients of Finsbury devices with head sizes \leq 48mm or Biomet devices with a 50 to 54 mm head size.

Fig 3 shows revision performance for the Birmingham hip, Biomet and Finsbury RS devices in male ASA1 and ASA2 grade patients when head size-patient categories were dichotomized into those predicted to satisfy and not satisfy the NICE benchmark. Refinement by selecting for age within head sizes generally improved the revision profile.

The cost-effectiveness of the Birmingham Hip, Biomet and Finsbury devices satisfying the NICE benchmark for revision were compared with THR devices in male ASA 1 and ASA 2 grade patients. For the base case economic analysis we compared the most widely used RS (Birmingham hip, within NICE benchmark) with the most widely used THR device (CeMoP) in male grade ASA 1 and ASA grade 2 patients. Inputs for the economic analysis are summarised in Table 2. This analysis indicated that the probability that RS was cost-effective compared to THR remained low (<4%) at a willingness to pay of £20,000/QALY (for CEAC see S10 Fig). Birmingham Hip accumulated fewer lifetime QALYs for 40, 50 and 60 year old men; lifetime costs were greater than for RS by at least £2,900 and RS was dominated by THR for 60 year old men.

Since the Birmingham Hip was the best performing RS device, we performed a sensitivity analysis in which it was compared with the best performing THR device (CeCoP). In this

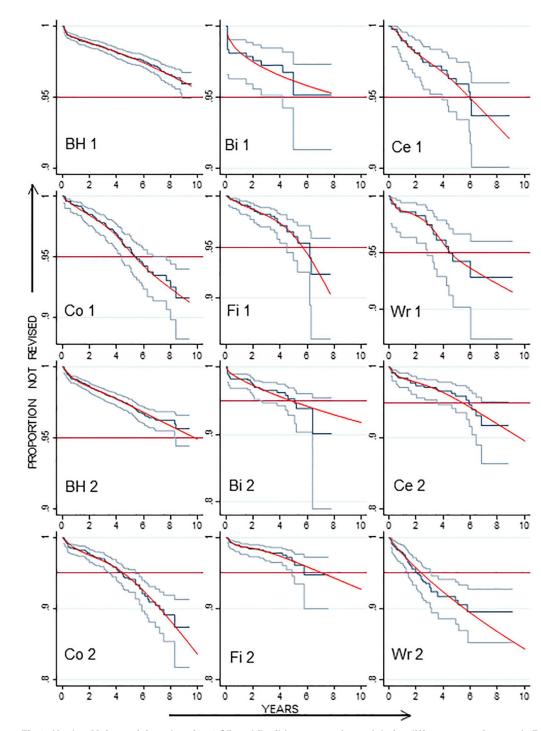


Fig 2. Kaplan-Meier revision plots (95% CI) and flexible parametric models for different manufacturer's RS devices implanted in men graded as ASA 1 (upper panel) or ASA 2 (lower panel). *BH* = *Birmingham Hip; Bi* = *Biomet; Ce* = *Centerpulse; Co* = *Corin; Fi* = *Finsbury; Wr* = *Wright UK.*

doi:10.1371/journal.pone.0165021.g002

comparison the probability that RS was cost-effective was 46% for 40 year old men, and less for older men.

PLOS ONE

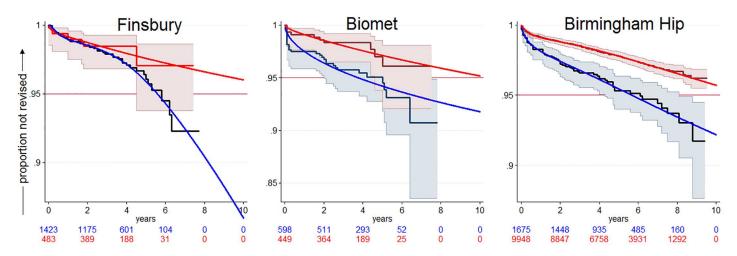


Fig 3. Estimated ten-year revision rates dichotomized by head size-patient combinations satisfying and not satisfying the ten year benchmark of 5%. The data are for male patients of ASA 1 plus ASA 2 grade receiving RS devices from different manufacturers (the subgroups within the NICE benchmark for revision were as follows: Finsbury (mean age 51.3 years): head sizes 48 or less and head size 50 if patient age was less than 50 years at intervention; Biomet (mean age 50.4 years): head size 50 if age less than 55 years, head sizes 52, and 54 if age less than 60 years; Birmingham Hip (mean age 55.5 years) head sizes 50 or greater and head size 48 if age less than 45 years). Note the more mature data for Birmingham Hip. For clarity the 95% CI of the Kaplan Meier plot for the Finsbury below-benchmark subgroup has been omitted.

doi:10.1371/journal.pone.0165021.g003

Since the mean age for the Birmingham Hip recipients was less than that for the CeMoP and CeCoP THR devices, we performed a further sensitivity analysis comparing the Birmingham Hip with the CeLCoC THR since this has been used in a younger population than the other THRs. In this comparison, the probability that the Birmingham Hip was cost-effective was ~76%. However, using alternative plausible models of lifetime revision resulted in a drop in probability of the Birmingham Hip being cost-effective to less than 10% due to poor predicted performance of RS.

We compared the Biomet RS and Finsbury devices (patient device combinations within the NICE benchmark for revision shown in Fig 3) with the best performing THR device (CeCoP) in male grade ASA 1 and ASA grade 2 patients, the probability that RS was cost-effective was <6% at a willingness to pay of £20,000/QALY.

| Table 2. Cost-effectiveness results for base case analysis Birmingham hip) versus CeMoP comparison for ASA1 plus ASA 2 male patients aged |
|---|
| 40, 50 and 60 years. |

| | Age | Age 40 | | Age 50 | | Age 60 | |
|--------------------------|--------|---------|--------|-----------|--------|-----------|--|
| | BHIP | CeMoP | BHIP | CeMoP | BHIP | CeMoP | |
| Men: 10-year time horizo | on | | | | , | | |
| Total mean costs £ | 12,211 | 10,348 | 12,133 | 10,033 | 12,024 | 9,829 | |
| Total mean QALYs | 7.326 | 7.321 | 7.515 | 7.512 | 7.4850 | 7.4841 | |
| Incremental cost £ | 1,8 | 1,863 | | 2,100 | | 2,194 | |
| Incremental QALYs | 0.0 | 0.0054 | | 0.0026 | | 0.0009 | |
| ICERs (£/QALY) | 344, | 344,570 | | 811,430 | | 2,376,140 | |
| Men: Lifetime horizon | | | | | | | |
| Total mean costs £ | 21,479 | 18,571 | 19,187 | 15,908 | 16,421 | 13,130 | |
| Total mean QALYs | 16.587 | 16.581 | 14.706 | 14.705 | 12.109 | 12.110 | |
| Incremental cost £ | 2,9 | 2,908 | | 3,278 | | 3,291 | |
| Incremental QALYs | 0.0059 | | 0.0013 | | -0.001 | | |
| ICERs (£/QALY) | 488, | 488,836 | | 2,493,847 | | Dominated | |

doi:10.1371/journal.pone.0165021.t002

When manufacturer's device costs were used instead of NHS Supply Chain costs, the probability that the Birmingham Hip was cost-effective relative to the CeMoP THR device remained below 5%. In further sensitivity analyses, we applied the one year QOL advantage for RS reported by Edlin *et al.* (2012) in the Birmingham Hip versus CeMoP comparison; the Birmingham Hip was more costly and accumulated more QALYs, and the probability that Birmingham Hip was cost-effective was 100% for 40, 50 and 60 year old men (with NHS Supply Chain prosthesis costs) [26].

Discussion

Conceptual advantages proposed for resurfacing relative to THR include preservation of bone and improved durability from metal-on-metal bearing surfaces; features leading to the perception that resurfacing is suitable for young and active patients. The age profile of RS recipients in National Joint Registry reflects this perception, but there is a lack of randomised or other comparative evidence to underpin this usage and, the observed revision rates for RS are alarmingly poor relative to THR. The single RCT so far conducted indicated a lack of short term advantage for RS in a mix of male and female patients with a mean age of 56 years [30]. National Joint Registry data for women who have received resurfacing devices highlights poor revision performance; even when the data are stratified according to device manufacturer, device head size and controlled for patient age, poor revision rates are still found and almost no subgroup of device-patient-head size combinations was predicted to satisfy the NICE benchmark for revision. This registry evidence points to a high probability of RS failure relative to THR, and suggests that resurfacing should be abandoned for women until good comparative evidence is available that shows that in young active women RS is at least as successful as THR.

For male recipients of RS devices it was possible to identify patient-head size-device manufacturer subgroups predicted to satisfy benchmark performance retrospectively. However, for five of the six manufacturers of the most commonly used devices, such subgroups represented less than half of device recipients. Only the Birmingham Hip, Biomet and Finsbury devices delivered appreciable proportions of patients predicted to perform within benchmark (85%, 43% and 25% respectively). When the cost-effectiveness of resurfacing relative to alternative THR prostheses was compared using these manufacturer device-patient subgroups, there appeared little likelihood that resurfacing in these groups has represented a cost-effective deployment of health provider resources. Furthermore, it is clear that without retrospective selection of better performing RS subgroups, the proposition that resurfacing should be continued for male patients on the grounds of cost-effectiveness cannot be supported.

Strengths, limitations and previous analyses

The most significant limitation is the discrepancy in age distribution between resurfacing and THR recipients. This means that comparing the two types of intervention requires modelling THR revision rates outside of the observed age distribution, by controlling for age as a covariate. Unfortunately, there is no viable alternative to this approach because of the lack of comparative studies. A further difficulty is the inability to control for physical activity of patients or surgeon experience, which are likely to impact on the probability of device failure. Our approach to some of these difficulties has followed that of others in using flexible parametric models [5,12,13]. McMinn (2015) [31] has suggested that to gain experience in RS a surgeon would need to conduct about 1,000 operations; a large number in the context of the total interventions for some RS devices recorded in the NJR. Whether a similarly prolonged learning curve may be required for THR is unknown. McMinn has suggested poor performance of

small cup size RS devices in female recipients may be attributable to their use by relatively inexperienced surgeons [31].

Several weaknesses in our cost-effectiveness analyses must be acknowledged, stemming from uncertainties about model input parameters. In particular, there is no information about long term quality of life following implantation of the different types of hip replacement of interest, or about long term device survival following the different implants examined here. The Alberta Hip Improvement Project study compared 3, 12 and 24 month SF-36 physical function changes from baseline for propensity matched Birmingham Hip and THR patients. In this study there was considerable missing data and a 3 month advantage for RS almost disappeared by 2 years [32]. A further limitation is that NHS Supply Chain costs are unlikely to perfectly reflect real world costs because of variable and individual contractual arrangements between NHS Trusts and prosthesis manufacturers, and potential economies of scale. Our analyses do not include costs for monitoring plasma cobalt levels; now recommended for patients following MOM implants, and this might slightly bias results in favor of RS [33–34]. Nevertheless, our analyses use IPD which reflect real world use of hip replacements in England and Wales over the recent decade, and provide estimates of lifetime cost-effectiveness that will be of interest to decision makers. Estimating life time revision rates requires modelling substantially beyond the observed data and the results are sensitive to the model chosen.

This is the first lifetime cost-effectiveness analysis using data from the National Joint Registry England and Wales on RS devices satisfying the ten year NICE benchmark. An early analysis by Vale *et al* (2002) compared RS with THR as a generalized intervention but was limited by the immaturity of available revision data [25]. Edlin *et al.* undertook cost-effectiveness analysis over a one year time horizon using cost and clinical data simultaneously collected from a randomized controlled trial [26]. This analysis did not capture important differences between devices in terms of long term revision requirements. Heintzbergen *et al.* (2013) undertook a 15 year analysis and compared the best performing RS device (Birmingham Hip) with the generality of THR devices, most of which were used for older patients [35]. This analysis tends to bias in favor of RS, and since RS is now mainly justified on the grounds of its potential long term benefit in delaying requirement for revision a longer time horizon appears more appropriate.

Like other cost-effectiveness analyses of hip replacement we assumed equal mortality for recipients of different devices [17, 36, 37,38]. Two recent UK observational studies proposed better survival after RS than THR, but the authors acknowledged their conclusions were problematic due to the influence of hidden confounders [10, 39].

Conclusion

In conclusion, the cost-effectiveness case for the use of RS as a general class of intervention for young patients with osteoarthritis is weak. We would suggest that much of the past use of RS has probably been wasteful of NHS resources. Alternative THR devices are likely to be equally or more cost-effective. In the absence of good comparative evidence, RS is difficult to justify on the grounds of either cost-effectiveness or on the basis of preferable revision rates.

Supporting Information

S1 Fig. Relative past use of different RS devices according to RS head manufacturer. (DOCX)

S2 Fig. ASA grade distribution of recipients of six major RS head manufacturers. (DOCX)

S3 Fig. Age distribution of recipients of six major RS head manufacturers. (DOCX)

S4 Fig. Device head size distribution for recipients of six major RS head manufacturers. (DOCX)

S5 Fig. Kaplan-Meier revision plots (95% CI) with flexible parametric models for six major RS head manufacturer's implanted in women graded as ASA 1 or ASA 2. (DOCX)

S6 Fig. Female recipients (ASA grade 1 + 2) of the Birmingham hip of various head sizes. (DOCX)

S7 Fig. Male recipients (ASA grade 1 + 2) of the Birmingham hip of various head sizes. (DOCX)

S8 Fig. Male recipients (ASA grade 1 + 2) of the Biomet device of various head sizes. (DOCX)

S9 Fig. Male recipients (ASA grade 1 + 2) of the Finsbury device of various head sizes. (DOCX)

S10 Fig. Cost-effectiveness acceptability curves for Birmingham Hip versus CeMoP THR using bath tub fit ASA1 grade 40, 50, 60 year old men. (DOCX)

S11 Fig. Cost-effectivenessscatter plots for Birmingham Hip versus CeMoP THR (using Bath tub fit) ASA1 grade 40, 50, 60 year old men. (DOCX)

S1 Table. Characteristics of the five THR categories. (DOCX)

S2 Table. Utility parameters for the sensitivity analysis using Edlin *et al.*(2012) utility difference of RS versus THR.

(DOCX)

S3 Table. Cost of RS prosthesis. (DOCX)

S4 Table. Cost parameters for the sensitivity analysis using manufacturer's device cost. (DOCX)

Author Contributions

Conceptualization: RPJ MC N-BK HM AG KF MC PS AC.

Formal analysis: RP-J MC N-BK HM.

Funding acquisition: PS AC.

Methodology: RPJ MC N-BK HM AG KF MC PS AC.

Project administration: AG.

Supervision: PS AC.

Validation: RPJ MC N-BK HM.

Writing - original draft: RPJ MC.

Writing - review & editing: RPJ MC N-BK HM AG KF MC PS AC.

References

- NICE 2014. Updated NICE guidance on hip replacement and resurfacing recommends more durable artificial joints. https://www.nice.org.uk/news/press-and-media/updated-nice-guidance-on-hipreplacement-and-resurfacing-recommends-more-durable-artificial-joints. (date last accessed 16 August 2015).
- Department of Health. NHS Reference Costs 2013–2014 London: Department of Health, 2010 https://www.gov.uk/government/publications/nhs-reference-costs-2013-to-2014. (date last accessed 16 August 2015).
- 3. The National Audit Office. Report on Hip replacements: Getting it right first time, HC 417, Session 1999–00, April 2000.
- Vanhegan IS, Malik AK, Jayakumar P, UI Islam S, Haddad FS. A financial analysis of revision hip arthroplasty: The economic burden in relation to the national tariff. Journal of Bone & Joint Surgery [Br], 2012; 94-B(5):619–623.
- National Joint Registry for England and Wales: 11th Annual Report. National Joint Registry. [Internet] 2014. http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Reports/11th_annual_ report/NJR%2011th%20Annual%20Report%202014.pdf (date last accessed 10 August 2015).
- Cohen D. How safe are metal-on-metal hip implants?. BMJ 2012; 344:e1410. doi: <u>10.1136/bmj.e1410</u> PMID: 22374741
- Smith AJ, Dieppe P, Vernon K, Porter M, Blom AW. On behalf of the National Joint Registry for England and Wales. Failure rates of stemmed metal-on-metal hip replacements: analysis of data from the National Joint Registry of England and Wales. Lancet 2012; 379:1199–1204. doi: 10.1016/S0140-6736(12)60353-5 PMID: 22417410
- Wilkinson JW. Metal-on-metal hip prostheses: where are we now? BMJ 2012; 345:e7792 doi: 10.1136/ bmj.e7792 PMID: 23160785
- Sedrakyan A. Metal-on-metal failures—in science, regulation, and policy. Lancet 2012; 319:1174– 1175.
- McMinn DJ, Snell KI, Daniel J, Treacy RB, Pynsent PB, Riley RD. Mortality and implant revision rates of hip arthroplasty in patients with osteoarthritis: registry based cohort study. BMJ 2012; 344:e3319. doi: 10.1136/bmj.e3319 PMID: 22700782
- Jameson SS, Baker PN, Mason J. Independent predictors of revision following metal-on-metal hip resurfacing: a retrospective cohort study using National Joint Registry data. Journal of Bone & Joint Surgery [Br] 2012, 94-B:746–754.
- 12. Kandala NB, Connock M, Puliottil-Jacob R, Sutcliffe P, Grove A, Mistry H, Clarke A. Setting benchmark revision rates for total hip replacement: analysis of registry evidence. BMJ 2014; 350:h756.
- Smith AJ, Dieppe P, Howard PW, Blom AW. On behalf of the National Joint Registry for England and Wales. Failure rates of metal-on-metal hip resurfacings: analysis data from the National Joint Registry for England and Wales. Lancet 2012; 380(9855):1759–66. doi: <u>10.1016/S0140-6736(12)60989-1</u> PMID: 23036895
- de Verteuil R, Imamura M, Zhu S, Glazener C, Fraser C, Munro N, Hutchison J, Grant A, Coyle D, Coyle K, Vale L. A systematic review of the clinical effectiveness and cost-effectiveness and economic modelling of minimal incision total hip replacement approaches in the management of arthritic disease of the hip. Health Technology Assessment 2008; 12(26). PMID: 18513467
- 15. Lambert PC, Royston P. Further development of flexible parametric models for survival analysis. The Stata Journal 2009,265–290.
- Pulikottil-Jacob R, Connock M, Kandala N-B, Mistry H, Grove A, Costa M, Sutcliffe P, Clarke A. Costeffectiveness of total hip replacements for women and men with hip osteoarthritis: comparison of devices with differing bearing surfaces and modes of fixation. Bone Joint J 2014; 97-B:449–57.
- Fitzpatrick R, Shortall E, Sculpher M, Murray D, Morris R, Lodge M. Primary total hip replacement surgery: a systematic review of outcomes and modelling of cost-effectiveness associated with different prostheses. Health Technology Assessment. 1998; 2:20:1–64. PMID: 10103353
- 18. Mujica-Mota R. Cost-effectiveness analysis of early versus late total hip replacement in Italy. Value in Health 2013; 16:267–279. doi: 10.1016/j.jval.2012.10.020 PMID: 23538178
- McKenzie L, Vale L, Stearns S, McCormack K. Metal on metal hip resurfacing arthroplasty. An economic analysis. Eur J Health Econom 2003; 4:122–129.

- Office for National Statistics. Health and Social Care. 2012. Available from: http://www.ons.gov.uk/ ons/taxonomy/index.html?nscl=Health+and+Social+Care (date last accessed 16 August 2015).
- 21. National Institute for Health and Clinical Excellence. Guide to methods of technology appraisal 2013. http://www.nice.org.uk/article/pmg9/chapter/Forward (date last accessed 26 January 2016).
- 22. National Joint Registry for England and Wales: 9th Annual Report. National Joint Registry. [Internet] 2012. http://www.njrcentre.org.uk/NjrCentre/Portals/0/Documents/England/Reports/9th_annual_report/NJR%209th%20Annual%20Report%202012.pdf (date last accessed 1 August 2015).
- New Zealand Joint Registry: Thirteen Year Report January 1999 to December 2011. HEALTHFIRST: Canterbury District Health Board's gateway to health information for everyone [Internet] 2012. <u>http://www.cdhb.govt.nz/njr/reports/A2D65CA3.pdf</u> (date last accessed 16 August 2015).
- Patient Reported Outcome Measures (PROMS). Health and Social Care Information Centre 2013. http://www.hscic.gov.uk/proms (date last accessed 17 August 2015).
- Vale L, Wyness L, McCormack K, McKenzie L, Brazzelli M, Stearns SC. A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease. Health Technology Assessment 2002; 6,15:1–109. PMID: 12137721
- 26. Edlin R, Tubeuf S, Achten J, Parsons N, Costa M. Cost-effectiveness of total hip arthroplasty versus resurfacing arthroplasty: economic evaluation alongside a clinical trial. BMJ Open 2012; 2:5:e001162. doi: 10.1136/bmjopen-2012-001162 PMID: 23065450
- 27. Briggs A, Sculpher M, Claxton K. Decision modelling for health economic evaluation. 1 ed. England: Oxford University Press, 2006.
- Personal Social Services Research Unit. Unit costs of health & social care. 2010. <u>https://www.education.gov.uk/publications/eOrderingDownload/PSSRU-1368-230X.pdf</u> (date last accessed 16 August 2015).
- 29. National Institute for Health and Care Excellence. Final appraisal determination. Total hip replacement for end-stage arthritis of the hip (review of technology apprasial guidance 2 and 44). National Institute for Health and Care Excellence. 2014. <u>http://www.nice.org.uk/nicemedia/live/13690/66423/66423.pdf</u> (date last accessed 20 August 2015).
- 30. Costa ML, Achten J, Parsons NR, Edlin RP, Foguet P, Prakash U, Griffin DR, Young Adult Hip Arthroplasty team. Total hip arthroplasty versus resurfacing arthroplasty in the treatment of patients with arthritis of the hip joint: single centre, parallel group, assessor blinded, randomised controlled trial. BMJ 2012; 344:e2147. doi: 10.1136/bmj.e2147 PMID: 22517930
- McMinn, D.The McMinn Centre. Women do well with hip resurfacing in may hands. 2015 http://www.mcminncentre.co.uk/research-lectures-women-resurfacing.html (date last accessed 28 January 2016).
- **32.** The Alberta Hip Improvement Project. Functional outcomes for 2 years comparing hip resurfacing and Total Hip Arthroplasty. J Arthroplasty 2012; 27,5:750–757. doi: 10.1016/j.arth.2011.10.004 PMID: 22285258
- Prentice JR, Clark MJ, Hoggard N, Morton AC, Tooth C, Paley MN, Stockley I, Hadjivassiliou M, Wilkinson JM. Metal-on-Metal Hip Prostheses and Systemic Health: A Cross-Sectional Association Study 8 Years after Implantation. PLOS ONE 2013 8,6:e66186. doi: <u>10.1371/journal.pone.0066186</u> PMID: 23762480
- 34. Penny JØ, Varmarken J-E, Ovesen O, Nielsen C, Overgaard S. Metal ion levels and lymphocyte counts: ASR hip resurfacing prosthesis vs. standard THA 2–year results from a randomized study. Acta Orthop 2013; 84,2:130–137. doi: 10.3109/17453674.2013.784657 PMID: 23597114
- Heintzbergen S, Kulin NA, Ijzerman MJ, Steuten LMJ, Werle J, Khong H, Marshall DA. Cost-Utility of Metal-on-Metal Hip Resurfacing Compared to Conventional Total Hip Replacement in Young Active Patients with Osteoarthritis. Value in Health 2013; 16:942–952. doi: <u>10.1016/j.jval.2013.06.021</u> PMID: 24041344
- Pennington M, Grieve R, Sekhon JS, Gregg P, Black N, Van Der Meulen JH. Cemented, cementless, and hybrid prostheses for total hip replacement: cost-effectiveness analysis. BMJ 2013; 346:f1026. doi: 10.1136/bmj.f1026 PMID: 23447338
- Briggs AF, Sculpher MF, Dawson JF, Fitzpatrick RF, Murray DF, Malchau H. The use of probabilistic decision models in technology assessment: the case of total hip replacement. Appl Health Econ Health Policy 2004; 3,2:79–89. PMID: <u>15702945</u>
- Higashi H, Barendregt JJ. Cost-effectiveness of total hip and knee replacements for the Australian population with osteoarthritis: discrete-event simulation model. PLoS ONE 2011; 6,9:e25403. doi: 10. 1371/journal.pone.0025403 PMID: 21966520
- Kendal A, Prieto-Alhambra D, Arden N, Carr A, Judge A. Mortality rates at 10 years after metal-onmetal hip resurfacing compared with total hip replacement in England: retrospective cohort analysis of hospital episode statistics. BMJ 2013; 347:f6549. doi: 10.1136/bmj.f6549 PMID: 24284336