

# Hip Resurfacing (Re-Review)

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## Final Evidence Report

October 14, 2013

**Health Technology Assessment Program (HTA)**

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# Hip Resurfacing (Re-Review)

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October 14, 2013

This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.



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## Executive Summary

### Introduction

Total hip arthroplasty (THA) is a well-established and effective treatment for severe degenerative diseases of the hip that has historically been performed in older, relatively inactive patients between 60 and 80 years of age. Over the past 10 to 15 years, however, THA has become increasingly common in patients less than 65 years of age. As the growth of joint replacement continues in younger patients, the demand for THA among patients under 65 years was expected to exceed 50% of all THAs by 2011, up from 44% in 2005. Younger patients receiving hip replacement often have more active lifestyles than those who are older, causing concern about the longevity of the implant. Evidence suggests that higher rates of implant failure occur as the age of patients receiving the implant gets younger.

Total hip resurfacing (HR) is proposed as a bone-conserving alternative to the conventional THA for young and active patients after optimal medical therapy fails. In contrast to THA, total HR preserves the femoral head and neck, which may facilitate future revision surgery should it be necessary, and additionally, enable the patient to take advantage of newer technology or treatments in the future. Furthermore, hip resurfacing was designed to more closely mimic normal joint biomechanics and load transfer, and may be associated with a lower local morbidity rate at the time of revision surgery.

In the fall of 2009, a HTA on hip resurfacing was completed for the State of Washington. Since the publication of that report, metal-on-metal (MoM) hip systems (both THA and HR) have received wide spread usage. As a result, more information has become available regarding the safety profile and clinical performance of these MoM systems. Data from national total joint registries as well as peer-reviewed journal publications and presentations at scientific meetings have suggested increasing rates of potential safety issues associated with MoM hip systems including:

- (1). Local complications such as osteolysis, pseudotumors and aseptic lymphocytic vasculitis-associated lesions (ALVAL)
- (2). Early device failure and the need for revision surgery
- (3). Systemic complications from metal ion exposure

As a result of these safety concerns, there has been a dramatic reduction in the use of MoM hip replacement, including hip resurfacing, among the orthopedic community. For example, the Australia National Joint Replacement Registry reports a 69% reduction in HR in 2012 compared to the peak use in 2005, while the National Joint Registry of England and Wales reports a 59% decrease from 2009 to 2011.

Given the recent safety concerns with MoM hip resurfacing, an update to the 2009 HTA report was commissioned to bring the latest evidence to bear on the following Key Questions:

**Key Question 1:** What is the evidence of efficacy and effectiveness of hip resurfacing (HR) compared with total hip arthroplasty (THA)?

**Key Question 2:** What is the evidence about the safety profile for hip resurfacing compared with THA?

**Key Question 3:** What is the evidence of efficacy, effectiveness and safety of revisions of hip resurfacing compared with revisions of THA?

**Key Question 4:** Is there evidence of differential efficacy or safety issues with use of hip resurfacing?

**Key Question 5:** What is the evidence of cost implications and cost effectiveness of hip resurfacing?

## Methods

We searched electronic databases from January 1, 2009 through 2 June, 2013 to determine new publications since our original report. We attempted to pool functional outcomes when two or more randomized controlled studies presented identical outcomes over similar time periods. We did not pool the functional outcomes from observational studies due to heterogeneity between studies. However, we did pool observational studies to assess the risk for revisions but display them separately from RCTs.

### *Outcome Assessed*

For efficacy and effectiveness, we assessed functional outcomes using patient-reported functional and quality of life outcomes measures, as well as activity scores. We also included clinician-based outcomes measures such as the Harris Hip Score. For safety, we assessed revision and complications, and addressed issues around blood ion concentrations.

## Results

Results for this updated HTA are presented in the executive summary alongside the findings from the original report to assist the reader in identifying differences.

### *Studies Selected*

We identified 5 new randomized controlled trials; three are new studies and two are subsequent follow-up studies of clinical results from an earlier RCT. We also found eight new controlled observational studies, three updated annual reports from three national total hip registries, and two new cost effectiveness studies. In addition, we reviewed 13 studies that report revision risks comparing HR with THA from one or more of the three national total hip registries. Since these reports represent older registry data, we not report results from these studies, but rather we report revision risks from the latest annual reports of each registry. However, each of the 13 studies was abstracted and their data can be found in the appendices.

### **Studies Included**

Key Questions	Original	Update	Total
KQ 1,2,4	(n = 4 RCTs) (n = 20 observational studies) (n = 3 total hip registry reports)	(n = 5 RCTs) (n = 3 observational studies) (n = 3 total hip registry reports)	(n = 9 RCTs) (n = 12 observational studies) (n = 3 total hip registry reports)
KQ 3	(n = 2)	(n = 5)	(n = 7)
KQ 5	(n = 4)	(n = 2)	(n = 6)

*Updated Health Technology Reports since the Washington State 2009 HTA*

Three HTAs summarized in Washington State's 2009 report underwent updated reviews since the publication of our first report. These updates were a result of safety concerns around metal-on-metal bearing hip replacement systems to include HR. In addition, we found a new HTA from the American Academy of Orthopaedic Surgeons and a new report from the FDA. We provide a summary of these 5 reports below, both from the previous and current report (blue column).

Assessment (Year)	Results from 2009 HTA Report	Results from this 2013 Updated HTA Report
<b>California Technology Assessment Forum: 2007</b>  <b>Update : 2011</b>	<p><b>Efficacy:</b> Because no RCTs with FDA-approved devices are available, MoM HR has not been shown to improve health outcomes in an investigational setting</p> <p><b>Safety:</b> A national review of femoral neck fractures associated with BHR report an incidence of 1.46%. Chronic exposure to metal ions a concern</p>	<p><b>Efficacy:</b> Recent studies, particularly registry evidence shows an increased revision rate with HRA compared with THA</p> <p><b>Safety:</b> Increasing concerns about metal ion levels; need to prove safety and efficacy in RCTs before subjecting young patients to significant potential harm over their lifetimes</p> <p>MoM HR using the BHR, Cormet 2000, or Conserve Plus devices does not meet CTAF criteria 3-5 for safety, efficacy and improvement in health outcomes for patients as an alternative to THA</p>
<b>Ontario Health Technology Assessment Series: 2006</b>  <b>Update: 2012</b>	<p><b>Efficacy:</b> MoM HR has been shown to be effective as tested in younger patients. However, there are no RCTs that compare MoM HR with THA</p> <p><b>Safety:</b> Concern remains on the potential adverse effects of metal ions</p> <p><b>Economic:</b> MoM HR is more cost effective compared with watchful waiting followed by THA. MoM HR is not more cost effective when compared directly with THA</p>	<p><b>Efficacy:</b> Not addressed in 2012 report</p> <p><b>Safety:</b> Only three of MoM HR implants (BHR, Conserve Plus, Cormet 2000) met the NICE criteria for revision rates of 10% or less at 10 years (two (ReCap, Durom) had short-term f/u and one (ASR) failed to meet the criteria). Concerns about adverse tissue reactions and biological effects of high metal ion levels in the blood were reported by several studies</p> <p><b>Economic:</b> Not addressed in 2012 report</p>
<b>The Canadian Coordinating Office for Health Technology Assessment: 2003</b>  <b>Update: 2012</b>	<p><b>Efficacy:</b> MoM HR was recommended as one option for active, younger patients with advanced hip disease</p> <p><b>Safety:</b> Patient selection is important for prosthesis viability</p> <p><b>Economic:</b> Need for cost-benefit analysis was stated</p>	<p><b>Efficacy:</b> MoM HR allows for greater bone preservation, lower wear rates, and equal or better functional outcomes compared with THA</p> <p><b>Safety:</b> MoM HR patients experienced higher rates of revision, femoral neck fractures, and component loosening than THA recipients</p> <p><b>Economic:</b> No evidence found</p>

Assessment (Year)	Results from 2009 HTA Report	Results from this 2013 Updated HTA Report
<b>American Academy of Orthopaedic Surgeons (AAOS) 2011</b>	No previous HTA report	<p><b>Efficacy:</b> HRA had better 1- and 2-year WOMAC scores, although there was no clinical relevance in the difference between HR and THA</p> <p><b>Safety:</b> Concerns about increased revision rates, local metal debris release, adverse tissue reactions, and elevated serum metal ion levels in MoM articulations, although not enough data to report clinical significance</p> <p><b>Economic:</b> Not addressed in 2011 report</p>
<b>FDA Executive Summary Memorandum 2012</b>	No previous report	<p><b>Efficacy:</b> Not addressed</p> <p><b>Safety:</b> Concerns with local complications, early device failure and the need for revision surgery, and systemic complications from metal ion exposure</p> <p><b>Economic:</b> Not addressed in 2012 report</p>

### ***Results from the Washington State HTA Report***

We provide a summary of the results by key question from the current report next to the summary of results from the 2009 report.

**Key question 1: What is the evidence of efficacy and effectiveness of hip resurfacing (HR) compared with total hip arthroplasty (THA)?**

Results From 2009 HTA Report	Results From This 2013 Updated HTA Report
<p><b>Efficacy (<math>\leq 1</math> year):</b> There is MODERATE evidence from three small randomized controlled trials that total HR is similar to THA with respect to short-term (1 year) functional, quality of life, and activity outcome.</p> <p><b>Efficacy (<math>&gt;1</math> year):</b> There are NO DATA available to assess efficacy beyond one-year follow-up.</p> <p><b>Effectiveness (Short-term, <math>&lt;5</math> years):</b> There is LOW evidence from studies directly comparing total HR with THA to suggest that short-term (<math>\leq 5</math> years) patient-reported outcomes, clinician-based outcomes, and pain are similar comparing total HR and THA. Activity scores tend to be slightly higher (better) in total HR patients.</p>	<p><b>Efficacy (<math>\leq 2</math> year):</b> There is MODERATE evidence from three small randomized controlled trials that total HR is similar to THA with respect to short-term (<math>&lt;2</math> year) functional, quality of life, and activity outcome.</p> <p><b>Efficacy (<math>&gt;2</math> year):</b> There are NO DATA available to assess efficacy beyond two-year follow-up.</p> <p><b>Effectiveness (Short-term, <math>&lt;5</math> years):</b> There is LOW evidence from studies directly comparing total HR with THA to suggest that short-term (<math>\leq 5</math> years) patient-reported outcomes, clinician-based outcomes, and pain are similar comparing total HR and THA. Activity scores tend to be slightly higher (better) in total HR patients.</p>

Results From 2009 HTA Report	Results From This 2013 Updated HTA Report
<b>Effectiveness (Mid-term, 5-10 years):</b> There is VERY LOW evidence from one cohort study to suggest that at an average of 5.9 years follow-up, patients treated with total HR may have better quality of life and activity outcome scores, but similar functional scores, compared with those treated with THA.	<b>Effectiveness (Mid-term, 5-10 years):</b> There is INSUFFICIENT evidence from one cohort study to suggest that at an average of 5.9 years follow-up, patients treated with total HR may have better quality of life and activity outcome scores, but similar functional scores, compared with those treated with THA.

**Key question 2: What is the evidence related to the safety profile of hip resurfacing?**

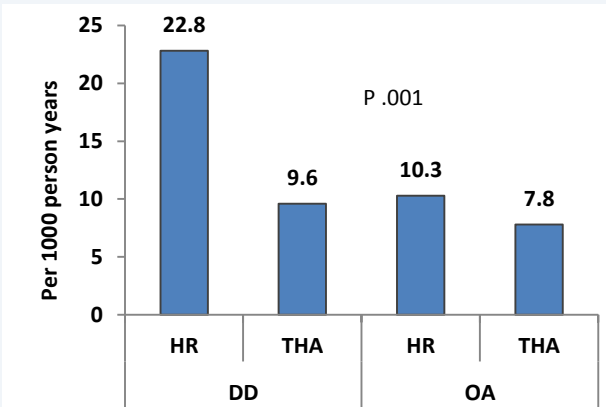
Results From 2009 HTA Report	Results From This 2013 Updated HTA Report
<b>Revision (Short-term, ≤5 years)</b> There is MODERATE evidence that short-term revision rates are slightly higher in patients treated with total HR compared with those treated with THA. The difference in 3-year revision rates between total HR and THA in 3 registry studies range from 0.6% to 2.5% in favor of THA. The difference in 1-year revision rates in one RCT is 0.9% in favor of THA. The difference in short-term revision rates between total HR and THA in eight cohort studies varied: 4 favored THA, 2 favored total HR, and 2 reported equal rates.	<b>Revision (Short-term, ≤5 years)</b> There is HIGH evidence from three large registry studies that short-term revision risks are higher in patients treated with total HR compared with those treated with THA. At three years, there is between 20-50% higher risk of revision among those receiving HR vs. THA. The absolute risk is 3% in the HR group and between 2- 3% in the THA group. At five years, the higher risk is between 30-80%. The absolute risk ranges from 5 to 6% in the HR group and 1 to 4% in the THA group.
<b>Revision (Mid-term, 6-10 years)</b> There is LOW evidence from one large registry study that 7-year revision rates are higher in patients receiving total HR versus THA (hazard ratio = 1.42, rate difference = 1.3%). Data from one small cohort study with a mean follow-up of 5.9 years reports revision rates that are similar between total HR and THA.	<b>Revision (Mid-term, 6-10 years)</b> There is HIGH evidence from three large registry studies that 7 and 10-year revision risks are higher ranging from 40-100% in patients receiving total HR versus THA. The absolute risk at 7 years is between 6-9% in the HR group and between 3- 4% in the THA group.
<b>Revision (Long-term, 10+ years)</b> There is NO evidence comparing long-term revision rates between total HR and THA.	<b>Revision (Long-term, 10+ years)</b> There is LOW evidence from one registry study that 11-year revision risks are higher in patients receiving total HR (10%) versus THA (7%).
<b>Complications</b> Reported risks of other complications in the short-term for total HR are generally low except for heterotopic ossification; the risk of femoral neck	<b>Complications</b> There is HIGH evidence from up to 3 RCTs and up to 6 observational studies that <ul style="list-style-type: none"> <li>femoral component loosening occurs 8 times</li> </ul>

Results From 2009 HTA Report	Results From This 2013 Updated HTA Report
<p>fractures range from 0.4-2.6%, avascular necrosis from 0.4-2%, femoral component loosening from 0-3.6%, acetabular component loosening from 0-1.8%, acetabular component migration from 0-1.9%, and femoral component migration was not detected in any hips. Heterotopic ossification rates ranged from 0-42.7%</p>	<p>more frequently in HR patients than in THA patients, 2.7% vs. 0.3%</p> <ul style="list-style-type: none"> <li>• heterotopic ossification occurs nearly twice as often in HR patients compared with THA patients, 19.8% vs. 11.4%.</li> <li>• Dislocation occurs less frequently in HR vs. THA patients, 0.5% vs. 2.8%.</li> </ul> <p>There is MODERATE evidence that deep infection occurs less frequently in patients undergoing HR compared with THA, 0.4% vs. 1.8%.</p> <p>The risk of femoral neck fracture and avascular necrosis in HR patients is 2% and 1%, respectively.</p>
<p><b>Metal Ion Safety</b></p> <p>Patients with metal-on-metal total HR are likely to experience elevated metal serum levels (Co and Cr). Concerns have been raised regarding the safety of and risks associated with prolonged exposure to metal ions, and whether such exposure may increase the risk of cancers or metabolic disorders. However, an association between total HR and cancer or metabolic disorders has not been reported with the current length of follow-up. The results from long-term monitoring will be needed to assess the risk of metal ion exposure.</p>	<p><b>Metal Ion Safety</b></p> <p>There are consistently higher median concentrations of the primary metal ions cobalt and chromium in the blood or hair of HR patients compared with non-MoM THA (MoP and ceramic) patients in 5 studies with up to 3-year follow-up.</p> <p>High blood levels of cobalt and chromium are associated with poor outcomes (revision or poorly functioning hip) compared with low blood levels in patients receiving HR in 3 studies.</p> <p>Higher serum ion levels of cobalt and chromium are associated with pseudotumor formation following MoM HR and MoM THA in 3 studies.</p> <p>MoM hip prostheses (both HR and THA) are not associated with an increased risk of cancer compared with THA with other bearing surfaces in 3 registry studies.</p> <p>There is no negative impact on renal function across 6 studies evaluating patients following MoM HR or MoM THA.</p>

**Key Question 3: What is the evidence of efficacy, effectiveness and safety of revisions of hip resurfacing compared with revisions of THA?**

Results From 2009 HTA Report	Results From This 2013 Updated HTA Report
This was not a key question in the 2009 HTA report	There is INSUFFICIENT evidence from one small study reporting similar functional and quality of life outcomes comparing HR revision with THA revision at final follow-up (range, 2-7 years).

**Key Question 4: Is there evidence of differential efficacy or safety issues with use of hip resurfacing?**

Results From 2009 HTA Report	Results From This 2013 Updated HTA Report									
<p><b>Dysplasia vs. other arthritic conditions</b></p> <p>There is LOW evidence to suggest that short-term revision rates are twice as high in patients who receive total HR for a primary diagnosis of dysplasia compared with patients of primary osteoarthritis. The 5-year cumulative revision percent for dysplasia is four times greater in those receiving total HR compared with THA (12% vs. 3%) in one registry study. One small prognostic study supported this data, with 5.2% revision rates in dysplasia patients compared with 0% revision rates in osteoarthritic patients.</p>	<p><b>Dysplasia vs. other arthritic conditions</b></p> <p>There is HIGH evidence from a large registry study that the diagnosis of developmental dysplasia (DD) modifies the rate of revision in HR and THA; those with DD receiving HR have significantly higher revision rates than those receiving THA or those with other diagnoses receiving HR or THA.</p> <div><table><caption>Revision Rates per 1000 person years</caption><thead><tr><th>Diagnosis</th><th>HR</th><th>THA</th></tr></thead><tbody><tr><td>DD</td><td>22.8</td><td>9.6</td></tr><tr><td>OA</td><td>10.3</td><td>7.8</td></tr></tbody></table></div>	Diagnosis	HR	THA	DD	22.8	9.6	OA	10.3	7.8
Diagnosis	HR	THA								
DD	22.8	9.6								
OA	10.3	7.8								
<p><b>Gender</b></p> <p>There is MODERATE evidence from three registries that 3- and 5-year revision rates are higher in females than in males (hazard ratios range from 1.57 to 2.5). Much of the difference in rates between sexes disappeared in one study when controlling for femoral component head size; the smaller the head, the higher the failure rate.</p>	<p><b>Gender</b></p> <p>There is HIGH evidence from a large registry study that gender modifies the rate of revision in HR and THA; females receiving HR have significantly higher revision rates than females receiving THA or males receiving HR or THA</p>									

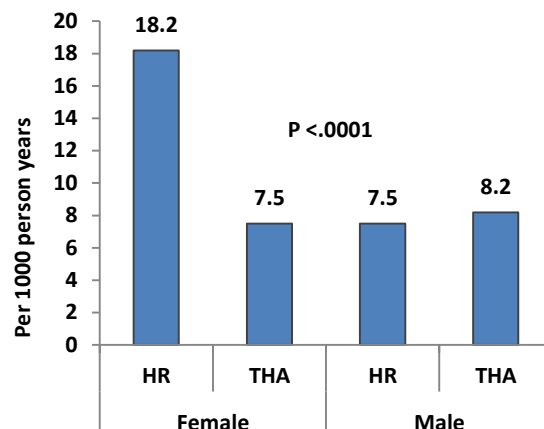


## Results From 2009 HTA Report

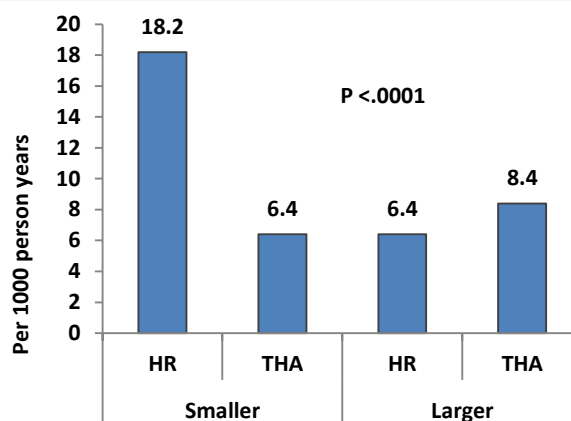
## Results From This 2013 Updated HTA Report

**Femoral component head size**

See gender above.

**Femoral component head size**

Smaller femoral component head size results in significantly higher revision rates for those receiving HR while larger femoral component heads result in higher revision rates in those receiving THA.



\*Smaller: HR <50 mm, THA ≤32 mm; Larger: HA ≥50 mm, THA >32 mm

**Obesity**

Two low quality studies evaluated the effect of obesity on total HR with conflicting results. One reported lower revision risk with increasing obesity, and one reported higher.

**Obesity**

No evidence that obesity has a differential effect on treatment.



**Key Question 5: What is the evidence of cost implications and cost effectiveness of hip resurfacing?**

Results From 2009 HTA Report	Results From This 2013 Updated HTA Report
<b>Cost Effectiveness</b>  There is limited evidence on the economic implications of hip resurfacing from two published articles and one HTA. Revision rates are important input factors in the prediction models, and no study estimated the revision rates using current data.	<b>Cost Effectiveness</b>  There is limited evidence on the economic implications of hip resurfacing from four published articles and one HTA. Revision rates are important input factors in the prediction models, and no study estimated the revision rates using current data.

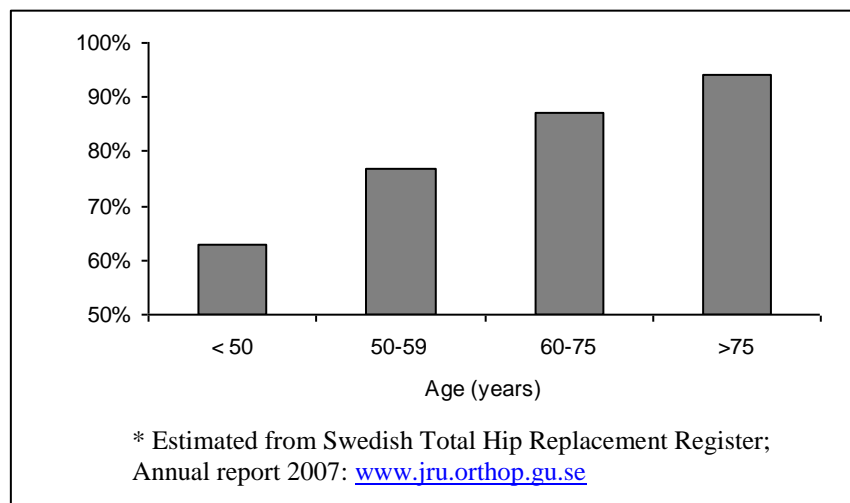
# 1. Appraisal

## 1.1. Rationale

Total hip arthroplasty (THA) has proven to be effective for elderly patients with hip pain and dysfunction from non-inflammatory arthritis such as osteoarthritis, traumatic arthritis, avascular necrosis, dysplasia, or inflammatory arthritis such as rheumatoid arthritis. Over the last decade, the prevalence of THA in younger patients (those under 65 years) has increased. As the growth of joint replacement continues in younger patients, the demand for THA among patients under 65 years is expected to exceed 50% of all THAs by 2011, up from 44% in 2005.<sup>84</sup> Younger patients receiving hip replacement are more likely to have a diverse set of causes leading them to undergo total hip replacement. For example, osteonecrosis is a common cause of hip pain in younger patients. Traditionally, patients with osteonecrosis have had worse outcomes after total hip arthroplasty than patients with osteoarthritis. Furthermore they often have more active life styles than those who are older, causing concern about the longevity of the implant. Evidence suggests that higher rates of implant failure occur as the age of patients receiving the implant get younger, Figure 1.

**Figure 1. Implant Survival (%) after 16 Years\***

Options for contemporary THA allow for use of multiple femoral and acetabular components. The femoral component consists of a metal stem that is placed into the center of the femur and may be cemented or uncemented ("press fit") into the bone. A metal or ceramic ball is placed on the upper part of the stem, replacing the damaged femoral head. The acetabulum ("socket") is



replaced with a solid metal cup, or a metal cup that may be lined with a plastic, ceramic or metal insert/liner between the head and socket. Solid metal cups must be completely removed during revision of the cup, whereas other implants may permit just an exchange of the liner. Screws or cement may be used to hold the socket in place. As with the femoral component, the acetabular component (socket) can be uncemented (press fit) as well. The different components allow for various combinations of bearing (articulating) surfaces including ceramic-on-ceramic, metal-on-plastic, and metal-on-metal. There is also a trend to use a ceramic-on-plastic bearing couple in young patients undergoing THA. Additionally, it is worth noting that traditional polyethylene acetabular liners can be used, and there is also growing interest in utilizing a highly cross-linked form of polyethylene.

Hip resurfacing is proposed as a bone conserving alternative to the conventional THA after optimal medical therapy fails. Unlike THA, hip resurfacing does not involve the removal of the entire femoral

head and neck or removal of bone from the femur. Rather, the head, neck and femur bone are preserved in an effort to facilitate future surgery should it be necessary and to enable the patient to take advantage of newer technology or treatments in the future. As a result of the larger bearing surface, proposed benefits of hip resurfacing include increased stability, flexibility, implant durability and range of motion. Younger patients needing full joint replacement that are expected to outlive the full replacement may benefit from symptom relief and increased bone preservation to better tolerate a subsequent replacement surgery later. Modern total HR components consist of high-carbide cobalt chrome metal-on-metal bearings that articulate against an intermediate synovial fluid film, a design that results in low surface wear.

Of recent, metal-on-metal (MoM) hip systems (both THA and HR) have received wide spread usage. As a result, more information has become available regarding the safety profile and clinical performance of these MoM systems. Data from national total joint registries as well as peer-reviewed journal publications and presentations at scientific meetings have suggested increases in potential safety issues associated with MoM hip systems to include:

- 1) Local complications such as osteolysis, and adverse local tissue reactions such as pseudotumors and aseptic lymphocytic vasculitis-associated lesions (ALVAL)
- 2) Early device failure and the need for revision surgery
- 3) Systemic complications from metal ion exposure

As a result of these safety concerns, there has been a reduction in the use of MoM hip replacement to include hip resurfacing. For example, the Australia National Joint Replacement Registry reports a 69% reduction in HR in 2012 compared to the peak use in 2005.<sup>7</sup> Similarly, the National Joint Registry of England and Wales reports a 59% decrease in the use of hip resurfacing from 2009 to 2011.<sup>123</sup> Furthermore, in 2003, 9.7% of hip replacements in the National Joint Registry of England and Wales were hip resurfacing compared with only 2.5% in 2011.

Given the recent safety concerns with MoM hip resurfacing, an update to the 2009 HTA report was commissioned to bring the latest evidence to bear on the following Key Questions:

## **1.2. Key Questions**

When used as an alternative in patients where total hip replacement is indicated:

### **Key Question 1:**

What is the evidence of efficacy and effectiveness of hip resurfacing (HR) compared with total hip arthroplasty (THA)?

### **Key Question 2:**

What is the evidence about the safety profile for hip resurfacing compared with THA?

### **Key Question 3:**

What is the evidence of efficacy, effectiveness and safety of revisions of hip resurfacing compared with revisions of THA?

### **Key Question 4:**

Is there evidence of differential efficacy or safety issues with use of hip resurfacing?

### **Key Question 5:**

What is the evidence of cost implications and cost effectiveness of hip resurfacing?

### 1.3. Outcomes Assessed

#### 1.3.1. Efficacy and effectiveness measures

Studies reported functional and activity scores from generic quality of life, disease specific clinician-based or patient-reported outcomes, and pain, Table 1.

- Four quality of life measures were used: the EQ-5D, SF-36, SF-12, and VAS outcomes measures. Domains assessed by the EQ-5D include patient mobility, self-care, usual activity, pain and anxiety/depression.<sup>77</sup> SF-36 and SF-12 include 8 subscales that assess physical function, role limitations due to physical health problems, pain, general health, vitality, limitations due to emotional problems, and mental health.<sup>180</sup> The SF-12 measures the same subscales as the SF-36 with fewer items.<sup>179</sup> The satisfaction domain of the VAS was used.<sup>152</sup>
- Four patient-reported disease specific outcomes measures were used, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Oxford Hip Score, the Disability Rating Index, and the Paffenbarger Physical Activity Questionnaire. The WOMAC assesses the patient's pain, stiffness and physical function.<sup>13</sup> The Oxford Hip Score uses 12 questions to assess perception of pain and function.<sup>41</sup> The Disability Rating Index is a 12 item questionnaire assessing disability perception. The Paffenbarger Physical Activity Questionnaire assesses perceived amounts of energy spent on physical and leisure activities on a weekly basis.<sup>32</sup>
- Two different clinician based outcomes, the Harris Hip Score (HHS)<sup>67</sup> and the Merle D'Aubigne Hip Score,<sup>34</sup> were also reported frequently; both combine a component of patient symptoms with physician assessment.
- Six activity scores were used. The activity score of Mont attempts to assess the frequency and duration of activity in which each patient regularly participates.<sup>117</sup> The UCLA activity scale seeks to determine how active a patient is on a 1-10 scale with one representing a person who is wholly inactive and dependent on others, and 10 representing a person who regularly participates in impact sports.<sup>4</sup> Additional activity scores include the Timed Up and Go (TUG), Hop on one leg, and Step tests. The TUG measured the amount of time a patient took to rise from sitting, walk ten feet, turn around and return to a seated position. The hop on one leg test counted how many times a patient was able to hop up and down on one leg for 10 seconds. The step test measured the amount of time taken to step up and down from an 18-inch step five times consecutively.<sup>93</sup>
- Pain was assessed by some studies using a visual analog scale (VAS).<sup>115</sup>

#### 1.3.2. Minimum Clinically Important Difference (MCID) & Minimum Detectable Change (MDC)

In order to more accurately observe the changes in patient recovery after total hip resurfacing or arthroplasty, parameters need to be defined that indicate what changes in patient reported or clinician based outcomes are clinically important. A search was conducted to find reports of the minimum clinically important difference (MCID) or the minimum detectable change (MDC) in outcomes used in a total hip population. The SF-36 and WOMAC were the only two outcomes of interest we found that established MCID/MDC in a total hip population.<sup>138</sup> Since MCID/MCD

values were not reported in a total hip population for other important outcomes, we searched for MCID/MDC in other musculoskeletal conditions such as total knee replacement or low back pain. Three additional outcomes measures with MCID/MDC were found in patients undergoing lumbar surgery: the EQ-5D, SF-12, and pain as measured by the VAS.<sup>18,58,133</sup> When results were reported as statistically significant between HR and THA groups, we sought to use MCID/MDC to establish clinical importance.

**Table 1. Outcome Measures**

Outcome Measure	Instrument Type	Components	Score Range	Interpretation	MCID
<b>PATIENT REPORTED OUTCOMES</b>					
WOMAC (Western Ontario and McMaster Universities OA index) <sup>13</sup>	Disease specific	Pain (20) Stiffness (8) Physical function (68)	0–96	Higher score = greater disability	<u>Total hip MCID:</u> 29.3 (pain) 26.5 (functional limitation) 25.9 (stiffness) <sup>138</sup>
Oxford hip score <sup>41</sup>	Disease specific	12 questions concerning the perception of pain and function (1–5 each)	12–60	Higher score = lower function	None found
EQ-5D (European Quality of Life) <sup>77</sup>	Generic	Mobility (1–3) Self-care (1–3) Usual activity (1–3) Pain (1–3) Anxiety/depression (1–3)	0–1 <sup>+</sup>	Optimal health: 1 Death: 0	<u>Spinal refusion MCID range:</u> 0.14–0.24 <sup>133</sup>
SF-36 (Short Form 36 health survey questionnaire) <sup>180</sup>	Generic	<u>8 subscales (# items)</u> Physical functioning (10) Role limitations due to physical health problems (4) Bodily pain (2) General health (5) Vitality (4) Social functioning (2) Role limitations due to emotional problems (3) Mental health (5)	0–100 for each subscale (total score not used)	Lower score = greater disability	<u>Total hip MCID</u> 20.4 (physical function) 10.8 (role physical) 14.7 (bodily pain) 0.4 (general health) 8.6 (social function) 10.1 (vitality) 9.0 (mental health) <sup>138</sup>
SF-12 (Short Form 12 health survey questionnaire) <sup>179</sup>	Generic	<u>2 subscales (no. of items)</u> <i>Physical health</i> General health (1) Physical functioning (2) Physical role limitations (2) Bodily pain (1) <i>Mental health</i> Emotional role limitations (2) Social functioning (1) Vitality/mental health (3)	0–100 for each subscale	Lower score = greater disability	<u>Low back pain MCID:</u> 8.8 points (physical) 9.3 points (mental) <sup>133</sup>

Outcome Measure	Instrument Type	Components	Score Range	Interpretation	MCID
UCLA activity scale <sup>4</sup>	Disease specific	Activity (10)	1–10	Unrestricted activity: 10 Bedridden: 1	None found
Mont Activity <sup>117</sup>	Disease specific	Each activity that the patient regularly participates in is assessed: Score = frequency (# times per week) x duration (hours) x weighed points (1–3; based on competitiveness)	0–?*	Low activity patients: 0–8 High-activity patients: ≥9*	None found
VAS pain (Visual Analogue Scale) <sup>115</sup>	Generic	Pain	0–10	No pain: 0 Worst pain imaginable: 10	<u>Low back pain MCID:</u> >1.5 unit improvement <sup>18</sup>  <u>Low back pain MCID:</u> >30% improvement <sup>58</sup>
<b>CLINICIAN BASED OUTCOMES</b>					
HHS (Harris hip score) <sup>67</sup>	Disease specific	Pain (44) Function (47) Deformity (4) Range of motion (5)	0–100	Excellent: 90–100 Good: 80–89 Fair: 70–79 Poor: <70	None found
Merle D'Aubigne hip score <sup>34</sup>	Disease specific	Pain (6) Mobility (6) Walking ability (6)	0–12‡	‡Very good: 11–12 Good: 10 Medium: 9 Fair: 8 Poor: <7	None found
TUG (Timed Up and Go) (Lavigne, 2010)	Generic	Functional	Timed	A shorter time reflects better physical mobility and speed	None found
Hop on one leg (Lavigne, 2010)	Generic	Functional	Timed	A shorter time reflects better functional recovery	None found
Step Test (Lavigne, 2010)	Generic	Functional	Number of hops possible in 10 sec.	A greater number of hops represents a better functional recovery	None found

\* Mont (2009): the maximum possible score was not reported.

† EQ-5D: final score is a 5-digit descriptor that corresponds to the level of disability in each subcomponent and ranges from 11111–33333; each score is assigned a preferential weight (e.g., 21111 = 0.85) to obtain a final score of 0 to 1.

‡ MA final score: the pain and walking ability scores are summed and then adjusted down by 1–2 grades based on the mobility score for the final clinical grade.

## **1.4. Key considerations highlighted by clinical experts:**

### **1.4.1. Intervention**

The issue the literature addresses focuses on a tension between slightly higher short-term complication and reoperation rates with total hip resurfacing (HR) (in the higher quality studies) versus the potential benefits of a more femoral bone-sparing approach and the possible increased durability of a metal-on-metal bearing couple. Issues which are unclear include the very long-term durability with conventional total hip arthroplasty (THA) using metal-on-polyethylene bearings in the very young/active/male population, which presumably will bring a high revision, reoperation, and complication rate, and the safety of metal-on-metal articulations pertaining to metal allergy and systemic deposition of metal ion species and corrosion products. "Advocates" of the procedures write much of the literature on total HR and THA, and this potential bias needs to be taken into account.

As with any orthopaedic intervention, the decision to proceed with surgery needs to be individualized. In the context of total hip resurfacing versus conventional total hip arthroplasty, one needs to consider the pros and cons of both. Hip resurfacing is intended for patients with high functional demands for whom traditional total hip arthroplasty would be a poor option because of anticipated future failure and subsequent revision surgery. Many clinical experts believe that total hip resurfacing is a bone sparing procedure best done in males under the age of 55 years with good bone stock, good health, an active lifestyle, and minimal femoral deformity or leg length discrepancy. There should be no history of renal disease or metal sensitivity. Patients with significant avascular necrosis, a history of infection, a strong history or family history of metabolic bone disease (osteoporosis) or women of childbearing age may not be suitable candidates for this procedure. Lastly, patients who are immunosuppressed should not undergo hip resurfacing.

Patients could consider hip resurfacing when: arthritis has been resistant to conservative measures; the patient is sufficiently healthy to undergo the procedure; the patient understands the risks and alternatives; the surgeon is trained and experienced in hip-resurfacing surgery; and no medical or surgical contraindication to hip resurfacing exists.

One risk of hip resurfacing is fracture of the preserved femoral neck. Infections are a rare but potentially catastrophic problem. Component loosening is an infrequent complication. Potential risks from the production of ions (cobalt and chromium) have yet to be clearly documented in the clinical literature. There is a theoretical concern that metal ions may pose a cancerous risk and there is in fact an increase in chromosomal aberrations in those with MoM hips. A patient who has kidney disease may have difficulty filtering these ions from the blood. Hip resurfacing is not recommended for women of childbearing age because of the uncertainty regarding the effects of metal ions on the developing fetus. Hypersensitivity to metal ions is a risk that is being increasingly recognized, and therefore patients with a history of metal allergy should not undergo this procedure.

#### **1.4.2. Costs**

Cost data is somewhat controversial and hard to decipher, but the metal-on-metal bearings (whether in a resurfacing or a replacement) will typically be more expensive. Since the hard-on-hard surfaces will be used in younger active patients (both in resurfacing and in replacement), comparing the average cost of a resurfacing to the average cost of a replacement will artificially bias the results: the cost of a resurfacing in a 50 year old male is being compared to a the cost of a cheaper cemented, metal-on-polyethylene replacement in a 75 year old female.

#### **1.4.3. Patient considerations**

In all women, the revision rate is higher for total HR compared to THA. In men over 65 years of age, revision rates for total HR are higher than for THA, while revision rates for resurfacing are comparable tp THA in men under 65 years. Therefore, resurfacing can be recommended for select young men (those with good bone quality, minimal hip deformity and degenerative joint disease (DJD) from a source other than post infectious arthritis), and young women in only exceptionl circumstances.

#### **1.4.4. Professional considerations**

Because hip resurfacing devices have received approval only recently in the United States, many communities do not have surgeons trained in this procedure. For FDA-approved devices, the device manufacturers require that surgeons who implant their devices be properly trained for technique. There is a definite learning curve for this procedure. To reduce complications, this procedure should be performed by surgeons with extensive experience in this surgery. This has been well documented.<sup>118</sup>

### ***1.5. Inclusion of non FDA-approved devices***

We included data from studies that used both FDA-approved and non FDA-approved total HR devices that otherwise met our inclusion/exclusion criteria. Our clinical experts believed that total HR devices are similar enough that including all devices in this review was appropriate, and that the results using one device could be reasonably generalized to other devices as well. Including all devices in this review provides more information to inform readers of this report on efficacy, effectiveness and safety of the procedure of hip resurfacing.



## 1.6. Washington State utilization and cost data

The following data were provided from the Washington State Health Care Authority and represent estimates for costs and utilization from the Uniform Medical Plan, Labor and Industry and Medicaid.

**Table 2: Count of Procedures by Year, Washington State**

**Figure 2a: All Agency Historic Count of Procedures by Year 2005-2008**

ICD-9 Procedure Codes	2005	2006	2007	2008	Total
00.85 (total hip resurfacing)	0	3	20	22	45
00.86 (resurfacing, femoral head)	0	1	2	2	5
00.87 (resurfacing, acetabulum)	0	0	0	0	0
81.51 (total hip replacement)	432	471	487	614	2004
81.52 (partial hip replacement)	108	100	82	102	392
<b>Total</b>	<b>540</b>	<b>575</b>	<b>591</b>	<b>740</b>	<b>2446</b>

**Table 2b: PEBB Count of Procedures by Year (partial resurfacing procedures were not found in the agency data)**

ICD-9 Procedure Codes	2009	2010	2011	2012	Total
00.85 (total hip resurfacing)	13	10	8	7	38
81.51 (total hip replacement)	421	443	505	533	1902
81.52 (partial hip replacement)	43	43	58	40	184
<b>Total</b>	<b>477</b>	<b>496</b>	<b>571</b>	<b>580</b>	<b>2124</b>

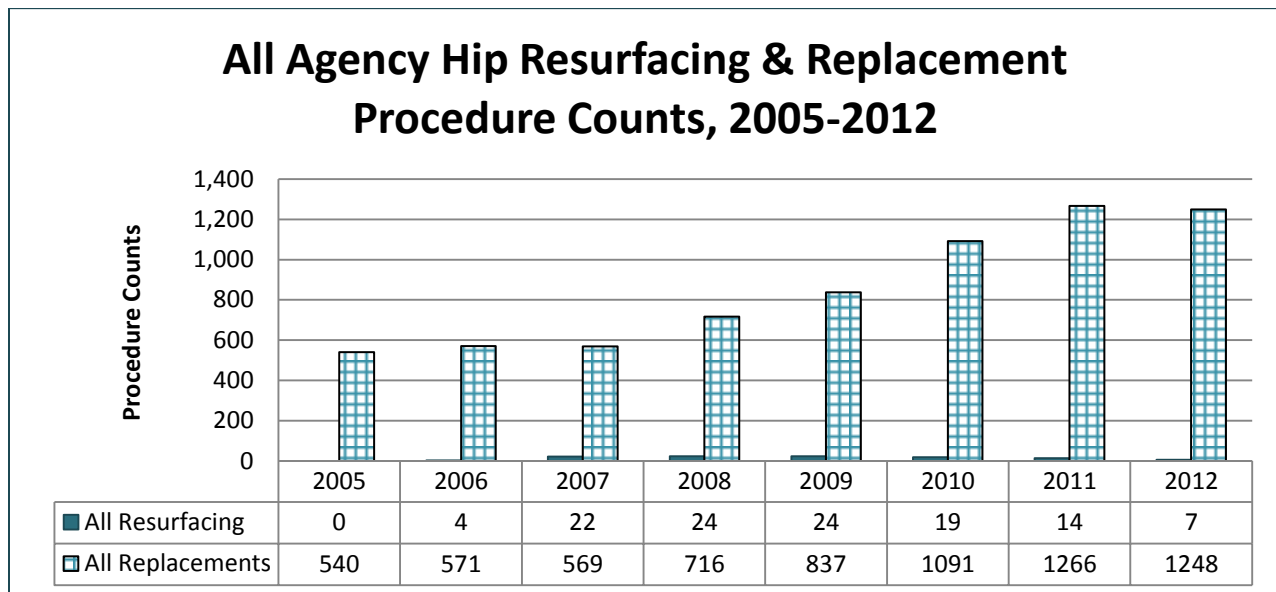
**Table 2c: Medicaid Count of Procedures by Year 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	Total
00.85 (total hip resurfacing)	9	7	4	0	20
81.51 (total hip replacement)	253	403	458	439	1553
81.52 (partial hip replacement)	28	119	169	161	477
<b>Total</b>	<b>290</b>	<b>529</b>	<b>631</b>	<b>600</b>	<b>2050</b>

**Table 2d: L&I Count of Procedures by Year 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	Total
00.85 (total hip resurfacing)	2	2	2	0	6
81.51 (total hip replacement)	85	81	72	70	308
81.52 (partial hip replacement)	7	2	4	5	18
<b>Total</b>	<b>94</b>	<b>85</b>	<b>78</b>	<b>75</b>	<b>332</b>

Figure 2: All Agency Procedure Counts by Year 2005-2012



**Table 3: Amount Paid\* by Procedure by Year**

**Table 3a: All Agency Historic Amount Paid\* for Procedures by Year (partial resurfacing codes 00.86/00.87 were not found in 2009-2012 usage data)**

**UMP, L&I, & Medicaid**

ICD-9 Procedure Codes	2005	2006	2007	2008	Total
00.85 (total hip resurfacing)	\$0	\$69,406	\$404,120	\$454,032	<b>\$927,558</b>
00.86 (resurfacing, femoral head)	\$0	\$19,991	\$36,344	\$60,457	<b>\$116,792</b>
00.87 (resurfacing, acetabulum)	\$0	\$0	\$0	\$0	<b>\$0</b>
81.51 (total hip replacement)	\$5,639,160	\$6,378,458	\$6,389,632	\$9,036,877	<b>\$27,444,126</b>
81.52 (partial hip replacement)	\$1,264,504	\$940,592	\$957,011	\$1,246,261	<b>\$4,408,368</b>
<b>Total</b>	<b>\$6,903,663</b>	<b>\$7,408,447</b>	<b>\$7,787,107</b>	<b>\$10,797,626</b>	<b>\$32,896,844</b>

\* includes facility, professional and other payments

**Table 3b: PEBB Amount Paid for Procedures by Year 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	Total
00.85 (total hip resurfacing)	\$360,943	\$203,250	\$172,690	\$198,528	<b>\$935,411</b>
81.51 (total hip replacement)	\$5,891,420	\$6,161,986	\$7,603,839	\$7,432,837	<b>\$27,090,082</b>
81.52 (partial hip replacement)	\$200,536	\$212,717	\$202,715	\$90,076	<b>\$706,044</b>
<b>Total</b>	<b>\$6,452,899</b>	<b>\$6,577,953</b>	<b>\$7,979,244</b>	<b>\$7,721,441</b>	<b>\$28,731,537</b>

\* includes facility, professional and other payments

**Table 3c: Medicaid Amount Paid\* for Procedures by Year 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	Total
00.85 (total hip resurfacing)	\$94,856	\$7,705	\$1,897	\$0	<b>\$104,458</b>
81.51 (total hip replacement)	\$4,103,593	\$1,476,176	\$703,657	\$712,110	<b>\$6,995,536</b>
81.52 (partial hip replacement)	\$478,946	\$134,395	\$82,107	\$183,220	<b>\$878,668</b>
<b>Total</b>	<b>\$4,677,395</b>	<b>\$1,618,276</b>	<b>\$787,660</b>	<b>\$895,330</b>	<b>\$7,978,662</b>

\* includes facility, professional and other payments

**Table 3d: L&I Amount Paid for Procedures by Year 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	Total
00.85 (total hip resurfacing)	\$45,193	\$36,114	\$32,759	\$0	<b>\$114,066</b>
81.51 (total hip replacement)	\$1,553,195	\$1,569,076	\$1,476,288	\$1,269,552	<b>\$5,868,111</b>
81.52 (partial hip replacement)	\$120,391	\$31,299	\$62,664	\$77,284	<b>\$291,637</b>
<b>Total</b>	<b>\$1,718,779</b>	<b>\$1,636,489</b>	<b>\$1,571,711</b>	<b>\$1,346,836</b>	<b>\$6,273,814</b>

\* includes facility, professional and other payments

**Table 4 Amount Paid\* by Procedure by Year****Table 4a: All Agency Historic Amount Paid per Procedure by Year**

UMP, L&amp;I, &amp; Medicaid

ICD-9 Procedure Codes	2005	2006	2007	2008
00.85 (total hip resurfacing)	0	\$23,135	\$22,451	\$20,638
00.86 (resurfacing, femoral head)	0	\$19,991	\$18,172	\$30,229
00.87 (resurfacing, acetabulum)	0	0	0	0
81.51 (total hip replacement)	\$17,902	\$18,650	\$18,361	\$20,037
81.52 (partial hip replacement)	\$20,071	\$17,102	\$21,750	\$21,487

\* includes facility, professional and other payments, amount paid divided by procedure count. Medicare and Secondary coverage patients were excluded from averages.

**Table 4b: PEBB Amount Paid\* per Procedure by Year, 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	All Year Average
00.85 (total hip resurfacing)	\$26,213	\$28,361	\$24,644	\$32,827	\$27,580
81.51 (total hip replacement)	\$26,989	\$28,451	\$31,181	\$28,919	\$28,937
81.52 (partial hip replacement)	\$37,175	\$32,465	\$41,222	\$20,584	\$33,990

\*includes facility, professional and other payments, amount paid divided by procedure count. Medicare coverage patients were excluded from averages

**Table 4c: Medicaid Amount Paid\* per Procedure by Year, 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	All Year Average
00.85 (total hip resurfacing)	\$11,844	\$1,101	\$486	\$0	\$5,773
81.51 (total hip replacement)	\$16,504	\$5,857	\$2,967	\$3,321	\$7,412
81.52 (partial hip replacement)	\$18,655	\$4,807	\$2,316	\$4,353	\$6,794

\* includes facility, professional and other payments, amount paid divided by procedure count. Medicare coverage patients were excluded from averages

**Figure 4d: L&I Amount Paid\* per Procedure by Year, 2009-2012**

ICD-9 Procedure Codes	2009	2010	2011	2012	All Year Average
00.85 (total hip resurfacing)	\$22,596	\$18,057	\$16,380	\$0	\$19,011
81.51 (total hip replacement)	\$18,273	\$19,371	\$20,504	\$18,136	\$19,367
81.52 (partial hip replacement)	\$17,199	\$15,649	\$15,666	\$15,457	\$16,202

\* includes facility, professional and other payments, amount paid divided by procedure count.

**Table 5: Patient Age and Sex by Procedure Type****Table 5a: All Agency Historic Age and Sex by Procedure****UMP, L&I, & Medicaid**

Age	Gender	00.85	00.86	81.51	81.52	Total
0-19	F	0	0	1	3	4
	M	0	0	0	0	0
20-44	F	3	0	66	9	78
	M	6	1	116	11	134
45-64	F	7	2	579	74	662
	M	27	2	588	53	670
65-74	F	1	0	243	37	281
	M	1	0	193	10	204
75-84	F	0	0	115	64	179
	M	0	0	67	31	98
85+	F	0	0	26	76	102
	M	0	0	8	24	32
<b>Total</b>		<b>45</b>	<b>5</b>	<b>2002</b>	<b>392</b>	<b>2444</b>

**Table 5b PEBB Patient Age and Sex by Procedure Type, 2009-2012**

Age	Gender	00.85	81.51	81.52	Total
0-20	F	0	1	0	1
	M	0	2	0	2
21-34	F	0	0	0	0
	M	1	4	0	5
35-49	F	2	45	2	49
	M	8	25	0	33
50-64	F	4	381	9	394
	M	15	279	1	295
65-79	F	0	506	43	549
	M	2	344	16	362
80+	F	0	104	77	181
	M	0	43	32	75
<b>Total</b>		<b>32</b>	<b>1734</b>	<b>180</b>	<b>1946</b>

\*Counts differ from procedure counts due to patients with two procedures in different years counted only once

**Table5c: Medicaid Patient Age and Sex by Procedure Type, 2009-2012**

Age	Gender	00.85	81.51	81.52	Total
0-20	F	0	4	0	4
	M	0	4	0	4
21-34	F	0	34	0	34
	M	3	37	5	46
35-49	F	3	164	10	179
	M	8	182	8	200
50-64	F	3	482	65	550
	M	4	309	42	355
65-79	F	0	214	95	309
	M	0	66	53	119
80+	F	0	45	153	198
	M	0	13	41	54
<b>Total</b>		<b>21</b>	<b>1555</b>	<b>472</b>	<b>2053</b>

\*Counts differ from procedure counts due to patients with two procedures in different years counted only once

**Table 5d: L&I Patient Age and Sex by Procedure Type, 2009-2012**

Age	Gender	00.85	81.51	81.52	Total
21-34	F	0	0	0	0
	M	0	10	0	10
35-49	F	0	9	0	9
	M	1	70	2	73
50-64	F	0	56	4	60
	M	5	137	3	145
65-79	F	0	10	3	13
	M	0	13	4	17
80+	F	0	0	1	1
	M	0	2	1	3
<b>Total</b>		<b>6</b>	<b>307</b>	<b>18</b>	<b>331</b>

\*Counts differ from procedure counts due to patients with two procedures in different years counted only once

**Related Medical Codes**

ICD9 Proc	Description
00.85	Resurfacing hip, total, acetabulum and femoral head
00.86	Resurfacing hip, partial, femoral head
00.87	Resurfacing hip, partial, acetabulum
81.51	Total hip replacement, replacement of both femoral head and acetabulum by prosthesis, total reconstruction of hip
81.52	Partial hip replacement, Bipolar endoprosthesis
CPT	Description
27130	Total Hip Arthroplasty (Professional code for either hip resurfacing or replacement )

## 2. Background

### 2.1. *History of Hip Resurfacing*

Total hip arthroplasty (THA) is a well-established and effective treatment for severe degenerative diseases of the hip. Originally designed for elderly patients,<sup>26,84,144</sup> most THAs have historically been performed in patients between 60 and 80 years of age (late middle-aged and elderly) who are relatively inactive. Over the past few years, however, THA has become increasingly common in young, active patients. Data from the Swedish National Hip Arthroplasty Register suggests that younger patients are more likely to need revision surgery following THA than their older counterparts. Survival rates increase with age (at the time of the primary THA): while patients aged 60 years or older have a survival rate greater than 82% 16 years following surgery, those aged 50 to 59 years have a survival rate of ~76%, and patients younger than 50 years of age have a 16-year survival rate of only ~65%.<sup>157</sup> Therefore, the longevity of THA for this patient population is of concern. The need for hip prostheses in younger patients is only expected to increase: by 2011, patients under 65 years of age are projected to account for over half of THAs, and by 2030 the number of these procedures in the United States is expected to triple.<sup>84</sup>

Total HR is an alternative to THA for young and active patients. In contrast to THA, total HR conserves femoral bone, attempts to maintain normal joint biomechanics and load transfer, and may be associated with a lower morbidity rate at the time of revision surgery.

Total HR prostheses were initially introduced to the medical community in the late 1970s, but most surgeons abandoned the technique in the 1980s due to high failure rates. These first generation total HR prostheses failed largely due to the wear created by the metal-on-polyethylene design, which resulted in early component loosening, osteolysis, and subsequent femoral neck fractures.<sup>3,120</sup>

The redesign of total HR prostheses in the 1990s spurred renewed interest in this procedure for the treatment of younger, active patients. With correct patient selection, surgeon education, and operative technique, survivorship at five years initially was thought to be comparable with that of conventional hip replacements.<sup>12,169</sup> Modern total HR components consist of high-carbide cobalt chrome metal-on-metal bearings that articulate against an intermediate synovial fluid film, a design that results in low surface wear. Ingrowth fixation, which utilizes cementless fixation of acetabular components, has been correlated with a lower incidence of early acetabular component failure. Modern total HR has been associated with promising early and mid-term results. Early studies of survivorship in younger patients reported 99.8% of total HR surviving at a mean of 3.3 years in 446 osteoarthritic hips<sup>37</sup>; 94.4% at 4 years in 400 hips<sup>1</sup>; and 99.1% at a mean of 3 years follow-up in a prospective study of 230 resurfaced hips.<sup>75</sup> However, subsequent comparative studies and registry studies with longer follow-up as reported in the first HTA suggest that the revision rate for total HR exceed those of THA.

### 2.2. *Potential Advantages of Hip Resurfacing versus Total Hip Replacement*

During a total hip arthroplasty procedure, the entire femoral head is removed and replaced with a metal, ceramic, or ceramicized metal prosthetic ball. In contrast, during a hip resurfacing procedure,



only the surface of the femoral head is removed and replaced with a hollow cap inserted into the hollow part of the femoral neck. On the pelvic side, both procedures involve replacing the acetabulum with a metal cup, which functions as the socket of the new hip joint. With total HR, the cup consists of a solid single piece of metal. With MoM THA the cup is either solid metal or a metal cup that accepts various liners.

One of the major alleged advantages of total HR is the preservation of femoral bone stock.<sup>4,33,174</sup> Following a conventional THA, osteolysis of the periprosthetic bone may occur because the load has been transferred to the implant thus bypassing the bone. As a result of this stress shielding, the bone becomes weaker, and more prone to fracture. In contrast, normal femoral loads are maintained following total HR, which helps to maintain normal bone density and quality.<sup>83</sup> Preservation of the femoral head also may improve function and allows for conversion to a THA in the future if needed.<sup>60,61</sup> Total HR is associated with lower morbidity at the time of revision surgery than THA.<sup>11,22</sup> Other theoretical advantages of hip resurfacing over THA are a decreased risk of dislocation due to the larger femoral head and better replication of normal anatomy,<sup>2,113</sup> and a greater range of motion.<sup>23,48,78,141</sup>

### **2.3. Target Population**

The ideal candidates for metal-on-metal hip resurfacing are younger, active adults with isolated degenerative diseases of the hip, good proximal femoral bone quality and morphology, and normal kidney function.<sup>12</sup> The aim of hip resurfacing is to allow the patient to resume a more physically active lifestyle after pain relief is achieved.

### **2.4. Indications for Hip Resurfacing**

Total HR is intended for reduction or relief of pain and improved hip function in skeletally mature patients with non-inflammatory degenerative arthritis such as osteoarthritis, traumatic arthritis, dysplasia or avascular necrosis.

*Primary or secondary osteoarthritis (OA)*, or degenerative arthritis, is the most common form of arthritis and typically occurs after middle age. OA is characterized by the chronic breakdown of articular cartilage and underlying subchondral bone in the joints. This may be due to the combination of wear and tear with a variety of hereditary, developmental, and metabolic factors; or it may result from a specific cause such as an injury or obesity. The hip and knee are the most commonly affected joints. Clinical symptoms of OA may include joint pain, tenderness, stiffness, inflammation, creaking, locking of joints, and disability.<sup>15,121</sup>

*Rheumatoid arthritis (RA)* is a chronic, systemic inflammatory disorder that primarily affects the joints. Inflammation of the synovial membrane lining the joint, or synovitis, can lead to the destruction of articular cartilage and ankylosis of the joints. Women are three times more likely than men to have RA and onset occurs most often between ages 40 and 60 years.<sup>104</sup> It should be noted here that there is a growing concern that inflammatory arthritis can cause cysts and softening of the bone which can compromise HR with early loosening or neck fractures.

*Avascular necrosis (AVN) or osteonecrosis*, results from temporary or permanent loss of blood supply to an area of bone. This debilitating disorder primarily affects the joints at the shoulder, knee, and hip, and can lead to the destruction of the articular surface of the joint. Total HR is contraindicated if osteonecrosis affects more than half of the femoral head. Osteonecrosis following a hip fracture may occur if the fracture interrupts blood flow to the femoral head, resulting in slow and incomplete healing or even bone death. If severe enough damage to the hip socket has occurred, replacement surgery becomes necessary.

*Ankylosing spondylitis (AS)* is a chronic, inflammatory arthritis that affects the joints of spine and the sacroiliac joint of the pelvis and causes eventual fusion of the spine. Medication and physical therapy are common treatments for AS, but in severe cases joint replacement may be necessary, particularly in the knees and hips.

*Perthes disease* occurs only in children, usually between 4 and 10 years of age, and is characterized by a temporary loss of blood to the femoral head resulting in bone death, inflammation, and irritation around the hip joint.

*Hip dysplasia* is a congenital or acquired deformity of the hip joint and often causes osteoarthritis of the hip at a relatively young age. Arthroplasty, in conjunction with osteotomy, is sometimes used to correct the misalignment.

## **2.5. Contraindications for hip resurfacing**

Contraindications for hip resurfacing include the following<sup>166,167</sup>:

- Severe osteoporosis or osteopenia
- Skeletal immaturity
- Multiple femoral neck cysts greater than 1 cm in diameter
- Infection or sepsis
- Vascular insufficiency, muscular atrophy, or neuromuscular disease severe enough to compromise implant stability or postoperative recovery
- Avascular necrosis involving more than 50% of the femoral head
- Moderate to severe renal insufficiency
- Immunosuppression (ie, AIDS) or high doses of corticosteroids
- Females of child-bearing age due to the unknown effect of metal ion release on the fetus
- Severely overweight (BMI > 35)
- Known or suspected metal sensitivity

## **2.6. Metal-on-metal bearings and current safety concerns**

Metal-on-metal (MoM) hip implants provide the ability to use larger diameter femoral head sizes compared to other articulating combinations. These sizes more closely mimic natural anatomy and are intended to improve the joint stability and reduce postoperative dislocation.

Following MoM hip resurfacing or replacement, the articulating MoM surfaces can lead to the

production and accumulation of metal ions (e.g., cobalt and chromium) and/or debris within the peri-prosthetic space. While some patients have no significant reaction to these materials, others may experience a significant inflammatory response that can lead to peri-prosthetic bone and tissue destruction. The reaction may be referred to by the terms “adverse local tissue reactions” (ALTR) or “adverse reaction to metal debris” (ARMD), and can lead to complications of bone osteolysis, aseptic lymphocytic vasculitis-associated lesions (ALVAL), and pseudotumors. Resulting soft tissue destruction may lead to pain, implant loosening, device failure, and the need for revision surgery.

In addition to local complications, there is a suggestion from case reports that high serum levels of metal ions may be associated with cardiomyopathy<sup>102</sup> and neurological and psychological changes.<sup>160</sup>

### **Recent Regulatory Actions Regarding Metal-on-Metal Implants**

The FDA summarizes the actions from regulatory bodies across the world as they have responded to emerging data on MoM hip systems:<sup>162</sup>

- December 2009: withdrawal of Depuy ASR hip systems from the Australian market as overseen by the Australia’s Therapeutic Goods Administration (TGA). Action taken after data from the Australian National Joint Replacement Registry (NJRR) showed higher-than-anticipated revision rates for those products.
- April 2010: the United Kingdom’s Medicines and Healthcare products Regulatory Agency (MHRA) issued a Medical Device Alert that included specific follow-up recommendations regarding blood tests, imaging for patients with painful MoM hip implants, soft tissue reactions and revision surgery. In February 2012 the MHRA published a medical device alert and updated it in June 2012 with advice on the management and monitoring of patients with MoM hip systems.
- February 2011: FDA posted a summary of the safety issues as well as providing considerations to orthopaedic surgeons for pre-implantation evaluation, intra-operative evaluations, post-operative evaluations and follow-up. It also included considerations for general primary care physicians regarding potential systemic effects of metal ions.
- February 2012: the FDA launched a metal-on-metal hip implant webpage providing updated safety information and recommendations to patients and health care providers.
- May 2012: Health Canada issued a public health communication to orthopaedic surgeons and patients regarding MoM hip implants.
- September 2012: The Therapeutic Goods Administration of Australia published their safety information for healthcare professionals on MoM hips.

## **2.7. Potential complications/harms of hip resurfacing**

### *Femoral neck fracture*

Short-term failure of hip resurfacing prostheses is most commonly due to periprosthetic femoral neck fractures, which account for 37% to 47 % of revisions.<sup>130</sup> Risk factors include a combination of patient-associated (i.e., poor bone quality, obesity, and female gender), technique-related (i.e., notching of the superior part of the femoral neck, varus femoral placement relative to the

anatomical neck, poor exposure, incomplete seating of the femoral implant), and post-operative factors.<sup>19,55,147</sup>

#### *Osteonecrosis*

Osteonecrosis has been a common histological finding in failed resurfaced hips. Extensive involvement has been noted in femoral heads that failed by fracture, thus the role of osteonecrosis in the causation of these fractures has been questioned.<sup>97</sup>

#### *Osteolysis*

In hip resurfacing, osteolysis, or active bone resorption, arises from an inflammatory reaction to wear debris, primarily to polyethylene particulates, but also to metal debris. Osteolysis has been reported as a common complication in hip arthroplasty and a major cause of component loosening and failure.<sup>156</sup>

#### *Prosthetic loosening*

Aseptic loosening of the implant over time is a potential complication of hip resurfacing and is most likely related to inadequate initial fixation of the femoral component. Wear failure of the underlying cement-bone interface is another possible cause of loosening.<sup>146</sup>

#### *Heterotopic ossification*

Heterotopic ossification has been noted around total hip arthroplasty in numerous studies. Since hip resurfacing may require a larger incision and exposure, and more muscle trauma than that of total hip arthroplasty, the rate of heterotopic ossification and its effect on function following resurfacing remains a concern.<sup>8</sup>

#### *Metal wear debris*

Concerns have been raised regarding the effect of metal wear debris from the metal-on-metal (MoM) bearing surfaces. The main metals used in MoM bearings are cobalt (Co) and chromium (Cr), however, the long-term biological consequences of the exposure to the particles and ions remain largely unknown and are poorly defined. Possible adverse consequences include local soft tissue toxicity, hypersensitivity reactions, bone loss, and carcinogenesis, as well as possible chromosomal aberrations and the risk of passing on those genetic abnormalities.<sup>99</sup> Compared to traditional metal-on-polyethylene (MoP) bearings, published reports on second generation MoM bearings have consistently revealed higher levels of serum Co and Cr when compared to preoperative values<sup>9,16,27,101,143</sup> and there is evidence to suggest that Co and Cr levels are influenced by factors such as the type, design, size, and positioning of the prosthesis.<sup>99</sup> Osteolysis has also been correlated with wear rate<sup>49</sup> and has been reported in association with MoM total hip arthroplasty in a small number of cases.<sup>99</sup> Though the wear rate for MoM bearings has been reported to be substantially lower than for MoP bearing, the number of particles generated can be up to 500 times greater.<sup>150</sup>

#### *Lack of long term follow-up*

The current implants have only been used for about 10 years so the only data available is on short-term (1-5 years) and mid-term (5-10 years) follow-up. Data on longer-term follow-up ( $\geq 10$  years) is needed.

*Deep infection*

Instances of both early and chronic infections are causal for revision.<sup>32,152,173</sup> There are some indications that there is less risk of infection for total hip arthroplasty than resurfacing arthroplasty. It has been suggested that this may be due to a difference in the amount of soft tissue dissection needed for the two procedures.<sup>32</sup>

*Intraoperative acetabular fissure of proximal femoral fissure*

Fissure or fracture of the femur is a complication that can occur intraoperatively. Explanations include a stiffer acetabular component used for resurfacing.<sup>173</sup>

## **2.8. Implant designs**

The majority of total HR systems available today employ hybrid fixation, which includes cementless press-fit fixation of the acetabular component and cemented fixation of the femoral component. Although a few femoral components are designed for cementless applications, the majority of currently available femoral component designs employ cement as the means of implant fixation.<sup>63</sup>

*Cemented femoral implants*

There is variability in the amount and distribution of bone cement employed into the dome portion of the femoral implant. In one study, the proportion of retrieved femoral-head sections that were filled with cement ranged from 11% to 89%.<sup>19</sup> Another study reported that greater amounts of cement were measured in loosened femoral heads (51% versus 36% of fractured heads and 40% of nonfemoral failures), indicating cement volume as a possible cause for implant failure.<sup>130</sup> Excessive cementing may also lead to decreased bone-loading and thus increased stress-shielding in the proximal portion of the femur<sup>139</sup> and also may promote thermal necrosis.<sup>19</sup>

*Cementless femoral implants*

Cementless femoral design attempt to address concerns regarding thermal necrosis from cementing, cement penetration, and controlling uniform mantle thickness. Excellent survival rates and significant improvements in pain and function at 2 years follow-up have been shown with a hydroxyapatite-coated (cementless) femoral design.<sup>96</sup> Many different aspects related to this type of design will need to be considered and addressed but as contemporary implants continue to mature, there is definite potential for cementless fixation in hip resurfacing.

## **2.9. Common hip resurfacing devices**

Three total HR devices are approved currently by the FDA (**one since the index HTA in 2009**):

1. Birmingham Hip Resurfacing (BHR) System (MoM, high carbon, cobalt-chromium alloy; acetabular component coated with hydroxyapatite) – Approved by the FDA in May 2006. Manufactured by Smith & Nephew, Inc., Memphis TN
2. Cormet Hip Resurfacing System (MoM, cobalt chromium alloy; acetabular component has a bi-coating of plasma sprayed titanium and hydroxyapatite) - Approved by the FDA in July 2007. Corin USA, Tampa FL.

3. CONSERVE Plus Total Resurfacing Hip System (MoM, cobalt-chromium alloy) – Approved by the FDA in November, 2009. Manufactured by Wright Medical Technology, Inc., Arlington TN. (FDA approval after the index HTA in 2009)

Other common devices are found in Table 6.

**Table 6. Common current devices**

Device Name	Company	FDA-Approved	Where Used
ASR*	Depuy (J & J)	No	Canada, Europe, India, Australia
Birmingham	Smith and Nephew	Yes (May 06)	Globally
Cormet	Styker/Corin Medical	Yes (Jul 07)	USA
Conserve Plus	Wright Medical Technology	Yes (Nov 09)	USA, Europe and Asia
Durom	Zimmer	No	UK, North America outside USA
ReCap	Biomet Orthopedics	No	Canada

ASR: Articular Surface Replacement

\*Withdrawn from worldwide market in 2010 due to higher than anticipated revision rates as reported by the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR)

## 2.10. Operative approach

Briefly, an incision is made on the upper part of the thigh, allowing the surgeon to see both the femoral head and the acetabulum. The femoral head is dislocated out of the socket and its surface smoothed down and shaped so that the new metal cap will fit snugly on top of the bone. The femoral cap is then cemented into place; a small peg is also inserted down into the bone. The hip socket may remain unchanged but more often it is replaced by a thin metal cup. Friction holds the metal liner in place until bone grows into the holes in the surface and attaches the metal to the bone.

Total HR is substantially more technically demanding than a standard hip replacement and the optimal operative approach is controversial. Most current generation metal-on-metal hip resurfacing procedures are performed using a posterior approach. This approach employs circumferential capsulotomy at the acetabulum, which maximizes acetabular exposure. In addition, the short external rotator muscles are released in order to access the femoral head, which sacrifice the primary blood supply to the femoral head (the ascending branch of the medial circumflex artery). While the posterior approach provides excellent exposure, preserves the hip abductor muscles, and is easily reproducible, the possible intraoperative disruption of blood flow to the femoral head can lead to osteonecrosis.<sup>146</sup>

The lateral and anterior approaches are also performed in the US, but are much less common. The lateral approach provides very good exposure and also preserves femoral head blood flow but can be associated with abductor muscle weakness. The anterior approach preserves blood flow to the femoral head and makes visualization of the socket easy, though it makes visualization of the femur

more difficult. This technique is also unfamiliar to many surgeons and may require a specialized surgical table.<sup>146</sup>

Without prior femoral neck resection, exposure of the acetabulum can present technical challenges. Accurate placement of a guide pin in the femoral neck is necessary to avoid varus positioning of the component and notching of the femoral neck. The use of a computer navigation system has been suggested as a possible way to improve the performance and accuracy of procedure. There is a high learning curve associated with total hip resurfacing<sup>108</sup> and surgeons are strongly encouraged to undergo additional training to properly prepare themselves for the technical challenges.

## **2.11. Clinical Guidelines**

### **2.11.1. National Guideline Clearinghouse**

A search of the National Guideline Clearinghouse for metal-on-metal hip resurfacing retrieved one guideline for the use of hip resurfacing.

#### **American College of Occupational and Environmental Medicine (2011)**

Hip resurfacing arthroplasty is recommended with a grade of “C” for select patients with osteonecrosis or bilateral osteoarthritis or hip joint disease.

Recommendations are made under the following categories:

Strongly recommended, “A” level

Moderately recommended, “B” level

Recommended, “C” level

Insufficient-recommended (consensus-based), “I” level

### **2.11.2. National Institute for Health and Clinical Excellence**

The National Institute for Health and Clinical Excellence (NICE), (which provides guidance on health technologies and clinical practice for the National Health Service in England and Wales) provided the following guidance in 2012:

a. Metal on metal (MoM) hip resurfacing arthroplasty is recommended as one option for people with advanced hip disease who would otherwise receive and are likely to outlive a conventional primary total hip replacement. In considering hip resurfacing arthroplasty, it is recommended that surgeons take into account activity levels of potential recipients and bear in mind that the current evidence for the clinical and cost effectiveness of MoM hip resurfacing arthroplasty is principally in individuals less than 65 years of age.

b. When MoM hip resurfacing arthroplasty is considered appropriate, the procedure should be performed only in the context of the ongoing collection of data on both the clinical effectiveness and cost effectiveness of this technology. Ideally, this data collection should form part of a UK national joint registry.

c. This guidance should be read in conjunction with the Institute's guidance on devices for total hip replacement (Guidance on the selection of prostheses for primary total hip replacement: NICE Technology Appraisal Guidance No 2. April 2000). In that guidance, the Institute recommended that the best prostheses (using long-term viability as the determinant) should demonstrate a 'benchmark' revision rate (the rate at which they need to be replaced) of 10% or

less at 10 years or, as a minimum, a 3 year revision rate consistent with this 10-year benchmark. Establishing and confirming similar benchmarking criteria will be necessary for MoM hip resurfacing arthroplasty and will be facilitated by a UK national joint registry. In the interim, the 3 year minimum benchmark should apply to MoM hip resurfacing devices.

c. MoM hip resurfacing arthroplasty should be performed only by surgeons who have received training specifically in this technique.

d. Surgeons should ensure that patients considering MoM hip resurfacing arthroplasty understand that less is known about the medium- to long-term safety and reliability of these devices or the likely outcome of revision surgery than for conventional total hip replacements. This additional uncertainty should be weighed against the potential benefits claimed for MoM devices.

## ***2.12. Previous Systematic Reviews/Technology Assessments***

Previously conducted reviews and assessments have not reached definitive conclusions regarding the safety and efficacy of hip resurfacing procedures. There is limited long-term data available. Table 7 summarizes the systematic reviews and Table 8 summarizes the previous technology assessments. **Note that original information from the previous report is in light print and updated information is in dark print in the tables.**



Table 7. Overview of previous systematic reviews of hip resurfacing.

Assessment (Year)	Lit search dates	Prosthesis evaluated	Purpose	Inclusion criteria	Evidence base available*†	Follow-up range	Comments	Primary Conclusions
Smith (2010)	through January 2010	BHR, Durom, Conserve Plus, Cormet, Tharies, Indian Conservative, McMinn components, DePuy articular and stemless system, Metasul	To compare the clinical and radiological outcomes and complication rates between HRA and THA	All RCTs and non-randomized controlled trials comparing HRA and THA	<ul style="list-style-type: none"> <li>10 RCTs (N = 1313)</li> <li>28 prospective observational (N = 409)</li> <li>8 retrospective (N = 867)</li> </ul>	Efficacy: NR  Safety: 6-71 months	Conclusions based on a meta-analysis of the results	<p><u>Efficacy:</u> Functional outcomes for HRA patients were better (WOMAC, HHS, step test) than or the same (MA, UCLA, Oxford hip score, hop test, pain scores, patient satisfaction, range of motion) as for subjects with a THA.</p> <p><u>Safety:</u> Statistically significant greater incidences of heterotopic ossification, aseptic loosening, and revision surgery with HRA compared to THA.</p> <p><u>Economic:</u> Not addressed</p>
Jiang (2011)	through June 2009	NR	To compare the clinical results of HRA to THA for the treatment of hip disease in young, active patients	All RCTs and CCTs with: <ul style="list-style-type: none"> <li>Younger than 65 years</li> <li>Skeletally mature</li> <li>End-stage hip disease</li> <li>&gt;12 month f/u</li> </ul>	<ul style="list-style-type: none"> <li>4 RCTs (N = 968)</li> </ul>	Min >12 months  (12-120 months)	Conclusions based on a meta-analysis of the results	<p><u>Efficacy:</u> Functional scores were similar between the two groups, although the HRA group showed higher activity levels. Insufficient evidence to determine whether HRA offers clinical advantages over THA.</p> <p><u>Safety:</u> Increased rates of revision, femoral neck fractures, and component loosening in HRA patients. No significant differences in rates of mortality, dislocation, or deep hip joint infection.</p> <p><u>Economic:</u> Not addressed</p>

Assessment (Year)	Lit search dates	Prosthesis evaluated	Purpose	Inclusion criteria	Evidence base available*†	Follow-up range	Comments	Primary Conclusions
Kuzyk (2011)	through December 2010	BHR, ASR, Durom, Cormet 2000	To summarize the findings of studies that compare metal ion production from HR to that of MoM THA	<ul style="list-style-type: none"> <li>Comparative trials, HR vs. MoM THA</li> <li>Analysis of chromium or cobalt ions, or both, in patient serum or whole blood, at a min. of 1 year after implantation</li> </ul>	<ul style="list-style-type: none"> <li>2 RCTs (N = 143)</li> <li>8 retrospective studies (N = 1082)</li> </ul>	Min >12 months  (12-60 months)	Conclusions based on a meta-analysis of the results	<p><u>Efficacy</u>: Not addressed</p> <p><u>Safety</u>: Mean differences for serum cobalt and chromium metal ions were not significantly different between HR and MoM THA patients, although there was a tendency for lower serum cobalt ion levels in patients receiving HR.</p> <p><u>Economic</u>: Not addressed</p>
Zywił (2011)	NR	NR	To determine survival rates for stemmed MoM THA, HR, CoC THA, and CoM THA	<ul style="list-style-type: none"> <li>Reported the survival rates of MoM THA, HR, CoC THA, or CoM THA in humans</li> <li>Min. of 25 hips</li> <li>Min. mean 24 month f/u</li> <li>No studies limiting inclusion of patients based on pre-op diagnosis (except OA)</li> </ul>	<ul style="list-style-type: none"> <li>10 RCTs (N = 1031)</li> <li>54 comparative (Level III and IV) studies (N = N/A)</li> </ul>	Mean >24 months  (2-336 months)	Conclusions based on results from RCTs	<p><u>Efficacy</u>: Not addressed</p> <p><u>Safety</u>: Mean survival at 38 to 60 months for MoM THA was between 96% and 100%; mean survival at 56 and 33 months for HR was 94% and 98%, respectively; CoC THA reported survival from 100% at mean 51 months to 96% at 8 years.</p> <p><u>Economic</u>: Not addressed</p>

BHR: Birmingham Hip Resurfacing System

THA: Total Hip Arthroplasty

HR/HRA: Hip Resurfacing / Hip Resurfacing Arthroplasty

MoM: Metal-on-Metal

CoC: Ceramic-on-Ceramic

NR: Not Reported

N/A: Not Available

HHS: Harris Hip Score; MA: Merle d'Aubigne; WOMAC:

\*Percent follow-ups are weighted based on sample size, and were calculated using the N reported in the assessment. Percent follow-ups were not given for all RCTs or case series. Mean time to follow-up is reported here.

†N reflects numbers before loss to follow-up

**Table 8. Overview of previous technology assessments of hip resurfacing (original information in light print, update in dark print).**

Assessment (Year)	Lit search dates	Prosthesis evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
California Technology Assessment Forum (2007)  <i>Metal-on-Metal total HR as an alternative to THA</i>	through 2007	BHR, Cormet 2000	<ul style="list-style-type: none"> <li>No RCTs comparing FDA-approved BHR and Cormet 2000</li> <li>2 RCTs (90% f/u, 12 months); N = 234; compared earlier MoM non FDA-approved devices</li> <li>7 case series (f/u NR; N = 1,150)</li> </ul>	Yes	Assessed only FDA-approved devices	<p><b>Efficacy:</b> Because no RCTs with FDA-approved devices are available, MoM HR has not been shown to improve health outcomes in an investigational setting</p> <p><b>Safety:</b> A national review of femoral neck fractures associated with BHR report an incidence of 1.46%. Chronic exposure to metal ions a concern.</p> <p><b>Economic:</b> Not addressed</p>
2011 update	through 2011	BHR, Cormet 2000, Conserve Plus	<ul style="list-style-type: none"> <li>6 RCTs (N = 438)</li> <li>16 cohorts (2 registry studies) (N = 316,078)</li> <li>2 meta-analyses (N = 18,582)</li> <li>8 case series (N = 4957)</li> </ul>	Yes	MoM HR using the BHR, Cormet 2000, or Conserve Plus devices does not meet CTAF criteria 3-5 for safety, efficacy and improvement in health outcomes for patients as an alternative to THA	<p><b>Efficacy:</b> Recent studies, particular registry evidence shows an increased revision rate with HRA compared with THA</p> <p><b>Safety:</b> Increasing concerns about metal ion levels; need to prove safety and efficacy in RCTs before subjecting young patients to significant potential harm over their lifetimes</p> <p><b>Economic:</b> Not addressed</p>

Assessment (Year)	Lit search dates	Prosthesis evaluated	Evidence base available**	Critical Appraisal‡	Comments	Primary Conclusions
BlueCross BlueShield Technology Evaluation Center Assessment (2007) <i>Metal-on-Metal HR</i>	through 01/2007	BHR, Cormet, Conserve Plus	<ul style="list-style-type: none"> <li>1 RCT (% f/u NR, 12 months); N = 210</li> <li>12 case series (% f/u NR, 3 years); N = 2,076</li> </ul>	No		<p><u>Efficacy:</u> HR represents a safe and effective means to defer a first THA in properly selected patients who require a THA</p> <p><u>Safety:</u> See Efficacy</p> <p><u>Economic:</u> Not addressed</p>
Alberta Bone and Joint Health Institute (2006)  <i>Metal-on-Metal HR for young, active adults with degenerative hip disease</i>	through 2006	BHR, Conserve Plus, Cormet 2000, ReCap, Durum, ASR	<ul style="list-style-type: none"> <li>6 SR/HTA</li> <li>2 RCTs (90% f/u, 12 months); N = 234; compared THA with HR</li> <li>13 case series / case control (95% f/u, 5 years); N = 2,209</li> </ul>	No	Most studies had limited follow-up (less than 2 years), thus it was difficult to assess long-term device performance	<p><u>Efficacy:</u> Based on two RCTs, HR and THA confer similar satisfaction rates in younger patients, but HR may offer better functional performance</p> <p><u>Safety:</u> No significant differences were found for revision rates due to complications, although long-term (&gt;5 years) safety is unknown</p> <p><u>Economic:</u> MoM HR could be more cost-effective than THA after year 1, but long-term revision rates are unknown</p>
Ontario Health Technology Assessment Series (2006)  <i>Metal-on-Metal total HRA</i>	January 1, 1997 through October 27, 2005	BHR, Conserve Plus, Cormet 2000, ReCap, Durum, ASR	<ul style="list-style-type: none"> <li>1 RCT (100% f/u, 8.5 years); N = 24; compared THA with HR</li> <li>8 case series (96% f/u, 4 years); N = 1,539</li> </ul>	Yes	RCT not used for assessment because newer generation of implants are now used	<p><u>Efficacy:</u> MoM HRA has been shown to be effective as tested in younger patients. However, there are no RCTs that compare MoM HR with THA</p> <p><u>Safety:</u> Concern remains on the potential adverse effects of metal ions</p> <p><u>Economic:</u> MoM HR is more cost effective compared with watchful waiting followed by THA. MoM HR is not more cost effective when compared directly with THA</p>
2012 update	January 1, 2009 to February 13, 2012	BHR, Conserve Plus, Cormet 2000, ReCap, Durom, ASR	<ul style="list-style-type: none"> <li>2 RCTs (N = 280)</li> <li>2 Registry studies (N = 314,673)</li> <li>18 cohorts (N = 8,446)</li> <li>24 case series (N = 15,261)</li> </ul>	Yes		<p><u>Efficacy:</u> Not addressed</p> <p><u>Safety:</u> Only three of MoM HRA implants (BHR, Conserve Plus, Cormet 2000) met the NICE criteria for revision rates of 10% or less at 10 years (two (ReCap, Durom) had short-term f/u and one (ASR) failed to meet the criteria). Concerns about adverse tissue reactions and biological effects of high metal ion levels in the blood were reported by several studies</p> <p><u>Economic:</u> Not addressed</p>

Assessment (Year)	Lit search dates	Prosthesis evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
Agency for Healthcare Research and Quality (2006) <i>Horizon Scan on hip replacement surgery</i>	through 2006	N/A	<ul style="list-style-type: none"> <li>3 RCTs ongoing (still in recruitment or data collection stage)</li> </ul>	No	Review focused on THA	<p><u>Efficacy:</u> Data on effectiveness of HR are limited, but this conclusion was based on older literature</p> <p><u>Safety:</u> Most common complication is periprosthetic fracture of the femoral head</p> <p><u>Economic:</u> Not addressed</p>
Center for Clinical Effectiveness (2002)  <i>Hip resurfacing in patients with osteoarthritis</i>	through 11/2002	BHR	<ul style="list-style-type: none"> <li>1 SR (case series only included for review; f/u inclusion criteria &gt; 5 years; N = NR; compared BHR with THA)</li> <li>1 HTA</li> </ul>	Yes	Most recent literature available now	<p><u>Efficacy:</u> MoM resurfacing of the hip may be a viable and bone-conserving option for adults who are likely to outlive THA</p> <p><u>Safety:</u> Short-term revision rates were comparable between MoM and THA</p> <p><u>Economic:</u> THA was calculated to be more cost-effective than MoM, but there was a lack of long-term data on health outcomes and revision rates</p>
The Canadian Coordinating Office for Health Technology Assessment (2003) <i>MoM HR</i>	Through 02/2003	BHR, Conserve Femoral Surface Replacement device	<ul style="list-style-type: none"> <li>7 HTAs</li> </ul>	No	More recent literature available now	<p><u>Efficacy:</u> MoM HR was recommended as one option for active, younger patients with advanced hip disease</p> <p><u>Safety:</u> Patient selection is important for prosthesis viability</p> <p><u>Economic:</u> Need for cost-benefit analysis was stated</p>
2012 update	January 1, 2007 through October 18, 2012	BHR, Durom, Conserve Plus	<ul style="list-style-type: none"> <li>2 meta-analyses (N = 7157)</li> <li>1 systematic review (N = 1979)</li> </ul>	Yes		<p><u>Efficacy:</u> MoM HRA allows for greater bone preservation, lower wear rates, and equal or better functional outcomes compared with THA</p> <p><u>Safety:</u> MoM HRA patients experienced higher rates of revision, femoral neck fractures, and component loosening than THA recipients</p> <p><u>Economic:</u> No evidence found</p>

Assessment (Year)	Lit search dates	Prosthesis evaluated	Evidence base available*†	Critical Appraisal‡	Comments	Primary Conclusions
Alberta Heritage Foundation for Medical Research (2002) <i>MoM HR for young active adults with degenerative hip disease</i>	through 2002	BHR, Conserve plus, Cormet 2000	<ul style="list-style-type: none"> <li>• 5 HTAs</li> <li>• 0 RCTs</li> <li>• Several case series (not evaluated)</li> </ul>	No	More recent literature available now	<p><u>Efficacy</u>: MoM resurfacing may be a viable and bone-conserving option for adults with degenerative hip disease who are likely to outlive THA.</p> <p><u>Safety</u>: Concern of the toxicity of the metals over time if shed into the body. Patient selection is important; good bone stock required</p> <p><u>Economic</u>: Costs for BHR and THA were comparable in the UK</p>
9. American Academy of Orthopaedic Surgeons (AAOS) (2011)  <i>MoM HR</i>	through July 15, 2011	BHR, Durom, Metasul	<ul style="list-style-type: none"> <li>• 2 joint registries</li> <li>• 5 RCTs (N = 630)</li> <li>• 6 cohorts (N = 1433)</li> <li>• 8 case series (N = 3658)</li> </ul>	Yes		<p><u>Efficacy</u>: HRA had better 1- and 2-year WOMAC scores, although there was no clinical relevance in the difference between HRA and THA</p> <p><u>Safety</u>: Concerns about increased revision rates, local metal debris release, adverse tissue reactions, and elevated serum metal ion levels in MoM articulations, although not enough data to report clinical significance</p> <p><u>Economic</u>: Not addressed</p>
10. FDA Executive Summary Memorandum  <i>Metal-on-Metal HR</i>	January 1, 2005 to April 2, 2012	BHR, Cormet, Conserve Plus	<ul style="list-style-type: none"> <li>• 6 RCTs (N = 683)</li> <li>• 117 observational studies (N = N/A)</li> <li>• 3 retrieval analyses (N = 286)</li> <li>• 1 meta-analysis (N = 7081)</li> <li>• 4 systematic reviews (N = N/A)</li> </ul>	No	There are no FDA cleared or approved tests to measure cobalt or chromium levels in patient samples	<p><u>Efficacy</u>: Not addressed</p> <p><u>Safety</u>: Concerns with local complications, early device failure and the need for revision surgery, and systemic complications from metal ion exposure</p> <p><u>Economic</u>: Not addressed</p>

BHR: Birmingham Hip Resurfacing System; THA: Total Hip Arthroplasty; HR/HRA: Hip Resurfacing / Hip Resurfacing Arthroplasty; MoM: Metal-on-Metal; NR: Not Reported

N/A: Not Available

\*Percent follow-ups are weighted based on sample size, and were calculated using the N reported in the assessment. Percent follow-ups were not given for all RCTs or case series. Mean time to follow-up is reported here.

†N reflects numbers before loss to follow-up

‡Critical appraisal refers to formal evaluation of individual study quality using criteria such as the Jadad or GRADE methods of scoring and the determination of overall strength of evidence.

### **2.13. Medicare and Representative Private Insurer Coverage Policies**

Coverage policies are consistent for hip resurfacing for CMS and selected bell-weather payers. The payers will provide coverage for hip resurfacing as long as an FDA-approved device is used and certain patient conditions are met. Table 9 provides an overview of policy decisions.

- **Medicare**

No national coverage decisions were found for hip resurfacing.

- **Aetna**

Aetna considers metal-on-metal hip resurfacing a medically necessary alternative to total hip arthroplasty for physically active members with osteoarthritis of the hip, or osteonecrosis of the femoral head. Aetna also considers MoM HR experimental and investigational for developmental dysplasia of the hip and for all other indications because its effectiveness for these indications has not been established.

- **Blue Cross/Blue Shield**

Total hip resurfacing arthroplasty, using an FDA-approved / cleared prosthesis, is considered medically necessary in fit, active individuals who:

- Have normal proximal femoral bone geometry and bone quality, and
- Would otherwise receive a conventional primary THA, and
- Are likely to live longer than a current conventional THA prosthesis is expected to last

- **Cigna**

Cigna covers total hip resurfacing arthroplasty as medically necessary when an individual has met all of the following criteria:

- Diagnosis of noninflammatory arthritis including osteoarthritis or osteonecrosis, traumatic arthritis, or inflammatory arthritis involving the hip
- Candidate for total hip replacement
- Age less than 65 years
- Failed nonsurgical management

- **Harvard Pilgrim**

Total hip resurfacing arthroplasty is covered with FDA-approved devices for the treatment of hip disease in patients who are younger than age 55 and who meet the following criteria:

- Have chronic, persistent pain and/or disability.
- Are otherwise fit and active.
- Have normal proximal femoral bone geometry and bone quality.
- Would otherwise receive a conventional primary total hip arthroplasty, but are likely to live longer than a conventional THA is expected to last.

**Table 9. Overview of payer technology assessments and policies for hip resurfacing (original information in light print, update in dark print).**

Payer (Year)	Pub date	Prosthesis	Evidence base available*†	Policy	Rationale/comments
Centers for Medicare and Medicaid Services (2007)	through 2007	BHR	<ul style="list-style-type: none"> <li>FDA premarket approval letters (2006-2007)</li> <li>6 case series (f/u, N NR)</li> </ul>	<p>The Centers for Medicare and Medicaid Services (CMS) will deem total HR medically necessary in select patients requiring primary HR due to the following conditions:</p> <ul style="list-style-type: none"> <li>Non-inflammatory arthritis (degenerative) such as osteoarthritis, traumatic arthritis, avascular necrosis, or dysplasia/developmental hip dislocation</li> <li>Inflammatory arthritis, such as rheumatoid arthritis</li> </ul>	<ul style="list-style-type: none"> <li>Policy only valid for FDA-approved devices</li> <li>CPT codes if criteria are met: 00.85, 00.86, 00.87</li> </ul>
2013 update	through 2013			No policy found for CMMS	
Aetna Clinical Policy Bulletin (2008)	through 2007	BHR	<ul style="list-style-type: none"> <li>3 HTAs</li> <li>3 case series (% f/u NR, 5 years) N = 506</li> <li>Listed 40 other references policy is based upon</li> </ul>	Aetna considers MoM HR a medically necessary alternative to THA for physically active members with osteoarthritis of the hip, or osteonecrosis of the femoral head	<ul style="list-style-type: none"> <li>No rationale for policy stated</li> <li>CPT codes if selection criteria are met: 27125</li> </ul>
2012 update	through 2012	BHR, Cormet	<ul style="list-style-type: none"> <li>3 HTAs</li> <li>4 cohorts (N = 269 pts with 290 hips, f/u 2-7 years, % NR)</li> <li>6 case series (N = 654 patients with 734 hips, f/u 2-10 years, % NR)</li> <li>Listed 49 other references policy is based upon</li> </ul>	<p>Aetna considers metal-on-metal HR:</p> <ul style="list-style-type: none"> <li>A medically necessary alternative to THA for physically active members with osteoarthritis of the hip, or osteonecrosis of the femoral head</li> <li>Experimental and investigational for developmental dysplasia of the hip and for all other indications because its effectiveness for these indications has not been established</li> </ul>	<ul style="list-style-type: none"> <li>No rationale for policy stated</li> <li>CPT codes if selection criteria are met: 27125</li> <li>HCPCS codes covered if selection criteria are met: S2118</li> </ul>
BCBS Medical Policy (2006)	N/A	BHR	<ul style="list-style-type: none"> <li>2 case series (f/u NR, N = NR)</li> </ul>	<p>Total HRA with an FDA-approved device may be considered medically necessary for patients with degenerative hip joint disease, or severe arthritis, or rheumatoid arthritis, or advanced avascular necrosis of the hip and meet all of the following criteria:</p> <ul style="list-style-type: none"> <li>Skeletally mature and 55 years of age or less, and</li> <li>Patient with BMI of 39 or less, and</li> <li>Have failed conservative management, and</li> <li>Would otherwise require THA surgery</li> </ul>	<ul style="list-style-type: none"> <li>Hemi HR of the femoral head is an established procedure for patients with osteonecrosis of the femoral head</li> <li>While long-term studies are needed to address the use of total HR in most patient populations, there is adequate evidence to support the use of this procedure in patients at low risk for failure of the procedure</li> </ul>
2012 update	through	BHR,	<ul style="list-style-type: none"> <li>2 RCTs (N = 313, f/u 1-7 years,</li> </ul>	Total HRA, using an FDA-approved/cleared prosthesis,	<ul style="list-style-type: none"> <li>Hemi HR of the femoral head is an</li> </ul>



Payer (Year)	Pub date	Prosthesis	Evidence base available*†	Policy	Rationale/comments
	2012	Cormet, Conserve Plus	<ul style="list-style-type: none"> <li>% NR)</li> <li>2 case series (N = 4478, f/u 3-5 years, % NR)</li> <li>Listed 52 other peer reviewed and government agency references policy is based upon</li> </ul>	<p>is considered medically necessary in fit, active individuals who:</p> <ul style="list-style-type: none"> <li>Have normal proximal femoral bone geometry and bond quality, and</li> <li>Would otherwise receive a conventional primary THA, and</li> <li>Are likely to live longer than a current conventional THA prosthesis is expected to last</li> </ul>	<p>established procedure for patients with osteonecrosis of the femoral head</p> <ul style="list-style-type: none"> <li>CPT codes if selection criteria are met: 27299</li> <li>HCPCS codes if selection criteria are met: S2118</li> </ul>
Cigna Medical Coverage Policy (2009)	through 2008	BHR, Cormet (FDA-approved)	<ul style="list-style-type: none"> <li>10 case series (% f/u NR); N = 403</li> </ul>	<p>Cigna covers total HRA as medically necessary as an alternative to THA when all of the following criteria are met:</p> <ul style="list-style-type: none"> <li>Age less than 65 years</li> <li>Diagnosis of osteoarthritis or inflammatory arthritis</li> <li>Individual has failed nonsurgical management and is a candidate for THA</li> </ul>	<ul style="list-style-type: none"> <li>Policy is designed for treatment of osteonecrosis of the femoral head when there is failure, contraindication or intolerance of nonsurgical management</li> <li>CPT codes if selection criteria are met: 27125, 27130, 27299</li> </ul>
2013 update	through 2013	BHR, Cormet, Conserve Plus	<ul style="list-style-type: none"> <li>1 RCT (N = 71, f/u 2 years, % NR)</li> <li>4 systematic reviews (N = 24,577, f/u 5-10 years, % NR)</li> <li>6 HTAs</li> <li>10 case-series (N = 7163, f/u 2-10 years, % NR)</li> <li>Listed 70 other references policy is based upon</li> </ul>	<p>Cigna covers total HRA as medically necessary when an individual has met all of the following criteria:</p> <ul style="list-style-type: none"> <li>Diagnosis of noninflammatory arthritis including osteoarthritis or osteonecrosis, traumatic arthritis, or inflammatory arthritis involving the hip</li> <li>Candidate for total hip replacement</li> <li>Age less than 65 years</li> <li>Failed nonsurgical management</li> </ul>	<ul style="list-style-type: none"> <li>Policy is designed for treatment of osteonecrosis of the femoral head when there is failure, contraindication or intolerance of nonsurgical management</li> <li>CPT codes if selection criteria are met: 27125, 27130, 27299</li> </ul>
Harvard Pilgrim (2008)	through 2007	BHR, Cormet	<ul style="list-style-type: none"> <li>1 HTA</li> <li>4 case series (f/u NR, N = NR)</li> </ul>	<p>Total HRA is covered with FDA-approved devices for the treatment of hip disease in patients who are younger than age 55 and who meet the following criteria:</p> <ul style="list-style-type: none"> <li>Have chronic, persistent pain and/or disability</li> <li>Are otherwise fit and active</li> <li>Have normal proximal femoral bone geometry and bone quality, and</li> <li>Would otherwise receive a conventional primary THA, but are likely to live longer than a conventional THA is expected to last</li> </ul>	<ul style="list-style-type: none"> <li>Used BCBS, United, Cigna, and Aetna as benchmarks for policy decision</li> <li>CPT codes if selection criteria are met: S2118, 27299, 27130</li> </ul>

Payer (Year)	Pub date	Prosthesis	Evidence base available*†	Policy	Rationale/comments
2012 update	through 2012	BHR, Cormet	<ul style="list-style-type: none"> <li>2 HTAs</li> <li>1 systematic review</li> <li>5 case series (N = NR, f/u &amp; % NR)</li> <li>Listed 12 other references policy is based upon</li> </ul>	<p>Total HRA is covered with FDA-approved devices for the treatment of hip disease in patients who are younger than age 55 and who meet the following criteria:</p> <ul style="list-style-type: none"> <li>Have chronic, persistent pain and/or disability</li> <li>Are otherwise fit and active</li> <li>Have normal proximal femoral bone geometry and bone quality, and</li> <li>Would otherwise receive a conventional primary THA, but are likely to live longer than conventional THA is expected to last</li> </ul>	<ul style="list-style-type: none"> <li>Used BCBS, United, Cigna, and Aetna as benchmarks for policy decision</li> <li>CPT codes if selection criteria are met: S2118, 27299, 27130</li> </ul>
Washington State Payers					
Group Health Cooperative (2007)	through 2006	BHR, Cormet	<ul style="list-style-type: none"> <li>2 SR (no information provided)</li> <li>2 RCTs used for critical appraisal (% f/u NR, 8.5 years – one study only); N = 128</li> </ul>	<p>Group Health members are covered when all of the following criteria are met:</p> <ul style="list-style-type: none"> <li>The patient is 55 years of age or younger</li> <li>The device is FDA-approved</li> <li>The patient has been diagnosed with arthritis of the hip</li> <li>The patient would otherwise require a THA</li> </ul>	<ul style="list-style-type: none"> <li>No rationale for policy stated</li> </ul>

BHR: Birmingham Hip Resurfacing System

HR / HRA: Hip Resurfacing / Hip Resurfacing Arthroplasty

THA: Total Hip Arthroplasty

NR: Not Reported

\*Formal critical appraisals were not reported in any of the payer HTAs except Group Health. Percent follow-ups were not given for RCTs or case series. Mean time to follow-up is reported here

†N reflects numbers before loss to follow-up

Aetna: [http://www.aetna.com/cpb/medical/data/600\\_699/0661.html](http://www.aetna.com/cpb/medical/data/600_699/0661.html)

BCBS: [http://www.anthem.com/medicalpolicies/policies/mp\\_pw\\_a053350.htm](http://www.anthem.com/medicalpolicies/policies/mp_pw_a053350.htm)

Cigna: [https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/mm\\_0460\\_coveragepositioncriteria\\_hip\\_resurfacing\\_arthroplasty.pdf](https://cignaforhcp.cigna.com/public/content/pdf/coveragePolicies/medical/mm_0460_coveragepositioncriteria_hip_resurfacing_arthroplasty.pdf)

Harvard Pilgrim: [https://www.harvardpilgrim.org/pls/portal/docs/PAGE/PROVIDERS/MEDMGMT/STATEMENTS/TOTAL\\_HIP\\_RESURFACING\\_1012.PDF](https://www.harvardpilgrim.org/pls/portal/docs/PAGE/PROVIDERS/MEDMGMT/STATEMENTS/TOTAL_HIP_RESURFACING_1012.PDF)

Group Health: [http://www.ghc.org/all-sites/clinical/criteria/pdf/mom\\_hip.pdf;jsessionid=BZBIVEMOUUPJLJCISQ3SHPO](http://www.ghc.org/all-sites/clinical/criteria/pdf/mom_hip.pdf;jsessionid=BZBIVEMOUUPJLJCISQ3SHPO)

United / Comment on Medicare/Medicaid (p. 7) <http://www.aaos.org/govern/federal/issues/UHCHipResurfacingArthroplasty.pdf>

### 3. The Evidence

#### 3.1. *Methods of the Systematic Literature Review*

##### 3.1.1. Inclusion/exclusion

Inclusion and exclusion criteria are summarized in Table 10.

- *Population.* Studies of adults who underwent primary total HR for arthritis (non-inflammatory or inflammatory) developmental dysplasia, osteonecrosis were included.
- *Intervention.* Included studies evaluated total HR using modern commercially available devices designed for hybrid (i.e. using cementless acetabular fixation) resurfacing: FDA-approved or unapproved devices in Phase III trials with  $\geq 1$  year of follow-up data in a peer-reviewed journal. Studies reporting on non-hybrid or hemi-resurfacing or minimally invasive surgery were excluded.
- *Comparator.* Included studies compared hybrid total HR to primary THA: FDA-approved or unapproved devices in Phase III trials with  $\geq 1$  year of follow-up data in a peer-reviewed journal. Studies that reported on revision THA were excluded.
- *Outcomes.* Eligible studies reported on at least one of the following outcomes: physical function/disability (clinical success (e.g., Harris Hip Score, pain, activity, and motion), revision, or complications (including femoral neck fracture, femoral head collapse, avascular necrosis, dislocation, osteolysis, device migration or loosening, heterotopic ossification, impingement, infection or radiolucencies).
- *Study design.* Eligible studies compared total HR with THA utilizing a randomized or cohort study design. National total joint registries were used for key questions 2 and 4. Formal economic analyses published in peer-reviewed journals were eligible for inclusion to help answer key question 5 as were cost data reported in other systematic reviews or technology assessments.

**Table 10. Summary of inclusion and exclusion criteria.**

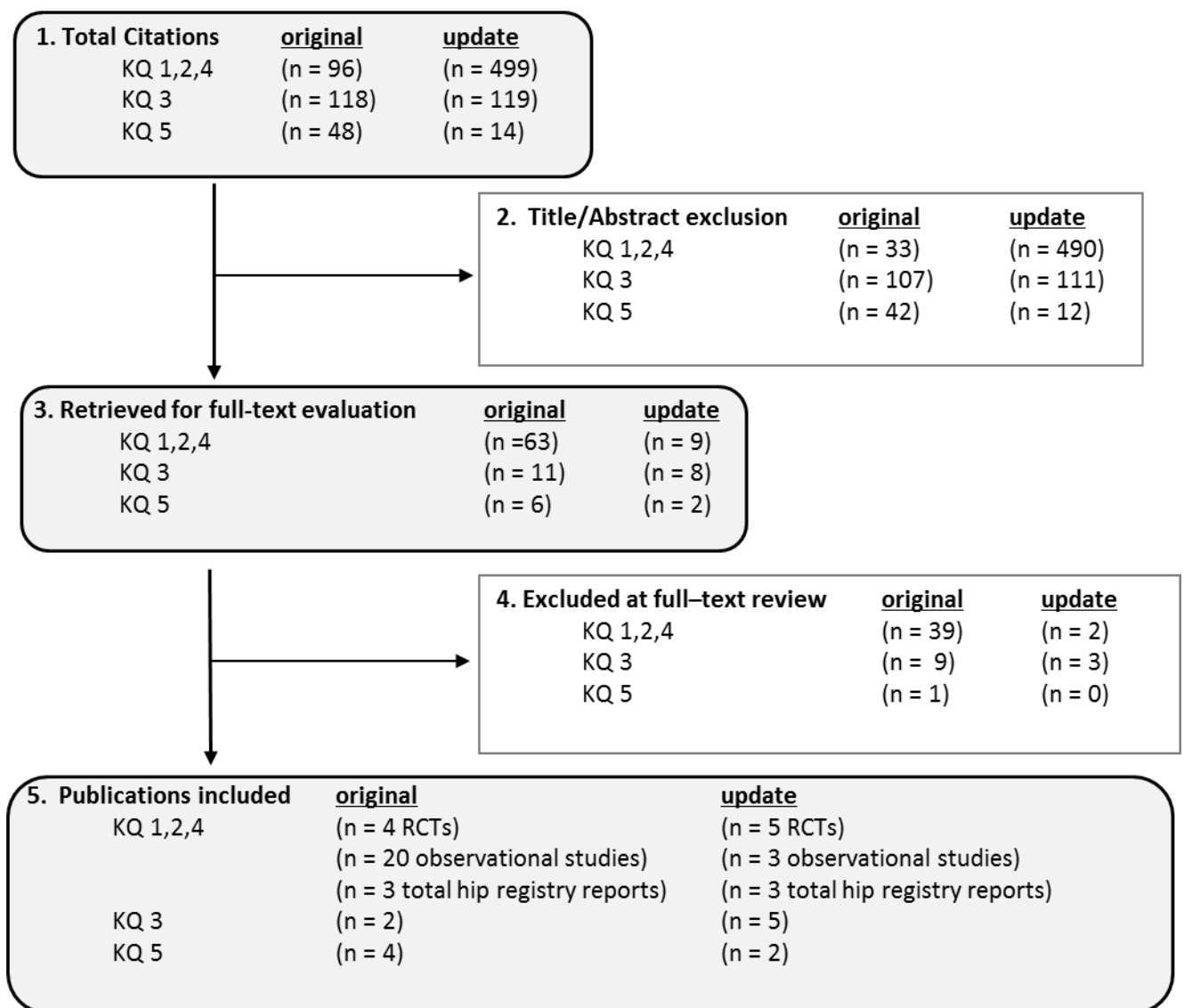
Study Component	Inclusion	Exclusion
<b>Population</b>	<ul style="list-style-type: none"> <li>Patients undergoing primary total HR</li> </ul>	<ul style="list-style-type: none"> <li>Patients with contraindications to receive total HR</li> </ul>
<b>Intervention</b>	<ul style="list-style-type: none"> <li>Total HR with a modern commercially available device designed for hybrid resurfacing: FDA-approved or un-approved devices in Phase III trials with <math>\geq 1</math> year of follow-up data</li> </ul>	<ul style="list-style-type: none"> <li>Non-hybrid or hemi resurfacing or use of minimally invasive surgery</li> </ul>
<b>Comparator</b>	<ul style="list-style-type: none"> <li>Primary THA</li> </ul>	<ul style="list-style-type: none"> <li>Revision THA</li> </ul>
<b>Outcomes</b>	<p>Studies must report on at least one of the following:</p> <ul style="list-style-type: none"> <li>Physical function/disability (clinical success, pain, activity, or motion)</li> <li>Revision</li> <li>Complications (e.g., femoral neck fracture, infection, avascular necrosis, dislocation, osteolysis, device migration or loosening, heterotopic ossification, infection, and others)</li> </ul> <p>The following secondary outcomes are reported if presented with studies meeting the above criteria:</p> <ul style="list-style-type: none"> <li>Quality of life (SF-36, SF-12, or EQ-5D)</li> </ul>	<ul style="list-style-type: none"> <li>Non-clinical outcomes</li> </ul>
<b>Study Design</b>	<ul style="list-style-type: none"> <li>Randomized controlled trials (RCTs) and comparative studies with concurrent controls were considered for key question 1.</li> <li>RCTs and observational comparative studies with concurrent controls for key questions 2, 3, 4</li> <li>Total joint hip registries for questions 2 and 4.</li> <li>For question 5, formal economic analyses (e.g., cost-utility study) were sought. In the absence of formal economic analyses, cost data reported in other systematic reviews or technology assessments were briefly summarized.</li> </ul>	<ul style="list-style-type: none"> <li>For question 1, studies other than RCTs or comparative studies with concurrent controls were excluded.</li> <li>Case reports</li> <li>Case series</li> </ul>
<b>Publication</b>	<ul style="list-style-type: none"> <li>Studies published in English in peer reviewed journals</li> <li>FDA SSED to supplement peer reviewed reports</li> <li>Annual reports from National Total Joint Registries</li> </ul>	<ul style="list-style-type: none"> <li>Abstracts, editorials, letters</li> <li>Duplicate publications of the same study which do not report on different outcomes</li> <li>Single-site reports from multicenter trials</li> <li>White papers or narrative reviews</li> <li>Articles identified as preliminary reports when results are published in later versions</li> </ul>

### **3.1.2. Data sources and search strategy**

The clinical studies included in this report were identified using the algorithm shown in Appendix A. The search took place in four stages. The first stage of the study selection process consisted of a comprehensive literature search using electronic means and hand searching. We then screened all possible relevant articles using titles and abstracts in stage two. This was done by two individuals independently. Those articles that met a set of *a priori* retrieval criteria based on the criteria above were included. Any disagreement between screeners that were unresolved resulted in the article being included for the next stage. Stage three involved retrieval of the full text articles remaining. The final stage of the study selection algorithm consisted of the selection of those studies using a set of *a priori* inclusion criteria, again, by two independent investigators. Those articles selected form the evidence base for this report.

We searched electronic databases from January 1, 2009 through 2 June, 2013 to determine new publications since our original report. Electronic databases searched included PubMed, EMBASE, CINAHL, ClinicalTrials.gov, CRISP, HSTAT, *The Cochrane Library*, EconLIT, PsychINFO, AHRQ, and INAHTA for eligible studies, including health technology assessments (HTAs), systematic reviews, primary studies and FDA reports. Annual reports from National Total Joint Registries and reference lists of all eligible studies were also searched. The search strategies used for PubMed and EMBASE, are shown in Appendix B. Figure 2 shows a flow chart of the results of all searches for included primary studies. Articles excluded at full-text review are listed in Appendix C.

Figure 3. Flow chart showing results of literature search from the original report



### **3.1.3. Data extraction**

Reviewers extracted the following data from the included clinical studies: study population characteristics, study type, study period, patient demographics and preoperative diagnoses, study interventions, follow-up time, study outcomes (functional and clinical, motion, radiographic), adverse events (revision, femoral neck fracture, avascular necrosis, osteolysis, heterotopic ossification, device loosening or migration, elevated serum (etc.) ion concentrations, death), and other complications (intraoperative cracks or notching, radiographic lucency, infection, myocardial infarction, deep vein thrombosis, pulmonary embolism, etc.). An attempt was made to reconcile conflicting information among multiple reports presenting the same data. For economic studies, data related to sources used, economic parameters and perspectives, results, and sensitivity analyses were abstracted.

### **3.1.4. Study quality assessment: Class of evidence (CoE) evaluation**

The method used by Spectrum Research, Inc. (SRI) for assessing the quality of evidence of individual studies as well as the overall quality of evidence incorporates aspects of the rating scheme developed by the Oxford Centre for Evidence-based Medicine,<sup>136</sup> precepts outlined by the Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group,<sup>6</sup> and recommendations made by the Agency for Healthcare Research and Quality (AHRQ).<sup>182</sup>

Details of the Class of evidence (CoE) methodology are found in Appendix D. Each clinical/human study chosen for inclusion was given a CoE rating based on the quality criteria listed in Appendix D. Standardized abstraction guidelines were used to determine the CoE for each study included in this assessment.

## **3.2. *Quality of Literature Available***

### **3.2.1. Number and quality of studies retained**

We identified 632 citations from our electronic search since our last report in 2009 using the search strategy in Appendix B. From among these, we identified five new randomized controlled trials (RCT): three were new studies<sup>32,79,152</sup>, one was a subsequent follow-up of clinical results from an earlier RCT<sup>173</sup> and one was a follow-up of ion concentrations to that same earlier RCT.<sup>177</sup> We also found eight new controlled observational studies<sup>10,31,82</sup>, three updated annual reports from three national total hip registries, and two new cost effectiveness studies. In addition, we reviewed 13 studies that report revision risks comparing HR with THA from one or more of the three national total hip registries. Since these reports represent older registry data, we report revision risks from the latest annual reports of each registry rather than from these articles. However, we provide a summary of the articles in Appendix E.

### **3.2.2. Analysis**

We attempted to pool functional outcomes when two or more randomized controlled studies presented identical outcomes over similar time periods. We did not pool the functional

outcomes from observational studies due to heterogeneity between studies. However, we did pool observational studies to assess the risk for revisions but display them separately from RCTs. To compare the estimates of procedure effectiveness across studies using continuous outcomes, differences in means were computed. First, the pre- and post-procedure means were differenced within each treatment arm to arrive at a measure of change induced by each procedure. The mean change for each arm was then compared with the other. The difference between them was used as the effect size estimate for the meta-analysis. When necessary, pooled standard deviations of the change within treatment groups were calculated assuming a correlation of 0.8. Standard deviations and standard errors across groups were found using the formulas below:

$$s_i = \sqrt{\frac{(n_{1i} - 1)sd_{1i}^2 + (n_{2i} - 1)sd_{2i}^2}{N_i - 2}} \quad SE\{MD_i\} = \sqrt{\frac{sd_{1i}^2}{n_{1i}} + \frac{sd_{2i}^2}{n_{2i}}}$$

**Where for study i:**  $s_i$  is the pooled standard deviation,  $n_i$  is the sample size,  $N_i$  is the pooled sample size, and  $sd_{j,i}$  is the standard deviation of treatment  $j$ .

When preoperative scores were not reported, as in the UCLA- Activity outcome, the postoperative scores for each procedure were compared directly. When standard deviations were not reported, estimated values were imputed as an average of the remaining studies as suggested by the Cochrane handbook.<sup>74</sup>

To compare proportions for risk of revision, we calculated the risk ratios across treatments. The Mantel-Haenszel method was implemented to weight the studies and generate pooled estimates. To estimate the risk of other complications, we pooled risks from multiple studies weighted by sample size.

Forest plots of the effect size were constructed with 95% confidence intervals. A random effects model was assumed to address heterogeneity. Calculations and plots were implemented in Review Manager 5.2.1.

To explore the possibility of differential effectiveness, we compared the difference in revision rates between HR and THA within each subgroup stratum. We tested the difference between subgroups by calculating the  $I^2$ -statistics. Measuring statistical heterogeneity,  $I^2$  approximates the likelihood that the observed discrepancies between subgroups are due to inherent differences in effect sizes or are a consequence of sampling error (i.e. result of chance).  $I^2$  is calculated by first summing the weighted squared difference of each subgroup rate ratio and the pooled estimate. This quantity is known as Cochran's Q. Assuming a null hypothesis that the effect size estimates are equivalent across subgroups, Cochran's Q follows a chi-squared distribution with  $N - 1$  degrees of freedom (where  $N$  is the number of subgroups). Reported as a percentage,  $I^2$  is then the quotient of the degrees of freedom and Cochran's Q which is then subtracted from 1 and multiplied by 100. For instance, an  $I^2 = 75\%$  suggests a 75% likelihood that the variation across subgroup effect sizes is due to heterogeneity. We displayed the estimates visually with forest plots to demonstrate the differential effect. When the stratum specific rate ratios and their confidence intervals fall on opposite sides of the overall effect, this represents a differential effect.



### 3.2.3. Critical Appraisal (APPENDIX F)

#### *Randomized controlled trials*

##### *Garbuz (2010)*

Garbuz et al.<sup>57</sup> published the results of a randomized controlled trial (RCT) in which 107 patients with an unreported number of hips were randomized to undergo either total HR with metal-on-metal (MoM) Durom components (48 patients underwent surgery) or MoM total hip arthroplasty (THA) with a large femoral head. Both groups received the same acetabular cup; all surgeries were performed using the posterior approach. The preoperative diagnosis was not reported; patients were included if they were considered suitable for total HR by the operating surgeon and were between 19 and 70 years of age. Mean patient age was 51.8 years, and 89.4% of patients were male. Although randomization was achieved using permuted blocks of two and four, patient treatment groups were placed in sealed but not necessarily opaque envelopes that were opened the day prior to surgery. Patients were blinded to their treatment group, though the authors did not discuss whether the patients remained blinded throughout the follow-up period. There was no indication of intention-to-treat. The objectives of this study were to evaluate whether there were differences between the groups in quality of life outcomes as well as serum metal ion concentrations; interestingly, although the PAT-5D (Paper Adaptive Test in 5 Domains of Quality of Life in Arthritis Questionnaire) was the primary outcome, the outcome scores were not reported. A complete follow-up rate of only 68% was reported; most outcomes were reported at one or two years follow-up. The institution of one or more of the authors for this study received funding from Zimmer, Inc. (Warsaw, IN). This study received a class of evidence (CoE) grade of II.

##### *Lavigne (2010)*

Lavigne et al.<sup>93</sup> conducted a RCT in which 48 patients with 48 hips were randomized to undergo total HR with MoM Durom prostheses (24 patients) or THA with a MoM large femoral head (24 patients). The acetabular component was identical in both groups; all surgeries were performed using the posterior approach. The majority of patients had osteoarthritis (77.1%); other diagnoses included developmental dysplasia (6.3%), protrusion acetabuli (4.2%), posttraumatic osteoarthritis (2.1%), avascular necrosis of the femoral head (6.3%), postseptic arthritis (2.1%), and rheumatoid arthritis (2.1%). Mean patient age was 49.7 years, which ranged from 33 to 63 years, and 60.4% of patients were male. Patients were randomly assigned to a treatment group using a random number generator; corresponding sealed and numbered opaque envelopes contained the type of procedure and were opened by the surgeon the day of surgery. Unlike most surgical studies, most patients (85%) remained blinded to the treatment until one year postoperatively. Although one of the primary objectives of the study was to determine whether total HR patients had better walking speeds at one year, there was a significant difference in the preoperative normal walking speeds (and step length) between treatment groups that was not controlled for using stratification or multivariate analysis. Otherwise, baseline patient demographics (age, gender, body mass index, and diagnosis) were similar between treatment groups. The complete follow-up rate was 87.5%; the mean follow-up was 14 months, though most outcomes were reported at one year. With respect to conflict of interest for this study, one or more of the authors received funding from Zimmer, Inc. (Warsaw, IN). This study received a CoE grade of II (downgraded from a score of I due to inadequate sample size and lack of control adjusting for baseline walking speed differences).

*Vendittoli (2006, 2010), Rama (2009), and Vendittoli, Roy (2010)*

Vendittoli et al.<sup>173</sup> performed a RCT in which 202 patients with 219 hips were randomized to receive either total HR with MoM Durom components (112 hips) or MoM THA (107 hips). Ten patients (ten hips) were excluded before surgery (3 in the HR group and 7 in the THA group) because of exclusion criteria missed at selection (n = 5), patients unfit for surgery (n = 2), and patients deciding to postpone surgery (n = 3), leaving 209 hips in 192 patients (109 HR and 100 THA) to form the basis of the study. The posterior surgical approach was used for all patients. Most hips had a preoperative diagnosis of osteoarthritis (77.5%); other diagnoses included Perthes (2.9%), hip dysplasia (8.1%), osteonecrosis (2.4%), inflammatory arthritis (6.2%), postseptic arthritis (0.5%), and 2.4% of hips were posttraumatic. Mean patient age was 50.1 years, which ranged from 23 to 65 years, and 65.6% of patients were male. Although randomization was performed with statistical software that used a block randomization table, the authors did not disclose who had access to the program and when. Intention-to-treat was not used, as one patient was excluded following intraoperative conversion from total HR to THA. A research nurse not blinded to the treatment groups made all follow-up assessments. Although most demographics were similar between groups, the THA group tended to have a higher body mass index (BMI) (30.0 versus 27.0 for the total HR group) that was not controlled for in the analysis. Complete follow-up rates of 97.6% at one year and 92.7% at 4.7 years were achieved. Due to limitations in study design, this RCT received a CoE grade of II.

Rama et al.<sup>140</sup> reported heterotopic ossification rates and risk factors for the same population reported in Vendittoli et al.<sup>173</sup> Although radiographs were used to evaluate HO, the authors did not disclose whether they were assessed by independent or blinded evaluators. Rama had a complete follow-up rate of 95.2%; outcomes were reported at one year or later. This study also received a CoE grade of II.

Vendittoli, Roy et al.<sup>173</sup> recruited 117 patients (64 HR and 53 THA) from the original 202 RCT patients for blood sampling analysis of metal ions, after excluding patients with other metallic implants such as previously replaced joints and internal fixation devices. Concentrations of whole blood and serum chromium (Cr), cobalt (Co), and titanium (Ti) ions released after surgery were compared between the HR and THA patients at three, six, twelve, and twenty-four months postoperatively. A complete follow-up of 80.3% was reported at 24 months. The authors did not disclose whether independent or blinded evaluators assessed the blood samples. This study also received a CoE grade of II.

*Smolders (2010, 2011)*

Smolders et al.<sup>152</sup> conducted an ongoing RCT in which 82 patients (75 patients originally from the 2010 study<sup>153</sup>) with an unreported number of hips were randomized to either undergo total HR with MoM Conserve Plus components (n = 42) or MoM THA (n = 40). All surgeries were performed using the posterior approach. The majority of patients had a preoperative diagnosis of osteoarthritis (93.0%); other diagnoses included avascular necrosis (1.4%) and congenital hip dysplasia (5.6%). Patients were aged between 24 and 65 years old, with a mean of 58.5 years, and 59.2% of patients were male. Patient randomization was computer-generated using a variable block schedule with an independent statistician placing treatment groups in sealed, opaque envelopes. Patients and surgeons were blinded to the randomization groups prior to surgery, however neither could be blinded to the eventual type of implant and no independent or blind assessment was disclosed postoperatively. There was no indication of intention-to-treat.

Both Smolders et al. studies used the same patient population; however they differed in their objectives. Smolders et al. (2010) sought to evaluate changes in bone mineral density (BMD) at the femoral neck and proximal femur after HR compared with THA. Smolders et al. (2011) compared the functional results and metal ion blood levels of patients who received HR compared with those who underwent MoM THA. Baseline demographic characteristics and co-interventions were similar between the two groups. Smolders et al. (2010) reported BMD outcome levels at 12 months, with an average follow-up of 16.6 months and 78.7% follow-up rate. Smolders et al. (2011) reported functional and blood level outcomes at 12 and 24 months, with a mean follow-up time of 20 months and 48.8% follow-up rate at 24 months. Regarding conflicts of interest for this study, benefits have been or will be received by one or more of the authors to be directed solely to a research fund, foundation, educational institution, or other nonprofit organization. Due to numerous limitations in study design, this RCT received a CoE grade of II.

*Jensen (2011)*

Jensen et al. performed a RCT in which 43 patients with 43 hips were randomized to receive either total HR with ASR components (n = 21) or standard THA with Biomet polyethylene liner and a ceramic head and titanium stem (n = 22). All surgeries were performed by two experienced surgeons using the posterior approach. All patients had a preoperative diagnosis of unilateral primary osteoarthritis. Mean patient age was 56.0 years, ranging from 44-65 years, and 73.0% of patients were male. There were no significant differences between any of the baseline group variables. Blocked randomization was used with sealed envelopes prior to surgical intervention. Investigator and patient blinding was not possible after surgery because of the size of surgical incision and movement restrictions. There was no indication of intention-to-treat. The objective of this study was to evaluate the recovery in mechanical muscle strength following HR versus THA. Mean follow-up time was 52 weeks, with an 86% complete follow-up rate. There were no conflicts of interest reported. This study received a CoE grade of II.

*Costa (2012)*

Costa et al. conducted a RCT in which 126 patients with an unreported number of hips were randomized to receive either total HR with large diameter head (n = 60) or THA (n = 66). The type of THA implant varied, with 44% receiving ceramic-on-ceramic bearings, 41% metal-on-metal, 5% ceramic-on-polyethylene, and 8% metal-on-polyethylene. The majority of patients had a primary preoperative diagnosis of osteoarthritis (96%); other diagnoses included developmental dysplasia (1.6%), ankylosing spondylitis (0.8%), Perthes disease (0.8%), and post-traumatic arthritis after a previous fracture of the acetabulum (0.8%). Mean patient age was 56.5 years, and 58.7% of patients were male. Baseline characteristics were similar between the two groups. Treatment allocation was determined using a computer generated, randomized number sequence and stratified by the supervising orthopaedic surgeon to balance any potential surgeon effects, and outcomes were assessed by blinded evaluators. Intention-to-treat analysis was performed for hip function at 12 months postoperatively. The objective of the study was to compare the clinical effectiveness of THA with HR in patients with severe arthritis of the hip. Outcomes were reported at a mean follow-up time of 12 months, with 95.2% complete follow-up rate. Funding from the National Institute of Health Research, University of Warwick, and University Hospitals Coventry and Warwickshire NHS trust; consultant surgeons at the University Hospitals Coventry and Warwickshire NHS trust have received research project funding and provided paid educational support to meetings sponsored by manufacturers of both

THA and HR arthroplasty implants, but not in relation to this study. This study received a class of evidence (CoE) grade of I.

#### *Prospective cohort studies*

##### *Fowble (2009)*

Fowble et al.<sup>54</sup> reported outcomes from a prospective cohort study in which 85 patients with 94 hips received either total HR using Conserve Plus prostheses under an FDA investigational device exemption (IDE) (50 patients with 50 hips) or THA with either a cross-linked polyethylene bearing (Marathon) (30 hips) or metal bearing (Ultamet) (14 hips); all surgeries were performed via the posterolateral approach. All patients who underwent total HR were self-referred, which is a potential source of bias. Preoperative diagnoses included osteoarthritis (93.6% of hips) and osteonecrosis (4.3% of hips). The mean patient age was 49.7 years, which ranged from 27 to 75 years, and 53.4% of patients were male. Patients were followed for a mean of 34.7 months, and a complete follow-up rate of 94.1% was obtained. One total HR patient had revision surgery and was excluded from all clinical outcomes, which may be a source of bias. Independent or blind assessment was not reported. Of note, there were several significant differences between the groups that were not controlled for, including (but not limited to): gender (62% male (total HR); 41% male (THA), ( $P = .03$ )), mean age (46 (total HR); 55 (THA), ( $P = .0001$ )), BMI (27.3 (total HR); 31.3 (THA), ( $P = .001$ )), Harris hip score (HHS) ( $P = .005$ ), and UCLA activity score ( $P = .02$ ). It is noted that financial support for this study was provided by Wright Medical Technology and the Los Angeles Orthopaedic Hospital Foundation. One investigator has a financial interest in the total hip replacement prostheses used in this research study (DePuy Pinnacle™, Summit™, and Ultamet™). The study received a CoE grade of III.

#### *Retrospective cohort studies*

##### *Li (2009)*

Li et al.<sup>95</sup> published the results of a retrospective cohort study in which 49 ankylosing spondylitis patients with 80 hips received either total HR (Durom) (24 consecutive patients with 39 hips) or ceramic-on-ceramic cementless THA (Secur-Fit HA) (25 patients with 41 hips). All surgeries were performed via the posterolateral approach. The mean patient age was 30.9 years, and ranged from 20 to 47 years, and 81.2% of patients were male. A complete follow-up rate of 100% was achieved, but the length of follow-up was not reported. One total HR patient who underwent revision due to a femoral neck fracture was excluded from all clinical outcomes, which may skew the results for this group. This study received a CoE grade of III due to inadequate sample size, lack of independent or blind assessment, and for not controlling for possible confounding.

##### *Li (2008)*

Li et al.<sup>94</sup> evaluated outcomes of 42 patients (52 hips) with developmental dysplasia in a retrospective cohort study. MoM total HR (Durom) was performed in 21 consecutive patients with 26 hips, while the same number of matched patients (and hips) received ceramic-on-ceramic (Secur-Fit HTA) THA; all procedures were done via the posterolateral approach. Mean patient age was 47.4 years (range of 37 to 64 years), and 71.4% of patients were female. The complete follow-up rate at a mean of 26.5 months was 100%. A CoE grade of III was given for the same reasons as Li (2009).

*Mont (2009)*

Mont et al.<sup>117</sup> prospectively followed both total HR and THA patients before performing retrospective matching. Fifty-four patients with 54 hips in the total HR group received the Conserve Plus prosthesis (as part of an FDA IDE study) via the anterolateral approach, while the same number of matched patients and hips underwent THA (approach not disclosed). Patients in the total HR group came to the authors' institution specifically to request the procedure, creating a potential source of bias between the groups. The mean patient age was 55 years, and ranged from 35 to 79 years, and two-thirds of patients were male. Surgical indications included osteoarthritis, osteonecrosis, or hip dysplasia (percentages were not reported). Complete follow-up of 92.6% of patients was achieved with a mean follow-up of 39 months. Although patients were matched, total HR patients had a significantly higher mean preoperative activity score than their THA counterparts ( $P = .01$ ); another limitation was that the two cohorts received different postoperative rehabilitative treatments. The primary author for this study acknowledges that he is a consultant for and has received funding from Stryker Orthopaedics (Mahwah, NJ) and Wright Medical Technology (Arlington, TN). This study was assigned a CoE grade of III.

*Pattyn (2008)*

Pattyn et al.<sup>134</sup> reported outcomes of 440 patients (number of hips not reported) who underwent either Birmingham MoM total HR via the posterolateral approach (250 consecutive patients) or ceramic-on-ceramic THA (Ancafit; uncemented) via the Harding lateral (73.7%) or posterolateral (26.3%) approach (190 patients). Patients had a mean age of 48.3 years, with a range of 14 to 78 years, and 63.0% were male. Preoperative diagnoses included osteoarthritis (70.1%), avascular necrosis (17.0%), rheumatoid arthritis (4.5%), and trauma (1.9%). The complete follow-up rate was 99.5%, and follow-up ranged from 36 to 72 months. One limitation of the study was notable differences in patient demographics (mean age, gender, and surgical indications) between groups that were not controlled for by stratified or multivariate analysis. In addition, outcomes were not assessed in a blinded or independent manner. The study was given a CoE grade of III.

*Pollard (2006)*

Pollard et al.<sup>137</sup> retrospectively reviewed 113 patients with 117 hips who underwent Birmingham total HR or hybrid THA via the posterior approach. In the total HR group, the first 63 Birmingham total HR hips treated by the senior author were included; however, the authors excluded three hips that underwent revision within the first postoperative year as well as six hips not available for follow-up. One additional hip in the total HR group was lost to follow-up, thus clinical outcomes for the total HR group were reported for 53 hips (complications were reported for 56 hips). The THA group was comprised of 54 matched hips and was selected from a 64-month period, however three patients were lost to follow-up, leaving 51 hips available for review. Overall, the complete follow-up rate included 88.5% of all patients. The primary surgical indication was osteoarthritis (75.9%); other indications included avascular necrosis (10.2%) and dysplasia (5.6%). Mean patient age was 50.1 years (range of 18 to 67 years), and 76.9% of patients were male. Outcomes did not appear to be assessed by an independent or blinded observer. Although patient demographics were relatively similar between groups, the authors did not report whether there were any statistically significant differences. Interestingly, the authors excluded from clinical outcomes three patients from the total HR group who underwent revision in the first year following the procedure; however one total HR patient who

underwent revision surgery at 62 months and four THA patients with planned revisions were all included in the clinical outcomes, making the reported clinical outcomes difficult to interpret. This study was the only one with mid-term (as opposed to short-term) follow-up, as patients were followed for an average of 5.9 years (range: 3.5–10 years) (THA: 6.7 (3.5–10) years; total HR: 5.1 (4.3–5.9) years). This study received a CoE grade of III.

*Stulberg (2008)*

Stulberg et al.<sup>156</sup> evaluated 603 patients with as many hips in a retrospective cohort study. A total of 337 patients were enrolled as part of a randomized FDA IDE study for the Cormet 2000 total HR System. The THA group was comprised of 266 matched patients who received the ceramic-on-ceramic Osteonics ABC System as part of a nonrandomized IDE study of this device. One potential source of bias is that the THA group served as an historical control, treated between 1996 and 1998, while the total HR patients were enrolled between 2001 and 2003. Preoperative diagnoses were osteoarthritis (84.9%), osteonecrosis (14.5%), and rheumatoid arthritis (0.7%). The mean patient age was 51.5 years (range was not reported), but was significantly higher in the THA group (53.3 years versus 50.1 years in the total HR group), and 65.2% of patients were male. The authors did perform propensity analysis to assess the comparability of patient demographics and baseline HHS between the cohorts and found no differences that would affect a conclusion of non-inferiority of total HR. A complete follow-up rate of 90.8% was achieved, and only patients with a minimum of 24 months of follow-up were included in clinical outcomes. Of note, 16 patients in the total HR group and three patients in the THA group were excluded from all clinical outcomes because they received revision surgery with the first two postoperative years, while an additional eight patients in the total HR group and two in the THA group underwent revision after 24 months and were included in all clinical outcomes. The exclusion of some revision patients from clinical outcomes makes these data more difficult to interpret. The authors acknowledge that one or more of them received outside funding or grants from Stryker Orthopaedics. In addition, one or more of the authors or a member of his or her immediate family received payments or other benefits, or a commitment or agreement to provide such benefits from a commercial entity (Corin, Tampa, Florida). This study was given a CoE grade of III.

*Vail (2006)*

Vail et al.<sup>169</sup> published the results of a retrospective review of 231 patients with 261 hips who underwent MoM total HR (Conserve Plus) as part of an FDA IDE study or metal-on-polyethylene THA. Because the authors excluded patients with less than two years follow-up, only 55 patients (57 hips) and 84 patients (93 hips) were included in the outcomes for the total HR and THA groups, respectively. Total HR prostheses were implanted via the posterior approach, while the approach used for the THA procedures was not disclosed. The most common indication for surgery (prior to loss to follow-up) was osteoarthritis; others included osteonecrosis, dysplasia, posttraumatic arthritis, and rheumatoid arthritis. Prior to loss to follow-up, the mean patient age was 53.2 years (range: 17 to 92 years), and 52.9% of patients were female. There were several significant differences between the groups in terms of demographics and preoperative scores; however these differences were controlled for with the use of multivariate analysis. Outcomes were not assessed in an independent or blinded manner. The complete follow-up rate was only 59.6%, and patients were followed for a mean of 36 months. Each author in this study certifies that he has or may receive payments or benefits from a commercial entity related to this work (Wright Medical Technology, Inc). This study received a CoE grade of III.



*Zywiell (2009)*

Zywiell<sup>191</sup> conducted a retrospective cohort study of 66 patients with 66 hips. The total HR group consisted of 33 patients who received the Conserve Plus prosthesis as part of an FDA IDE study; the THA group consisted of 33 matched patients who underwent THA with either metal-on-polyethylene or ceramic-on-polyethylene prostheses. The anterolateral approach was used in all total HR procedures, however the approach used for THA was not reported. Although the total HR group originally consisted of 54 consecutive hips, the authors were unable to match and hence excluded 21 of these hips, providing an opportunity for bias. Surgical indications were not disclosed. The mean patient age was 53 years, and ranged from 37 to 79 years, and 69.7% of patients were male. Because patients were closely matched, preoperative demographics, HHS, and activity scores were similar between cohorts. The primary outcomes were patient-reported and considered as reliable evidence in a retrospective study. Patients were followed for a mean of 43.5 months, and the complete follow-up rate was not reported. A senior author is a consultant for Stryker Orthopedics and Wright Medical Technology. This study was given a CoE grade of III.

*Costa (2011)*

Costa et al.<sup>31</sup> conducted a retrospective cohort study comparing 67 patients (73 hips) who underwent MoM hip resurfacing with 125 patients (137 hips) treated with standard total hip arthroplasty in the same time period. Details regarding the surgical procedure/approach and postoperative care were not provided. Surgical indications were not disclosed. Mean age was similar across the two groups (resurfacing: 51 years; THA: 54 years); however, there was a significantly fewer number of females in the HR group (6% vs. 48%) and patients undergoing hip resurfacing were more active and healthy preoperatively as indicated by the significantly higher mean Harris hip score. Because the patients/hips were not matched for specific pre-operative factors and the authors did not control for these differences the results are subject to bias. Pre- and post-operative data were collected prospectively in a database and analyzed retrospectively. No mention was made of independent or blinded assessment of outcomes. Only patients with a minimum of 24 months follow-up were included in the analysis; mean follow-up period for both groups was 30 months and the complete follow-up rate was not reported. The senior author is a paid consultant for Stryker Orthopaedics and Wright Medical Technologies. This study received a CoE grade of III.

*Killampalli (2009)*

Killampalli et al.<sup>82</sup> conducted a retrospective review of 255 consecutive hip arthroplasties from which they compared the results of 58 patients who had undergone MoM hip resurfacing with 58 patients who had undergone uncemented THA matched for age, sex and pre-operative activity level. The total number of hips was not reported. Mean patient age was 57.9 years in the hip resurfacing group and 58.5 years in the THA group. The sex distribution of the patients was not reported. All prostheses were implanted via the posterior approach. The most prevalent indication for both surgical procedures was osteoarthritis. Co-interventions were the same for both groups with full weight-bearing allowed post-surgery and impact activities commenced at week 12. No mention was made of independent or blinded assessment of outcomes. Patients were followed for a mean of 5 years and the authors state that no patient was lost to follow-up. The authors declare no conflicts of interest and that no financial support was received. This study received a CoE grade of III.

*Australian Joint Replacement Registry (2012)*<sup>7</sup>

In 1999, the Australian Commonwealth Department of Health and Ageing established a Joint Replacement Registry with a staged implementation. The Registry became national in 2002 and receives information from some 299 public and private hospitals that perform joint replacement. Data for the Registry are collected on Registry forms completed at the participating hospitals at the time of surgery. Data validation is by multilevel comparison to data provided by state and territory health departments. For some territories, individual level patient/procedure validation is performed. For the 2011 Registry data, the initial validation resulted in 93.9% of Registry records verified against health department data. Follow-up on unreported and unmatched records yielded an almost complete set of data relating to hip replacement in Australia. The Twelfth Annual Report details the findings from the Registry through December 2011, and includes analyses on 332,351 total hip arthroplasties, and 14,901 hip resurfacings. The primary outcome is time to first revision described using Kaplan-Meier survival estimates.

*The National Joint Registry for England and Wales (NJR) (2011)*<sup>123</sup>

The NJR was established in October 2002 and began collecting and studying data on hip replacement surgeries in April 2003. Data are provided to the NJR by the National Health Service (NHS) and independent healthcare providers throughout England and Wales. The analyses are based on data on primary hip replacement undertaken between 1st April 2003 and 31 March 2012 that are linked to an episode in the Hospital Episode Statistics (HES) database. Linkage was not available for independently funded hip procedures in the private sector (estimated at 15% of the total number of procedures in the NJR during the above time frame). The main outcome of interest is survival to revision of implants in primary hip replacement surgeries. The 9th Annual Report was used for this Technology Assessment. In 2011-2012 80,314 hip replacements were carried out, 71,672 primary and 8,641 revisions. Resurfacing accounted for 2% of the primary hip procedures. Exeter V40 stem was the most used (64%) for cemented fixation, Corail stem was most used (47%) for uncemented fixation, and Birmingham hip resurfacing was the most used for hip resurfacing.

*The Swedish Hip Arthroplasty Register (2011)*<sup>158</sup>

The Swedish Hip Arthroplasty Register has been in existence for over 30 years. The registry includes such variables as patient-reported outcomes, short-term complications and 10-year survival. The national completeness for 2011 was 97.6%. During 2011, 167 resurfacing implants were placed, with BHR being the most commonly used (83.2%), followed by Adept (15%) and Durom (1.8%). Since 1992 there have been 1,959 resurfacings done. Since 2009, nearly 48,000 hip replacement surgeries were added to the registry.



## 4. Results

### 4.1. Key question 1: What is the evidence of efficacy and effectiveness of total HR compared with THA?

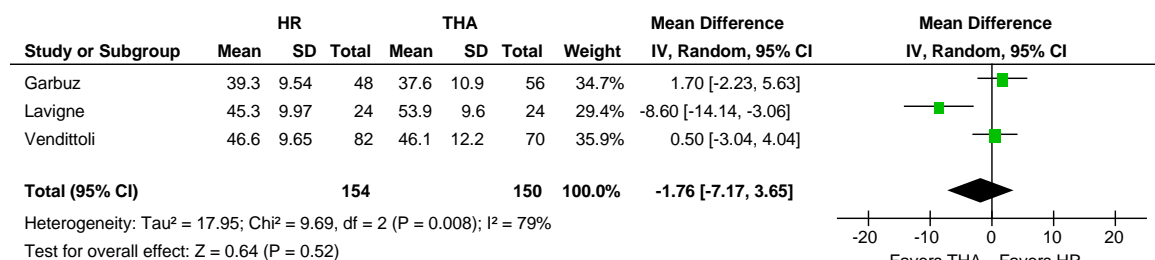
#### 4.1.1. Efficacy

We report on six RCTs that produced nine separate publications. Study characteristics are described in Table 11. Detailed results for each study can be found in Appendix G.

#### WOMAC scores (Figure 3)

A patient-reported outcome measure, WOMAC scores account for pain, stiffness, and physical functioning. The pooled estimate in the difference in mean change between pre- and postoperative WOMAC scores was not statistically significant between total HR and THA groups at one-year follow-up as reported by three RCTs.<sup>56,92,175</sup> In evaluating the change in mean scores between 1 and 2 years, Vendittoli et al. (2010)<sup>173</sup> reported a statistical difference between groups between a one and two year period ( $P = .007$ ) in WOMAC scores favoring HR. However, differences in scores were small,  $2.3 \pm 2.1$  for HA vs.  $1.2 \pm 1.3$  for THA. The authors concluded that these small differences were only of slight clinical relevance.

**Figure 4. Difference in mean change in WOMAC scores from pre- to 1-year postoperative hip resurfacing or conventional total hip arthroplasty.**



**Table 11 Hip Resurfacing Demographic Table, randomized controlled trials**

Author (Year)	Study Type Study Period	No. of Patients No. of Hips	Mean Age (Years) (Range) Sex	Preop Diagnosis (N, %)	Intervention	Follow-up (F/U) Time % F/U	Conflict of Interest
1. Vendittoli (2006) (Index study)	Randomized controlled trial 2003-2006 (randomization period)	N = 202* patients with 219 hips	Mean age: 50.1 (23-65) 65.6% male	<ul style="list-style-type: none"> <li>• Osteoarthritis (n = 162, 77.5%)</li> <li>• Perthes (n = 6, 2.9%)</li> <li>• Hip dysplasia (n = 17, 8.1%)</li> <li>• Osteonecrosis (n = 5, 2.4%)</li> <li>• Post trauma (n = 5, 2.4%)</li> <li>• Inflammatory arthritis (n = 13, 6.2%)</li> <li>• Post septic arthritis (n = 1, 0.5%)</li> </ul>	<ul style="list-style-type: none"> <li>• HR [hybrid Durom with a cemented femoral and uncemented acetabular components] (n = 109, 52.2%)</li> <li>• THA [titanium, uncemented CLS-Spotorno femoral stem and Allofit acetabular cup with Metasul chrome-cobalt insert and femoral head] (n = 100, 47.8%)</li> </ul>	Vendittoli/Rama (2006/2009): <u>F/U: 12 months</u> (95.2-97.6% for perioperative, NR for other outcomes)	Although none of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article, benefits have been or will be received but will be directed solely to a research fund, foundation, educational institution, or other nonprofit organization with which one or more of the authors are associated.
2. Rama (2009) (HO eval from index study)						Vendittoli, Ganapathi (2010): <u>F/U 12 months:</u> 93% for perioperative safety (203/219) 87% for subjective outcomes (190/219) 69% for functional questionnaires† (152/219) <u>F/U 24 months:</u> 83% for subjective outcomes 69% for functional questionnaires† <u>Final F/U:</u> mean 56 months range: 36-72 months 92.7% complete F/U	
3. Vendittoli, Ganapathi (2010) (F/U to Index study)							
4. Vendittoli, Roy (2010) (metal ion eval from index study)						Vendittoli, Roy (2010): Mean F/U: NR 80.3% F/U at 24 months	

Author (Year)	Study Type Study Period	No. of Patients No. of Hips	Mean Age (Years) (Range) Sex	Preop Diagnosis (N, %)	Intervention	Follow-up (F/U) Time % F/U	Conflict of Interest
Garbuz (2010)	Randomized controlled trial 2005-2008 (patient recruitment period)	N = 107 patients (number of hips NR)	Mean age: 51.8 (range NR) (inclusion criteria: 19–70 years) 89.4% male	NR	<ul style="list-style-type: none"> <li>• HR [Durom femoral component and acetabular cup (fixation NR)] (n = 48, 46.2%)</li> <li>• LDH THA [Durom femoral component and M/L Taper stem with Metasul large femoral head (fixation NR)] (n = 56, 53.8%)</li> </ul>	<u>F/U: 12 months</u> Functional outcomes (68%) 73/107 Safety outcomes F/U: 24 months Safety outcomes 68% complete F/U <ul style="list-style-type: none"> <li>• 8/107 patients lost to F/U, 3 of which did not undergo surgery</li> <li>• 23 patients had not reached 1-yr F/U at time of publication</li> </ul>	The institution of one or more of the authors has received funding from Zimmer, Inc. (Warsaw, IN)
Lavigne (2010)	Randomized controlled trial 2006-2007 (patient recruitment period)	N = 48 patients with 48 hips	Mean age: 49.7 (33-63) 60.4% male	<ul style="list-style-type: none"> <li>• Osteoarthritis (n = 37, 77%)</li> <li>• Mild developmental dysplasia (n = 3, 6.3%)</li> <li>• Protrusion acetabuli (n = 2, 4.2%)</li> <li>• Posttraumatic osteoarthritis (n = 1, 2.1%)</li> <li>• Avascular necrosis of the femoral head (n = 3, 6.3%)</li> <li>• Postseptic arthritis (n = 1, 2.1%)</li> <li>• Rheumatoid arthritis (n = 1, 2.1%)</li> </ul>	<ul style="list-style-type: none"> <li>• HR [Durom acetabular cup and cemented Durom femoral component] (n = 24, 50%)</li> <li>• LDH THA [Durom acetabular cup and CLS femoral stem] (n = 24, 50%)</li> </ul>	Mean F/U: 14 months F/U range: 12-18 months 87.5% complete F/U <ul style="list-style-type: none"> <li>• 100% F/U for patient reported outcomes and radiographic analyses</li> <li>• 87.5% F/U for gait analysis</li> </ul>	One of the authors has received funding from Zimmer, Warsaw, IN.

Author (Year)	Study Type Study Period	No. of Patients No. of Hips	Mean Age (Years) (Range) Sex	Preop Diagnosis (N, %)	Intervention	Follow-up (F/U) Time % F/U	Conflict of Interest
Smolders (2011)  (includes Smolders 2010 data which is not as complete)	Randomized controlled trial 2007-2010 (patient recruitment period)	N = 82 patients (number of hips NR)	Mean age: 58.5 (24-65) 59.2% male	<ul style="list-style-type: none"> <li>• Osteoarthritis (n = 66, 93.0%)</li> <li>• Avascular necrosis (n = 1, 1.4%)</li> <li>• Congenital hip dysplasia (n = 4, 5.6%)</li> </ul>	<ul style="list-style-type: none"> <li>• HR [Conserve Plus, both components made of a cast, heat-treated solution-annealed Co-Cr alloy] (n = 42, 51.2%)</li> <li>• THA [uncemented, metal-on-metal; metal stem and a threaded titanium cup with a polyethylene insert and metal head, Zweymuller Classic] (n = 40, 48.8%)</li> </ul>	Smolders (2011): Mean F/U: 20 months 85.4% complete F/U at 1-year 48.8% complete F/U at 2-years	Although none of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article, benefits have been or will be received but will be directed solely to a research fund, foundation, educational institution, or other nonprofit organization with which one or more of the authors are associated.
Jensen (2011)	Randomized controlled trial NR	N = 43 patients with 43 hips	Mean age: 56.0 (44-65) 73.0% male	<ul style="list-style-type: none"> <li>• Unilateral primary osteoarthritis (N = 43, 100%)</li> </ul>	<ul style="list-style-type: none"> <li>• HR [ASR, cementless cup and cemented femoral component] (n = 21)</li> <li>• THA [Mallory-Head cup (Biomet) with polyethylene liner, 28mm ceramic femoral head on a titanium Bimetric stem] (n = 22)</li> </ul>	Mean F/U: 52 weeks F/U range: 48-56 weeks 86% complete F/U <ul style="list-style-type: none"> <li>• 6/43 patients lost to F/U, 4 of which did not undergo surgery</li> </ul>	There were no conflicts of interest.

Author (Year)	Study Type Study Period	No. of Patients No. of Hips	Mean Age (Years) (Range) Sex	Preop Diagnosis (N, %)	Intervention	Follow-up (F/U) Time % F/U	Conflict of Interest
Costa (2012)	Randomized controlled trial 2007–2010 (patient recruitment period)	N = 126 patients (number of hips NR)	Mean age: 56.5 (range NR) 58.7% male	<ul style="list-style-type: none"> <li>• Osteoarthritis (n = 121, 96%)</li> <li>• Developmental dysplasia (n = 2, 1.6%)</li> <li>• Ankylosing spondylitis (n = 1, 0.8%)</li> <li>• Perthes disease (n = 1, 0.8%)</li> <li>• Post-traumatic arthritis after a previous fracture of the acetabulum (n = 1, 0.8%)</li> </ul>	<ul style="list-style-type: none"> <li>• HR [large diameter metal-on-metal bearings; specific implants NR] (n = 60, 47.6%)</li> <li>• THA [29 (44%) implants had ceramic-on-ceramic bearings, 27 (41%) metal-on-metal, 3 (5%) ceramic-on-polyethylene, 5 (8%) metal-on-polyethylene; 3 femoral and 5 acetabular components were cemented, all other components were implanted uncemented] (n = 66, 52.4%)</li> </ul>	Mean F/U: 12 months 95.2% complete F/U <ul style="list-style-type: none"> <li>• 6/126 patients lost to F/U, 4 of which did not undergo surgery</li> </ul>	Funding from the National Institute of Health Research, University of Warwick, and University Hospitals Coventry and Warwickshire NHS trust; consultant surgeons at the University Hospitals Coventry and Warwickshire NHS trust have received research project funding and provided paid educational support to meetings sponsored by manufacturers of both THA and HR arthroplasty implants, but not in relation to this study.

HR: hip resurfacing

LDH: large diameter head

THA: total hip arthroplasty

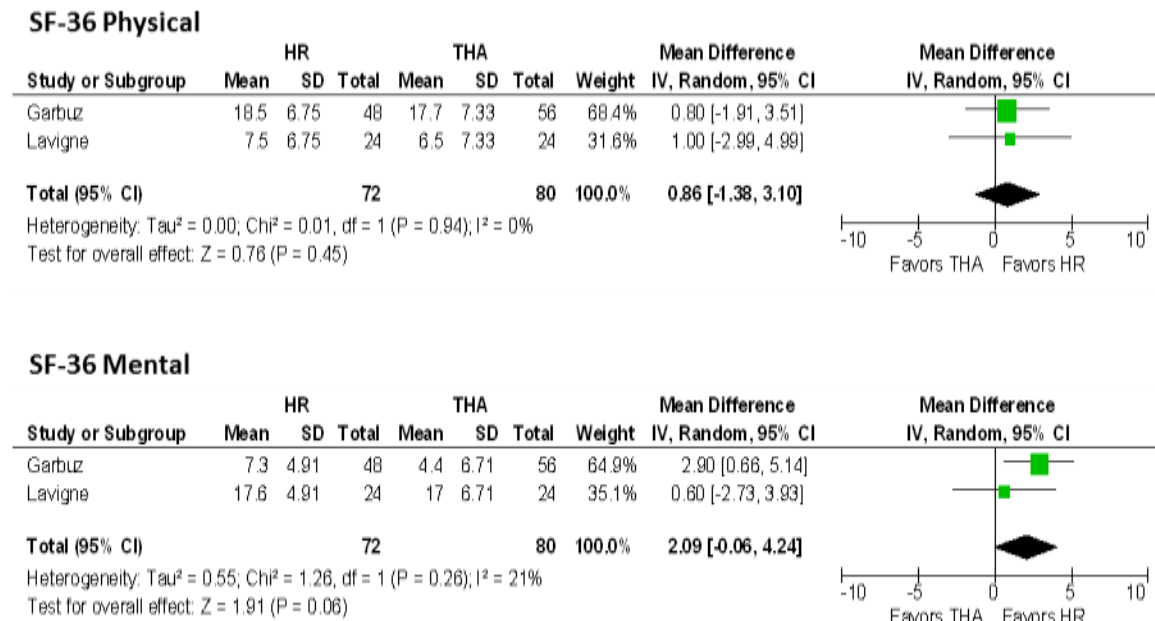
\*N varied between 191-202 patients for the first three studies (10 of which did not undergo surgery and 1 patient unable to be accounted for); Vendittoli, Roy (2010) used a subset of the patients (N = 117) for blood analysis only

†n=70 hips for THA and n=82 hips for HR eligible to complete the functional questionnaires, the rest were excluded due to bilateral cases or being excluded for other reasons. However, the number who completed the questionnaires at each time period (1 and 2 years) is not given.

*SF-36 scores (Figure 4)*

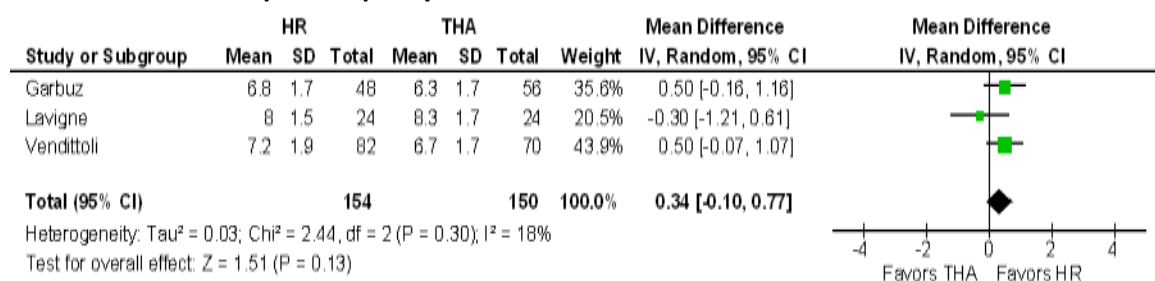
There was no significant difference in the pooled difference in mean change in the SF-36 quality of life scores between treatment groups at one-year follow-up as reported in two RCTs.<sup>56,92</sup> The mean differences in SF-36 physical scores ranged from 6.5 to 17.7 in the THA group and from 7.5 to 18.5 in the total HR group; mean differences in the mental SF-36 scores ranged from 4.4 to 17 in the THA group and from 7.3 to 17.6 in the total HR group.

**Figure 5 Difference in mean change in SF-36 scores from pre- to 1-year postoperative hip resurfacing or conventional total hip arthroplasty.**

*UCLA activity scores (Figure 5)*

There was no significant difference in the pooled mean change in the UCLA Activity Score between treatment groups at one-year follow-up as reported in three RCTs.<sup>56,92,175</sup> In the THA group, postoperative scores ranged from 6.3 to 8.3; in the total HR group, postoperative scores ranged from 6.8 to 8.0. Using medians instead of means, Smolders et al.<sup>152</sup> reported similar results (HR 8, range 4 to 10; THA 7, range 2 to 9).

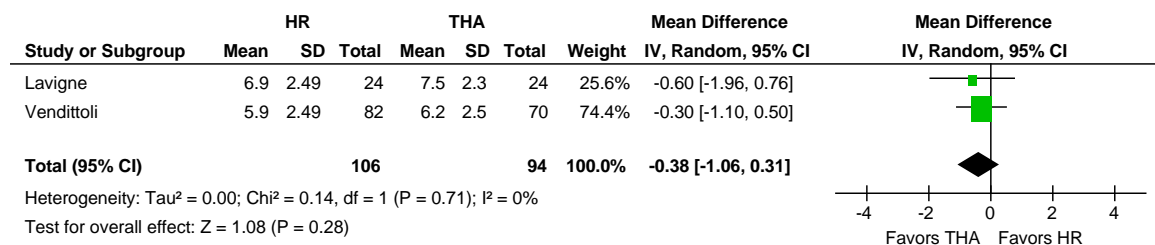
**Figure 6. Mean change in UCLA Activity Scores 1-year postoperative hip resurfacing or conventional total hip arthroplasty.**



### Merle D'Aubigné (MA) scores (Figure 6)

The Merle D'Aubigné score is a clinician-reported outcome measure that includes pain, ability, and walking ability components. There was no significant difference in the pooled difference in mean change in the Merle D'Aubigné Score between treatment groups at one-year follow-up as reported by two RCTs.<sup>92,175</sup> The mean differences ranged from 6.2 to 7.5 in the THA group and 5.9 to 6.9 in the HR group.

**Figure 7 Mean change in Merle D'Aubigné scores 1-year postoperative hip resurfacing or conventional total hip arthroplasty.**



### Oxford Hip Score

Two RCTs reported results using the Oxford Hip Score (OHS), one reporting means<sup>32</sup> and one reporting medians.<sup>152</sup> Each found similar scores after 1 year. Costa et al reports a mean OHS of 40.4 (range, 37.9 to 42.9) in the HR group and 38.2 (range, 35.3 to 41.0) in the THA group, while Smolders et al. reports a median score of 35 in the HR group and 33 in the THA group. (Note that Smolders et al. reported the OHS values such that lower values represent higher function rather than lower function as intended. The scores available for the OHS range from 0 [lowest function] to 48 [highest function]. We converted the values by subtracting the reported values from 48.

### Harris Hip Score

Two RCTs reported results using the Harris Hip Score (HHS). Costa et al. reported no statistical difference between means at 1-year follow-up, 88.4 (95% CI 84.4, 92.4) for HR compared with 82.3 (95% CI 77.2, 87.5) for THA.<sup>32</sup> Likewise, Smolders et al reported statistically similar medians at 1-year follow-up, 98 (range 60, 100) for HR compared with 96 (range 49, 100) for THA.<sup>152</sup>

### 4.1.2. Effectiveness

We report on six RCTs that produced nine separate publications. Study characteristics are described in Table 12. Detailed results for each study can be found in Appendix H.

### Quality of life (Figures 7,8)

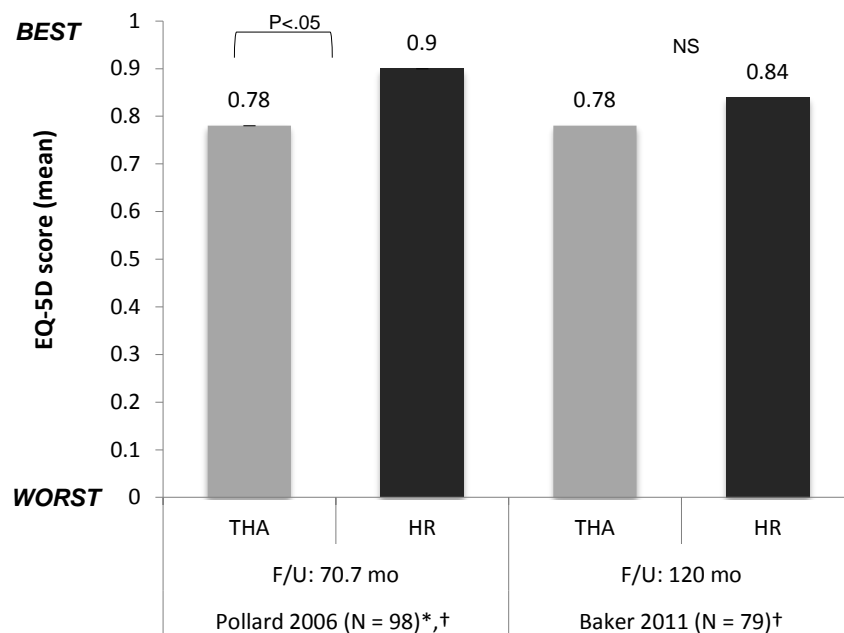
#### EQ-5D

Postoperative EQ-5D scores were statistically higher in the total HR group (0.9) compared to the THA group (0.78) as reported by Pollard et al. a mean 71 months following surgery.<sup>137</sup> Preoperative scores were not reported. A follow-up at 120 months demonstrated no difference in the EQ-5D. Details of this study are provided in the preceding paragraph. The EQ-5D score is a patient-reported outcome measure that includes subscales to assess mobility, self-care, activity, pain, and mental health.

#### SF-12

Postoperative SF-12 physical scores were significantly higher in the total HR (53.6) group versus the THA (47.0) group as reported by one prospective cohort study ( $P = .002$ ).<sup>54</sup> Although the preoperative scores were not significantly different between groups ( $P = .2$ ), it is possible that at least some of the 6.6-point difference in the postoperative scores between groups may be accounted by a 7.8-point difference in the preoperative scores (THA: 25.8, total HR: 33.6). There was no significant difference in the SF-12 mental scores between groups either postoperatively (THA: 52.5, total HR: 54.6) or preoperatively (THA: 35.2, total HR: 44.2). Only short-term follow-up was available. The SF-12 is a patient-reported health survey.

**Figure 8. EQ-5D Scores from controlled observational studies.**



HR: total hip resurfacing.

NS: not statistically significant ( $P > .05$ ).

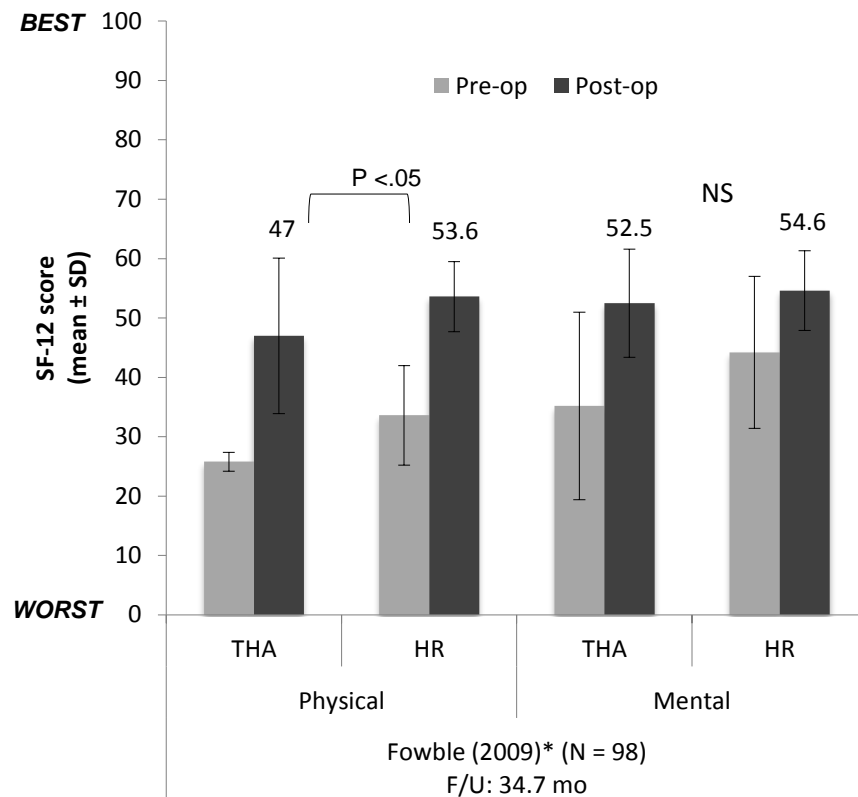
THA: total hip arthroplasty.

\*Author excluded patient(s) who underwent revisions from all clinical outcomes: three hips in the total HR group underwent early revision (due to avascular necrosis). Note that an additional five revisions were NOT excluded (one in the total HR and four planned revisions in the THA group).

†Standard deviation not reported.



Figure 9. SF-12 scores



HR: total hip resurfacing.

NS: not statistically significant ( $P > .05$ ).

THA: total hip arthroplasty.

\*Author excluded patient(s) who underwent revisions from all clinical outcomes: one hip in the total HR group underwent revision (due to avascular necrosis).

**Table 12. Hip Resurfacing Demographic Table, observational comparative studies.**

Author (Year)	Study Type Study Period	N	Age (Years) (Range), Sex	Preop diagnosis (N, %)	Intervention	Mean F/U Time	Conflict of Interest
Fowble (2009)	Prospective cohort study NR	N = 85 patients with 94 hips	Mean age: 49.7 (27–75) 53.4% male	Osteoarthritis (88 hips, 93.6%), osteonecrosis (4 hips, 4.3%), other (not specified) (2 hips, 2.1%)	HR [Conserve Plus (fixation NR)] (n = 50 patients with 50 hips, 58.8%); THA [Summit and Pinnacle femoral and acetabular components with cementless fixation; cross-linked poly bearing (30 hips) or metal bearing (14 hips)] (n = 35 patients with 44 hips, 41.2%)	Mean F/U: 2.9 years F/U range: 2.0–4.2 years 94.1% complete F/U rate (1 HR patient had revision and not included in F/U)	Financial support for this study was provided by Wright Medical Technology and the Los Angeles Orthopaedic Hospital Foundation. Thomas P. Schmalzried, M.D., has a financial interest in the total hip replacement prostheses used in this research study (DePuy Pinnacle™, Summit™, and Ultamet™)
Li (2009)	Retrospective cohort study 2005–2007	N = 49 patients with 80 hips	Mean age: 30.9 (20–47) 81.2% male	Ankylosing spondylitis (100%)	HR [Durom resurfacing system with cementless acetabular and cemented femoral fixation] (n = 24 patients with 39 hips); THA [Secur-Fit HA ceramic-on-ceramic system with cementless acetabular and femoral fixation] (n = 25 patients with 41 hips)	Mean F/U: NR F/U range: NR 100% complete F/U rate	Authors state that “no benefits or funds were received in support of the study”

Author (Year)	Study Type Study Period	N	Age (Years) (Range), Sex	Preop diagnosis (N, %)	Intervention	Mean F/U Time	Conflict of Interest
Li (2008)	Retrospective cohort study 2005–2007	N = 42 patients with 52 hips	Mean age: 47.4 (37–64) 71.4% female	Developmental dysplasia of the hip: Crowe type I (n = 38 hips, 73.1%), Crowe type II (14 hips, 26.9%)	HR [Durom resurfacing system with cementless acetabular and cemented femoral fixation] (n = 21 patients with 26 hips, 50%); THA [Secur-Fit HA ceramic-on-ceramic total hip system with cementless acetabular and femoral fixation] (n = 21 matched patients with 26 hips, 50%)	Mean F/U: 2.2 years F/U range: 1.3–3.1 years 100% complete F/U rate	Unclear
Mont (2006)	Retrospective cohort study 2000–2003	N = 78 patients with 85 hips	Mean age: 42 (18–64) †† 68.8% male ††	<u>Osteonecrosis</u> of the femoral head (n = 37 patients with 43 hips); <u>Osteoarthritis</u> (n = 41 matched patients with 42 hips)	HR [Conserve Plus prosthesis with cementless press-fitted acetabular and cemented femoral fixation] (n = 78 patients with 85 hips, 100%)	Mean F/U: 3.4 years †† F/U range: 2.0–5.1 years †† 98.7% complete F/U rate	One or more of the authors received grants or outside funding from Wright Medical Technology, Inc. as well as payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Wright Medical Technology, Inc.)

Author (Year)	Study Type Study Period	N	Age (Years) (Range), Sex	Preop diagnosis (N, %)	Intervention	Mean F/U Time	Conflict of Interest
Mont (2009)	Retrospective cohort study 2002–2005	N = 108 patients with 108 hips	Mean age: 55 (35–79) 66.7% male	Osteoarthritis, osteonecrosis, or hip dysplasia (n = NR)	HR [Conserve Plus prosthesis with press-fitted acetabular and cemented femoral fixation] (n = 54 patients with 54 hips, 50%); THA [Stryker Howmedica Osteonics Trident cup with Accolade femoral component (fixation details NR) and press-fitted femoral fixation] (n = 54 matched patients with 54 hips 50%)	Mean F/U: 3.3 years F/U range: 2–5 years 92.6% complete F/U rate <sup>††</sup>	Primary author is a consultant for and has received funding from Stryker Orthopaedics (Mahwah, NJ) and Wright Medical Technology (Arlington, TN)
Pattyn (2008)	Retrospective cohort study 1998–2003	N = 440 patients (number of hips NR)	Mean age: 48.3 (14–78) 63.0% male	Osteoarthritis (70.1%), avascular necrosis (17.0%), rheumatoid arthritis (4.5%), and trauma (1.9%) <sup>***</sup>	HR [Birmingham metal-on-metal, fixation NR] (n = 250, 56.8%); THA [Ancafit ceramic-on-ceramic, fixation details NR] (n = 190, 43.2%)	Mean F/U: NR F/U range: 3–6 years 99.5% complete F/U rate	Authors state that there are “no relevant financial relationships to disclose”
Pollard (2006) Baker (2010)	Retrospective cohort study 1996–2001	N = 113 patients with 117 hips <sup>†††</sup>	Mean age: 50.1 (18–67) <sup>†††</sup> 76.9% male <sup>†††</sup>	Osteoarthritis (82 hips, 75.9%), avascular necrosis (11 hips, 10.2%), developmental dysplasia (6 hips, 5.6%), rheumatoid arthritis (1 hip, 0.9%), other (slipped capital femoral epiphysis, Perthes’ disease, ankylosing spondylitis, post-traumatic osteoarthritis (8 hips, 7.4%) <sup>†††</sup>	HR [Birmingham prosthesis with cemented femoral and uncemented acetabular fixation] (n = 51 patients with 54 hips, 49%) <sup>†††</sup> THA [cemented femoral stem, uncemented acetabular component and a press-fit polyethylene liner] (n = 53 matched patients with 54 hips 51%) <sup>†††</sup>	Mean F/U: 5.9 years (3.5–10) 88.5% complete F/U rate <sup>†††</sup>  10 years (7.5–14.5) (69.9%)	Authors state that “no benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article”

Author (Year)	Study Type Study Period	N	Age (Years) (Range), Sex	Preop diagnosis (N, %)	Intervention	Mean F/U Time	Conflict of Interest
Stulberg (2008) (2010)	Retrospective cohort study (historical control) 1996–2003 (dates of enrollment)	N = 603 patients with 603 hips	Mean age: 51.5 (range: NR****) 65.2% male	Osteoarthritis (84.9%), osteonecrosis (14.5%), rheumatoid arthritis (0.7%)	HR [Cormet 2000 Hip Resurfacing System with cemented femoral fixation and uncemented acetabular fixation] (n = 337 patients with 337 hips, 55.9%); THA (historical control) [ceramic-on-ceramic Osteonics ABC System I or II; fixation NR] (n = 266 patients with 266 hips, 44.1%)	Mean F/U: NR F/U range: NR (>2 years) 90.8% complete F/U rate  Note: HHS score F/U: 2 year: 86.6% 3 year: 45.3%	One or more of the authors received outside funding or grants from Stryker Orthopaedics. In addition, one or more of the authors or a member of his or her immediate family received payments or other benefits, or a commitment or agreement to provide such benefits from a commercial entity (Corin, Tampa, Florida).
Vail (2006)	Retrospective cohort study 2000–2003	N = 231 patients with 261 hips	Mean age: 53.2 (17-92) +++++,++++ 52.9% female +++++,++++	Osteoarthritis (n = 110, 79.1%), osteonecrosis (n = 25, 18.0%), developmental dysplasia (n = 6, 4.3%), posttraumatic arthritis (n = 3, 2.2%), rheumatoid arthritis (n = 6, 4.3%) +++++	HR [Conserve Plus prosthesis system with press-fit acetabular fixation and cemented femoral fixation] (n = 55 patients with 57 hips) THA [press-fit femoral stem fixation (acetabular fixation NR)] (n = 84 patients with 93 hips) +++++	Mean F/U: 3 years F/U range: 2–4 years 59.6% complete F/U rate	Each author certifies that he has or may receive payments or benefits from a commercial entity related to this work (Wright Medical Technology, Inc).
Zywił (2009)	Retrospective cohort study 2002–2005	N = 66 patients with 66 hips	Mean age: 53 (37–79) 69.7% male	NR	HR [Conserve Plus prosthesis system (fixation NR)] (n = 33 patients with 33 hips); THA [Stryker acetabular cup and Accolade stem and either ceramic or metal femoral head (fixation NR)] (n = 33 matched patients with 33 hips)	Mean F/U: 3.6 years F/U range: 2–5.7 years Complete F/U: NR	Yes - MA. Mont, M.D., is a consultant for Stryker Orthopedics and Wright Medical Technology. None of the other authors have a financial or proprietary interest in the subject matter or materials discussed

Author (Year)	Study Type Study Period	N	Age (Years) (Range), Sex	Preop diagnosis (N, %)	Intervention	Mean F/U Time	Conflict of Interest
Costa (2011)	Retrospective cohort study 2007-NR	N = 192 patients with 210 hips	Mean age: 53 (14-89) 66.7% male	NR	HR [Cormet 2000] (n = 67 patients with 73 hips); THA [Stryker system with Accolade stem and Trident cup] (n = 125 patients with 137 hips)	Mean F/U: 30 months F/U range: 24-37 months Complete F/U: NR	M.A. Mont, M.D. is a paid consultant for Stryker Orthopaedics and Wright Medical Technologies, receives royalties from Stryker Orthopaedics and has received institutional or research support from: Stryker Orthopaedics, Wright Medical Technologies, Biomet, BrainLab, DePuy, Finsbury, Smith and Nephew, and Salient Surgical Technologies.
Killampalli (2009)	Retrospective cohort study NR	N = 116 patients (number of hips NR)	Mean age: 58.2 (34-68) % male NR	Osteoarthritis (n = 99, 85.3%), rheumatoid arthritis (n = 3, 2.6%), avascular necrosis (n = 9, 7.8%), dysplastic hip (n = 5, 4.3%)	HR [NR] (n = 58 patients with hips NR) THA [uncemented, NR] (n = 58 patients with hips NR)	Mean F/U: 5 years F/U range: 4-7 years Complete F/U: 100%	No conflicts of interest

*Activity (Figure 9,10)**UCLA*

Postoperative UCLA activity scores were higher in the total HR group in all four studies that reported this outcome,<sup>54,82,95,137</sup> this difference reached statistical significance in two of the four studies,<sup>54,137</sup> one of which had mid-term follow-up with a mean of 5.9 years.<sup>54</sup> Postoperative UCLA activity scores ranged from 3.6 to 6.8 in the THA group, and from 6.1 to 8.4 in the total HR group. Although the preoperative UCLA score was significantly higher in the total HR group (4.2) compared to the THA group (3.6) in one study<sup>54</sup> ( $P = .02$ ), there was a 4-point increase between pre- and post-operative scores in the total HR group compared to a more modest 2.3-point increase in the THA group in this study. One study reported a *decrease* in postoperative UCLA activity scores compared to their preoperative counterparts, but this is because the authors reported activity scores before patients were limited by pain and became an indication for arthroplasty.<sup>137</sup> The UCLA score is a patient-reported measure of activity.

*Mont's scoring system*

Using a scoring system devised by Mont (2009), two studies reported significantly higher activity scores for the total HR group compared to the THA group<sup>117,191</sup> ( $P = .0004$ ,  $P < .001$ ). Postoperative scores were reported at a mean of 39 and 43.5 months for each of the two studies, and ranged from 5.3 to 7.0 in the THA group and from 10.0 to 11.5 in the total HR group. Although preoperative activity scores were significantly higher in the total HR group in one study (3 versus 2 in the THA group, ( $P = .01$ )), there was a pre- to postoperative 8.5-point increase in activity score in the total HR group compared to a 5-point increase in the THA group.<sup>117</sup> This activity scoring system is patient-reported, and takes into account the duration, frequency, and level of competitiveness of each activity the patient regularly participates in. From the description of the scoring system, there appears to be no maximum possible score.

Figure 10. UCLA Activity Scores from controlled observational studies.

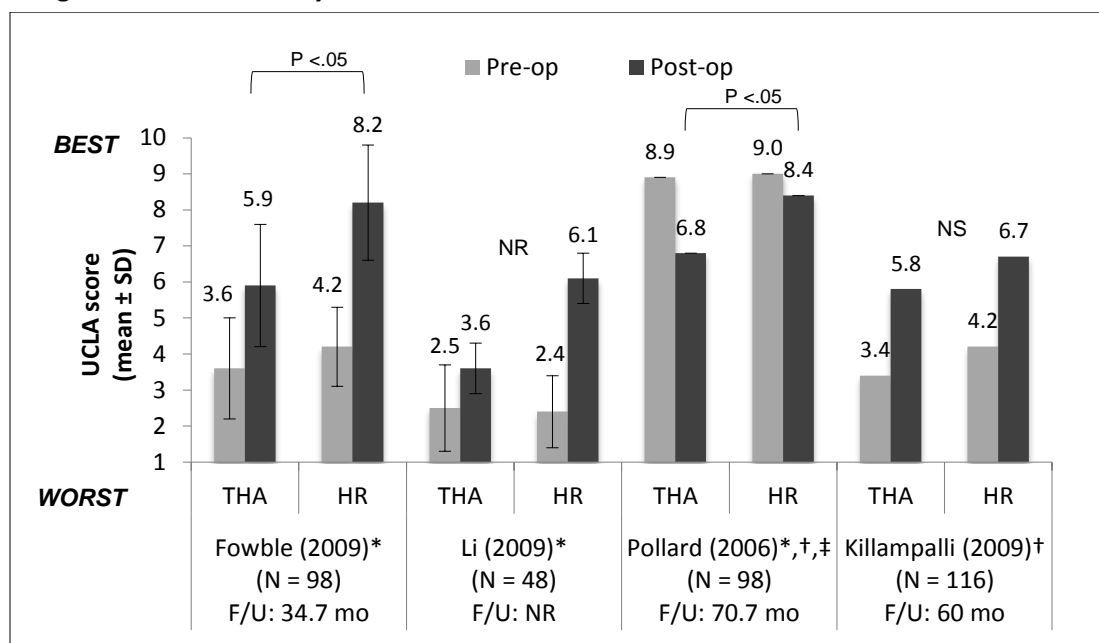
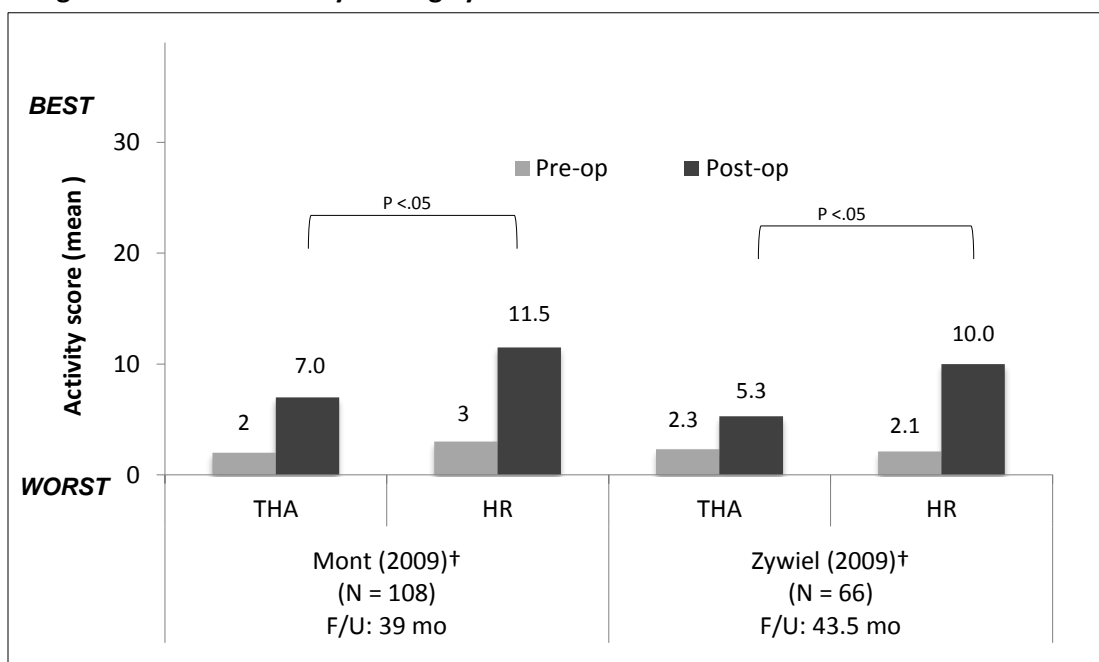


Figure 11 Mont's Activity Scoring System from controlled observational studies



HR: total hip resurfacing.

NR: P-value not reported.

NS: not statistically significant ( $P > .05$ ).

THA: total hip arthroplasty.

\*Author excluded patient(s) who underwent revisions from all clinical outcomes:

Fowble: one hip in the total HR group underwent revision (due to avascular necrosis).

Li (2009): one hip in the total HR group underwent revision (due to femoral neck fracture).



Pollard: three hips in the total HR group underwent early revision (due to avascular necrosis). Note that an additional five revisions were NOT excluded (one in the total HR and four planned revisions in the THA group).

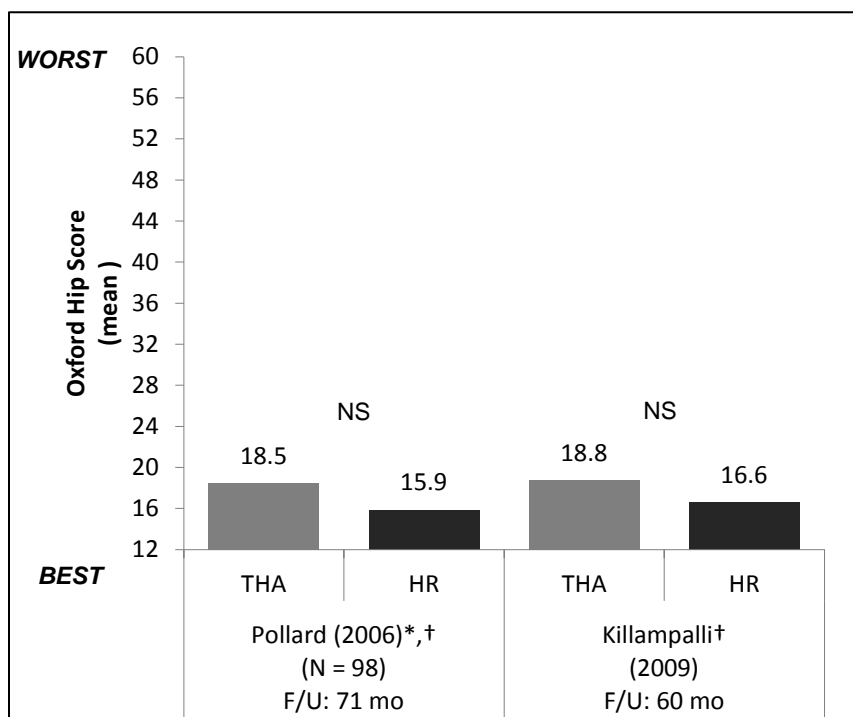
†Standard deviation not reported.

‡ Preoperative scores were reported *before* patients were limited by pain; UCLA score was modified for the British population.

#### *Oxford score (Figure 11)*

No significant differences were found in postoperative Oxford scores as reported by Pollard et al (THA: 18.5, total HR: 15.9).<sup>137</sup> and by Killampalli et al (THA: 18.8, total HR: 16.6).<sup>82</sup> Mid-term follow-up was available for this study, with a mean follow-up of 70.7 months (5.9 years). However, Pollard excluded three hips in the total HR group yet included a total of five other hips that underwent revision (one in the total HR group and four planned revisions in the THA group), which makes the results somewhat difficult to interpret. Preoperative scores were not reported in either study. The Oxford score is a patient-reported outcome measure that includes pain and function components.

**Figure 2. Oxford Hip Scores from controlled observational studies.**



HR: total hip resurfacing.

NS: not statistically significant ( $P > .05$ ).

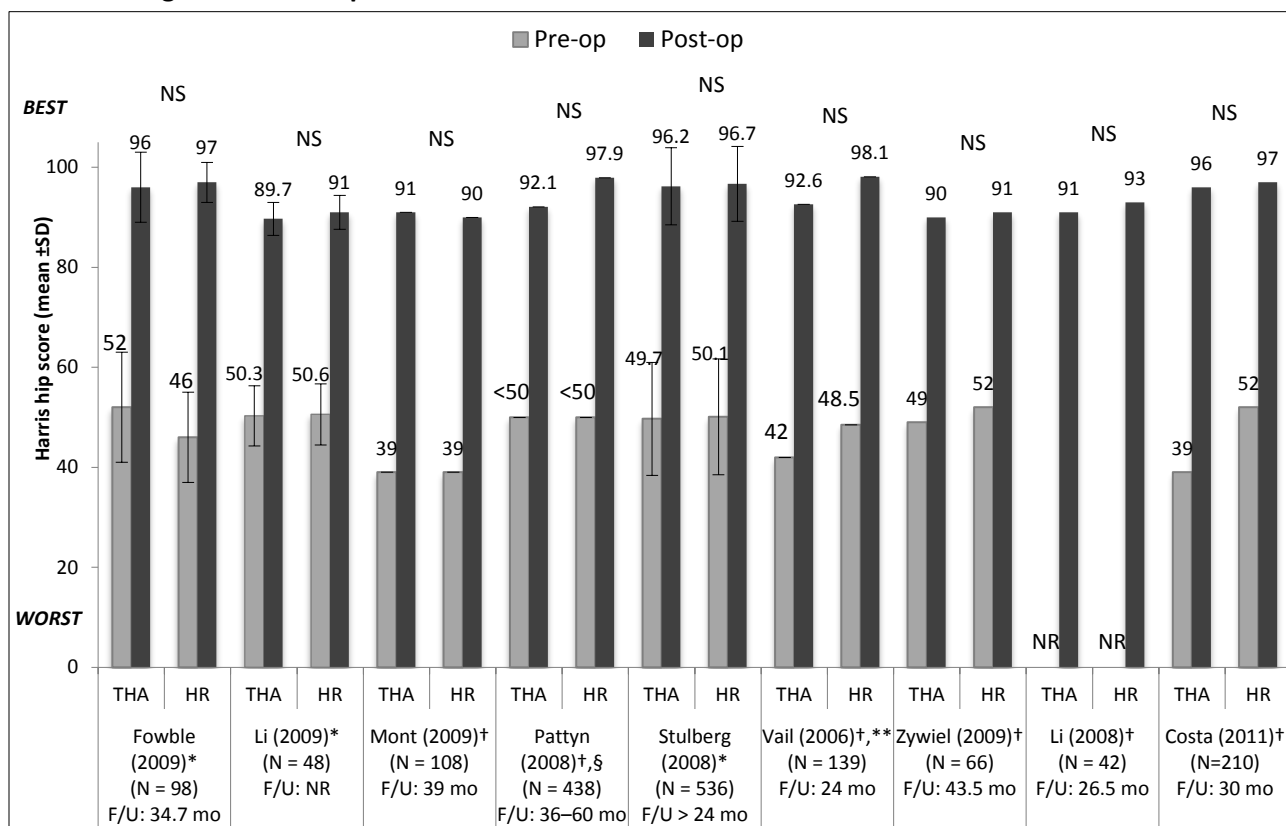
THA: total hip arthroplasty.

\*Author excluded patient(s) who underwent revisions from all clinical outcomes: Pollard: three hips in the total HR group underwent early revision (due to avascular necrosis). Note that an additional five revisions were NOT excluded (one in the total HR and four planned revisions in the THA group).

†Standard deviation not reported.

*Harris hip scores (HHS) (Figure 12)*

No significant differences were identified in postoperative HHS as reported by one prospective<sup>54</sup> and eight retrospective cohort studies.<sup>31,94,95,117,134,156,169,191</sup> Only short-term follow-up was available, as scores were obtained between a mean of 24 to 43.5 months in most studies. The mean postoperative HHS ranged from 90 to 97 in the THA group and from 90 to 98 in the total HR group. There were no statistical differences in the postoperative HHS. Preoperative HHS were significantly higher in the THA group in one study by Fowble<sup>54</sup>; another study had significant differences in the preoperative HHS, however this difference was controlled for using multivariate statistical analysis.<sup>169</sup> Three studies excluded some or all patients who underwent revision surgery from this clinical outcome: Fowble excluded one hip in the total HR group, Li (2009) excluded one hip in the total HR group<sup>95</sup>, and Stulberg<sup>156</sup> excluded 16 hips in the total HR group and three hips in the THA group but included an additional 10 hips that underwent revision (eight in the total HR group and two in the THA group). Although all these hips are accounted for in the safety section, exclusion of patients that underwent revision surgery could bias results. The HHS is a clinician-reported outcome measure that accounts for pain, function, deformity, and range of motion.

**Figure 3 Harris Hip Scores from controlled observational studies.**

HR: total hip resurfacing.

NS: not statistically significant ( $P > .05$ ).

THA: total hip arthroplasty.

\*Author excluded patient(s) who underwent revisions from all clinical outcomes:

Fowble: one hip in the total HR group underwent revision (due to avascular necrosis).

Li (2009): one hip in the total HR group underwent revision (due to femoral neck fracture).

Stulberg: 16 hips in the total HR group and 3 hips in the THA group underwent early revision (< 24 months) and were excluded from clinical outcomes.

†Standard deviation not reported.

§All patients had a preoperative HHS of less than 50, but the mean preoperative HHS was not reported.

\*\* Statistical significance for the postoperative scores was calculated *after* adjusting for age, gender, and preoperative values (the difference in the preoperative scores for THA versus total HR was statistically significant; there were also substantial differences in patient age and gender between the two groups (see patient demographics)).

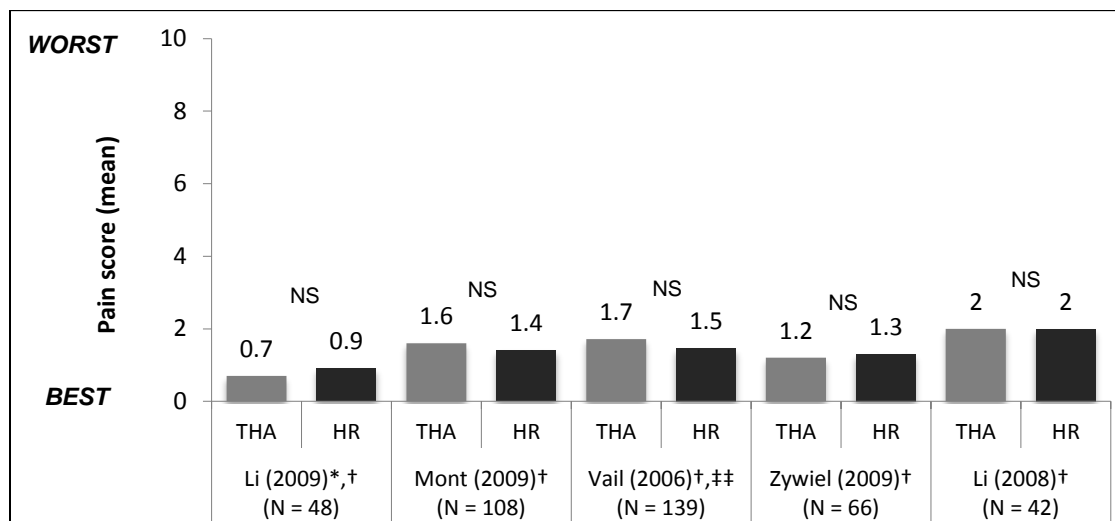
‡‡ Authors reported the 45-point HHS pain score, which ranges from 0–44 (higher score indicates less pain). This score was normalized to an 11-point 0-10 scale with 10 indicating the worst pain: new pain score = 11 - (HHS pain score/4.5).

### *Pain (Figure 13)*

There appears to be no significant differences in the postoperative level of pain between total HR and THA treatment groups as reported by five retrospective cohort studies.<sup>94,95,117,169,191</sup>

Postoperative pain scores ranged from 0.7 to less than 2 in the THA group, and from 0.9 to less than 2 in the total HR group, and were measured during short-term follow-up only (maximum mean of 43.5 months). All but one study reported pain scores from the VAS (visual analogue scale); Vail et al. reported Harris hip pain component scores, which were normalized here.<sup>169</sup>

There were no significant differences in preoperative pain scores between groups as reported by two studies.<sup>95,169</sup> VAS pain scores were patient-reported, with 0 indicating no pain and 10 indicating worst pain imaginable.

**Figure 14. Pain Scores from controlled observational studies.**

HR: total hip resurfacing.

NS: not statistically significant ( $P > .05$ ).

THA: total hip arthroplasty.

\*Author excluded patient(s) who underwent revisions from all clinical outcomes:

Li (2009): one hip in the total HR group underwent revision (due to femoral neck fracture).

†Standard deviation not reported.

‡ P-value reflects postoperative scores adjusted for age, gender, and preoperative values using multiple regression analysis because there were statistically significant differences in preoperative values and demographics.

‡‡ Vail (2006): Authors reported the 45-point HHS pain score, which ranges from 0–44 (higher score indicates less pain). This score was normalized to an 11-point 0–10 scale with 10 indicating the worst pain: new pain score =  $11 - (\text{HHS pain score}/4.5)$ .

#### **4.2. Key Question 2: What is the evidence about the safety profile for hip resurfacing compared with THA?**

We present safety information in four sections: revisions, complications, surgical learning curve and metal ion safety. For revisions and complications, we stratified by follow-up period: short-term = 1 to 5 years, mid-term = 6 to 10 years, and long-term = >10 years. Short- and mid-term data are presented from available comparative studies and from the annual reports of three international total joint registries: the Australian National Joint Replacement Registry (ANJRR) (2012 report), the Swedish Hip Arthroplasty Register (2011 report), and the National Joint Registry for England and Wales (2012 report). Mid-term data are presented from two cohort studies and the same three international registries. One registry reported 11-year revision rates in a small number of patients with that length of follow-up.

#### **4.2.1. Revision**

##### ***Short-term follow-up***

Most of the evidence from national registries and comparative studies suggest that short-term follow-up revision rates are higher for total HR than THA.

##### ***Registry Studies***

Three national registry studies are consistent in reporting significantly higher revision rates in those receiving total HR compared with THA after three and five year of follow-up (Table 13).

##### **The Australian National Joint Replacement Registry (ANJRR), Australia<sup>122</sup>**

The cumulative 3- and 5-year revision risks are 2.8% and 3.9% for conventional THA and 3.4% and 5.2% for total HR. The two most frequent reasons for revision in the short-term include fracture and loosening/lysis. The incidence of revision for fracture increases rapidly in the first year (approximately 1.2% of patients), then increases at a slower rate. Loosening/lysis demonstrates a linear increase and exceeds fracture to become the most common reason for revision at just over four years.

##### **Swedish Hip Arthroplasty Register<sup>157</sup>**

The cumulative 3- and 5-year revision risks are 2.6% and 3.1% for uncemented THA and 3.4% and 5.7% for total HR. The adjusted relative risk comparing HR with cemented and uncemented metal on polyethylene THA is 1.9; 95% CI 1.5, 2.4 (adjusted for age, gender and diagnosis).

Two main causes of early revision after resurfacing prostheses include increased occurrences of fracture of the femoral neck, partly due to osteonecrosis, and the presence of pseudotumor around the hip joint.

##### **National Joint Registry for England and Wales<sup>122</sup>**

The NJR overall 3- and 5-year revision risk varied according to type of prosthesis. The risks were lowest in patients who received cemented ceramic on polyethylene prostheses (0.85% and 1.3%) and highest after hip resurfacing (2.9% and 4.6%). The most frequent reason for revision per 1000 person-years include pain (3.82), aseptic loosening (2.62) and periprosthetic fracture (1.61)

**Table 13. Short term revision risks for three international total joint registries.**

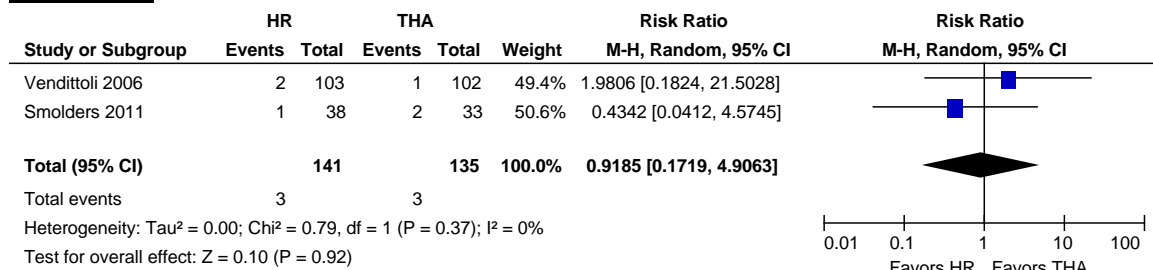
Total Hip Class`	3 years	5 years
<b>Australia NJRR</b>		
THA (conventional)	2.8% (2.7, 2.9)	3.9% (3.8, 4.0)
Hip Resurfacing	3.4% (3.1, 3.7)	5.2% (4.9, 5.6)
<b>Sweden Registry</b>		
THA (uncemented)	2.6% (2.3, 2.9)	3.1% (2.8, 4.0)
Hip Resurfacing	3.4 % (2.5, 4.4)	5.7% (4.4, 6.7)
<b>England NJR</b>		
THA (cemented CoP)	0.85% (0.68, 1.04)	1.3% (1.04-1.6)
(cemented MoP)	0.97% (0.92-1.03)	1.4% (1.4-1.5)
(uncemented CoP)	1.5% (1.3, 1.7)	2.1% (1.85, 2.35)
(uncemented MoP)	1.9% (1.8, 2.1)	2.5% (2.3, 2.7)
Hip Resurfacing	2.9% (2.7, 3.1)	4.6% (4.3, 4.9)

*Comparative Studies*

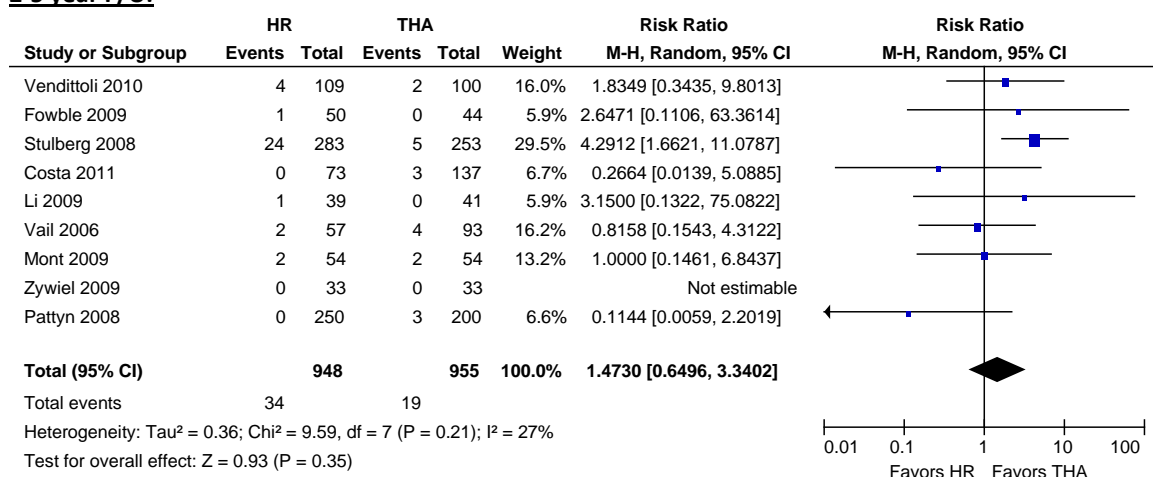
Revision risks were similar in two RCTs with 1-2 year follow-up; pooled risk estimates: 2.2% for THA compared with 2.1% for HR (RR 0.92; 95% CI 0.17, 4.91).<sup>152,175</sup> The risk of revision pooling across eight cohort studies with 2 to 5 year follow-up was 2.0% in the THA group and 3.6% in the HR group (RR 1.47; 95% CI 0.65, 3.34), Figure 14.

**Figure 4. Risk of revision 1-2 and 2-5 years following total hip arthroplasty (THA) or hip resurfacing (HR).**

**1-2 year F/U:**



**2-5 year F/U:**



Common causes for short-term revision in the THA group include deep infection (n = 6, 2 studies)<sup>156,169</sup>, periprosthetic fracture (n = 5) (4 studies)<sup>31,134,156,169</sup>, and dislocation (n = 5) (4 studies)<sup>134,156,169,175</sup>, Table 14. Common causes for short-term revision in the HR group include femoral component migration or loosening (n = 13) (2 studies)<sup>156,175</sup> and femoral neck fracture (n = 10) (4 studies).<sup>156,95,117,169</sup>

**Table 14 Short-term causes for revision by number of studies and number of patients.**

	THA		HR	
Cause for revision	No. studies	Total No. patients	No. studies	No. patients
Femoral component migration/loosening	2 <sup>156,169</sup>	2	2 <sup>156,175</sup>	13
Femoral head collapse			1 <sup>175</sup>	4
Femoral component failure			1 <sup>54</sup>	1
Femoral neck fracture			4 <sup>95,117,156,169</sup>	10
Acetabular component migration/loosening	3 <sup>31,117,175</sup>	4	1 <sup>156</sup>	4
Periprosthetic Fracture	4 <sup>31,134,156,169</sup>	5		
Heterotopic Ossification			1 <sup>175</sup>	1
Avascular Necrosis			1 <sup>54</sup>	1
Dislocation	4 <sup>134,156,169,175</sup>	5	1 <sup>156</sup>	1
Deep infection	2 <sup>156,175</sup>	6	1 <sup>169</sup>	1
Superficial infection	2 <sup>117,134</sup>	2		
Hip pain	1 <sup>156</sup>	1	1 <sup>175</sup>	2
Leg length discrepancy	1 <sup>175</sup>	1		

**Mid-term follow-up***Registry Studies*

All three registries present 7- to 10-year follow-up which continues to show higher revision risks for HR compared with THA, Table 15.

**The National Joint Replacement Registry (NJRR), Australia<sup>122</sup>**

The Australian National Joint Replacement Registry reports results on 7963 HR patients with 5 year follow-up and 654 with 10 year follow-up. A comparison of time to revision revealed a significantly higher revision risk for total HR compared with conventional THA after 7 years, adjusted hazard ratio = 1.42 (1.24, 1.63),  $P < .001$ .<sup>122</sup> The cumulative 10-year revision risk for THA is 6.7% and for total HR, 9.5%. The three most frequent reasons for revision include loosening/lysis (33.6%), fracture (25.7%), and metal sensitivity (16.6%).

**Swedish Registry<sup>157</sup>**

The Swedish Registry reports 7-year data. The cumulative 7-year risk for revision is 3.8% for THA and 6.5% for HR. The adjusted relative risk comparing HR with cemented and uncemented metal on polyethylene THA is 1.9; 95% CI 1.5, 2.4 (adjusted for age, gender and diagnosis).

**National Joint Registry, UK<sup>122</sup>**

The NJR overall 7- and 8-year revision risk varied according to type of prosthesis. The risks were lowest in patients who received cemented ceramic on polyethylene prostheses (1.7% and 2.0%) and highest after hip resurfacing (6.4% and 7.4%). In general, there was a 2 to 3 fold increase in risk comparing HR to any type of THA prosthesis. The most frequent reason for revision per 1000 person-years include pain (3.82), aseptic loosening (2.62) and periprosthetic fracture (1.61)



**Table 2. Mid-term revision risks for three international total joint registries**

Total Hip Class <sup>c</sup>	7 years	8 years	10 years
<b>Australia Registry</b>			
THA (conventional)		-----	6.7 (6.5, 6.9)
Hip Resurfacing		-----	9.5 (8.7, 10.3)
<b>Swedish Registry</b>			
THA (uncemented)	3.8% (3.4, 4.3)	-----	-----
Hip Resurfacing	6.5% (5.0, 7.9)	-----	
<b>England NJR</b>			
THA (cemented CoP)	1.7% (1.4, 2.1)	2.0% (1.5, 2.7)	-----
(cemented MoP)	1.9% (1.8-2.0)	2.2% (2.1-2.4)	
(uncemented CoP)	2.5% (2.2, 2.8)	2.5% (2.3, 2.8)	
(uncemented MoP)	3.2% (2.9, 3.5)	3.6% (3.2, 4.1)	
Hip Resurfacing	6.4% (5.9, 6.8)	7.4% (6.8, 8.0)	-----

*Cohort studies*

Mid-term revision risks (F/U: 5 – 10 years) were reported in two retrospective cohorts<sup>10,82,137</sup> with mean follow-up times ranging from 5.9 to 10 years. Overall, revision risks ranged from 1.7-18.4% of hips in the THA group and 0-15.4% in the HR group, Table 16. All of the studies reported a higher revision risk for THA (risk difference ranged from 0.3-3%). Two publications with different follow-up times (5.9 and 10 years) report on the same population.<sup>10,137</sup> The absolute risk difference increased from 0.3% to 3% with a longer follow-up time.

The most common causes for revision at mid-term follow-up in the THA group include osteolysis (n = 11) and dislocation (n = 2) (all 1 study each), Table 17. The most common causes for revision at mid-term follow-up in the HR group include avascular necrosis (n = 6), femoral component failure (n = 4), and femoral neck fracture (n = 3).

**Table 36. Mid-term revision risks (%) from comparative studies**

Author	Study design	Prosthesis FDA status	Mean F/U yrs (range)	n/N (% revised)	
				THA	HR
Pollard (2006) <sup>137</sup>	Retrospective cohort	Approved	5.9 (3.5-10)	4/54 <sup>†</sup> (7.4%)	4/56 <sup>†</sup> (7.1%)
Baker 2011 <sup>10*</sup>			10 (7.5-14.5)	9/49 <sup>†</sup> (18.4%)	8/52 <sup>†</sup> (15.4%)
Killampalli (2009) <sup>82</sup>	Retrospective cohort	NR	5 (4-7)	1/58 (1.7%)	0/58 (0%)

FDA: Food and Drug Administration; F/U: Follow-up; THA: Total hip arthroplasty; HR: Hip resurfacing;

\*Pollard, 2006 and Baker report on the same population with different follow-up times.

<sup>†</sup>Denominator includes revisions and deaths before 1 year, but not those lost to follow-up.

Includes revisions planned (all revisions in THA group planned)

**Table 17. Mid-term causes for revision by number of studies and number of patients.**

Cause for revision	THA		HR	
	No. studies	No. patients	No. studies	No. patients
Femoral component failure	---	---	1 <sup>137</sup>	4
Femoral neck fracture	---	---	1 <sup>137</sup>	3
Dislocation	1 <sup>10,137</sup>	2	1 <sup>82</sup>	1
Avascular Necrosis	---	---	1 <sup>10,137</sup>	6
Osteolysis	1 <sup>10,137</sup>	11	---	---

**Long-term follow-up**

One registry, the NJRR from Australia, reported on 11 year follow-up. The cumulative risk of revision for THA was 7.4% (95% CI 7.1, 7.7) and for HR, 9.8% (95% CI 8.9, 10.8). No other comparative study evaluating long-term follow-up was found.

**4.2.1. Complications**

Femoral component loosening, femoral neck fracture, and heterotopic ossification occur more frequently in patients receiving HR versus THA, Table 18. Femoral component loosening is more than eight times more likely to occur in HR hips than THA hips, RR 8.4 (95% CI 2.0, 36.2),  $p < .001$ . Heterotopic ossification is nearly two times more likely in HR hips, RR 1.8 (95% CI 1.2, 2.5),  $p = .002$ . One study limited results to only symptomatic heterotopic ossification.<sup>173</sup> This study reported a slightly higher incidence of symptomatic heterotopic ossification in HR hips than THA (1.8%, 0%). Dislocation and deep infections occurred less frequently in HR than THA hips, RR 0.17 (95% CI 0.06, 0.49), RR .21 (95% CI 0.05, 0.90). There was no difference in frequency of avascular necrosis, sciatic nerve palsy/neuropraxia, or deep vein thrombosis between the two groups.

**Table 48. Complication risks (%) from comparative studies**

Complication	Study design	No. of studies	Risk		RR (95% CI)	P-value
			THA	HR		
Femoral component loosening	RCT	2 <sup>32,93</sup>	0.0% (0/124)	4.5% (6/133)	not calculable	.018
	Cohort	6 <sup>54,94,95,117,155,169</sup>	0.4% (2/511)	2.2% (11/509)	5.5 (1.2, 24.8)	.012
	All studies	8	0.3% (2/635)	2.7% (17/642)	8.4 (2.0, 36.2)	<.001
Acetabular component loosening	RCT	1 <sup>96</sup>	0.0% (0/24)	0.0% (0/24)	not calculable	
	Cohort	6 <sup>55,97,98,120,158,173</sup>	0.6% (4/648)	1.0% (6/582)	1.7 (0.5, 5.9)	.531
	All studies	7	0.6% (4/672)	1.0% (6/606)	1.7 (0.5, 5.9)	.531
Femoral neck fracture	RCT	0				
	Cohort	5 <sup>95,117,134,155,169</sup>	0.0% (0/641)	1.8% (12/683)	not calculable	<.001
	All studies	5	0.0% (0/641)	1.8% (12/683)	not calculable	<.001

Complication	Study design	No. of studies	Risk		RR (95% CI)	P-value
			THA	HR		
Heterotopic ossification	RCT	1 <sup>140</sup>	29.4% (30/102)	42.7% (44/103)	1.5 (1.0, 2.1)	.047
	Cohort	5 <sup>54,94,95,117,169</sup>	4.3% (11/258)	9.3% (21/225)	5.5 (1.2, 24.8)	.012
	All studies	6	11.4% (41/360)	19.8% (65/328)	1.8 (1.2, 2.5)	.002
Avascular necrosis	RCT	1 <sup>152</sup>	0.0% (0/33)	2.6% (1/38)	not calculable	1.00
	Cohort	2 <sup>54,134</sup>	0.0% (0/244)	0.7% (2/300)	not calculable	.500
	All studies	3	0.0% (0/277)	0.9% (3/338)	not calculable	.256
Dislocation	RCT	3 <sup>32,152,173</sup>	4.0% (8/199)	0.5% (1/207)	0.12 (0.02, 0.95)	.018
	Cohort	4 <sup>54,134,155,169</sup>	2.4% (14/590)	0.5% (3/639)	0.20 (0.06, 0.69)	.006
	All studies	7	2.8% (22/789)	0.5% (4/846)	0.17 (0.06, 0.49)	<.001
Deep Infection	RCT	3 <sup>32,152,173</sup>	4.5% (9/199)	0.0% (0/207)	not calculable	.002
	Cohort	2 <sup>155,169</sup>	0.3% (1/346)	0.7% (2/310)	2.2 (0.20, 24.5)	.605
	All studies	5	1.8% (10/545)	0.4% (2/517)	0.21 (0.05, 0.90)	.038
Sciatic nerve palsy or neuropraxia	RCT	1 <sup>173</sup>	2.0% (2/100)	0.9% (1/109)	0.5 (0.04, 5.0)	.608
	Cohort	2 <sup>31,54</sup>	0.0% (0/181)	1.64% (2/122)	not calculable	.161
	All studies	3	0.7% (2/281)	1.3% (3/231)	0.5 (0.31, 10.8)	.662
DVT	RCT	2 <sup>32,173</sup>	1.8% (3/166)	3.0% (5/169)	1.6 (0.4, 6.7)	.723
	Cohort	1 <sup>169</sup>	1.1% (1/93)	0.0% (0/57)	not calculable	1.00
	All studies	3	1.5% (4/259)	2.2% (5/226)	1.4 (0.4, 5.3)	.740

THA: Total hip arthroplasty; HR: Hip resurfacing;

### Learning curve threshold

It has been suggested that there is a steep learning curve associated with hip resurfacing arthroplasty. A number of factors may affect the success of this procedure that are often improved with increased surgeon experience, including patient selection,<sup>108,119</sup> optimal component positioning,<sup>119,125,187</sup> and component size<sup>108,119</sup>. The following studies were identified that address the association between patient outcomes and surgical experience.

Marker et al (2007)<sup>108</sup> performed 550 MoM total HR arthroplasties between 2000 and 2006. Although the overall risk for femoral neck fracture was 2.5% (14 fractures), 12 of these occurred in the first 69 hips treated (86% of fractures; incidence of 17.4%), while only two occurred in the remaining 418 hips (0.4%). Surgeons who treated patients that developed femoral neck fractures had significantly less experience performing total HR surgeries compared to those who treated patients who did not develop fractures (mean of 69 previous total HR procedures in the fracture group versus 279 in the non-fracture group ( $P < .001$ )). In addition, the authors found over the course of the study that they could reduce femoral neck notching by decreasing the thickness of the acetabular shell from 10 to 6 mm. This change took place after patient 78, and allowed for the use of a larger femoral component and improved femoral and acetabular bone conservation. Other changes were also made in surgical technique, including not cementing the femoral

component on femoral neck or cysts and limiting the femoral component cement mantle to 2 mm. The authors also placed additional restrictions in total HR patient selection, and began to exclude patients who would need more than minimal notching of the femoral neck.

In a subsequent study of what appears to be a subset of the patients from the 2007 study, Marker et al (2010)<sup>109</sup> evaluated 361 hip resurfacing arthroplasties that had a minimum of 28 month follow-up. The objectives were to determine if implant positioning changed with surgeon experience, and if the positioning and component size were associated with implant longevity. They found no significant difference in the antero-posterior and lateral stem shaft angles over time. However, they noted a small but statistically significant difference in the cup inclination angles.

Mont et al (2007)<sup>119</sup> compared the outcomes of the first 292 patients treated with total HR (Conserve Plus) to the subsequent 724 patients. The authors evaluated their techniques and patient outcomes after treating the first group of patients and made a number of changes to their surgical indications and techniques in the 724 subsequent total HR patients. Three types of risk factors for failure were identified, which included preoperative (femoral head cysts, abnormalities in the head-neck junction, inadequate bone density), operative (not covering reamed femoral bone, using smaller femoral component to conserve acetabular bone, malpositioning of the acetabular component, and leaving the femoral component proud), and postoperative risk factors (patient does not heed postoperative restrictions, traumatic events). The improved patient selection and operative technique led to a decrease in the rate of femoral neck fractures from 7.2% to 0.8% ( $P = .0001$ ) and in the revision rate from 13.4% to 2% ( $P < .001$ ).

Nunley et al.<sup>126</sup> (2009) evaluated the first 100 hip resurfacing procedures performed by each of five surgeons. None of the surgeons had prior training in this technique yet all performed a high volume of other joint reconstruction surgeries (mean of 220 hip arthroplasties per year) and had many years in clinical practice (mean of 21.4 years). The rate of major complications (femoral neck fracture, nerve injury, dislocation, infection, and acetabular bone in-growth) was stratified by the first 25 cases per surgeon, the second set of 25 cases, etc. The rate of major complications for all surgeons was significantly higher in the first 25 cases (5.6%) compared to the second 25 cases (1.6%) ( $P < .002$ ); the third and fourth subsequent sets of 25 cases each had a major complication rate of 1.6%.

O'Neill et al (2009)<sup>127</sup> evaluated the first 50 cases performed by each of five surgeons with no prior training in hip resurfacing but who performed at least 100 THA per year, and found a postoperative revision rate of 3.2%. The authors suggested that this relatively low revision rate may be due to the surgeons' high-volume practices.

Sielbel et al (2006)<sup>149</sup> noted a decrease in the revision rate with increased surgical experience, from 5% in the first 100 cases to 2% in the next 100 to 1% in the last 100 resurfacing procedures. However, this trend was not statistically significant ( $P = .308$ ). Although longer follow-up time was available for the first set of patients, the mean follow-up in this study was quite short at 202 days.

Witjes et al (2009)<sup>187</sup> evaluated the learning curve for optimal component positioning in the first 40 cases performed by a single surgeon. Implant positioning was determined radiographically and compared against a set of predetermined "optimal" measurements for cup abduction angle, stem

shaft angle, and cup head angle. Although the number of cases was too small to achieve statistical significance, a trend towards more optimal component positioning was found.

#### **4.2.2. Metal Ion Safety**

##### *Background and significance*

Patients with metal-on-metal (MoM) joint replacements are likely to experience elevated blood metal levels throughout the life of the prosthesis. Metal release is a potential issue not just for MoM total HR, but for MoM THA as well. Concerns have been raised regarding the safety of and risks associated with prolonged exposure to metal ions, and whether such exposure may increase the risk of cancers or metabolic disorders.<sup>81</sup>

The primary metals used in MoM prostheses are cobalt (Co) and chromium (Cr). Although these metals are essential trace elements that are important for many biological processes in the human body (and are found in food and water supplies), they are considered toxic and hazardous by inhalation. Cobalt and chromium exposure is regulated by the Occupational Safety and Health Administration (OSHA). According to OSHA's occupational safety and health standards limits for air contaminants (expressed as milligrams of substance per cubic meter of air [mg/m]), cobalt metal, dust, and fume (as Co) has a limit of 0.1 mg/m and chromium metal and insoluble salts (as Cr) has a limit of 1 mg/m.<sup>168</sup> To date, no OSHA regulations exist regarding metal levels following orthopaedics procedures.

MoM articulations generate a much larger number of particles every year than do conventional metal-on-polyethylene components. However, the particles produced through MoM wear are smaller (generally < 50 nm)<sup>47</sup> than those generated by polyethylene wear (generally > 100 nm)<sup>52</sup>, which results in a lower actual volumetric wear. The processes by which these particles are taken up by cells in the human body differ depending on their size. While smaller metal particles (< 150 nm) are taken up by cells through endocytotic processes (non-specific receptor-mediated endocytosis and pinocytosis),<sup>148</sup> larger particles (> 150 nm) stimulate phagocytosis in specialized cells called macrophages.<sup>161</sup> The response of macrophages to wear debris is thought to be responsible for implant loosening in patients with metal-on-polyethylene bearings. In contrast, the smaller particles created by MoM bearings have limited ability to activate macrophages.<sup>116,184</sup> Once internalized into a cell, metal particles can induce cytotoxicity,<sup>66</sup> chromosomal abnormalities,<sup>35</sup> and oxidative stress.<sup>154</sup> Metal ions released from orthopaedic implants have also been shown to induce apoptosis and/or necrosis in a range of cells, with Co(II) and V(III) among the most cytotoxic.<sup>66,76</sup> The major theoretical concerns regarding MoM hip resurfacing include hypersensitivity-related failures, allergic reaction, aseptic lymphocytic vasculitis-associated lesions (ALVAL), local tissue toxicity, impaired renal function, chromosomal damage, and possible malignant cellular transformation/cancer.

The variability of methods used to assess metal levels in orthopaedic studies, such as analytical technique, time of collection, units of measurement, and specimen can make reliable comparisons difficult between studies.<sup>81</sup> Historically, metal ion concentrations in total HR and THA patients have been measured using serum plasma levels; other methods include whole blood, red blood cells, and urine specimens. However, whole blood measurement has been shown to be more accurate than serum plasma levels to indirectly measure metal wear and

systemic metal exposure,<sup>9,90,190</sup> as has daily output of metal ions in urine.<sup>39</sup> One study found a significant difference between serum and whole blood cobalt and chromium concentrations such that there was an over-estimation of cobalt and chromium ion concentrations in serum levels compared with whole blood levels.<sup>176</sup>

#### *MoM hip resurfacing compared with conventional THA*

Patients with MoM articulations are likely to experience elevated metal levels throughout the life of the prosthesis. We analyzed the degree to which these levels differ between MoM hip resurfacing and conventional non-metal-on-metal THA.

Five cohort studies were found (2 included in the previous version of this report) that compared median levels of metal ions in patients who received MoM hip resurfacing with those that received metal-on-polyethylene (MoP) or ceramic-on-ceramic (CoC) THA.<sup>5,72,98,135,186</sup> Sample sizes ranged from 22 to 88 patients in the HR groups and from 18 to 58 in the THA groups across four studies; one study did not report the number of patients in each group.<sup>186</sup> Patients undergoing HR tended to be younger and primarily male, as compared with those in the control groups. Follow-up periods ranged from 12 to 35 months across all studies. The type of sample used to test for metal ion levels varied, with three studies using whole blood, one using serum, and one using hair.

Regardless of the type of sample used, all studies reported significantly higher concentrations of the primary metal ions cobalt and chromium in the HR groups at all follow-up periods assessed (3, 6, 12, 24, 35 months), Table 19. Across four studies that used either whole blood or serum samples, median levels of cobalt at latest follow-up ranged from 1.18 to 3.02 µg/L in the HR groups compared with 0.34 to 1.65 µg/L in the conventional THA groups.<sup>5,72,135,186</sup> In the study that used hair samples, the median level of cobalt at 12 months was 47.40 µg/g following HR versus 4.22 µg/g following MoP THA.<sup>98</sup> For chromium, whole blood or serum samples yielded median levels ranging from 0.5 to 2.33 µg/L versus 0.06 to 1.72 µg/L in the HR and THA groups, respectively, while the median level found in patients' hair at 12 months was 23.48 µg/g versus 2.32 µg/g, respectively.

Other metals analyzed included molybdenum (1 study)<sup>5</sup> and nickel and titanium (1 study)<sup>186</sup> with no difference found between groups in the levels of these metal ions in either whole blood or serum.

**Table 19. Median levels of metal ions in patients following metal-on-metal (MoM) hip resurfacing (HR) compared with conventional metal-on-polyethylene (MoP) or ceramic-on-ceramic (CoC) total hip arthroplasty (THA).**

Author	Specimen	Timing	Metal	MoM HR	Conventional THA*	P-value
Antoniou (2008)	Whole blood	6 months	Co	2.3 µg/L	1.65 µg/L	< .001
			Cr	0.5 µg/L	0.05 µg/L	≤ .001
			Mo	1.30 µg/L†	1.65 µg/L†	NS
		12 months	Co	2.4 µg/L	1.65 µg/L†	< .001
			Cr	0.5 µg/L	0.06 µg/L†	< .001
			Mo	1.60 µg/L†	1.60 µg/L†	NS
Hart (2009)‡	Whole blood	35 months	Co	1.71 µg/L	0.34 µg/L	< .001
			Cr	2.33 µg/L	0.51 µg/L	< .001
Pattyn (2011) <sup>§</sup>	Whole blood	3 months	Co	1.03 µg/L	0.55 µg/L	< .05
			Cr	0.87 µg/L	0.50 µg/L	< .05
		6 months	Co	1.31 µg/L	0.49 µg/L	< .05
			Cr	1.02 µg/L	0.50 µg/L	< .05
		12 months	Co	1.31 µg/L	0.49 µg/L	< .05
			Cr	1.05 µg/L	0.50 µg/L	< .05
		24 months	Co	1.18 µg/L	0.49 µg/L	< .05
			Cr	1.12 µg/L	0.49 µg/L	< .05
Win (2012)	Serum	24 months	Co	3.02 ± 1.52 µg/L	1.19 ± 0.32 µg/L	.002
			Cr	2.31 ± 1.12 µg/L	1.72 ± 0.30 µg/L	.04
			Ni	8.76 ± 2.03 µg/L	21.75 ± 26.34 µg/L	.21
			Ti	1.53 ± 1.51 µg/L	0.88 ± 0.31 µg/L	.10
Liu (2011)	Hair	6 months	Co	53.29 ± 11.84 µg/g	3.39 ± 1.69 µg/g	< .01
			Cr	18.30 ± 5.64 µg/g	2.03 ± 0.71 µg/g	< .01
		12 months	Co	47.40 ± 10.04 µg/g	4.22 ± 2.46 µg/g	< .01
			Cr	23.48 ± 9.9 µg/g	2.32 ± 0.93 µg/g	< .01

Co: Cobalt; Cr: Chromium; Mo: Molybdenum; Ni: Nickel; NS: not significant; Ti: Titanium.

\*Antoniou, Win, and Liu used MoP THA; Pattyn used CoC THA; Hart used both MoP and CoC.

†Estimated from figures in article.

‡Results for the MoP and CoC groups were combined under the conventional THA group.

§All metal ion levels were estimated from figures in article. Both the MoM HR and CoC THA groups used 2 different devices and reported the results separately by device type. Within both groups, the levels of ions for each device type were averaged in order to get an overall metal ion level for both HR and THA (i.e. regardless of type of device used).

#### ***Association of metal ion levels with outcome following MoM hip resurfacing***

Histopathological analysis of inflammatory tissue surrounding poorly functioning implants<sup>19,21,131,184</sup> as well as the presentation of patients with unexplained pain requiring revision<sup>42</sup> has led many to hypothesize that adverse soft-tissue reactions are responsible for the majority of MoM hip arthroplasty revisions due to unexplained hip pain. At the current time,

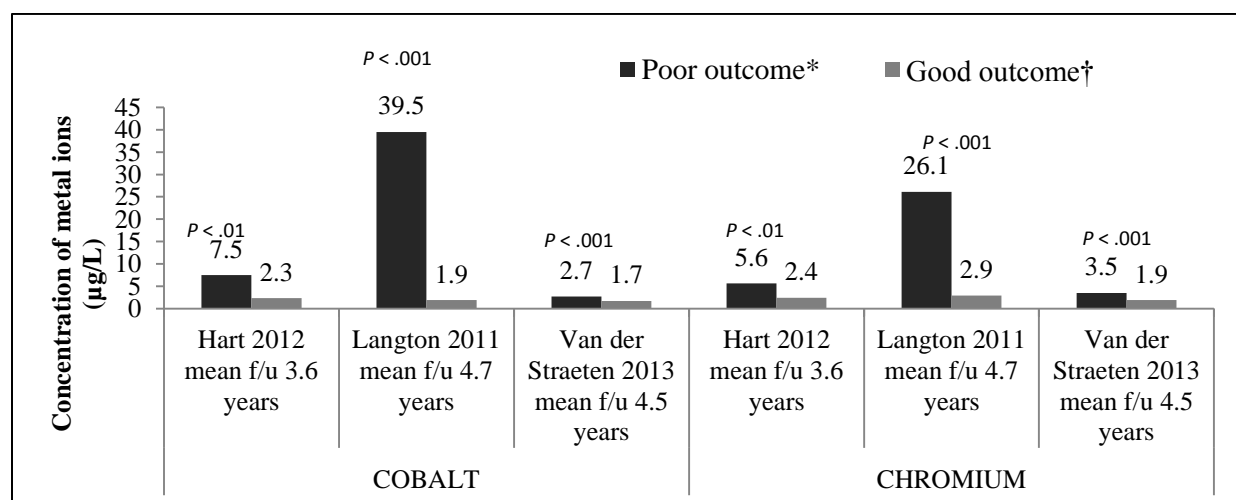


the FDA believes there is insufficient evidence in the U.S. demonstrating a correlation between a metal ion level and the presence of localized lesions, clinical outcomes and/or the need for revision surgery.<sup>164</sup> We identified four studies that investigated whether metal ion levels were associated with clinical outcome following MoM hip resurfacing.

Three studies divided their patients into groups based on whether they had a poor outcome (i.e. revision/poorly functioning hip) or a good outcome (i.e. asymptomatic/well-functioning hip) and compared the levels of cobalt and chromium ions between the two groups.<sup>69,89,170</sup> Across these studies the sample sizes ranged from 55 to 283 in the poor outcome groups and from 42 to 734 in the good outcome groups. Mean follow-up periods ranged from 3.6 to 4.7 years. The type of sample used to test for metal ion levels included serum in two studies and whole blood in one study. All three studies reported significantly higher levels of both cobalt and chromium in patients with a poor outcome compared to those with a good outcome following HR, Figure 15. Median levels of cobalt ranged from 2.7 to 39.5 µg/L in the poor outcome groups versus 1.7 to 2.3 µg/L in the good outcome groups. Median levels of chromium ranged from 3.5 to 26.1 µg/L and from 1.9 to 2.9 µg/L, respectively.

A fourth study stratified 299 patients according to the concentration of cobalt in whole blood samples (< 1 µg/L, 1–2 µg/L, 2–5 µg/L, 5–10 µg/L, > 10 µg/L) and reported the proportion of patients in each group that underwent revision within 9 years of HR.<sup>91</sup> The mean follow-up period was 5.8 years. A dose response was seen such that with each increase in the level of cobalt ions, a subsequently higher proportion of hips underwent revision, Figure 16.

**Figure 56. Median levels of cobalt and chromium in patients who had a good outcome versus a poor outcome following MoM hip resurfacing.**

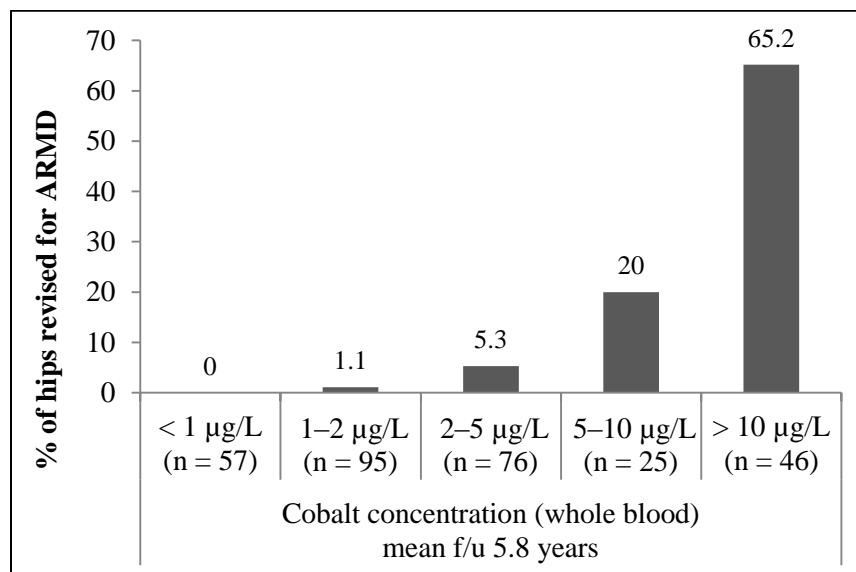


\*Revision/poorly-functioning hip.

†Asymptomatic/well-functioning hip



**Figure 67. Proportion of hips that underwent revision within 9 years following MoM hip resurfacing stratified by the concentration of cobalt in whole blood.**



ARMD: adverse reaction to metal debris.

#### Concerns regarding metal ion debris

Results from studies conducted in patients with MoM bearings have raised the possibility of serious adverse consequences from exposure to metal ion debris, including negative effects on cellular and biological processes, diseases such as cancer and pseudotumors, and teratogenicity. The Food and Drug Administration (FDA) has also raised concerns regarding other systemic and general health complications that may occur in patients who have received a MoM hip implant specifically cardiomyopathy, neurological (i.e sensory) and psychological changes, renal function impairment, and thyroid dysfunction.<sup>162</sup>

#### *DNA and chromosomal damage*

In a study conducted by Davies et al. in THA patients, samples of synovial fluid retrieved at revision arthroplasty and cultured for human fibroblast cells revealed that all six samples from MoM implants and four of six samples from metal-on-polyethylene implants had statistically significant higher levels of DNA damage compared with control levels in human fibroblasts in vitro.<sup>40</sup>

Chromosomal translocation and aneuploidy (an increased number of chromosomes) are genetic changes that occur in the general population as a result of increasing age and environmental factors. We identified two studies that investigated the association between ion levels and chromosomal aberrations in patients with cobalt-chromium alloy THA implants. These studies reported a 2.5-fold increase and a 2- to 4-fold increase in aneuploidy, as well as a 3.5-fold and 1.5-fold increase in chromosomal translocations in peripheral blood lymphocytes that could not be explained by confounding factors.<sup>46,87</sup> A third study reported a significantly elevated number of chromosomal abnormalities (aneuploidy and structure anomalies) in patients with MoM hip implants compared with an age- and sex-matched control group.<sup>50</sup> Furthermore, the Committee

on Mutagenicity in the United Kingdom (UK) has reported that internal exposure to orthopaedic metals is associated with increased genotoxicity.<sup>29</sup> The clinical consequences of such DNA and chromosomal aberrations are unknown.

#### *Hypersensitivity and immunological responses*

Cell-mediated hypersensitivity has been implicated as a cause of tissue damage in the presence of low wear following MoM hip arthroplasty procedures.<sup>20,103,132</sup> This abnormal tissue reaction associated with the release of metal ions, referred to as aseptic lymphocytic-vasculitis-associated lesions (ALVAL), has been shown to be associated with a variety of factors leading to the failure of MoM implants.<sup>86,103,128,184,188</sup> The prevalence of wear debris osteolysis and allergic reactions appears to be < 1% but longer-term, more inclusive data is needed to delineate the true prevalence of these complications.<sup>146</sup>

Changes in the lymphocyte count have also been reported in patients with MoM hip replacements, specifically reduced peripheral blood counts of T (primarily) and B lymphocytes.<sup>68,70</sup> One possible explanation for the low levels of T cells found in circulation and the elevated numbers in tissues<sup>132,184,188</sup> relates to the segregation of T cells into the tissues, as occurs in the autoimmune disorder rheumatoid arthritis. Metal wear debris could signal this process, but as yet the causal factor has not been identified.<sup>65</sup>

#### *Cancer*

The International Agency for Research on Cancer (IARC), has classified soluble cobalt as possibly carcinogenic and metallic chromium and chromium III compounds and implanted orthopaedic alloys as unclassifiable.<sup>111</sup> Currently, there is no consensus regarding safe exposure limits for these metals in hip arthroplasty.<sup>100</sup>

Earlier studies evaluated whether total joint replacement irrespective of the bearing surfaces was associated with an increase in cancer risk. In 2006, Onega et al. summarized seven population-based studies reporting standardized incidence ratios (SIRs) for cancer following large joint arthroplasty. The population consisted of both total hip (MoM and MoP bearings) and total knee arthroplasty and comprised 1,435,356 person-years of follow-up. The overall cancer risk among patients with arthroplasty was found to be similar to that of the general population; however, the results did suggest a late increase in melanoma and prostate cancer among arthroplasty patients.<sup>129</sup> While the authors placed the results in the context of multiple comparisons (i.e. likely due to chance), others are more likely to see a real association which raises the question of whether the increased cancers are related to metal exposure.<sup>114</sup>

We found three studies published since our initial report that assessed cancer risk comparing patients implanted with a MoM hip prosthesis (either HR or THA) versus a THA with other bearing surfaces (e.g. metal-on-polyethylene, ceramic-on-polyethylene, ceramic-on-ceramic).<sup>88,105,151</sup> The mean follow-up periods ranged from 3 to 5 years. In all three studies, MoM implants were not associated with an increased risk of cancer.

Another study looked at the cancer mortality among Finnish patients with MoM compared with MoP total hip prostheses.<sup>178</sup> The MoM THA group comprised 579 patients while the MoP THA group consisted of 1585 patients. Standardized mortality ratios (SMRs) were calculated. Mean

follow-up time was 18 years for MoM and 17 years for MoP patients. The overall SMR was 0.95 for the MoM group and 0.90 for the MoP group as compared to the normal population. During the first 20 years after surgery, the SMR for the MoM group was higher compared with the MoP group (RR 1.36; 95% CI 1.02, 1.79). After 20 years, however, there was no difference in SMRs between groups.

It is important to note that, in order to detect a rise in such adverse events, large numbers of patients would be required to be followed for several decades.<sup>100</sup> The effects of accumulating concentrations over time remain to be determined and continual monitoring of patients with MoM bearings is encouraged until a better understanding of the possible risks associated with metal ions in circulating blood is achieved.

### *Pseudotumors*

Pseudotumors (i.e. soft tissue masses) are a well-recognized complication following both MoM hip resurfacing and THA procedures and most commonly present with pain and discomfort in the region, presence of a mass, skin rash, and nerve palsy. Potential causes of pseudotumors include foreign-body reaction, hypersensitivity, and wear debris.<sup>36</sup> Symptomatic pseudotumors usually require a revision arthroplasty in order to eliminate the pain. Pseudotumors are not exclusively symptomatic, however, and a large number of pseudotumors are “silent”/do not present with any pain. The clinical impact of asymptomatic pseudotumors is as of yet unknown.<sup>145</sup> The prevalence of pseudotumors varies widely across the literature and depends upon the population being assessed and the type of diagnostic modality employed.

Wiley et al. conducted a meta-analysis of 14 studies including a total of 13,898 MoM hips (both resurfacing and THA) and reported a prevalence of pseudotumor or acute lymphocytic vasculitis associated lesions (ALVAL) ranging from 0% to 6.5% with a pooled estimated prevalence of 0.6%.<sup>183</sup> Mean follow-up ranged from 1.7 to 12.3 years across the studies. This review only included studies in symptomatic patients and all but one study included used either radiographs or histology (or both) to diagnosis the pseudotumor/ALVAL. More recent studies that included both symptomatic and asymptomatic patients and employed primarily magnetic resonance imaging (MRI) and/or high-resolution ultrasound to diagnoses the presence of a pseudotumor reported a much higher prevalence in patients with MoM hip implants. Seven studies including a total of 869 symptomatic and asymptomatic hips that had undergone MoM hip resurfacing or THA reported a prevalence of pseudotumor ranging from 2.7% to 69% across mean follow-up periods of 1.3 to 5.1 years<sup>25,71,73,85,171,172,185</sup>, with only one study reporting a prevalence of less than 25%.<sup>85</sup> When stratified by symptom status, the prevalence of pseudotumor in patients with a symptomatic/painful hip was 2.7%, 6.8% and 57% in three studies<sup>71,73,172</sup> and remained high in patients with asymptomatic hips across four studies (4%, 25%, 27.3%, 61%)<sup>71,85,172,185</sup>

There is some evidence to suggest that patients who have a revision from a total HR to a THA as a result of a pseudotumor have poorer outcomes than those who have revision for other reasons. Grammatopolous et al. reported worse Oxford hip scores following revision for pseudotumor than for fracture or for other causes.<sup>62</sup> The clinical outcome of revision for pseudotumor was also significantly worse than the outcome of matched primary total hip replacements. By contrast, the outcome for fracture and other causes was not significantly different from that of matched primary total hip replacements. After revision for pseudotumor there were three cases of recurrent dislocation, three of femoral nerve palsy, one of femoral

artery stenosis and two of component loosening. The authors concluded that outcome of revision for pseudotumor is poor, while outcome of resurfacing revision for other causes is good.

Three studies were found that explored the association of metal ion levels with pseudotumor formation.<sup>85,171,185</sup> Sample sizes ranged from 75 to 256 with mean follow-ups ranging from 2 to 5.1 years. In two studies, which looked at asymptomatic patients following MoM HR and MoM THA<sup>85,185</sup>, the median serum metal ion levels (cobalt and chromium) were greater in patients with pseudotumor formation compared with those without pseudotumor formation; however the difference was only statistically significant in one study. The third study included both symptomatic and asymptomatic patients who had undergone MoM HR and found an association between serum metal ion levels and pseudotumor formation.<sup>171</sup> When the patients were stratified by median serum cobalt and chromium levels, a greater proportion of patients with levels > 7 µg/L versus < 7 µg/L had developed pseudotumors: 77.8% versus 34.0% and 73.3% versus 33.2%, respectively.

#### *Teratogenicity*

Teratogenicity, or the capability of producing fetal malformation, has been raised as a potential concern for women of child-bearing age who receive a MoM hip implant. Cobalt and chromium ions generated from these implants can cross the placental barrier, and data has shown that the placenta plays a modulatory (and possibly protective) role in the rate of metal transfer and that the transfer rate is different with different metals.<sup>17,44,190</sup> Exposure to cobalt and chromium has been shown to induce teratogenicity in animal studies; however, there is insufficient data to confirm this in humans.<sup>65</sup> To date, there has never been a report of birth defects/fetal malformation associated with MoM hip implants.<sup>28,44</sup> Because the potential effects of transplacental transfer of metal ions are currently unknown, young female patients should be educated to avoid problems in the future.<sup>124</sup>

#### *Other systemic/general health complications*

Metal toxicity in patients treated who were treated with a MoM hip implant has been reported throughout the medical literature and can result in severe systemic complications and changes in general health including new or worsening symptoms outside of the hip. Cobalt appears to be the metal most commonly associated with metal toxicity complications, though chromium has been also been elevated in some cases. Cardiomyopathy, a disease that weakens and enlarges the heart muscle, has been associated with toxic levels of cobalt in case reports of patients who had MoM hip replacements.<sup>102,159</sup> Neurological changes (e.g. headaches, tinnitus, vertigo, hearing loss, visual changes/optic nerve atrophy, hand tremor, incoordination, cerebellar signs/ataxia/dysdiadochokinesis, muscle fatigue)<sup>106,107,142,159</sup> as well as psychological changes (e.g. cognitive decline, memory difficulties, poor concentration, depression, anxiety, irritability)<sup>106,159</sup> have also been reported in conjunction with toxic levels of metal ions.

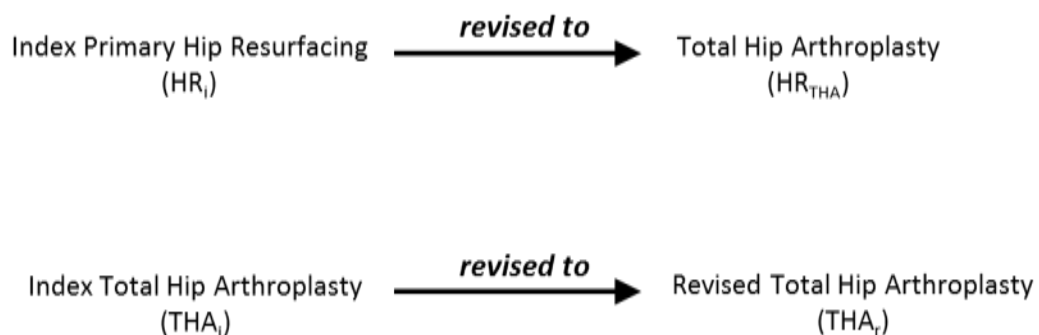
Renal function impairment is another concern in this patient population. One study was found which looked at the 9-year risk of developing renal disease after primary MoM THA in 1709 patients without preexisting renal disease treated in a Department of Veterans Affairs (VA) medical center.<sup>24</sup> The 9-year risk of chronic renal disease and severe/end-stage renal disease was 14% and 6%, respectively, in their population. For chronic renal disease, the risk was not different compared with that of the general population (14.8%).<sup>80</sup> In various other studies

looking at both short and longer-term results, no negative impact on renal function was reported following MoM hip resurfacing or THA.<sup>30,38,64,110,189</sup> In all patients who had symptoms in the above studies, revision of the implant resulted in a significant decrease or resolution of symptoms as well as a subsequent decrease in the level of metal ions, indicating that these adverse reactions are at least partially reversible by removing the MoM prosthesis.

The Federal Drug Administration (FDA) has raised concerns regarding the above complications and urges patients to be aware of signs and symptoms that may indicate a problem. Presently, the FDA does not have enough scientific data to specify the concentration of metal ions in a patient's body or blood necessary to produce adverse systemic effects. In addition, the reaction seems to be specific to individual patients, with different patients having different reactions to the metal wear particles.<sup>163</sup> Furthermore, there is not enough quality evidence to support the routine need for checking metal ion levels in the blood or soft tissue imaging if patients with MoM hip implants have none of the signs or symptoms described above and the orthopaedic surgeon feels the hip is functioning properly.<sup>162</sup> The FDA is recommending that asymptomatic patients with MoM hip implants continue to follow-up with their orthopaedic surgeon every 1 to 2 years to monitor for early signs of change in hip status. Follow-up of symptomatic patients should occur at least every six months.<sup>165</sup>

#### **4.3. Key Question 3: What is the evidence of efficacy, effectiveness and safety of revisions of hip resurfacing compared with revisions of THA?**

We approached this key question by searching for studies that addressed the safety and successfulness of converting a total HR to a THA. We included revisions to a HR when the revision included the femoral component. We followed the framework diagramed below:



We first looked for studies that compared HR hips revised to THA (HR<sub>THA</sub>) with THA hips revised to another THA (THA<sub>r</sub>). One such study by Desloges et al was found.<sup>45</sup> The authors of this study retrospectively compared 23 HR<sub>THA</sub> hips (22 patients) with a matched group of 23 patients undergoing a primary index THA hips (THA<sub>i</sub>), and 12 patients receiving THA revision (THA<sub>r</sub>). Mean patient age was 52.2 years in the HR<sub>THA</sub> group, 53.4 years in the THA<sub>i</sub> group, 53.0 years in the THA<sub>r</sub> group, and 73%, 78%, and 50% were male, respectively. Both components were revised in 15 of the 22 hip resurfacing revisions (HR<sub>THA</sub>), while the other 7 patients had only the femoral component revised. This study found similar outcomes between HR<sub>THA</sub> and THA<sub>r</sub> groups.

for SF-12 physical and mental scores and WOMAC pain, stiffness, function and total scores at final follow-up (24 to 84 months for HR<sub>THA</sub>, 24 to 48 months for and THA<sub>r</sub>).

Because only one study made the desired comparison, the search was expanded to studies that compared HR<sub>THA</sub> to index unrevised total hip arthroplasty hips, THA<sub>i</sub> or index unrevised hip resurfacing hips, HR<sub>i</sub>. We identified two studies that compared HR<sub>THA</sub> to both.<sup>43,53</sup> De Steiger et al compared 397 HR<sub>THA</sub> hips (247 femoral component only) to 141,611 THA<sub>i</sub> hips in the Australian National Joint Registry and found that HR<sub>THA</sub> hips revised only for the femoral component had over twice the risk for re-revision compared with the risk for revision of THA<sub>i</sub> hips (hazard ratio = 2,  $p = 0.001$ )<sup>43</sup> In a smaller study, Eswaramoorthy et al<sup>53</sup> retrospectively reviewed 29 HR<sub>THA</sub> patients and compared them to 236 and 523 THA<sub>i</sub> and HR<sub>i</sub> hips, respectively. Mean patient age was 54.4 years in the HR<sub>THA</sub> group, 54.7 years for THA<sub>i</sub> and 54.2 years for HR<sub>i</sub>. Oxford Hip Scores were similar between the HR<sub>THA</sub> and THA<sub>i</sub> groups at all follow-up times through 10 years. The HR<sub>THA</sub> group had slightly worse scores compared with HR<sub>i</sub> up to four years ( $p = .019$ ), but similar results beyond that point.

Two studies compared HR<sub>THA</sub> to only THA<sub>i</sub><sup>11 62</sup> while another two other studies compared HR<sub>THA</sub> to only HR<sub>i</sub>.<sup>59,181</sup> Ball et al<sup>11</sup> retrospectively evaluated outcomes of 20 HR<sub>THA</sub> patients (21 hips) due to femoral component failure and 58 THA<sub>i</sub> patients (64 hips). Mean patient age was 50.2 years (range, 23–72) in the total HR group, 50.8 years (range, 27–64) in the THA group, and 55% and 65% of patients were male, respectively. Grammatopoulos et al<sup>62</sup> conducted a retrospective analysis of 53 HR<sub>THA</sub> hips and a matched cohort of 103 THA<sub>i</sub> hips comparing the outcomes of those revised for the formation of a pseudotumor with those revised for other reasons. Mean age of both groups was 54 years (range, 20–71) and 36% and 38% of the patients were male in the total HR and THA groups, respectively. Wera et al prospectively compared 8 HR<sub>THA</sub> hips with 50 HR<sub>i</sub> hips.<sup>181</sup> Mean age of the HR<sub>THA</sub> group was 49.6 years and 50.4 years for the HR<sub>i</sub> group while 75% and 66% were male, respectively. Gilbert et al prospectively collected data on 63 HR<sub>THA</sub> hips revised for the femoral component only and 4,529 HR<sub>i</sub> hips with the mean age of each group 54.4 and 54.2 years, respectively.<sup>59</sup>

Of these four studies, only the largest found significant results indicating HR<sub>THA</sub> had worse outcomes than HR<sub>i</sub> ( $p < 0.001$  for Harris Hip Score, Merle d'Aubigine, and patient satisfaction scores).<sup>59</sup> One study noted that the reason for revision influenced outcomes; HR patients revised for pseudotumors had significantly worse outcomes than a matched THA<sub>i</sub> control group, whereas outcomes were similar across groups for patients revised for other reasons).<sup>62</sup>

#### **4.4. Key Question 4: Is there evidence of differential efficacy or safety issues with use of hip resurfacing?**

In our previous report, three exposures were identified as potential treatment modifiers: primary diagnosis, gender and size of the femoral head component. We explored differential efficacy, effectiveness and safety of these three exposures by looking for subgroup analyses. We did not find evidence of subgroup analyses in the RCTs; however, data were available from the Australian NJRR that permitted an evaluation of subgroups with revision as the outcome. We calculated stratum specific revision rates per 1000 observational years and compared HR

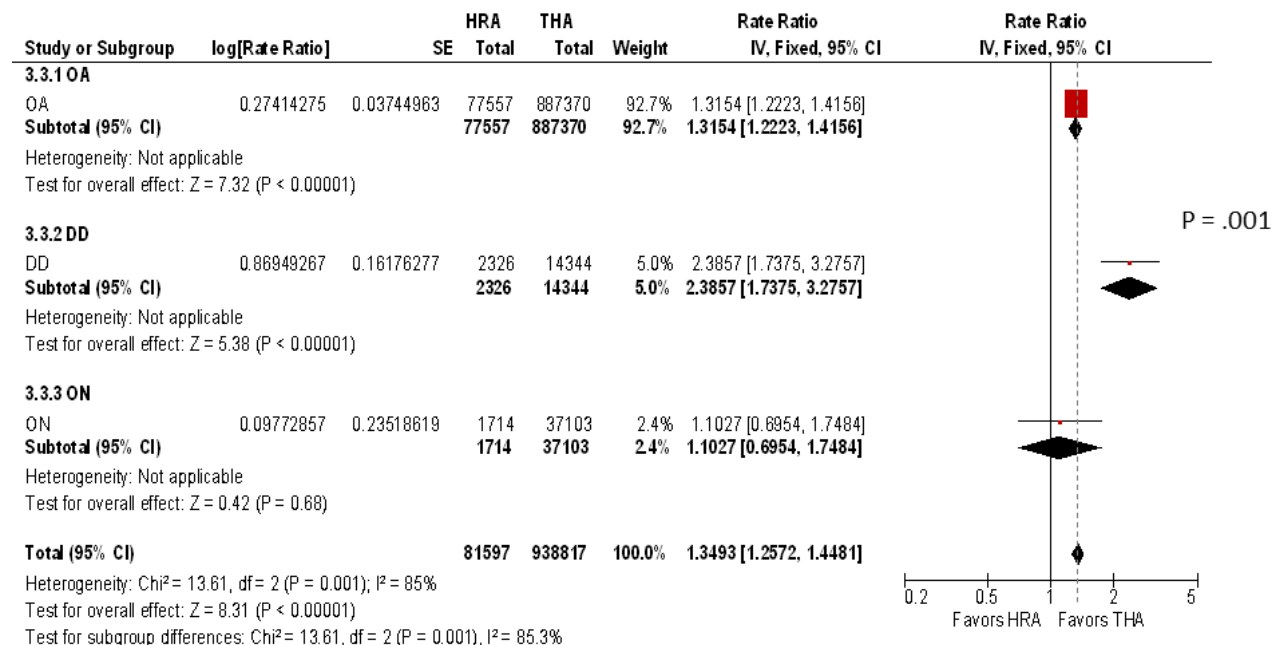


with THA in each stratum. We tested the null hypothesis that the effect size estimates are equivalent across subgroups. Additionally, we displayed the estimates visually with forest plots to demonstrate the differential effect. When the stratum specific rate ratios and their confidence intervals fall on opposite sides of the overall effect, this represents a differential effect.

### Primary Diagnosis

Three diagnoses were compared in the Australian National Joint Replacement Registry: osteoarthritis (OA), development dysplasia (DD) and osteonecrosis (ON). The rates per 1000 observational years for HR are 10.3, 22.8 and 11.1, and for THA 7.8, 9.6 and 10.1, respectively. The overall rate ratio is 1.31 (95% CI 1.22, 1.41) in favor of THA. There is evidence suggesting that the diagnosis of developmental dysplasia modifies the rate of revision in HR and THA; those with developmental dysplasia receiving HR have significantly higher revision rates than those receiving THA or those with other diagnoses receiving HR or THA, Figure 17.

**Figure 78. Stratum specific revision rates per 1,000 observational years and rate ratios comparing hip resurfacing (HR) and total hip arthroplasty (THA) by primary diagnosis.**

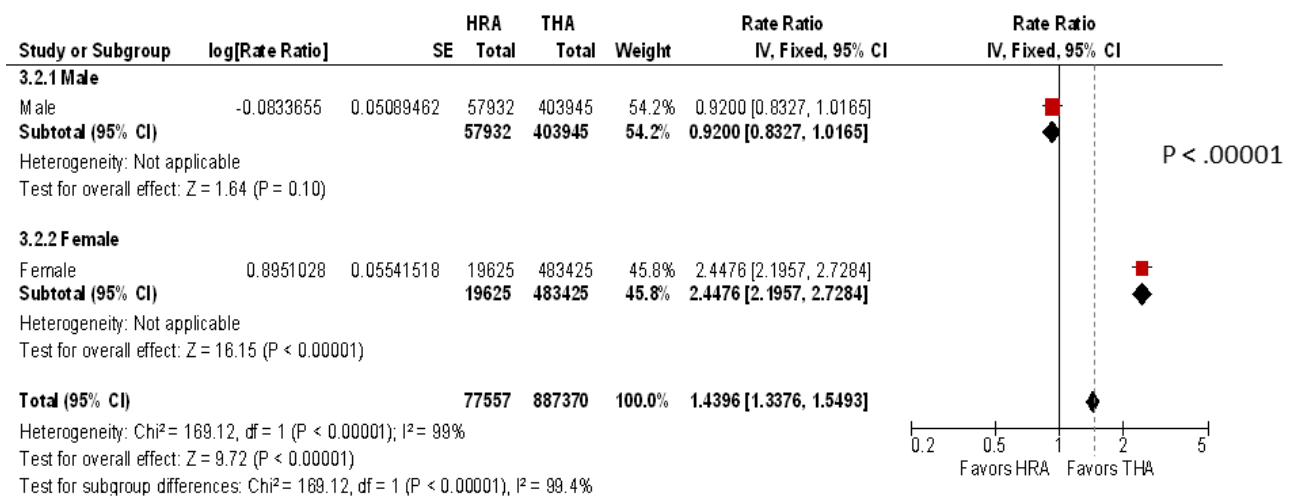


DD, developmental dysplasia; OA, osteoarthritis; ON, osteonecrosis

### Gender

The rates of revision in females receiving THA (7.5 per 1000 observational years) or males receiving HR or THA (7.5 and 8.2 per 1,000 observational years, respectively) are similar. However, in females receiving HR, the rate of revision is more than twice as high, 18.2 per 1,000 observational years, suggesting that gender modifies the rate of revision in HR and THA; females receiving HR have significantly higher revision rates than females receiving THA or males receiving HR or THA (P < .00001), Figure 18.

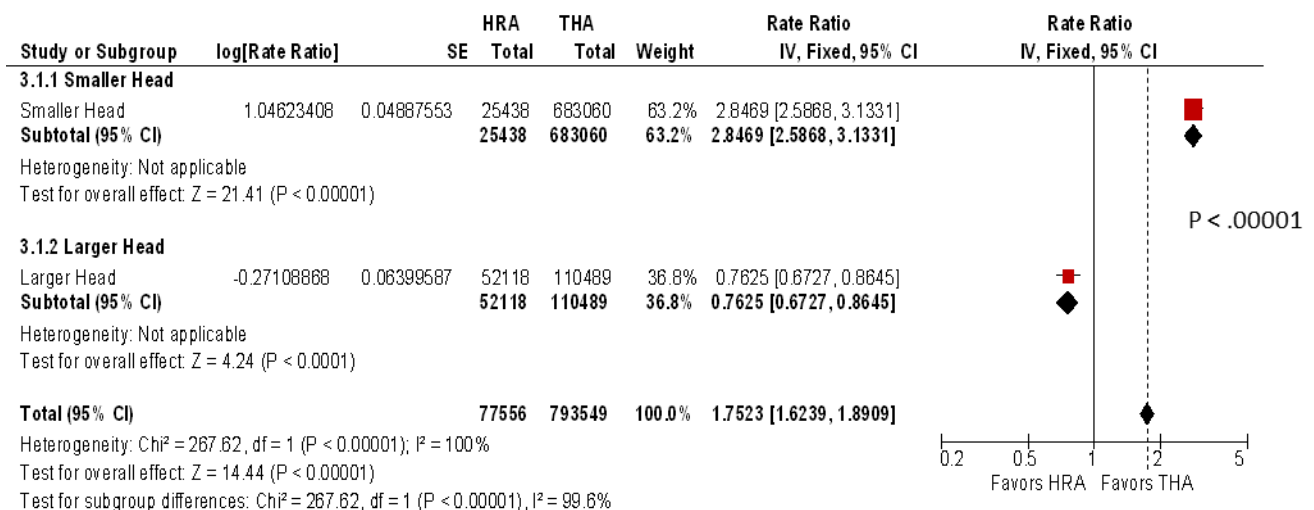
**Figure 89. Stratum specific revision rates per 1,000 observational years and rate ratios comparing hip resurfacing (HR) and total hip arthroplasty (THA) by gender.**



### Head Size

The rates of revision comparing HR with THA vary according to the femoral component head size. Larger component head size reduces the rate of revision in HR patients compared with a smaller femoral component head size (6.4 vs. 18.2 per 1,000 observational years) but increases the rate in patients receiving THA (8.4 vs. 6.4 per 1,000 observational years). This suggests that femoral component head size modifies the rate of revision in HR and THA; larger femoral component head size in those receiving HR result in significantly lower revision rates compared with smaller component head size, but larger femoral component head size in those receiving THA result in significantly higher revision rates compared with smaller component head size, Figure 19.

**Figure 9. Stratum specific revision rates per 1,000 observational years and rate ratios comparing hip resurfacing (HR) and total hip arthroplasty (THA\*) by femoral component head size†.**



\*Excluding metal on metal total hip arthroplasty

†Smaller: HR <50 mm, THA ≤32 mm; Larger: HA ≥50 mm, THA >32 mm



#### **4.5. Key Question 5. What is the evidence of cost implications and cost effectiveness of hip resurfacing?**

*Evidence from other Health Technology Assessments (HTAs).*

We found two previous HTAs that address the economic implications of hip resurfacing.

The Ontario HTA reports only on the McKenzie study, which we describe here in more detail (see below). They also conducted a very brief budget impact estimate for a Canadian setting, which includes only the cost per patient of hip resurfacing surgery. We did not include their impact estimate since it is not a complete economic evaluation and does not include any estimates for a US market.

The NICE HTA (Vale 2002) notes the lack of economic evaluations on hip resurfacing, but does give a fairly extensive assessment of the one "relatively complete economic evaluation" industry submission it received (Midland Medical Technologies, MMT) as part of the technology assessment process. The MMT study does not appear to have been subsequently published in the peer-reviewed literature. Details of the study, as reviewed by the HTA, are in Tables 20 and 21.

The Midland Medical Technologies submission included a cost-utility analysis submitted via spreadsheet. It compared Birmingham hip resurfacing (BHR) to either total hip arthroplasty or watchful waiting. As requested by NICE, the study took a health system perspective. The analysis was estimated for a hypothetical cohort of 1000 candidates for hip replacement at 5, 10, 15, and 20 years post-procedure, with focus on people age 45-65 based on the premise that THA was the superior option for people over 65. BHR effectiveness data were taken from internal industry data on 1693 BHRs conducted by four surgeons with limited follow-up for four years (complete follow-up data available for one percent, or 21 patients at four years); cost data were taken from NHS estimates and from the published literature; utility estimates were also from the published literature. Sensitivity analyses were conducted on varying levels of revision rate, cost, and QOL. Although Vale et al found this to be a reasonably well-conducted economic evaluation, they described several concerns that give reason for caution in the interpretation of the results—mainly the lack of long-term follow up data on BHR, and the model's assumption that patients do not exit watchful waiting for hip replacement but only for death.

*Economic studies on hip resurfacing*

We found four published, peer-reviewed articles on the economic impact of hip resurfacing. Each study varies in scope, perspective and methodology, and thereby warrants the consideration of all four when assessing the cost-effectiveness of hip resurfacing—especially given the lack of required evidence to draw a decisive conclusion. QHES scores ranged from 67 to 100 (mean of 88) [possible score 0 (worst) to 100 (best)].

One study, McKenzie et al.,<sup>112</sup> is a well-conducted economic evaluation whose main limitation is the paucity of clinical data available at that time on hip resurfacing, especially on revision rates. Weighted QHES score was 100 [possible score 0 (worst) to 100 (best)] for this study.

The McKenzie study was conducted in the UK on behalf of NICE. They conducted a cost utility analysis using a Markov model to integrate cost and outcomes of MoM hip resurfacing compared to either immediate THA or watchful waiting followed by THA. Taking a UK health service perspective

focusing only on direct medical costs, they created two separate models based on age of entry for younger and older “typical” patients with advanced hip disease. Costs were taken from literature and interviews with manufacturers, clinical data was from published literature and expert opinion, and utilities were from published literature. The main strengths of the study are the use of a cost utility model addressing several alternative clinical pathways and the 20-year time horizon. The main limitations are the use of expert opinion for some cost and clinical pathway inputs and the general lack of data on the effectiveness of BHR, especially revision rates, but overall it is a higher-quality economic study, and the authors’ conclusions are commensurate with the quality of the data available.

Another study (Buckland 2008) was brought to our attention in the initial report by Smith & Nephew, Inc. from a journal which does not appear to be indexed by Medline or EMBASE. We have included it as it provides some additional context and more recent data on the cost-effectiveness of hip resurfacing. Weighted QHES score was 67 [possible score 0 (worst) to 100 (best)] for this study.

Buckland and colleagues (2008) conducted a cost consequences study, which provides costs and QALYs separately. It takes a US health insurance payer perspective, comparing early hip resurfacing to five years of conservative management followed by THA. They provide estimates for a hypothetical population of people with moderate to severe hip disease at several age groups: 45-49, 50-54, and 55-59. Costs were estimated from Medicare fee schedules, average wholesale price for medications, and expert opinion; clinical pathways were determined by expert opinion; utility scores were based on published pain-related health states; and revision rates were from the Swedish National Hip Arthroplasty Register and the Oswestry Outcome Centre registry, which has 8-year follow up data on almost 5000 people receiving hip resurfacing. The sensitivity analysis is not clearly described but appears to be a threshold-type analysis of individual model inputs, including revision rate, cost, and discount rate. Overall, the quality of this study is undermined since many of the methods were not clearly described and the scope was relatively limited.

A more recent study conducted by Bozic et al.<sup>14</sup> in 2010 evaluated the cost effectiveness of MoM HR compared with THA. Its weighted QHES score was 100 [possible score 0 (worst) to 100 (best)] for this study.

Implementing a 30-year Markov decision model, Bozic and colleagues assumed a US healthcare system perspective and performed a full cost-utility economic analysis. Hypothetical patients age 50 years or older diagnosed with advanced osteoarthritis of the hip were stratified by gender and into age groups of 50-55, 55-64 and 65-74 years old. Authors sought data with a minimum follow up time of 5 years and assumed a constant rate of implant failure after 5-years. The 2008 Australian Orthopedic Association National Joint Replacement Registry (NJRR) Hip and Knee Arthroplasty Annual Report provided data on 9,956 HR patients and 109,972 THA patients detailing age, gender and types of revisions necessary for 5-7 years post procedure. The annual probability of revision was projected also using the NJRR data. In all, a total of 15 clinical outcomes were tracked in the model; the remainder of which were derived from published literature. Additionally, 8 relevant cost estimates were also monitored and obtained from averaged 2008 Medicare reimbursements of 544 primary lower extremity arthroplasty procedures and 545 revision procedures. To gauge effectiveness over time, QoL approximations were obtained from published literature. A strength of the Bozic 2010 study was its thorough sensitivity analysis that was presented to compensate for the models wide variability. Furthermore, the 30-year time horizon along with careful consideration of

data sources added to its legitimacy. Noted limitations included a lack of long-term data on implant failure rates for MoM HR and no direct estimate for QoL post-successful MoM HR or after conversion to THA. Overall, the study constructed a sound model, however, suffered from large degree of underlying parameter variability which ultimately restricted the scope of its conclusions.

The latest study reviewed, (Edlin 2012) was conducted in the UK. Its weighted QHES score was 85 [possible score 0 (worst) to 100 (best)] for this study.

Edlin et al.<sup>51</sup> relied on within-trial data to evaluate the cost-effectiveness of metal-on-metal HR against THA. It was centered in a large, single-site teaching hospital in the UK. The study consisted of 126 patients with severe hip joint arthritis. Patients were followed over the course of 1-year. The main strength of the Edlin 2012 study was that it was based on within-trial data. However, it was held back by several limitations. First, it had a small time horizon incapable of fully answering questions of devices durability and related long-term expenses and health outcomes. Furthermore, the study relied on a relatively small sample size, was a single-site location with hospital specific costs and presented UK based costs and effectiveness measures. Overall, being tied closely to a RCT the study offers additional firsthand insights into the cost effectiveness of hip resurfacing provided its limitations are taken into consideration.

### *Results*

The MMT submission described by Vale (2002) found that the cost utility of BHR increased dramatically over time. The cost per QALY at five years compared to THA was estimated to be £13,125, while BHR was dominant at 20 years. Compared to watchful waiting, Cost per QALY was £1101 at 5 years and BHR dominant (less costly, more effective) at 20 years. The improvement in QALYs for BHR was small at each time point and based on the assumption of a higher revision rate for THA. The submission indicated a “worst-case scenario” where THA revision rates equaled BHR revision rate; in this scenario THA would be dominant (less costly with same QALY improvements). Sensitivity analysis found that the break-even point of equal cost at 20 years for BHR compared with THA was if BHR revision rates were 85% of THA rates for a 55 year-old patient.

McKenzie found that that MoM hip resurfacing dominated the watchful waiting option at all time points in the younger population. Compared with THA, THA was found to be the dominant option in both the younger and older populations modeled. Hip resurfacing revision rate was influential in the model results, suggesting that with increasing THA revision rate, hip resurfacing ceases to be dominated when its revision rate is 80% of the THA rate. The model was not sensitive to prostheses cost up to 300% of the base case or variations in utility estimates up to 0.97, but was to watchful waiting costs (up to £620). The authors conclude that MoM hip resurfacing warrants further study given the lack of long-term data on hip resurfacing effectiveness, especially given how influential it was in model results.

Buckland (2008) found that for all age groups, immediate hip resurfacing was dominant over conservative management followed by THA. This study used implant survival rather than revision rate; e.g., a 81.6% implant survival at 13 years follow-up for a 50-59 year old, compared with 97.0% implant survival at eight years follow-up for a 50-54 year old. To illustrate further, consider the 50-54 age group, modeled to age 65, for conservative treatment. The cost per patient was \$22,160, and QALYs per patient were 10.03, compared to immediate total HR, which was both less costly (\$17,144 per patient) and saved more QALYs (11.51). Sensitivity analysis suggested that revision

rates do not change the overall results, even at equal revision rates for hip resurfacing and THA. The cost of drug treatment associated with conservative management would need to be between 26% and 42% of the estimated modeled, and the discount rate would need to be 10% or higher to change the study conclusions.

Bozic (2010)<sup>14</sup> reported highly variable ICERs across different demographics. In all age and gender subgroups reported, HR produced greater QALYs compared to THA while also incurring greater costs than THA. However, the modest improvements in QALYs (ranging from an increase of 0.002 QALYs to 0.052 QALYs when undergoing HR) coupled with differences in costs (ranging from HR being \$1,289 to \$4,131 more expensive than THA) resulted in erratic ICERs (ranging from \$28,614/QALY to \$2,483,435/QALY). To address the extreme variability produced by the model, the authors performed an extensive sensitivity analysis to glean further meaning. Applying one-way sensitivity analysis for both HR and THA, rates of failure, procedural costs, operative mortality, and the QoL after conversion from HR and THA were found to be highly influential parameters. Over a 30-year time horizon HR was cost saving if the incremental cost of HR implants versus THA implants were \$313, \$711 and \$175 less for men age < 55, 55-64, 65-74 respectively. Using two-way sensitivity analysis the authors demonstrated HR to be more favorable compared to THA for younger patients (age < 55) than older patients (age > 65) when varying values for the loss of QoL post HR conversion and incremental cost of HR conversion. Probabilistic sensitivity analysis mirrored the wide range of ICERs seen in the base case. Assuming a willingness to pay of \$100,000/QALY, the probability of HR being the preferred treatment was less than 75% for all strata. The authors conclude that while there exists some evidence that HR could be potentially cost effective for younger patients, given the model's sensitivity to clinical outcomes and QoL estimates more accurate measures are required to draw a definitive conclusion of cost effectiveness.

Edlin et al.<sup>51</sup> found evidence supporting the cost effectiveness of MoM HR over the initial 12-month period assuming a commonly accepted willingness-to-pay threshold of £20,000/QALY. In the 1-year base case analysis, HR costs an additional £564 and generated 0.032 more QALY, which yielded an ICER of £17,451/QALY. Following the base case, the authors tested a number of assumptions. First, the implant material was varied to the less common, though cheaper, metal-on-polyethylene bearing, which caused the ICER to increase to £39,318/QALY. Assuming a quicker recover time resulted in a more favorable ICER for HR of £14,310/QALY. If societal costs were taken into consideration, HR became relatively more expensive and the ICER increased to £19,435/QALY. Initial differences in baseline QoL and genders were adjusted using regression techniques and reported in the sensitivity analysis. With the QoL adjustments included, the ICER was reduced to £8,905/QALY. In that scenario, HR was found to be cost effective 78% of the time assuming a threshold of £20,000/QALY. The authors concluded that over a 1-year time horizon MoM HR was potentially a cost effective alternative to THA while noting the need for further research.

### *Discussion*

Overall, there is limited evidence to inform a strong recommendation about the economic value of hip resurfacing. It appears that the most convincing evidence of cost-effectiveness of hip resurfacing is in patients under age 65 and that there is little evidence of cost-effectiveness for extended watchful waiting/conservative management. Further study of the value of hip resurfacing is warranted.

Although each study provides some very interesting context and data, they differed from one another enough to preclude strong recommendations. The following are take-away points from synthesis of the three studies and directly inform recommendations for future economic evaluations that would provide more definitive evidence:

- The risk of revision for hip resurfacing appears to be an influential factor in all studies we reviewed. As such, the most long-term, comprehensive, and highest-quality follow-up data on hip resurfacing revision rates is crucial to understanding the economic value of hip resurfacing. Looking at studies conducted in the last few years the class of evidence is still insufficient and at times even contradictory. For example, revision risks used in Bozic et al (2010) disagree with risks reported in the 2013 hip registry with respect to whether HR or THA is more effective.
- Identifying potential subgroups (besides age) likely to benefit the most from this intervention would also be useful, including pre-surgical health and activity levels.
- Only one study, Edlin et al.,<sup>51</sup> addressed a societal perspective and doing so only minimally in a sensitivity analysis from a UK societal point of view. Considering the likely dramatic impact of hip disease on productivity, out of pocket costs, and quality of life of degenerative hip disease especially in younger people, a thorough economic evaluation would take a societal perspective and include factors such as pain relief, adverse effects from therapy, productivity, functional status, health-related quality of life and such as out-of-pocket costs for subsequent diagnostic or interventional costs, rehabilitation, lost productivity. Edlin and colleagues showed there to be a nontrivial impact on the ICER, which merits further inquiry.
- Studies used different comparators and forms of hip resurfacing, describing different clinical pathways—including one study that assumed that people choosing watchful waiting never proceed on to receive a hip replacement. As such it is difficult to compare the results of the studies as all made different assumptions about the costs and outcomes associated with conservative management or the exact clinical pathway through which patients receive THA or hip resurfacing.

### *Conclusion*

Although further study is necessary to include more current data, there remains insufficient evidence to warrant a conclusion about the economic value of hip resurfacing in a US setting. In particular, the estimates for revision used in these studies are not current and don't appear to match the contemporary data.

**Table 20. Summary demographic information for economic studies.**

Study	Design	Data sources and population	Model inputs	Primary strengths and limitations
McKenzie 2003	<p>Cost utility analysis Markov model: costs and outcomes for 20 cycles at 1 cycle/year; five year bands</p> <p>Intervention: Metal on metal hip resurfacing (MoM)</p> <p>Comparators: Total hip replacement (THA); watchful waiting (WW) plus THA</p> <p>UK health service perspective focused on direct medical costs</p> <p>20 year time horizon; 6% discount rate</p> <p>Sensitivity analysis: Altered key parameter values (revision rate, cost, QOL); time horizon assessed at 5-, 10-, and 15-year cycles</p>	<p>Separate models for persons aged 45-50 on entry and aged 65-70 on entry</p> <p>“Typical” patient with advanced hip disease (no other information provided)</p> <p>Costs: published literature, contact with manufacturers (Fitzpatrick 1998 updated to 2000 UK£)</p> <p>Probabilities: THA and MoM: published literature (MoM inputs largely from McKinn 1996); WW from contact with local medical staff</p> <p>QOL: published literature</p>	<p>Revisions: Hip resurfacing: 1.52% (1.133)</p> <p>THA: 1.36% (0.933)</p>	<p><u>Strengths:</u> Cost utility analysis with extended time horizon</p> <p>Use of several alternative management strategies</p> <p><u>Limitations:</u> Survival rates used to model outcome unlikely</p> <p>Lack of robust long term data about MoM</p>
Vale 2002	<p>NICE’s evaluation of industry submission received for NICE HTA (Midland Medical Technologies)</p> <p>Cost utility analysis provided via spreadsheet</p> <p>Time horizon: 20 years (analysis at 5, 10, 15, 20 years)</p> <p>Intervention: BHR Comparators: THA, watchful waiting</p> <p>Health services perspective</p> <p>Sensitivity analysis: Probabilistic analysis allowed variation of BHR revision rate, cost of surgery, utility.</p>	<p>Population: hypothetical cohort of 1000 pts. Not clear what ages were modeled, but submission focused recommendations for people ages 45-65, saying older patients are well managed with THA.</p> <p>Costs: UK Department of Health (interventions), Personal Social Services Research Unit data (hospital stay) reference costs for devices; published literature</p> <p>BHR effectiveness: Industry data on 1693 BHRs conducted by four surgeons (82% by one surgeon) with limited four-year follow-up (66% fu at 1 year, 1% at 4 years). Ages 15-86.</p> <p>THA revision: Swedish national hip register</p> <p>Watchful waiting: resource use measures for meds, GP visits, hospitalization</p> <p>Utilities: Published literature for THA</p>	<p>Revisions: Hip resurfacing: 0.5% (year 2) 2.5% (year 11+) [5.1]</p> <p>THA: 1.0% (year 2) 5% (year 11+) [4.2]</p>	<p><u>Strengths:</u> Use of person-level data</p> <p>“Reasonably complete” economic evaluation of BHR</p> <p><u>Limitations:</u> Survival rates used to model outcome unlikely</p> <p>Lack of data on long-term revision rates of BHR</p> <p>Questionable model assumption that people only exit WW for death.</p>



Study	Design	Data sources and population	Model inputs	Primary strengths and limitations
Buckland 2008	<p>Cost consequences analysis</p> <p>U.S. private insurance payer perspective</p> <p>Intervention: early hip resurfacing</p> <p>Comparator: Five years of conservative treatment (analgesics and anti-inflammatory rx) followed by THA</p> <p>Two time horizons: to age 65 and to death</p> <p>Net present value of direct costs and patient utilities</p> <p>Costs and utilities discounted at 4%</p> <p>Sensitivity analysis: not clearly described, but appeared to do a threshold-type analysis at varying levels of revision rate, cost, and discount rate</p>	<p>Hypothetical pts with mod to severe symptoms of degen hip disease (age groups: 45-49, 50-54, 55-59)</p> <p>Costs: 2006 Medicare fee schedule, CPT codes, average wholesale price for meds, interviews with managed care directors</p> <p>Clinical pathways and resource use: interviews with orthopedic surgeons and gastroenterologists</p> <p>Utility scores: published pain-related health states for people with degenerative hip disease</p> <p>Life expectancy: US life tables</p> <p>Revision rates: Swedish National Hip Arthroplasty Register (THA), Oswestry Outcome Center (HR) [registry of BHR outcomes since 1997—8 year follow-up on 4691 pts]</p>	<p>Survival: Hip resurfacing: 94.3% (age &lt;40) – 94.8% (age 70+)</p> <p>THA: 72.1% (age &lt;50) – 95.2% (age &gt;75)</p>	<p><b>Strengths:</b></p> <p>Use of recently available data on revision rates</p> <p>Clear description of clinical pathways</p> <p><b>Limitations:</b></p> <p>Survival rates used to model outcome unlikely</p> <p>Methods of sensitivity analysis unclear</p> <p>Patient characteristics not described beyond age</p> <p>Use of expert opinion to determine clinical pathways and some costs</p>
Bozic 2010	<p>Cost utility analysis</p> <p>Markov decision model with 1-year cycles</p> <p>Healthcare system perspective</p> <p>Intervention: Metal-on-Metal hip resurfacing (MoM HR)</p> <p>Comparator: THA</p> <p>Time horizons: 30-year</p> <p>Net present value of hospital costs and professional fees based on Medicare payments.</p> <p>Costs and utilities discounted at 5%</p> <p>Sensitivity analysis: conducted detailed one-way, two-way and Monte Carlo probabilistic sensitivity analysis.</p>	<p>Hypothetical patients age 50 years or older suffering from advanced osteoarthritis of the hip. Stratified by gender and age groups &lt;55, 55-64, 65-74.</p> <p>Costs: average of 2008 Medicare payment of 544 primary lower extremity arthroplasty procedures and 545 revision procedures.</p> <p>Implant failure data obtained from Australian Orthopedic Association with minimum of 5 year follow up time.</p> <p>QoL: published literature</p> <p>Life expectancy: US Life Tables</p> <p>Revision rates: obtained from published literature</p>	<p>Hip resurfacing failure:</p> <p>0.45% male &lt; 55</p> <p>Range for all age, gender and time after surgery: (0 – 2.25%)</p> <p>Primary THA failure:</p> <p>0.55% male &lt; 55</p> <p>Range for all age, gender and time after surgery: (0 – 0.84%)</p>	<p><b>Strengths:</b></p> <p>Thorough sensitivity analysis</p> <p>Justified rationale for data sources</p> <p>30-year time horizon</p> <p>Stratification by gender and age.</p> <p>In-depth clinical outcome tree model</p> <p><b>Limitations:</b></p> <p>Lack of long-term implant failure rate for MoM HR</p> <p>No direct estimate for QoL post-successful MoM HR or after conversion to THA.</p> <p>Australian based effectiveness rates</p>

Study	Design	Data sources and population	Model inputs	Primary strengths and limitations
Edlin 2012	<p>Cost utility analysis</p> <p>Intention-to-treat, single-center, single-blind RCT study</p> <p>Intervention: Metal on metal hip resurfacing (MoM)</p> <p>Comparator: Total hip replacement (THA); with ceramic-on-ceramic, metal-on-metal and metal-on-polyethylene bearing surfaces</p> <p>UK health service and Personal Social Services perspective.</p> <p>Considers 1-year follow up with outcomes assessed at 3, 6 and 12 month intervals; 1.9% annual discount rate</p> <p>Sensitivity analysis: One-way sensitivity analysis investigated influence of missing data, quicker recovery times, implant material for THA, and addition of societal costs.</p> <p>Baseline QoL and gender values adjusted using regression to compare with RCT</p>	<p>126 patients with severe arthritis of the hip, eligible if 18-years or older</p> <p>58 HR procedures, 64 THA procedures and 4 omitted.</p> <p>Single-center hospital in the UK</p> <p>Costs: broken into 6 categories: initial operation, inpatient care post-discharge, outpatient care, primary/community care, medications, and aids/adaptations required while in the community</p> <p>Hospital records and Healthcare Resource Group v.4 provided data</p> <p>RCT found no evidence of a difference in hip function between HR and THA at 12 months</p> <p>QoL: responses from EQ-5D-3L</p>	<p>Conducted alongside RCT</p>	<p><u>Strengths:</u> Relies on in-trial data</p> <p><u>Limitations:</u> Short term follow up</p> <p>Small sample size</p> <p>Single-site location with hospital specific costs</p> <p>UK based costs and effectiveness measures</p>



**Table 21. Summary of results for economic studies.**

	Relevant results	Results of sensitivity analysis	Author conclusions
McKenzie 2003	<p>MoM versus WW: MoM dominates WW in younger population (Additional cost for MoM= £-179, QALYs gained 3.73)</p> <p>MoM versus THA: THA dominates in both younger and older populations (additional cost for MoM=£1357 and £1362, QALYs gained -0.02 for both younger and older)</p>	<p>MoM becomes cost-effective as THA revision rate increases or MoM revision rate decreases; with increasing THA revision rate, MoM ceases to be dominated when MoM revision rate is 80% of THA rate. Decreasing MoM revision rate, MoM ceases to be dominated when the revision rate is 88% of THA rate.</p> <p>THA continued to dominate MoM at THA prostheses costs up to 300% of base case and at all time horizons MoM dominant over WW up to WW cost £620</p> <p>MoM dominant over WW even at QOL values 0.97.</p>	MoM warrants further study, especially since long-term data is not yet available and since revision rates were influential in the model and may substantially affect cost-effectiveness.
Vale 2002	<p>BHR versus THA: QALYs gained at 5 and 20 years: 29, 112 Cost gained at 5 and 20 years: £378,125, -£321,333 ICER (cost per QALY) at 5 and 20 years: £13,125; BHR dominates</p> <p>BHR versus WW: QALYs gained at 5 and 20 years: 2499, 8963 Cost gained at 5 and 20 years: £2.752,517, -£298,997 ICER (cost per QALY) at 5 and 20 years: £1101; BHR dominates</p>	<p>BHR vs THA: by year 20, BHR dominated 57% of the time; THA dominated 15% of the time, BHR less effective and less costly 28% of the time, BHR more costly and more effective 0% of the time.</p> <p>Improvement in QALYs for BHR was small and based on the assumption of a higher revision rate for THA. In a "worst-case scenario" where THA revision rates equaled BHR revision rate, THA would be dominant (less costly with same QALY improvements).</p> <p>Break-even point of equal cost at 20-years: BHR revision rates 85% of THA rates for a 55-year old patient.</p> <p>BHR vs WW: BHR continued to dominate at 20 year follow-up</p>	<p>Industry conclusions: equity issues with denying younger patients BHR if WW is the alternative.</p> <p>Vale et al conclusions: Evidence of utility gains at 5 years at reasonable cost, however some concern with model assumptions about revision rates, assumption that people only exited watchful waiting for death, not THA.</p> <p>Paucity of data, especially on revision rates, are reason for caution in recommending BHR beyond four years</p>

	Relevant results	Results of sensitivity analysis	Author conclusions
Buckland 2008	<p>For each age group, immediate total HR is the dominant option</p> <p>E.g.: For age group 50-54, to age 65: Conservative tx: Cost per patient: \$22,160; QALY per patient: 10.03</p> <p>Immediate total HR: Cost per patient: \$20,476; QALY per patient: 11.51</p>	<p>Revision rates influential, but does not change conclusions even at total HR rates=THA rates.</p> <p>Cost of drug treatment need to be between 26% and 42% of current estimate to change conclusions</p> <p>Discount rate would need to be 10% or higher to change conclusions</p>	<p>Total HR is superior to non-surgical management of degenerative hip disease. For younger, more active patients, hip resurfacing is superior to THA.</p>
Bozic 2010	<p>In all age and gender subgroups reported, HR produced greater QALYs compared to THA while also incurring greater costs than THA.</p> <p>MoM HR versus THA (30-year follow up): Male &lt; 55: <math>\Delta\text{Cost} = \\$1,687</math>; <math>\Delta\text{QALYs} = 0.035</math>; ICER = \$48,882/QALY</p> <p>Male 55-64: <math>\Delta\text{Cost} = \\$1,289</math>; <math>\Delta\text{QALYs} = 0.045</math>; ICER = \$28,614/QALY</p> <p>Male 65-74: <math>\Delta\text{Cost} = \\$1,825</math>; <math>\Delta\text{QALYs} = 0.022</math>; ICER = \$83,699/QALY</p> <p>Female &lt; 55: <math>\Delta\text{Cost} = \\$2,456</math>; <math>\Delta\text{QALYs} = 0.052</math>; ICER = \$47,468/QALY</p> <p>Female 55-64: <math>\Delta\text{Cost} = \\$4,131</math>; <math>\Delta\text{QALYs} = 0.009</math>; ICER = \$435,800/QALY</p> <p>Female 65-74: <math>\Delta\text{Cost} = \\$3,726</math>; <math>\Delta\text{QALYs} = 0.002</math>; ICER = \$2,483,435/QALY</p>	<p>For both MoM HR and THA rates of failure, procedural costs, operative mortality, and the QoL after conversion from MoM HR and THA were highly influential to the model results.</p> <p>MoM HR would be cost saving over a 30-year time horizon if the incremental cost of HR implants versus THA implants were \$313, \$711 and \$175 less for men age &lt; 55, 55-64, 65-74 respectively.</p> <p>Two way sensitivity analysis demonstrated MoM HR to be more favorable compared to THA for younger patients (age &lt; 55) than older patients (age &gt; 65) when varying values for the loss of QoL post HR conversion and incremental cost of HR conversion.</p> <p>Probabilistic sensitivity analysis mirrored the wide range of ICERs seen across the various gender and age strata reported. Range from \$28,614 – 2,483,435.</p> <p>Assuming a willingness to pay of \$100,000/QALY, the probability of MoM HR being the preferred treatment was less than 75% for all strata</p>	<p>Given the model's sensitivity to clinical outcomes and QoL estimates more accurate measures are required to draw a definitive conclusion of cost effectiveness.</p> <p>Evidence suggests the potential for MoM HR to be cost effective for younger patients.</p>

	Relevant results	Results of sensitivity analysis	Author conclusions
Edlin 2012	<p>Base case: during the initial 12 months, HR costs an additional £564 and generates 0.032 more QALY. ICER= £17,451/QALY</p> <p>Expense difference summary (HR – THA): Initial operation/care: £184 Subsequent inpatient: £ 279 Outpatient: £84 Societal costs: £629</p>	<p>Using a metal-on-polyethylene implant: ICER increases to £39,318/QALY</p> <p>Recover time of 6 weeks: more favorable ICER for HR of £14,310/QALY</p> <p>With societal cost: ICER increases to £19,435/QALY</p> <p>Baseline QoL gender adjustments: ICER is reduced to £8,905/QALY. HR is found to be cost effective 78% of the time assuming a threshold of £20,000/QALY</p>	<p>Over a 1-year time horizon assuming a willingness-to-pay of £20,000 and taking into consideration limitations of the study MoM HR is potentially a cost effective alternative to THA</p> <p>Further analysis is needed</p>

## 5. Summary by Key Question

Key Question 1: What is the evidence of efficacy and effectiveness of hip resurfacing (HR) compared with total hip arthroplasty (THA)?								Treatment groups		Effect size	
Outcome	Sample Size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	THA range of mean $\Delta$	HR range of mean $\Delta$	overall mean $\Delta$ diff (95% CI)	Favors
<b>WOMAC 1 year f/u</b>	3 RCTs N = 304	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious risk of imprecision*	Undetected	Moderate due to imprecision	38-54 points	29-47 points	<b>1.8 points lower</b> (7.2 lower to 3.7 higher)	<b>neither</b>
<b>SF-36 physical 1 year f/u</b>	2 RCTs N = 152	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious risk of imprecision*	Undetected	Moderate due to imprecision	7-18 points	8-19 points	<b>0.9 points higher</b> (1.4 lower to 3.1 higher)	<b>neither</b>
<b>UCLA Activity score 1 year f/u</b>	3 RCTs N = 304	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious risk of imprecision*	Undetected	Moderate due to imprecision	6-8 points	7-8 points	<b>0.3 points higher</b> (0.1 lower to 1.1 higher)	<b>neither</b>
<b>Merle D'Aubigné 1 year f/u</b>	2 RCTs N = 200	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious risk of imprecision*	Undetected	Moderate due to imprecision	6-8 points	6-7 points	<b>0.4 points lower</b> (1.1 lower to 0.3 higher)	<b>neither</b>

\*relatively small sample sizes, confidence interval includes benefit and harm.

Key Question 2: What is the evidence about the safety profile for hip resurfacing compared with total hip arthroplasty (THA)?								Treatment groups		Effect size	
Outcome	Sample Size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	THA range of risks (%)	HR range of risks (%)	Relative Risk (95% CI)	Favors
<b>Revision</b>											
<b>3 year f/u</b>	3 total joint registries N > 350,000	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	High	2 to 3%	3%	<b>1.2 to 1.5</b> (range of 3 registries)	<b>THA</b>
<b>5 year f/u</b>	3 total joint registries N > 228,000	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	High	1-4%	5-6%	<b>1.3 to 1.8</b> (range of 3 registries)	<b>THA</b>

Key Question 2: What is the evidence about the safety profile for hip resurfacing compared with total hip arthroplasty (THA)?								Treatment groups		Effect size	
Outcome	Sample Size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	THA range of risks (%)	HR	Relative Risk (95% CI)	Favors
<b>7 and 10 year f/u</b>	3 total joint registries N > 127,000	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	High	3-6%	6-10%	<b>1.4 to 2.0</b> (range of 3 registries)	<b>THA</b>
<b>11 year f/u</b>	1 total joint registry N > 2400	No serious risk of bias	Consistency unknown (one study)	No serious indirectness	Serious risk of imprecision†	Undetected	Moderate due to imprecision from single study	7.4%	9.8%	<b>1.32</b> (1.25, 1.40)	<b>THA</b>
<b>Complications</b>											
Femoral neck fracture	5 observational N = 1324	Serious risk of bias*	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	Low	0.0%	1.8%	Not calculable P < .001	<b>THA</b>
Avascular necrosis	1 RCT 2 observational N = 615	Serious risk of bias*	No serious inconsistency	No serious indirectness	Serious risk of imprecision†	Undetected	Insufficient due to risk of bias and imprecision	0.0%	0.9%	Not calculable P = NS	<b>neither</b>
Femoral component loosening	2 RCT 6 observational N = 1277	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	High	0.3%	2.7%	8.4 (2.0, 36.2) P < .001	<b>THA</b>
Heterotopic ossification	1 RCT 5 observational N = 688	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	High	11.4%	19.8%	1.8 (1.2, 2.5) P = .002	<b>THA</b>
Dislocation	3 RCT 4 observational N = 1635	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious risk of imprecision	Undetected	High	2.8%	0.5%	0.17 (0.06, 0.49) P < .001	<b>HR</b>

Key Question 2: What is the evidence about the safety profile for hip resurfacing compared with total hip arthroplasty (THA)?								Treatment groups		Effect size	
Outcome	Sample Size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	THA range of risks (%)	HR range of risks (%)	Relative Risk (95% CI)	Favors
Deep infection	3 RCTs 2 observational N = 1062	No serious risk of bias	Serious risk of inconsistency §	No serious indirectness	No serious risk of imprecision	Undetected	Moderate due to inconsistency	1.8%	0.4%	0.21 (0.05, 0.90) P = .038	HR

\*Serious risk of bias: the majority of studies did not meet two or more important criteria of a good quality RCT or cohort (see Appendix for details)

†Relatively small sample sizes, confidence interval includes benefit and harm.

‡Small sample size with relatively rare event

§Inconsistent risks between the RCTs and observational studies reduces our confidence in the size of the effect estimate.

	Sample Size	Conclusions
<b>Metal ion levels: MoM HR compared with conventional THA</b>	5 cohort studies N = 464, f/u: 1–3 yrs	<ul style="list-style-type: none"> <li>Regardless of the types of sample used (whole blood, serum, hair), all studies reported significantly (<math>P &lt; .001</math> to <math>.04</math>) higher median concentrations of the primary metal ions cobalt and chromium in the HR groups compared with the THA (MoP and ceramic) groups at all follow-up periods up to 3 years.</li> </ul>
<b>Association of metal ion levels with outcome following MoM HR</b>	3 case-control studies N = 1478, f/u: 3.6–4.7 yrs 1 cohort study N = 299, f/u: 5.8 yrs	<ul style="list-style-type: none"> <li>Evidence across three case-control studies showed significantly (<math>P &lt; .01</math>) higher levels of both cobalt and chromium in patients with a poor outcome (i.e. revision/poorly functioning hip) compared to those with a good outcome (asymptomatic/well-functioning hip) following HR.</li> <li>A dose response was seen in one retrospective cohort such that with each increase in the level of cobalt ions, a subsequently higher proportion of hips underwent revision within 9 years of surgery.</li> </ul>
<b>Pseudotumors</b>	2 case-control studies N = 233, f/u: 2–5.1 yrs 1 cohort study N = 256, f/u: 4.6 yrs	<ul style="list-style-type: none"> <li>Higher median serum ion levels of cobalt and chromium were associated with asymptomatic pseudotumor formation following MoM HR and MoM THA in two case-control studies.</li> <li>An association between serum metal ion levels and pseudotumor formation in symptomatic and asymptomatic patients following MoM HR was found in one cohort study: a greater proportion of patients with cobalt and chromium levels <math>&gt; 7 \mu\text{g/L}</math> versus <math>&lt; 7 \mu\text{g/L}</math> developed pseudotumors: for cobalt, 77.8% versus 34.0% and for chromium, 73.3% versus 33.2%, respectively.</li> </ul>
<b>Cancer</b>	4 comparative registries N = 332,238 f/u: 3–17 years	<ul style="list-style-type: none"> <li>Across three registries that compared the risk of cancer following implantation with a MoM hip prosthesis (both HR and THA) with THA with other bearing surfaces, MoM implants were not associated with an increased risk of cancer; likewise, when compared to the general population risks were similar.</li> <li>The fourth registry looked at the mortality and causes of death among patients with MoM compared with MoP total hip prostheses. Standardized mortality rates were similar between the hip arthroplasty patients and the general population; however, patients with MoM THA had higher cancer mortality than those with MoP THA, although after 20 years there was no difference between groups.</li> </ul>
<b>Renal function impairment</b>	2 cohort studies; 4 case-series N = 2452 f/u: 2–10 years*	<ul style="list-style-type: none"> <li>Across six studies evaluating patients following MoM HR or MoM THA, the evidence showed no negative impact on renal function (i.e. creatinine levels, creatinine and metal ion clearance, markers of renal damage, diagnosis of renal disease or renal insufficiency)</li> </ul>

Key Question 3: What is the evidence of efficacy, effectiveness and safety of revisions of HR compared with revisions of THA?								Treatment groups		Effect size	Favors
Outcome	Sample Size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	THA Median	HR		
<b>WOMAC SF-12 physical</b>	1 observational N = 45 f/u: 2-7 yrs	Serious risk of bias*	Consistency unknown (one study)	No serious indirectness	Serious risk of imprecision†	Undetected	Insufficient due to risk of bias, consistency & imprecision	83.9	79.1	N/A	<b>neither</b>
								37.3	33.1		

\*Serious risk of bias: the majority of studies did not meet two or more important criteria of a good quality cohort (see Appendix for details)

†small sample size

Key Question 4: Is there evidence of differential efficacy or safety issues with use of hip resurfacing?												
Outcome	Sample Size	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	THA rate/1000		HR rate/1000		Favors
								DD	OA	DD	OA	
<b>Revision DD vs. OA</b>	1 registry study N = 993,697 person years	No serious risk of bias	Consistency unknown (one study)	No serious indirectness	No serious risk of imprecision	Undetected	High due to magnitude of effect	9.6	7.8	22.8	10.3	<b>THA in DD pop</b>
male vs. female	1 registry study N = 887,370 person years	No serious risk of bias	Consistency unknown (one study)	No serious indirectness	No serious risk of imprecision	Undetected	High due to magnitude of effect	male	female	male	female	<b>THA in female pop</b>
								8.2	7.5	7.5	18.2	
smaller vs. larger femoral head size	1 registry study N = 793,549 person years	No serious risk of bias	Consistency unknown (one study)	No serious indirectness	No serious risk of imprecision	Undetected	High due to magnitude of effect	smaller	larger	smaller	larger	<b>THA in smaller femoral head size</b>
								6.4	8.4	18.2	6.4	



<b>Key Question 5:</b> What is the evidence of cost implications and cost effectiveness of hip resurfacing?			
<b>Studies</b>	<b>Countries</b>	<b>QHEs Range*</b>	<b>Conclusions</b>
4 cost-utility analyses	3 UK 1 US	67-100	<ul style="list-style-type: none"> <li>Revision rates are important input factors in the prediction models, and no study estimated the revision rates as presented in the latest registries of medium term follow-up.</li> </ul>
1 cost-consequence	1 US		<ul style="list-style-type: none"> <li>Studies used different comparators and forms of hip resurfacing, describing different clinical pathways—including one study that assumed that people choosing watchful waiting never proceed on to receive a hip replacement. As such it is difficult to compare the results of the studies as all made different assumptions about the costs and outcomes associated with conservative management or the exact clinical pathway through which patients receive THA or hip resurfacing.</li> </ul>

\*Quality of Health Economic Studies (QHEs) scores which primarily reflect the quality of reporting on specific factors that are important in economic analyses. It does not provide for evaluation of quality with respect to modeling assumptions or extensive consideration of data quality and included outcomes measures relevant to a specific topic.

## Glossary of Terms

<b>Ankylosing spondylitis (AS)</b>	A chronic, inflammatory arthritis that affects the joints of spine and the sacroiliac joint of the pelvis and causes eventual fusion of the spine. Though genetics play a role, its cause is largely unknown. AS causes pain and stiffness of low back and hip, progressing to the neck and chest.
<b>Anteversion</b>	The tipping forward of an entire organ or part. In this report it is used to describe acetabular component positioning.
<b>Apoptosis</b>	A natural process of self-destruction in certain cells that is determined by the genes and can be initiated by a stimulus or by removal of a repressor agent. Also called <i>programmed cell death</i> .
<b>Articular Surfacing Replacement (ASR) Device</b>	A metal-on-metal prosthesis that is manufactured by DePuy Orthopaedics, Inc., Warsaw, IN. The ASR is not FDA-approved. It is currently marketed in Canada, Europe, India, and Australia.
<b>Avascular necrosis (AVN)</b>	Bone death due to temporary or permanent cessation of blood flow to the bone.
<b>Birmingham Hip Resurfacing (BHR) System</b>	The first FDA-approved (May 2006) hip resurfacing system available for use in the US; it is also manufactured globally. It is a metal-on-metal prosthesis composed of high carbon and cobalt-chromium alloy; the acetabular component has a hydroxyapatite coating. The BHR is manufactured by Smith & Nephew, Inc., Memphis TN.
<b>Body mass index (BMI)</b>	A measurement that has replaced weight as the preferred determinant of obesity. The BMI can be calculated (in English units) as 703.1 times a person's weight in pounds divided by the square of the person's height in inches.
<b>Conserve Plus Hip Resurfacing</b>	A metal-on-metal prosthesis composed of cobalt-chromium alloy. It is manufactured by Wright Medical Technology, Inc., Arlington, TN. It is currently being marketed in Europe and Asia and is awaiting FDA approval in the US.
<b>Cormet Hip Resurfacing System</b>	Approved for use in the US by the FDA in July 2007. The Cormet is a metal-on-metal prosthesis composed of cobalt-chromium alloy; the acetabular component has a bi-coating of plasma sprayed titanium and hydroxyapatite. It is manufactured by Stryker/Corin Medical, Ltd., USA, Tampa, FL.
<b>Cytotoxicity</b>	The degree to which an agent possesses a specific destructive action on certain cells. Most often used to describe decomposition of cells by immune mechanisms.
<b>Dislocation</b>	Displacement of the bone.

<b>Durom Hip Resurfacing</b>	A metal-on-metal prosthesis composed of a wrought-forged high carbon and cobalt-chromium alloy; the acetabular component has a coating of pure sprayed titanium. It is manufactured by Zimmer, Inc., Swindon, UK. The Durom is not FDA-approved but is marketed in North America outside of the US and in the UK.
<b>Dysplasia of the hip</b>	A hereditary disease that, in its more severe form, can eventually cause crippling lameness and painful arthritis of the hip. The term dysplasia refers to an abnormality in maturation of cells within a tissue.
<b>Endocytosis</b>	A process of cellular ingestion by which the plasma membrane folds inward to bring substances into the cell.
<b>European Quality of Life (EQ-5D) measure</b>	A generic, patient-reported outcome measures that assesses mobility, self-care, usual activity, pain, and anxiety/depression.
<b>Harris Hip Score (HHS)</b>	A disease-specific, clinician-reported outcome measure that assesses a patient's pain, function, deformity, and range of motion, and classifies their overall hip function as excellent, good, fair, or poor based on the sum of all domain scores ranging 0 (poor) to 100 (excellent).
<b>Heterotopic ossification (HO)</b>	Unwanted bone growth in the soft tissues around an implant that causes pain and reduces range of motion.
<b>Hydroxyapatite</b>	A naturally occurring mineral form of calcium apatite and is commonly used as a coating to promote bone ingrowth into prosthetic implants.
<b>Macrophage</b>	A large white blood cell, found primarily in the bloodstream and connective tissue, that helps the body fight off infections by ingesting the disease-causing organism. They are usually immobile but become actively mobile when stimulated by inflammation.
<b>Merle D'Aubigne hip score</b>	A disease-specific, clinician-reported outcome measure that assesses a patient's pain, mobility, and walking ability and classifies their overall hip function as very good, good, medium, fair, or poor based on the sum of all domain scores ranging from 0 (poor) to 12 (very good).
<b>Mont Activity measure</b>	A disease-specific, patient-reported outcome measure that assesses each activity that the patient regularly performs and interprets patients as "low-activity" or "high-activity" based on an established scoring system.
<b>Osteopenia</b>	A condition where bone density is lower than normal. It is considered by many doctors to be a precursor to osteoporosis.
<b>Osteoporosis</b>	The thinning of bone tissue and loss of bone density over time, that leads to an increased risk of fracture, even after minimal trauma.

<b>Osteoarthritis (OA)</b>	Also referred to as degenerative joint disease (DJD), OA is a non-inflammatory, progressive disorder of the joints caused by gradual loss of cartilage and resulting in the development of bony spurs and cysts. It is caused by “wear and tear” on the joint and most commonly affects the knee and hip.
<b>Osteolysis</b>	Dissolution of bony tissues; applied especially to the removal or loss of the calcium of bone.
<b>Osteonecrosis</b>	Destruction and death of bone tissue due to ischemia (disruption of the blood supply), infection, malignant disease, or trauma.
<b>Osteophyte</b>	Unwanted bone growth.
<b>Oxford hip score</b>	A disease-specific, patient-reported outcome measure comprised of 12 questions (1–5 points each) concerning the perception of pain and function. The higher the score, the lower the function.
<b>Oxidative stress</b>	Any of various pathologic changes seen in living organisms in response to excessive levels of cytotoxic oxidizing agents and free radicals, which are generated by various stressors in the environment (e.g., tobacco, alcohol, toxic metals, quinones).
<b>Perthes disease</b>	A degenerative disease of the hip joint, where growth/loss of bone mass leads to some degree of collapse of the hip joint and to deformity of the ball of the femur and the surface of the hip socket. It is typically found in young children, and it can lead to osteoarthritis in adults.
<b>Phagocytosis</b>	A process by which a white blood cell envelopes and digests debris and microorganisms to remove them from the blood.
<b>Quality-adjusted life years (QALYs)</b>	A way of measuring both the quality and the quantity of life lived, as a means of quantifying in benefit of a medical intervention. They are based on the number of years of life that would be added by the intervention.
<b>Rheumatoid arthritis (RA)</b>	A chronic, systemic disease that affects the lining of peripheral joints. It causes inflammatory responses, which destroy the articular cartilage and the tissues around the joints, causing joint deformity.
<b>Sepsis</b>	A serious medical condition characterized by a whole-body inflammatory state and infection due to the overwhelming presence of pathogenic organisms in the bloodstream.
<b>Short Form 36 health survey questionnaire (SF-36)</b>	A generic, patient-reported outcome measure comprised of 8 subscales with various #'s of items: physical functioning, role limitation due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. Each subscale is scored separately (0–100 points); a total score is not used. The lower the score, the greater the disability.

<b>University of California-Los Angeles (UCLA) activity scale</b>	A disease-specific, patient-reported outcome measure that classifies a patient's activity level on a scale from 1 ("bedridden") to 10 ("unrestricted").
<b>Visual Analogue Scale (VAS) for pain</b>	A generic, patient-reported outcome measure in which a patient rates their level of pain on a scale from 0 (no pain) to 10 (worst pain imaginable).
<b>Western Ontario and McMaster Universities OA index (WOMAC)</b>	A disease-specific, patient-reported outcome measure assessing pain, stiffness, and physical function. The higher the total score, the greater the disability.

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