Washington State Health Care Authority

Safety and Efficacy of Hip Resurfacing Procedures

Introduction

A Comparative Effectiveness Review (CER) titled: Hip Resurfacing, was originally released in October 2009 by the Health Technology Clinical Committee and summarized below.

Health Technology Clinical Committee
Findings and Coverage Decision
Topic: Hip Resurfacing
Meeting Date: November 20, 2009
Final Adoption: May 14, 2010

HTCC Coverage Determination

Hip Resurfacing is a **covered benefit with conditions.**

HTCC Reimbursement Determination

- **Limitations of Coverage**
  - Total hip resurfacing arthroplasty as medically necessary as an alternative to total hip arthroplasty when all of the following conditions are met:
    - Diagnosis of osteoarthritis or inflammatory arthritis;
    - Individual has failed nonsurgical management and is a candidate for total hip arthroplasty; and
    - The device is FDA approved
- **Non-Covered Indicators**
  - Not applicable

Health Technology Background

The Hip Resurfacing topic was selected and published in December 2008 to undergo an evidence review process. Total Hip Arthroplasty (THA) was originally designed for older, relatively inactive patients. Historically, 60 to 80 years of age. The need for hip prostheses in younger patients is increasing. By 2011, more than half of all THA's are estimated to be < 65 years. Total Hip Replacement or Total Hip Arthroscopy (THA) is a proven, effective technique that results in excellent pain relief and function in most patients for many years. Hip resurfacing has had its ups and downs—with implants that were introduced in the early 1990s, then withdrawn from the market, and reintroduced a decade later.

History of Hip Resurfacing (HR): Initial design (1970-80s) abandoned due to high failure rates caused by metal-on-polyethylene design. New design (1990s) includes high-carbide cobalt chrome metal-on-metal bearings and hybrid fixation (cemented femoral component, uncemented acetabular component). Design of HR versus THA: THA – femoral head removed and replaced with a metal prosthetic ball; HR – surface of the femoral head is removed and replaced with a metal cap inserted into the femoral shaft; and both HR and THA replace the acetabulum with a metal cup.

Theoretical advantages of HR versus THA -- reduction in stress-shielding as more normal femoral loads are maintained; improved function due to preservation of femoral head; lower morbidity at time of revision surgery than that which occurs in THA patients; lower risk of dislocation; better replication of normal anatomy; and greater range of motion. Indication for HR (FDA) -- Adults who may not be suitable for THA due to increased risk of ipsilateral hip joint revision as a result of their younger age and/or increased activity level, and who have pain due to: Non-inflammatory degenerative arthritis (e.g., osteoarthritis, traumatic arthritis, avascular necrosis with < 50% involvement of the femoral head, or developmental hip dysplasia), or inflammatory arthritis (e.g., rheumatoid arthritis).

Contraindications for HR (FDA) – Infection or sepsis; skeletal immaturity; conditions that could compromise implant stability or postoperative recovery (i.e., vascular insufficiency, muscular atrophy, neuromuscular disease); inadequate bone stock to support the device, including: severe osteopenia or osteoporosis, severe avascular necrosis (> 50% of the femoral head), and multiple femoral neck cysts (< 1 cm in diameter); females of child-bearing age; BMI > 35; known or suspected metal sensitivity; moderate or severe renal insufficiency; and immunosuppression (i.e., AIDS, those receiving high doses of corticosteroids).

Unlike total hip replacement (THA), hip resurfacing does not involve the removal of the femoral head and neck or removal of bone from the femur. Rather, the head, neck and femur bone is preserved in an effort to facilitate future surgery should it be necessary. Hip resurfacing is anatomically and biomechanically more similar to the natural hip joint. Purported benefits include: increased stability, flexibility and range of motion; risk of dislocation; lower and higher activity level possible with less risk than THA; and younger patients needing full joint replacement that are expected to out-live the full replacement may benefit from symptom relief and more bone preservation to tolerate a subsequent replacement surgery later. Questions remain about: unknown longevity and durability of the procedure; reported higher failure rates; appropriate patient selection criteria (e.g., age, gender, tried and failed therapies); impact on long term health outcome; and health system impacts of a surgery designed to delay but not eliminate need for later surgery.

In September 2009, the HTA posted a draft and then followed with a final report from a contracted research organization that reviewed publicly submitted information; searched, summarized, and evaluated trials, articles, and other evidence about the topic. The comprehensive, public and peer reviewed, Hip Resurfacing report is 138 pages, and identified a relatively large amount of literature.

An independent group of eleven clinicians who practice medicine locally meet in public to decide whether state agencies should pay for the health technology based on whether the evidence report and other presented information shows it is safe, effective and has value. The committee met on November 20th, reviewed the report, including peer and public feedback, and heard agency comments. Meeting minutes detailing the discussion are available through the HTA program or online at http://www.hta.hca.wa.gov under the committee section.

Committee Findings

Having considered the evidence based technology assessment report and the written and oral comments, the committee identified the following key factors and health outcomes, and evidence related to those health outcomes and key factors:

1. Evidence availability and technology features

The committee concludes that the best available evidence on Hip Resurfacing has been collected and summarized.

- Severe hip disease is a prevalent and burdensome disease. Current treatment using surgical total joint replacement (THA) is effective and well established in older patients (aged 60 to 80). However, for younger patients the risk of the artificial joint wearing out, and of its' durability for more active lifestyles has led to need for alternative.
- Hip resurfacing (HR) acts to preserve the bone and is thought to be more durable because the femoral head and neck are preserved, thus it may be an ideal "bridge" therapy to delay the need for later hip replacement. HR a more invasive and technically difficult surgery than THA (size and placement of cup; and soft tissue disruption).
- In general, the committee noted that for a significant and invasive surgery, there is a paucity of high quality evidence (three RCTs are small and methodologically challenged and apply to non-FDA approved device) while remaining studies are mostly retrospective cohort studies. Countrywide data registries may provide the best information to date on critical issue of revision and complications. Committee agreed with evidence suggesting that more experienced surgeons have better outcomes and fewer complications, but that training for device implantation is not uniform or reviewed for quality.
- The committee acknowledged that HR has had several iterations, being introduced and then discredited earlier, and now re-introduced with new materials and techniques, and that modern techniques were reviewed here, though lessons from earlier introduction may apply. The committee noted that even modern era HR has had dissemination issues: the Durom was recalled by the FDA due to mislabeling in 2007 and subsequently in 2008, the manufacturer, Zimmer, pulled the device due to surgeons not having adequate training for implantation (this is the device used in the RCTs).

2. Is the technology safe?

The committee concludes that the comprehensive evidence reviewed showed insufficient evidence to conclude that HR is safe: with five committee members voting unproven; three committee members voting equivalent; and two less safe. Key factors to the committee's conclusion included:

- The committee agreed that the main safety question was whether HR provided lower morbidity, lower revision, or lower other complications. In general, evidence demonstrates a higher revision rate; and no difference in morbidity and complications.
- The primary concern is the revision rates, but also identified femoral neck fracture (which leads to revisions) as another important complication.
    - Femoral neck fractures: a primary theoretical advantage of HR is the durability and preservation of the hip bones, so the complication of a femoral neck fracture undermines this advantage and generally requires revision with THA. Femoral neck fracture rates ranged from .4 to 2.6% in short term and up to 5.4% in mid-term follow up. There may be an association with appropriate cup size and with smaller femoral component sizes (generally female) more prone to fracture.
    - Revision rates: overall evidence demonstrates higher revision rates in HR than THA; ranging from 0% to 7.8% in HR group and 0% to 4.3% in THA group. Rates in the Australian Joint Replacement Registry, with longest follow up (7 yr) and includes 125,004 THA and 10,263 HR, indicates that the cumulative revision rate for HR is 4.6% and THA is 3.4%. Analysis also revealed a significant difference in dysplasia patients' revision rates: 2% to 3% THA and 5% to 14% HR. Committee agreed that when needed, revision in THA patients is a more invasive and difficult surgery (with potential for more complications) than HR revision.

- The committee acknowledged the concern regarding metal ions and agreed with the evidence report that more data and longer term information is needed. However, this issue is present with both THA and HR devices that are metal on metal.
- The committee agreed that most perioperative adverse events stemmed from the technique of implantation itself, and reinforced the adequacy of training and experience.

3. Is the technology effective?

The majority of committee members conclude that the comprehensive evidence reviewed indicates that Hip Resurfacing is equivalent to THA.

- The committee agreed that one key assumption is that patients cannot be active with THA; the other key assumption is that relatively younger patients may outlive a prosthesis and will have an easier second surgery (THA) if the first surgery is an HR.
- The physical procedure does conserve bone; clinical expert experience indicates that a second THA surgery is much more complicated than a THA surgery after an HR.
- Overall, there is agreement with the evidence report showing low level data of short to mid-term time frame that functional and pain outcomes are same and activity scores slightly higher for HR.
- From evidence, data demonstrates two procedures are equivalent with tradeoffs in different benefits. Both surgeries appear equivalent at alleviating pain and improving function from severe hip disease.
- HR is a more complicated surgery with higher (double) revision rates, but if successful, can provide a better opportunity for a second THA surgery and may provide slightly better activity level.
- THA is surgically less complex with lower complication and revision rate, but second surgeries, if needed are more difficult and complicated and activity level may be more limited.
- Committee members expressed concern that endorsement of HR may lead to encouragement of more surgery and in patients not previously being considered for surgery. Comparative trials and evidence are limited to patients that would otherwise be treated with THA.

4. Is the technology cost-effective?

The committee split on whether the evidence sufficiently addressed cost: with five members voting that costs are equivalent and five voting unproven (not sufficient data yet).

- Committee acknowledged that the limited agency utilization experience to date indicated that HR and THA are equivalent in cost.
- Committee agrees with the evidence report that most cost studies utilized outdated revision rates (generally lower than showed for HR) and this significantly impacts cost analysis.

5. Evidence about the technology's special populations, patient characteristics and adjunct treatment

- The committee discussed selected population and patient characteristics of gender and component size, as well as dysplasia patients within the revision context.

6. Medicare Decision and Expert Treatment Guidelines

Committee reviewed and discussed the Medicare coverage decision and expert guidelines as identified and reported in the technology assessment report.

- Centers for Medicare and Medicaid Services (clarification at meeting) – does not have a national coverage decision. One local Wisconsin carrier covers HR as medically necessary in select patients requiring primary hip resurfacing due to the following conditions:

- Non-inflammatory arthritis (degenerative joint disease) such as osteoarthritis, traumatic arthritis, avascular necrosis, or dysplasia / developmental dislocation of the hip.
- Inflammatory arthritis, such as rheumatoid arthritis.

- Guidelines – a search of the National Guideline Clearinghouse (NGC) returned zero potential guidelines on HR. No clinical guidelines related to HR procedures were found when the NGC database was searched.
  - Additional searching of the AAOS web site did not yield any guidelines specific to HR.
- The following provides a summary of the National Institute for Health and Clinical Excellence (NICE) guidelines:
  - The NICE 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.
  - Although there is sufficient short-term evidence to conclude that MOM hip resurfacing can be as effective as total hip replacement (THA) in patients less than 55 years, NICE acknowledges that there are no randomized controlled trials comparing MOM hip resurfacing arthroplasty with conventional THA. There are also no long-term (> 10 years) observational data on the outcomes associated with MOM HR devices.

Committee Decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, agency and state utilization information. The committee considered all the evidence and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. The committee concluded that there is sufficient evidence to cover with conditions the use of Hip Resurfacing as an alternative to total hip arthroplasty. Primary considerations were that a majority of committee members concluded evidence demonstrated that HR is equivalent to THA in treating severe hip disease. With equivalence in efficacy at treating the condition demonstrated, this procedure is one where the trade-offs between THA and HR are between potentially better activity levels but higher risk of revision and complications, and these trade-offs should be discussed by patient and physician, within certain limits (the conditions imposed). Cost was not a significant factor.

Based on these findings for Hip Resurfacing, the committee voted 10 to 0 for coverage with conditions.

Hip Resurfacing is a covered benefit with conditions. Total hip resurfacing arthroplasty as medically necessary as an alternative to total hip arthroplasty when all of the following conditions are met:

1. Diagnosis of osteoarthritis or inflammatory arthritis;
2. Individual has failed nonsurgical management and is a candidate for total hip arthroplasty; and
3. The device is FDA approved

Health Technology Clinical Committee Authority

Washington State's legislature believes it is important to use a scientific based, clinician centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority, through its Health Technology Assessment program to gather and assess the quality of the latest medical evidence using a scientific research company and take public input at all stages. Pursuant to RCW 70.14.110 a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State

Health Technology Clinical Committee (HTCC) determines how selected health technologies are covered by several state agencies. RCW 70.14.080-140. These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases their decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to comply with the decisions of the HTCC. Selected technologies are considered for re-review on the basis of new evidence.

Purpose

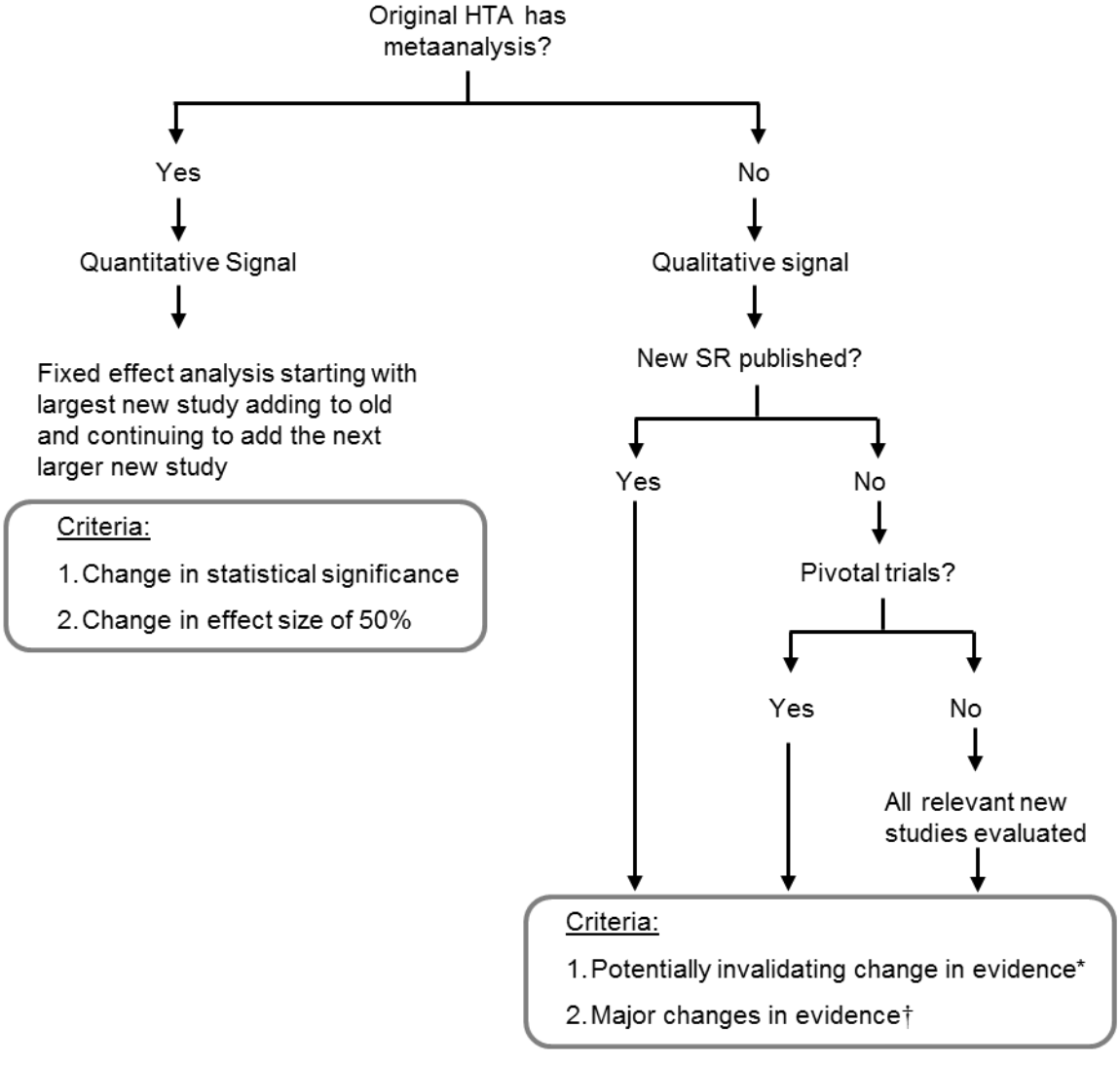
To determine whether the HTA on hip resurfacing performed for the Washington State HCA should be updated based on the presence of preset signal criteria.

Methods

3.1 Check for qualitative and quantitative signals

We followed the Ottawa method of identifying signals for updates, Figure 1. Since this CER did not contain meta-analyses, all signals for this report are qualitative.

Figure 1. Alogrithm of the Ottawa Method of Identifying Signals for SR Updates



*A-1. Opposing findings: Pivotal trial or SR including at least one new trial that characterized the treatment in terms opposite to those used earlier

A-2. Substantial harm: Pivotal trial or SR whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making

A-3. Superior new treatment: Pivotal trial or SR whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm.

†A-4. Important changes in effectiveness short of "opposing findings"
A-5. Clinically important expansion of treatment
A-6. Clinically important caveat
A-7. Opposing findings from discordant meta-analysis or nonpivotal trial

3.2 Literature Searches

Following the paradigm from Figure 1, we sought new systematic reviews published between January 2009 and June 2012 using a similar search strategy as that used for the original report. We searched MEDLINE, EMBASE, the gray literature and the Cochrane Library. We used key words to detect articles

that used the term "hip resurfacing" in combination with "total hip arthroplasty" or "THA." We also checked the FDA website for any updates on this technology. Having identified new systematic reviews, we did not look for additional pivotal studies. Full text of potential articles meeting the inclusion criteria were reviewed by two independent investigators to obtain the final collection of included studies, Figure A-1. Appendix A includes the search methodology for this topic.

3.3 Study selection

We sought systematic reviews that included articles that met inclusion and exclusion criteria similar to the original CER. Having found some, we did not evaluate individual studies.

3.4 Compilation of Findings and Conclusions

For this assessment we sought new systematic reviews published after the search strategy dates employed in the original report. We abstracted the data from the included studies and constructed a demographics table (Appendix B). We also constructed a summary table that included the key questions, the original conclusions, new sources of evidence, new findings, and conclusions based on available signals, Table 1. Our conclusions are based on the following algorithm:

- Original HTA has meta-analysis?
  - No → Examine qualitative signals
- New SR published?
  - Yes → Examine criteria
    1. Potentially invalidating change in evidence
       - A-1. Opposing findings?
       - A-2. Substantial harm?
       - A-3. Superior new treatment?
    2. Major changes in evidence
       - A-4. Important changes in effective short of "opposing findings"?
       - A-5. Clinically important expansion of treatment?
       - A-6. Clinically important caveat?
       - A-7. Opposing findings from discordant meta-analysis or non-pivotal trial?

Results

3.1 Search

The literature search identified 40 titles. After title and abstract review, we further reviewed the full text of 8 publications. The remaining 32 systematic reviews were rejected because they did not include topics of interest or did not include randomized trials in their inclusion. Among the 8 systematic reviews that went on to full text review, 4 were rejected because subjects did not meet the inclusion criteria and/or did not include a comparison of interest (Appendix C). Of the four publications included, 3 were stand-alone systematic reviews and 1 was a systematic review in the context of a Health Technology Assessment. All four were abstracted into an evidence table (Table 2). In addition, we found one FDA executive summary published in 2012 that evaluated the clinical performance as well as adverse events of metal-on-metal hip systems. New data from registries and peer-reviewed journals were investigated in this FDA report specifically looking for potential safety issues, including local complications such as pseudotumors and aseptic lymphocytic vasculitis-associated lesions (ALVAL), early device failure and the need for revision surgery, and systemic complications from metal ion exposure.

3.2 Identifying signals for re-review

Table 1 shows the original key questions, conclusions of the original report, new sources of evidence, new findings, and recommendations of Spectrum Research, Inc. (SRI) regarding the need for update.
Key Question 1: Original conclusions are still valid. New findings confirm HR may have some greater benefits in terms of better functional outcome scores, including Harris Hip Score, UCLA scores, and WOMAC scores, compared with THA, although there is some inconsistency across the studies. HR tends to have better postop activity levels and return to activity, especially in younger, more active patients. Longer-term outcomes are still uncertain.
Key Question 2: There is new evidence to suggest that this section of the report is no longer valid and needs updating. There is evidence reported consistently in all new systematic reviews that the risk of revision surgery following HR is more frequent compared with THA (relative risk ranging from 1.7 to 2.6). Older age, female sex, smaller femoral head size, and primary diagnosis of developmental dysplasia of the hip (DDH) all had greater risk of revision rates. There is also evidence of risks of other complications associated with both HR and THA, including component loosening, aseptic loosening, and heterotopic ossification. The risks of these other complications tend to be higher after HR procedures. There is new evidence regarding metal ion safety for patients with metal-on-metal procedures. Elevated levels of metal ions are concerning in HR patients, although the clinical significance of these elevated levels is still uncertain.
Key Question 3: Original conclusions are still valid. New findings confirm HR is promoted for younger patients with arthritis for whom conventional THA is not expected to last their lifetime. Sex-specific HR revision rates ranged much higher for women (0-28%) compared with men (1-9%).
Key Question 4: Original conclusions are still valid. There is limited evidence evaluating the cost-effectiveness of HR.

4. Conclusions

4.1 *Key Question 1:* What is the evidence of efficacy and effectiveness of hip resurfacing?

4.1a Efficacy

Conclusion is still valid and this portion of the CER does not need updating.

4.1b Effectiveness

Conclusion is still valid and this portion of the CER does not need updating.

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

4.2a Revision

There is evidence to suggest this portion of the CER is no longer valid and needs updating.

4.2b Other complications

There is evidence to suggest this portion of the CER is no longer valid and needs updating.

4.2c Learning curve threshold

Conclusion is still valid and this portion of the CER does not need updating.

4.2d Metal ion safety

There is evidence to suggest this portion of the CER is no longer valid and needs updating.

4.3 *Key Question 3:* Is there evidence of differential efficacy or safety issues with use of hip resurfacing?

4.3a Dysplasia vs. other arthritic conditions

Conclusion is still valid and this portion of the CER does not need updating.

4.3b Osteonecrosis (AVN) vs. other arthritic conditions

Conclusion is still valid and this portion of the CER does not need updating.

4.3c Gender

Conclusion is still valid and this portion of the CER does not need updating.

4.3d Obesity

Conclusion is still valid and this portion of the CER does not need updating.

4.3e SARI Index

Conclusion is still valid and this portion of the CER does not need updating.

4.4 *Key Question 4:* What is the evidence of cost implications and cost effectiveness of hip resurfacing?
Conclusion is still valid and this portion of the CER does not need updating.

5. Recommendations for update

Based on qualitative signals, there is evidence of potentially invalidating change in evidence with respect to A-2, substantial harm. Therefore, the recommendation for update to this HTA is ***HIGH***.

	Yes	No
Potentially invalidating change:		
A-1: Opposing findings		X
A-2: Substantial harm	X	
A-3: Superior new treatment		X
Major change in evidence:		
A-4: Effectiveness short of "opposing findings"		X
A-5: Expansion of treatment		X
A-6: Caveat		X
A-7: Discordant meta-analysis or non-pivotal trial opposing findings		X

Table 1. Hip Resurfacing Summary Table

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from SRI
Key Question 1: What is the evidence of efficacy and effectiveness of total hip resurfacing (HR) compared with conventional total hip arthroplasty (THA)?			
1. a) Efficacy (≤1 year): • 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 **b) Efficacy (>1 year):** • There are no data available to assess efficacy beyond one-year follow-up **2. a) Effectiveness (Short-term, <5 years):** • There is low evidence from studies directly comparing total HR with THA to suggest that short-term (≤5 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 **b) Effectiveness (Mid-term, 5-10 years):** • 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	[1] Jiang (2011); [3] Smith (2010); [4] Walsh (CTAF) (2011);	• There is moderate evidence from two systematic reviews [1,3] and two HTAs [4,5] that HR has some better functional outcome and activity scores than THA with a majority of studies > 1 year f/u ○ HR significantly higher: ▪ ROM of HHS ($p < .001$) and overall HHS ($p = .001$)*; ▪ SF-12 physical component scores ($p = .02$); ▪ UCLA activity level scores ($p = .037$); ▪ Percentage of patients return to heavy or moderate activities (72% vs. 39%; $p = .007$) ▪ Postop functional performance ○ THA significantly higher: ▪ WOMAC scores (indicating poorer functional ability) ($p = .001$); ▪ Greater difficulty in undertaking a step test ($p < .0014$) ▪ Slower recovery in maximal lower limb strength *One study [3] found significantly higher HHS scores for HR patients while the other two studies [1,4] found no significant differences between HR and THA	• This section of the report is still valid and does not need updating
Key Question 2: What is the evidence related to the safety profile of hip resurfacing?			
1. a) Revision (Short-term, <5 years) • 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	[1] Jiang (2011); [3] Smith (2010); [4] Walsh (CTAF) (2011) [5] FDA executive summary (2012)	• There is moderate evidence from two systematic reviews [1,3] and one HTA [4] that revision rates are higher in HR compared with THA patients in short to mid-term follow-up ○ Revision rates ranged from a relative risk of 1.7-2.6 times higher in HR than THA patients in the short to mid-term follow-up ○ Older age (>55 years), smaller femoral head size (≤44mm), and primary diagnosis of developmental dysplasia of the hip	• There is new evidence to suggest that this section of the report is out of date and needs updating

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from SRI
in eight cohort studies varied: 4 favored THA, 2 favored total HR, and 2 reported equal rates **b) Revision (Mid-term, 5-10 years)** • 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 **c) Revision (Long-term, 10+ years)** • There is no evidence comparing long-term revision rates between total HR and THA		(DDH) all had greater risk of revision rates (3.51, 5.87, and 1.94, respectively) • The 2012 FDA executive summary reported: ○ The rate of revision for MoM HR is likely not lower than the rate of revision for other articulating surfaces ○ Rate of revision may be higher with HR compared to THA ○ Women may be more at risk than men ○ There is insufficient evidence to describe differences in revision by age, ion level, and femoral head size	
2. Other complications • Reported risks of other complications in the short-term for total HR are generally low except for heterotopic ossification; the risk of femoral neck 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%	[1] Jiang (2011); [3] Smith (2010); [4] Walsh (CTAF) (2011) [5] FDA executive summary (2012)	• Two systematic reviews [1,3] and one HTA [4] reported mixed results of other complications in HR and THA patients ○ HR had a higher incidence of: ▪ Component loosening at 1 and 5 years, statistically significant at 2 years (RR = 6.10, p = .02) ▪ Aseptic loosening: 3 times greater risk in HR than THA (RR = 3.1, p = .03) ▪ Heterotropic ossification (RR = 1.6, p = .006) ○ THA had a higher incidence of: ▪ Dislocation (p < .001 for one study [3] and p = .19 for another study [1]) • The 2012 FDA executive summary reported: ○ Known local adverse events include localized immune response, adverse local tissue reaction (ALTR), and dislocation ○ The occurrence rates and severity for these events are not well defined in the literature ○ Pain and tissue necrosis were noted with revision ○ Insufficient evidence to describe systemic outcomes such as neurotoxicity, cardiomyopathy, endocrine symptoms, and cancer	• There is new evidence to suggest that this section of the report is out of date and needs updating

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from SRI
		○ In February 2011, FDA posted a public health communication on its website containing a summary of the safety issues with the MoM devices, as well as providing considerations to orthopaedic surgeons, general primary care physicians, and patients who had or will have a HR procedure ○ In May 2011, FDA issued orders for postmarket surveillance studies (e.g., "Section 522 studies") to each manufacturer of MoM THR systems requiring them to submit a study protocol to the FDA that addresses specific safety issues related to these devices.	
3. Learning curve threshold • A number of studies identified that the rate of major complications (including femoral neck fracture and revisions) decrease as surgeons gain experience performing total HR. The studies suggested that experience is associated with improved surgical technique and patient selection. However, with respect to identifying the number of procedures necessary for improved outcome, no consistent threshold was identified	[4] Walsh (CTAF) (2011)	• Hip resurfacing is considered by most to be a more challenging operation for the surgeon than THA and requires specialized training and a significant learning curve	• This section of the report is still valid and does not need updating
4. Metal ion safety • 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.	[2] Kuzyk (2011) [4] Walsh (CTAF) (2011) [5] FDA executive summary (2012)	• One systematic review [2] and two HTAs [4,5] report an increase level of metal ion levels in the blood for HR patients ○ One study [2] found mixed results in their review, reporting one LoE III study found HR produced significantly greater serum chromium and cobalt ions that THA, while five other LoE III studies found no significant difference between the two ○ One study [4] reported an elevation of ion levels in HR patients that fluctuated over time ○ Elevated levels of serum metal ion concentrations were reported in MoM hip articulations [5], however there was no difference in ion concentrations between MoM HR and MoM THA • The 2012 FDA executive summary reported:	• There is new evidence to suggest that this section of the report is out of date and needs updating

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from SRI
		○ MoM patients demonstrated higher Co and Cr ion levels in comparison to the reference groups at the early (6 months – 2 years) and later (3-33 years) stages of having the implant ○ Bilateral MoM HR patients have higher levels of metal ions in comparison to unilateral patients ○ Patients with high Co and Cr levels are at higher risk for revision	
Key Question 3: Is there evidence of differential efficacy or safety issues with use of hip resurfacing?			
1. Dysplasia vs. other arthritic conditions • 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.	[4] Walsh (CTAF) (2011)	• MoM HR has been promoted for younger patients with end-stage osteoarthritis of the hip or rheumatoid arthritis, traumatic arthritis, hip dysplasia, or avascular necrosis for whom conventional THA is not expected to last their lifetime	• This section of the report is still valid and does not need updating
2. Osteonecrosis (AVN) vs. other arthritic conditions • There is low evidence to suggest that short-term revision rates are slightly higher in patients who receive total HR for a primary diagnosis of ostenecrosis (AVN) compared with patients of primary osteoarthritis. The 5-year cumulative revision percent for osteonecrosis is two times greater in those receiving total HR compared with THA (6% vs. 3%) in one registry study and rates are the same in one small prognostic study	[4] Walsh (CTAF) (2011)	• One expert points out that the posterior approach favored in resurfacing devascularizes the femoral head, possibly permanently, potentially leading to avascular necrosis over time	• This section of the report is still valid and does not need updating
3. Gender • There is moderate evidence from three registries that 3- and 5-year revision rates are higher in females than in males (hazard ratios range	[5] FDA executive summary (2012)	• Sex-specific revision rates ranged between 0 and 27.6% for women and 1.4% and 8.97% for men	• This section of the report is still valid and does not need updating

Conclusions from CER Executive Summary	New Sources of Evidence	New Findings	Conclusion from SRI
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.		• One study (Ollivere, 2009) indicated a relative risk of revision 4.94 (95% CI, 1.33-18.31) times as high among women compared to men	
4. 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.			• This section of the report is still valid and does not need updating
5. SARI Index • Two low quality studies evaluated the effect of the SARI index on total HR. Both suggest a SARI score > 3 preoperatively results in an increased risk of early complications and revision.			• This section of the report is still valid and does not need updating
Key Question 4: What is the evidence of cost implications and cost effectiveness of hip resurfacing?			
Cost Effectiveness • 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.			• This section of the report is still valid and does not need updating

References:

[1] Jiang, Y., K. Zhang, et al. (2011). "A systematic review of modern metal-on-metal total hip resurfacing vs standard total hip arthroplasty in active young patients." J Arthroplasty **26**(3): 419-426.

[2] Kuzyk, P. R., M. Sellan, et al. (2011). "Hip resurfacing versus metal-on-metal total hip arthroplasty - are metal ion levels different?" Bull NYU Hosp Jt Dis **69 Suppl 1**: S5-11.

[3] Smith, T. O., R. Nichols, et al. (2010). "The clinical and radiological outcomes of hip resurfacing versus total hip arthroplasty: a meta-analysis and systematic review." Acta Orthop **81**(6): 684-695.

[4] Walsh, J. (2011). "Metal on Metal Hip Resurfacing as an alternative to Total Hip Arthroplasty." California Technology Assessment Forum Oct 2011: 1-30.

[5] FDA Executive Summary (2012). "Metal-on-Metal Hip Implant Systems." Food and Drug Administration Memorandum, June 2012: 1-58.

Appendix A.

The detailed strategy below is presented in Medline and EMBASE syntax.

Search Strategy
(2009 – June 2012)
Limited to English language, human population

Database: MEDLINE

1 ("Surface replacement arthroplasty" AND HIP) OR "hip resurfacing" OR ((MoM OR "METAL ON METAL") AND HIP)
2 (Hip[TI] AND (Resurfacing[TI] OR Metal-On-Metal[TI] OR Birmingham OR Conserve Plus OR Wagner Resurfacing)
3 "Finite Element Analysis"[Mesh] OR Engineer*
4 "Case Reports "[Publication Type] OR cadaver OR IN VITRO
5 #1 OR #2
6 #5 NOT (#3 OR #4)
7 limit English/abstracts
8 ("Comparative Study "[Publication Type] OR "Clinical Trials, Phase III as Topic"[Mesh])
9 #7 AND #8
1 ("Surface replacement" AND HIP[TI]) OR (hip[TI] AND resurfacing*[TI])
2 "Finite Element Analysis"[Mesh] OR Engineer*
3 "Case Reports "[Publication Type] OR cadaver OR IN VITRO
4 #1 NOT (#2 OR #3)
5 limit English/abstracts
6 SAFE* OR COMPLICATION*
7 #5 AND #6

Database: EMBASE

1 (("surface replacement arthroplasty" and hip) or "hip resurfacing" or ((mom or "metal on metal") and hip)).mp.
2 (Hip and (Resurfacing or Metal-On-Metal or Birmingham or Conserve Plus or Wagner Resurfacing)).mp.
3 ("Finite Element Analysis" or Engineer).mp.
4 1 or 2
5 limit 4 to abstracts
6 limit 5 to (human and (article or report or "review"))
7 comparative study/ or clinical trial/
8 6 and 7
9 perioperative complication/ or peroperative complication/ or postoperative complication/ or complication/ or safety.mp.
10 6 and 9
11 "cost utility analysis"/ or "cost benefit analysis"/ or "cost minimization analysis"/ or "cost"/ or "cost effectiveness analysis"/
12 6 and 11

Parallel strategies were used to search the Cochrane Library and others listed below. Keyword searches were conducted in the other listed resources.

Electronic Database Searches

The following databases have been searched for relevant information:

Agency for Healthcare Research and Quality (AHRQ)

Cumulative Index to Nursing and Allied Health (CINAHL)

Cochrane Database of Systematic Reviews (through 2009, Issue 2)

Cochrane Registry of Clinical Trials (CENTRAL) (through 2009, Issue 2)

Cochrane Review Methodology Database (through 2009, Issue 2)

Computer Retrieval of Information on Scientific Projects (CRISP)

Database of Reviews of Effectiveness (Cochrane Library) (through 2009, Issue 2)

EMBASE (1985 through July 23, 2009)

PubMed (1975 through July 23, 2009)

Informational Network of Agencies for Health Technology Assessment (INAHTA)

NHS Economic Evaluation Database (Cochrane Library through 2009, Issue 2)

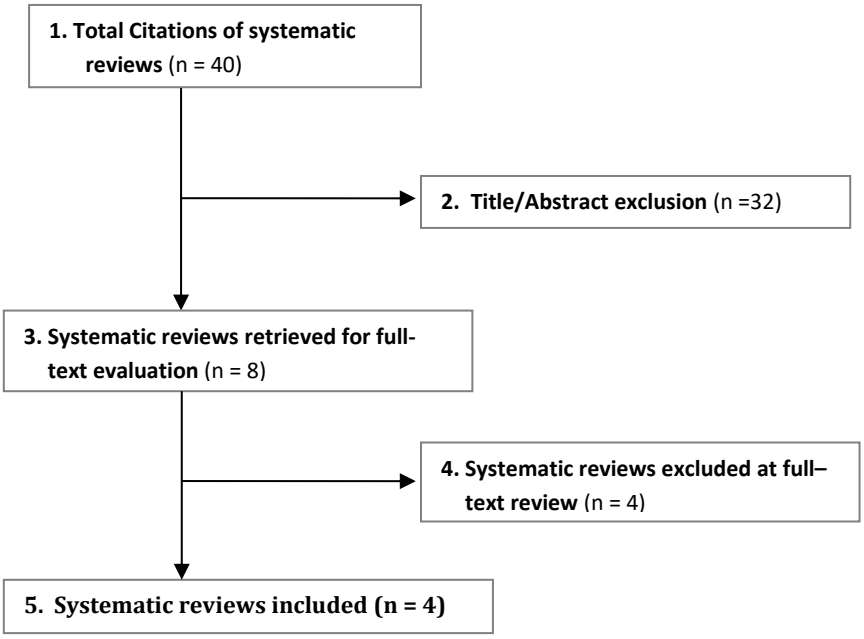
HSTAT (Health Services/Technology Assessment Text)

EconLIT

Additional Economics, Clinical Guideline and Gray Literature Databases

AHRQ- Healthcare Cost and Utilization Project
Canadian Agency for Drugs and Technologies in Health
Centers for Medicare and Medicaid Services (CMS)
Food and Drug Administration (FDA)
Google
Institute for Clinical Systems Improvement (ICSI)
National Guideline Clearinghouse

Figure A-1. Flow chart showing results of literature search



Appendix B. Abstraction table

Table B-1. Hip resurfacing systematic reviews abstraction table

Author	Studies; Demographics	Results	Conclusion
Jiang (2011)	RCT I: 3 RC III: 1 N = 968 MoM HR n = 503 Male: NA Age: NA Comparator: Standard THA (n = 465)	**Efficacy:** • The WOMAC and Merle d'Aubigne-Postel scales detected no significant differences • The UCLA scores showed significantly higher activity levels in the HR group than in the THA group (6.3 vs. 7.1; *P* = .037) and a greater percentage of HR patients who had returned to heavy or moderate activities (72% vs. 39%; *P* = .007) • Total HHS, function, and pain scores were similar at 2 years after surgery • HR group had higher activity scores than the THA group (14 vs. 13; *P* < .001) **Safety:** • Higher incidence of revision in the MoM group than in the THA group (RR 2.60; 95% CI, 1.31-5.15, *P* = .006) • THA group had a higher incidence of dislocation than the HR group at 1 year (RR, 0.14; 95% CI, 0.01-2.70; *P* = .19) and 2 years (RR, 0.33; 95% CI, 0.05-2.25; *P* = .26) after surgery, although no statistically significant differences between the two groups • No significant differences in mortality rate 3 years after surgery (RR, 1.05; 95% CI, 0.24-4.66; *P* = .95) • Femoral neck fracture was a complication unique to HR due to surgery technique • HR showed higher incidences of component loosening at 1 and 5 years after surgery; this difference was only significant at 2 years (RR, 6.10; 95% CI, 1.41-26.39; *P* = .02) • No significant difference in the rate of deep hip joint infection • Significantly shorter mean surgical time in the THA group (85 minutes; range, 50-150 min) than in the HR group (101 min; range, 65-155 min; *P* < .001) • No significant differences between mean incision length, mean volume of blood loss, or amount of acetabular bone removal	• Increased rates of revision, femoral neck fractures, and component loosening among patients who received modern MoM HR • No significant differences in the rates of mortality, dislocation, or deep hip joint infection between the two groups • Hip function scores were similar, but the HR group showed higher activity levels • There is insufficient evidence to determine whether modern MoM HR offers clinical advantages over standard THA in active, young patients
Kuzyk (2011)	RCT I: 2 RC III: 7	**Safety:** *HR vs. 28 mm MoM THA:*	• HR tends to produce a lesser degree of serum cobalt ions than MoM THA procedures

Author	Studies; Demographics	Results	Conclusion
	N = 1002 hip resurfacings Male: 59% Age: 54.5 (range, 25-85) years Comparator: MoM THA (n = 473)	• One level III study found that HR produced significantly greater serum chromium and more cobalt ions than MoM THA • The other five level III studies and one level I study found no significant differences between the groups • Pooling data from 5 studies (taking out 2 outliers): • Cobalt ion levels had an almost significant mean difference (p = .05) between HR and MoM THA of -0.28 µg/L (95% CI of -0.56 to 0.00) • Cobalt ion levels tended to be lower in the HR group than the MoM THA group, while chromium levels were not different between groups *HR vs. Large Head MoM THA* • All 3 studies found higher cobalt ion levels in MoM THA than HR	• The difference noted in most studies is small and may not represent a clinically significant difference
Smith (2010)	RCT: 10 PC: 28 RC: 8 N HRs (patients) = 3,799 (3,279) Male: 66% Age: 51 ± 7 years Comparator: THA n THAs (patients) = 3,282 (2,910)	**Efficacy:** • Significantly higher WOMAC score for THA patients, indicating poorer functional ability (MD = -2.4, CI: -3.9, -0.9; p = .001) • HR better ROM of HHS (MD = -0.05, CI: -0.1, -0.03; p < .001) and overall HHS (MD = 2.5, CI: 1.2, 3.8; p = .001) compared to THA • THA had significantly greater difficulty in undertaking a step test task than HR (RR = 0.3, CI: 0.1, 0.6; p < .0014) • No significant difference in Merle d'Aubigne index, UCLA, Oxford hip score, or hop test results (p > .05) • Difference in SF-12 physical component scores (MD = 3.5, CI: 0.6, 6.5; p = .02), but not in mental component or EQ-5D scores (p > .05) • No statistically significant difference regarding mean incision length, pain scores, presence of groin or thigh pain, and patient satisfaction outcomes • Radiological outcome: higher presence of heterotropic ossification (RR = 1.6, CI: 1.2, 2.1; p = .006) in HR than in THA **Safety:** • Risk of revision surgery following HR almost doubled compared to THA (RR = 1.7, CI: 1.2, 2.5; p = .003) • Three times greater risk of aseptic loosening in HR than in THA (RR = 3.1; 95% CI: 1.1, 8.5; p = .03)	• On the basis of the current evidence base, HR may have better functional outcomes than THA, but the increased risks of heterotropic ossification, aseptic loosening, and revision surgery following HR indicate that THA is superior in terms of implant survival

Author	Studies; Demographics	Results	Conclusion
		• Reduced incident of dislocation following HR (RR = 0.2, CI: 0.1, 0.5; p < .001) • No significant differences regarding the incidence of postoperative fracture, VTE or pulmonary embolism, joint infection, acetabular component mal-positioning, trochanteric malunion, peroneal or sciatic nerve palsy, trochanteric bursitis, clinical leg length discrepancy, squeaking, positive Trendelenburg sign, or mortality between HR and THA (p > .05) • No significant difference between the adverse reaction to metal debris	
Walsh CTAF (2011) (including 2007 and 2010)	RCT: 6 Cohorts: 9 articles (6 studies) Registries: 2 N = 926 HRs Male: NA Age: NA Comparator: THA (n = 769)	**Efficacy:** • No difference in satisfaction or complication rates, but MoM HR group had better postop functional performance • No difference in quality of life outcomes between MoM HR and large diameter MoM THA • No difference in gait speed, postural balance, and clinical scores between HR and large diameter THA; both groups achieved similar function to a healthy control group by 3 months • Slower recovery in maximal lower limb muscle strength in THA compared to MoM HR • No significant difference in gait outcomes between THA and MoM HR • No difference in HHS (including pain, function, satisfaction, and ROM) **Safety:** • Increased serum cobalt and chromium ion levels in both groups, but highest in MoM large head THA • The two main types of adverse outcomes are 1) early failure and revision rates and 2) elevated levels of metal ions in the blood	• Although HR may have some benefits, particularly in younger, active individuals, there are also potential risks • Revision rates appear to be higher in patients receiving HR procedures than those receiving THA • High revision risk in women • Elevated levels of metal ions risk in HR • Although the clinical significance of these elevated ion levels is still uncertain, they are implicated in the development of ALVAL, often seen in aseptic failure of HR • Pseudotumors appear to be more severe manifestation of ALVAL • There is clearly no evidence that the potential benefits of HR outweigh the potential risks

Abbreviations: ALVAL: aseptic lymphocytic-vasculitis-associated lesions; CoC: ceramic on ceramic; CTAF: California Technology Assessment Forum; f/u: follow-up; HHS: Harris hip score; HR: hip resurfacing; MoM: metal-on-metal; NA: not available; NICE: National Institute of Clinical Excellence; PC: prospective cohort; RC: retrospective comparative; ROM: range of motion; SF-12: short form-12; THA: total hip arthroplasty; WOMAC: Western Ontario and McMaster Universities index

Appendix C. Excluded articles after full-text review

Table C-1. List of excluded articles after full-text review

Study	Reason for Exclusion:
Corten K, Ganz R, Simon JP, Leunig M. Hip resurfacing arthroplasty: current status and future perspectives. Eur Cell Mater. 2011;21:243-258	Important RCTs missing
van der Weegen W, Hoekstra HJ, Sijbesma T, Bos E, Schemitsch EH, Poolman RW. Survival of metal-on-metal hip resurfacing arthroplasty: a systematic review of the literature. J Bone Joint Surg Br. Mar 2011;93(3):298-306	Purpose to evaluate the survival of HR using primarily case-series
van Gerwen M, Shaerf DA, Veen RM. Hip resurfacing arthroplasty. Acta Orthop. Dec 2010;81(6):680-683	Important RCTs missing
Zywiel MG, Sayeed SA, Johnson AJ, Schmalzried TP, Mont MA. Survival of hard-on-hard bearings in total hip arthroplasty: a systematic review. Clin Orthop Relat Res. Jun 2011;469(6):1536-1546	Purpose to evaluate the survival of hard on hard bearings in total hip arthroplasty; HR a subset subsumed in other SRs