HEALTH TECHNOLOGY ASSESSMENT REPORT

ALTERNATIVE PRIMARY HIP IMPLANTS
AND BUDGET IMPACT FOR BRITISH COLUMBIA

A report for the BC Health Technology Review Office, on behalf of health authorities and the Ministry of Health. Vancouver. August 2016.

Acknowledgements

This study was supported by the Health Technology Review (HTR), Government of British Columbia.

The views expressed herein are those of the authors and do not necessarily represent the views or official policy of the Government of British Columbia, British Columbia health authorities, or any other agency.

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

95% CI: 95% confidence interval
95% CrI: 95% credible interval
AHS: Alberta Health Services
ALSTR: Adverse local soft-tissue reaction
ALTR: Adverse local tissue reaction (also known as pseudotumour)
AOANJRR: Australian Orthopedic Association National Joint Replacement Registry
BCCSS: BC Clinical and Support Services
BCPSQC: BC Patient Safety & Quality Council
CADTH: Canadian Agency for Drugs and Technologies in Health
CIHI: Canadian Institute for Health Information
CJRR: Canadian joint replacement registry
CMoPxl: Ceramicised metal (head)-on-crosslinked polyethylene
CMPc: Ceramicised metal on conventional polyethylene (also known as oxinium)
CMPxl: Ceramicised metal-on-crosslinked polyethylene (also known as oxinium)
CoC: Ceramic-on-ceramic
CoP: Ceramic on polyethylene (comparison combined conventional and crosslinked poly)
CoPxl: Ceramic-on-crosslinked polyethylene
DGSC: Deal Governance Steering Committee
HA: Health authorities
HTA: Health technology assessment
HTR: Health Technology Review
ICER: incremental cost-effectiveness ratio
LOS: Length-of-stay
MoM: Metal-on-metal
MoP: Metal-on-polyethylene (comparison combined conventional and crosslinked poly)
MoPxl: Metal-on-crosslinked polyethylene
MSP: Medical service plan
NICE: National Institute for Health and Care Excellence UK
NJR: National Joint Registry (of England and Wales)
NMA: Network meta-analysis
NNT: Number needed to treat for the outcome
OR: Odds ratio
PICOs: Clinical question (Population, Intervention, Comparator, Outcomes)
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PVN: Patient Voices Network
QALY: Quality-adjusted life year
RCT: Randomized controlled trial
RD: Risk difference

RR: Risk ratio
SoPc: Steel on conventional polyethylene
SUCRA: Surface under the cumulative rank curve
THR: Total hip replacement
WTP: Willingness-to-pay

Chapter 1: Background and Problem

1.1 Definition of technologies under assessment

Total hip replacement (THR) involves replacing the head of the femur with an artificial head that fits into an acetabular component which is secured to the pelvis. These mechanical components will then function as the hip joint, allowing mobility that was previously limited because of injury or disease. In general, there are four implant components for a THR: the acetabular cup/shell, the liner, the head and the stem. In some cases, the head and stem, or the acetabular cup and liner, come in one piece. Interchangeable pieces of the head, neck, stem, or liners are also available (Figure 1). Modular components allow different combinations of head sizes, femoral neck lengths, and different materials for each component. This flexibility allows surgeons to choose a combination tailored to the needs of each patient. The area of contact between the acetabular liner insert and the femoral head is usually known as the bearing surface. Both the acetabular cup and femoral stem can be fixed to the patient bone with (cemented) or without bone cement (uncemented or cementless).

Figure 1: Different THR hip component combinations

[Figures extracted from vendors websites.]

According to the Canadian Joint Replacement Registry (CJRR), the number of total hip replacement surgeries has been rising over the last decade, mostly due to the aging population(1). Total hip replacement is one of the most important advances in the treatment of degenerative hip disease. Candidates for total hip replacement usually experience symptoms such as inadequate pain control from analgesics and limited mobility at the hip, which can cause a significant decrease in quality of life. Without intervention, patients are likely to progress to more serious limitations or even disability. Thousands of patients in British Columbia (BC), who would otherwise have severe limitation in their hips, benefit from total hip replacement surgery each year (1). Due to advances in new material used in the components of total hip replacement, surgeons and patients now have a variety of choices, such as ceramic or metal femoral head, modulated stem, or different types of acetabular liners.

Although advances have been made in this area, the clinical and economic consequences of these new components are not clear. While at first promising, metal-on-metal implants (MoM) has fallen out of favour in the last few years due to a higher rate of early revision compared to other types of implants (2, 3). At present time, most total hip replacements in BC use a cobalt-chromium femoral head (on uncemented titanium stems) against crosslinked polyethylene cup liners. The recent discovery of pseudotumours (defined below) in total hip replacement patients raises the need to review whether the current components used in total hip replacement may lead to the formation of pseudotumours or a higher revision rate compared to other available materials. Pseudotumours are granulomatous lesions, large focal solid, cystic or mixed masses around the prostheses mimicking the local effect of neoplasia or infection in the absence of either disease. These are considered to be related to adverse reactions to cobalt and chromium metal ions or debris, more specifically secondary to mechanically assisted tribocorrosion of the morse taper of a femoral stem of a hip replacement (4, 5). Particles from the bearing surface and corrosion at the metal interface are two possible sources of debris (3). Therefore, changing the material of the femur head could possibly reduce the incidence of pseudotumours. One case series found that the prevalence of pseudotumour was around 1.1% in metal-on-poly patients (6). Symptoms of pseudotumours include pain, inflammation, swelling and limited mobility. However, about 60% patients could be asymptomatic (7).

In some cases, some of these pseudotumours have been described as locally destructive masses requiring early revision surgery. However, as this is a recent discovery, earlier studies and registry data may have misclassified the reason for revision as infection or other causes(8). As such, it is important to closely examine both the incidence of pseudotumour and early revision rates.

1.2 Current usage in BC

According to the Canadian Institute for Health Information (CIHI), over 5,000 total primary hip replacements are performed in BC per year (Table 1) (9, 10). The number of total primary hip replacements has been rising, increasing from 4,671 in 2012–2013 to 5,117 in 2014–2015 (9.5% increases). The number of *revisions* for hip replacement, however, has only increased from 505 to 511 per year in the same time period (1.2% increases). Most of the hip replacements in Canada are due to degenerative arthritis or fractures (>89%), which reflects an aging population. (10)

Table 1: Total Hip Replacements, BC, 2010-2011 to 2014-2015

Type of total hip	2010-11	2011-12	2012-13	2013-14	2014-15
Primary	4,320	4,579	4,671	4,722	5,117
Revision	470	519	505	514	511
Primary: Revision	9:01	9:01	9:01	9:01	10:01

Source: Hospital Morbidity Database, BC, 2010–2011 to 2014–2015, Canadian Institute for Health Information.(9)

Most of the hip replacements in Canada use metal-on-poly prostheses (93.4%)(10). In BC, while 80% of total hip replacements between 2012 and 2015 used metal-on-crosslinked poly, the proportion of ceramic-on-crosslinked poly had almost doubled during the same time period (Table 2) (9, 10).

Table 2: Total primary hip replacements (all diagnoses), by bearing surface, BC, 2012-13 to 2014-15.

Bearing Surface	2012-13	2013-14	2014-15
Metal/Metal	2.0%	1.1%	1.0%
Metal/XLPE	86.2%	84.6%	84.1%
Metal/Non-XLPE	1.5%	0.7%	0.2%
Ceramic/Ceramic	4.8%	4.1%	2.9%
Ceramic/XLPE	4.7%	7.6%	8.7%
Ceramic/Non-XLPE	<0.1%	0.0%	0.0%
Ceramic/Metal	0.3%	0.1	0.2%
Ceramicized metal/XLPE	0.4%	<0.1%	0.2%
Ceramicized metal/Non-	0.0%	0.0%	0.0%
Other	0.1%	1.8%	2.8%

Notes XLPE – crosslinked polyethylene; Bearing surface information was available for 12,722 (97.8%) of total hip replacements submitted to CJRR for BC; The coverage rate for CJRR in BC for any hip replacements for fiscal years between 2012-13 and 2014-2015 was 72.5%, 94.1% and 95.0%, respectively.
Source: Canadian Joint Replacement Registry, BC, 2012–2013 to 2014–2015, Canadian Institute for Health Information.

1.3 Regulatory status

The current standard of care for THR devices in BC is metal (head)-on-crosslinked polyethylene (acetabular liner or all poly acetabular components) or “metal-on-poly,” for quick reference in this report. That device and related hospital services are fully covered by the province for beneficiaries[1]. Patients who choose a different device can pay out-of-pocket for the difference in cost between the patient-preferred product (ceramic-on-poly, etc.) and the medically insured standard, and for any additional hospital services/procedures that result from the patient-preferred product.

BC Ministry of Health is interested in evaluating the safety profile of the different types of hip implants, specifically (but not limited to) with regard to the incidence rate of pseudotumours following device implantation. While corrosion of the implant is inevitable, it has been suggested that ceramic heads, which do not contain cobalt and chromium ions, would eliminate the risk posed by metal debris. Therefore, ceramic (head)-on-crosslinked polyethylene (acetabular linear) or “ceramic-on-poly” hip replacement devices are being evaluated whether should be considered medically necessary and be fully covered by the public healthcare system (in addition to the current metal-on-poly insured standard). In the same way, ceramic (head)-on-ceramic (acetabular liners or cups) or “ceramic-on-ceramic” devices, and ceramicised metal (head)-on-crosslinked polyethylene (Oxinium-on-poly) are under the same evaluation. These implants are also listed under the patient pay list as alternative primary hip implants being used in clinical practice in BC.

[1] BC residents who are enrolled in the Medical Services Plan in accordance with section 7 of the *Medicare Protection Act.*

1.4 Decision problem

There are four options to be considered for primary hip replacement devices in BC, based on their relative safety, effectiveness, and cost-effectiveness:

- Metal-on-poly remains the sole insured standard for hip replacement
- Ceramic-on-poly becomes the new sole standard of care (with metal-on-poly provided on a patient-pay basis or not at all)
- Both metal-on-poly and ceramic-on-poly be publicly funded
- Ceramic-on-ceramic and Oxinium-on-poly be publicly funded as further options

1.5 Intervention and comparators

Four types of implants were compared against each other in this health technology assessment (HTA): the current standard of care and three alternative primary implants included in the patient pay list in BC:

- Metal-on-poly (standard of care)
- Ceramic-on-poly
- Ceramic-on-ceramic
- Oxinium-on-poly (ceramicised metal head)

1.6 Overall objective

The objective of this HTA is to evaluate the safety, effectiveness, and cost-effectiveness of four different hip implants (i.e., metal-on-poly, ceramic-on-poly, ceramic-on-ceramic, oxinium-on-poly), as well as assessing the budget impact for BC for primary total hip replacement. Patients of any age submitted for total hip replacement (unilateral or bilateral) due to any condition are included in the review. The hierarchy of outcomes is listed below:

Clinical outcomes

- All-cause mortality
- Revision (rates, interval between revisions)
- Functional score and quality of life
- Patient experience
- Complications (pseudotumours, aseptic loosening, infection, etc.)

Economic outcomes

- Costs (devices, procedure, revision)
- Quality-adjusted life years (QALYs)
- Resource use (hospital admissions, readmissions, length-of-stay (LOS))

1.7 Structure of report

Patient and physician input are outlined in the next two sections. Following this, a Canadian jurisdictional scan is provided and then an assessment of the clinical and economic evidence is presented in detail. The economic model is found in the next section, and is followed by the budget impact. The executive summary provides a brief overall discussion of the findings.

Chapter 2: Patient Experience

Summary of Patient Experience

The main issues faced by this patient population are pain, loss of mobility, loss of independency, loss of active lifestyle, loss of workplace productivity, impaired social relationships and depression - with impacts on family members. Severe pain before the procedure seems to affect their ability to make decisions about the implant, and they place a great deal of trust in the physicians to make that choice. Perceived harm from joint infection and revision seems to amplify all the issues abovementioned. Patients seem to value physiotherapy pre- and post- operatively as well as education for early detection of complications.

2.1 Objective

To gain an understanding of the outcomes important to patients, in order to guide the evaluation of the clinical literature and health policy.

2.2 Patient experience from literature

A rapid review of qualitative studies was conducted by Canadian Agency for Drugs and Technologies in Health (CADTH) (11) on behalf of the Health Technology Review (HTR) Office from the BC Ministry of Health to aid in meeting the overall objectives of this HTA.

They found that "the main perceived benefit of total hip replacement from the perspective of patients that emerged is the desire to return to everyday life without limitations. While everyday life looks different for each individual, participating in everyday life without limitations can include returning to work and activities of daily living, re-engaging in social relationships, and participating in leisure activities and hobbies. Returning to everyday life without limitations aligns with a desire for autonomy, independence, and dignity and a fear of being dependent on others." (pg 2)

One perceived harm from the patient perspective was described in the CADTH review: "prosthetic joint infection and the corresponding need for one or more revision surgeries. For study participants, this experience prevented them from returning to life without limitations, and had a considerable and extended impact on themselves and their family members and caregivers. Infection and revision surgery introduced further pain and mobility restrictions, the need for lengthy antibiotic treatment, and considerable distress due to lost independence, an uncertain future, and the need for ongoing support through symptom onset, treatment and revision surgery, and recovery after treatment." (pg 2)

The report further stated that, "Side effects that emerged as important to patients include pain and reduced mobility, worry and anxiety, frustration and time needed to adjust to a new and foreign body part. Participants within most of the included studies described these side effects as barriers to them returning to everyday life without limitations but also acknowledged these as necessary experiences to healing. It is possible that younger people are more frustrated than older people by the limitations to everyday life introduced by hip replacement, including the need for caregiver support, mobility restrictions, the need to limit social interactions and an inability to work and drive." (pg 2) CADTH notes that with a range of implant material types available, it is possible that people's perceptions of the benefits and harms of each differ but they were unable to explore this issue due to poor reporting of hip implant material in studies (p.13).

2.3 Patient input from focus group

2.3.1 Methods

Patients were invited to a focus group through the Patient Voices Network (PVN), which is administered by the BC Patient Safety & Quality Council (BCPSQC) Patient & Public

Engagement network. The invitation was published on the BCPSQC website and sent to the volunteer network mailing list. Respondents were contacted and asked to sign a 'Consent and non-disclosure agreement.' The questions for the focus group discussion were piloted with a hip replacement patient (Appendix A). Notes were taken during the focus group but the session was not recorded. All notes were anonymized with no personally identifiable information included. A summary of the discussion was circulated by email to participants as a feedback check for accuracy on their views/ responses.

2.3.2 Focus group participants

Four patients volunteered for the focus group. However one dropped out shortly before the meeting and could not be replaced on short notice. Three patients attended the meeting, two in person (both female) and one by phone (1 male). The average age of the participants was 66 years. Only one of them had experienced revisions/ complications.

2.3.3 Summary of focus group discussions

Patients experience a range of physical and mental health issues from the conditions which necessitate hip replacement surgery. These included pain, loss of mobility, loss of active lifestyle, loss of workplace productivity, impaired social relationships and depression. These affect family members as well. Each of the participants indicated a dramatic change in quality of life following their hip replacement surgery. Two patients undertook physiotherapy prior to surgery but it reportedly had minimal impact. All three patients were taking painkillers prior to surgery. Expectations for the surgery included return to full mobility and being pain free. Words used by patients following surgery included 'life changing' and 'pain free for the first time ever.' One of the patients required an immediate revision due to the prosthetic failing. All three participants reported having limited information about what type of prosthetic they were receiving and the pros and cons of different types. Two participants did not know what kind of hip they were given and one ‘thought’ they knew. All three remembered hearing from the surgeon that they were getting the ‘standard’ type of hip. The participants recognized the importance of post-surgical physiotherapy, yet acknowledged that this was not covered by the Province thus there would be ‘two tier’ recovery for those that can afford private rehab and those that cannot.

2.3.4 Conclusions

The literature review shows the main issues experienced by this patient population are pain, losses in many domains (mobility, independency, active lifestyle, productivity, social relationships) and spillovers in family members. Perceived harm from infections and revisions seem to amplify all the issues experienced during the primary surgery. The impression from the focus group is that patients are in severe pain before the procedure, which affects their ability to make decisions regarding the implant, even when they are given the opportunity. It seems there is an understanding that not all the new technologies are necessarily better and there is a great deal of trust in the surgeons to make that choice. However, patients do have questions on the specifics of the implants and related post-surgical consequences. On the very limited number of patients spoken to, there may be opportunities for better information, education and follow-up. Patients seem to value physiotherapy and see it potentially as a decisive factor for their surgical outcomes.

Chapter 3: Physician Input

Summary of Physician Input

The initial scope of this health technology assessment (HTA) was very comprehensive, capturing most of the outcomes described by the surgeons. Auxiliary outcomes and focus on early revisions were included in the review. Considerations about early revisions and need for ceramic-on-ceramic revisions were included in the economic analysis plan.

3.1 Objective

To verify that all the relevant outcomes are included when comparing different types of total hip replacement and that relevant comparators for local clinical practice are included in the evaluation.

3.2 Methods

Six BC surgeons were contacted by email or telephone and invited to provide feedback on the project scope. The Health Technology Review (HTR) process in BC was explained to the surgeons, and a draft of the project scope was sent by email. Feedback was anonymized with no personally identifiable information included. A summary of the discussion was circulated by email to participants as a feedback check for accuracy on their views/responses. Three surgeons returned some feedback either by email or over the phone. Two surgeons practice in the Greater Vancouver area and one on Vancouver Island.

3.3 Summary of surgeons' input

The surgeons made several key points in response to the request for information. First, to focus on the rates of early revision to capture any difference between the bearings caused by pseudotumours, since all the implants can show natural wear over time (>10-15 years). Pseudotumour is quite a recent finding in this field but, ultimately, monitoring early revision rates would capture their effects on patients. Second, in terms of outcomes included in the initial scope they suggested to include squeaking and fractures related to the ceramic type implants. Third, as the term pseudotumour is quite recent in the literature, to enhance the search strategies for studies on these outcomes should include the terms *"adverse local soft-tissue reaction (ALSTR)" or "fluid collections"* as they might have been described in the past. Fourth, when looking at the evidence on ceramic, it was noted to be aware that some types of ceramic were discontinued and therefore mixing data from older ceramics with newer ones might confuse the results.

Important points for implementation of technology monitoring is to also look at the difference in metal between stems and heads, and the size of metal heads being utilized. It might be that in implants with some metal in the stems and heads, or the use of small metal heads, corrosion and pseudotumours might not be a problem.

3.4 Conclusions

The scope of this HTA was comprehensive including most of the important outcomes when evaluating these technologies. A few of other auxiliary outcomes were added to the data extraction form as suggested by the specialists, such as squeaking and early revisions. In addition, the search strategies for pseudotumour were complemented with "adverse local soft-tissue reaction (ALSTR)" and "fluid collections." The considerations about early revisions and need for ceramic-on-ceramic revision implants were included in the economic analysis.

Chapter 4: Jurisdictional Scan

Summary of Jurisdictional Scan

Eight Canadian jurisdictions responded to the request for information. No written policy limiting the use of different types of bearing surfaces was found and for the most part the choice of implant is made by physicians.

4.1 Objectives

To outline policies from across Canada on the publicly funded types of total hip implants.

4.2 Methods

An environmental scan of hip implants policies and regulations in the Canadian provinces and territories was conducted through communication with the appropriate contact person for each jurisdiction. The communication was done by the BC Ministry of Health. There were two main questions of interest: [1] Which types of hip implants are being publicly funded, and [2] Is there any written policy regulating or limiting the utilization of any specific hip implants. The results were gathered by the HTR office and incorporated into this report.

4.3 Results

Eight Provinces provided details in response to the request (Alberta, Manitoba, Nova Scotia, Northwest Territories, Prince Edward Island, Yukon, Ontario and Newfoundland and Labrador). None of them have a written policy restricting public coverage to any specific implant. Manitoba, Prince Edward Island, Nova Scotia, Northwest Territories and Newfoundland and Labrador confirmed that all different types of implants are being covered. Alberta leaves the choice of implant to the physician with input from Alberta Health Services (AHS) as to whether the type of prosthesis used is considered an enhanced good for the patient’s medical condition. In the Northwest Territories the most commonly used are metal-on-poly and oxinium-on-poly.

Yukon residents usually undergo THR in BC or Alberta, and their coverage follows the coverage rules in the province providing services. Ontario could not provide any input because the decision on the implants is made at the hospital level.

4.4 Conclusions

There is no policy within the respondent jurisdictions limiting the coverage of specific types of implants. In jurisdictions covered in this review it would seem the choice of implant relies primarily on physician judgment. Input from the more populated Provinces (Quebec and Ontario) could have led to further insight on current practice.

Chapter 5: Assessment of Evidence

Summary of Evidence

No significant differences between all the bearing surfaces were found in revision rates, functional scores or quality of life when data from only crosslinked polyethylene liner was used in the analysis. The only studies showing significant differences in revision rates combined data from conventional polyethylene liners, which is proven to have worse outcomes and drove the results in favour of the ceramic implants.

Ceramic-on-ceramic, when compared to metal-on-poly, showed lower risk of osteolysis, implant dislocation, and aseptic loosening. However, ceramic-on-ceramic showed higher risk of squeaking and implant fracture when compared to both metal-on-poly and ceramic-on-poly.

All levels of evidence (systematic reviews of randomized control trials (RCTs), direct comparison from RCTs and network meta-analysis of RCTs) are consistent in their results comparing the four bearing surfaces, and the risk of revision analysis between them remains such that no implant can be claimed superior at this time. . The probability rank analysis (SUCRA) does not mean ceramic-on-crosslinked poly was significantly better than other bearing surfaces but has the highest probability to be the best intervention in terms of risk of revision given the existing available evidence (ceramic on poly 0.84 vs metal on poly 0.58, out of 1).

Economic analysis in the UK context showed ceramic-on-poly was more cost-effective for patients <65 years, and metal-on-poly for those >65 years. In the UK context the costs of ceramic-on-poly implants are considerably lower than the metal-on-poly implant. All THR types were very similar in terms of QALY gains causing the cost-effectiveness to be very sensitive to small differences in the cost of implants.

The evidence available for Oxinium-on-poly implant was insufficient to support any robust conclusion.

5.1 Objectives

To assess the evidence on safety, effectiveness, and cost-effectiveness of the different hip implants (metal-on-poly, ceramic-on-poly, ceramic-on-ceramic, oxinium-on-poly) for primary total hip replacement.

5.2 Methods

5.2.1 Inclusion criteria

Table 3 defines the patient population, inclusion criteria and outcomes of interest.

Table 3 Inclusion criteria

Patient population	Intervention	Appropriate comparators	Outcomes
Patients of any age who are eligible to receive THR (unilateral or bilateral) due to any condition	Bearing surfaces – • metal-on-poly (XL) • ceramic-on-poly (XL) • ceramic-on-ceramic • oxinium -on-poly (XL)	The interventions compared to each other	Clinical outcomes • Mortality • All-cause revision ○ First 5-year revision rate • Functional score (ie, HHS) • Quality of life • Patient experience and satisfaction • Complications (ie, pseudotumours, aseptic loosening, infection, fractures, dislocation etc.)
			Economic outcomes • Resource use (hospital admissions, readmissions, LOS) • Cost (devices, procedure, revision) • Utility measures • ICERs, WTP, CEAC
Legend - CEAC: cost-effectiveness acceptability curves; HHS: Harris hip score; ICER: incremental cost-effectiveness ratio; THR: total hip replacement; LOS: length-of-stay; XL: crosslinked polyethylene; WTP: willingness-to-pay.			

5.2.2 Exclusion criteria

Non-English-language publications; abstract/conference proceedings; letters and commentaries; quality of life reported without utilities or QALYs; hip/knee data not reported separately.

5.2.3 Literature search overview

Initial scoping searches were undertaken in Medline in May 2016 to assess the volume and type of literature relating to the objectives. These scoping searches also informed development of the final search strategies (Appendix B). An iterative procedure was used to develop these strategies based on previous HTA reports. The strategies were designed to capture generic terms for total hip replacement and systematic reviews. Searches were date-limited to the last 10 years. Published articles were identified using the search strategy in Medline and Embase via Ovid. Search results were imported into Endnote® and Microsoft® Excel for screening. The search is considered up to date as of July 14, 2016.

Systematic reviews and HTA reports in clinical effectiveness and economic analysis were screened. Randomized controlled trials were screened when the information from systematic reviews was insufficient or to update their searches. Systematic reviews for clinical effectiveness and economic analysis were separated from the main search result by search filters and screened separately. A complimentary search using filters for economic studies was performed to update the results from the most recent systematic review found, and to investigate other existing models used to compare the different implants.

5.2.4 Study selection and data extraction

One reviewer screened titles and abstracts according to a pre-specified protocol. A second reviewer confirmed the relevance of included studies. The study flow was summarized using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (Figure 2). Data was extracted into a standardized data extraction sheet (Appendix C). A reviewer extracted all the data for clinical outcomes, while another reviewer extracted all the data from economic analyses. Data were cross checked by the two reviewers for errors. Any discrepancy was resolved by discussion.

5.2.5 Quality assessment

The systematic review was critically appraised using an adapted Cochrane checklist for critical appraisal of systematic reviews (Appendix D). The cost-effectiveness studies with decision-analytic models were assessed by one reviewer using the criteria of Philips et al (12) to keep consistency across HTA reports.

For the purposes of this project, the 2011 hierarchy of evidence from the Centre of Evidence-based Medicine at University of Oxford (13) was adopted. First, systematic reviews of RCTs or observational studies with dramatic effect (level 1, the highest level) were searched. If the amount of evidence was deemed insufficient at this level, large-scale randomized trials (level 2) were included in the screening. If the amount of evidence was deemed insufficient at this level, then cohort studies were considered, such as a national registry (level 3). Lower levels evidence were considered hypothesis-generating and deemed insufficient for policy decision making.

5.2.6 Data synthesis

Cochrane Review Manager software, RevMan 5.3.5, was used to synthesize data for clinical outcomes using direct comparison. Dichotomous outcomes were analyzed by using risk ratio (RR) or odds ratio (OR). When a statistically significant RR or OR was found, risk difference (RD) and number needed to treat for the outcome (NNT) were calculated when possible. The results from economic studies were presented in descriptive tables.

A Bayesian network meta-analysis using netmetaXL based on the Markov chain Monte Carlo method in WinBUGS 1.4 was conducted. The OR and 95% credible interval were calculated. Random effects model was used only if significant heterogeneity was found in the analysis. Otherwise, all comparison used a fixed effects model. The code generated by netmetaXL, which then was implemented in WinBUGS, can be found in Appendix E.

In order to be included in the network meta-analysis, studies must have been published in or after 2006 and must have been an RCT, included patients receiving THR, and reported revision rate by bearing surfaces. Bearing surfaces used in the RCT could have been a certain type of prosthesis not included in the objectives, such as metal-on-metal or metal-on-conventional polyethylene. The list of included studies from the systematic reviews was primarily used for study selection. A search for RCTs published within the last year only was performed, as the most updated search from the systematic review was in May 2015.

Heterogeneity was assessed by using Chi^2 and I^2 statistics. NetmetaXL assesses inconsistency using an inconsistency plot. Please refer to Brown 2014 for detailed methods regarding statistics used in NetmetaXL (14).

5.2.7 Subgroup analysis

When possible, subgroup analysis included:

1. Sex
2. Age
3. Different head size (ie, <28mm vs 28 to 36 mm vs >36mm)
4. Different types of ceramics (ie, alumina vs mixed ceramics)
5. Different types of head and stem material (ie, cobalt-chromium head and stem vs cobalt-chromium head and titanium stem)

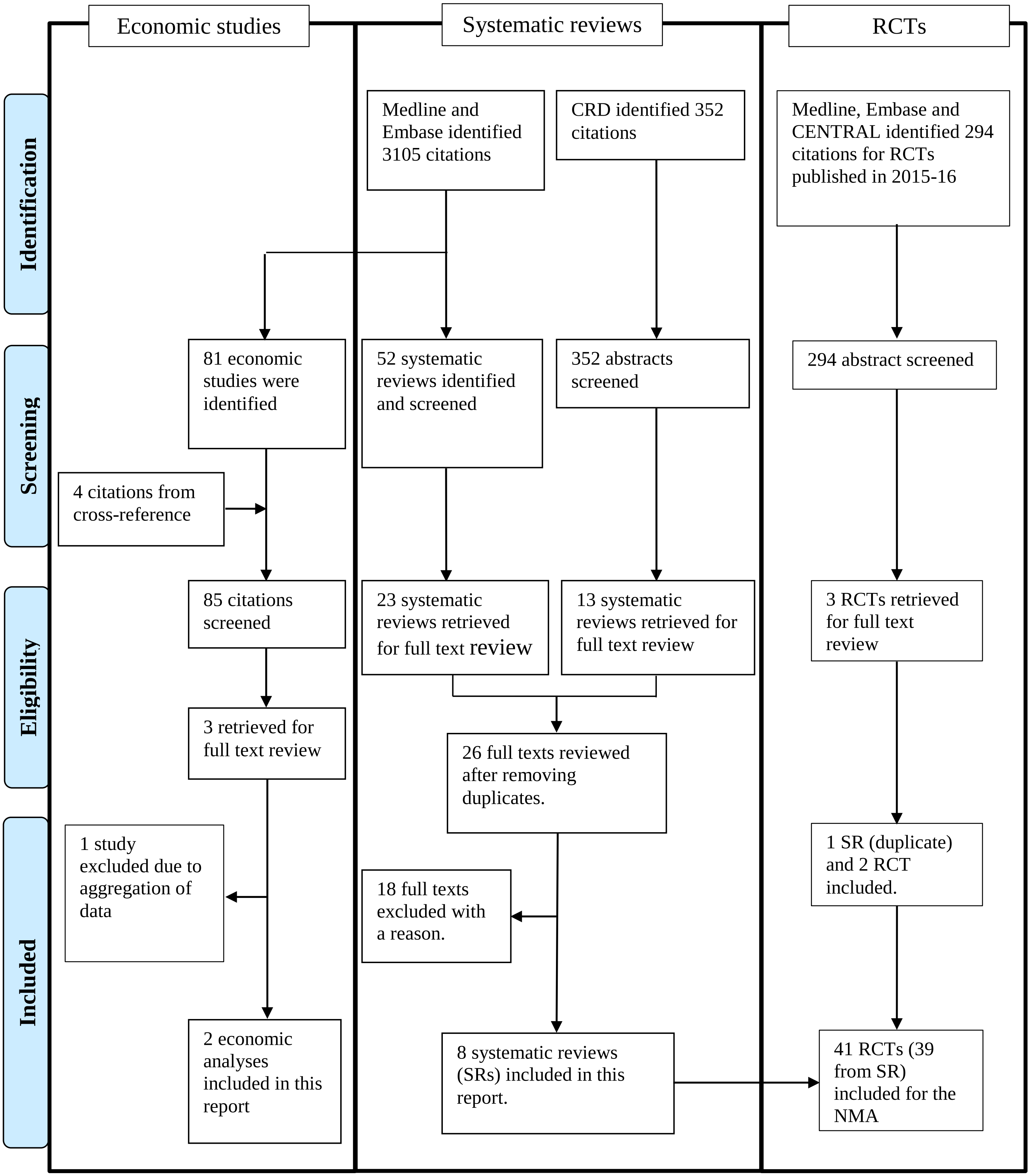
5.2.8 Search results

The detailed flow of study selection is presented in Figure 2. Medline and Embase identified 3,105 citations; after applying the filter for systematic reviews, 52 citations were screened. Of the 52 citations, 23 systematic reviews were retrieved for full text review. CRD identified an additional 352 citations, of which 13 were retrieved for full text review. After removing 10 duplicate publications, 26 full texts were reviewed and eight were included in this report. After filtering, Medline and Embase identified 81 citations as economic studies. With four additional citations from other HTA and systematic reviews, 85 citations were identified. After screening, 82 citations were excluded and three were retrieved for full text review. Two economic analyses were included.

A search filter for RCT was applied to Medline and Embase. In addition, RCTs were searched for in CENTRAL. The three databases found 294 citations from 2015 to 2016. Three articles were retrieved for detail reading. One of the articles was a systematic review already included through the search for systematic reviews. The other two RCTs were added to the analysis.

Two orthopedic surgeons suggested additional 17 citations to be considered. The references and descriptions are listed in Appendix F.

Figure 2: PRISMA diagram



5.3 Clinical effectiveness

5.3.1 Description of included studies

All of the included systematic reviews were reviews of RCTs with comparisons of the bearing surfaces. They included at least two of the bearing surfaces of interest in this report. Some of the reviews combined data from conventional polyethylene and crosslinked polyethylene in their analysis. The most updated search in the included systematic review was run in May 2015. All the systematic reviews reported revision rate as one of their outcomes. Functional scores and complications were reported in some of the reviews. Number of total participants in the reviews ranged from 897 (5 RCTs) to 5,321(40 RCTs). Mean duration of follow-up (if reported) ranged from 6.6 years to 8.4 years. Further details on the individual systematic review are presented in Appendix G. Additional screening was carried out for RCTs published from May 2015 to July 14, 2016.

5.3.2 Description of excluded studies

A list of citations excluded at full text screening and the reason for exclusion is located in Appendix H. The main reasons for exclusion were that the citation was either a conference abstract of a systematic review, or a narrative review.

5.3.3 Quality assessment

The quality of included studies was assessed using a modified version of the Cochrane collaboration checklist for systematic review. The overall quality of included systematic reviews was good with low risk of bias in multiple categories. Please refer to Appendix D for the detailed assessment of systematic reviews. Two reviews, CADTH 2013 and Si 2015 had higher risk of bias in search strategy and data collection. However, these two reviews only contributed a small amount of data to the analysis and did not affect the conclusion (15, 16). Imprecision of estimates due to low event rates of complications in some results might raise concerns. However, this had more to do with the quality of the included RCTs than the quality of the systematic reviews.

5.3.4 Effect of intervention

5.3.4.1 Results from systematic reviews of RCTs

Eight systematic reviews of RCTs were included. The number of RCTs included in these systematic reviews ranged from five RCTs to forty RCTs depending on the breadth of the research question. There were overlaps of RCTs included in these systematic reviews. However, not all RCTs included in these systematic reviews examined the bearing surfaces of interested. Outcomes reported in the included systematic reviews were all-cause revision, functional score (ie, Harris Hip Score), quality of life, and complications. Mortality, patient satisfaction, and some of the complication (ie, pseudotumours) were not reported in any of the systematic reviews. Detailed descriptions of each included systematic review can be found in Appendix G.

5.3.4.2 Revisions

All eight systematic reviews reported overall revision rate. Two provided results from both direct comparison and network meta-analysis (17, 18). Results of each included systematic review are summarized in Table 4, Hu 2015b found significant difference in revision rate between ceramic-on-poly and metal-on-poly (19). However, most of the significant effect was contributed by studies using non-crosslinked poly (no longer commonly used in clinical practice). Other systematic reviews that examined crosslinked poly did not show any significant difference between the bearing surfaces.

Table 4 Revision rates

Study Reference and Type	Comparison # of RCT (# of patients)	Effect estimates (95% CI)	Notes
Wyles 2015(17) SR	CoC vs CoPxl 3 RCTs (n=556)	RR 0.65 (0.19, 2.23)	Direct comparison p=0.5, I-square=0%
	CoC vs MoPxl 2 RCTs (n=223)	OR 0.39 (0.06, 2.69)	Direct comparison p=0.34, I-square=0%
	CoPxl vs MoPxl Didn't report number of RCTs	RR 4.88 (95% CrI 0.05, 134.7)	Indirect comparison
Yin 2015(18) SR	CoC vs MoPxl 2 RCTs (n=223)	RR 0.45 (0.06, 3.42)	Direct comparison
	CoC vs CoPxl 4 RCTs (n=666)	RR 0.71 (0.26, 1.92)	Direct comparison
	CoPxl vs MoPxl 3 RCTs (n=212)	RR 1.57 (0.31, 7.98)	Direct comparison
NHS 2015(20, 21) SR	CoC vs MoPc‡ 1 RCT (n=328)	5 year follow-up: RR 0.35 (0.12 to 1.00) 5-10 year follow-up: RR 0.38 (0.10 to 1.39)	p=0.045 p=0.08 (RCT mixed crosslinked poly and conventional poly in comparison)
	CoC vs CoPxl‡ 1 RCT (n=357)	5 year follow-up RR 3.01 (0.85 to 10.61)	p = 0.06 (RCT mixed crosslinked poly and conventional poly in comparison)
	Ceramicised metal head vs Metal (CoCr) head 1 RCT (n=100)	2 year follow-up RR 1.00 (0.06 to 15.50)	RCT did not report information on the type of cup surface.
Hu 2015(22) SR	CoC vs CoP 9 RCT (n=1747)	RR 0.95 (0.54, 1.68)	RCT mixed crosslinked poly and conventional poly in comparison
Hu 2015b(19) **SR**	**CoC vs MoP** **5 RCT (n=586)**	**RR 0.39 (0.2, 0.76)**	**p = 0.006** **RCT mixed crosslinked poly and conventional poly in comparison**

Study Reference and Type	Comparison # of RCT (# of patients)	Effect estimates (95% CI)	Notes
Dong 2015(23) SR	CoC vs CoP 8 RCTs (n=1,600)	RR 0.99 (0.54, 1.83)	RCT mixed crosslinked poly and conventional poly in comparison
CADTH 2013(15) SR	CoC vs CoPxl vs MoPxl 1 SR	See note	The only SR included did not conduct meta-analysis of trials as they varied in method. One RCT in the SR reported significant differences between CoC and MoP in revision (10/165 vs. 6/349). However, this trial likely included both conventional and crosslinked poly. All other comparisons did not find any significant difference.
Si 2015(16) SR	CoC vs CoP 5 RCTs (n=813)	RR 1.28 (0.6, 2.75)	RCTs mixed crosslinked poly and conventional poly in comparison.

Footnote:
‡The NHS report did not specify the type of poly used in this comparison. The type of poly was confirmed by reading the original publication of the included RCT.

95% CI: 95% confidence interval; CoC: ceramic-on-ceramic; CoP: ceramic on polyethylene (data combined conventional and crosslinked poly); CoPc: ceramic-on-conventional polyethylene; CoPxl: ceramic on polyethylene; MoP: metal-on-polyethylene (data combined conventional and crosslinked poly); MoPc: metal on conventional polyethylene; MoPxl: metal-on-crosslinked polyethylene; RCT: randomized controlled trial; OR: odds ratio; RR: risk ratio; SR: systematic review.
Studies in bold font contain statistically significant result.

5.3.4.3 Functional scores

Three systematic reviews reported functional score. Dong 2015 discussed functional score but did not report any number or meta-analysis regarding functional score (23). The results from the other two systematic reviews are listed in Table 5. None of the systematic reviews showed significant difference between the bearing surfaces in functional scores.

Table 5: Functional scores

Study Reference and Type	Comparison # of RCT (# of patients)	Effect estimates (SD)	Notes
NHS 2015(20, 21) SR	CMoPxl vs MoPxl 2 years f/up, 1 RCT	HHS: 92 (SD NR) vs. 92.5 (SD NR)	p = 0.159
	CoC vs. MoPc‡ 5 years f/up, 1 RCT 10 years f/up, 1 RCT	HHS: 96.4 (SD NR) vs. 97.0 (SD NR) 96.7 (SD NR) vs. 96.4 (SD NR)	p > 0.05 p > 0.05
	CoC vs. CoPxl‡ 5 years 1 RCT	HHS score NR	p > 0.05
	SoPc vs. CoCr-on-Pc vs. Ceramicised metal head -on-Pc vs. CoCr-on-Pxl vs. Ceramicised metal head -on-Pxl 2 years 1 RCT	HHS: 91 (10.8) vs. 91 (8.5) vs. 91(11.1) vs. 93 (11.3) vs. 88(9.5)	p = 0.7; ANOVA-based p = 0.5
	CMoPxl vs. MoPxl 2 years f/up, 1 RCT	Western Ontario and McMaster University Osteoarthritis Index 84.9 (SD NR) vs. 87.0 (SD NR)	p = 0.159
Hu 2015b(19)	CoC vs MoP 3 RCTs (n=475)	HHS: mean differences 0.82 [-0.24, 1.88]	P=0.13

Footnote:
‡The NHS report did not specify the type of poly used in this comparison. The type of poly was confirmed by reading the original publication of the included RCT.
95% CI: 95% confidence interval; CoC: ceramic-on-ceramic; CoCr: cobalt chrome head; CoP: ceramic on polyethylene (comparison combined conventional and crosslinked poly); CoPxl: ceramic-on-crosslinked polyethylene; f/up: follow-up; MoP: metal-on-polyethylene (comparison combined conventional and crosslinked polyethylene); MoPxl: metal-on-crosslinked polyethylene; CMoPxl: Ceramicised metal head on crosslinked polyethylene; NS: not statistically significant; OR: odds ratio; Pc: conventional polyethylene; Pxl: crosslinked polyethylene; RCT: randomized controlled trial; RR: risk ratio; SD NR: standard deviation not reported; SoPc: steal head-on-conventional polyethylene liner; SR: systematic review; HHS: Harris hip score.

5.3.4.4 **Quality of life**

One systematic review (NHS 2015 (20, 21)) reported quality of life data. SF-15 was used in the included RCT to examine quality of life. The SF-15 score was not significantly different when comparing ceramic-on-ceramic to ceramic-on-poly at 5-year follow-up or oxinium head to Cobalt-chromium head at two year follow-up. Quality of life was not reported for other comparisons.

5.3.4.5 **Complications**

Five systematic reviews (16, 19-23) reported various kinds of complications. The most commonly reported complications were implant dislocation, aseptic loosening, and osteolysis. The results from complications are summarized in Table 6. One systematic review showed significant difference that favour steel-on-poly, metal-on-poly and oxinium-on-poly. Both metal-on-poly and oxinium-on-poly groups used crosslinked poly in this comparison. The analysis showed ceramic-on-ceramic had a lower risk of implant dislocation, aseptic loosening and osteolysis when compared to metal-on-poly. However, these reviews included both crosslinked and non-crosslinked poly in the analysis. The result from crosslinked poly alone might not show similar results. In addition, ceramic-on-ceramic showed higher risk of squeaking and implant fracture when compared to both metal-on-poly and ceramic-on-poly.

Table 6 Complications

Outcomes	Study	Number of RCT (# of patients)	Effect estimates (95% CI)	Notes
Femoral head penetration	**NHS 2015(20, 21)**	**Steel-on-Pc vs. CoCr-on-Pc vs. CMoPc vs. CoCr-on-Pxl vs. CMoPxl 1 RCT**	**2 years follow-up (mm/year) 0.19 (0.16 to 0.23) vs. 0.40 (0.33 to 0.46) vs. 0.44 (0.37 to 0.51) vs. 0.19 (0.15 to 0.23) vs. 0.18 (0.13 to 0.22),**	**p < 0.001 (in favour of steel-on-Pc, ceramicised metal -on-Pxl and CoCr-on-Pxl)**

Infection	NHS 2015(20, 21)	CoC vs. CoPxl
		1 RCT
			5 years f/up, Superficial (n/N): 6/166 vs. 3/146, RR 1.75 (0.44 to 6.90)
			
			5 years f/up, Deep (n/N): 1/166 vs. 2/146, RR 0.43 (0.04 to 4.79)
				p = 0.357 (NS);
				
				p = 0.909 (NS);

		CMoPxl vs. MoPxl 1 RCT	2 years follow-up (n/N), 1/50 vs. 1/50, RR 1.00 (0.06 to 15.55),	p value NR
	Si 2015(16)	CoC vs CoP 4 RCTs (n=860)	>5 year follow-up RR 0.98 (0.27, 3.51)	p value NR
Implant dislocation	NHS 2015(20, 21)	CoC vs. CoPxl‡ 1 RCT	5 years follow-up (n/N), 10/166 vs. 9/146, RR 0.97 (0.40 to 2.33)	p = 0.672 (NS)
		CoC vs. MoPc‡ 1 RCT (low risk of bias)	10 years follow-up (n/N), 5/222 vs. 5/106, RR 0.47 (0.14 to 1.61),	p = 0.25 (NS)
		CMoPxl vs. MoPxl 1 RCT	2 years follow-up (n/N), 2/50 vs. 1/50, RR 2.00 (0.18 to 21.35)	p value NR
	Hu 2015(22)	CoC vs CoP 9 RCTs (N=1747)	RR 0.77 (0.47, 1.25)	p =0.29 RCT mixed crosslinked poly and conventional poly in comparison
	Hu 2015 b(19)	**CoC vs MoP 3 RCTs (N=586)**	**RR 0.23 (0.08, 0.67)**	**p=0.007, favour CoC RCT mixed crosslinked poly and conventional poly in comparison**
	Dong 2015(23)	CoC vs CoP 8 RCTs (N=1,692)	RR 0.73 (0.44, 1.19)	P=0.21 RCT mixed crosslinked poly and conventional poly in comparison
	Si 2015(16)	CoC vs CoP 7 RCTs (N=1,490)	RR 0.72 (0.43, 1.19)	RCT mixed crosslinked poly and conventional poly in comparison
Osteolysis	NHS 2015(20, 21)	CoC vs CoPxl‡ 1 RCT	5 years follow-up (n/N), 1/166 vs. 1/146 RR 0.87 (0.05 to 13.93)	p = 0.797
		CoC vs MoPc‡ 1 RCT	**10 years follow-up (n/N), 3/222 vs. 15/106, RR 0.10 (0.02 to 0.32)**	**p < 0.001 , favour CoC**

Outcomes	Study	Number of RCT (# of patients)	Effect estimates (95% CI)	Notes
	Hu 2015(22)	CoC vs CoP 7 RCTs (N=1,155)	RR 0.43 (0.11, 1.68)	p = 0.22 RCT mixed crosslinked poly and conventional poly in comparison
	Hu 2015 b(19)	**CoC vs MoP 5 RCTs (N=749)**	**RR 0.22 (0.14, 0.36)**	**p<0.00001, favour CoC RCT mixed crosslinked poly and conventional poly in comparison**
	Dong 2015(23)	CoC vs CoP 4 RCTs (N=636)	RR 0.39 (0.1, 1.56)	p=0.18 RCT mixed crosslinked poly and conventional poly in comparison
	Si 2015(16)	CoC vs CoP 4 RCTs (n=704)	RR 0.36 (0.08, 1.56)	RCT mixed crosslinked poly and conventional poly in comparison
Aseptic loosening	NHS 2015(20, 21)	Ceramicised metal femoral heads (oxinium) vs. CoCr femoral heads 1 RCT	2 years follow-up (n/N), 0/50 vs. 1/50 RR and 95% CI not estimated,	p value NR
	Hu 2015(22)	CoC vs CoP 6 RCTs (N=1,099)	RR 1.55 (0.59, 4.07)	p =0.38 RCT mixed crosslinked poly and conventional poly in comparison
	Hu 2015b(19)	**CoC vs MoP 4 RCTs (N=913)**	**RR 0.22 (0.07, 0.74)**	**p =0.01, favour CoC RCT mixed crosslinked poly and conventional poly in comparison**
	Dong 2015(23)	CoC vs CoP 7 RCTs (N=1,400)	RR 1.13 (0.48, 2.65)	p =0.79 RCT mixed crosslinked poly and conventional poly in comparison
	Si 2015(16)	CoC vs CoP 4 RCTs (n=919)	RR 0.74 (0.19, 2.86)	RCT mixed crosslinked poly and conventional poly in comparison
Deep-vein thrombosis	NHS 2015(20, 21)	CoC vs. CoPxl‡ 1 RCT	5 years follow-up (n/N), 3/166 vs. 2/146 RR 1.31 (0.22 to 7.78)	p = 0.909 (NS)

Outcomes	Study	Number of RCT (# of patients)	Effect estimates (95% CI)	Notes
	Si 2015(16)	CoC vs CoP 3 RCTs (n=970)	RR 0.96 (0.35, 2.65)	RCT mixed crosslinked poly and conventional poly in comparison
Squeaking	Hu 2015(22)	CoC vs CoP 5 RCTs (N=1033)	RR 8.07 (1.46, 44.49)	p =0.02 RCT mixed crosslinked poly and conventional poly in comparison
	Hu 2015b(19)	**CoC vs MoP 3 RCTs (N=690)**	**RR 8.27 (1.1, 62.16)**	**p =0.04 RCT mixed crosslinked poly and conventional poly in comparison**
	Dong 2015(23)	**CoC vs CoP 3 RCTs (N=670)**	**RR 14.73 (2.81, 77.17)**	**p=0.001 RCT mixed crosslinked poly and conventional poly in comparison**
	Si 2015(16)	**CoC vs CoP 3 RCTs (n=670)**	**RR 14.73 (2.81, 77.17)**	**RCT mixed crosslinked poly and conventional poly in comparison**
Implant fracture	Hu 2015(22)	CoC vs CoP intra: 4 RCTs (n=1234) post: 6 RCTs (N=1533) **Total implant fracture: 6 RCTs (n=1,533)**	RR 3.25 (0.69, 15.28) RR 3.54 (0.77, 16.33) **RR 5.1 (1.32, 19.71)**	p =0.14 p =0.11 **p =0.02 RCT mixed crosslinked poly and conventional poly in comparison**
	Hu 2015b(19)	**CoC vs MoP 3 RCTs (N=811)**	**RR 8.68 (1.12, 67.15)**	**p =0.04 RCT mixed crosslinked poly and conventional poly in comparison**
	Dong 2015(23)	**CoC vs CoP 5 RCTs (N=1,344)**	**RR 4.46 (1.16, 17.25)**	**p =0.03 RCT mixed crosslinked poly and conventional poly in comparison**
	Si 2015(16)	**CoC vs CoP 6 RCTs (n=1,814)**	**RR 6.02 (1.77, 20.51)**	**RCT mixed crosslinked poly and conventional poly in comparison**

Outcomes	Study	Number of RCT (# of patients)	Effect estimates (95% CI)	Notes
Footnote: ‡The NHS report did not specify the type of poly used in this comparison. The type of poly was confirmed by reading the original publication of the published RCT. 95% CI: 95% confidence interval; CoC: ceramic-on-ceramic; CoP: ceramic on polyethylene (comparison combined conventional and crosslinked poly); CoPxl: ceramic on polyethylene; f/up: follow-up; MoP: metal-on-polyethylene (comparison combined conventional and crosslinked poly); MoPxl: metal-on-crosslinked polyethylene; CMoPxl: Ceramicised metal head on crosslinked polyethylene; CMoPc**:** Ceramicised metal head on polyethylene (comparison combined conventional and crosslinked poly); NS: not statistically significant; OR: odds ratio; RCT: randomized controlled trial; RR: risk ratio; SD NR: standard deviation not reported; SR: systematic review. **Studies in bold contain significant results.**				

5.3.4.6 **Pseudotumours (adverse local tissue reaction)**

Pseudotumour or adverse local tissue reaction (ALTR) was not reported in any of the included systematic reviews. Most information in the literature regarding ALTR was related to metal-on-metal implants. No quantifiable data on the bearing surfaces of interest was found in the literature search. Following, summary of one RCT and one cohort study that examined the incidence of ALTR are presented.

One RCT that reported incidence of ALTR comparing metal-on-metal to metal-on-conventional poly was found (24). This RCT enrolled 50 patients receiving metal-on-metal and 55 patients receiving metal-on-conventional poly. Only 41 metal-on-metal patients returned for complete follow-up. ALTR was found by computer tomography in 22/41 (53.7%) patients that received metal-on-metal and 12/55 (21.8%) patients that received metal-on-conventional poly (RR 2.46 [1.38, 4.37], p=0.002). Three patients received revision in the metal-on-metal group and one received revision in the metal-on-conventional poly group (OR 3.38 [0.34, 33.64]). The authors did not report whether ATLR was the reason for the revisions.

Another cohort study conducted at Vancouver General Hospital examined the incidence of asymptomatic ALTR (25). In this study, thirty-one patients received metal-on-metal implants and twenty-four patients received metal-on-poly implants. After two years of follow-up, patients who received metal-on-metal had a significantly higher rate of ALTR (13/31) compared with metal-on-poly patients (3/24, $p = 0.015$). However, metal-on-metal is not a comparator in this HTA. Neither of the studies examined the differences in rate of revision between bearing surfaces due to ALTR.

5.3.4.7 Summary of findings from the systematic reviews

All of the included systematic reviews reported rate of revision for primary surgery. Most of the reviews did not show significant results between comparison groups (Table 4). Hu 2015b found that patients randomized to ceramic-on-ceramic had significantly fewer revisions compared to those randomized to metal-on-poly (19). However, the review included RCTs that used conventional polyethylene. NHS 2015 showed that the risk ratio for revision was significantly lower in patients that received crosslinked polyethylene liner compared to conventional polyethylene liner (RR 0.18 [95% CI 0.04 to 0.78], $p < 0.05$) (20, 21). Therefore, mixing the data from crosslinked and conventional cup liner might not be appropriate. Other systematic reviews that included only crosslinked polyethylene did not find significant differences in first revision rate between the bearing surfaces.

The most reported functional score was Harris Hip Score. There was no significant difference in any functional scores between the bearing surfaces (Table 5). There was no significant difference in quality of life between bearing surfaces.

Complications were reported in five of the included systematic reviews (Table 6). Prostheses with crosslinked liners showed significantly less wear compared to conventional liners based on femoral head penetration. Ceramic-on-ceramic showed lower risk of osteolysis when compared to metal-on-polyethylene in NHS 2015 and Hu 2015b (both $p<0.001$) (19-21).

Ceramic-on-ceramic prostheses showed lower risk of implant dislocation and aseptic loosening compared to metal-on-polyethylene in Hu 2015b (both $p<0.01$), which combined data from conventional and crosslinked liners, as mentioned previously (19). Ceramic-on-ceramic showed higher risk of squeaking and implant fracture compared to metal-on-poly and ceramic-on-poly in three systematic reviews (all $p <0.05$) which combined data from crosslinked and conventional polyethylene (16, 19, 23).

No systematic review was found examining pseudotumours in patients who received any of the three bearing surfaces in the objectives and inclusion criteria. Only two comparative studies, one RCT and one cohort study on pseudotumours were found, however, they compared metal-on-metal to metal-on-conventional poly and showed higher rates in the metal-on-metal arms.

5.3.5 Direct and indirect comparison of revision of primary hip replacement

Both direct comparison and network meta-analysis were conducted on revision of primary hip replacement. Any RCT from the systematic reviews that was published since 2006 were included, as well as any new published RCT from 2015 to present. In total, 12 RCTs (n=1826) were included in the direct comparison analysis and 41 RCTs (n=6100) were included in the network meta-analysis. The mean follow-up time of the RCTs was seven years, ranging from two to twelve years. Other patient demographic information was not reported in the systematic reviews.

5.3.5.1 Quality of included RCTs

The systematic reviews assessed the risk of bias for each of their included RCTs. Since most of the RCTs came from the systematic reviews, their prior assessment was taken into account when evaluating risk of bias in this analyses. Overall, the RCTs had adequate randomization (low risk of selection bias), low drop-out rate (low risk of attrition bias), and generally reported relevant outcomes (low risk of reporting bias). Some RCTs tried to blind the assessor and patients, but most of RCT did not have blinding. As such, the RCTs had high risk of detection bias and performance bias.

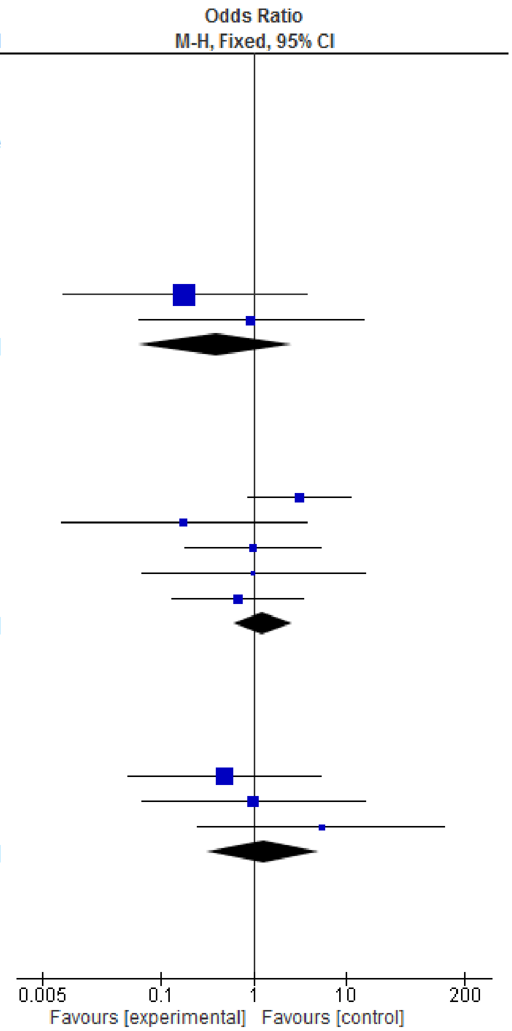
5.3.5.2 **Direct comparison**

The result from direct comparison is summarized in Figure 3. No significant difference in risk of revision was observed among different bearing surfaces in direct comparison. Effect estimate was not calculated for ceramic-on-crosslinked poly and metal-on-crosslinked poly comparisons due to the absence of the event. There was no significant heterogeneity in any of the comparisons.

Direct comparison was limited to four comparisons. There were no data comparing oxinium to other ceramic interventions. In addition, the confidence intervals were wide in two of the three estimates, possibly due to small sample size and absence of events.

Figure 3: Direct comparison of risk of revision between bearing surfaces.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.3.1 CoPxl v MoPxl						
Kawate 2009	0	32	0	30		Not estimable
Nakahara 2010	0	51	0	51		Not estimable
Subtotal (95% CI)		**83**		**81**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.3.2 CoC v MoPxl						
Bascarevic 2010	0	82	2	75	72.2%	0.18 [0.01, 3.77]
Nikolaou 2012	1	34	1	32	27.8%	0.94 [0.06, 15.68]
Subtotal (95% CI)		**116**		**107**	**100.0%**	**0.39 [0.06, 2.69]**
Total events	1		3			
Heterogeneity: Chi² = 0.63, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 0.96 (P = 0.34)						
1.3.3 CoC vs CoPxl						
Amanatullah 2011	11	196	3	161	24.5%	3.13 [0.86, 11.42]
Beaupre 2013	0	48	2	44	20.3%	0.18 [0.01, 3.75]
Hamilton 2010	4	177	2	87	20.7%	0.98 [0.18, 5.47]
Kim 2013	1	100	1	100	7.8%	1.00 [0.06, 16.21]
Lombardi 2010	3	65	3	45	26.7%	0.68 [0.13, 3.52]
Subtotal (95% CI)		**586**		**437**	**100.0%**	**1.27 [0.60, 2.66]**
Total events	19		11			
Heterogeneity: Chi² = 4.15, df = 4 (P = 0.39); I² = 4%						
Test for overall effect: Z = 0.62 (P = 0.53)						
1.3.4 CMoPxl vs MoPxl						
Jassim 2015	1	135	2	133	58.3%	0.49 [0.04, 5.46]
Lewis 2008	1	50	1	50	28.6%	1.00 [0.06, 16.44]
Morison 2014	2	24	0	24	13.1%	5.44 [0.25, 119.63]
Subtotal (95% CI)		**209**		**207**	**100.0%**	**1.29 [0.31, 5.26]**
Total events	4		3			
Heterogeneity: Chi² = 1.49, df = 2 (P = 0.48); I² = 0%						
Test for overall effect: Z = 0.35 (P = 0.73)						
Test for subgroup differences: Chi² = 1.29, df = 2 (P = 0.53), I² = 0%						



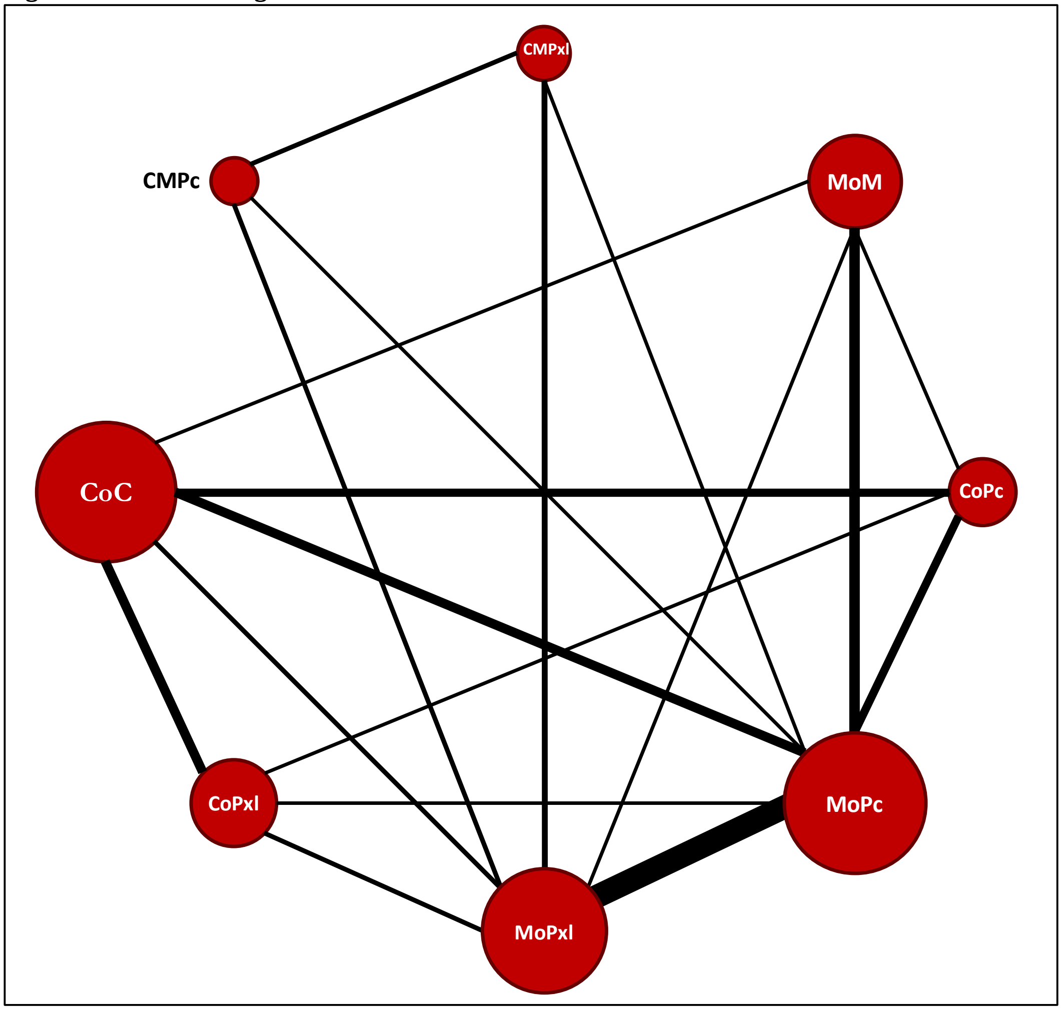
5.3.5.3 Indirect comparison

A network meta-analysis (NMA) was useful to this project by producing estimates for comparisons that had no direct comparison data or a narrower credible interval than the confidence interval in direct comparison. Since the direct comparison provided limited information, a network meta-analysis was conducted using 39 RCTS from the systematic reviews and two newly published RCTs found in the updated search. The 41 RCTs (n=6100) included in the NMA examined eight interventions leading to 28 possible pairwise comparisons. The quality assessment of the RCTs can be found in section 5.3.5.1.

The network diagram can be found in Figure 4. In the diagram, the width of the line is proportional to the number of RCTs included in the comparison and the size of the node is proportional to the number of patients randomized to that particular intervention. Table 7 summarizes the number of RCTs, patients and events in each bearing surface group.

Bearing surfaces that were not a part of the objectives were included to strengthen the network. As a result, a dynamic network was generated and is demonstrated by the spider web shape of the network diagram. The ceramic-on-ceramic group and metal-on-conventional poly group contained the largest sample size. Comparison between metal-on-conventional poly and metal-on-crosslink poly was the largest among the comparisons.

Figure 4: Network diagram.



CMPc: ceramicised metal-on-conventional poly; CMPxl:ceramicised metal-on-crosslinked poly; CoC: ceramic-on-ceramic; CoPc: ceramic-on-conventional poly; CoPxl: ceramic-on-crosslinked poly; MoM: metal-on-metal; MoPc: Metal-on-conventional poly; MoPxl: Metal-on-crosslinked poly.

Table 7: Characteristics of interventions

Treatment	# Studies	# Events	# Patients
CoC	15	42	1746
CoPxl	7	12	520
MoPxl	20	14	1083
MoPc	26	61	1490
CoPc	6	8	300
MoM	8	25	597
CMoPxl	3	4	209
CMoPc	2	3	155
CMoPc: ceramicised metal (oxinium)-on-conventional poly; CMoPxl: ceramicised metal (oxinium)-on-crosslinked poly; CoC: ceramic-on-ceramic; CoPc: ceramic-on-conventional poly; CoPxl: ceramic-on-crosslinked poly; MoM: metal-on-metal; MoPc: Metal-on-conventional poly; MoPxl: Metal-on-crosslinked poly.			

The effect estimates of revision risk and 95% credible intervals (95% CrI) can be found in Table 8. In the league table, an effect estimate smaller than one means the odds ratio favours the intervention listed on top of the column. If the 95% CrI does not cross the value of one, it indicates a statistically significant result. The most apparent advantage of the NMA was that it provided an estimate and 95% credible interval for comparison between ceramic-on-crosslinked poly and metal-on-crosslinked poly, which was not estimated in direct comparison. In addition, estimates between oxinium and other ceramic bearing surfaces were also calculated. Overall the 95% credible intervals in the NMA were narrower than the 95% confidence intervals in the direct comparison. However, none of the comparisons of interest was statistically significant.

Table 8: League table for the network meta-analysis

CoPxl							
0.87 (0.41 – 1.78)	**CoC**						
0.58 (0.20 – 1.65)	0.67 (0.30 – 1.53)	**MoPxl**					
0.56 (0.16 – 1.96)	0.65 (0.23 – 1.82)	0.97 (0.30 – 3.25)	**CoPc**				
0.47 (0.08 – 2.74)	0.54 (0.11 – 2.82)	0.81 (0.19 – 3.63)	0.84 (0.13 – 5.45)	**CMPxl**			
0.44 (0.07 – 3.15)	0.51 (0.09 – 3.26)	0.76 (0.16 – 4.37)	0.78 (0.11 – 6.12)	0.93 (0.17 – 5.65)	**CMPc**		
0.25 (0.10 – 0.61)	0.29 (0.16 – 0.50)	0.43 (0.22 – 0.82)	0.44 (0.15 – 1.20)	0.53 (0.11 – 2.42)	0.57 (0.09 – 2.85)	**MoPc**	
0.10 (0.03 – 0.32)	0.12 (0.05 – 0.29)	0.18 (0.06 – 0.47)	0.19 (0.06 – 0.56)	0.22 (0.04 – 1.18)	0.24 (0.03 – 1.41)	0.42 (0.19 – 0.87)	**MoM**

Note: Range in parenthesis is 95% credible interval. Point estimates smaller than one favour the interventions in the column.
CoPxl: ceramic-on-crosslinked poly; CoC: ceramic-on-ceramic; MoPxl: Metal-on-crosslinked poly; CoPc: ceramic-on-conventional poly; CMoPxl: ceramicised metal (oxinium)-on-crosslinked poly; CMPxl: ceramicised metal (oxinium)-on-crosslinked poly; CMPc: ceramicised metal (oxinium)-on-conventional poly; crosslinked poly MoM: metal-on-metal; MoPc: Metal-on-conventional poly;

Since the effect estimates were not statistically significant, a probability rank analysis provided useful information. Results from the probability rank analysis can be found in Figure 5 and Table 9. Ceramic-on-crosslinked poly achieved the highest rank according to surface under the cumulative rank curve (SUCRA) analysis, followed by ceramic-on-ceramic and then metal-on-crosslinked poly. Similarly, ceramic-on-crosslinked poly had the highest probability to be the best treatment on the rankogram. A rankogram is a graphic representation of the probabilities of which position an intervention will assume in a rank. For example, the probability of metal-on-crosslinked poly being ranked number one (best intervention) in the NMA was 0.0413, which was represented by the green section on the bar labeled one. Rankogram and SUCRA are useful tools to show the result of probability rank analysis.

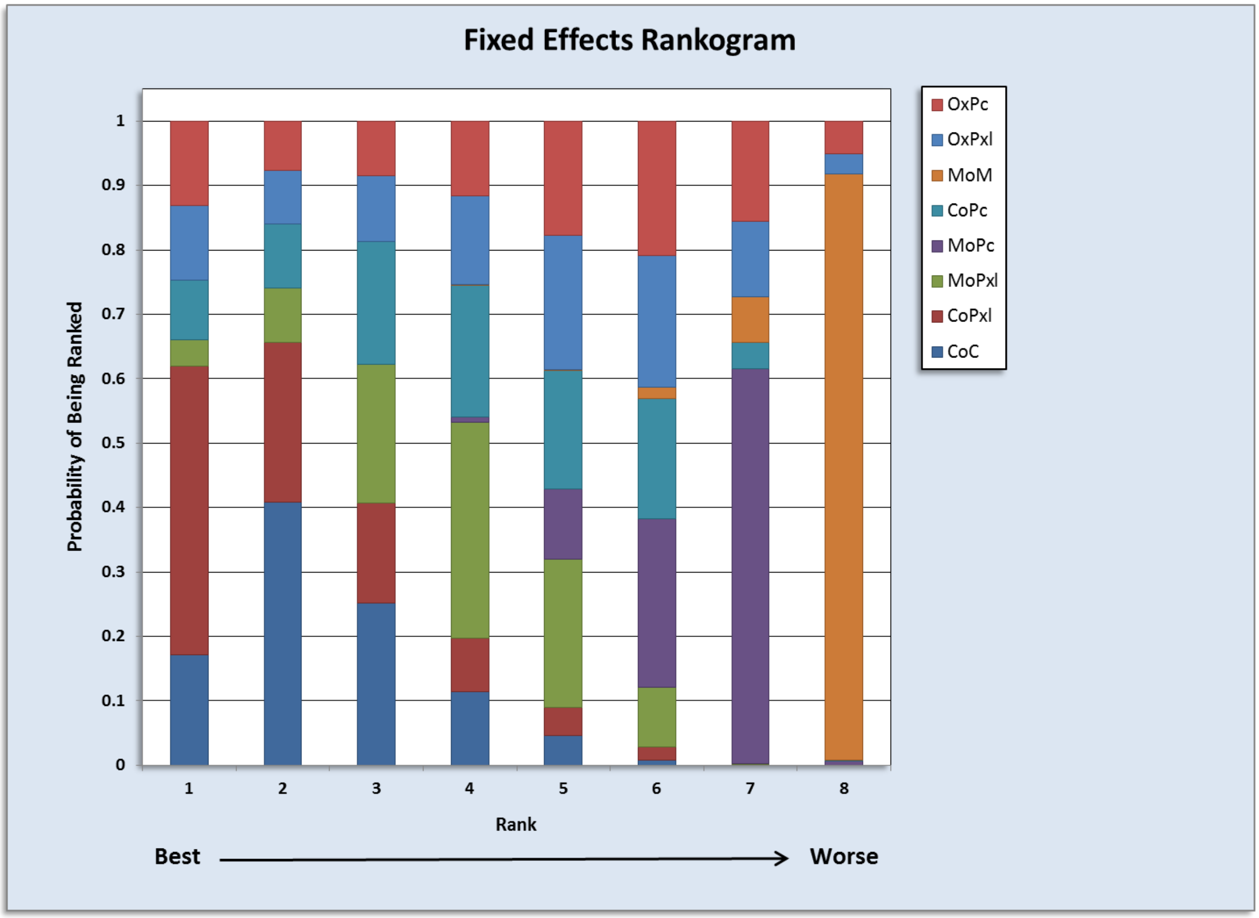
Probability rank analysis must be interpreted carefully because it is prone to bias. It should only be used as a supplement for effect estimate and should not replace the result of effect estimate. In this case, although ceramic-on-crosslinked poly received the highest rank, it did not mean that ceramic-on-crosslinked poly was significantly better than other bearing surface but it's most likely to be the best choice given the available evidence at the moment. The effect estimates remained not significant.

Table 9: SUCRA ranking

Treatment	SUCRA
CoPxl	0.8444
CoC	0.7886
MoPxl	0.5843
CoPc	0.5687
CMPxl	0.5036
CMPc	0.481
MoPc	0.2139
MoM	0.01565

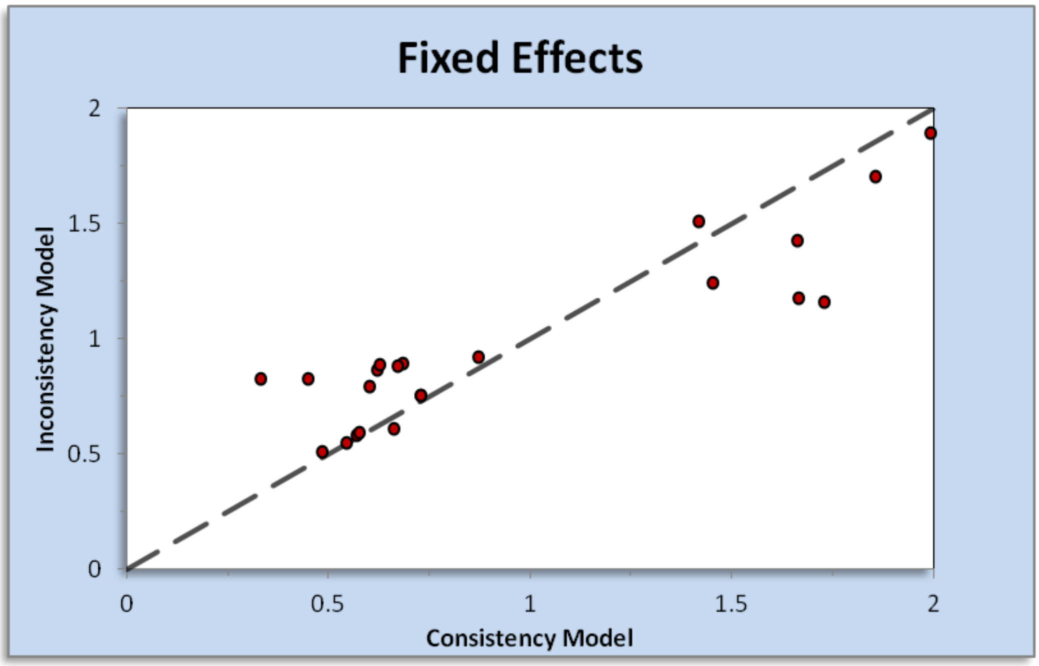
CoPxl: ceramic-on-crosslinked poly; CoC: ceramic-on-ceramic; MoPxl: Metal-on-crosslinked poly; CoPc: ceramic-on-conventional poly; CMoPxl: ceramicised metal (oxinium)-on-crosslinked poly; CMPxl: ceramicised metal (oxinium)-on-crosslinked poly; CMPc: ceramicised metal (oxinium)-on-conventional poly; crosslinked poly MoM: metal-on-metal; MoPc: Metal-on-conventional poly;

Figure 5: Rankogram



The result of the inconsistency analysis can be found in Figure 6. There was no significant inconsistency between direct and indirect comparison, which was demonstrated by the paucity of RCTs around the lower right corner of the inconsistency plot.

Figure 6: Inconsistency plot



5.3.6 Overall summary of clinical effectiveness

- Eight systematic reviews that included good quality RCTs did not show any statistically significant differences in rate of first revision between metal-on-poly, ceramic-on-poly and ceramic-on-ceramic. The direct comparison and network meta-analysis conducted by the HTA reviewers, which included forty one RCTs (n=6,100), showed similar results.
- Rate of first revision was not significant due to wide confidence interval in the comparisons. The confidence interval was wide because revision was a rare event. A

large sample size is required to show differences in rare events. The sample size in the systematic review and analyses was not large enough to find significant differences.

- Although all levels of evidence could not detect statistically significant differences between the implants, the average point estimates show some direction of the results in terms of first revision in the NMA [95% Crl]:
    - Ceramic-on-poly vs metal-on-crosslinked poly: odds ratio 0.58 [0.2, 1.65], favours ceramic-on-poly.
    - Ceramic-on-ceramic vs metal-on- crosslinked poly: odds ratio 0.67 [0.3, 1.53], favours ceramic-on-ceramic.
    - Ceramic-on-poly vs ceramic-on-ceramic: odds ratio 0.87 [0.41, 1.78], favours ceramic-on-poly.
    - Metal-on-crosslinked poly vs Oxinium-on-poly: odds ratio 0.81 [0.19, 3.63], favours metal-on-crosslinked poly.
    - The rankogram does not imply that ceramic-on-poly was significantly better than other bearing surface but pointed this implant as most likely to be the best choice given the available evidence at the moment.
    - If uncertainty is ignored, the point estimate trends toward favoring ceramic-on-poly. However, the 95% Crl suggests a large amount of imprecision that needs to be taken into account in the economic analysis and decision making for policy changes.
- There were no significant differences in functional scores or quality of life scores between the bearing surfaces.

- Ceramic-on-ceramic, when compared to metal-on-poly, showed lower risk of osteolysis, implant dislocation, and aseptic loosening. However, ceramic-on-ceramic showed higher risk of squeaking and implant fracture when compared to both metal-on-poly and ceramic-on-poly.

5.3.7 Limitations

The two most important outcomes (mortality and revision) were not statistically significant due to either lack of data (in the case of mortality) or the rarity of events (in the case of revision). Both outcomes are rare events which require large sample size to detect significant differences between bearing surfaces, which were not possible with the available sample sizes.

There was a concern that post-surgery treatment might be different between intervention groups, which could influence the rate of first revisions (risk of performance bias and detection bias) due to most of the studies not being double-blinded (blinding patients and outcome assessors can minimize bias, when is not possible to blind the surgeons). Early revision (revision within 5 years) was a relevant outcome as bearing surfaces that caused more complications were likely to cause more early revision. However, paucity of data did not allow the analysis of early revision. In addition, paucity of data also prevented any of the pre-specified subgroup analysis with RCTs.

All RCTs used generic names for the bearing surfaces in their publications. Insufficient data on specific brand was available from RCTs to allow individual analysis by brand. The Australian registry provided revision data for some of the most common brands used in Australia. However, unmatched, unadjusted registry data are prone to bias and must be interpreted with great caution. Registries are discussed in the next section.

5.4 Joint registry

5.4.1 Description of national joint registries

National joint registries have been an important source of information for joint replacement. Before the establishment of national joint registries, it was very difficult to determine the outcome prognosis of total hip replacements. In the last 10 years, the quality of data has made significant improvements in the two leading joint registries in the world. Both the National Joint Registry (NJR) of England and Wales and the Australian Orthopedic Association National Joint Replacement Registry (AOANJRR) are the gold standard of joint registries (26, 27). NJR contains 670,732 total hip replacement recipients followed for 11 years. AOANJRR contains 329,240 total hip replacement recipients followed for 14 years. The registries provide statistics for number of total hip replacements performed and number of revisions according to the primary bearing surfaces.

Although these national registries contained a much larger sample size than those included in the previous RCTs, no data was synthesized in the clinical effectiveness section because the annual reports only presented unmatched data, which is prone to various biases. Stand-alone, unadjusted data from national registries is not suitable evidence for policy making since there are multiple factors affecting those results. However, because the results synthesized in the clinical effectiveness analysis were limited by the amount and type of data available in RCTs, some data was extracted from these two registries to fill the gaps of information when running the economic model, and to compare with the evidence extracted from the RCTs.

5.4.2 Information synthesized from national registries

The information obtained from the two national registries is listed in the tables below. Were extracted data for 90-day mortality after primary surgery and after first revision (

Table 10), the yearly revision rate after primary surgery divided by bearing surfaces, age and sex (Table 11), and the cumulative rate of second revision according to the time of first revision (Table 12).

Table 10: 90-day mortality after primary and first revision in NJR

Outcomes	N	Cumulative rate (95% CI)
90-day mortality after primary surgery	704,274	0.49% (0.47, 0.5)
90-day mortality after first revision	70,696	1.31% (1.22, 1.44)

Table 11: Cumulative revision rate from national registries (NJR and AOANJRR)

Bearing surface	subgroups	n	1 year	3 years	5 years	7 years	10 years
MoP¥	Overall	104,028	1.08%	1.88%	2.42%	3.05%	4.40%
	Male <55	2,390	0.81%	2.19%	3.69%	5.41%	6.35%
	Male 55-64	8,564	0.98%	2.32%	3.11%	4.04%	6.22%
	Male 65-74	17,773	1.00%	1.83%	2.30%	3.03%	4.79%
	Male 75+	13,244	1.32%	2.07%	2.63%	3.16%	3.94%
	Female <55	3,031	1.38%	2.23%	3.00%	4.04%	5.33%
	Female 55-64	11,553	0.86%	1.93%	2.49%	3.16%	4.91%
	Female 65-74	25,627	1.00%	1.66%	2.09%	2.61%	3.40%
	Female 75+	21,785	1.26%	1.76%	2.25%	2.58%	3.53%
CoP¥	Overall	43,056	0.85%	1.56%	2.12%	2.59%	3.56%
	Male <55	2,850	1.20%	2.30%	3.51%	3.92%	4.50%
	Male 55-64	6,309	0.86%	1.63%	2.30%	2.68%	3.22%
	Male 65-74	7,085	0.68%	1.23%	1.42%	1.74%	2.44%
	Male 75+	2,421	1.23%	1.73%	2.20%	2.20%	2.78%
	Female <55	3,523	0.79%	1.44%	2.28%	3.26%	3.87%
	Female 55-64	8,124	0.73%	1.55%	2.28%	2.83%	4.45%
	Female 65-74	9,121	0.86%	1.55%	2.08%	2.64%	3.68%
	Female 75+	3,590	0.98%	1.64%	1.83%	2.22%	3.40%
CoC¥	Overall	93,873	0.95%	1.82%	2.46%	3.09%	4.22%
	Male <55	12,897	0.91%	2.23%	3.15%	4.18%	5.44%
	Male 55-64	16,326	0.94%	1.88%	2.69%	3.38%	4.63%
	Male 65-74	11,205	1.22%	1.93%	2.54%	3.07%	3.92%

	Male 75+	2,727	1.19%	2.11%	2.25%	2.25%	2.25%
	Female <55	14,811	0.75%	1.82%	2.52%	3.38%	5.37%
	Female 55-64	18,774	0.93%	1.66%	2.31%	2.79%	3.80%
	Female 65-74	13,521	0.81%	1.46%	1.78%	2.22%	2.50%
	Female 75+	3,566	1.49%	1.89%	2.02%	2.43%	2.43%
CMoPxl‡	Overall	14,016	1.50%	2.00%	2.30%	2.60%	3.30%
‡ Data in this category came from AOANJRR. ¥ Data in the category came from NJR. CMoPxl: ceramicised metal-on-crosslinked poly; CoC: ceramic-on-ceramic; CoP: ceramic-on-poly; MoP: metal-on-poly.							

Table 12: Cumulative rate of second revision according to time to first revision in NJR

Time when first revision took place	N	Cumulative risk of second revision at 1 year	Cumulative risk of second revision at 3 year
< 1 year after primary	5,189	6.24% (5.59-6.95)	11.55% (10.62-12.54)
1-3 years after primary	4,482	5.17% (4.54-5.88)	9.81% (8.90-10.79)
3-5 years after primary	3,651	4.59% (3.94-5.34)	8.50% (7.55-9.57)
5+ years after primary	4,594	3.83% (3.28-4.47)	6.79% (5.91-7.79)

During consultation with stakeholders, two specific types of stems (M/L Taper and Taperloc) currently in use with both metal and ceramic heads were mentioned as of interest for potential cost reduction. Table 13 summarizes the 3-year cumulative revision rates of the two stems from NJR and the odds ratio comparing M/L taper with Taperloc. Table 14 summarizes the 3-year cumulative revision rates of ceramic heads and metal heads on Taperloc stems and the odds ratio comparing them.

There was no significant difference in the 3-year cumulative revisions rate between M/L Taper and Taperloc stems. In addition, there was no significant difference in 3-year cumulative revisions rate between ceramic heads and metal heads on Taperloc stems. Taperloc has longer follow-up period (7 years) than M/L Taper (3 years) in the NJR.

Table 13 : Three-year cumulative number of revisions of hip replacements using Taperloc and M/L Taper stems in NJR, and calculated OR (regardless of bearing surface)

Outcome	Taperloc:	M/L Taper:	Calculated OR [95% CI]
# revisions/ # subjects (%)	247/15829 (1.56%)	45/2535 (1.77%)	0.88 [0.64, 1.2]

#: number.

Table 14 Three-year cumulative number of revisions of hip replacements using Taperloc by bearing surface, and calculated OR (regardless of bearing surface)

Outcome	CoP	MoP	Calculated OR [95% CI]
# revisions/ # subjects (%)	32/2675 (1.20%)	87/4881 (1.79%)	0.67 [0.44, 1.00]

#: number; M/L Taper did not have a minimum follow-up by bearing surface to be reported in the registry; MoP: metal-on-poly; CoP: ceramic on poly.

5.4.3 BC data from CIHI

Hip replacement data of BC was obtained from a collaboration with CIHI(9). The BC data had a much smaller sample size (n=43,064). The 3-year cumulative rate of revision for metal-on-poly in BC was similar to rates reported in NJR. However, the 3-year cumulative rates of revision in ceramic-on-ceramic, ceramic-on-poly and oxinium-on-poly were lower in BC compared with NJR. The differences could be the result of larger variation due to the smaller sample size. Table 15, Table 16, Table 17, Table 18, and Table 19 summarize the data obtained from CIHI.

Table 15: Total hip replacements, BC, 2010-11 to 2014-15 fiscal years.

Type of total hip	Metric	2010-11	2011-12	2012-13	2013-14	2014-15
Primary	Count	4,320	4,579	4,671	4,722	5,117
Revision	Count	470	519	505	514	511
Primary: Revision	Ratio	9:1	9:1	9:1	9:1	10:1

Source: Hospital Morbidity Database, BC, 2010–2011 to 2014–2015, Canadian Institute for Health Information.

Table 16: Risk of first revision (any) for primary total hip replacements by sex, BC, 2010–11 to 2014–15.

Sex	1-year risk of revision	2-year risk of revision	3-year risk of revision
Males	1.54%	1.94%	2.15%
Females	1.40%	1.72%	2.06%
All	**1.46%**	**1.82%**	**2.10%**

Source: Hospital Morbidity Database, BC, 2010–2011 to 2014–2015, Canadian Institute for Health Information.

Table 17: Risk of first revision (any) of primary total hip replacements by age group, BC, 2010–11 to 2014–15.

Age group	1-year risk of revision	2-year risk of revision	3-year risk of revision
<41	0.77%	1.01%	1.08%
41–50	1.78%	1.55%	2.21%
51–60	1.20%	1.51%	1.96%
61–70	1.43%	1.97%	2.39%
71–80	1.38%	1.79%	1.81%
80+	2.09%	2.25%	2.35%
All	**1.46%**	**1.82%**	**2.10%**

Source: Hospital Morbidity Database, BC, 2010–2011 to 2014–2015, Canadian Institute for Health Information.

Table 18: Proportion of total primary hip replacements (all diagnoses), by bearing surface, BC, 2012-13 to 2014-15.

Bearing Surface	2012-13	2013-14	2014-15
Metal/Metal	2.0%	1.1%	1.0%
Metal/XLPE	86.2%	84.6%	84.1%
Metal/Non-XLPE	1.5%	0.7%	0.2%
Ceramic/Ceramic	4.8%	4.1%	2.9%
Ceramic/XLPE	4.7%	7.6%	8.7%
Ceramic/Non-XLPE	<0.1%	0.0%	0.0%
Ceramic/Metal	0.3%	0.1	0.2%
Ceramicized metal/XLPE	0.4%	<0.1%	0.2%
Ceramicized metal/Non-	0.0%	0.0%	0.0%
Other	0.1%	1.8%	2.8%

Notes : XLPE – crosslinked polyethylene; Bearing surface information was available for 12,722 (97.8%) of total hip replacements submitted to CJRR for BC; The coverage rate for CJRR in BC for any hip replacements for fiscal years between 2012-13 and 2014-2015 was 72.5%, 94.1% and 95.0%, respectively.
Source: Canadian Joint Replacement Registry, BC, 2012–2013 to 2014–2015, Canadian Institute for Health Information.

Table 19 Proportion of revised total primary hip replacements for females and males (all diagnoses) by bearing surface and age, 2012-13 to 2014-15 combined.

	Cementless Metal/ XLPE (MoP)	Ceramic/ Ceramic (CoC)	Ceramic/ Polyethylene (CoP)	Ceramicized metal/ XLPE (HyMoP)
Sex: Female				
Age: <41	0.0281	0.0114	0.0135	0.0000
41–50	0.0170	0.0125	0.0041	0.0137
51–60	0.0097	0.0110	0.0102	0.0070
61–70	0.0177	0.0074	0.0118	0.0174
71–80	0.0189	0.0588	0.0142	0.0000
80+	0.0227	0.0000	0.0303	0.0000
Total	0.0178	0.0112	0.0107	0.0112
Sex: Male				
Age: <41	0.0209	0.0110	0.0396	0.0000
41–50	0.0188	0.0110	0.0000	0.0000
51–60	0.0186	0.0143	0.0093	0.0000
61–70	0.0142	0.0040	0.0110	0.0088
71–80	0.0174	0.0000	0.0098	0.0000
80+	0.0278	0.0000	0.0000	0.0000
Total	0.0177	0.0111	0.0097	0.0025
Overall total (male and female)	0.0178	0.0112	0.0102	0.0067

N = 43,064.

Note: Cementless – fixation method for prosthesis designed to be used without cement. XLPE – crosslinked polyethylene; Polyethylene – includes both crosslinked (XLPE) and non-crosslinked (non-XLPE), unless otherwise noted.

Sources: Canadian Joint Replacement Registry, BC, MB and ON, 2012–2013 to 2014–2015, Canadian Institute for Health Information; Hospital Morbidity Database, 2010–2011 to 2014–2015, Canadian Institute for Health Information.

Despite this observational data being prone to various types of bias, when comparing ceramic-on-poly with metal-on-poly using the 3-year cumulative number of revisions from BC data the OR for risk of first revision is 0.57 [95% CrI 0.41, 0.78]. The mean estimate is very similar to the OR found in the NMA (0.58 [95% CrI 0.20, 1.65]).

5.5 Literature review of cost-effectiveness data

5.5.1 Description of included studies

A systematic review of economic studies with cost-effectiveness analysis was retrieved (28). The review comprised a high quality full HTA conducted by the National Institute for Health and Care Excellence (NICE) in the UK. It included 10 studies comparing different techniques and types of THR, published from 2002 to 2012 (details in Appendix J). Eight of the included studies were based on decision-analytic models (29-36); however, only two studies provided relevant data on model framework, costs and utilities (30, 34) to support the economic evaluation carried by NICE (28). NICE also carried out their own economic evaluation to compare cost-effectiveness of five types of THR to each other (described below), and provided subgroup results by age and gender. Later, another study derived from the same UK model was published reporting only the results for the elderly population (37).

Five most common types of THR implants used in the United Kingdom (UK):

A. **CeMoP**: Metal head (cemented stem) on cemented polyethylene cup;
B. **CeLMoP**: Metal head (cementless stem) on cementless hydroxyapatite-coated metal cup (polyethylene liner);
C. **CeLCoC**: Ceramic head (cementless stem) on cementless hydroxyapatite-coated metal cup (ceramic liner);
D. **HyMoP**: Hybrid metal head (cemented stem) on cementless hydroxyapatite-coated metal cup (polyethylene liner);
E. **CeCoP**: ceramic head (cemented stem) on cemented polyethylene cup.

The costs were calculated (in UK pounds) for prosthesis, surgery (excluding prosthesis), hospital admission, successful primary THR, revision surgery and successful revision surgery. The primary outcomes were measured as QALYs using EQ-5D-3L. A Markov model was stipulated for 10 years, and lifetime horizon applying discount rate at 3.5% to both costs and outcomes. The incremental cost per QALY gained was reported on willingness-to-pay (WTP) thresholds of £20,000/QALY.

5.5.1 Description of excluded studies

The remaining economic studies were excluded primarily because they conducted partial economic evaluation and/or analyzed other techniques (i.e. resurfacing, different bearing surfaces in an aggregate form, focused on implant fixation other than the bearings) (29, 31-33, 35, 36).

5.5.2 Quality assessment

The studies were critically appraised for quality and completeness using an adapted checklist from Philips et al for economic models, and the standard Cochrane checklist for systematic review(12). The systematic review was evaluated as good quality with clear research questions and a thorough search. However, it was not appropriate to combine the results of the included studies due to different comparators and outcomes in the primary studies. Having said that, the quality of the individual included economic models was good. Model characteristics such as model design/structure, cycle length, and perspective of analysis, time horizon, and discount rates were clearly stated. Data sources were appropriately selected and/or supported with relevant literature. The tables on critical appraisal of systematic review and economic studies can be found in Appendix I and Appendix J.

5.5.3 Results of the review of cost-effectiveness

Findings from two of the included economic studies (28, 37) from the same model are elaborated as a single cost-effectiveness analysis in order to simplify results for subgroups. The main model inputs are described in Table 20 to allow interpretation of generalizability of the results.

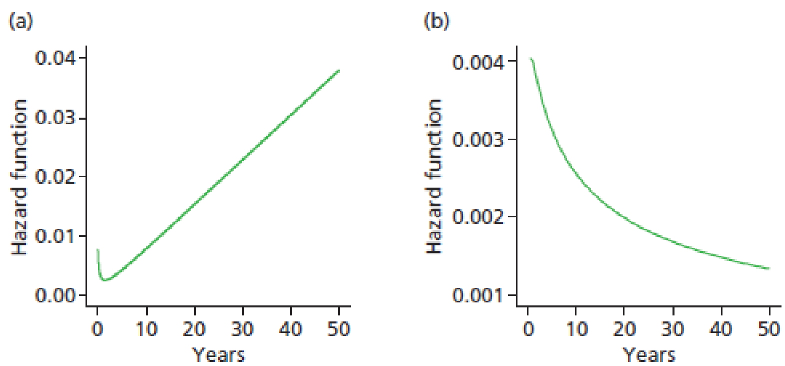
Table 20: Model Inputs for the UK HTA comparing different types of THR

Inputs	Mean value	SE	Distribution		Source
Transition probabilities					
Surgical mortality	0.0050	0.001			NJR(38)
Risk of re-revision	0.0326	NA			DePuy submission(20, 28)
			Beta distribution		
Utilities			**alpha**	**beta**	
Age 50–60 years	0.7529	0.004	1296	488	PROMs(39)
Age 60–70 years	0.7789	0.002	7397	2427	
Age 70–80 years	0.7637	0.002	22,244	6315	
Age 80+ years	0.7210	0.003	28,054	8681	
Revision surgery	0.5624	0.340	9092	3518	
Costs (£)			**Gamma distribution**		
Different types of prosthesis			**alpha**	**beta**	
Category A – CeMoP	1557	NA	NA	NA	NHS Supply Chain(20, 28)
Category B – CeLMoP	3017	NA	NA	NA	
Category C – CeLCoC	3869	NA	NA	NA	
Category D –HyMoP	2650	NA	NA	NA	
Category E – CeCoP	1996	NA	NA	NA	
Other costs (£)					
Surgery costs (excluding prosthesis)	1485	NA	NA	NA	Vale et al.(36)
Hospital inpatient stay	1687	NA	NA	NA	Edlin et al.(40)
Successful primary THR	394	30	169	2	Edlin et al.(40)
Revision surgery	16,517	456	1314	13	Vanhegan et al.(41)
Successful revision surgery	394	30	169	2	Edlin et al.(40)

The most relevant assumptions from this model are as follows: the risk of re-revision was considered constant regardless of when the first revision occurred); surgical mortalities for primary and revision surgeries were assumed to be the same; and the cost of revision surgeries was assumed to be the same regardless of the primary implant.

For extrapolation of revision rates beyond the observed data (9-10 years), this model used the bathtub hazard functions for people <65 years, which assumes an increase in revision rates after 5 years predicting the natural wear and tear of the implant components. For people >65 years, lognormal hazard function was applied assuming a decrease in revision rates over time predicting the natural relative lack of clinical imperative to undertake revision, in a situation where an extrapolation with an increasing hazard becomes less appropriate (example in Figure 7)

Figure 7 Example of a bathtub hazard functions (a) and lognormal hazard functions (b) predicting risk of revision



Both the deterministic and probabilistic analysis revealed age and gender differences in costs and QALYs associated with various THR types. The findings were robust to sensitivity analysis. The key findings from a probabilistic analysis of the multi-state Markov model for a lifetime horizon are summarized in Table 21.

The probabilistic estimates from a lifetime analysis suggested ceramic-on-poly as the most cost-effective strategy for men and women <65 years (i.e. incurred least cost and generated more QALYs) compared to all other THR types. The probability of ceramic-on-poly being cost-effective was 97% at WTP of £20,000/QALY (28). On the other hand, for men and women >65 years, the mean cost for metal-on-poly was slightly lowered and resulted in more QALYs gained. The probability of metal-on-poly being cost-effective in this population was 100% at WTP of £20,000/QALY.(37). As one can observe from Table 21, the differences in QALY gains between total hip replacement types were small (<0.01 QALY), which leaves the cost-effectiveness estimates very sensitive to small differences in costs. Additionally, the model estimates were sensitive to the discount rates, and to the choice of model for extrapolation of revision rates beyond the observed data. In sensitivity analysis, applying lognormal distributions to all age groups favored ceramic-on-poly in all groups compared to the other types; however, the differences in QALY gains were still under 0.01 QALYs.

Table 21: Probabilistic estimates based on lifetime horizon

Age groups	Men					Women				
	CeMoP	CeLMoP	CeLCoC	HyMoP	CeCoP	CeMoP	CeLMoP	CeLCoC	HyMoP	CeCoP
40 Years										
QALY	16.6662	16.657	16.6646	16.6577	16.6651	7.1843	7.1881	7.189	7.1916	7.1954
Cost (£)	18,556	21,877	21,304	21,069	19,587	10,502	11,630	12,405	10,967	9,983
50 Years										
QALY	48.8108	14.8041	14.8085	14.8074	14.8124	7.3355	7.3371	7.3368	7.3393	7.3426
Cost (£)	15,626	19,032	18,581	17,608	16,071	10,049	11,384	12,253	10,849	9,936
60 Years										
QALY	12.2174	12.2128	12.2155	12.2155	12.2188	7.4075	7.4072	7.4061	7.4077	7.41111
Cost (£)	12,957	16,029	15,831	14,617	13,113	9,673	11,147	12,075	10,749	9,849
70 Years										
QALY	8.9914	8.991	8.9907	8.9913	8.9915	9.4341	9.4313	9.4313	9.4314	9.4315
Cost (£)	10,099	11,732	12,778	11,243	10,485	10,363	12,168	13,006	11,708	10,919
80 Years										
QALY	5.6873	5.6868	5.6864	5.6873	5.6872	6.0579	6.0581	6.058	6.0582	6.0581
Cost (£)	8,395	10,133	11,164	9,508	8,866	8,690	10,356	11,205	9,774	8,995
Overall (Men and women of all ages)										
QALY	14.7881	14.7856	14.7849	14.7878	14.7935	-				
Cost (£)	14,834	16,801	17,972	15,976	13,954					

CeCoP: Ceramic-on- all poly cup (cemented stem, cemented cup).
CeLCoC: Ceramic-on-ceramic (cementless stem, cementless metal cup);
CeLMoP: Metal-on-crosslinked poly liner (cementless stem, cementless metal cup);
CeMoP: Metal-on-crosslinked all poly cup (cemented stem, cemented cup);
HyMoP: Metal-on-crosslinked poly liner (cemented stem, cementless metal cup);

The NICE report included other modeling studies that contributed to model framework and cost parameters of their own model, but the results were deemed not relevant for the bearing surface comparison and are not mentioned in this report (cemented fixation vs cementless fixation vs hybrid fixation) (30, 34).

5.5.4 Overall summary of cost-effectiveness and discussion

Cost-effectiveness analysis of certain total hip replacement types appeared to demonstrate some benefit over others. Ceramic-on-poly was more effective (superior in <0.01 QALY) and dominated all other total hip replacement types for men and women younger than 65 years. However, for men and women older than 65 years, metal-on-poly remained the cost-effective choice.

All total hip replacement types were similar in terms of QALY gains (in 10 years or in a lifetime) causing the cost-effectiveness ratios to be very sensitive to small differences in the implant cost or gains in QALY. In the UK, the cost of the ceramic-on-poly implants are lower than the cementless metal-on-poly implants (~£1,000), which is the reverse scenario compared to BC. Therefore, an analysis with local costs of the implants is required to verify if the same dominance situation and differences in QALY gains between implants remain.

Chapter 6: Economic Analysis for British Columbia

Summary of Economic Analysis for BC

QALY counts and number of revisions over a 20-year period are similar for all four types of implants. Given the similarities and high degree of parameter uncertainty around revision rates and cost estimates, it is difficult to recommend one type of device over another based solely on cost-effectiveness.

The best available evidence suggests that ceramic-on-poly has the highest expected value of benefit at the current prices and is likely to be the most cost-effective option. However, cost-effectiveness estimates are very sensitive to small differences in cost units. Further research on oxinium-on-poly implants is needed before making any robust conclusions about this type of implant.

6.1 Objectives

To evaluate the cost-effectiveness of the different types of total hip replacement (THR) for the BC population.

6.2 Methods

A decision-analytic model of THR outcomes was created to estimate the costs, health outcomes, and quality-adjusted life years (QALYs) associated with each implant type over a 20-year time horizon in British Columbia.

6.2.1 Target population and subgroups

BC population was estimated into 10 subgroups defined by age and sex. The identification of age groups (41 to 50, 51 to 60, 61 to 70, 71 to 80, 80+ years) was consistent with other published results to facilitate comparisons. The analysis was performed separately within each subgroup. Subgroup-specific results were weighted-averaged with weights being the prevalence of each subgroup in BC, to arrive at overall results for total hip replacement recipients in BC in 2014.

6.2.2 Setting and location

The public healthcare system in BC, covering the entire population of the province, in the reference year of 2014.

6.2.3 Study perspective

A publicly funded health system perspective was chosen. Out-of-pocket expenses and productivity loss were not included.

6.2.4 Comparators

Four types of implants were compared against each other: the current standard of care and three alternative primary implants included in the patient pay list in BC:

- Metal-on-poly (standard of care)
- Ceramic-on-poly
- Ceramic-on-ceramic
- Oxinium-on-poly (ceramicised metal head)

6.2.5 Time horizon

A 20-year time horizon was used in the base-case analysis. 10-year and lifetime time horizons were investigated in the sensitivity analyses.

6.2.6 Discount rate

A three-percent discount rate was applied to both costs and outcomes. Alternative values were explored in sensitivity analyses.

6.2.7 Choice of health outcomes

The main outcome of interest was quality-adjusted life years (QALY), which captures both the length and quality of life associated with each type of primary implant and the impact of corresponding revisions and complications. The secondary outcome of number of subsequent revisions was also examined, considering its clinical relevance and that it captures all causes of implant failure requiring new surgery (e.g., pseudotumour, osteolysis, dislocations, implant fractures, or other causes).

6.2.8 Model structure

After evaluating other published economic models comparing hip implants (28, 37, 42-45), a new Markov model was created to improve on the previous models in an important aspect: to accommodates the time dependency of revisions and re-revisions; this is necessary to take into account the differences between the technologies in early revision rates that is also correlated with the their difference in the timing of subsequent revisions (Figure 8). Each red rectangle represents a surgical event and each blue circle represents a mutually exclusive health state. In this model, the time shifts one year at a time in each cycle and each patient can be at only one health states in any given cycle. No half-cycle correction was applied.

At baseline, the patient receives the primary surgery and immediately moves to the post-surgery state (PP). Patients stay in PP until they either require the first revision or die. A patient who undergoes the first revision surgery (R1) moves to one of the six post-first revision (PR1) tunnel states (PR1.1.1 to PR1.6+.1). The tunnel states model the variable time between primary surgery and the first revision, which previous studies have suggested is a strong predictor of the time between the first and second revisions (27). Patients who survive the first year after revision enter a second set of tunnel states (PR1.1.2 to PR1.6+.2) that separate the first, second, and third and subsequent years after the first revision. This second set of tunnel states was modeled to accommodate the time-dependent risk of second and subsequent revisions. Patients remain in any given tunnel state only for one year. Patients may experience subsequent revisions, or may die at any time in the model, according to the background risk of death or due to the complications of the primary surgery or any of the revisions.

6.2.9 Parameter sources and assumptions

Input parameters from the model came from a mix of data from the literature review in Chapter 5 as well as data gathered from CIHI and health authorities to tailor the cost-effectiveness analysis to the BC context. Two other Canadian models in arthroplasty were used to complement other input parameters with relevant Canadian data (46, 47). Although these models do not compare bearing surfaces, they provided parameter estimates for costs of complications and follow-up after any THR.

6.2.9.1 The effectiveness of technologies

The rate of revisions associated with each implant type in the study is a key parameter in the cost-effectiveness results. The literature and the approaches undertaken by other modeling studies were evaluated. The largest source of data for inference on revision rates is the UK registry (27). However, because the registry data is observational, the comparative revision rates may be substantially confounded by other factors that motivate patients and care providers to choose a particular bearing surface. Therefore, evidence from randomized controlled trials was utilized to estimate the comparative revision rates, defined as the odds ratio (OR) of revision between any of the technologies and the reference technology (metal-on-poly). The registry data were used to estimate the revision rate of the reference technology and to derive the shape of the hazard function (i.e., rate of revision as a function of time since the primary surgery) associated with each implant. This approach resulted in the following steps:

Step 1: Reproducing survival curves for risk of first revisions by bearing surface

The shapes of the survival curves (risk of first revision) from the 2012 UK registry (metal-on-poly, ceramic-on-poly, ceramic-on-ceramic) and the 2015 Australian registry (oxinium-on-poly) (26, 27) were reproduced. The UK registry has the largest sample size (n= 670,732), long follow-up, and an analysis of the best distribution fit with extrapolation (28). The Australian registry includes the oxinium-on-poly bearing surface, which is not reported separately in the UK registry. The oxinium-on-poly cohort reported in this registry was 14,016 patients with 10 years of follow-up.

In the UK registry, the bathtub hazard function provided the best fit to reproduce survival curves for the hazard of first revisions in patients younger than 65 years, and a lognormal hazard function for patients over 65 years. The distribution parameters published in the UK and Australian registries were used to recreate the shape of the survival curves, adjusted for age (28). Parameters for the subgroup of females aged 40, 50, 60 in the metal-on-poly arm were not published in the UK registry. To determine the shape of the survival curve for those females, the corresponding function from the male subgroup was used and calibrated to reproduce the 10-year revision rate observed among females in the UK registry.

For oxinium-on-poly, the revision rates published in the Australian registry was used to create a survival curve assuming a lognormal distribution for patients over 65 years. The primary data from this registry were not available to conduct a distribution fit analysis or recreate the bathtub hazard function for patients younger than 65 years. For this subgroup, the same shape of survival curve as the ceramic-on-poly arm from the UK Registry was assumed.

Step 2: Calibrating the curves to the reference technology (metal-on-poly) rates of first revision

All survival curves, regardless of implant type or distribution assumed, were calibrated to reproduce the same 10-year revision rates for the metal-on-poly arm published in the 2015 UK registry (27). This way, the survival curves of each bearing surface maintained their original shape for time to revision, but were brought to the same revision rates over 10 years so that the ORs of revisions identified in the systematic review of the literature could be applied.

Step 3: Applying relative rate of revision for different implant types from the review of randomized controlled trials

First, the evidence from the direct comparison of RCTs, estimated through meta-analysis (section 5.3.5.2) was assessed. The total sample sizes for many comparisons were very small, resulting in confidence intervals that were too wide. Then, the ORs from the indirect comparisons estimated through a network meta-analysis (NMA, Table 8) comparing all alternative hip implants to metal-on-poly was chosen. NMA enables the propagation of evidence across the entire network of comparators and results in consistent estimates of treatment effect (e.g., if OR= 0.74 for Technology 1 versus Technology 2, and OR= 0.89 for Technology 2 versus Technology 3, then OR= 0.74*0.89 for Technology 1 versus Technology 3; this is not necessarily the case in conventional meta-analysis).

The OR of first revisions was applied to the calibrated survival curves, simulating the differences between the implant types in the time for first revision.

6.2.9.2 Re-revisions

Two sets of parameters were used for re-revisions: probability of second revision and probability of further revisions. Probability of second revision was calculated using the cumulative rates published in the 2015 UK registry. This probability depended on the time of first revision for the first three years (Table 12) and was constant afterwards (27). Probability of further revisions was extracted from the UK HTA and assumed to be constant. These probabilities were applied in the model regardless of types of implant, sex, and age groups (28).

6.2.9.3 **Mortality**

Surgical mortality after primary and revision surgery was calculated from the UK registry data (

Table 10) (27). Mortality from other causes was extracted from Canadian life tables for BC (2008-2010) published by Statistics Canada (48).

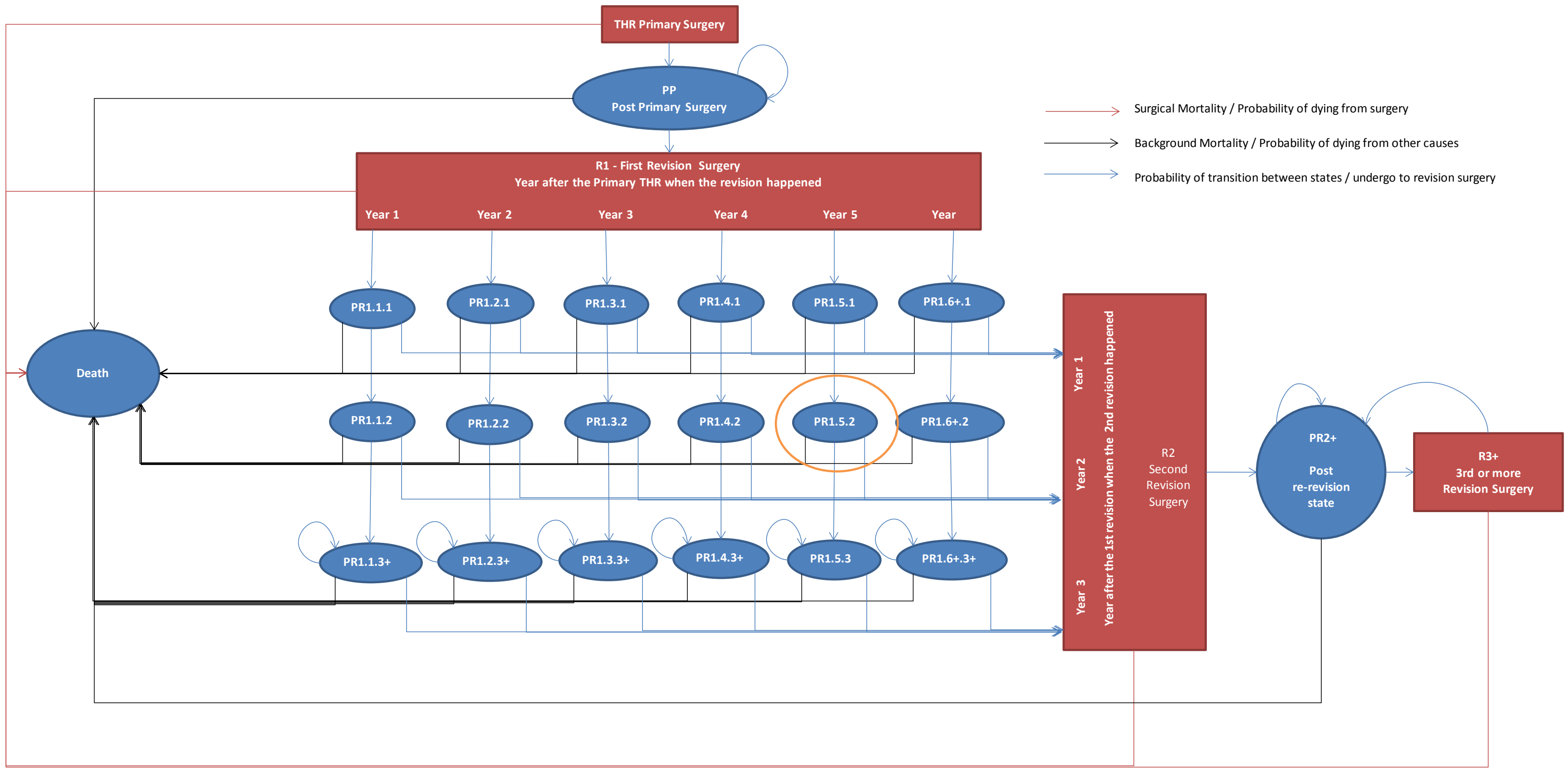
6.2.9.4 **Complications**

Rates of non-surgical complications were reported in Canadian trials and applied in the model after every surgery (primary or revision) (47).

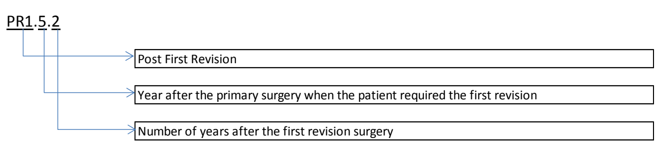
6.2.9.5 **Utilities**

The utility values (by age and sex) for the post-primary state, post-revision state, and revision surgery decrement (disutility) reported in the UK HTA (28) were used. These values were calculated from two patient-reported outcome measures (PROMs) datasets from patients who had a THR (total sample size more than 240,000) and used EQ-5D scores. Utility decrements for complications after primary and revision surgeries were calculated from the utility values published by Heintzbergen et al., 2013 (47), measured in two Canadian trials carried out in Alberta (total sample size more than 1,300).

Figure 8. Markov model structure



Example of how to interprete the tunnel states: If in state 1.5.2, it means that patient had the first revision 5 years after the primary surgery, survived, and is in the second year after the first revision surgery. From this state, this patient can die from natural causes, OR go to the second revision surgery, OR move to state 1.5.3+ (which means he survived another year without requiring another revision).



Notes: the red rectangles represent surgical events; the blue circles represent 1-year health states; light blue circles represent tunnels states and patients remain in those for only 1 year.

6.2.9.6 **Costs**

The cost of the various primary hip implants was calculated from the BC Clinical and Support Services (BCCSS) database (49). BCCSS provided the history of implant purchases in BC from February 2015 to January 2016. There was no patient-level information to provide the exact cost per person, so the weighted price for each type of implant was based on a series of assumptions to build each implant construct: 1. categorize all implant parts by generic names with consultation with the vendors (acetabular components, femoral components, ceramic heads, metal heads, etc.); 2. determine the weighted price per component per vendor; 3. calculate the weighted price of the primary total implant constructs (per type and per vendor); 4. validated costs based on BCCSS information.

Hospital cost of primary surgeries was extracted from the CIHI patient cost estimator (BC fiscal year 2014) and adjusted to exclude the cost of the primary implants. Physician costs were calculated from the MSP fee schedule, operative time from a public guide from Ontario, and volumes of the different types of revision surgeries, using expert opinion associated with CIHI data about replaced parts in revision surgeries in Canada (50-53).

Cost of revision surgeries was also extracted from the CIHI patient cost estimator. First, the weighted average price for revision surgery was calculated, adjusting for age group and surgeries with infection from the reported volumes for the province. Then, this cost was adjusted to incorporate incremental cost of revision implants depending on the type of primary implant, to account for the need for ceramic-on-ceramic revision implants for patients whose primary implants have ceramic components (as pointed out during physician consultation in Chapter 3). The incremental cost of revision implants was calculated as the cost difference between primary implants. Patients receiving oxinium-on-poly as the primary were assumed to receive the same oxinium-on-poly implants, if revision occurred.

Healthcare costs associated with the first year after THR surgery (primary or revision), non-surgical major complications, or follow-ups after the first year post surgeries were assumed to be the same in every arm of the model, regardless of the primary implant. The cost of first year after THR surgery and non-surgical major complications were extracted from the Alberta THR model (47) and the follow-ups from a CADTH THR model (46).

6.2.9.7 Weighted population for cost-effectiveness

To produce an overall estimate of cost-effectiveness for BC, the cohort of patients modeled in the base-case analysis was weighted by the age and sex distribution of all hip replacement recipients in Canada in 2013–2014, published by CIHI in the 2015 CJRR report (1).

6.2.10 Currency, price date, and conversion

All costs were inflated to 2015 Canadian dollars using the annual health and personal care Consumer Price Index for BC (54).

6.2.11 Analytic methods

For the base-case analysis, a single set of outcomes were calculated for each technology by weighted-averaging outcomes within each subgroup. Weights represented the age distribution of patients who underwent total hip implant surgery in BC in 2014. Base-case results and all subgroup-specific results were calculated from a deterministic analysis. A probabilistic analysis was performed with 10,000 iterations to evaluate the degree of uncertainty in the base-case results. Results of the probabilistic analysis are reported as the cost-effectiveness plane and the cost-effectiveness acceptability curve. For the probabilistic analysis, probability distributions were assigned to each uncertain model parameter:

- Beta distributions for probabilities (e.g., risk of complications) and utilities (and utility decrements). Normal distribution was assigned for probability of surgical mortality and further revisions. For the probability of further revisions an arbitrary 0.25 coefficient of variance was used to the probability of third or further revisions, due to lack of evidence on the variance of this parameter in the literature.
- Normal distribution operative time (in estimating Medical Services Plan (MSP) fees).
- Gamma distributions for all cost parameters.

The price of primary implants was not assumed to be uncertain, because price is subject to negotiation. Univariate deterministic sensitivity analyses were conducted to evaluate the effect of changes in key assumptions on the results. Higher incremental prices of revision implants, alternative discounting values (0% and 5%), variations of the OR of first revision, and changes in the price of the primary implants were evaluated.

In determining the most efficient scenarios, the efficiency frontier approach was used. The scenario with the lowest ICER compared with the standard of care (metal-on-poly) was identified (55). This scenario then became the default scenario to identify the next-best scenario (the one with the lowest ICER). This iterative process stopped when no scenario with a positive ICER could be identified.

6.2.12 Study parameters

Table 22, Table 23, and Table 24 describe the study parameters used in the model.

Table 22. Model input for probability of first revision

Probability of First Revision							
Survival curves shape							
Age 40, 50, 60 years							
Male	**Hazard function**	**Alpha**	**Beta**	**Gamma**	**Age coeff**	**Calib coeff**	**Source**
Metal-on-poly	Bathtub	0.00104	0.02454	4.82273	-0.00247	0.87675	UK HTA (28)
Ceramic-on-poly	Bathtub	0.00047	0.00337	1.78261	-0.03277	11.81127	
Ceramic-on-ceramic	Bathtub	0.00062	0.02127	3.03246	-0.01108	1.71126	
Oxinium-on-poly	Bathtub	0.00018	0.01500	3.32721	0.00000	1.89705	
Female	**Hazard function**	**Alpha**	**Beta**	**Gamma**	**Age coeff**	**Calib coeff**	
Metal-on-poly	Bathtub	0.000833	0.019629	4.822729	-0.002468	0.860227	UK HTA (28)
Ceramic-on-poly	Bathtub	0.000470	0.007181	3.211915	-0.007823	2.252069	
Ceramic-on-ceramic	Bathtub	0.000615	0.021500	3.952961	-0.008873	1.269982	
Oxinium-on-poly	Bathtub	0.000180	0.015000	3.327210	0.000000	1.489596	
Age 70 and 80+ years							
Males	**Hazard function**	**Mu**	**Sigma**		**Age coeff**	**Calib coeff**	
Metal-on-poly	lognormal	10.52551	4.554688		-0.0483328	42.58022311	UK HTA (28)
Ceramic-on-poly	lognormal	10.54446	3.971899		-0.0407056	45.67192698	
Ceramic-on-ceramic	lognormal	9.611438	4.12394		-0.0448092	30.37791958	
Oxinium-on-poly	lognormal	11.0000	30		0	0.569720213	AUS Registry (26)
Females	**Hazard function**	**Mu**	**Sigma**		**Age coeff**	**Calib coeff**	
Metal-on-poly	lognormal	12.10535	5.138115	-0.024137	7.8705	12.10535	UK HTA(28)
Ceramic-on-poly	lognormal	10.1304	3.562737	0.063183	0.0333	10.1304	
Ceramic-on-ceramic	lognormal	11.4710	4.744101	-0.028743	11.2723	11.4710	
Oxinium-on-poly	lognormal	11.0000	30	0	0.4434681	11.0000	AUS Registry(26)

2015 UK Registry 10-year cumulative revision rates for metal-on-poly as targets for calibration					
Males					**Source**
<55-64 years	0.0622				UK NJR(27)
>65 years	0.0443				
Females					
<55-64 years	0.0491				UK NJR(27)
>65 years	0.0346				
OR First Revision compared to metal-on-poly					
	Distribution	**Mean**	**95% CI**		**Source**
Metal-on-poly	*Reference*	-	**lb**	**ub**	
Ceramic-on-poly	lognormal	0.58	0.20	1.65	NMA 5.3.5.3
Ceramic-on-ceramic		0.67	0.30	1.53	
Oxinium-on-poly		1.23	0.28	5.26	

Note: age coeff: UK published age coefficients that are outputs from the stgenreg Stata package when calculating the bathtub hazard, which was then integrated to give cumulative hazard and survival curves. It adjust for patient age at the primary implant to patient ; calib coeff: calibration coefficient determined through model calibration to provide the metal-on-poly observed 10-year revision rate in the 2015 UK Registry, such that the ORs from the literature could be applied. Metal-on-poly group was also calibrated because the bathtub hazard parameters were calculated on data from the 2012 UK Registry; UK: United Kingdom; HTA: health technology assessment; AUS: Australian; NJR: national joint registry; NMA: network meta-analysis; OR: odds ratio; lb: low boundary; ub: upper boundary; CI: confidence interval

Table 23. Model input for probability of re-revisions

Probability of Second Revision									
		First year			Second year	Third year			
			95% CI		Average		95% CI		
		Mean	**lb**	**ub**	**Mean***	**Mean**	**lb**	**ub**	**Source**
If R1 in the 1year	lognormal	0.0624	0.0559	0.0695	0.0890	0.1155	0.1062	0.1254	UK NJR (27)
If R1 in the 2-3 years		0.0517	0.0454	0.0588	0.0749	0.0981	0.089	0.1079	
If R1 in the 3-5 years		0.0459	0.0394	0.0534	0.0655	0.085	0.0755	0.0957	
If R1 in the 5+ years		0.0383	0.0328	0.0447	0.0531	0.0679	0.0591	0.0779	
Probability of third+ Revisions		**Mean**	**SE**						
P(R3+)		0.01205	0.00815						DePuy submission, UK HTA (20, 28)

R1: first revision; P: probability; NJR: national joint registry; UK: United Kingdom; HTA: health technology assessment; lb: low boundary; ub: upper boundary; CI: confidence interval; *: calculated average between first year and third year; SE; standard error

Table 24 Model input for other parameters

Inputs	Distribution	Mean	SE	Parameters		Source
Transition probabilities				**alpha**	**beta**	
Surgical mortality – primary THR	Normal	0.0049	7.6530^{-5}			Calculated from NJR 2015(27)
Surgical mortality – revision	Normal	0.0131	5.6122^{-4}			Calculated from NJR 2015(27)
Post-operative complications(non-surgical)	Beta	0.01205	0.00691	3.0	245	Alberta THR model(47)
Utilities						
Post-Primary (PP) or Post-revision (PR) states						
Males		**Mean**	**SE**	**alpha**	**beta**	
Age 50–60 years	Beta	0.7360	0.0179	443.35	159.03	PROMs(39)
Age 60–70 years	Beta	0.7670	0.0066	3132.76	951.67	
Age 70–80 years	Beta	0.7920	0.0038	9112.12	2393.08	
Age 80+ years	Beta	0.7900	0.0034	11487.96	3053.76	

Inputs	Distribution	Mean	SE	Parameters		Source
Revision surgery	Beta	0.7450	0.0071	2816.14	963.91	
Females						
Age 50–60 years	Beta	0.7200	0.0129	871.75	339.02	PROMs(39)
Age 60–70 years	Beta	0.7420	0.0057	4333.77	1506.89	
Age 70–80 years	Beta	0.7690	0.0032	13128.34	3943.62	
Age 80+ years	Beta	0.7470	0.0029	16731.74	5666.84	
Revision surgery	Beta	0.7100	0.0048	6305.38	2575.44	
Disutility post-operative complications (non-surgical)		**Mean**	**SE**	**alpha**	**beta**	
Complications disutility after primary	Beta	0.132	0.177	0.3520	2.3145	Alberta THR model (47)
Complications disutility after revision	Beta	0.107	0.170	0.2474	2.0646	
Costs (2015 CAD$)		**Mean**		**alpha**	**beta**	
THR Primary Surgery						
Implants						
Metal-on-poly	-	confidential				BCCSS(49)
Ceramic-on-poly	-	confidential				
Ceramic-on-ceramic	-	confidential				
Oxinium-on-poly	-	confidential				
Other costs		**Mean**	**SE**	**alpha**	**beta**	
Surgery Costs + Hospital Stay (excluding implants/physician costs)	Gamma	6,454	1,613	16	403.38	CIHI Patient Cost Estimator (56) (adjusted to exclude implant cost)
Physician fees (surgery)		1,501				MSP schedule(52)
First year after surgery	Gamma	1,157	828	1.95	592.40	Alberta THR model(47)
Complications (non-surgical)	Gamma	6,948	4,562	2.32	2,995.37	
Follow-up (yearly)	Gamma	23	6	16	1.44	
Revision Surgery						

Inputs	Distribution	Mean	SE	Parameters		Source
Implants incremental cost depending on primary implant		**Mean**				
Metal-on-poly	-	-				BCCSS(49)
Ceramic-on-poly	-	confidential				
Ceramic-on-ceramic	-	confidential				
Oxinium-on-poly	-	confidential				
Other costs		**Mean**	**SE**	**alpha**	**beta**	
Revision surgery (includes implant + surgery + stay, excludes physicians)	Gamma	14,477	3,619	16	904.81	CIHI Patient Cost Estimator(56)
Physician fees (surgery)		3770				
First year after surgery	Gamma	1,157	828	1.95	592.40	
Complications (non-surgical)	Gamma	6,948	4,562	2.32	2,995.37	Alberta THR model(47)
Follow-up (yearly)	Gamma	23	6	16	1.44	CADTH THR model(46)
Operative Time for physician fees estimate (in minutes)		**Mean**	**SE**	**Range**		
				lb	**ub**	
Primary surgery	Normal	165	7.65	150	180	Mount Sinai Patient booklet(50)(Toronto)
Revision surgery	Normal	210	15.30	180	240	London health Science Centre (51)(Ontario)

THR: total hip replacement; NJR: national joint registry; sd; standard error; PROMs: patient-reported outcome measures; BCCSS: BC Clinical and Support Services database; CIHI: Canadian institute for health information; MSP: Medical services plan; CADTH: Canadian agency for drugs and technology in health
lb: low boundary; ub: upper boundary

6.3 Results

6.3.1 Total costs and outcomes – population level

Over a 20-year time horizon in BC, the number of revision surgeries per thousand patients submitted to primary THR is estimated to be 147 if patients receive metal-on-poly, 98 if they receive ceramic-on-poly, 92 if they receive ceramic-on-ceramic, and 192 if they receive oxinium-on-poly as their primary implant. The total (discounted) per-patient costs (including downstream revisions and re-revisions) are expected to be $13,832 for metal-on-poly, $13,875 for ceramic-on-poly, $15,027 for ceramic-on-ceramic, and $15,173 for oxinium-on-poly. The (discounted) QALYs are estimated at 9.452 years for metal-on-poly, 9.463 years for ceramic-on-poly, 9.462 years for ceramic-on-ceramic, and 9.444 years for oxinium-on-poly implants (Table 25).

Table 25. Total number of revisions, total costs, and total QALYs per patient over a 20-year time horizon

Deterministic	20-year Time Horizon		
	Revisions	**Cost***	**QALY***
Metal-on-poly	0.147	13,832	9.452
Ceramic-on-poly	0.098	13,875	9.463
Ceramic-on-ceramic	0.092	15,027	9.462
Oxinium-on-poly	0.192	15,173	9.444

QALY(s): quality –adjusted life years
* Costs and QALYs are discounted

6.3.2 Incremental costs and outcomes – population level

All the alternative implants were compared against the standard of care in BC and against each other (Table 26). Over a 20-year time horizon, ceramic-on-poly implants are estimated to offer an incremental 0.011 QALYs and avoid 0.05 revisions per recipient compared to metal-on-poly, for an additional cost of $43 per patient. This result in $3,944 per QALY gained and $863 per revision avoided. Ceramic-on-ceramic implants are estimated to offer similar benefits (0.011 QALYs, 0.06 revisions avoided) for an additional cost of $1,194 per patient, resulting in an

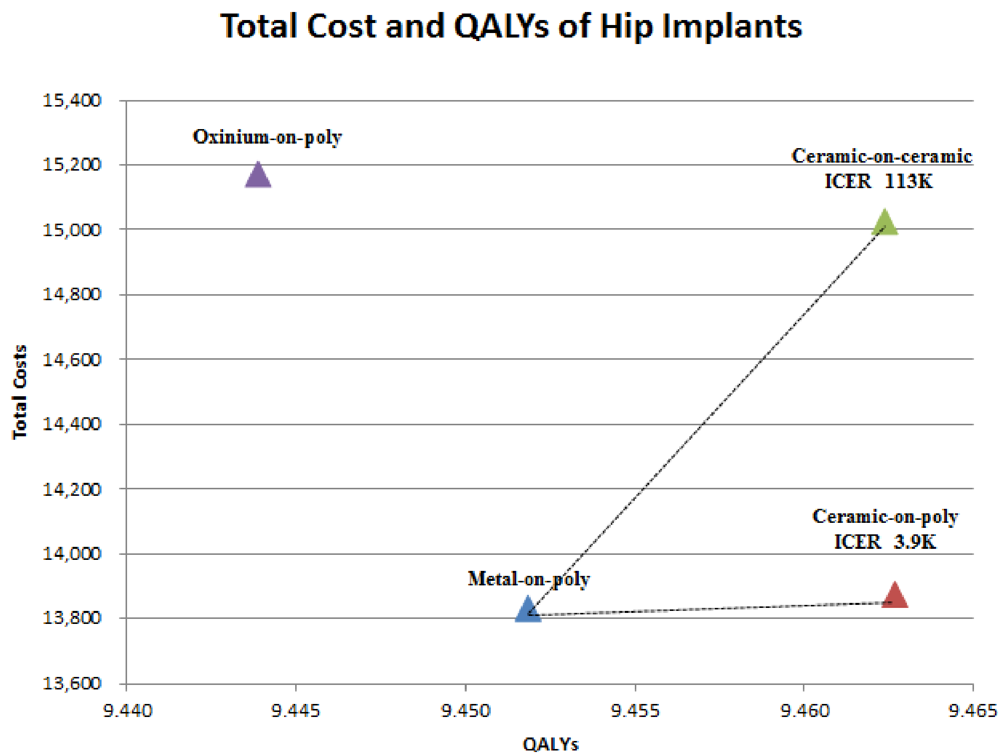
ICER of $113,455 per QALY gained and $21,607 per revision avoided. Oxinium-on-poly is estimated to be more costly with no additional benefits, and is therefore dominated by metal-on-poly. Comparing alternative implants against each other, ceramic-on-poly dominates ceramic-on-ceramic and oxinium-on-poly, and ceramic-on-ceramic dominates oxinium-on-poly. Ceramic-on-poly dominates all the other types in the efficiency frontier. For this reason, mainly the results for ceramic-on-poly will be reported (Figure 9). Uncertainty in the estimates, especially for the oxinium-on-poly implants, is discussed in the next section.

Table 26. Cost-effectiveness of the different types of hip implants in BC over a 20-year time horizon (results are expresses per patient).

Implant type	ICER / QALY	ICER / Revisions Avoided	Incremental Costs	Incremental QALYs	Revisions Avoided
Metal-on-poly vs Ceramic-on-poly	3,944	863	43	0.011	0.05
Metal-on-poly vs Ceramic-on-ceramic	113,455	21,607	1,194	0.011	0.06
Metal-on-poly vs Oxinium-on-poly	dominant	dominant	1,340	-0.008	-0.04
Ceramic-on-poly vs Ceramic-on-ceramic	dominant	197,817	1,152	0.000	0.01
Ceramic-on-poly vs Oxinium-on-poly	dominant	dominant	1,298	-0.019	-0.09
Ceramic-on-ceramic vs Oxinium-on-poly	dominant	dominant	146	-0.018	-0.10

ICER: incremental cost-effectiveness ratio; QALY(s): quality –adjusted life years

Figure 9. Cost-effectiveness plane



ICER: incremental cost=effectiveness ratio

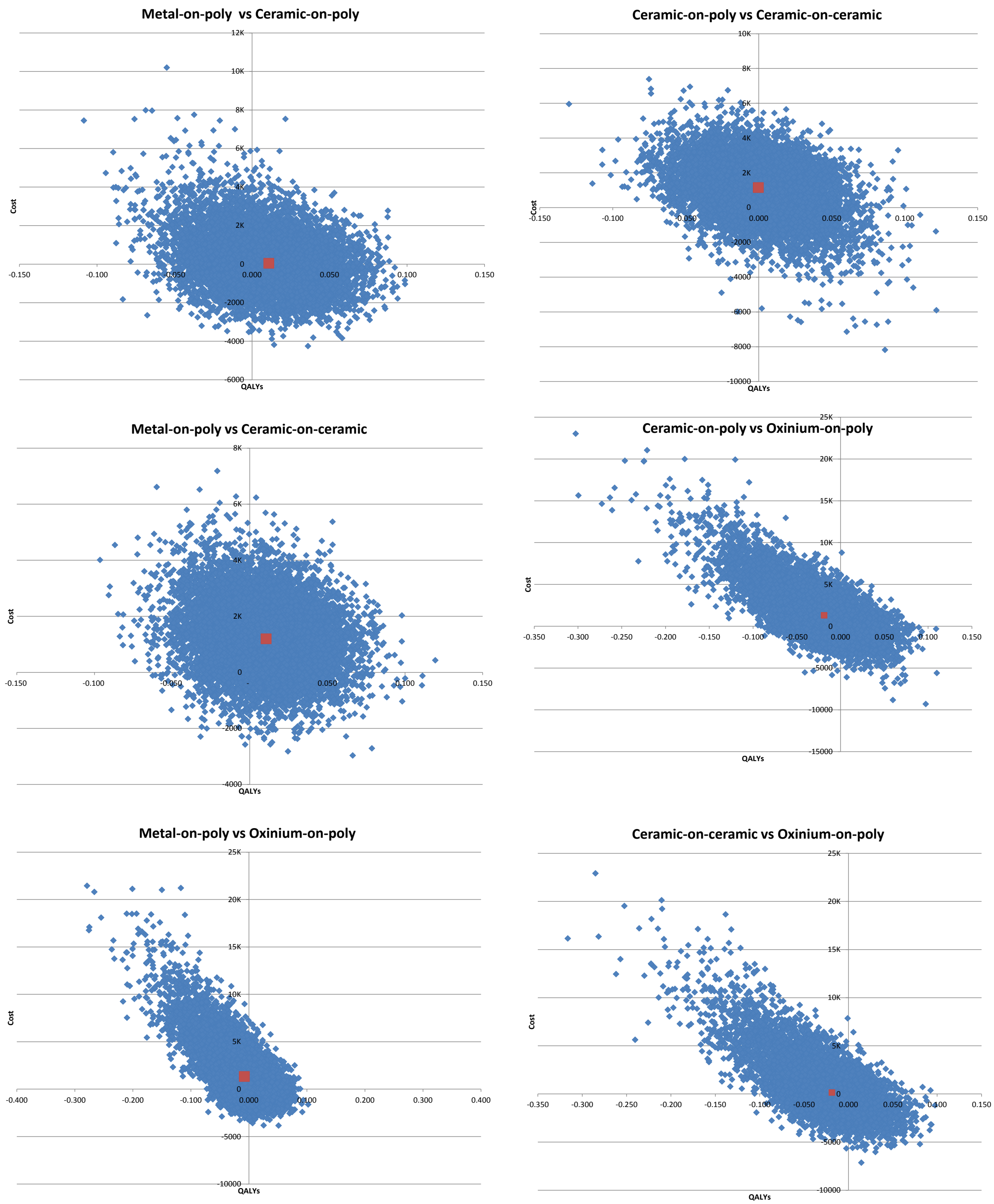
6.3.3 Characterizing uncertainty

The probabilistic model for a 20-year time horizon showed a high degree of uncertainty in the estimates for all outcomes for all implant comparisons. The clouds in the cost-effectiveness planes spread over the four quadrants, showing that any choice of implant could be more costly and less effective than another (Figure 10). The cost-effectiveness acceptability curve quantifies the uncertainty by demonstrating the probable cost-effectiveness of a particular strategy at a given willingness-to-pay (WTP) (Figure 11.b). All the implants have a low probability of being cost-effective. For example, for a WTP of $50,000/QALY gain in a 20-year period, the probability of metal-on-poly, oxinium-on-poly, and ceramic-on-ceramic being cost-effective is 25% or less, while the probability of ceramic-on-poly being cost-effective is just over

40%. Despite the low numbers, all the available evidence shows that, at a WTP of $50,000/QALY, ceramic-on-poly implants have the highest probability of cost-effectiveness among the four implants. This occurs because there is still a great amount of uncertainty around models parameters, for instance, odds ratios with wide confidence intervals. When the probabilistic model samples from within these confidence intervals, the new technology performs better than the comparator, and sometimes worse, which leads to a scenario where there is not a clear pattern, and none of the options has a huge advantage over the others in terms of probability of being cost-effective. The 95% CrI demonstrated the incremental costs for ceramic-on-poly ranged from -$2,279 to $3,262, and the incremental QALYs ranged from -0.047 to 0.062, when compared to metal-on-poly.

A deterministic sensitivity analysis was conducted considering a 10-year time horizon to avoid extrapolations beyond the observed data from the registries. Results were similar to those from the base-case analysis (Table 27). Even with a shorter period to offset the incremental costs of the implants, the ICER for ceramic-on-poly was estimated to be $46,000/QALY (Table 28). At a WTP of 50,000/QALY, ceramic-on-poly would have similar probabilities of cost-effectiveness to metal-on-poly (Figure 11.a). Univariate deterministic sensitivity analyses confirmed the results favoring ceramic-on-poly (Table 29). In the worst-case scenario, if the incremental cost of revision implants for patients who received primary ceramic-on-poly implants were five times higher than the costs used in the base-case, the ICER was estimated at $53,000/QALY. Sensitivity analyses with price reductions of the alternative primary implants were robust and would change the cost-effective ratio such that ceramic-on-poly dominated metal-on-poly, assuming the cost of metal-on-poly remained the same.

Figure 10 Cost-effectiveness plane of probabilistic analysis over a 20-year time horizon



Note: the red squares represent the ICERS from the deterministic analysis.

Figure 11. CEACs for 10-year, 20-year and lifetime time horizon

Fig 11.a

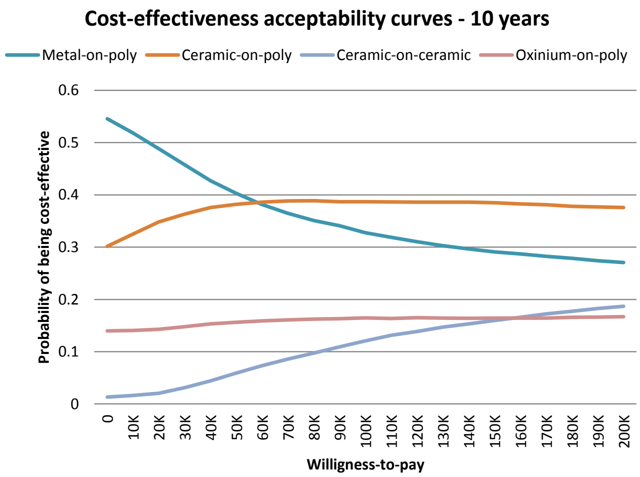


Fig 11.b

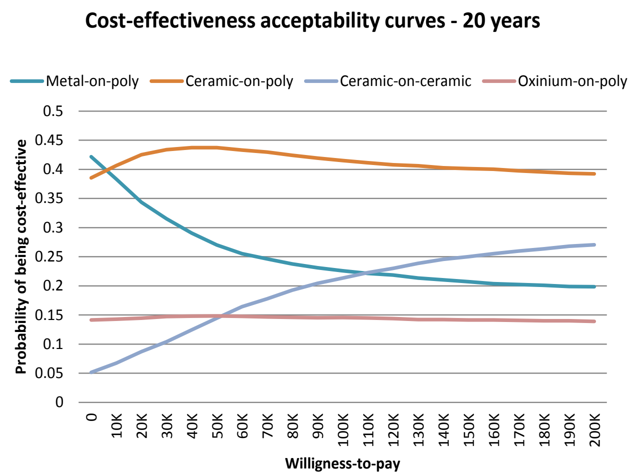


Fig 11.c

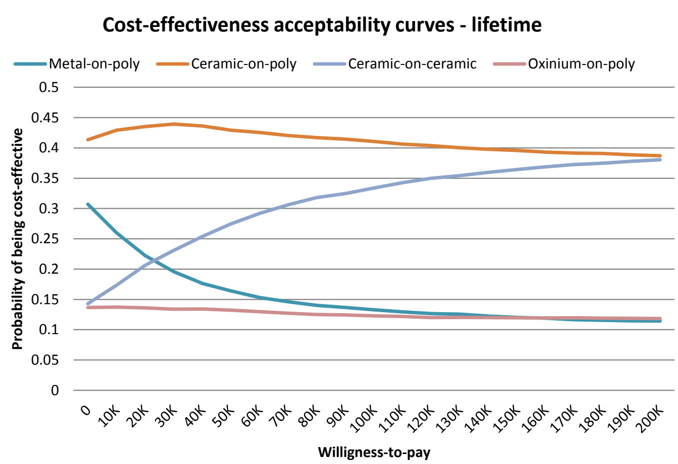


Table 27 Total number of revisions, total costs and total QALYs per patient over a 10-year time horizon

Deterministic	20-year	Time Horizon	
Implant type	**Revisions**	**Cost**	**QALY**
Metal-on-poly	0.064	12,672	6.042
Ceramic-on-poly	0.038	12,942	6.048
Ceramic-on-ceramic	0.043	14,247	6.046
Oxinium-on-poly	0.078	13,589	6.039

QALY(s): quality –adjusted life years

Table 28 Cost-effectiveness of the different types of hip implants in BC over a 10-year time horizon.

Cost-Effectiveness	ICER / QALY	ICER / Revision Avoided	Incremental Costs	Incremental QALYs	Revisions Avoided
Metal-on-poly vs Ceramic-on-poly	46,343	10,454	270	0.006	0.03
Metal-on-poly vs Ceramic-on-ceramic	371,396	76,976	1,574	0.004	0.02
Metal-on-poly vs Oxinium-on-poly	dominant	dominant	916	-0.003	-0.01
Ceramic-on-poly vs Ceramic-on-ceramic	dominant	dominant	1,304	-0.002	-0.01
Ceramic-on-poly vs Oxinium-on-poly	dominant	dominant	646	-0.009	-0.04
Ceramic-on-ceramic vs Oxinium-on-poly	93,355	18,957	-658	-0.007	-0.03

ICER: incremental cost-effectiveness ratio; QALY(s): quality –adjusted life years

Table 29 Univariate deterministic sensitivity analysis

Sensitivity Analysis - Univariate Deterministic		Parameter value: Base case	Parameter value: Sens Anal	ICER/QALY: Metal-on-poly vs Ceramic-on-poly	ICER/QALY: Metal-on-poly vs Ceramic-on-ceramic	ICER/QALY: Metal-on-poly vs Oxinium-on-poly	ICER/QALY: Ceramic-on-poly vs Ceramic-on-ceramic	ICER/QALY: Ceramic-on-poly vs Oxinium-on-poly	ICER/QALY: Ceramic-on-ceramic vs Oxinium-on-poly
Base Case Results				3,944	113,455	dominant	dominant	dominant	dominant
Incremental cost of revisions implants for primary implants with ceramic components - 3x times higher	Ceramic-on-poly	confidential		28,546	138,191	dominant	dominant	dominant	dominant
	Ceramic-on-ceramic								
	Oxinium-on-poly								
Incremental cost of revisions implants for primary implants with ceramic components - 5x times higher	Ceramic-on-poly	confidential		53,149	162,928	dominant	dominant	dominant	798
	Ceramic-on-ceramic								
	Oxinium-on-poly								
Discount - lower		3%	0%	dominated	64,750	dominant	2,609,550	dominant	dominant
Discount - higher			5%	12,722	151,565	dominant	dominant	dominant	6,343
Odds ratio of first revision - 20% higher	Ceramic-on-poly	0.58	0.70	48,682	211,903	dominant	dominant	dominant	dominant
	Ceramic-on-ceramic	0.67	0.80						
	Oxinium-on-poly	1.23	1.48						
Odds ratio of first revision - 20% lower	Ceramic-on-poly	0.58	0.46	dominated	64,421	dominant	dominant	dominant	6,954
	Ceramic-on-ceramic	0.67	0.54						
	Oxinium-on-poly	1.23	0.99						

Sensitivity Analysis - Univariate Deterministic		Parameter value: Base case	Parameter value: Sens Anal	ICER/QALY: Metal-on-poly vs Ceramic-on-poly	ICER/QALY: Metal-on-poly vs Ceramic-on-ceramic	ICER/QALY: Metal-on-poly vs Oxinium-on-poly	ICER/QALY: Ceramic-on-poly vs Ceramic-on-ceramic	ICER/QALY: Ceramic-on-poly vs Oxinium-on-poly	ICER/QALY: Ceramic-on-ceramic vs Oxinium-on-poly
Price of alternative primary implant – price reduction 1	**Metal-on-poly** **Ceramic-on-poly** **Ceramic-on-ceramic** **Oxinium-on-poly**	confidential		dominated	31,240	dominant	dominant	dominant	dominant
Price of alternative primary implant – price reduction 2	**Metal-on-poly** **Ceramic-on-poly** **Ceramic-on-ceramic** **Oxinium-on-poly**	confidential		dominated	72,347	dominant	dominant	dominant	dominant

6.3.4 Subgroup analysis

Results for different age and sex subgroups are shown in Table 30. None of the input parameters pertaining to the decisions under evaluation (e.g., OR of revision, costs of primary and revision surgeries, rate of complications) were age- or sex-specific. As a result, the observed differences in the outcomes among subgroups are due to non-technology-related components such as sex- or age-dependent variations in the underlying background survival and utility values.

6.4 Discussion

Incorporating the best available evidence into a decision-analytic simulation model showed that ceramic-on-poly is the cost-effective option compared with the current standard of care (metal-on-poly) and alternative technologies. However, the QALY gains and number of revisions avoided over a 20-year period were generally similar and accompanied by a substantial level of uncertainty for all four types of implants, making the cost-effectiveness ratios uncertain and sensitive to small differences in costs. Ceramic-on-poly had the highest probability of cost-effectiveness at a wide range of WTP value for QALYs.

<u>Given such small differences and high degrees of uncertainty, it is difficult to recommend of one type of device over another based solely on cost-effectiveness</u>. The choice of implants (between metal-on-poly and ceramic-on-poly) should, in this context, be determined not just by their cost and effectiveness profile but also by the preference of the surgeon and the patients, bearing in mind that ceramic-on-poly has the highest expected benefit and probability of being cost-effective. Further research on oxinium-on-poly implants is suggested to strengthen the evidence base, followed by re-evaluation of its cost-effectiveness.

Oxinium-on-poly implants are the most recent technology, with the shortest follow-up in registries and fewer RCTs. Also, due to lack of survival data for this type of implant in the UK registry, the analysis had to be complemented with data coming from smaller samples from the Australian registry. No RCT comparing oxinium-on-poly with metal-on-poly was found, and the OR of first revision for this technology came exclusively through indirect comparison. The confidence intervals were very wide, resulting in a higher degree of uncertainty for the comparisons of metal-on-poly with oxinium-on-poly than for the comparison with the other ceramic type implants. The clouds in Figure 10 show the skewness in the data. In several simulations, the oxinium-on-poly was more expensive and less effective than its comparators.

The economic analysis has some limitations due to lack of available data about some cost parameters. Physician fees were calculated to estimate fees incurred by primary and revision surgery. Other physician fees incurred within those hospital admissions were not captured. Cost of revisions surgeries were based on CIHI public data on the average cost of such surgeries, regardless of the type of implant. In the event of a new study showing that revisions surgeries have considerably different cost depending on the primary implant, the corresponding model parameters need to be updated. While rehabilitation services were deemed relevant, it was not explicitly incorporate the associated cost. However, the cost for the first year after surgery was extracted from the Alberta HIP study, which included cost for physiotherapy (47).

Table 30 Subgroup analysis by age group and sex

	Males 41-50 years old			Females 41-50 years old		
	Revisions	**Cost**	**QALY**	**Revisions**	**Cost**	**QALY**
Metal-on-poly	0.247	15,238	11.085	0.199	14,554	10.911
Ceramic-on-poly	0.224	15,769	11.092	0.132	14,410	10.925
Ceramic-on-ceramic	0.166	16,209	11.100	0.132	15,667	10.923
Oxinium-on-poly	0.441	18,658	11.051	0.269	16,243	10.899
	Males 51-60 years old			**Females 51-60 years old**		
	Revisions	**Cost**	**QALY**	**Revisions**	**Cost**	**QALY**
Metal-on-poly	0.231	15,015	11.081	0.189	14,413	10.996
Ceramic-on-poly	0.157	14,751	11.098	0.119	14,207	11.011
Ceramic-on-ceramic	0.143	15,848	11.097	0.118	15,444	11.009
Oxinium-on-poly	0.316	16,858	11.068	0.243	15,870	10.987
	Males 61-70 years old			**Females 61-70 years old**		
	Revisions	**Cost**	**QALY**	**Revisions**	**Cost**	**QALY**
Metal-on-poly	0.203	14,622	10.392	0.172	14,168	10.512
Ceramic-on-poly	0.102	13,906	10.413	0.102	13,944	10.526
Ceramic-on-ceramic	0.116	15,420	10.408	0.101	15,172	10.524
Oxinium-on-poly	0.208	15,319	10.393	0.209	15,389	10.505
	Males 71-80 years old			**Females 71-80 years old**		
	Revisions	**Cost**	**QALY**	**Revisions**	**Cost**	**QALY**
Metal-on-poly	0.088	13,066	8.336	0.074	12,853	8.716
Ceramic-on-poly	0.053	13,229	8.344	0.047	13,120	8.723
Ceramic-on-ceramic	0.060	14,548	8.342	0.051	14,397	8.722
Oxinium-on-poly	0.104	14,074	8.330	0.085	13,755	8.713
	Males 80+ years old			**Females 80+ years old**		
	Revisions	**Cost**	**QALY**	**Revisions**	**Cost**	**QALY**
Metal-on-poly	0.039	12,208	5.187	0.043	12,296	5.692
Ceramic-on-poly	0.024	12,658	5.190	0.059	13,309	5.689
Ceramic-on-ceramic	0.027	13,899	5.189	0.028	13,932	5.696
Oxinium-on-poly	0.080	13,642	5.177	0.067	13,409	5.687

Chapter 7: Budget Impact

Summary of Budget Impact

The BC healthcare system should expect a progressive increase in the number of primary THRs due to population growth and aging, and should expect to adjust capacity accordingly. Policy changes that increase the use of ceramic-on-poly will increase cost for the province and the health authorities, based on the current prices of primary implants.

In a scenario where ceramic-on-poly and metal-on-poly share the market equally, the overall budget impact for BC over 20 years is expected to be $15.3 million. The higher cost of the more expensive primary implant ($41.1 million) would be partially offset by the reduction in healthcare costs with revision surgeries over time ($25.8 million overall, comprising $5.8 million in physician fees, and $21.2 million in health authority costs).

If a price reduction of the primary ceramic-on-poly implant occurs, the technology can become cost-saving over time. However, if its use surpasses metal-on-poly, there would still be higher costs for health authorities, requiring more aggressive price negotiations.

Conducting a costing exercise is suggested to more accurately determine the costs incurred during the first year after primary and revision surgeries for each device, for further calibration of the budget impact analysis.

According to CIHI data (Table 18), among the four types of implants in BC, metal-on-poly devices currently have the largest market share (87%). In recent years, there has been an increase in the use of ceramic-on-poly, a slight decrease in use of the ceramic-on-ceramic, and steady, low-level use of oxinium-on-poly. These three devices together represented 12.2 percent of implants in 2014 (9). In the UK, ceramic-on-poly and ceramic-on-ceramic implants accounted for 57.8 percent of uncemented primary implants in 2014 (27).

7.1 Objectives

To evaluate the budget impact of a policy change in BC to accommodate ceramic-on-poly implants.

7.2 Methods

Assuming a policy change would accommodate coverage for ceramic-on-poly implants according to physician and patient preference, three scenarios were created to evaluate the budget impact in BC (Table 31).

The *status quo* scenario represents the current market share of the four types of implants included in this HTA. Scenario A assumes that the market share would be equal between ceramic-on-poly and metal-on-poly implants after the policy change. Scenario B assumes that the market share of the ceramic-on-poly implants would be higher than the metal-on-poly after the policy change, equal to the UK levels of ceramic implant use.

Only the use of metal-on-poly and ceramic-on-poly for primary THR were varied. The market shares of ceramic-on-ceramic and oxinium-on-poly implants remained unchanged. In all scenarios, it was assumed that all healthcare costs, including cost of implants, were paid by the public healthcare system.

Table 31 Market share of the different types of implant in three scenarios

	Status quo	Scenario A Equal market share between metal-on-poly and ceramic-on-poly	Scenario B Ceramic-on-poly market share higher than metal-on-poly (up to the UK level)
Metal-on-poly	87.8%	48.4%	42.1%
Ceramic-on-poly	9.1%	48.4%	54.8%
Ceramic-on-ceramic	3.0%	3.0%	3.0%
Oxinium-on-poly	0.2%	0.2%	0.2%

The same Markov model as in the economic evaluation (Figure 8) was used to simulate a dynamic population impact over 20 years (2016 to 2035). However, a dynamic population based on staggered entry of new cohorts eligible for THRs every calendar year was used. The subgroup weights were assigned based on Statistics Canada's projected population growth and aging during this period (57).

It was assumed that surgery capacity would increase to accommodate the THR of the aging population, based on the numbers of THR performed in 2014(9). Therefore, no changes in the existing wait time were implemented in the model. Every year, a new cohort of patients entered the model after their primary implant, and the number of revisions and costs were cumulative, including the health consequences of all cohorts over time (starting from 2016). Revision surgeries for patients who had their primary THR before 2016 were not included in the budget impact. As such, the reported cost estimates only pertain to the primary surgeries after 2015 and revision surgeries whose primary surgery was conducted after 2015.The overall budget impact on the province is presented, and an estimation of the health authorities (HAs) and MSP portions.

Number of surgeries and costs were not discounted, and inflation was not applied. Costs were expressed in 2015 Canadian dollars. No changes in price units during the period were assumed (meaning that any nominal change in price in the future would equate the inflation rate).

7.3 Results

Table 32 shows the main results for the budget impact evaluation. Given the growth and aging of the population in BC, it is estimate that the number of primary hip replacements will increase from 5,453 surgeries per year in 2016 to 11,108 surgeries per year in 2035 (relative change +104 percent), for a total of 156,602 primary THR surgeries over 20 years. Results for each individual year are available in Appendix K.

7.3.1 Status quo

The status quo scenario of primary hip implant use in BC estimates the healthcare costs for the treatment of patients requiring THR (and its consequences) at $2 billion over 20 years. It is predicted to increase from $64.2 million per year in 2016 to $151.9 million per year in 2035 (Table 32). This scenario estimates 8,894 revision surgeries (Table 33).

Cost of primary implants is estimated at $361 million over 20 years, increasing from $12.6 million per year in 2016 to $25.6 million per year in 2035 (Table 34), mainly due to the growth and aging of the population. Cost of revision surgeries is estimated at $186 million over 20 years, increasing from $1.4 million per year for the first cohort of patients in 2016 to $21.2 million in the cumulative population in 2035 (Table 35). These estimates do not include cost of revision surgeries for patients who received their primary THR before 2016. Estimates for each individual year are available in Appendix K, Appendix L, Appendix M, and Appendix N.

7.3.2 Equal market share between metal-on-poly and ceramic-on-poly (Scenario A)

Assuming that a policy change would accommodate coverage for ceramic-on-poly implants according to physician and patient preference and that the market share would be equal between ceramic-on-poly and metal-on-poly implants, a cost increase of $21.2 million to the health authorities (hospital costs, devices, follow-ups, etc.) is estimated and a decrease in physicians fees related to revision surgeries of $5.8 million, for an overall cost increase of $15.3 million to the health system over 20 years (Table 32). The annual budget impact decreases from $1.1 million per year in 2016 to $354,000 per year in 2035 as a result of the reduced healthcare costs associated with revision surgeries, estimated to decrease 16.3 percent among the future cohorts of patients requiring THR (1,453 revisions avoided, Table 33). The higher cost to health authorities are also expected to start at $1.2 million per year in 2016 to $961,000 per year in 2035. Physician fees associated with surgeries are expected to decrease from $71,000 per year in 2016 to $600,000 per year in 2035. The increased cost of primary implants is estimated around $41.1 million (11.3 percent, Table 34). The decrease in cost of revision is estimated around $25.8 million overall ($5.8 million in physician fees and $20 million in health authority costs, Table 35). These estimates do not account for revision surgeries for patients who received their primary THR before 2016. Therefore, the increased costs observed in practice will be lower than the estimated. Estimates for each individual year are available in Appendix K, Appendix L, Appendix M, and Appendix N.

7.3.3 Ceramic-on-poly market share higher than metal-on-poly, up to the UK level (Scenario B)

Assuming that a policy change accommodating coverage for ceramic-on-poly implants would result in market share change similar to the UK levels of ceramic head use (57.8 percent), the overall increased cost to the healthcare system would be $17.8 million over 20 years (Table 32). This would be the result of a cost increase of $24.6 million to the health authorities (for hospital costs, devices, follow-ups, etc.) and a decrease of $6.8 million in physician fees related to revision surgeries. The annual budget impact decreases from $1.3 million per year in 2016 to $424,000 per year in 2035 as a result of the reduced healthcare costs associated with revision surgeries, which are estimated to decrease 18.9 percent among future cohorts of patients requiring THR (1,688 revisions avoided, Table 33). The higher cost to health authorities are expected to start at $1.3 million per year in 2016 to $1.1 million per year in 2035. Physician fees associated with surgeries are expected to decrease $82,000 per year in 2016 to $692,000 per year in 2035. The higher cost of primary implants is estimated at $47.8 million (13.2%, Table 34). The decrease in cost for revisions surgeries is estimated at $30 million overall ($6.8 million in physician fees, and $23.2 million in health authority costs, Table 35). These estimates do not account for revision surgeries for patients who received their primary THR before 2016. Therefore, the incremental costs observed in practice will be lower than the estimated. Estimates for each individual year are available in Appendix K, Appendix L, Appendix M, and Appendix N.

7.3.4 Sensitivity analysis

Sensitivity analysis considering a substantial price reduction of the ceramic-on-poly primary implants was conducted. In a scenario where market share would be equal between ceramic-on-poly and metal-on-poly implants (Scenario A), there would be an overall decrease of costs to the healthcare system over 20 years, with cost savings for both the HAs and MSP. The cost of treating the new cohort of patients would increase up to the sixth year of the policy change for the province (to the tenth year for HAs), and then cost savings resulting from the reduced healthcare costs associated with revision surgeries would be expected.

In scenario B, where ceramic-on-poly implants assume a larger market share than metal-on-poly implants, over 20 years, overall cost savings are still observed mainly due to reduced MSP fees associated with revisions surgeries. However, the incremental costs for health authorities would not be completely offset by the simulated price reduction of the primary implants.

Table 32. Total Cost and annual budget impact for BC for management of THR and its consequences in year 1, year 10, year 20 and cumulative over 20 years

Cost of health care for patients requiring total hip replacement over 20 years				
Year	**2016**	**2025**	**2035**	**Total Cumulative**
N. of primary THR	**5,453**	**7,302**	**11,108**	**156,602**
Growth over 20 years				**104%**
Total Cost				
Status quo - Metal-on-poly with largest market share (87%)	64.2 M	92.9 M	151.9 M	2.0 B
MSP Fees - Surgeons	8.5 M	12.4 M	20.7 M	270.9 M
HA Costs	55.8 M	80.5 M	131.2 M	1.7 B
Scenario A - Equal market share between Metal-on-poly and Ceramic-on-poly	65.3 M	93.7 M	152.3 M	2.0 B
MSP Fees - Surgeons	8.4 M	12.2 M	20.1 M	265.0 M
HA Costs	56.9 M	81.5 M	132.1 M	1.8 B
Annual Budget Impact of the police change (MSP + HA) in Scenario A	1.1 M	789.0 K	365.2 K	15.3 M
MSP Annual Budget Impact	-71.2 K	-251.7 K	-595.9 K	-5.8 M
HA Budget Impact	1.2 M	1.0 M	961.1 K	21.2 M
Scenario B - Ceramic-on-poly market share higher than Metal-on-poly	65.5 M	93.8 M	152.3 M	2.0 B
MSP Fees - Surgeons	8.4 M	12.1 M	20.1 M	264.1 M
HA Costs	57.1 M	81.7 M	132.3 M	1.8 B
Annual Budget Impact of the police change (MSP + HA) in Scenario B	1.3 M	916.7 K	424.3 K	17.8 M
MSP Annual Budget Impact	-82.7 K	-292.4 K	-692.4 K	-6.8 M
HA Budget Impact	1.3 M	1.2 M	1.1 M	24.6 M

Table 33 Number of revisions surgeries estimated for BC and annual impact in year 1, year 10, year 20 and cumulative over 20 years

	2016	2025	2035	Total Cumulative
Status quo	67	363	1012	8894
Equal market share between Metal-on-poly and Ceramic-on-poly	49	301	864	7441
Annual Impact (n. revision surgeries) in Scenario A	-18	-63	-148	-1453
S2 - Ceramic-on-poly market share higher than Metal-on-poly	46	291	840	7206
Annual Impact (n. revision surgeries) in Scenario B	-21	-73	-172	-1688

Table 34 Costs with primary implants in each scenario and budget impact in year 1, year 10, year 20 and cumulative over 20 years

	2016	2025	2035	Total Cumulative
Status quo	12.6 M	16.8 M	25.6 M	361.3 M
Scenario A - Equal market share between Metal-on-poly and Ceramic-on-poly	14.0 M	18.8 M	28.5 M	402.4 M
Annual Budget Impact of the police change $ in Scenario B	1.4 M	1.9 M	2.9 M	41.1 M
Scenario B - Ceramic-on-poly market share higher than Metal-on-poly	14.2 M	19.1 M	29.0 M	409.0 M
Annual Budget Impact of the police change $ in Scenario B	1.7 M	2.2 M	3.4 M	47.8 M

Table 35 costs of revision surgeries in each scenario and budget impact in year 1, year 10, year 20 and cumulative over 20 years (includes implants + hospital + complications + MSP fees)

	2016	2025	2035	Total Cumulative
Status quo	1.4 M	7.6 M	21.2 M	186.1 M
MSP Fees - Surgeons	267.5 K	1.5 M	4.1 M	35.7 M
HA Costs	1.1 M	6.1 M	17.1 M	150.4 M
Scenario A - Equal market share between Metal-on-poly and Ceramic-on-poly	1.0 M	6.5 M	18.6 M	160.3 M
MSP Fees - Surgeons	196.3 K	1.2 M	3.5 M	29.9 M
HA Costs	846.7 K	5.3 M	15.2 M	130.4 M
Annual Budget Impact of the police change (MSP + HA) in Scenario A	-347.4 K	-1.1 M	-2.6 M	-25.8 M
MSP Annual Budget Impact	-71.2 K	-251.7 K	-595.9 K	-5.8 M
HA Budget Impact	-276.2 K	-876.3 K	-2.0 M	-20.0 M
Scenario B - Ceramic-on-poly market share higher than Metal-on-poly	986.8 K	6.3 M	18.2 M	156.1 M
MSP Fees - Surgeons	184.8 K	1.2 M	3.4 M	29.0 M
HA Costs	802.0 K	5.1 M	14.8 M	127.2 M
Annual Budget Impact of the police change (MSP + HA) in Scenario B	-403.6 K	-1.3 M	-3.0 M	-30.0 M
MSP Annual Budget Impact	-82.7 K	-292.4 K	-692.4 K	-6.8 M
HA Budget Impact	-320.9 K	-1.0 M	-2.3 M	-23.2 M

7.4 Discussion

The budget impact analysis took into account population growth and aging in BC over the next 20 years. In the status quo scenario, the healthcare system should expect an average increase of four percent per year in the number of THRs, assuming the prevalence of disease leading to THR remains the same within subgroups. The anticipated cost over this time is around 2 billion.

Policy changes that increase the use of ceramic-on-poly implants (which are currently 30 percent more expensive on average than metal-on-poly) will increase costs for the province and health authorities. If the efficacy of ceramic-on-poly in reducing revisions compared to metal-on-poly is confirmed in clinical practice, the cost increase expected from the more expensive primary implants (41.1 million, in Scenario 1) would be partially offset by the reduction in healthcare costs for revision surgeries over time ($25.8 million overall, comprising $5.8 million in physician fees, and $20 million in health authority costs), resulting in an net budget impact of $15.3 million over 20 years.

For future cohorts of patients requiring THR, in a balanced scenario with equal market share between the new technology and the current standard of care, a substantial price reduction in the cost of primary ceramic-on-poly implants would translate into cost savings with revisions surgeries over time. However, if ceramic-on-poly assumes a larger market share, system costs would still increase despite lower revision rates.

Carrying out a costing exercise is suggested to determine more accurately the cost of the first year after surgery and if the costs of subsequent revision surgeries differ by primary bearing surface. Although the cost-effectiveness ratios are not highly sensitive to this parameter, it may have considerable impact on the budget over time.

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Appendix A **Questions addressed on Focus Group**

1. Please describe how the conditions/reasons that led to your hip replacement affected your day-to-day life prior to your surgery.

2. What did you expect (or hope for) as a result of the hip replacement? Thinking about one year following the surgery, were your expectations met? Were there any things you were unhappy with (relatively to the implant? Or to other adverse events/complications)? Did anything unexpected occur?
    a. How about five years afterward?

3. Were you given options of different types of implant prior to surgery? If yes, were potential risks and benefits related to the different implants presented to you? If you had a choice among implants, what factors influenced the final decision you made among the options?

4. Following the original surgery, have you had any subsequent surgeries on that same hip to deal with any of the implant parts? If yes, what were the reasons for these?

Appendix B **Search strategies**

B.1 **Medline**

Database: Ovid MEDLINE(R) 1946 to Present with Daily Update
Search Strategy:
----

1 Arthroplasty, Replacement, Hip/ (19491)

2 Hip Prosthesis/ (19886)

3 ((hip or hips) adj8 (arthroplast$ or replac$ or prosthe$ or endoprosthe$)).tw. (29870)

4 Hip/ (10730)

5 (hip or hips).tw. (98141)

6 Hip Joint/ (23385)

7 4 or 5 or 6 (106323)

8 Arthroplasty/ (7457)

9 Arthroplasty, Replacement/ (5018)

10 Joint Prosthesis/ (9330)

11 "Prostheses and Implants"/ (41099)

12 8 or 9 or 10 or 11 (58706)

13 7 and 12 (5089)

14 Hip Joint/su [Surgery] (6444)

15 total hip arthroplasty.kw. (388)

16 total hip replacement.kw. (115)

17 artificial hip joint.kw. (7)

18 or/1-3,13-17 [Hip Arthroplasty] (42638)

19 Ceramics/ (10443)

20 (ceramic or ceramics).kw. (93)

21 (ceramic or ceramics).tw. (16377)

22 bearing surface$.tw. (1429)

23 "Bearing surfaces".kw. (3)

24 bearing coupl$.tw. (113)

25 or/19-24 [Bearing surfaces] (20510)

26 18 and 25 (1867)

****

B.2 Embase

Database: Embase <1980 to 2016 May 20>
Search Strategy:
----

1 total hip prosthesis/ (24873)

2 Hip/ and prosthesis/ (1097)

3 Hip arthroplasty/ (14954)

4 1 or 2 or 3 (38095)

5 arthroplasty.mp. (68896)

6 joint prosthesis.mp. (11176)

7 joint replacement.mp. (7118)

8 (arthroplast$ or replace$ or prosthe$ or artificial$).mp. (1043870)

9 5 or 6 or 7 or 8 (1043870)

10 hip/ (41321)

11 (hip or hips).mp. (166127)

12 10 or 11 (166127)

13 9 and 12 (57971)

14 4 or 13 (57971)
Annotation: [Hip arthroplasty]

15 bearing surface$.mp. (1698)

16 bearing coupl$.mp. (164)

17 ceramics/ (12376)

18 ceramic$.mp. (25406)

19 15 or 16 or 17 or 18 (26793)
Annotation: [Bearing surfaces]

20 14 and 19 (2616)

Appendix C **Data Extraction Sheet**

Article Number	
Database (if applicable)	
Type of Article	
Search Period	
Title and Reference (First author)	
Year of publication	
n. patients (studies in case of SR)	
Inclusion criteria	
Patients	
Intervention & comparator	
Follow-up period & outcome measured	
Exclusion criteria	
Study Characteristics	
Population	
Intervention and comparisons	
List of included studies	
Outcomes	
Mortality	
Revision	
Pseudotumour	
Functional score (ie Harris Hip score)	
QoL (ie EQ-5D)	
Femoral head pentration rate	
Post-revision complication	
Peri or post operation adverse events	
Infection	
Bleeding	
wound problem	
Implant dislocation	
Osteolysis	
Aseptic loosening	
Femoral fracture	
DVT	
Muscle weakness	
Nerve palsy	
Pulmonary embolism	
Squeking	
Implant fracture	

Appendix D **Critical Appraisal for SR**

Assessment Criteria	Wyles 2015	Yin 2015	NHS 2015	Hu 2015	Hu 2015b	Dong 2015	CADTH 2013	Si 2015
Research Question	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
1. Was the research question clearly stated (PICOS)?	Y	Y	Y	Y	Y	Y	Y	Y
2. Was the type of **participants** appropriate to the research question?	Y	Y	Y	Y	Y	Y	Y	Y
3. Was the type of **interventions and comparators** appropriate?	Y	Y	Y	Y	Y	Y	Y	Y
4. Was the type of **outcomes** appropriate? Is adverse effect included?	Y	Y	Y	Y	Y	Y	Y	Y
5. Was the type of **study design** appropriate?	Y	Y	Y	Y	Y	Y	Y	Y
Search strategy								
1. Was the search strategy comprehensive, adequate and reasonably unbiased?	Y	Y	Y	Y	Y	U	N	Y
2. Was the selection of studies carried out independently by two reviewers?	Y	Y	Y	Y	Y	Y	N	Y
Quality assessment of included studies								
1. Was the quality of included studies assessed in a reliable manner with clearly stated criteria?	U	Y	Y	Y	Y	Y	Y	Y
2. Was the quality assessment performed independently by two reviewers?	N	Y	Y	Y	Y	Y	N	Y
Data collection								
1. Did the reviewers include all relevant studies?	Y	Y	Y	Y	Y	Y	N	Y
2. Was the reason for excluding studies	Y	Y	Y	Y	Y	Y	Y	N

stated?								
3. Was the process of obtaining missing information stated?	Y	U	N	Y	Y	N	N	N
Data synthesis								
1. Was the outcomes (primary and secondary) defined in advance and clearly described?	Y	Y	Y	Y	Y	Y	Y	N
2. If the results of included studies were combined, was it reasonable to do so? (Similar PICOS, baseline)	Y	Y	Y	Y	Y	Y	N	Y
3. Was the method of analysis and statistical tool appropriate?	Y	Y	Y	Y	Y	Y	U	Y
Result reporting								
1. Was the baseline characteristics of included studies reported?	Y	Y	Y	Y	Y	Y	Y	Y
2. Was all results in the method (available or not) reported?	Y	Y	Y	Y	Y	Y	Y	Y
3. Was results reported with appropriate statistics? (95%CI, p value, I^2)	Y	Y	Y	Y	Y	Y	Y	Y
4. Was the issue with missing information, if any, addressed?	Y	U	N	NA	NA	U	U	U
5. Was the amount of missing information small enough that the result was not impacted?	Y	U	N	NA	NA	U	U	U
6. Was the issue with heterogeneity, if any, addressed?	Y	U	Y	NA	NA	U	U	Y

Footnote: In this table, a yes (Y) answer indicates low risk of bias in the category, a no (N) answer indicate high risk of bias, an unknown answer (U) indicates unknown risk of bias. NA indicates not applicable in that category.

Appendix E **WinBUGS coded generated by NetmetaXL**

Inits and data tables

Inits Random Effects (Vague)

```
list(d=c(NA,1.5,0.5,0,1.5,1.5,2,2), sd=1.5,
mu=c(1,1.5,1.5,2,1.5,1,1.5,0,0.5,1,2,0.5,1,0.5,0.5,1,1.5,2,1,1.5,0,1,1,1,0.5,1,0.5,1.5,2,1,1,1.5,0,0.5,1.5,0,1,1.5,0,1,0.5))
list(d=c(NA,1,0.5,1.5,0,1.5,1.5,1.5), sd=2,
mu=c(0.5,0.5,1.5,2,2,0,0,0,0,0.5,1,0.5,1,1.5,1,2,1,1.5,0,2,1,1.5,1,0.5,2,0.5,1,1,1.5,0,1.5,0,0,0,1,0.5,0.5,2,1.5,1,0))
list(d=c(NA,1,1.5,1.5,1,0.5,0,1), sd=1.5,
mu=c(1,0.5,1,0.5,0.5,2,1,1.5,0.5,2,0.5,1.5,1.5,0.5,0,0.5,0.5,1.5,1,1.5,2,1,0.5,0,0,1,0.5,0.5,1,1.5,1,0.5,0.5,1,1.5,1.5,0.5,1,1,0.5,1))
```

Inits Random Effects (Informative)

```
list(d=c(NA,0.5,1,1.5,0.5,0.5,0.5,1.5), var=1,
mu=c(1.5,1,1,2,0.5,2,0.5,1,1.5,2,1,1,1,0.5,1.5,0.5,1,0.5,0.5,1,1.5,0,1,0,1.5,0.5,1.5,1.5,1.5,1,1.5,1.5,1,1.5,0.5,2,2,1,0.5,1,1))
list(d=c(NA,2,0.5,0.5,0,1.5,1,1.5), var=1,
mu=c(2,0,2,1,1,0.5,1,1,1.5,0.5,1.5,1,1,1,2,0.5,0.5,2,1.5,1.5,0.5,0,1,0.5,1,1,1,0,0,0.5,1.5,0.5,2,0.5,0,1,0.5,0.5,1,2,1.5))
list(d=c(NA,0,1.5,1.5,0,0.5,0.5,2), var=1.5,
mu=c(0.5,1.5,0,0.5,0.5,0,2,1.5,1.5,1,0.5,1.5,1,1,0.5,0.5,1,1,1.5,0.5,2,1.5,0,0,1,1.5,2,1.5,1,2,1,0.5,0,0,1,1,1,1,2,1.5,0))
```

Inits Fixed Effects

```
list(d=c(NA,1.5,0.5,1.5,1.5,2,2,0),
mu=c(1.5,0.5,1,1.5,0.5,0.5,1,1,1.5,1,0.5,0.5,1.5,1,1,0.5,1.5,2,0,1,0.5,1,1,0.5,0,1.5,2,1,1,1,0,1,1,0.5,1.5,0,0.5,1,0.5,1.5,1))
list(d=c(NA,1.5,0.5,0,1.5,1.5,2,2),
mu=c(1,0.5,0,1.5,2,1.5,0.5,0.5,1,0.5,0.5,0,0.5,1.5,0,1.5,0.5,0.5,2,2,1.5,1.5,1,1,2,2,1.5,1.5,0.5,0.5,0.5,0.5,0,1.5,0.5,0.5,2,1.5,0,1.5,1))
list(d=c(NA,1,0.5,1,0.5,1.5,1,1.5),
mu=c(0,1,0.5,1,0.5,0.5,2,1,2,1.5,0.5,1.5,1.5,1.5,1,0.5,1,2,1.5,1,0,0.5,1,0.5,0,0.5,1,1.5,0.5,1,1.5,2,1,2,0,1,1.5,0.5,1.5,0.5,1.5))
```

WinBUGs Data Table and List Statement

```
list(NS=41, NT=8)
```

Study ID	Study Name	r[,1]	n[,1]	r[,2]	n[,2]	r[,3]	n[,3]	r[,4]	n[,4]	r[,5]	n[,5]	r[,6]	n[,6]	r[,7]	n[,7]	r[,8]	n[,8]	t[,1]	t[,2]	t[,3]	t[,4]	t[,5]	t[,6]	t[,7]	t[,8]	na[]
1	Amanatullah 2011	11	196	3	161	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	2	NA	NA	NA	NA	NA	NA	2
2	Beaupre 2013	0	48	3	44	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	2	NA	NA	NA	NA	NA	NA	2
3	Hamilton 2010	4	177	2	87	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	2	NA	NA	NA	NA	NA	NA	2
4	Kim 2013	0.516129	32.51613	0.483871	30.48387	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	2	NA	NA	NA	NA	NA	NA	2
5	Lombardi 2010	3	65	3	45	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	2	NA	NA	NA	NA	NA	NA	2
6	Bascarevic 2010	0.5	51.5	0.5	51.5	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	3	NA	NA	NA	NA	NA	NA	2
7	NikoLaou 2012	1	34	1	32	2	36	NA	1	NA	1	NA	1	NA	1	NA	1	1	3	4	NA	NA	NA	NA	NA	3
8	Kawate 2009	0	32	0	30	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	2	3	NA	NA	NA	NA	NA	NA	2
9	Morison 2014	0	24	2	21	2	24	1	22	NA	1	NA	1	NA	1	NA	1	3	4	7	8	NA	NA	NA	NA	4
10	Nakahara 2010	0	51	0	51	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	2	3	NA	NA	NA	NA	NA	NA	2
11	Engh 2012	0.5	27.5	0.5	27.5	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
12	Garcia-Rey 2013	1	45	0	45	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
13	Johanson 2012	2	31	1	30	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
14	Geerdink 2009	0	22	1	26	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
15	Thomas 2011	0	27	0	27	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
16	Mutimer 2010	0.495798	59.4958	0.504202	60.5042	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
17	Digas 2007	0.5	27.5	0.5	27.5	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
18	Geerdink 2006	0	66	2	67	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
19	Triclot 2007	1	49	1	53	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
20	Calvert 2009	0	59	0	60	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
21	Glyn-Jones 2008	0	27	0	27	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
22	Lewis 2010	1	30	1	26	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	5	NA	NA	NA	NA	NA	NA	2
23	Ochs 2007	1	35	1	31	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	5	NA	NA	NA	NA	NA	NA	2
24	Cai 2012	2	51	3	62	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	5	NA	NA	NA	NA	NA	NA	2
25	Vendittoli 2013	1	71	8	69	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	4	NA	NA	NA	NA	NA	NA	2
26	D'Antonio 2012	6	194	10	95	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	4	NA	NA	NA	NA	NA	NA	2
27	Seyler 2006	6	158	3	52	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	4	NA	NA	NA	NA	NA	NA	2
28	Engh 2014	1	37	1	63	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	6	NA	NA	NA	NA	NA	NA	2
29	Desmarchelier 2013	1	125	3	125	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	6	NA	NA	NA	NA	NA	NA	2
30	Engh 2006	0	116	2	114	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	4	NA	NA	NA	NA	NA	NA	2
31	Lewis 2008	0.45098	23.45098	0.54902	28.54902	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	3	7	NA	NA	NA	NA	NA	NA	2
32	Jassim 2015	2	133	1	135	2	133	NA	1	NA	1	NA	1	NA	1	NA	1	3	7	8	NA	NA	NA	NA	NA	3
33	Bjorgul 2013	3	137	1	131	8	129	NA	1	NA	1	NA	1	NA	1	NA	1	4	5	6	NA	NA	NA	NA	NA	3
34	Zijlstra 2010	2	98	4	102	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	6	NA	NA	NA	NA	NA	NA	2
35	Hanna 2012	0.5	30.5	0.5	30.5	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	6	NA	NA	NA	NA	NA	NA	2
36	Zijlstra 2014	0	54	4	50	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	6	NA	NA	NA	NA	NA	NA	2
37	Malviya 2011	2	50	2	50	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	6	NA	NA	NA	NA	NA	NA	2
38	Dahl 2013	2	23	2	20	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	5	NA	NA	NA	NA	NA	NA	2
39	Kraay 2006	0	30	0	30	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	5	NA	NA	NA	NA	NA	NA	2
40	Van der Veen 2015	1	54	3	50	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	4	6	NA	NA	NA	NA	NA	NA	2
41	Capello 2008	4	380	5	95	NA	1	NA	1	NA	1	NA	1	NA	1	NA	1	1	4	NA	NA	NA	NA	NA	NA	2
		END																								

Fixed effect model

```
model                  # this code for this model was adapted from WinBUGS code from the
{                      multi-parameter Evidence Synthesis Research Group at the University of
                       Bristol:  Website: www.bris.ac.uk/cobm/research/mpes
    for(i in 1:NS)
     {

        mu[i] ~ dnorm(0,.0001)
    # vague priors for baselines                        # vague priors for all trial baselines
        for (k in
    1:na[i])                                            # LOOP THROUGH ARMS
            {
            r[i,k] ~ dbin(p[i,k],n[i,k])                     # binomial likelihood
                                                              # model for linear
            logit(p[i,k]) <- mu[i] + d[t[i,k]] - d[t[i,1]]    predictor
                                                              # expected value of the
            rhat[i,k] <- p[i,k] * n[i,k]                      numerators
            #Deviance contribution
            dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k])) +  (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k])
            - log(n[i,k]-rhat[i,k])))
            }
                                              # summed residual deviance contribution for this
    resdev[i] <- sum(dev[i,1:na[i]])          trial
     }
    totresdev <- sum(resdev[])     # Total Residual Deviance

    d[1]<-
    0

    for (k in 2:NT)
    {
            d[k] ~ dnorm(0,.0001) #  vague priors for basic parameters
    }



    # ranking best and probability
    for (k in 1:NT)
    {
                                              #events good
            rk[k]<- rank(d[],k)               #events bad
            best[k]<-equals(rk[k],1)

            for (h in 1:NT)
            {
                    prob[k,h]<-equals(rk[k],h)
```

```
		}
	}
	for (k in 1:NT)
	{
		for (h in 1:NT)
		{
			cumeffectiveness[k,h]<-sum(prob[k,1:h])   # The cumulative ranking
			probability of treatment i to be among the j best treatments.
		}
	}
	for(i in 1:NT)
	{
	   SUCRA[i]<-sum(cumeffectiveness[i,1:(NT-1)])/(NT-1) # The surface under the
	cumulative rankings for treatment i.
	}

	# pairwise ORs
	for (c in 1:(NT-
	1))
	{
		for (k in (c+1):NT)
		{
			OR[c,k] <- exp(d[k] - d[c] )
			lOR[c,k]<-d[k]-d[c]
		}
	}

}	#END Program
```

Fixed effect inconsistency model

```
#Fixed effects model for multi-arm trials (any number of arms) - developed based on WinBUGS code
from  Multi-parameter Evidence Synthesis Research Group at the University of Bristol  Website:
www.bris.ac.uk/cobm/research/mpes
model
{
		for(i in 1:NS)		# LOOP THROUGH STUDIES
		{
				mu[i]~ dnorm(0,.0001)	# vague priors for trial baselines
				for (k in 1:na[i])	# LOOP THROUGH ARMS
				{
						r[i,k] ~ dbin(p[i,k],n[i,k])	# binomial likelihood
```

```
                    logit(p[i,k]) <- mu[i] + d[t[i,1],t[i,k]]    #model for
                    linear predictor
                    rhat[i,k]<- p[i,k] * n[i,k]     # expected value of the
                    numerators
                    dev[i,k] <- 2* (r[i,k] * (log(r[i,k])-log(rhat[i,k])) +
                    (n[i,k]-r[i,k]) *(log(n[i,k]-r[i,k]) - log(n[i,k]-
                    rhat[i,k]))) #Deviance contribution

            }
            resdev[i] <- sum(dev[i,1:na[i]])   # summed residual deviance
            contribution for this trial
        }
        totresdev <- sum(resdev[])      # Total Residual Deviance
        for (k in 1:NT)     # set effects of k vs k to zero
        {
            d[k,k]<- 0
        }
        for (c in 1:(NT-1))      # priors for all mean treatment effects
        {
            for (k in (c+1):NT)
            {
                    d[c,k] ~ dnorm(0,.0001)
            }
        }
}  #PROGRAM ENDS
```

Fixed effect script

```
#open log file
display('log')
# check model
check('C:/Users/gavinw/Documents/WinBUGS14 data/Fixed Effect Model.txt')
#load datalist
data('C:/Users/gavinw/Documents/WinBUGS14 data/Data List.txt')
#load data table
data('C:/Users/gavinw/Documents/WinBUGS14 data/Data Table.txt')
#compile with 3 chains
compile(3)
#load datalist
inits(1,'C:/Users/gavinw/Documents/WinBUGS14 data/Fixed Effect Inits1.txt')
#load datalist
inits(2,'C:/Users/gavinw/Documents/WinBUGS14 data/Fixed Effect Inits2.txt')
#load datalist
```

```
inits(3,'C:/Users/gavinw/Documents/WinBUGS14 data/Fixed Effect Inits3.txt')
#generate inits
gen.inits()
#run burn in
update(10000)
#monitor
dic.set()
set(rk)
set(best)
set(OR)
set(prob)
set(resdev)
set(totresdev)


set(SUCRA)


set(dev)
#run model
update(10000)
# View Results
stats(*)
dic.stats()
gr(OR)
trace(OR)


# save results
save('C:/Users/gavinw/Documents/WinBUGS14 results/Fixed Effect Results 7 20 2016 2 59 39
PM.txt')
save('C:/Users/gavinw/Documents/WinBUGS14 results/Fixed Effect Results 7 20 2016 2 59 39
PM.odc')
quit()
```

Appendix F **List of references from specialists**

Name	Reference and comment	
Lash 2016	Lash N. J., Whitehouse M. R., Greidanus N. V., Garbuz D. S., Masri B. A., Duncan C. P. Delayed dislocation following metal-onpolyethylene arthroplasty of the hip due to 'silent' trunnion corrosion. Bone and Joint Journal. 2016;98B(2):187-93.	
	Comment	Included only in background. This was a case series that examined the formation of ALTR in MoP patients (n=10).
Konan 2016	Konan S., Garbuz D. S., Masri B. A., Duncan C. P. Modular tapered titanium stems in revision arthroplasty of the hip the risk and causes of stem fracture. Bone and Joint Journal. 2016;98B(1 Supplement A):50-3.	
	Comment	Excluded. This is a case series examining modular stems.
Whitehouse 2015	Whitehouse M. R., Endo M., Zachara S., Nielsen T. O., Greidanus N. V., Masri B. A., et al. Adverse local tissue reactions in metal-onpolyethylene total hip arthroplasty due to trunnion corrosion: The risk of misdiagnosis. Bone and Joint Journal. 2015;97-B(8):1024-30.	
	Comment	Included only in background. This was a case series that examined the formation of pseudotumour
Daivajna 2015	Daivajna S. C., Duncan C. P., Masri B. A., Garbuz D. S. Ultrasound: Optimal screening test for pseudotumor detection. Seminars in Arthroplasty. 2015;26(3):no pagination.	
	Comment	Excluded. This is a narrative review of using ultrasound to diagnose ALTR.
Munro 2014	Munro Jacob T., Masri Bassam A., Duncan Clive P., Garbuz Donald S. High complication rate after revision of large-head metal-on-metal total hip arthroplasty. Clinical orthopaedics and related research. 2014;472(2):523-8.	
	Comment	Excluded. This was a case series about the complication (including ALTR) of large head MoM.
Konan 2014	Konan S., Garbuz D. S., Masri B. A., Duncan C. P. Non-modular tapered fluted titanium stems in hip revision surgery: gaining attention. The bone & joint journal. 2014;96-B(11 Supple A):56-9.	
	Comment	Excluded. This is a review of case series that examined the use of Non-modular fluted, tapered titanium stems.
Garbuz 2014	Garbuz Donald S., Hargreaves Brian A., Duncan Clive P., Masri Bassam A., Wilson David R., Forster Bruce B. The John Charnley Award: Diagnostic accuracy of MRI versus ultrasound for detecting pseudotumors in asymptomatic metal-on-metal THA.	

	Clinical orthopaedics and related research. 2014;472(2):417-23.	
	Comment	Excluded. This was a diagnostic study comparing ultrasound and MRI in diagnosis of ALTR.
Whitehouse 2013	Whitehouse Michael R., Endo Makoto, Masri Bassam A. Adverse local tissue reaction associated with a modular hip hemiarthroplasty. Clinical orthopaedics and related research. 2013;471(12):4082-6.	
	Comment	Excluded. This was a case report of the outcome of a partial hip replacement patient. (Level IV)
Almousa 2013	Almousa Sulaiman A., Greidanus Nelson V., Masri Bassam A., Duncan Clive P., Garbuz Donald S. The natural history of inflammatory pseudotumors in asymptomatic patients after metal-on-metal hip arthroplasty. Clinical orthopaedics and related research. 2013;471(12):3814-21.	
	Comment	Excluded. This was a case series examining the natural history of ALTR. (n=20)
Williams 2011	Williams Daniel H., Greidanus Nelson V., Masri Bassam A., Duncan Clive P., Garbuz Donald S. Prevalence of pseudotumor in asymptomatic patients after metal-on-metal hip arthroplasty. The Journal of bone and joint surgery American volume. 2011;93(23):2164-71.	
	Comment	Included as summary. This was a cohort study examining the rate of ALTR and other surrogate outcomes in MoM, MoP and resurfacing patients.
McGrory 2015	McGrory BJ, MacKenzie J, Babikian G. A High Prevalence of Corrosion at the Head–Neck Taper with Contemporary Zimmer Non-Cemented Femoral Hip Components. The Journal of Arthroplasty. 2015;7(30):1265–1268.	
	Comment	Excluded.Background information only. This was a case series of different stem used and the incidence of ALTR.
Pitto 2015	Pitto RP; Garland M; Sedel L. Are ceramic-on-ceramic bearings in total hip arthroplasty associated with reduced revision risk for late dislocation? Clinical Orthopaedics & Related Research. 2015;473(12):3790-5.	
	Comment	Excluded. This was an analysis of New Zealand registry with matched population, reporting only revision due to dislocation.
Paxton 2015	Paxton EW; Inacio MC; Namba RS; Love R; Kurtz SM. Metal-on-conventional polyethylene total hip arthroplasty bearing surfaces have a higher risk of revision than metal-on-highly crosslinked polyethylene: results from a US registry. Clinical Orthopaedics & Related Research. 2015;473(3):1011-21.	
	Comment	Excluded. This was an analysis of the registry comparing crosslinked

		poly to conventional poly.
ICOR 2015	Sedrakyan A; Graves S; Bordini B; Pons M; Havelin L; Mehle S; Paxton E; Barber T; Cafri G. Comparative effectiveness of ceramic-on-ceramic implants in stemmed hip replacement: a multinational study of six national and regional registries. Journal of Bone & Joint Surgery - American Volume. 2014;96 Suppl 1:34-41. Furnes O; Paxton E; Cafri G; Graves S; Bordini B; Comfort T; Rivas MC; Banerjee S; Sedrakyan A. Distributed analysis of hip implants using six national and regional registries: comparing metal-on-metal with metal-on-highly crosslinked polyethylene bearings in cementless total hip arthroplasty in young patients. Journal of Bone & Joint Surgery - American Volume. 2014;96 Suppl 1:25-33. Paxton E; Cafri G; Havelin L; Stea S; Palliso F; Graves S; Hoeffel D; Sedrakyan A. Risk of revision following total hip arthroplasty: metal-on-conventional polyethylene compared with metal-on-highly crosslinked polyethylene bearing surfaces: international results from six registries. Journal of Bone & Joint Surgery - American Volume. 2014;96 Suppl 1:19-24. Allepuz A; Havelin L; Barber T; Sedrakyan A; Graves S; Bordini B; Hoeffel D; Cafri G; Paxton E. Effect of femoral head size on metal-on-HXLPE hip arthroplasty outcome in a combined analysis of six national and regional registries. Journal of Bone & Joint Surgery - American Volume. 2014;96 Suppl 1:12-8. Sedrakyan A; Graves S; Bordini B; Pons M; Havelin L; Mehle S; Paxton E; Barber T; Cafri G. Comparative effectiveness of ceramic-on-ceramic implants in stemmed hip replacement: a multinational study of six national and regional registries. Journal of Bone & Joint Surgery - American Volume. 2014;96 Suppl 1:34-41.	
	Comments	Excluded. These references were publications from the same research project which used unmatched patients from registry.
Pulikottil 2015	Pulikottil-Jacob R; Connock M; Kandala NB; Mistry H; Grove A; Freeman K; Costa M; Sutcliffe P; Clarke A. Cost-effectiveness of total hip arthroplasty in osteoarthritis: comparison of devices with differing bearing surfaces and modes of fixation.Bone & Joint Journal. 2015;97-B(4):449-57.	
	Comment	Included as a part of NHS 2015.
Jameson 2013	Jameson SS; Baker PN; Mason J; Rymaszewska M; Gregg PJ; Deehan DJ; Reed MR. Independent predictors of failure up to 7.5 years after 35 386 single-brand cementless	

	total hip replacements: a retrospective cohort study using National Joint Registry data. Bone & Joint Journal. 2013;95-B(6):747-57.	
	Comment	Excluded. This was a study of only one brand.
Kurtz 2013	Kocagoz SB; Underwood RJ; MacDonald DW; Gilbert JL; Kurtz SM. Ceramic Heads Decrease Metal Release Caused by Head-taper Fretting and Corrosion.[Erratum appears in Clin Orthop Relat Res. 2016 May;474(5):1344; PMID: 26956249] Clinical Orthopaedics & Related Research. 2016;474(4):985-94. Kurtz SM; Kocagoz SB; Hanzlik JA; Underwood RJ; Gilbert JL; MacDonald DW; Lee GC; Mont MA; Kraay MJ; Klein GR; Parvizi J; Rimnac CM. Do ceramic femoral heads reduce taper fretting corrosion in hip arthroplasty? A retrieval study. Clinical Orthopaedics & Related Research. 2013;471(10):3270-82.	
	Comment	Excluded. These were cohort studies that examined the material loss in MoP and CoP.

Appendix G **Characteristics of included studies**

Article Number	Wyles 2015	Yin 2015	NHS 2015	Hu 2015
Database (if applicable)	Medline	Medline	CRD	Medline
Type of Article	SR	SR	Overview of RCT & SR	SR of RCT
Search Period	Inception to Jan, 2014	Inception to May 2015	2002 to Dec 2012	To Oct 2013
Title and Reference (First author)	Wyles CC	Yin S	Clarke A	Hu DC
Year of publication	2015	2015	Jan 2015	2015
n. patients (studies in case of SR)	18 RCT	40 RCT	16 RCT, 8 SR 13 RCT, 5 SR comparing different THR Limited to publication since 2008 & n>100	9 RCT
Inclusion criteria				
Patients	<65 y/o	<75 y/o	Expand Patients with end-stage arthritis and failed non surgical management	Pt with THR
Intervention & comparator	CoC, CoPxl, MoPxl	Expand MoM, MoPxl, MoPc, CoC, CoPxl, CoPc	Expand Different types of THR vs hip RS Different types of THR compare to each other	CoC vs CoP (mix XL & Pc)
Follow-up period & outcome measured	>2 year Revision	> 2 year Revision	Expand Outcomes: mortality validated functional/pain and health-related quality of life total scores revision rate implant survival rate	Expand demographic data revisons osteolysis radiolucent line aseptic loosening Intra/post-operative implant fracture

			femoral head penetration rate (measure of prosthesis movement) Adverse events included incidence of peri-/postprocedural complications (i.e. implant dislocation, infection, osteolysis, aseptic loosening, femoral fracture and deep-vein thrombosis)	squeaking dislocation deep infections heterotopic ossifications
Exclusion criteria	Expand row Zirconia ceramic, uncrosslinked poly, inclusion of revision cases, non clinical study, report based only on radiography follow-up or component wear	Did not state	Expand indications for hip replacement other than end-stage arthritis of the hip l revision surgery as the primary procedure of interest l abstract/conference proceedings, letters and commentaries l non-English language publications Sample size <100	NR
Study Characteristics				
Population	Data 2599 pt THA with 72 subsequent revision, average follow-up 7 years, range 3-12 years	Data 5321 THR randomized, average f/up 6.6 years	Data RCTs: n=3175, f/up range from 3 mo to 20 years	Data 9 RCT, w 1-10 year f/up, 1575 pts, 1747 hips. 4 RCT sponsored by companies 4 RCTs limited pt to <61 year old
Intervention and comparisons	MoPxl vs CoPxl vs CoC	Expand MoM, MoPxl, MoPc, CoC,	Expand This review compared	CoC vs CoP

		CoPxl, CoPc	different types of THR components including acetabluar cup, shell, femeral stem and bearing surface. Bearing surfaces included in comparison were CoC vs MoPE CoC vs CoPE Ox vs CoCr Steel on PE vs CoCr on PE vs Ox on PE vs CoCr on XLPE vs Ox on XLPE	
List of included studies	CoC versus CoPxl Kim, 2013 Beaupre, 2013 Hamilton, 2010 CoC versus MoPxl Nikolaou, 2012 **Bascarevic, 2010(58)** CoC versus MoPc Venditolli, 2013 D'Antonio, 2012 Nikolaou, 2012 MoPxl versus MoPc García-rey, 2013 Geerdink, 2009 **Engh, 2006** (59) Mutimer, 2010 Nikolaou, 2012 Digas, 2007 Digas, 2004 Geerdink, 2006 Calvert, 2009 CoC versus CoPc Lewis, 2010 Amanatullah, 2011 Cai, 2012	MoPc VS MoPxl VS CoPc VS CoPxl **Morison 2014(60)** MoPc VS MoPxl VS CoC **Nikolaou 2012(61)** MoPc VS MoM VS CoPc **Bjørgul 2013(62)** MoPc VS MoPxl **Engh 2012(63)** **García-Rey 2013 (64)** **Johanson 2012(65)** **Geerdink 2009(66)** **Thomas 2011(67)** **Mutimer 2010(68)** **Digas 2007(69)** **Geerdink 2006(70)** **Triclot 2007(71)** **Calvert 2009(72)** **Glyn-Jones 2008(73)** **Zijlstra 2010(74)** Lombardi 2004 **Hanna 2012(75)** **Zijlstra 2014(76)** **Malviya 2011(77)** CoC vs CoPc	1. Cup fixation (2) Bjørgul 2010, Angadi 2012 2. Cup liner bearing surface (2) McCalden 2009, Engh 2012 3. Cup shell design (1) Capello 2008 4. Cup/stem fixation (1) Corten 2011 5. Femoral head size (1) Howie 2012 6. Femoral head bearing (1) **Lewis 2008(88)** 7. Femoral head-on-cup liner bearing surface (3) Amanatullah 2011, **Capello 2008(89)**, Kadar 2011 8. Stem composition (1) Healy 2009 9. Stem design (1) Kim 2011 10. Stem fixation (1) Kim 2011	**Amanatullah 2011(90)** **Beaupre 2013(91)** **Cai 2012(92)** **Hamilton 2010(93)** **Kim 2013(94)** **Lewis 2010(95)** **Lombardi 2010(96)** **Ochs 2007(78)** Sonny 2005

		Lewis 2010 **Ochs 2007(78)** Amanatullah 2011 Cai 2012 CoC vs CoPxl Kim 2013 Lombardi 2010 Beaupre 2013 Hamilton 2010 CoC VS MoPc **Vendittoli 2013(79)** **D'Antonio 2012(80)** **Seyler 2006(81)** MoPc vs CoPc **Dahl 2013(82)** Kim 2005 **Kraay 2006(83)** MoPxl vs CoPxl **Nakahara 2010(84)** **Kawate 2009(85)** MoPxl vs MoM **Engh 2014(86)** Jacobs 2004 CoC vs MoPxl Bascarevic 2010 CoPc vs MoM Pabinger 2003 **Desmarchelier 2013(87)**		

Article Number	Hu 2015	Dong 2015	CADTH 2013	Si 2015
Type of Article	SR of RCT	SR of RCT	Rapid review	SR of RCT
Search Period	To March 2014	NR	Sep-13	Aug-14
Title and Reference (First author)	Hu DC	Dong YL	NR	Si HB
Year of publication	2015	2015	2013	2015

n. patients (studies in case of SR)	5 RCT	8 RCT	1 SR	11 RCT
Inclusion criteria				
Patients	Pt wth THR	Pt with THR	Pt with THR	Pt with THR
Intervention & comparator	CoC vs MoP (mix XL and Pc)	CoC vs CoP (mix XL and Pc)	CoC vs CoP vs MoPxl	CoC vs CoP
Follow-up period & outcome measured	Expand hip function complication radiographic outcomes	Expand f/up > 24 mo Revision complications radiographic outcomes	Clinical benefit and harm	Expand Follow-up 1-12 y Revision and complications
Exclusion criteria	NR	NR	Expand Studies were excluded if they did not meet the selection criteria if it was unclear as to whether acetabular liners were standard or crosslinked polyethylene if the report was published prior to 2008	
Study Characteristics				
Population	Data 5 RCT, mean f/up 8.4 year, 897 patients w 974 hips. Mean age 54.5	Data 8 RCT, 1508 patients with 1702 hips. Follow-up 2 to 12 years. Included a self controlled study Kim 2013.	Data The identified systematic review included clinical trials, observational studies, and registry data. A total of 18 comparative studies examining 3,404 hips in 3,129 patients were included, four of which were relevant to the comparisons of interest in this review. The mean age of patients ranged between	Data 13 RCTs with 2488 THR, 1 to 12 year follow-up.

			42 and 71 and the percentage of female participants ranged from 26 to 88%.	
Intervention and comparisons	CoC vs MoP	CoC vs CoP	CoC vs CoP vs MoPxl	CoC vs CoP
List of included studies	Bascarevic 2010 D'Antonio 2012 Nikolaou 2012 Vendiittoli 2007 Zhou 2006	Kim 2013 Lauren 2013 Bal 2005 Derek 2011 Lombardi 2010 Cai 2012 Lewis 2010 Hamilton 2010	Sedrakyan 2011	Kim et al 2013 Beaupre et al Cai et al 2012 Amanatullah et al 2011 Lombardi et al 2010 Lewis et al 2010 Hamilton et al 2010 Poggie et al 2007 Kim et al 2007 Bal et al 2005 Nygaard et al 2004 Pitto et al 2003 Pitto et al 2000

Additional RCTs found through updated search:**Jassim 2015 (97); Van der Veen 2015 (98)**

The RCTs in bold followed by their reference number were included in the meta-analysis and network meta-analysis conducted by the HTA reviewers

Appendix H **Characteristics of excluded studies**

Name	Reference and comment	
Bozic 2012	Bozic KJ, Browne J, Dangles CJ, Manner PA, Yates AJ, Jr., Weber KL, et al. Modern metal-on-metal hip implants. The Journal of the American Academy of Orthopaedic Surgeons. 2012;20(6):402-6.	
	Comment	Metal-on-metal only.
Campbell 2014	Campbell PA, Kung MS, Hsu AR, Jacobs JJ. Do retrieval analysis and blood metal measurements contribute to our understanding of adverse local tissue reactions? Clinical orthopaedics and related research. 2014;472(12):3718-27.	
	Comment	This was a SR that investigated serum metal level and it's relation to ALTR.
Carli 2011	Carli A, Reuven A, Zukor DJ, Antoniou J. Adverse soft-tissue reactions around non-metal-on-metal total hip arthroplasty: A systematic review of the literature. Bulletin of the NYU Hospital for Joint Diseases. 2011;69(SUPPL. 1):S47-S51.	
	Comment	This was a SR of case reports of non MoM ALTR.
Gallo 2012	Gallo J, Goodman SB, Lostak J, Janout M. Advantages and disadvantages of ceramic-on-ceramic total hip arthroplasty: a review. Biomedical papers of the Medical Faculty of the University Palacky, Olomouc, Czechoslovakia. 2012;156(3):204-12.	
	Comment	This was a narrative review.
Gosling 2015	Gosling O, Hussain N, Ferreri T, Schemitsch E, Atrey A. Implant wear in total hip arthroplasty: A systematic review and meta-analysis of metal-on-polyethylene versus ceramic on polyethylene components. HIP International. 2015;25:S26.	
	Comment	This was a conference abstract about implant wear.
Hussain 2015	Hussain N, Gosling O, Ferreri T, Schemitsch E, Atrey A. Taper corrosion of the modular total hip arthroplasty: A systematic review and meta-analysis of survivorship between metal and ceramic heads. HIP International. 2015;25:S98.	
	Comment	This was a conference abstract about neck corrosion.
Marques 2016	Marques EMR, Humphriss R, Welton NJ, Higgins JPT, Hollingworth W, Lopez-Lopez JA, et al. The choice between hip prosthetic bearing surfaces in total hip replacement: A protocol for a systematic review and network meta-analysis. Systematic Reviews. 2016;5(1):no pagination.	
	Comment	This was a protocol.
Mihalko 2014	Mihalko WM, Wimmer MA, Pacione CA, Laurent MP, Murphy RF, Rider C. How have alternative bearings and modularity affected revision rates in total hip arthroplasty? Clinical orthopaedics and related research. 2014;472(12):3747-58.	
	Comment	This was a qualitative review of observational studies.
Nieuwenhuijse 2014	Nieuwenhuijse MJ, Nelissen RGHH, Schoones JW, Sedrakyan A. Appraisal of evidence base for introduction of new implants in hip and knee replacement: a systematic review of five widely used device technologies. BMJ (Clinical research ed). 2014;349:g5133.	
	Comment	This review combined CoP and MoP results.
Sedrakyan 2014	Sedrakyan A, Graves S, Bordini B, Pons M, Havelin L, Mehle S, et al. Comparative effectiveness of ceramic-on-ceramic implants in stemmed hip replacement: a multinational study of six national and regional registries. The Journal of bone and joint surgery American volume. 2014;96 Suppl 1:34-41.	
	Comment	This was an analysis of unmatched registries data.
Sedrakyan 2011	Sedrakyan A, Normand SLT, Dabic S, Jacobs S, Graves S, Marinac-Dabic D. Comparative assessment of implantable hip devices with different bearing surfaces: Systematic appraisal of evidence. BMJ (Online). 2011;343(7835):no pagination.	

	Comment	This was a SR of RCT and registry, RCT data was combined with registry data.
Shetty 2011	Shetty V, Shitole B, Shetty G, Thakur H, Bhandari M. Optimal bearing surfaces for total hip replacement in the young patient: a meta-analysis. International orthopaedics. 2011;35(9):1281-7.	
	Comment	This was a SR of observational studies. This review included studies that had no control.
Walker 2015	Walker R, Gee M, Wong F, Shah Z, George M, Bankes M, et al. Functional outcomes of total hip arthroplasty in patients aged 30 years or less. HIP International. 2015;25:S38.	
	Comment	This was a conference abstract.
Zywiel 2011	Zywiel MG, Sayeed SA, Johnson AJ, Schmalzried TP, Mont MA. Survival of hard-on-hard bearings in total hip arthroplasty: A systematic review. Clinical Orthopaedics and Related Research. 2011;469(6):1536-46.	
	Comment	This was a narrative review.
Qu 2011	Qu X, Huang X, Dai K. Metal-on-metal or metal-on-polyethylene for total hip arthroplasty: a meta-analysis of prospective randomized studies. Archives of Orthopaedic and Trauma Surgery. 2011;131(11):1573-83. PubMed PMID: 12012011537.	
	Comment	This review compared MoM to MoP.
Shan 2014	Shan L, Shan B, Graham D, Saxena A. Total hip replacement: a systematic review and meta-analysis on mid-term quality of life. Osteoarthritis and Cartilage. 2014;22(3):389-406. PubMed PMID: 12014005003.	
	Comment	This was a qualitative review of non-RCT.
Stanat 2012	Stanat SJ, Capozzi JD. Squeaking in third- and fourth-generation ceramic-on-ceramic total hip arthroplasty: meta-analysis and systematic review. Journal of Arthroplasty. 2012;27(3):445-53. PubMed PMID: 12012011684.	
	Comment	This review combined RCT and non-RCT data.
Tilbury 2014	Tilbury C, Schaasberg W, Plevier JW, Fiocco M, Nelissen RG, Vliet Vlieland TP. Return to work after total hip and knee arthroplasty: a systematic review. Rheumatology. 2014;53(3):512-25. PubMed PMID: 12013069588.	
	Comment	This was a qualitative review of work status in hip replacement.

Appendix I **Critical appraisal of the included systematic review of economic studies**

Type of Article	Systematic Review of Economic Studies + Economic Evaluation Markov Model
Title and Reference	Clarke et al 2015(28)
Year	2015
Search period	2002-Nov 2012
Clinical question or Context	1. Compared different types of primary Total Hip Replacements to each other 2. Compared Primary Resurfacing of the Hip vs Primary Total Hip Replacement Subgroup results: (**Ages < 65 years)**
Included Studies	Without decision-analytic models Davies C et al 2010(99) Laupacis A et al 2002 (100) Fordham R et al 2012 (101) Hulleberg G et al 2008 (102) Economic evaluation with decision-analytic models Briggs AF et al 2004 (30) (Charnley vs Spectron hip implants) Pennington M et al 2013(34) (cemented vs. cementless vs. hybrid) Marinelli M et al 2008(33) (cemented vs cementless) Bozic KJ 2006 (29)(other alternative bearing surfaces aggregated vs metal-on-common poly) di Tanna GL et al 2011(32) (cementless vs. hybrid) Cummins JS et al 2009(31) (cement with antibiotic vs. without) Bozick KJ et al 2010(35) (metal-on-metal vs resurfacing) Vale L et al 2002(36) (metal-on-metal vs resurfacing)

Research question	**Yes /No/Unclear (Comments)**
1. Was the research question clearly stated (PICOS)?	Y
2. Was the type of participants appropriate to the research question?	Y
3. Was the type of interventions and comparators appropriate?	Y
4. Was the type of outcomes appropriate? (Cost, QALYs, utility, ICERs, WTP, CEACs)	Y
5. Was the type of study design appropriate?	Y

Search strategy	
1. Was the search strategy comprehensive, adequate and reasonably unbiased?	Y
2. Was the selection of studies carried by two reviewers?	Y (First reviewer extracted, Second reviewer checked)
Quality assessment of included studies	
1. Was the quality of included studies assessed in a reliable manner with clearly stated criteria?	Y (CHEC-list)
2. Was the quality assessment performed independently by two reviewers?	Y (First reviewer extracted, and Second reviewer checked)
Data collection	
1. Did the reviewers include all relevant studies?	Y
2. Was the reason for excluding studies stated?	Y
3. Was the process of obtaining missing information stated?	Y
Data synthesis	
1. Was the outcomes (primary and secondary) defined in advance and clearly described?	Y
2. If the results of included studies were combined, was it reasonable to do so?	N (Not reasonable to combine)
3. Were the results appropriately describe?	Y (Descriptive of keys points)
Result reporting	
1. Was the baseline characteristics of included studies reported?	Y
2. Was all results in the method (available or not) reported?	Y
3. Was results reported with appropriate statistics? (95%CI, p value, I^2)	N – not appropriate
4. Was the issue with missing information, if any, addressed?	UN
5. Was the amount of missing information large enough to affect the validity of the result?	UN
6. Was the issue with heterogeneity, if any, addressed?	N –addressed on the primary studies

(N, no; NA, not applicable; UN, unclear; Y, yes)

Appendix J **Critical appraisal of included economic studies**

Type of Article	Systematic Review of Econ Studies + Economic Evaluation Markov Model	Markov Model	Markov Model	Markov Model
Title and Reference	Clarke et al.	Pulikottil-Jacob et al.	Pennington et al.	Briggs et al.
Year	2015	2015	2013	2004
Search period	2002-Nov 2012	NA	NA	NA
Clinical question or Context	1. Different types of primary THR to each other 2. Primary Resurfacing vs. Primary THR	Compared different types of primary Total Hip Replacements to each other. Same model as Clarke et al 2015. Subgroup results: (**Ages >65 years**)	Cemented vs. Cementless vs. Hybrid Subgroup results: **(Ages >65 years)**	Charnley vs. Spectron hip implants
Structure	**Yes /No/Unclear (Comments)**			
1. Is there a clear statement of the decision problem?	Y	Y	Y	Y
2. Is the objective of the model specified and consistent with the stated decision problem?	Y	Y	Y	Y
3. Is the primary decision-maker specified?	Y	Y	N	Y
4. Is the perspective of the model stated clearly?	Y	Y	Y	Y
5. Are the model inputs consistent with the stated perspective?	Y	Y	Y	Y
6. Is the structure of the model consistent with a coherent theory of the	Y	Y	Y	Y

health condition under evaluation?				
7. Are the sources of the data used to develop the structure of the model specified?	Y	Y	Y	Y
8. Are the structural assumptions reasonable given the overall objective, perspective and scope of the model?	Y	UN Revision THA state is 1-year state Should it be an event instead?	UN	Y
9. Is there a clear definition of the options under evaluation?	Y	Y	UN	Y
10. Have all feasible and practical options been evaluated?	Y	N	Y	N
11. Is there justification for the exclusion of feasible options?	NA	Y	UN	N
12. Is the chosen model type appropriate given the decision problem and specified casual relationships within the model?	Y	Y	Y	Y
13. Is the time horizon of the model sufficient to reflect all-important differences between the options?	Y	Y	Y	Y
14. Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	Y	UN Revision THA state is 1-year state Should it be an event instead?	Y	Y
15. Is the cycle length defined and justified in terms of the natural history of disease?	Y	UN Revision THA state is 1-year state Should it be an event instead?	Y	UN
Data				
1. Are the data identification methods	Y	Y	Y	Y

transparent and appropriate given the objectives of the model?				
2. Where choices have been made between data sources are these justified appropriately?	Y	Y	Y	UN
3. Where expert opinion has been used are the methods described and justified?	NA	NA	NA	NA
4. Is the choice of baseline data described and justified?	Y	Y	Y	Y
5. Are transition probabilities calculated appropriately?	Y	Y	UN	Y
6. Has a half-cycle correction been applied to both costs and outcomes?	N	UN	N	NA
7. If not, has the omission been justified?	NA	NA	N	NA
8. Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified?	Y	Y	Y	Y
9. Are the costs incorporated into the model justified?	Y	Y	Y	Y
10. Has the source for all costs been described?	Y	Y	Y	Y
11. Have discount rates been described and justified given the target decision-maker?	Y	Y	Y	Y
12. Are the utilities incorporated into the model appropriate?	Y	Y	Y	Y
13. Is the source of utility weights referenced?	Y	NA	Y	Y
14. If data have been incorporated as distributions, has the choice of distributions for each parameter been	Y	Y	N	Y

described and justified?				
15. If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified?	Y	Y	NA	NA
16. Has heterogeneity been dealt with by running the model separately for different subgroups?	Y	Y	Y	Y
17. Have the results been compared with those of previous models and any differences in results explained?	Y	Y	N	NA

(N, no; NA, not applicable; UN, unclear; Y, yes)

Appendix K **Budget impact for BC in total costs of management of THR its consequences**

Cost of health care for patients requiring total hip replacement over 20 years																					
Year	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**2031**	**2032**	**2033**	**2034**	**2035**	**Total**
N. of primary THR	5,453	5,625	5,793	5,953	6,129	6,344	6,550	6,793	7,050	7,302	7,587	8,020	8,423	8,806	9,192	9,566	9,923	10,297	10,688	11,108	156,602
Annual growth		3%	3%	3%	3%	3%	3%	4%	4%	4%	4%	6%	5%	5%	4%	4%	4%	4%	4%	4%	104%
Total Cost																					
Status quo	64.2 M	66.9 M	69.5 M	72.1 M	74.8 M	78.1 M	81.3 M	85.0 M	89.0 M	92.9 M	97.3 M	103.5 M	109.5 M	115.3 M	121.2 M	127.1 M	132.8 M	138.8 M	145.2 M	151.9 M	2.0 B
MSP Fees - Surgeons	8.5 M	8.8 M	9.2 M	9.5 M	9.9 M	10.4 M	10.8 M	11.3 M	11.9 M	12.4 M	13.0 M	13.9 M	14.7 M	15.5 M	16.4 M	17.2 M	18.0 M	18.9 M	19.8 M	20.7 M	270.9 M
HA Costs	55.8 M	58.1 M	60.3 M	62.5 M	64.9 M	67.7 M	70.5 M	73.7 M	77.1 M	80.5 M	84.3 M	89.6 M	94.8 M	99.7 M	104.8 M	109.9 M	114.8 M	120.0 M	125.4 M	131.2 M	1.7 B
Scenario A - Equal market share between MoP and CoP	65.3 M	68.0 M	70.5 M	73.0 M	75.8 M	79.0 M	82.2 M	85.9 M	89.8 M	93.7 M	98.1 M	104.3 M	110.2 M	116.0 M	121.8 M	127.7 M	133.4 M	139.3 M	145.6 M	152.3 M	2.0 B
MSP Fees - Surgeons	8.4 M	8.7 M	9.1 M	9.4 M	9.8 M	10.2 M	10.6 M	11.1 M	11.6 M	12.2 M	12.8 M	13.6 M	14.4 M	15.2 M	16.0 M	16.8 M	17.5 M	18.4 M	19.2 M	20.1 M	265.0 M
HA Costs	56.9 M	59.2 M	61.5 M	63.6 M	66.0 M	68.8 M	71.6 M	74.8 M	78.2 M	81.5 M	85.3 M	90.7 M	95.8 M	100.8 M	105.9 M	110.9 M	115.8 M	121.0 M	126.4 M	132.1 M	1.8 B
Annual Budget Impact of the police change (MSP + HA)	1.1 M	1.0 M	1.0 M	970.9 K	937.1 K	909.8 K	878.3 K	851.3 K	822.9 K	789.0 K	757.0 K	748.8 K	727.0 K	694.1 K	655.3 K	607.4 K	549.9 K	489.9 K	427.5 K	365.2 K	15.3 M
MSP Annual Budget Impact	-71.2 K	-90.7 K	-107.9 K	-126.0 K	-144.4 K	-163.7 K	-183.8 K	-205.2 K	-227.8 K	-251.7 K	-277.2 K	-306.1 K	-336.6 K	-368.6 K	-402.3 K	-437.7 K	-474.5 K	-513.1 K	-553.5 K	-595.9 K	-5.8 M
HA Budget Impact	1.2 M	1.1 M	1.1 M	1.1 M	1.1 M	1.1 M	1.1 M	1.1 M	1.1 M	1.0 M	1.0 M	1.1 M	1.1 M	1.1 M	1.1 M	1.0 M	1.0 M	1.0 M	981.0 K	961.1 K	21.2 M
Scenario B - CoP market share higher than MoP	65.5 M	68.1 M	70.7 M	73.2 M	75.9 M	79.2 M	82.3 M	86.0 M	89.9 M	93.8 M	98.2 M	104.4 M	110.3 M	116.1 M	122.0 M	127.8 M	133.4 M	139.4 M	145.7 M	152.3 M	2.0 B
MSP Fees - Surgeons	8.4 M	8.7 M	9.1 M	9.4 M	9.7 M	10.2 M	10.6 M	11.1 M	11.6 M	12.1 M	12.7 M	13.5 M	14.3 M	15.1 M	15.9 M	16.7 M	17.5 M	18.3 M	19.1 M	20.1 M	264.1 M
HA Costs	57.1 M	59.4 M	61.6 M	63.8 M	66.2 M	69.0 M	71.8 M	74.9 M	78.3 M	81.7 M	85.5 M	90.9 M	96.0 M	101.0 M	106.1 M	111.1 M	116.0 M	121.1 M	126.5 M	132.3 M	1.8 B
Annual Budget Impact of the police change (MSP + HA)	1.3 M	1.2 M	1.2 M	1.1 M	1.1 M	1.1 M	1.0 M	989.1 K	956.1 K	916.7 K	879.6 K	869.9 K	844.6 K	806.4 K	761.4 K	705.7 K	638.9 K	569.2 K	496.7 K	424.3 K	17.8 M
MSP Annual Budget Impact	-82.7 K	-105.3 K	-125.4 K	-146.4 K	-167.7 K	-190.3 K	-213.5 K	-238.4 K	-264.7 K	-292.4 K	-322.1 K	-355.7 K	-391.1 K	-428.2 K	-467.5 K	-508.5 K	-551.3 K	-596.2 K	-643.1 K	-692.4 K	-6.8 M
HA Budget Impact	1.3 M	1.3 M	1.3 M	1.3 M	1.3 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.2 M	1.1 M	1.1 M	24.6 M

Appendix L **Number of revisions surgeries estimated for BC**

Year	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	Total
Number of revisions																					
Status quo	67	94	119	147	177	209	243	280	321	363	410	461	517	575	638	705	775	850	929	1,012	8894
Scenario A - Equal market share between MoP and CoP	49	71	93	116	141	168	198	229	264	301	341	385	433	484	538	596	657	722	791	864	7441
Annual Impact (n. revision surgeries)	-18	-23	-27	-31	-36	-41	-46	-51	-57	-63	-69	-76	-84	-92	-100	-109	-118	-128	-138	-148	-1453
Scenario B - CoP market share higher than MoP	46	67	88	111	135	162	190	221	255	291	330	373	419	469	522	578	638	702	769	840	7206
Annual Impact (n. revision surgeries)	-21	-26	-31	-36	-42	-47	-53	-59	-66	-73	-80	-89	-97	-107	-116	-127	-137	-148	-160	-172	-1688

Appendix M **Costs with primary implants**

Year	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	Total
Cost of primary implants																					
Status quo	12.6 M	13.0 M	13.4 M	13.7 M	14.1 M	14.6 M	15.1 M	15.7 M	16.3 M	16.8 M	17.5 M	18.5 M	19.4 M	20.3 M	21.2 M	22.1 M	22.9 M	23.8 M	24.7 M	25.6 M	361.3 M
Scenario A - Equal market share between MoP and CoP	14.0 M	14.5 M	14.9 M	15.3 M	15.7 M	16.3 M	16.8 M	17.5 M	18.1 M	18.8 M	19.5 M	20.6 M	21.6 M	22.6 M	23.6 M	24.6 M	25.5 M	26.5 M	27.5 M	28.5 M	402.4 M
Annual Budget Impact of the police change $	1.4 M	1.5 M	1.5 M	1.6 M	1.6 M	1.7 M	1.7 M	1.8 M	1.9 M	1.9 M	2.0 M	2.1 M	2.2 M	2.3 M	2.4 M	2.5 M	2.6 M	2.7 M	2.8 M	2.9 M	41.1 M
Scenario B - CoP market share higher than MoP	14.2 M	14.7 M	15.1 M	15.5 M	16.0 M	16.6 M	17.1 M	17.7 M	18.4 M	19.1 M	19.8 M	20.9 M	22.0 M	23.0 M	24.0 M	25.0 M	25.9 M	26.9 M	27.9 M	29.0 M	409.0 M
Annual Budget Impact of the police change $	1.7 M	1.7 M	1.8 M	1.8 M	1.9 M	1.9 M	2.0 M	2.1 M	2.2 M	2.2 M	2.3 M	2.4 M	2.6 M	2.7 M	2.8 M	2.9 M	3.0 M	3.1 M	3.3 M	3.4 M	47.8 M

Appendix N **Costs of revision surgeries**

Year	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	Total
Cost of revision surgeries (includes implants + hospital + complications + MSP fees)																					
Status quo	1.4 M	2.0 M	2.5 M	3.1 M	3.7 M	4.4 M	5.1 M	5.9 M	6.7 M	7.6 M	8.6 M	9.7 M	10.8 M	12.0 M	13.4 M	14.8 M	16.2 M	17.8 M	19.4 M	21.2 M	186.1 M
MSP Fees - Surgeons	267.5 K	376.3 K	480.1 K	591.8 K	710.7 K	839.7 K	977.5 K	1.1 M	1.3 M	1.5 M	1.6 M	1.9 M	2.1 M	2.3 M	2.6 M	2.8 M	3.1 M	3.4 M	3.7 M	4.1 M	35.7 M
HA Costs	1.1 M	1.6 M	2.0 M	2.5 M	3.0 M	3.5 M	4.1 M	4.7 M	5.4 M	6.1 M	6.9 M	7.8 M	8.7 M	9.7 M	10.8 M	11.9 M	13.1 M	14.4 M	15.7 M	17.1 M	150.4 M
Scenario A - Equal market share between MoP and CoP	1.0 M	1.5 M	2.0 M	2.5 M	3.0 M	3.6 M	4.2 M	4.9 M	5.7 M	6.5 M	7.3 M	8.3 M	9.3 M	10.4 M	11.6 M	12.8 M	14.2 M	15.6 M	17.1 M	18.6 M	160.3 M
MSP Fees - Surgeons	196.3 K	285.6 K	372.2 K	465.8 K	566.4 K	675.9 K	793.7 K	921.7 K	1.1 M	1.2 M	1.4 M	1.5 M	1.7 M	1.9 M	2.2 M	2.4 M	2.6 M	2.9 M	3.2 M	3.5 M	29.9 M
HA Costs	846.7 K	1.2 M	1.6 M	2.0 M	2.5 M	2.9 M	3.5 M	4.0 M	4.6 M	5.3 M	6.0 M	6.7 M	7.6 M	8.5 M	9.4 M	10.5 M	11.5 M	12.7 M	13.9 M	15.2 M	130.4 M
Annual Budget Impact of the police change (MSP + HA)	-347.4 K	-435.7 K	-512.4 K	-592.0 K	-672.1 K	-755.7 K	-841.3 K	-932.2 K	-1.0 M	-1.1 M	-1.2 M	-1.4 M	-1.5 M	-1.6 M	-1.8 M	-1.9 M	-2.1 M	-2.2 M	-2.4 M	-2.6 M	-25.8 M
MSP Annual Budget Impact	-71.2 K	-90.7 K	-107.9 K	-126.0 K	-144.4 K	-163.7 K	-183.8 K	-205.2 K	-227.8 K	-251.7 K	-277.2 K	-306.1 K	-336.6 K	-368.6 K	-402.3 K	-437.7 K	-474.5 K	-513.1 K	-553.5 K	-595.9 K	-5.8 M
HA Budget Impact	-276.2 K	-345.1 K	-404.5 K	-466.0 K	-527.7 K	-592.0 K	-657.5 K	-727.0 K	-800.1 K	-876.3 K	-957.8 K	-1.1 M	-1.1 M	-1.2 M	-1.4 M	-1.5 M	-1.6 M	-1.7 M	-1.8 M	-2.0 M	-20.0 M
Scenario B - CoP market share higher than MoP	986.8 K	1.5 M	1.9 M	2.4 M	2.9 M	3.5 M	4.1 M	4.8 M	5.5 M	6.3 M	7.1 M	8.1 M	9.1 M	10.2 M	11.3 M	12.5 M	13.8 M	15.2 M	16.7 M	18.2 M	156.1 M
MSP Fees - Surgeons	184.8 K	271.0 K	354.7 K	445.4 K	543.0 K	649.4 K	764.0 K	888.5 K	1.0 M	1.2 M	1.3 M	1.5 M	1.7 M	1.9 M	2.1 M	2.3 M	2.6 M	2.8 M	3.1 M	3.4 M	29.0 M
HA Costs	802.0 K	1.2 M	1.5 M	1.9 M	2.4 M	2.8 M	3.3 M	3.9 M	4.5 M	5.1 M	5.8 M	6.6 M	7.4 M	8.3 M	9.2 M	10.2 M	11.3 M	12.4 M	13.6 M	14.8 M	127.2 M
Annual Budget Impact of the police change (MSP + HA)	-403.6 K	-506.3 K	-595.4 K	-687.8 K	-780.8 K	-878.0 K	-977.4 K	-1.1 M	-1.2 M	-1.3 M	-1.4 M	-1.6 M	-1.7 M	-1.9 M	-2.0 M	-2.2 M	-2.4 M	-2.6 M	-2.8 M	-3.0 M	-30.0 M
MSP Annual Budget Impact	-82.7 K	-105.3 K	-125.4 K	-146.4 K	-167.7 K	-190.3 K	-213.5 K	-238.4 K	-264.7 K	-292.4 K	-322.1 K	-355.7 K	-391.1 K	-428.2 K	-467.5 K	-508.5 K	-551.3 K	-596.2 K	-643.1 K	-692.4 K	-6.8 M
HA Budget Impact	-320.9 K	-400.9 K	-470.0 K	-541.4 K	-613.1 K	-687.8 K	-763.9 K	-844.7 K	-929.6 K	-1.0 M	-1.1 M	-1.2 M	-1.3 M	-1.5 M	-1.6 M	-1.7 M	-1.8 M	-2.0 M	-2.1 M	-2.3 M	-23.2 M