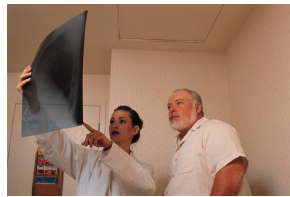
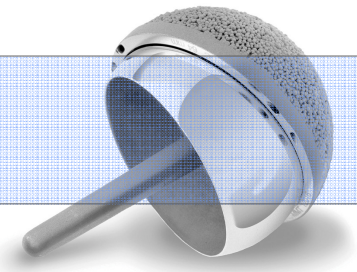


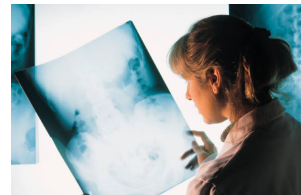
Metal-On-Metal Hip Resurfacing for Young Active Adults with Degenerative Hip Disease

November 1, 2006



Life is Movement

ALBERTA BONE & JOINT HEALTH INSTITUTE



ALBERTA
BONE & JOINT
INSTITUTE HEALTH

www.albertaboneandjoint.com



TABLE OF CONTENTS

The Alberta Bone & Joint Health Institute 2

Request 2

Distribution of Technote 2

Abbreviations 3

Background 4

 Degenerative joint diseases 4

 Alberta rates of hip replacement 4

Conventional Hip Replacements 5

 Metal-on-Polyethylene hip replacements 5

 Ceramic-on-Ceramic hip replacements 5

Metal-on-Metal Hip Resurfacing 6

 Metal-on-metal hip resurfacing 6

Canada Regulatory Status for Hip Resurfacing Devices 7

Review of Literature 8

 Results of literature search 8

 Systematic reviews and health technology assessments 8

 Experimental studies 10

 Observational studies 13

 Industry submitted reports 25

Complications and Risk Factors Associated with Hip Resurfacing 26

 Failure rates and revisions 26

 Osteolysis 28

 Femoral neck fractures 28

 Dislocations 28

 Osteoporosis 28

 Metal ion release and safety 29

 Hypersensitivity 31

 Fertility and reproduction 31

 Learning curve 31

 Surface arthroplasty risk index 32

Alberta Hip Improvement Project (HIP) 33

 Study design and ethical concerns 33

 Ethical approvals 33

 Study background 33

 Alberta HIP Advisory Committee 36

 Analyses at year 2 36

 General cohort characteristics 36

 3 month effectiveness outcomes 37

 Readmissions and metal ion findings 38

 Cost and cost effectiveness results 40

 Summary of findings to date 45

 Limitations to study findings 45

Recommendations for MOM hip resurfacing 46

Value and importance of independent post marketing research 47

Next Steps 47

Appendix 1 48

Reference List 49



The Alberta Bone and Joint Health Institute (ABJHI)

The ABJHI was founded in 2004 as a not-for-profit centre of excellence for the advancement of bone and joint patient treatment, research and education. The ABJHI vision is to significantly improve bone and joint health and healthcare for all Albertans to a standard that is the best in the world and a model for others to emulate. Goals of the ABJHI include creating an innovative and sustainable system of patient-centered care that efficiently provides the best quality of bone and joint health to all.

Request

This technote reports, critiques, and summarizes the current evidence and status of the use of metal-on-metal hip resurfacings for adults with degenerative hip disease in Alberta.

Distribution of Technote

This document has been circulated to the following:

- The Alberta HIP Advisory Committee
- Calgary Health Region
- Capital Health Authority
- David Thompson Health Region
- Alberta Health and Wellness

Recommendations are provided in the following context:

This technote was developed and written after careful consideration of the available evidence. This technote does not override the individual responsibility of health professionals to make appropriate decisions for their individual patients, in consultation with the patient and/or guardian or care giver.

Technotes are brief reports that draw on limited reviews of evidence and research, analysis of relevant literature, expert opinion and regulatory status where appropriate. They are not subject to an external review process.



Abbreviations

ABJHI	Alberta Bone and Joint Health Institute
AHW	Alberta Health and Wellness
BHR	Birmingham Hip Replacement
BMD	Bone Mineral Density
CIHI	Canadian Institute for Health Information
COC	Ceramic-on-Ceramic
DJD	Degenerative Joint Disease
DXA	Dual Energy X-ray Absorption
FDA	Food and Drug Administration
FFS	Fee for Service
HIP	Hip Improvement Project
HRA	Hip Resurfacing Arthroplasty
HRQL	Health-related Quality of Life
HTA	Health Technology Assessment
HUI-3	Health Utilities Index Mark-3
LOS	Length of Stay
MOM	Metal-on-Metal
NICE	National Institute for Clinical Excellence
OA	Osteoarthritis
QALYs	Quality-adjusted Life Years
OR	Operating Room
PMA	Postel Merle d'Aubigne
RA	Rheumatoid Arthritis
RCT	Randomized Control Trial
SF-36	Short-Form-36 Health Assessment Questionnaire
SrCr	Serum Chromium
SrCo	Serum Cobalt
THR	Total Hip Replacement
UrCr	Urine Chromium
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index



Degenerative Joint Diseases

Degenerative joint disease (DJD) results in the deterioration of cartilage and underlying bone that support weight-bearing joints and is directly associated with chronic pain and stiffness.^{1,2} The main cause of DJD is osteoarthritis (OA), which in Alberta affects 1 in 10 people (approximately 278,000).³ That estimate does not include rheumatoid arthritis (RA), which affects 1 in 100 Albertans,³ avascular necrosis, congenital hip dysplasia, or arthritic trauma as other causes of DJD.^{1,4} OA, one of the most common forms of arthritis, is caused by the breakdown of cartilage and disruption of adjacent bone and primarily affects the hips, knee, hands and spine. Under normal conditions cartilage acts as a shock absorber between adjoining bones allowing for smooth movement, but as OA progresses the joint cartilage splits, fibrillates, and wears away, with the underlying bones becoming thicker and stiffer causing pain as the joint moves, especially in weight bearing joints such as the hip and knee. Another cause for chronic pain, inflammation and reduced mobility results from irritation of the surrounding joint tissue from pieces of cartilage that break off.

RA is an autoimmune disease causing a person's immune system to attack the lining of joints, producing inflammation and swelling, leading to pain and discomfort. Avascular necrosis is a condition that prevents blood flow to bones causing the bone tissue to die and collapse. Avascular necrosis generally affects the ends of the femur causing the joint spaces to collapse, which leads to symptoms similar to OA. Congenital hip dysplasia is a birth defect that causes malformation the hip joint. Trauma to a joint can cause cartilage damage that can lead to arthritis. As DJD, more specifically OA advances, considerable functional and symptomatic problems arise and which significantly curtail a person's activity level. As the population ages and the prevalence of DJD and OA increases, national and international concern is escalating.

Alberta Rates of Hip Replacement

Over the past 40 years, total hip replacements (THR) have been recognized as one of the most effective surgical interventions to relieve pain and improve function for patients with severe OA of the hip, after all conservative treatment options are depleted, such as activity modification, analgesic and anti-inflammatory medication, exercise, and weight

reduction.^{1,2,3,4,5} Although pain is the primary indication for a THR, disability and reduced function are increasingly seen as additional indications. Between 2000/2001 Alberta reported the highest rate of THR in Canada to the Canadian Institute for Health Information (CIHI), and as the population ages, the rate and overall number of total hip replacements are expected continually to rise. Between 1994/1995 and 2000/2001 there was an 11.5% increase in the number of total hip replacements in Alberta and a growing number of these procedures were performed on younger patients (Figure 1). According to a report released by CIHI, the number of total hip replacements on people under the age of 55 had increased by 30% in that 7 year period. Although 70% of total hip replacements were performed on people over the age of 65, the increasing trend for total hip replacements in the younger age groups is important to monitor as these patients are more likely to outlive their devices and, subsequently, require a surgical revision.

There are excellent long-term clinical data on the effectiveness of total hip replacements.⁶ The overall results conclude that elderly people (>65 years) have a decrease in pain and increased mobility post-surgery.^{1,2} Although the outcomes with elderly patients receiving a THR are good, of note THR is a fairly invasive procedure can be associated with bone loss and weakening of existing bone and may only last 10 years before the patient needs another new artificial hip (revision hip replacement).

By comparison, the treatment of younger patients with severe hip disease with a conventional THR presents a challenge. There is growing evidence to suggest that younger patients (particularly those with active lifestyles) experience high implant failure rates with the need of revision. Long-term results indicate that THR in younger patients may be associated with overall revision rates up to 25–30% within 15 years⁷⁻⁹, with specific subgroups of young active patients, primarily with secondary OA, experiencing rates of 50%.^{10,11} That contrasts with the revision rates of less than 5% at 10 years for older patients who receive THR.¹² Furthermore, patients that are expected to outlive the lifespan of the prosthesis often must wait and rely on non-surgical interventions before they reach an age that is considered appropriate for THR. Moreover, revision hip replacements are more difficult to perform and generally have poorer outcomes than the primary replacement.^{1,13}

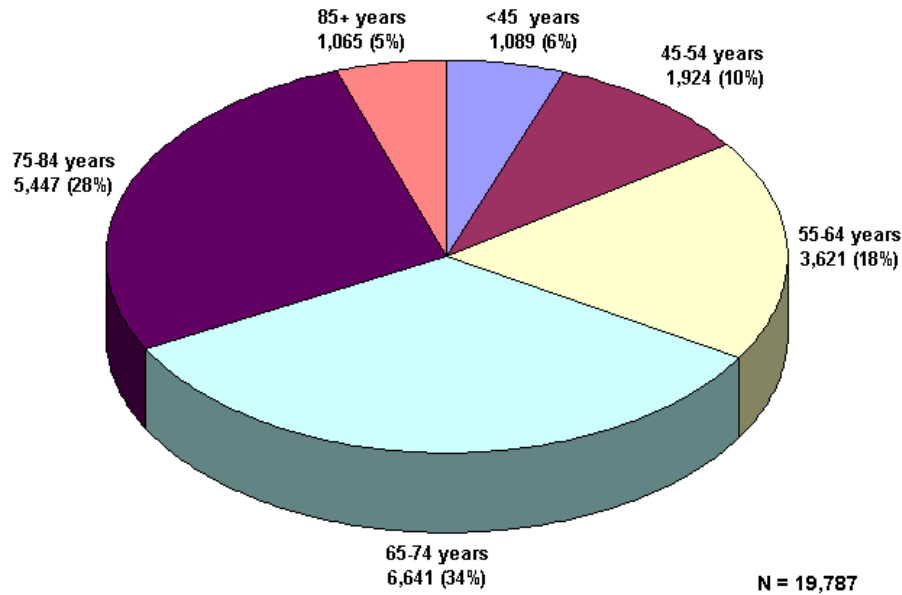


Figure 1: Distribution of THR by patient age 2000/2001 in Canada

Conventional Hip Replacements Metal-on-Polyethylene THR

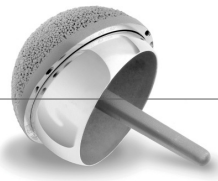
Although many different prostheses are available, they generally consist of three parts: an ultra-high molecular weight polyethylene cup that replaces the hip socket, a metal ball to replace the femoral head, and a metal stem that is inserted into the shaft of the femur to add stability to the prosthesis. Currently, the most common bearing surface used in THR is metal-on-polyethylene. With a traditional THR the diseased bone in the hip joint, femoral head, part of the upper femur and the acetabulum, are removed and replaced with a prosthesis device.

The problems with polyethylene wear and reaction to debris are recognised as major concerns in polyethylene on metal THR. Consequently, the development of alternative device material with lower wear rates have become an alluring option, especially for young and active patients. Although developed in the 1970's in Europe, in February 2003, the Food and Drug

Administration (FDA) approved two new hip replacement devices both constituted of ceramic instead of the conventional metal and high-density polyethylene. The ceramic surface is smoother and, purportedly, the device produces less friction with activity and will take a longer time to revision compared to the traditional THR.

Ceramic-on-Ceramic THR

Three clinical studies have evaluated the performance of a ceramic-on-ceramic (COC), also known as alumina-on-alumina, bearing surfaces in THR. Hamadouche and colleagues¹⁴ retrospectively studied 108 consecutive alumina-on-alumina bearing surfaces in THR at 20-years follow-up. Both components (femoral head and acetabular cup) were cemented in 85 hips, 29 hips were implanted without cement, and 4 hybrids (COC with a conventional stem) were used. The mean age of the patients in the series was 62.2 years. At 20 years follow-up, 46 patients (comprising 51 hips) were still alive and had not undergone revision, 25 patients (25 hips) had



undergone revision, 29 patients (30 hips) had died from unrelated causes, and 12 patients (12 hips) were lost to follow-up. Using revision as the end point, the survival rate was 88.5% for cementless sockets vs. 59.7% for cemented sockets ($p = .0058$). Survival of the stem was 88.0% for cementless stems vs. 83.5% for cemented stems (log-rank, $p = .65$). On X-ray, no wear could be measured, and osteolysis was not significant. The authors concluded that uncemented sockets performed significantly better than cemented sockets, and the absence of osteolysis in this long-term study was most likely related to a low wear rate. Accordingly, they proposed that ceramic-on-ceramic bearing surface in THR was a safe option with good long-term results.

D'Antonio and colleagues¹⁵ presented the results of a multicentre, prospective, randomized study comparing alumina-on-alumina ceramic bearing surfaces to cobalt-chrome-on-polyethylene bearing surfaces. Patients with a preoperative diagnosis of non-inflammatory arthritis (mean age, 53 years) presented with 514 hips for THR; 349 received the alumina-ceramic bearing, and 165 received the cobalt-chrome-on-polyethylene bearing. All patients received the same press-fit hydroxyapatite coated femoral stem. At a minimum of 2 years follow-up (mean, 2.9 years), there was no significant difference in clinical performance between the patient cohorts. With the exception of one post-traumatic femoral stem subsidence, there was no loss of fixation of implants. No ceramic fracture or alumina ceramic bearing failure occurred. According to the authors, the alumina-on-alumina ceramic bearings had superior wear resistance and did not carry a significant risk of ion release.

Another study reported by DiCaprio and colleagues¹⁶ evaluated the medium-term (range, 5.8 to 14.8 years; mean, 10.2 years) follow-up results of 27 consecutive COC THR in a young population (range, 16 to 55 years; mean, 36 years). The preoperative diagnoses included 13 patients with osteoarthritis, 11 with avascular necrosis, and 1 with rheumatoid arthritis. All cups were of the same design. The stems were all uncemented; 16 were straight proximal-porous, 9 were straight non-porous, and 2 were tapered non-porous. Five hips were revised, 4 for mechanical failure and 1 for infection. Of the 4 THR revised for mechanical reasons, 1 was due to a cup fracture at 5 years, and the other 3 were due to loosening at 10.6, 10.9, and 11.0 years. Stem revision was performed in 2 of those 4 revisions because of loosening at 10.6 and 11.0 years. Of the 22 THR that remained in place, the mean Harris Hip score was 38 preoperatively, 94 at 2-year follow-up, 92 at 5-year follow-up,

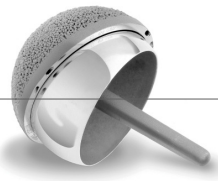
and 88 at 10-year follow-up. Twenty of the 22 remaining cups were stable, and 2 were loose; 23 of the 24 remaining stems were stable, and 1 was loose. The authors reported no incidence of either acetabular or femoral radiographic osteolysis and concluded that ceramic-on-ceramic articulation was a good choice for young patients with high activity demands.

Although alumina wear is well recognised, the use of COC hip replacements is limited due to the risk associated with ceramic component fracture. In the 1990's ceramic devices were recalled due to the higher than expected fracture rates¹⁷, however the introduction of the newer ceramics has rendered this a very uncommon complication.¹⁸ Although COC bearings have demonstrated very low in vivo wear, as with other foreign particles, ceramic debris can induce granulation tissue along the implant bone interface, potentially resulting in osteolysis and aseptic loosening^{19,20}. In the past, breakage of ceramic articulations was a significant problem, but there are no studies in the literature reporting systemic adverse effects with the use of COC THR.

COC bearings appear to be a safe option for young and active patients, demonstrating a very low wear rate and good clinical results, but this does not come without a cost. The COC THR are more costly compared to traditional polyethylene on metal THR devices. Additional long-term studies are needed to elucidate completely the role of COC articulation in THR. In addition to the evidence in the literature, the Alberta Orthopaedic Society, Alberta Health and Wellness (AHW) and the Alberta Regional Authorities have identified the need for additional research of the alternative hip bearing surfaces, including COC THR, to understand more fully the short term and long term effectiveness, safety and cost effectiveness of alternative bearing THR devices.

Metal-on-Metal Hip Resurfacing

Metal-on-metal (MOM) Hip Resurfacing (also known as resurfacing arthroplasty, surface replacement, or alternative bearing) surgery has recently been introduced as a bone-conserving hip replacement option for patients. Hip resurfacings are offered in MOM bearing surfaces. This form of arthroplasty involves the replacement of the both femoral head surface and acetabular cup with metal surfaces.



There are a number of proposed advantages of MOM hip resurfacing over conventional THR.²¹ These advantages include minimal bone resection and conservation of femoral bone, and maintenance of normal femoral loading and stresses by elimination of the conventional long stem on a femoral prosthesis. MOM is thought to allow higher levels of post-surgery activity with fewer risks than a conventional THR, where the increased stability would allow for physical activities with a more nearly normal range of motion of the hip. The current generation of MOM hip resurfacing devices feature improvements in metallurgy, bearing geometry, fixation techniques and produce significantly less wear debris than the previous generation of MOM devices.²²

Hip resurfacing is not a new concept; the first hip resurfacing using a teflon-on-teflon bearing surfaces were implemented in the early 1950s by Charnley²³, but due to rapid wear and high failure rates, that approach was discontinued.²⁴ The next hip resurfacing was designed in 1960 by Townley²⁵ using a metal-on-polyurethane,; it too was discontinued because of excessive wear. Years after those initial attempts at hip resurfacing several more attempts were made using high density polyethylene-on-metal, cobalt chromium and ceramic; all of these failed due to cup loosening and excessive wear.^{26,27,28,29} In the late 1980s MOM total hip replacements, with improved wear characteristics, were being widely implemented in Europe³⁰, which lead to the re-design of hip resurfacings using

MOM bearings. The first re-design was introduced in 1991 in Germany, but it was discontinued due to implanting difficulties.³¹ In that same year, McMinn from the United Kingdom introduced the first press-fit cobalt-chrome hip resurfacing, but that too was later discontinued due to cup loosening.³² It wasn't until 1996 that McMinn along with Midland Medical Technologies (now Smith and Nephew) and Corin Medical developed new MOM hip resurfacings known as the Birmingham Hip Resurfacing (BHR) and the Cornet-2000, respectively.³² Newer MOM models with improved design, composition and fixation techniques have emerged, and the most commonly used current MOM hip resurfacing device in Alberta clinical practice today is the BHR.

Despite the reported successes of MOM hip resurfacing THR, the long-term postoperative failure and safety profiles of MOM hip resurfacing are not well understood due to a current lack of long-term prospective studies. The evidence on the short-term safety characteristics of MOM implants is quickly developing in the literature.^{1,33,34} Postoperative safety concerns with these devices have been centered on at three areas: health consequences related to metal ion debris release, femoral neck fracture risk and dislocation risk. Additionally, compared to conventional polyethylene THR, hip resurfacing devices have higher implant costs, and there could be negative consequences of using MOM prosthesis, such as early failure or biological responses to metal ion debris.

Canada Regulatory Status for Hip Resurfacing Devices

There are several MoM hip resurfacing devices currently licensed in Canada (Table 1). These prostheses include the Birmingham hip resurfacing (Smith & Nephew), Conserve Plus hip (Wright Medical Technology), Cormet hip (Corin), Durom hip (Zimmer GMBH), and the ReCap resurfacing device (Biomet UK).

Table 1. Hip Resurfacing Systems Licensed by Health Canada

Device	Manufacturer	Licensed date	License No.	Class
Birmingham Hip Resurfacing System	Smith & Nephew Orthopaedics	2002	60640	III *
Conserve Plus Hip System	Wright Medical Technology	2003	61779	III *
ReCap Resurfacing Hip System	Biomet UK Ltd.	2004	72082	III *
Cormet Resurfacing Hip System	Corin Ltd.	2005	70449	III *
Durum Hip Resurfacing System	Zimmer GMBH	2005	68144	III *
ASR Hip Resurfacing System	Depuy International Ltd.	2006	70004	III *

* Class III: denotes medium risk devices such as hip implants and surgically-invasive devices that are intended to be absorbed into the body, or that are intended to remain in the body for at least 30 consecutive days. Data attained from Health Canada's Medical Device License Listing database (www.mdall.ca) on 04-Oct-06



In the United States, Smith & Nephew gained FDA approval on May 9, 2006 for the Birmingham Hip Resurfacing System (registration No. 3005623319; from FDA Device Listing Database www.accessdata.fda.gov). Since its introduction in the United Kingdom in 1997, the Birmingham Hip has been used in 26 other countries and has been implanted in 60,000 patients. Currently, the FDA is reviewing clinical evidence towards the approval of the Conserve Plus Hip Resurfacing System (Wright Medical Technology). Wright Medical anticipates FDA approval for their device in 2006.

Review of Literature on the Effectiveness of MOM Hip Resurfacing

The objective of the technology assessment review of the literature was to assess the outcomes of MOM hip resurfacing with respect to effectiveness, safety and cost-effectiveness, particularly in comparison to conventional THR results for the same patient population.

Searches of the major medical electronic databases (Cochrane DSR, Ovid MEDLINE, PubMed, EMBASE, CINAHL) were conducted with the following search strategy:

Search Term: (resurfacing OR surface OR alternative-bearing) AND (arthroplasty OR replacement) AND hip AND (comparison OR outcome OR assessment OR evaluation OR analysis) AND English[la]

The selection criteria for published studies were as follows:

- Studies comparing outcomes (effectiveness for revision rate, pain relief and functioning, safety, cost-effectiveness) of MOM hip replacement arthroplasty (HRA) compared to THR
- Studies that report on the effectiveness of MOM HRA with respect to post-surgical revision rates, and changes in pain and function levels
- Studies wherein the primary diagnosis was OA
- Studies that report on safety outcomes following MOM HRA
- Studies that assess the cost-effectiveness associated with MOM HRA
- Studies limited to English-language reporting

Exclusion criteria included:

- Studies that did not contain patient data
- Studies that reported on hip resurfacing prostheses other than MOM, e.g., metal-on-polyethylene hip resurfacings

Results of Literature Search Process

Over 400 citations were identified in the literature search. Several systematic reviews and technology assessment reports were included in this review, along with 15 experimental and observation studies that met the inclusion criteria (Table 2).

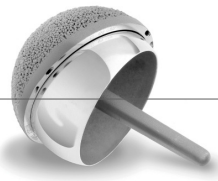
Table 2: Type and Number of Studies Included that Met Inclusion Criteria of Review

Study Design	Type of Study	Number of Studies
Review	Systematic, Tech assessment	6
Experimental	Randomized controlled trial	2
Observational	Case series, Case controlled	13

Systematic Reviews and Health Technology Assessments

The included systematic reviews and health technology assessments on MOM HRA identified in the literature search are as follows:

- Metal on metal resurfacing hip arthroplasty (hip resurfacing). 2000. New and Emerging Technology Briefing, National Horizon Scanning Centre.¹¹
- Metal-on-metal hip resurfacing for young, active adults with degenerative hip disease. 2002. Alberta Heritage Foundation for Medical Research: Health Technology Assessment Unit. Technote.³⁵
- Guidance on the use of metal on metal hip resurfacing arthroplasty. 2002. Technology Appraisal Guidance No.44; National Institute of Clinical Excellence (NICE).¹
- A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease. 2002. Vale et al. Health Technol. Assess. 6(15): 1-109.³³
- The effectiveness of metal on metal hip resurfacing: a systematic review of the available evidence published before 2002. 2004. Wyness, L. et al.³⁴
- Metal-on-metal total hip resurfacing arthroplasty. 2006. Health technology policy assessment: Medical advisory Secretariat of Ontario.³⁶



Description of Reviews

The National Horizon Scanning Centre (NHSC) published a report ¹¹ in December 2000 for the Department of Health of England on the new and emerging use of MOM hip resurfacing arthroplasty. This report reviewed evidence from a limited number of case series studies that reported on clinical efficacy and costs associated with the emerging use of hip resurfacings in the UK. One proposition of this report was that the evidence suggests hip resurfacing compares favourably with the outcomes of conventional THR across all age groups, particularly in younger patients. The NHSC concluded that although hip resurfacing appears to be a promising alternative to THR in younger patients with the potential to reduce overall long-term service costs, there is a lack of randomized trials and well designed studies with adequate follow-up.

In March 2002, the Alberta Heritage Foundation for Medical Research (AHFMR) published a technote titled “Metal-on-metal Hip Resurfacing for Young, Active Adults with Degenerative Hip Disease” ³⁵ which assessed the current status of the use of MOM hip resurfacings in young, active adults aged 65 or less. This technote concluded that the available evidence suggests that MOM hip resurfacing could be a viable, bone-conserving option for adults who would outlive a THR, particularly in patients less than 65 years of age and/or active adults who may require multiple THRs. A recommendation of this report was for larger studies with longer outcomes data.

The National Institute for Clinical Excellence (NICE) published their guidance on the use of metal on metal hip resurfacing arthroplasty ¹ in June 2002. This report utilized eight observational studies, including three from manufacturers. Only four of these were published. The NICE appraisal committee recommended that MOM hip resurfacing should be considered to be an alternative form of THR with the same criteria applied to it as applied to conventional THR in terms of benchmarking revision rates. The committee recommended that data from long-term use is required to confirm the clinical and cost effectiveness of hip resurfacing arthroplasty.

The National Coordinating Center for Health Technology Assessment (NCCHTA) review ³³, prepared by Vale et al. in 2002, systematically assessed the effectiveness of MOM hip resurfacing for the treatment of hip disease compared to THR,

osteotomy, watchful waiting, arthrodesis and arthroscopy. Inclusion criteria of this review included studies which examined active individuals less than 65 years of age who would likely outlive a THR. Twenty articles (1990 to 2001) were included in this review, although the authors noted that the data from these reports was limited. Over a three-year period, revision rates for hip resurfacing ranged from 0-14%, compared to THR revision rates of $\leq 10\%$ over a 10 year follow-up period. Another finding was that 91% of hip resurfacing patients were pain free at four years post-surgery, compared to 84% at 11 years for THR. This report concluded with a call for additional, larger studies with longer follow-up periods.

Wyness et al. (2004) ³⁴ conducted a systematic review on the effectiveness of MOM hip resurfacing based on studies published prior to 2002. Studies that reported on the effectiveness of hip resurfacing, THR and watchful waiting were included in this review. In total, data was abstracted from four published MOM studies, four published THR studies, and one watchful waiting study. In addition, four unpublished studies supplied from manufacturers were also included. No comparative studies were identified in this report. The authors stated that the majority of included studies rated poorly in terms of study sample descriptions and control of bias. This report concludes with a call for more rigorous research that is large-scale, long-term, and utilize standard outcome measures pre- and post-operatively.

In February, 2006 the Ontario Health Technology Advisory Committee published a health technology assessment titled “Metal-on-Metal Total Hip Resurfacing Arthroplasty.” ³⁶ This report assessed the effectiveness, safety and costs associated with MOM hip resurfacing. Eleven studies (one experimental and 10 observational) met the inclusion criteria of this report. A conclusion of this review was that, based on the limited number of observational studies, the short- and medium-term outcomes of hip resurfacing are satisfactory and comparable to THR. An average revision rate of 1.5% was reported for a mean follow-up period range of 2.8 to 3.5 years, and the incidences of complications were low. Furthermore, MOM hip resurfacing significantly reduced pain and restored joint function. This technology assessment concludes that the current lack of long-term data does not allow definitive conclusions to be reached on MOM hip resurfacing arthroplasty.



Experimental Studies

Two RCTs were identified in the literature that specifically assessed the clinical outcomes of patients who received MOM hip resurfacing in comparison with patients who received THR. These studies are listed in Table 3.

Table 3: Description of Experimental MOM Hip Resurfacing Studies

Study	Study Period	Number of hips per group	Mean Patient Age (range)	Preoperative Diagnosis by % *	Prosthesis
Howie et al. 2005	1993-1995	Resurfacing: 11 THR: 13	46 (16-55) 50 (22-54)	<u>Resurfacing group:</u> OA: 64% <u>THR group:</u> OA: 62%	Resurfacing device: McMinn THR device: Exeter system by Howmedica
Vendittoli et al. 2006	2003-2006	Resurfacing: 107 THR: 103	49.1 (23-64) 50.6 (24-65)	<u>Resurfacing group:</u> OA: 75.7% Hip dysplasia: 9.3% Osteonecrosis: 2.8% Traumatic: 2.8% Inflammatory arthritis: 4.7% RA: 3.7% Ankylosing spondylitis: 0.9% Post septic arthritis: 1.9% <u>THR group:</u> OA: 75.7% Hip dysplasia: 6.8% Osteonecrosis: 1.9% Traumatic: 1.9% Inflammatory arthritis: 10.7% RA: 8.7% Ankylosing spondylitis: 1.9% Post septic arthritis: 0%	Resurfacing device: Durom system THR device: Metal-on-metal Zimmer THR system

* Preoperative diagnoses are not mutually exclusive.



Description of Included Experimental Studies

Howie et al. (2005)³⁷ compared the results of MOM hip resurfacing with THR in an RCT with 24 patients aged 55 or younger. Between 1993 and 1995, 11 patients (mean age 46, range 16-55) randomly received a McMinn resurfacing device, while 13 patients (mean age 50, range 22-54) received an Exeter THR device. The main preoperative diagnosis was OA in hip resurfacing group (64%) and THR group (62%). Furthermore, the outcome comparisons in this study included the Harris hip and pain scores and range of motion analyses. The RCT portion of this study was stopped after 2 years of patient recruitment due to a high incidence of failure of the cemented McMinn hip resurfacing. At an average follow-up period of 8.5 years (range, 8 to 10 years), 8 of the 11 (73%) hip resurfacings had been revised to THR (7 of this 8 revisions were performed within five years postoperatively). The stated reasons for these failures were 2 femoral neck fractures, loosening of the cemented acetabular component in 5 patients, and 1 patient with a previous femoral neck surgery who experienced a loosening of the hip resurfacing femoral component. The THR group had a revision rate of 15% (2/13 patients), both due to acetabular component loosening. There were no significant differences in flexion range of abduction to adduction or rotation between the hip resurfacing and THR groups at 2 years postoperatively. The average Harris pain score of the hip resurfacing group (40/44) was also comparable to the average of the THR group (44/44) at the two-year follow up.

Two big limitations of this RCT are the very small sample sizes involved and the device fixation technique used. In fact, the results of this study, along with others,³⁸ led to the abandonment of cement fixation of the acetabular component in hip resurfacing. Therefore, the results of this trial may not be indicative of the performance characteristics of the current generation of hip resurfacing prostheses.

Vendittoli et al. (2006)³⁹ recently conducted an RCT which compared the clinical outcomes of patients who randomly received MOM hip resurfacings (107 hips) with those who randomly received MOM THR (103 hips) over a study period from 2003 to 2006. The age of the hip resurfacing group (49.1 years, range 23-64) was statistically similar to the age of the THR group (50.6 years, range 24-65), although the hip resurfacing group had a significantly lower BMI than the THR group (27.2 vs. 29.6, respectively). OA was the primary diagnosis for both groups and study outcome measures included the WOMAC, PMA functional assessment, and the UCLA activity score. Three surgeons participated in this study, and notable differences between the study groups include longer mean surgical time (101 min vs. 85 min) and shorter average length of hospital stays (5.0 days vs. 6.1 days) for the resurfacing group compared to the THR group. Five patients were lost to follow-up; four in the resurfacing group and one in the control group. At a follow-up period of one year, both groups had similar WOMAC and PMA scores, although the resurfacing group had a higher average UCLA activity score. Also, more resurfacing patients returned to work and resumed heavy or moderate activities at the one year mark compared to the control group. In terms of complications, no dislocations or femoral neck fractures were observed in the resurfacing group, although two cases of femoral aseptic loosening led to revision surgery (one at 6 months and the other at 9 months postoperatively). In the THR group, one revision was performed for recurrent dislocation. Vendittoli et al. concluded that hip resurfacing and conventional THR confer similar satisfaction rates in young patients, but resurfacing arthroplasty may offer better functional performance in terms of activity level and capacity to return to work. Although this RCT is the best experimental study conducted on MOM hip resurfacing thus far, it is limited by its very short-term follow-up period.



Clinical Outcomes of MOM HRA reported in Experimental Studies

A summary of the experimental studies is provided in the following tables. Table 4 is a summary of the studies with reported revision rates, Table 5 a summary of clinical outcomes and Table 6 is a summary of the reported postoperative complications.

Table 4. Summary of Revision Rates reported in Experimental Studies

Study	Study Period	Number of hips per group	Mean Patient Age (range)	Mean Follow-up Period (range)	Prosthesis	Revision Rate %
Howie et al. 2005	1993-1995	Resurfacing: 11 THR: 13	46 (16-55) 50 (22-54)	8.5 years (8-10)	Resurfacing device: McMinn THR device: Exeter system by Howmedica	Resurfacing: 73% THR: 15%
Vendittoli et al. 2006	2003-2006	Resurfacing: 107 THR: 103	49.1 (23-64) 50.6 (24-65)	1year, latest follow-up	Resurfacing device: Durom system THR device: Metal-on-metal Zimmer THR system	Resurfacing: 1.9% THR: 1.0%

Table 5. Summary of Clinical Measures

Study	Study Period	Prosthesis	Test	Pre-Surgery Comparison (resurfacing vs THR)	Follow-up Comparison (HRA vs THR)
Howie et al. 2005	1993-1995	Resurfacing device: McMinn THR device: Exeter system by Howmedica	Harris Hip Score Pain Range of motion (deg) Flexion Abduct-adduction	43 vs. 46 10 vs. 20 NR NR	89 vs. 93 @ 2 years 40 vs. 44 110 vs. 105 @ 2 yr 70 vs. 50 @ 2 yr
Vendittoli et al. 2006	2003-2006	Resurfacing device: Durom system THR device: Metal-on-metal Zimmer THR system	WOMAC Function PMA UCLA activity score	52.6 vs. 54.8 10.8 vs. 10.2 NR	9.2 vs. 11.7 @ 1 yr 16.7 vs. 16.6 @ 1 yr 7.1 vs. 6.3 @ 1 year *

Values are mean ± SD, if available. NR: Not Reported. * denotes statistically significant difference.



Table 6. Summary of Postoperative Complications

Study	Study Period	Number of hips per group	Complications
Howie et al. 2005	1993-1995	Resurfacing: 11 THR: 13	<p><u>Resurfacing group:</u> Femoral neck fracture: 3 (27.3%) Aseptic loosening of cemented acetabular component: 5 (45.5%)</p> <p><u>THR group:</u> Aseptic loosening of cemented acetabular component: 2 (15.4%) Loose acetabular component, awaiting revision: 1 (7.7%)</p>
Vendittoli et al. 2006	2003-2006	Resurfacing: 107 THR: 103	<p><u>Resurfacing group:</u> Femoral neck fracture: 3 (27.3%) Aseptic loosening of cemented acetabular component: 5 (45.5%)</p> <p><u>THR group:</u> Aseptic loosening of cemented acetabular component: 2 (15.4%) Loose acetabular component, awaiting revision: 1 (7.7%)</p>

Observational Studies

Numerous observational studies have been conducted on the clinical outcomes of MOM hip resurfacing arthroplasty. Studies that met this review’s inclusion criteria are listed in Table 7.



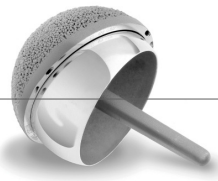
Table 7: Description of Observational MOM Hip Resurfacing Studies

Study	Study Period	Number of hips (patients)	Mean Patient Age (range)	Preoperative Diagnosis by %	Prosthesis
Beaule et al. 2004	1993-1996	42 (39)	47.5 (22-69)	OA: 55% Osteonecrosis: 16.7% Hip dysplasia: 9.5% Arthrokatachysis: 7% RA: 4.8% Slipped capital femoral epiphysis: 4.8% Legg-Calve-Perthes: 2.4%	McMinn
Beaule et al. 2004	NR	94 (83)	34.2 (15-40)	OA: 24.4% Developmental dysplasia: 19.1% Trauma: 18.1% Osteonecrosis: 18.1% Rheumatoid diseases: 6.4% Legg-Calve-Perthes: 6.4% Slipped capital femoral epiphysis: 4.3% Ankylosing spondylitis: 3.2%	Conserve Plus
Treacy et al. 2005	1997-1998	144 (130)	52.1 (17-76)	OA: 87% Avascular necrosis: 10% Developmental dysplasia: 2% RA: 1.3% Other diagnoses: 3%	BHR
Amstutz et al. 2004	1996-2000	400 (355)	48.2 (15-77)	OA: 66% Developmental dysplasia: 10.8% Osteonecrosis: 9% Posttraumatic c arthritis: 7.8% Previous operations: 6.3% Legg-Calve-Perthes: 2.5% Slipped capital femoral epiphysis: 1.8% Ankylosing spondylitis: 1% Juvenile rheumatoid arthritis: 0.8% RA: 0.8% Melorheostosis: 0.3%	Conserve Plus
Pollard et al. 2006	1999-2001	54 (53)	49.8 (18-67)	OA: 78% Avascular necrosis: 7% Developmental dysplasia: 6% Other diagnoses: 9%	BHR
Back et al. 2005	1999-2001	230	52.1 (18-82)	OA: 88.3% Avascular necrosis: 5.2% RA: 1.3% Neurometabolic: 0.9% Other diagnoses: 4.3%	BHR



Table 7: Description of Observational MOM Hip Resurfacing Studies - *continued*

Study	Study Period	Number of hips (patients)	Mean Patient Age (range)	Preoperative Diagnosis by %	Prosthesis
Daniel et al. 2004	1994-2001*	446 (384)	48.3 (26.8-54.9)	OA: 100%	BHR: 403 hips McMinn: 43 hips
Lilikakis et al. 2005	2001-2002	70 (66)	51.5 (23.3-72.7)	OA: 97% Osteonecrosis: 1% Chondrolysis: 1%	Cornet 2000
Vail et al. 2006	2000-2003	57 (52)	47 (22-64)	OA: 77.2% Osteonecrosis: 17.5% Posttraumatic arthritis: 3.5% RA: 1.8%	Conserve Plus
Grigoris et al. 2005	2001-2003	200 (186)	48 (22-72)	OA: 45% Slipped capital femoral epiphysis: 20% Developmental dysplasia: 18% Hip protusio: 4.5% Avascular necrosis: 4% Trauma: 2% Other diagnoses: 6.5%	Durom System
De Smet 2005	1998-2004	268 (252)	49.7 (16-75)	OA: 80.6% Necrosis: 7.3% Congenital dislocation of hip: 4.8% Rheumatoid: 3.6% Traumatic: 1.2% Neurometabolic: 0.4% Other diagnoses: 0.8%	BHR
Schmalzried et al. 2005	2000-2004	91 (79)	48 (30-67)	OA: 95% Ankylosing spondylitis: 2% Osteonecrosis: 1% RA: 1%	Conserve Plus
Siebel et al. 2006	2003-2005	300 (300)	56.8 (18-76)	OA-majority of patients: (NR) Trauma: (NR) Necrosis: (NR)	ASR



Description of Included Observational Studies

Beaule et al. (2004)⁴⁰ retrospectively examined the clinical outcomes of MOM hip resurfacing in a younger group of patients, where the average age was 34.2 years (range, 15 to 40). Ninety-four Conserve Plus MOM hip resurfacings were reviewed (83 patients) and the primary preoperative diagnosis was OA. All patients were evaluated preoperatively and at the latest follow-up with the UCLA hip score, SF-12 questionnaire, and range of motion analysis. In addition, prosthesis survival rate was also reported. Fourteen percent of these patients had a previous surgery on their affected hip, although the nature of that intervention was not reported. The mean follow-up period was 3 years (range, 2.0 to 5.6), and two patients (two hips) were lost to follow-up. Compared to before surgery, significant improvements were observed in UCLA hip scores and SF-12 component summaries. The range of motion of the resurfaced hips had significant improvements at follow-up; 116.2° for flexion and extension, 70.0° in abduction and adduction (measured in extension), and 74.5° in rotation (measured in extension). The survival rate in this study was 96.8% at follow-up. Three revisions to THR were performed at a mean of 27 months, with one due to a femoral neck fracture, one due to femoral component loosening, and the last revision due to persistent dislocation. The authors concluded by stating that the observed survivorship of the MOM hip resurfacing prosthesis was superior to the results conferred by THR devices for this younger patient population.

Limitations of study included a lack of a control group, short-term follow-up period, multiple surgical techniques used, and the procedure was not the primary treatment for all patients.

Beaule et al. (2004)⁴¹ retrospectively examined the midterm clinical outcomes and survivorship of MOM hip resurfacings performed between 1993 and 1996. Their study reported the outcomes of 39 patients, with a mean age of 47.5 years (range, 22 to 69), who received 42 McMinn MOM hip resurfacings. The primary pathology leading to surgery was OA, and 6 patients had received previous surgery on the affected hip (2 had proximal femoral osteotomy, 3 had metal-on-polyethylene resurfacing arthroplasty, and 1 had a hemi-resurfacing arthroplasty). The mean follow-up period was 8.7 years (range, 7.2 to 10.0), and 1 patient was lost to follow-up due to death. This study reported a dismal survival rate of 79% at 7

years follow-up. When aseptic-only failures were considered, the femoral and acetabular component survivorship at 7 years was 93% and 80%, respectively. Cement fixation was used for the acetabular component of the prosthesis. Previous studies (e.g., Howie et al. (2005) and Schmalzried TP et al. (1996)) have also found unacceptable acetabular component failure with this fixation technique. Consequently these data are not indicative of the survival rate of the current generation of hip resurfacing prosthesis that use cementless acetabular components. Supporting that premise was the finding by Beaule et al. that the survivorship of the cemented acetabular fixation (66%) was significantly less than those of cementless devices (95%) at 7 years follow-up.

Limitations of their study included a lack of a control group, small sample size, multiple fixation techniques used, and the procedure was not the primary treatment for all patients.

Treacy et al. (2005)⁴² examined the 5 year survivorship of 144 consecutive Birmingham hip resurfacings performed between 1997 and 1998. This study included men less than age 65 and women less than age 60, with the average age being 52.1 years (range, 17 to 76). The primary diagnosis was OA. The survival rate at 5 years postoperatively was 98%. The three implant failures that occurred were due to two infections and one femoral neck fracture. No patients were lost to follow-up, and radiographic analysis at 5 years follow-up was performed on 107 (76%) hips. No evidence was found on any radiograph to indicate component loosening. This included no indications of osteolysis or trabecular compression at the tip of the stem that could suggest femoral component migration. Treacy et al. concluded that the use of MOM hip resurfacing "...can provide a solution in the medium term for the younger more active adult who requires surgical intervention for hip disease."

Limitations of their study included a lack of a control group and the use of multiple device fixation techniques.

Amstutz et al. (2004)⁴³ conducted a prospective study on the clinical outcomes of 400 Conserve Plus MOM hip resurfacings in 355 patients performed between 1996 and 2000. The patients had an average age of 48.2 (range, 15 to 77), and the primary diagnosis for surgery in this group was OA. The average duration of follow-up was 3.5 years (range, 2.2 to 6.2),



and 3 patients were lost to follow-up. Two patients (3 hips) died of unrelated causes. Study outcomes included the UCLA hip-rating system, Harris hip scores, SF-12 quality of life questionnaire, and prosthesis survival. Compared to preoperative status, the clinical assessment at follow-up found significant improvements in UCLA hip scores (pain, walking, function and activity) and SF-12 physical and mental component summaries. The Harris Hip Score at follow-up had a mean of 93.5 out of 100. The survival rate for this patient population was 97%, with 12 resurfaced hips converted to THR. The stated reasons for revision included femoral component loosening (7 hips), femoral neck fracture (3 hips), recurrent dislocation (1 hip) and a deep infection (1 hip).

Limitations of this study included a lack of a control group and a short-term follow-up period

Pollard et al. (2006)⁴⁴ retrospectively reviewed the outcomes of 54 Birmingham hip resurfacings performed from 1999-2001 and 54 hybrid THRs performed from 1996-2001 by the same surgeon. Outcomes were based on changes between preoperative and postoperative radiological and clinical measures, such as the Oxford hip score, UCLA activity score and EQ-5D quality of life score. Patients in both groups were matched preoperatively for gender, age at surgery, BMI and preoperative activity levels prior to disease limitations. The primary diagnosis was OA for THR group (74%) and resurfacing group (78%). The post-surgical mean follow-up periods were 80 months (range, 42 to 120) for the THR group and 61 months (range, 52 to 71) for the BHR group. In the THR group, 3 patients were lost to follow-up due to unrelated death, leaving 51 patients in this group, and 2 patients were lost to follow-up due to 1 emigrating and another patient withdrawing from the study, thus leaving 52 in the resurfacing group for analysis. Pollard et al. reported that postoperative function was excellent in both groups, but that the hip resurfacing group had significantly higher postoperative activity scores and higher quality of life scores. The revision or intent-to-revise rates in this study were 8% in the hybrid THR group (due to osteolysis secondary to polyethylene wear or recurrent dislocation) and 6% (due to femoral component failure) in the Birmingham resurfacing group. The authors of that study stated that a reason for the revision rate of the resurfacing group (6%) could be attributed to the higher rate of technical errors incurred due to the surgeon's inexperience. The authors conclude by stating that hip resurfacing provides

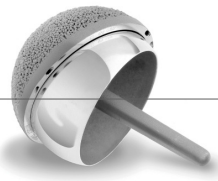
better clinical outcomes to younger patients as compared to total hip replacements. The authors stated that since a failed hip resurfacing can easily be revised to a THR, it was sensible to reserve THR for failed hip resurfacings.

The prime limitation of this study was its small sample size.

Back et al. (2005)⁴⁵ conducted a prospective study that examined the clinical and radiological outcomes of 230 consecutive Birmingham hip resurfacing patients performed between 1999 and 2001. The average age of the patients was 52.1 years (range, 18 to 82), and the primary preoperative diagnosis was OA. Study outcome measures included prosthesis survivorship, Harris hip scores and range of motion measures. All recipients were available for follow-up, which was performed at an average of 3 years postoperatively (range, 25 to 52 months). These authors reported a 99.14% survivorship (1 patient suffered a femoral neck fracture that required revision). Ninety-seven percent of patients reported their outcome as good or excellent. Significant improvements in Harris hip scores and mean hip flexion were also observed. The authors stated that the results with the Birmingham hip resurfacing prosthesis were superior to the earlier generation of hip resurfacing devices that used cement and metal-on-polyethylene bearings.

Limitations of this study included a lack of a control group, multiple surgeons, and short-term follow-up.

Daniel et al. (2004)⁴⁶ conducted a retrospective review of the outcomes of 446 hip resurfacings performed between the period of 1994 and 2001 by the same surgeon. Outcome assessments were based on the survival rate, Oxford hip scores and activity levels. The results of 186 patients who received their implant in 1996 were excluded due to prosthesis failure attributed to a different implant device. A total of 43 McMinn hip resurfacing implants and 403 Birmingham hip resurfacing implants were included in this study. The study population had a mean age of 48.3 years (range, 27 to 55), and the primary diagnosis of OA. The average follow-up period was 3.3 years (range, 1.1 to 8.2), and no patient was lost to follow-up. Six patients died due to unrelated reasons, while one suffered a femoral neck fracture. Two complications were noted in this review: a thromboembolic event and a non-fatal pulmonary embolism. The survival rate was 99.8% (1 revision was performed). Significant improvements in Oxford hip



scores and activity levels were observed. Most patients returned to their pre-arthritis activity level by 1 year post-surgery, and no patient changed her or his occupation after surgery. The authors concluded that although the limitations of their study prevented firm conclusions to be drawn, the results suggested that MOM hip resurfacing "...manifests evidence of significant superiority over existing treatments..." for younger patients with degenerative joint disease.

Limitations of this study included a lack of a control group, short-term follow-up period, and use of multiple prosthesis types.

Lilikakis et al. (2005)⁴⁷ performed a prospective study on the outcomes of 70 MOM hip resurfacings (Cormet 2000 prosthesis) performed from 2001 to 2002. Unique to this report was the use of hydroxyapatite coating on the femoral side of the hip resurfacing rather than the common use of cement fixation of the femoral component. Sixty-six patients with an average age of 51.5 years (range, 23.3 to 72.7) participated in this study, which measured changes in Harris hip scores, radiographic changes, complications development and prosthesis survival rates. The primary preoperative diagnosis was OA, and the mean follow-up period was 2.4 years (range, 2.0 to 3.2). The survival rate was 97.1%, with 2 revisions as a result of 1 infection and 1 aseptic loosening of the acetabular component. Without the revision due to the acetabular component loosening, the survival rate of the hydroxyapatite-coated femoral component was 98.6%. Mean Harris Hip Scores for pain and function had significantly increased from preoperative (12.0 and 28.3) to postoperative (39.3 and 43.1) follow-up scores, respectively.

Limitations of the study included a lack of a control group, short-term follow-up period and small hip resurfacing group sample size.

Vail et al. (2006)⁴⁸ recently conducted a retrospective comparison of the outcomes of two patient-matched groups; one group received hip resurfacings and the other conventional THR. The procedures were performed between 2000 and 2003. The MOM hip resurfacing group consisted of 57 Conserve Plus prostheses in 52 patients of average age 47 (range, 22 to 64 years). The control group included 204 THR in 176 patients of average age 57 (range, 17 to 92). The primary diagnosis for both groups was OA, and preoperative age, gender and function levels were matched between the

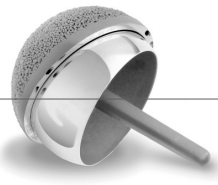
groups. The study compared outcomes of both groups based on Harris hip scores, range of motion, complication rates and device survival. The follow-up evaluation period for this study was a mean of 3.0 years (range, 2 to 4), and no patient was lost to follow-up. Comparison at follow-up after age, gender and preoperative functions were matched revealed several differences between the groups. The hip resurfacing group had significantly higher activity and range of motion scores and lower patient-reported limitations compared to the control group. Postoperative complication and revision rates were similar in the hip resurfacing and THR groups. In the hip resurfacing group, the survival rate was 96.5% as 2 patients required revision, 1 due to a femoral neck fracture and the other due to a deep infection. The survival rate in the control group was 95.7% as 4 THR patients required re-operation.

The major limitation of this study was its short-term follow-up period.

Grigoris et al. (2005)³² have reported their early results with the Durom hip resurfacing system in 186 consecutive patients (200 hips) performed between 2001 and 2003. The patients had a mean age of 48 years (range, 22-72), and the primary preoperative diagnosis was OA. The average follow-up time was at 2.2 years (range, 1.0-3.4), and no patients were lost to follow-up. Their early results indicated 100% prosthesis survivorship, with no observed indications of impending device failure, acetabular or femoral migration, and no evidence of focal osteolysis.

The limitations of study included a lack of a control group, multiple surgeons, and a short-term follow-up period

De Smet (2005)⁴⁹ conducted a prospective study on the outcomes of 268 consecutive Birmingham hip resurfacings performed on 252 patients from 1998 to 2004. The mean patient age at surgery was 49.7 years (range, 16 to 75), and the primary diagnosis was OA. The study outcomes involved Harris hip scores, Postel Merle d'Aubigne (PMA, functional assessment), range of movement, activity levels and prosthesis survival rates. The study's mean follow-up time was 2.8 years (range, 2 to 5), and 3 patients (4 prostheses) were lost to follow-up due to death. Outcomes at follow-up revealed that 97.8% had no pain, the total Harris Hip Score averaged 97.2, 61% of patients performed strenuous activities, hip flexion averaged 123°, 19.4% of patients experienced a clicking noise in the prosthesis that occurred within the first 6 months after



surgery but was painless and disappeared, and 2.8% of patients had a persistent slight groin pain. The survival rate in this sample was 98.8% as 3 patients required revision, 1 due to a femoral neck fracture, another due to a low-grade infection, and 1 developed avascular necrosis for the femoral head. The authors concluded that MOM hip resurfacing was a good alternative to young active surgical patients based on their promising short-term results.

Limitations of this study included a lack of a control group, short-term follow-up period and small hip resurfacing group sample size.

Schmalzried et al. (2005)⁵⁰ examined the outcomes of 91 Conserve Plus MOM hip resurfacings in 79 patients performed between 2000 and 2004. The patients had an average age of 48 (range, 30-67), and the primary diagnosis for surgery was OA. Outcome measures included UCLA activity scores, Harris Hip Scores, range of motion analyses and prosthesis survivorship. Of the 79 patients, 70 (81 hips) were available for a minimal 2-year follow-up. The mean follow-up period for this group was 2.6 years (range, 2.0-4.0). Significant improvements were observed at follow-up in Harris Hip Scores, UCLA activity scores, and range of motion as compared to preoperative measurements. The survivorship of the prostheses was 100% at follow-up in this patient population. They reported an association between preoperative radiographic grading of the proximal femur and postoperative pain, range of motion and limb length discrepancy, and they developed a radiographic grading system to assess the arthritic proximal femur preoperatively based on bone density, shape, biomechanics and focal bone defects. Hips that had less arthritic changes based on this grading system had better outcomes with hip resurfacing. The authors concluded that the use of relatively strict selection criteria for hip resurfacing results in the low occurrence of short-term failures.

Limitations of their study included a lack of a control group, use of multiple femoral cement fixation techniques, and a short-term follow-up period.

Siebel et al. (2006)⁵¹ reported early results of a prospective study that examined the clinical outcomes of 300 consecutive ASR MOM hip resurfacings performed between 2003 and 2005. The average age of the 300 patients at surgery was 56.8 years (range, 18-75.9), and the primary diagnosis leading to surgery was OA. Fifteen (5%) of patients had undergone a previous surgery on their affected hip. The mean follow-up period was 202 days (0.6 years). In total, 8 patients (2.7%) had to be revised, with 5 femoral neck fractures that occurred within 4 months of surgery, and 3 acetabular component revisions. An analysis of the the revision rates over the 300 consecutive implants (in successive groups of 50) provided evidence of a steep learning curve in MOM HRA. In particular, 7 revisions were performed in the first 150 patients, whereas 1 revision was required in the next 150 patients. That represented a drop in revision rates from 4.7% to 0.7% in this series of patients. Significant improvements were observed on the Harris hip and UCLA scores between preoperative and follow-up measurements.

Limitations of this study included a lack of a control group, very short-term follow-up period, and the procedure was not primary treatment for all patients



Clinical Outcomes of MOM HRA reported in Observational Studies

A summary of the observational studies is provided in the following tables. Table 8 is a summary of the studies with reported revision rates, Table 9 presents a summary of clinical outcomes and Table 10 is a summary of the reported postoperative complications.

Table 8. Summary of Revision Rates Reported in Observational Studies

Study	Study Period	Number of hips (patients)	Mean Patient Age (range)	Mean Follow-up Period (range)	Prosthesis	Revision Rate %
Beaule et al. 2004.	1993-1996	42 (39)	48 (22-69)	8.7 years (7.2-10.0)	McMinn	35.9%
Beaule et al. 2004.	NR	94 (83)	34 (15-40)	3 years (2.0- 5.6)	Conserve Plus	3.6%
Treacy et al. 2005	1997-1998	144 (130)	52 (17-76)	5 years	BHR	2.3%
Amstutz et al. 2004	1996-2000	400 (355)	48 (15-77)	3.5 years (2.2-6.2)	Conserve Plus	3.4%
Pollard et al. 2006.	1999-2001	54 (53)	50 (18-67)	5.1 years (4.3-5.9)	BHR	6%
Back et al. 2005.	1999-2001	230	52 (18-82)	3 years (2.1-4.3)	BHR	0.4%
Daniel et al. 2004	1994-2001*	446 (384)	48 (27-55)	3.3 years (1.1-8.2)	BHR: 403 hips McMinn: 43 hips	0.3%
Lilikakis et al. 2005	2001-2002	70 (66)	52 (23-73)	2.4 years (2.0-3.2)	Cormet 2000	2.9%
Vail et al. 2006.	2000-2003	57 (52)	47 (22-64)	3.0 years (2.0-4.0)	Conserve Plus	3.5%
Grigoris et al. 2005.	2001-2003	200 (186)	48 (22-72)	2.2 years (1.0-3.4)	Durom System	0%
De Smet 2005	1998-2004	268 (252)	50 (16-75)	2.8 years (2-5)	BHR	1.2%
Schmalzried et al. 2005	2000-2004	91 (79)	48 (30-67)	2.6 years (2.0-4.0)	Conserve Plus	0%
Siebel et al. 2006	2003-2005	300 (300)	57 (18-76)	0.6 years (NR)	ASR	2.7%

* 1996 data excluded due to prosthesis production problems, NR: Not Reported



Table 9. Summary of Clinical Measures Reported in Observational Studies

Study	Study Period	Prosthesis	Test	Pre-Surgery Score	Follow-up Score	Statistical Significance
Beaule et al. 2004.	1993-1996	McMinn	UCLA hip score Pain Walking Function Activity	3.9 6.2 5.8 4.6	9.3 9.2 8.5 6.6	<0.05 <0.05 <0.05 <0.05
Beaule et al. 2004.	NR	Conserve Plus	UCLA hip score Pain Walking Function Activity SF-12 Physical Mental Range of Motion Flex-extension Abduct-adduction Rotation	3.1 4.4 5.8 5.5 29.9 44.8 79.5° 28.9° 20.2°	9.1 9.2 9.1 7.1 47.7 51.5 116.2° 70.0° 74.5°	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 NR NR NR
Treacy et al. 2005	1997-1998	BHR	Oxford Hip Score	NR	NR	NR
Amstutz et al. 2004	1996-2000	Conserve Plus	UCLA hip score Pain Walking Function Activity SF-12 Physical Mental Harris Hip Score	3.5 (1-8) 6.0 (2-10) 5.7 (1-10) 4.5 (1-10) 31.2 (16.8-54.8) 46.8 (4.0-68.5) NR	9.5 (2-10) 9.6 (3-10) 9.4 (3-10) 7.7 (2-10) 50.0 (17.6-62.7) 53.1 (10.5-67.1) 93.5 (41-100)	<0.0001 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001 NR
Pollard et al. 2006.	1999-2001	BHR	Oxford Hip Score UCLA Score EQ-5D EQ-VAS		15.9 (12-42) 8.4 (4-10) 0.9 (0.08-1.00) 82.3 (20-100)	NR NR NR NR

Values are mean ± SD, if available. Range data provided in parentheses. NR: Not Reported



Table 9. Summary of Clinical Measures Reported in Observational Studies - *continued*

Study	Study Period	Prosthesis	Test	Pre-Surgery Score	Follow-up Score	Statistical Significance
Back et al. 2005.	1999-2001	BHR	Harris Hip Score			
			Charnley Catg. A	63.9 (8-93)	97.7 (60-100)	NR
			Pain	21.2	43.3	NR
			Movement	7.9	8.9	NR
			Function	34.8	45.5	NR
			Charnley Catg. B	56.2 (18-82)	99.4 (90-100)	NR
			Pain	16.3	43.9	NR
			Movement	7.6	8.8	NR
			Function	32.3	46.7	NR
			Charnley Catg. C	64.8 (30-98)	85.5 (30-100)	NR
			Pain	20.7	36.7	NR
			Movement	8.8	8.3	NR
			Function	35.3	40.5	NR
			SF-12			
Charnley Catg. A						
Physical	31.1	54.1	NR			
Mental	58.6	56.9	NR			
Charnley Catg. B						
Physical	30.3	54.1	NR			
Mental	60.5	57.7	NR			
Charnley Catg. C						
Physical	31.5	48.2	NR			
Mental	52.2	55.9	NR			
Oxford Hip Score	NR	13.5 (12-28)	NR			
Range of Motion						
flexion	91.5° (25-130)	110.4° (80-130)	NR			
Daniel et al. 2004	1994-2001*	BHR: 403 hips McMinn: 43 hips	Oxford Hip Score UCLA score	NR NR	12.0 8.7	NR NR
Lilikakis et al. 2005	2001-2002	Cormet 2000	Harris Hip Score Pain Function	12 (0-30) 28.3 (3-42)	39.3 (0-44) 43.1 (9-47)	<0.0001 <0.0001
Vail et al. 2006.	2000-2003	Conserve Plus	Harris Hip Score Pain Activity Function Range of Motion Flexion Abduction Adduction Rotation	48.5 11 8.5 28.8 86.4 23.0 12.6 17.3	98.1 42.9 14.0 46.2 110.9 41.6 21.2 41.6	<0.001 <0.001 NR NR NR NR NR NR NR
Grigoris et al. 2005.	2001-2003	Durom System	Charnley score Pain Movement Walking	3.0 3.0 2.5	6.0 5.0 5.8	NR NR NR
De Smet 2005	1998-2004	BHR	Harris Hip Score PMA Flexion	All < 60	97.2 ± 7.6 17.7 ± 0.9 123° ± 13°	NR NR NR
Schmalzried et al. 2005	2000-2004	Conserve Plus	Harris Hip Score UCLA score	46.2 4.3 ± 1.5	95.3 ± 6.6 8.2 ± 1.5	<0.001 <0.001
Siebel et al. 2006	2003-2005	ASR	Harris Hip Score UCLA score	44 ± 11 4.0 ± 1.5	89 ± 13 6.1 ± 1.3	NR NR

Values are mean ± SD, if available. Range data provided in parentheses. NR: Not Reported



Table 10. Summary of Complications Reported in Observational Studies

Study	Study Period	Number of hips (patients)	Complications
Beaule et al. 2004.	1993-1996	42 (39)	Aseptic loosening of cemented acetabular component: 9 Aseptic loosening of cementless acetabular component: 1 Aseptic loosening of femoral component: 3 Aseptic loosening due to hematogenous sepsis: 1 Femoral neck fracture: 1 (2.6%) Osteolysis: 1 (2.6%)
Beaule et al. 2004.	NR	94 (83)	Femoral neck fracture: 1 at 2 months, led to revision Component loosening: 1 at 29 months, led to revision Subluxation: 1 at 50 months, led to revision Osteolysis: 2.1% Component size mismatch: 1 Trochanteric bursitis: 1
Treacy et al. 2005	1997-1998	144 (130)	Femoral neck fracture: 1 (0.7%), due to deep infection Avascular necrosis: 1 (0.7%) at 9 months Heterotopic bone: 28% of hips
Amstutz et al. 2004	1996-2000	400 (355)	Femoral component loosening: 7, led to revision Femoral neck fracture: 3, led to revision Recurrent dislocations: 1, led to revision Late hematogenous infection: 1, led to revision Heterotopic bone: 106 Dislocation: 6 Component size mismatch: 1 Heterotopic bone removal: 2 hips in 1 patient Trochanteric bursitis: 1
Pollard et al. 2006.	1999-2001	54 (53)	Femoral component loosening: 4, led to revision Deep vein thrombosis: 2 Pulmonary embolism: 1 Superficial infection: 1
Back et al. 2005.	1999-2001	230	Femoral neck fracture: 1 at 6 weeks Heterotopic bone: 59.6% of hips Notched femoral neck: 5 Nerve palsy: 5 Vascular injury: 3 Deep vein thrombosis: 11 Pulmonary embolism: 2 Superficial infection: 11 Urinary tract infection: 9 Sinus tachycardia: 5 Hypotension: 14 Pressure sores: 4



Table 10. Summary of Complications Reported in Observational Studies - *continued*

Study	Study Period	Number of hips (patients)	Complications
Daniel et al. 2004	1994-2001*	446 (384)	Avascular necrosis: 1, led to revision Pulmonary embolism: 1
Lilikakis et al. 2005	2001-2002	70 (66)	Aseptic loosening: 1 Deep infection: 1 Superficial infection: 1 Intraoperative notching: 16 Displacement of the cup: 1 Pulmonary embolism: 1 Wound hematoma: 1
Vail et al. 2006.	2000-2003	57 (52)	Femoral neck fracture: 1, led to revision Fatal pulmonary embolus: 1 Deep infection: 1, led to revision
Grigoris et al. 2005.	2001-2003	200 (186)	Pulmonary embolism: 2 Bone/cup impingement leading to neck narrowing: 1
De Smet 2005	1998-2004	268 (252)	Femoral neck fracture: 1 (0.4%) at 6 weeks Avascular necrosis: 1 (0.4%) Osteolysis: 2 (0.8%) Heterotopic bone: 4 (1.6%) Dislocation: 1 (0.4%) Infection: 1 (0.4%) Sciatic nerve palsy: 2 (0.8%) Deep vein thrombosis: 1 (0.4%) Pulmonary embolism: 1 (0.4%)
Schmalzried et al. 2005	2000-2004	91 (79)	Femoral component loosening: 1 at 17 months, led to revision
Siebel et al. 2006	2003-2005	300 (300)	Femoral neck fracture: 5 all within 4 months, led to revision Notched femoral neck: 7 Potentially notched femoral neck: 5 Incomplete seating of head: 2 Dislocation: 1, led to revision Persistent post-op pain: 1, led to synovectomy Peroneal palsy: 1



Industry-submitted Reports

Hip resurfacing device manufacturers and private organizations have also reported on MOM hip resurfacing arthroplasty outcomes. Summaries of these industry-submitted reports on MOM hip resurfacing surgery outcomes are provided in Table 11.

Table 11. Summary of Industry-submitted Reports on MOM HRA Outcomes

Study	Study Setting	Resurfacing Device	Number of hips	Mean Follow-up period (range)	Mean patient age (range)	Revision Rate
Corin Group Ltd. 2001.	Four hospitals, one clinic (UK)	Cormet 2000	CIC	21.4 months	50.8 years (26-69)	CIC
Wright Cremascoli Ortho Ltd. 2001.	NR	Conserve Plus	100	(24-51.6 months)	NR	3%
Midland Medical Technologies Ltd. 2001.	Hospitals in Birmingham, Southampton and Liverpool (UK) and Belgium	Birmingham Hip Resurfacing	1382	NR	49.2 years (15-86)	0.6%
Oswestry Outcome Centre. 2001.	UK	McMinn Hip Resurfacing	1378	(0-48 months)	53.1 years	0.5%
Oswestry Outcome Centre. 2001.	UK	Various resurfacing devices	4424	(0-48 months)	49.2 years	0.77%

Note: Data from Wyness L et al. (2004); CIC – data marked as “Commercial in confidence” in industry report.



Complications and Risk Factors associated with Hip Resurfacing THR

Failure Rates and Revisions

There are currently no long-term results available on the new generation of MOM hip resurfacing devices available in the market. Table 4 summarizes the revision rates for second generation MOM hip resurfacing reported in the studies included in this review. Significantly, the second generation of MOM hip resurfacing devices use cementless acetabular component fixation. Consequently, the revision rate (35.9%)

reported in by Beaulé et al. (2004)⁵² is not indicative of the new generation of implants that used cemented acetabular fixation. The latest generation of MOM resurfacing devices was introduced earlier this decade with improvements in metallic composition, bearing geometry, and acetabular and femoral fixation techniques.⁵³ The short-term results of the newest generation of MOM devices are presented in Table 8 and Figure 2.

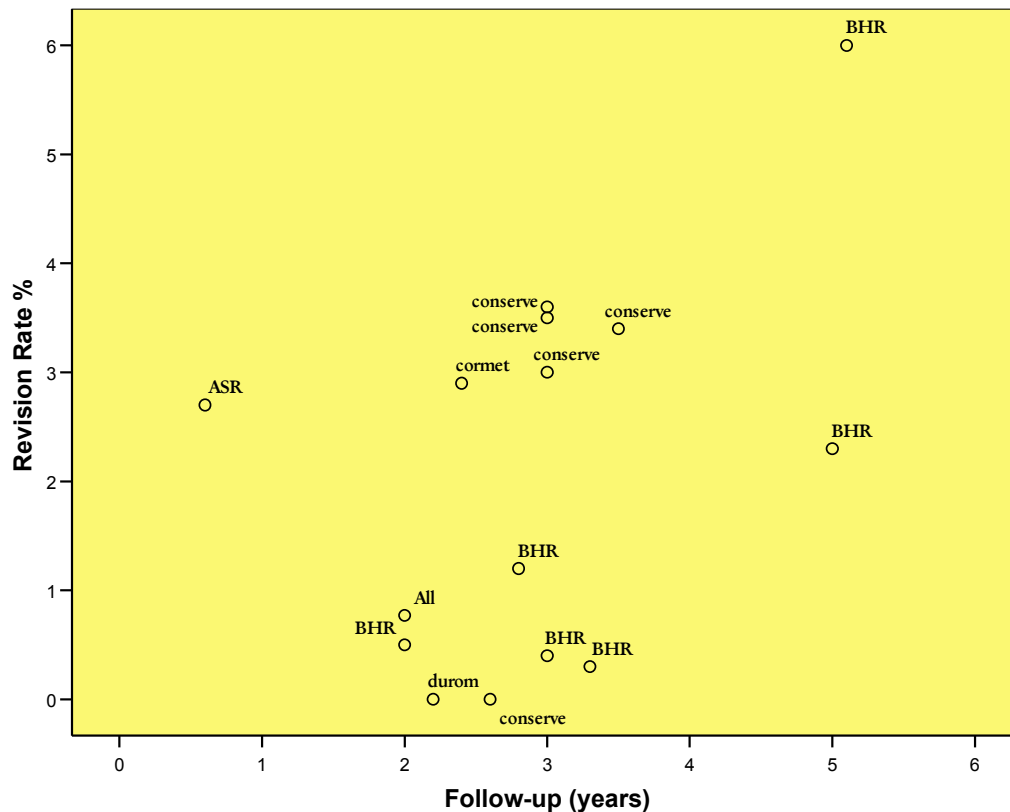
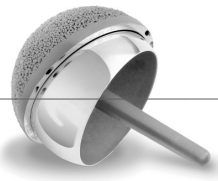


Figure 2. Summary of reported MOM hip resurfacing revision rates in the literature by manufacturer type (excluding cemented acetabular prosthesis rates)



As younger patients are more likely to outlive their THR, they experience high long-term THR failure rates. Joshi et al (1993)⁵⁴ reported that in a group of 219 THR performed on patients aged 40 or less that the overall prosthesis survival rate was 75% at a mean follow-up time of 16 years. That figure dropped to 51% when only active patients with OA were considered. That dramatically contrasts with the revision rates for older THR patients where failure rates tend to be below 5% at 10 years.⁵⁵ Head-to-head comparisons of MOM hip resurfacing and THR survival rates do not currently exist. Vail et al. (2006)⁵⁶ retrospectively compared the outcomes of 57 resurfaced hips with 93 cementless THR and reported a trend toward better overall outcomes with hip resurfacing. The

MOM hip resurfacing patients had lower rates of failure (3.5%) and complications (5.3%) at a mean follow-up time of 3 years as compared to THR patients (4.3% and 14.0%, respectively). Daniel et al. (2004)⁵⁷ superimposed the survival rate of their 403 Birmingham hip resurfacing performed between 1997 and 2001 with the results of male patients (cohort 1988 to 1998) aged 54 or less with OA from the Swedish Hip Register 2000 (see Figure 3). Although this comparison is weakened by the lack of proper controls, it suggests that MOM hip resurfacing may provide younger patients with higher short-term prosthesis survival rates compared to conventional THR.

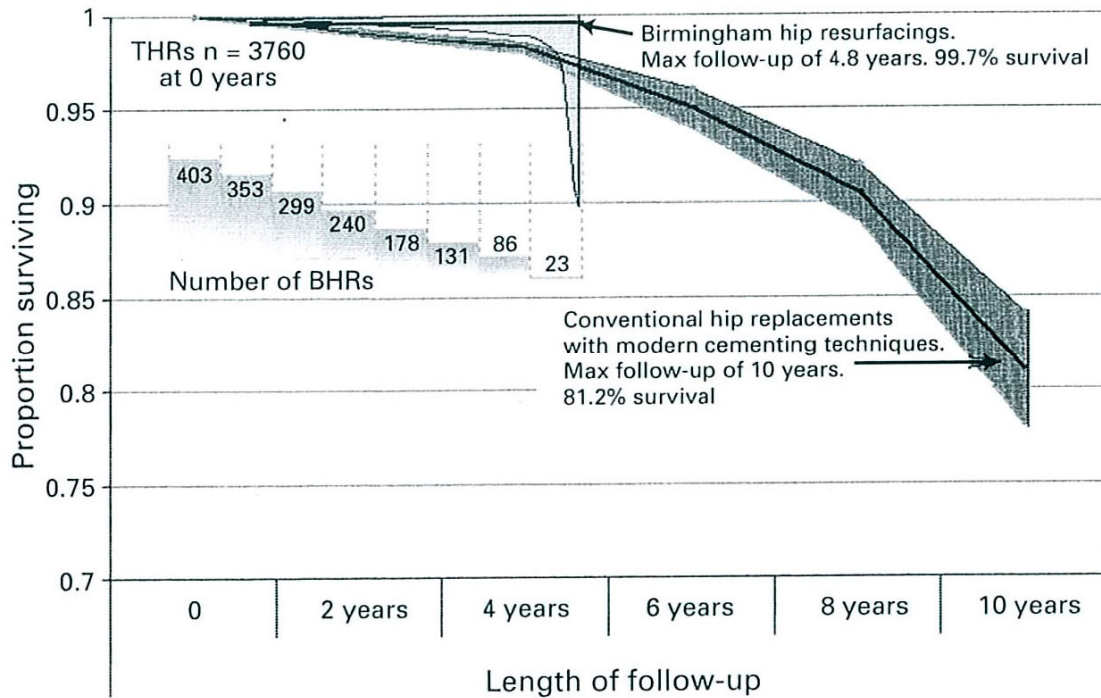


Figure 3. Survival curves of BHR patients (male and female) and THR patients (male only) aged < 55 years with OA as the primary diagnosis. Adapted from Daniel et al. 2004



Osteolysis

Osteolysis refers to the dissolution of bone around the prosthesis due to the production of wear particles released from the device. Compared to MOM implants, osteolysis is more prevalent with the use of metal-on-polyethylene devices where there is significant polyethylene wear. Several studies^{58,59} found polyethylene wear 0.2mm or more per year, and Wan and Dorr reported a volumetric wear rate of 150 cubic mm per year. On the other hand, MOM hip resurfacing implants produce less wear particles. Schmalzried et al (1996)⁶⁰ conducted a wear analysis on MOM THRs retrieved after a mean of 21.3 years and reported a worst case estimate of combined femoral and acetabular wear of 4.2 microns per year - approximately 25 times less than that typically observed with polyethylene. Nevertheless, histology studies of tissues retrieved from revised MOM prostheses have indicated mild-to-moderate macrophage infiltration with metal debris localized in macrophages.⁶¹ Whether this will lead to osteolysis in the long term following MOM HRA remains unknown.

Femoral Neck Fractures

MOM patients may have an elevated risk for femoral neck fractures shortly after surgery due to a combination of patient, surgical and postoperative factors.⁶² A recent audit of the first 3429 Birmingham hip resurfacing recipients found a femoral neck fracture rate of 1.46% at an average time of 15 weeks after surgery⁶³. Amstutz et al 2004⁶⁴ reported a femoral neck fracture rate of 0.83% in a series of 600 MOM HRA. A review of the complications list from the included case series studies (see Table 10) indicates that femoral neck fractures were a common occurrence but affected a small percentage of MOM hip resurfacing patients.

De Smet KA (2005)⁶⁵ outlined several risk factors associated with femoral neck fracture in hip resurfacing patients. These are summarized in Table 12 below.

Table 12: Risk factors for the Development of Femoral Neck Fracture

Surgical Factors	Patient Factors
Femoral neck notching	Severe osteoporosis
Malpositioning of central guide pin	
Varus placement of the head component	
Incomplete coverage of reamed bone	
Removal of soft tissue around femoral neck	
Impact too hard and too long	
Impacting in wrong direction	
Removal of too much femoral neck bone	

Dislocations

A review of the complications reported in the literature (see Table 6) showed that the majority of studies reported no incidence of a dislocation. Among studies where dislocation was reported, the incidence was minor: Amstutz et al (2004) 1.5%, De Smet (2005) 0.4%, Siebel et al. (2006) 0.3%.

Osteoporosis

Osteoporosis is a disease characterized by the loss of normal bone mass and density, which increases the risk of bone fractures. The success of hip arthroplasty is dependent on the strength of existing bone, and decreased bone quality increases the risk of prosthesis failure. Although osteoporosis affects men and women, its prevalence is greater in women due to hormonal changes that happens during and after menopause. Using World Health Organization criteria, in 2000 the incidence of osteoporosis of the femoral neck in Canadian men and women aged 50 or more was 4.8% and 7.9%, respectively.⁶⁶ Approximately 35% of men and 55%



of women also have osteopenia, which is characterized by bone below-normal mineral density but not as low as osteoporosis. Therefore, osteoporosis represents a general contraindication that must be considered prior to MOM HRA. As Roberts et al (2005)⁶⁷ stated, the difficulty is determining to what extent femoral head deficiency or what degree of femoral head and neck osteoporosis is incompatible with the long-term success of hip resurfacing arthroplasty. Duijsens et al (2005)⁶⁸ suggested that patients with severe proximal femoral osteoporosis may not benefit from hip resurfacing. Currently, the relation is not well understood between osteoporosis of the femoral head and neck to prosthesis failure. Consequently, diligence must be exercised in patients with osteoporosis when considering MOM hip resurfacing. This is of particular importance to post-menopausal women and young patients with inflammatory arthritis, or other osteoporosis risk factors.

Metal Ion Release and Safety

The current generation of MOM resurfacing prostheses feature femoral and acetabular components made of Co-Cr alloy bearing surface. Despite the lower overall wear⁶⁹, studies have indicated that MOM resurfacing systems generate cobalt and chromium particles that exceed the accumulated particles with previous metal implants and non-metal implants.⁷⁰ Analyses of the blood of BHR patients before and after surgery suggested that cobalt levels peaked at 6 months postoperatively and gradually declined, and chromium levels peaked at 9 months and then declined.⁷¹ That raises legitimate concerns for systemic and local toxicities with the MOM implants.

Although cobalt is essential to the human diet (it is a constituent of vitamin B12), higher doses of cobalt and chromium can cause severe biological effects, including cancer, respiratory and renal conditions, and implant loosening.^{72,73,74}

A recent study by Visuri et al. (2006)⁷⁵ assessed the relation between hip replacements and the incidence of cancer in a large cohort of Danish, Norwegian and Swedish patients. Specifically, they found that 579 MOM THR patients with a primary diagnosis of OA and at a mean follow-up period of 16 years had virtually the same rate of all-site cancer (standardized incidence ratio - SIR of 1.03) as compared to age- and sex-matched healthy population. The SIR for each cancer type was calculated by the observed cases of cancer

among the MOM hip replacement patients with that expected in the general population. Visuri et al. did note that the incidence of lung cancer was lower than expected, especially among male patients, but was significantly more in cases with unknown primary site among females. Signorello et al. (2001)⁷⁶ assessed the incidence of cancer among 116,727 patients who underwent hip replacement surgery in Sweden between 1965 through 1994 and reported that, relative to the population, THR patients had no overall cancer excess (SIR = 1.01).

A study by Brodner and colleagues⁷⁷ presented a randomized trial of metal levels in 100 uncemented THRs, 50 with MOM and 50 with ceramic-on-polyethylene articulation. All patients received titanium acetabular and femoral components. Measurements of metal blood levels were done preoperatively and at 3, 6, 12, and 24 weeks postoperatively; measurements were then repeated every 6 months. Serum cobalt was analyzed using atomic absorption spectrometry. In the metal-on-metal group, the median serum cobalt concentration was 1 mcg/L at 1 year, 0.55 mcg/L at 2.5 years, and 0.7 mcg/L at 5 years. The median serum cobalt in the ceramic-on-polyethylene group was consistently below the detection limit. The difference in median serum cobalt between the 2 groups was significant ($P < .0001$). This study demonstrated a systemic cobalt release from metal-on-metal bearing surfaces over a 5-year postoperative period. Skipor and colleagues⁷⁸ measured the levels of serum chromium (SrCr), serum cobalt (SrCo), and urine chromium (UrCr) in 14 MOM hip resurfacing procedures. According to the results of this study, SrCr and SrCo levels increased as postoperative time increased. UrCr showed increases at 6 months, but decreased at 12 months. Concentrations at 12 months were 19 times greater for SrCr, 14 times greater for UrCr, and 6 times greater for SrCo compared with values seen in patients with metal-on-polyethylene bearing surfaces. The authors concluded that there was a substantial elevation in serum and urine metal content following metal-on-metal hip resurfacing, but the toxicologic significance remained unclear. Indeed, although studies have shown an increased incidence of some cancers in patients with MOM hip resurfacing, other cancers were significantly reduced in the treated population. These data suggest that the clinical significance of the elevated metal levels in MOM hip resurfacing remains to be established, and its relevance for toxicity and carcinogenesis is equivocal. A summary of metal ion debris measurements identified in past studies is illustrated in Figure 4.

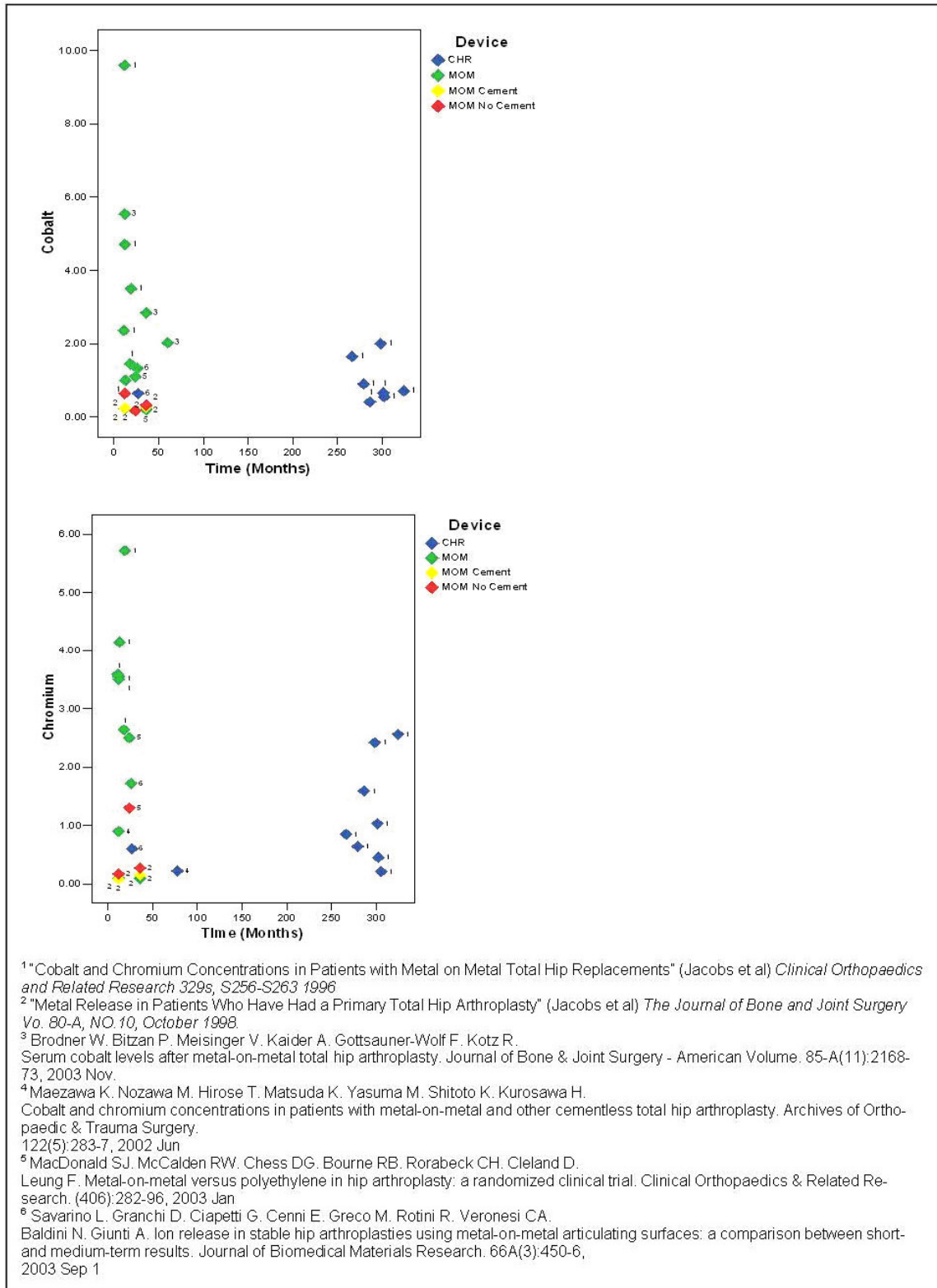


Figure 4. Summary of Cobalt and Chromium Ion Measurements from Previous MOM Prostheses Studies



Hypersensitivity to Metal Ions

The systemic dissemination of metal debris has led to concerns about the response to the particles in other body tissues. Another potential systemic effect of metallic wear debris is the development of hypersensitivity to the released metal ions. Metal hypersensitivity could potentially lead to implant failure, or worse, a systemic immune response. MOM implants more than their metal-PE counterparts are thought to be at particular risk due to the high numbers of potentially allergenic metal particles produced.⁷⁹

Fertility and Reproduction

Studies are limited that document metal ion effects on reproductivity in humans. Elbethieha and Al-Hamood⁸⁰, however, showed that ingestion of trivalent and hexavalent Cr compounds by adult male and female mice caused adverse effects on fertility and reproduction.

Although the cause and effect relation has not been conclusively proved between metal debris and local or systemic disease, complications potentially arising from metal wear products are subject for concern.⁸¹ MOM devices should be monitored with regular clinical, laboratory and radiologic investigations to detect possible complications at the earliest possible stage.

Learning Curve associated with Hip Resurfacing THR

MOM hip resurfacing has a significant learning curve associated with the procedure. This is in part because, although the surgical approach is similar to that of conventional THR surgery, hip resurfacing has more dissection as the femoral head is preserved and displaced to allow visualization of the acetabulum.⁸² The learning curve associated with hip resurfacing is evident in an inverse relationship between revision rates and surgeon's experience. For example, Mont et al (2005) reported a 25% failure rate among the first 50 MOM hip resurfacings, which was then followed by a 1% failure rate among the next 150 procedures. More recently, Siebel et al. (2006)⁸³ reported a failure rate of 4.7% among the first 150 patients, followed by a 0.7% failure rate for the next 150 hip resurfacings. This learning curve is illustrated in Table 13.

Table 13: The Learning Curve Profile Based on the Number of Failures for Consecutive Groups of 50 Hip Resurfacings.

		1-50	51-100	101-150	151-200	201-250	251-300	TOTAL
Revisions	NO	48	47	48	50	49	50	274
	YES	2 (4.0%)	3 (6.0%)	2 (4.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	8 (2.7%)
	TOTAL	50	50	50	50	50	50	300

Adapted from Siebel et al. 2006.



Surface Arthroplasty Risk Index

Beaule et al (2004)⁴⁵ developed a grading system to predict the survivorship of MOM hip resurfacing prostheses based on radiographic evaluation and patient history. An underlying basis for such a grading system was to identify patients with MOM HRA at risk of revision. This mirrored the development and use of the Chandler index⁸⁴, which was published in 1981 and identified THR patients at risk of prosthesis failure. Since the MOM HRA prostheses differed considerably from THR devices, Beaule et al. developed the Surface Arthroplasty Risk Index (SARI)⁴⁵ to facilitate optimized patient selection and implant survivorship.

In the SARI, 2 points are given to femoral head cyst of greater than 1 cm, 2 points for a body mass below 82 kg, 1 point for previous surgery, and 1 point for a high activity level of 7 or greater on the UCLA activity scale. In comparison to the THR-based Chandler index, the SARI assigns 2 points for a femoral cyst because femoral cysts have a direct relation with the femoral component fixation in MOM HRA. A comparison of the items of the Chandler index and SARI are provided in Table 14.

Table 14: Items of the Chandler Index and SARI

Item	Chandler Index	SARI
Absence of collagen disease	1	-
Activity level (UCLA score)	1	1
Avascular necrosis	1	-
Femoral cyst >1cm	-	2
Previous surgery	1	1
Unilateral hip disease	1	-
Body mass	1 if > 82kg	2 if < 82kg

Adapted from Beaule et al. 2004

In the SARI, high scores are associated with higher risk of failure. Beaule et al.⁴⁵ found that patients who experienced postoperative problems following MOM HRA had significantly higher SARI scores than patients who had low SARI scores. Patients with SARI scores great than 3 were found to be 12 times more likely to experience early problems than patients with a SARI of 3 or less.⁴⁵ Amstutz et al. (2004)

⁸⁵ also reported that SARI scores above 3 were significantly correlated with earlier revisions following MOM hip resurfacing. The survival rate of the MOM prostheses at 4 years follow-up for patients with low SARI scores (below or equal to 3) was 97%, compared with 89% for patients with SARI scores above 3.



Alberta Hip Improvement Project (HIP)

In collaboration with the Calgary Health Region, Capital Health, Alberta Health and Wellness, and the orthopaedic surgeons, it was determined to be essential to conduct a prospective clinical trial to determine the appropriateness for use of newer hip replacement devices for younger adults in Alberta. The Alberta Bone and Joint Health Institute was approached to design and implement a study to determine the effectiveness, cost-effectiveness and safety of new alternative hip bearing devices.

The study design aimed to provide orthopaedic surgeons and decision makers with the requisite evidence to determine the appropriate use of new hip devices for patients requiring THR in Alberta. Prior to the HIP study, no formal system was implemented to capture the necessary health related information pertaining to the appropriate use of orthopaedic devices or techniques in Alberta.

A review of the existing literature coupled with consensus of the leading orthopaedic surgeons resulted in the development of criteria for patients receiving hip resurfacing in Alberta. The inclusion criteria defined for the study inception (June 2004) was agreed to by the project partners and included the following:

1. Patient less than 56 years at time of surgery.
2. Patient must consent to participate in a prospective study to evaluate the effectiveness and safety of hip resurfacing compared to other device options.
3. Patient must have appropriate femoral anatomy.
4. Orthopaedic surgeon must be appropriately trained to perform hip resurfacing.
5. Patient must not have compromised renal function.
6. Female patients must not be of child bearing potential.

Patient must be a resident of Alberta (for administrative access for complete patient follow up).

Study Design and Ethical Concerns

Assessment of innovative surgery is recognized as an important ethical issue. However, it is notoriously difficult to devise research methods to assess new forms of surgery. A study of arthroscopic surgery involving a placebo arm gathered

both praise and criticism for the methodology used. For more invasive forms of surgery, classical clinical trial methodology with randomization to one or other arm, or randomization to one arm and a placebo can raise ethical issues and concerns with patients.

The design chosen for the Alberta HIP study was a compromise between randomizing patients to one or another procedure, which was felt not to be acceptable to the patient and not acceptable to the surgeons performing the surgery. The Alberta HIP study, thus was a prospective case control design whereby the surgeon consults with each patient to determine which type of surgery is best for the patient. The patients are entered into a common database (registry) that compares and tracks patient progress over the years for a minimum of 10 years. This methodology has been used to assess new devices (e.g., in cardiology) and has proven effective in providing acceptable evidence of efficacy and listing of complications.

Ethical Approvals

The Alberta HIP study received ethical approval by the University of Calgary Conjoint Ethics Review Board as well as the University of Alberta Ethics Review Board. The Principal Investigators of the study are Dr. Cy Frank (University of Calgary) and Dr. Greg O'Connor (University of Alberta). All patients are required to sign consent to participate in the study. It was also agreed by the orthopaedic surgeons and the Regional Health Authorities, that due to the uncertainties regarding the long term outcomes of MOM hip resurfacing, all patients receiving MOM hip resurfacing must consent to participate in the study.

Study Background

Beginning in June 2004, patients under the age of 56 years requiring hip arthroplasty were recruited and consented to participate in this prospective longitudinal study. Figure 5 illustrates the study flow diagram.

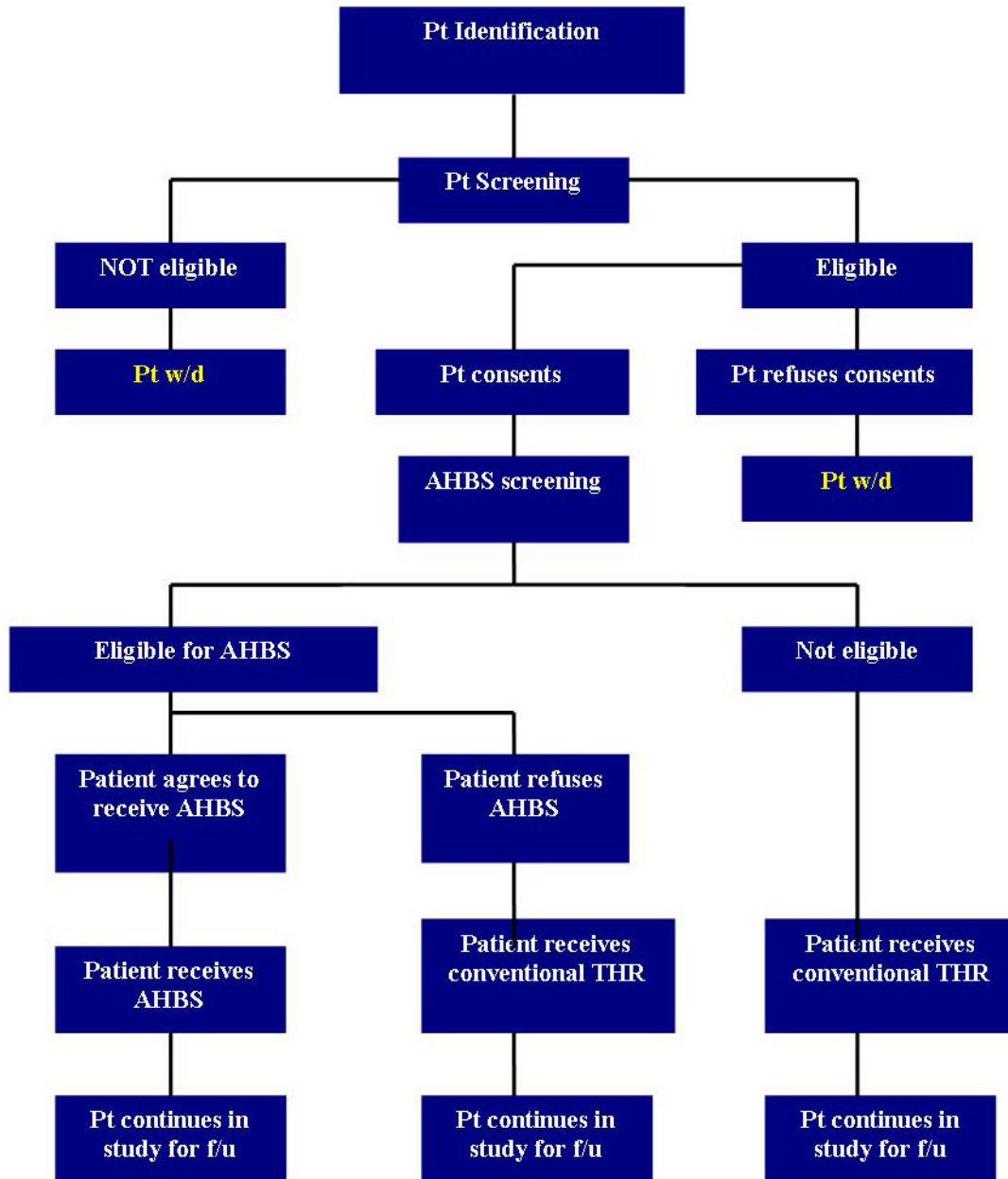


Figure 5. Alberta HIP Study Flow Diagram



As of July 31, 2006, 478 patients were recruited into the Alberta Hip Study. Data are continually being captured from a number of sources consented to by the participating patients, including patient questionnaires, clinic and hospital charts, as well as administrative data from Alberta Health and Wellness, the Regional Health Authorities and Vital Statistics. Data collected via the patient questionnaires include patient demographics, co-morbidity status, direct and indirect costs, and validated general and disease specific health related quality of life surveys. Patient questionnaires are administered to all patients pre surgery (baseline) as well as at timed intervals post-surgery (3 months, 6 months and annually thereafter for 10 years).

Patient co-morbidity is estimated based on methodology developed by Clark et al (1995).⁸⁶ Specifically, a measurement of comorbidity status, based on the utilization of prescription drugs is calculated using the Chronic Disease Score (CDS) which is a weighted index of prescription medications whereby higher scores are a result of more classes of medications dispensed, especially medications used to treat serious diseases. The CDS has strong evidence of validity, including a high correlation with physician ratings of physical disease severity and high year-to-year stability. Further tests of reliability and predictive validity using Alberta administrative databases found the CDS to be a significant predictor of hospitalization and health resource utilization.⁸⁷ As the scoring table for the CDS was originally developed in 1995, a consensus of Alberta specialists updated the table to include classes of medications introduced to the market since the development of the co-morbidity scoring tool. For the purposes of the Alberta HIP study cohort, the use of analgesic medications for the treatment of their hip pain were eliminated from the calculations of subject's CDS.

To assess and compare the effectiveness and cost utility of new hip devices a number of generic and disease specific health related quality of life (HRQOL) questionnaires were captured in the study. The Western Ontario and McMasters University Osteoarthritis Index (WOMAC) survey is a valid and reliable instrument used specifically for accessing lower limb function pain, and stiffness in patients suffering from OA. It is a self assessment questionnaire that asks patients questions regarding

their pain, stiffness and function in the hip and knee areas affected by OA.⁸⁸

The SF-36 Health Survey is a multi-purpose, short-form health survey containing 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically based physical and mental health summary measures and a preference-based health utility index. It is a generic measure as opposed to one that targets a specific disease or group. The SF-36 has been documented in over 4,000 publications and the usefulness in estimating disease burden and comparing disease specific benchmarks with general population norms is illustrated in articles describing over 200 diseases and conditions, including osteoarthritis and other musculoskeletal disorders.⁸⁹ Studies to date have shown concurrent, criterion, construct and predictive evidence of validity of the SF-36 questionnaire.

The HUI-3 is a generic health profile and preference-based system for the purpose of measuring health status, reporting HRQOL and producing utility scores.⁹⁰ HUI-3 measure has a strong theoretical foundation and has been shown to be both a valid and reliable health questionnaire.⁹¹ HRQOL is defined as the value assigned to the duration of life as modified by the impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, treatment or policy.⁹² HUI-3 has been used in hundreds of clinical studies covering diverse health problems and in numerous large general population surveys since 1990.⁹³ Marginal utility scores are being used more frequently by decision makers for the decision to fund new and existing health interventions.

To assess the safety of metal ion debris release in patients receiving MOM hip resurfacing a subcohort of 200 patients is providing baseline (when available) and annual blood samples for the measurement of cobalt and chromium ions. The sub-cohort is being followed due to the study budget and the high costs associated with the measurement of metal ions. Blood samples are collected in Royal Blue (Trace Metals) vacutainer tubes, obtained from Calgary Laboratory Services, and stored at 4C until delivery (within five days of collection) to the University of Calgary Toxicology Centre for analysis. The



whole blood samples are diluted 20 times with a 1% nitric acid and 0.5% hydrochloric acid solution. Similarly, whole blood controls are diluted using the same diluent. Calibrators are made up in the diluent before each batch. Internal standard is added to each sample, calibrator and control. A minimum of 10 samples and a maximum of 50 samples are run in a batch. The diluted blood is analyzed for chromium and cobalt using an Agilent 7500ce Inductively Coupled Plasma Mass Spectrometer (ICP-MS). A calibration is run at the beginning of the analysis. Three whole blood controls (low, medium and high) are included at the beginning and every 10 samples throughout the run. The controls must be within 20% of the reference values for the batch to be acceptable. One duplicate sample is run in each batch for every 25 samples. The limit of quantitation for chromium and cobalt is 0.4ng/mL.

Alberta HIP Advisory Committee

The Hip Advisory Committee was appointed to bring the appropriate experience and expertise to the study. This committee is comprised of a representative from each of the project partners as well as additional research expertise. The role of the Hip Advisory Committee is to develop and approve the research proposal, to monitor study progress, and to interpret study results. Any amendments to the original proposal as a result on interim reports are the responsibility of the Hip Advisory Committee. All publications arising from the Alberta HIP Study must be signed-off by the Alberta HIP Advisory Committee.

Alberta HIP Advisory Committee Membership (as of September 2006)

Dr. Brian Burkart
Orthopaedic Surgeon, Calgary

Dr. Cy Frank, Principal Investigator
Orthopaedic Surgeon, Calgary

Katherine Gooch
Chief Operating Officer, ABJHI, Calgary

Dr. James MacKenzie
Orthopaedic Surgeon, Calgary

Dr. Greg O'Connor, Principal Investigator
Orthopaedic Surgeon, Edmonton

Dr. Jim Powell
Orthopaedic Surgeon, Calgary

Dr. Jason Werle
Orthopaedic Surgeon, Calgary

Dr. Ron Zernicke
Executive Director, ABJHI, Calgary

Tracy Wasylak
Vice-President, Southwest Community Portfolio,
Calgary Health Region

Analyses Completed at Year 2

The total cohort included in the interim analyses comprises 329 patients under age 56 at the time of surgery. Of the 329 patients, 188 received MOM hip resurfacings, 87 received COC THR and the remaining 54 received other THA (22 S-ROM, 12 MOM, 13 polyethylene, and 7 hybrid). The aim of the interim analyses was to compare the outcomes of MOM hip resurfacings to other THR devices. The first patient was enrolled into the study in June 2004.

General Cohort Characteristics

The average age of patients receiving MOM hip resurfacing was 47.6 years compared to 47.7 years for patients receiving other THA devices. Table 11 illustrates the statistically significant differences in patient characteristics (i.e., age, gender, co-morbidity, pre-surgery WOMAC, body mass index (BMI) and socioeconomic statuses) before surgery. A p value of ≤ 0.05 was deemed a statistically significant difference between groups.



Table 15: Summary of Patient Characteristics Prior to Surgery

Patient Characteristic	MOM Hip resurfacing	Other total hip replacements	p value
Age Mean Standard deviation	47.64 6.29	47.69 7.46	0.947*
Gender % female	46.42	53.57	<0.001**
Co-morbidity status Mean Standard deviation	568.61 1024.33	1134.60 1532.18	<0.001*
WOMAC Mean Standard deviation	49.01 15.44	54.61 14.30	0.001*
Body mass index Mean Standard deviation	27.22 4.07	29.00 6.07	0.001*
Socioeconomic status % Low % Medium % High	17.17 25.75 57.07	38.57 30.0 31.42	<0.001**

* t-test used to determine differences in continuous data
 ** chi-square test used to determine differences in categorical data

The patient characteristics illustrated in Table 15 show that with the study design, the average age of patients receiving a MOM hip resurfacing or THR was not significantly different. The differences that existed in this patient cohort showed a higher percentage of men receiving MOM hip resurfacings than women. Baseline pain, function and stiffness (as obtained by WOMAC) were worse in patients receiving THR than those receiving MOM hip resurfacing. In addition patients receiving THR tended to have more co-morbidities, with lower socioeconomic status, than patients receiving MOM hip resurfacing. A statistically significant difference was found in patient baseline BMI, with patients receiving THR having greater average BMI scores than patients receiving MOM hip

resurfacing. With an average difference of 1.78 BMI, however, the clinical significance is equivocal.

3-Month Effectiveness Outcomes

One hundred and ninety one patients were included in an analysis to compare the effectiveness of MOM hip resurfacing to other THR at 3 months post surgery (see Table 16). Effectiveness was defined as a clinically relevant change in WOMAC scores from pre-surgery to 3-months post surgery. One hundred and twelve patients received MOM hip resurfacing, and 79 patients received another THR device. There was no significant difference in WOMAC scores at 3 months (16.38 hip resurfacing vs. 16.79 for other THR,



p=0.834). On average, WOMAC differences between baseline and 3 months were 31.96 for hip resurfacing patients compared to 35.60 for other THR patients (p=0.141). Univariate analysis was undertaken whereby all associations < 0.2 were added in a multivariate linear regression model. The primary outcome was tested and met criteria for linearity. Results of the final model indicated that patient co-morbidity and exposure to analgesics were both statistically significant predictors of improvement in WOMAC scores at 3 months post surgery.

The results of that analysis suggested that at 3 months following surgery, there were no differences in patient WOMAC scores between hip resurfacing vs. other THR patients. When comparing effectiveness of hip resurfacing, it is important to consider the differences in patient characteristics as seen in this subset of patients compared to other young patients receiving other types of THR.

Table 16. Paired samples statistics between BHR and THR patients

Patient Characteristic	BHR	THR	Significance
n = 191	n = 112	n = 79	
DIFFWOMAC	31.96 ± 17.1	35.60 ± 16.3	p = 0.141
WOMAC (3month)	16.38 ± 14.2	16.79 ± 12.1	p = 0.834

Patient Samples Test		95% CI of Difference	
WOMAC(baseline) - WOMAC(3month)	33.47 ± 16.81	31.07 - 35.87	p < 0.0001

Patient Safety Results, Readmissions and Metal Ion Findings

Readmissions were defined as a readmission to hospital for any reason within 30 days after the primary surgery or for any joint specific reason greater than 30 days after the primary surgery. Readmission information was obtained from the administrative databases within the participating regional health authorities (Calgary Health Region and Capital Health). The differences in event rates by patient group are shown in Table 17. Further investigation and longer patient follow-up are required to determine the differences in readmission rates between THR device types.

Table 17: Readmission rates by prosthesis type

Prosthesis Type	Readmission Rate 0-3 month	Revision Rate
MOM Hip resurfacing	2.6	0
COC THR	1.1	0
Other THR	1.8	0



MOM Hip Resurfacing Metal Ion Trends

The cohort for metal ion analysis consisted of patients who received a MOM hip resurfacing between 2002 and 2005 and gave blood samples at baseline and post surgery. Due to the short term follow up of metal ions, no analysis has been undertaken to identify any negative health consequences due to metal ion release post MOM hip resurfacing THR. Figures 6 and 7 illustrate the trend of serum cobalt and serum chromium levels post MOM hip resurfacing as seen in the HIP study patients.

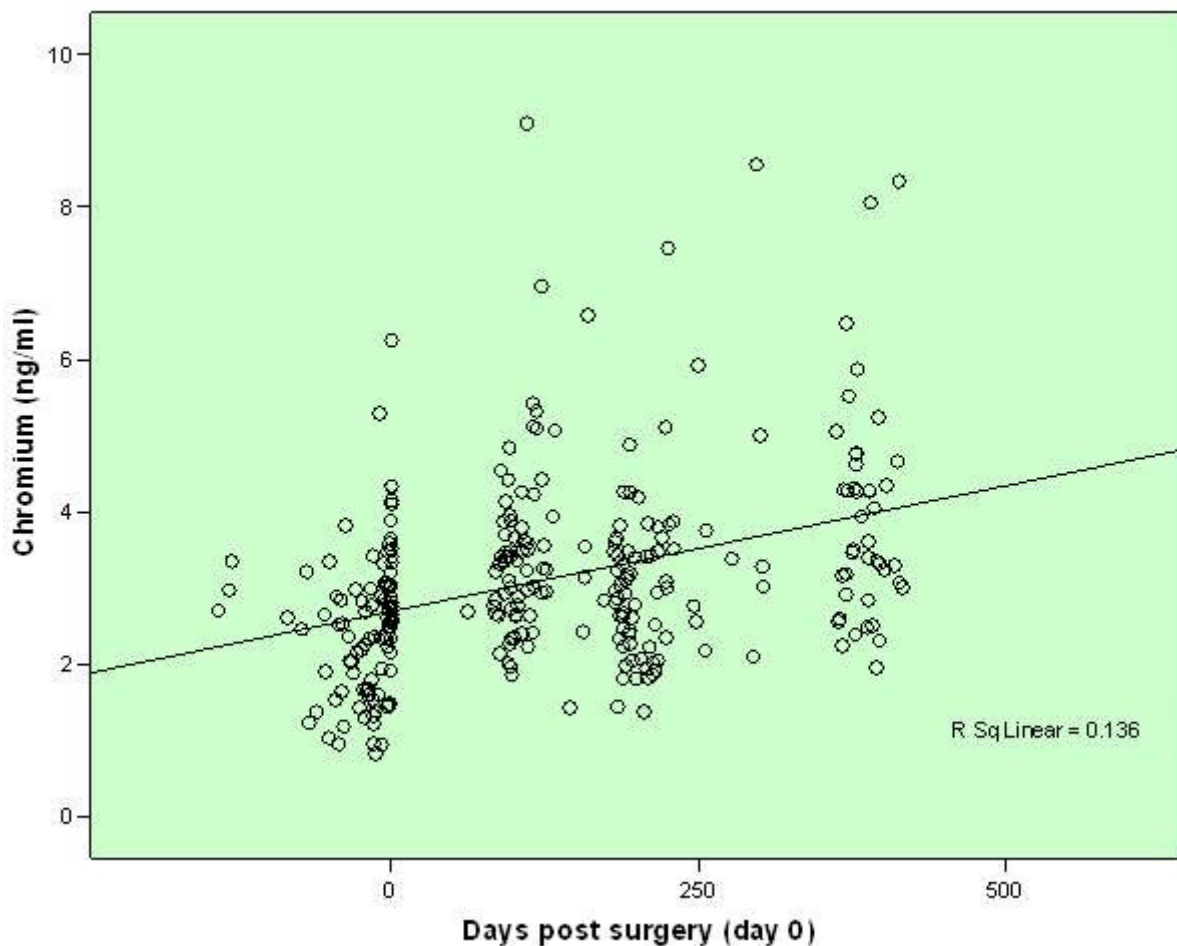


Figure 6. Scatterplot illustrating Relation between Chromium Release and Days Following MOM Hip Resurfacing.

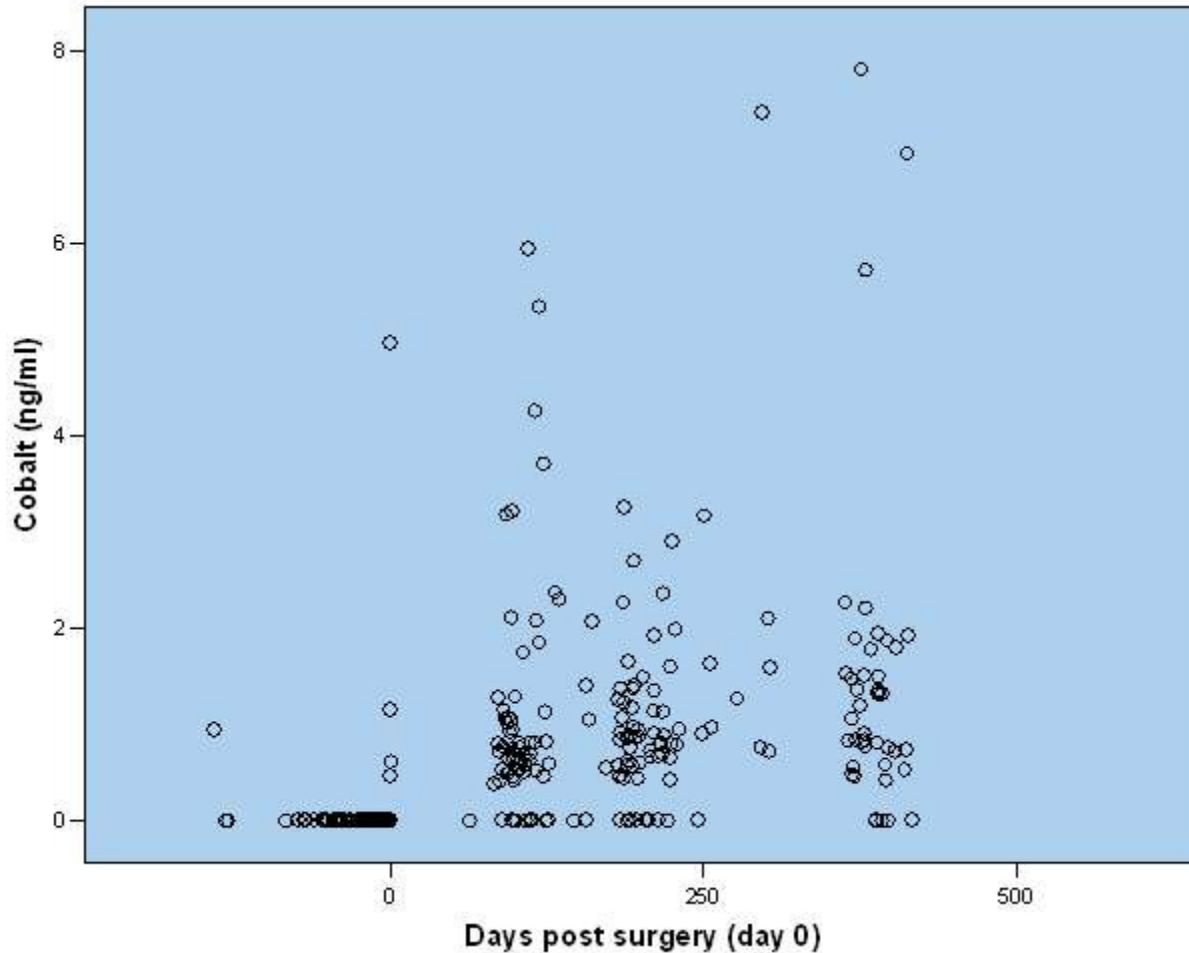


Figure 7. Scatterplot illustrating Relation Between Cobalt Release and Days Following MOM Hip Resurfacing.

Cost and Cost Effectiveness Results

The Alberta Hip and Knee Replacement Pilot Project (www.albertaboneandjoint.com/hipandknee.asp) developed a provincial standardized costing model to compare the costs of the new developed hip and knee replacement continuum to the current standard of care. Inputs for the costing model resulted from consultations with costing experts from the participating

regional health authorities. The final costing model inputs are shown in Table 18. Costs for all components were obtained from financial representatives from within each of the participating healthcare regions and were standardized and validated by an independent accounting firm. The final model was used to determine the direct inpatient costs for this study. Pre and post inpatient costs, as well as provincial expenses were not included in this analysis as they are not costs incurred directly by the regional health authorities.



Table 18: Costing Model Inputs for Operation and Acute Inpatient Stay. Modified Version of Alberta Hip and Knee Replacement Costing Model

Costs	Cost Driver	Payer
Operating Room (OR) Costs		
Anaesthetist	encounter	Alberta Health and Wellness
Surgical Assist	encounter	Alberta Health and Wellness
Orthopaedic Surgeon	minutes per patient	Alberta Health and Wellness
Nursing Compensation	minutes per patient	Regional Health Authority
OR Tech Compensation	minutes per patient	Regional Health Authority
Autologous Blood / Transfusion	per patient	Regional Health Authority
CSR Compensation	minutes per patient	Regional Health Authority
Anaesthesia Compensation (Tech Only)	minutes per patient	Regional Health Authority
OR Support Compensation	minutes per patient	Regional Health Authority
Nursing Compensation (PARR)	per patient	Regional Health Authority
Drugs	per patient	Regional Health Authority
Supplies (Excluding Prosthesis)	per patient	Regional Health Authority
Equipment Amortization	per patient	Regional Health Authority
Indirect Costs	per patient	Regional Health Authority
Prosthesis	actual per patient	Regional Health Authority
In-patient Costing		
Nursing Compensation	per day	Regional Health Authority
Nursing Administration & Support	per day	Regional Health Authority
Rehab Compensation	per day	Regional Health Authority
Drug	per day	Regional Health Authority
Meals	per day	Regional Health Authority
Linen	per day	Regional Health Authority
Other Supplies	per day	Regional Health Authority
In-patient Lab (Excluding Transfusion)	per day	Regional Health Authority
Equipment Amortization	per day	Regional Health Authority
Other Direct Costs	per day	Regional Health Authority
Indirect Costs	per day	Regional Health Authority



Operating Room Minutes and Inpatient Length of Stay

Descriptive statistics were used to compare costs and components of costs (operating room (OR) and inpatient) for MOM hip resurfacing versus all other THR. A comparison of patients receiving MOM hip resurfacing to other THR devices showed no significant difference in OR minutes (mean, 129.6 minutes for hip resurfacing vs. 130.0 minutes for other hip devices), but a significant difference was seen in length of stay (LOS) as patients receiving MOM hip resurfacing were discharged 0.64 days less, on average, than patients receiving other hip devices (average LOS of 4.10 days for hip resurfacing patients vs. 4.74 days for patients receiving other hip devices).

Cost Effectiveness Modeling

To determine the potential benefits of MOM hip resurfacing against its cost, a cost effectiveness analysis was undertaken to complete an economic evaluation of MOM hip resurfacing,

COC THR compared to all other THR in patients under 56 years of age. A cost per quality QALY was calculated in the analysis due to the availability of utility information from the patient reported HUI-3 scores pre- and post-surgery. Advantages to evaluating costs per QALY included the ability to compare results to other estimates within and externally to bone and joint care, as well as it is the most useful tool in a decision making realm. Various health authorities, including the United Kingdom, have adapted the process of estimating QALYs to rank interventions and inform priority setting.

A Markov model (Figure 8) was developed that requires 3 data inputs including costs, event rates and patient benefit (utility).

The model standardized OR cost and inpatient LOS between the patient groups. Readmission costs were based on Alberta Health and Wellness Case Mix Index estimates and were standardized for all cohort readmission diagnoses. Because of the short duration of the model, discounting was unnecessary. Comparison of cost utility estimates are displayed in Table 19.

Table 19: Comparison of Cost Utility Estimates

	Cost (\$)	Effectiveness (QALY)	Cost utility ratio (actual LOS)	Cost utility ratio (LOS – 4 days)
MOM Hip Resurfacing	11661	2.41	4827	4788
COC THR	10929	2.07	5267	5158
Other THR	11226	2.02	5567	5332

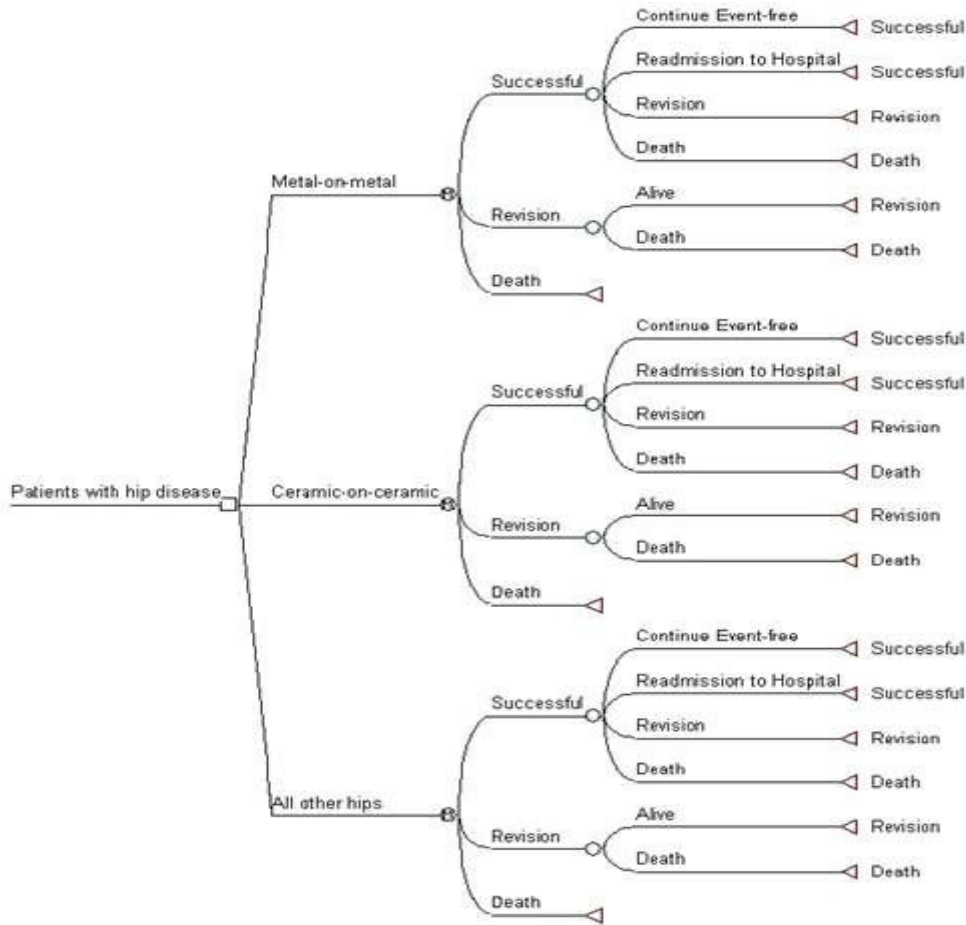


Figure 8: Markov Model Used to Analyze the Cost-Effectiveness

These results indicated that MOM hip resurfacing had a greater pre- and post-utility difference compared to COC THR and other THR. When investigating the difference of costs compared to the utility gains, however, COC THR were the more cost-effective choice for patients under 56 years, if it is assumed that all patients under 56 years should have an average LOS of 4 days. MOM hip resurfacing became more cost effective if the actual LOS averages as seen in the study cohort were applied to the model. Due to the differences seen in MOM hip resurfacing patients compared to other THRs, it is

difficult to determine if the differences seen in LOS are due to the THR prosthesis type or direct patient influences.

Sensitivity analyses examined the changes in cost-effectiveness comparisons based on changes in various costing inputs. A decrease in MOM hip resurfacing costs by 18%, as well as a LOS of 3 days to reflect the new provincial care path for MOM hip resurfacing were forced into the model.



Table 20: Results of Sensitivity Analysis

Cost-Utility Ratio (\$/QALY)			
	MOM Hip Resurfacing	COC THR	Other THR
Resurfacing device = \$4500	4383	5267	5569
Resurfacing device = \$4500 Resurfacing LOS = 3 days	4104	5267	5569
Resurfacing device = \$4500 Resurfacing LOS = 3 days Other LOS = 4 days	4104	5135	5336

Results of the sensitivity analysis (Table 20) suggested that such decreases in health resource costs (device cost and reduced LOS to 3 days) would result in MOM hip resurfacing being the most cost effective choice at 1 year follow up for patients under 56 years in Alberta.

These results indicated that MOM hip resurfacing had a greater pre- and post-utility difference compared to COC THR and other THR. When investigating the difference of costs compared to the utility gains, however, COC THR were the more cost-effective choice for patients under 56 years, if it is assumed that all patients under 56 years should have an

average LOS of 4 days. MOM hip resurfacing became more cost effective if the actual LOS averages as seen in the study cohort were applied to the model. Due to the differences seen in MOM hip resurfacing patients compared to other THRs, it is difficult to determine if the differences seen in LOS are due to the THR prosthesis type or direct patient influences.



Summary of Alberta Hip Study Findings (to date)

- There are significant differences between the patient characteristics MOM hip resurfacing and THR patients.
- At 3 months post surgery, there are no significant differences in the effectiveness of MOM hip resurfacing compared to other THR devices.
- On average all patients under 56 years of age receive newer, more expensive devices than older patients.
- Cost effectiveness results indicate that in 2004/2005 COC THR was the most cost effective option for patients less than 56 years of age in Alberta. However, an 18% decrease in MOM hip resurfacing prosthesis cost couple with a standardized 3 day LOS could result in MOM hip resurfacing being the most cost effective in year 1.
- Valid short term and longer term revision rates and consequences of metal ion release remain unclear.

Limitations to the Alberta Hip Study Findings (to date)

The following limitations are acknowledged in the Alberta HIP study.

- The inability to randomize patients into study groups resulted in many statistically significant differences in patient characteristics between groups. Such differences included the severity of patient hip disease before surgery, gender

distribution, the number of coexisting comorbidities, socioeconomic status and body mass index pre surgery. Any differences in outcomes must account for these differences in patient characteristics between groups, and although there is an attempt to control for patient differences in multivariate analyses models, other models such as the cost effectiveness results are not controlled, and therefore the results may be biased.

- Only 72% of all patients receiving MOM hip resurfacing were recruited into the Alberta HIP study that limits generalisability of the results for all patients that receive MOM hip resurfacing in Alberta.
- Re-admission and revision rates were unattainable for those patients that were not recruited into the Alberta HIP study.
- No long-term data exists about the safety of metal ion release post MOM hip resurfacing, and thus, that factor remains unknown.
- Cost results were based on a standardized model based on financial data from the Regional Health Authorities participating in the Alberta Hip and Knee Replacement Pilot Project; those data may be inaccurate and not applicable to all Alberta Regional Health Authorities or other Canadian provinces.
- The cost effectiveness analysis is only based on 1 year follow-up as the long term revision rates are unknown and therefore the cost effectiveness post 1 year is unknown.



Recommendations for MOM Hip Resurfacings

By integrating current findings from the Alberta HIP study with other existing studies, recommendations for the use of hip resurfacing have been developed by the ABJHI and the Alberta HIP Advisory committee

- **Age Criteria.** The current international age criterion trends for hip resurfacing are:
 - Males ≤ 65 years of age
 - Females ≤ 56 years of age
- The appropriateness of hip resurfacing in patients with osteoporosis remains unclear. For this reason, to continue to define eligibility for hip resurfacing, a hip and spine bone mineral scan (DEXA) is recommended for females ≥ 50 years of age and males ≥ 65 years of age.
- **Obese** patients with a BMI of 35 or greater should not be eligible for a MOM hip resurfacing.
- Women of child-bearing potential should not be eligible for MOM hip resurfacings due to unknown consequences of metal ion debris on the unborn fetus.
- Patients with renal failure should not be eligible for MOM hip resurfacings.
- All patients receiving MOM hip resurfacings should undergo annual toxicology tests to monitor metal ion levels in the blood.

- All patients receiving MOM hip resurfacings in Alberta should read, understand and sign a consent form acknowledging the unknown risks associated with receiving a MOM hip resurfacing and must agree to be studied long-term by the Alberta HIP Study.

The ABJHI and the Alberta HIP Advisory Committee strongly advise surgeons to be guided by future long-term data when deciding the type of procedure to use in young, active patients.

A screening form outlining these recommendations has been developed for physician use (Appendix 1).

These recommendations however, do not override the individual responsibility of the physician to make the appropriate decisions for his or her individual patients.



The Value and Importance of Independent Post-Marketing Research

With the continuing and growing introductions of new health technologies, it is important to understand the relative value of new health technologies that treat the same medical conditions, and especially whether increases in cost can be justified. Recent reports have indicated that new approaches for new health technology post-marketing evaluations need to be undertaken to ensure that new technologies are used in the most appropriate and cost-effective manner possible. To obtain market licensing, biotechnology and pharmaceutical industries must successfully implement and submit research results to national regulatory authorities. However, once new technologies are on the market and are prescribed by physicians to real-world patients, their costs, long-term effectiveness and safety may vary considerably. The variation in results can be attributed to the fact that carefully monitored RCT (Phase III trials) are undertaken in ideal conditions with relatively short-term follow-up (typically 12 months). Additionally in the real-world, new health drugs and devices are used not only for the relatively healthy patients who are enrolled in Phase III studies, but also for younger and older patients and patients with co-morbidities. Commonly, physicians, patients and policy makers base their decisions on the very limited available information from these inconclusive Phase III studies. Unlike the United States, Canadian requirements for medical device marketing do not always require the clinical evidence obtained from Phase III RCT. This, therefore, lessens the physicians' confidence of efficacy and long-term safety in the patients that receive the new devices. Post-marketing studies, otherwise known as Phase IV

trials, that are less frequently used, attempt to determine the safety and effectiveness under real-world conditions for a longer period of time. These observational longitudinal studies such as the Alberta HIP study conducted after licensure, increase the real-world evidence that is required to monitor effectively the use of new health technologies. With this information, payers and decision makers may be more assured of their decisions to fund new health technologies knowing that their decisions would be re-evaluated regularly over time. This would in turn enable them to amend their decisions based on the support of evidence. One of the more powerful tools in post-marketing evaluations is the use of administrative databases to link information to clinical research.⁹⁴

Next Steps

The ABJHI and the HIP Advisory Committee will continue its study of MOM hip resurfacings for a minimum of eight more years.

Further recommendations may be forthcoming as new information becomes available from the study.

For further information

Contact Dr. Ron Zernicke (Executive Director, Alberta Bone and Joint Health Institute)
Email: rzernike@albertaboneandjoint.com



Appendix 1

Alternative Hip Bearing Surfaces Screening Form for Surgeons

INCLUSION CRITERIA
All answers must be "YES"

Patient is able to consent to participate in the HIP study.

YES NO

Patient does not have a history of renal failure.

YES NO

Orthopedic Surgeon has received the appropriate training to implant re-surfacing device.

YES NO

Patient has appropriate femoral anatomy.

YES NO

Patient is not obese and has a BMI < 35.

YES NO

Patient is not of childbearing potential.

YES NO

CONSIDERATIONS

Historically, bone quality has been of concern in women over the age of 50 and men over the age of 65. For this reason, a Hip/Spine DEXA is required as input into continuing to define eligibility for hip resurfacing.

DEXA of Hip and Spine completed:

NO YES Result _____

Please note the indication(s) for a patient receiving a hip resurfacing device:

Physical Activity

Bone Conservation

Age

Other: _____

Physician Name (print): _____

Date: _____
DAY MONTH YEAR

Physician Signature: _____



Reference List

- 1 National Institute for Clinical Excellence (2002) Guidance on the use of metal on metal hip resurfacing arthroplasty (Technology appraisal Guidance No. 44 edn)
- 2 Australian Society and Efficacy Register of New Interventional Procedures (2001) Metal hip resurfacing prosthesis (ASERNIPs, ed),
- 3 Arthritis Canada (2006) Osteoarthritis. Available: www.arthritiscanada.com. Accessed Feb, 2002.
- 4 Rottensten K (2002) Monograph series on age-related diseases IX (17 edn) (Ottawa,O.H.C., ed), Chronic Diseases in Canada
- 5 Faulkner,A. *et al.* (1998) Effectiveness of hip prostheses in primary total hip replacement: a critical review of evidence and an economic model. *Health Technol. Assess.* 2, 1-133
- 6 Berry,D.J. *et al.* (2002) Twenty-five-year survivorship of two thousand consecutive primary Charnley total hip replacements: factors affecting survivorship of acetabular and femoral components. *J. Bone Joint Surg. Am.* 84-A, 171-177
- 7 Northmore-Ball,M.D. (1997) Young adults with arthritic hips. *BMJ* 315, 265-266
- 8 Bisset AF (2001) *Hip resurfacing in younger people with osteoarthritis*, Wessex Institute for Health Research and Development, University of Southampton
- 9 McAuley,J.P. *et al.* (2004) Total hip arthroplasty in patients 50 years and younger. *Clin. Orthop. Relat Res.*, 119-125
- 10 Joshi,A.B. *et al.* (1993) Long-term results of Charnley low-friction arthroplasty in young patients. *J. Bone Joint Surg. Br.* 75, 616-623
- 11 National Horizon Scanning Centre (2000) Metal on metal resurfacing hip arthroplasty (hip resurfacing) (National Horizon Scanning Centre, ed), National Horizon Scanning Centre
- 12 Fitzpatrick,R. *et al.* (1998) Primary total hip replacement surgery: a systematic review of outcomes and modelling of cost-effectiveness associated with different prostheses. *Health Technol. Assess.* 2, 1-64
- 13 Northmore-Ball,M.D. (1997) Young adults with arthritic hips. *BMJ* 315, 265-266
- 14 Hamadouche,M. *et al.* (2002) Alumina-on-alumina total hip arthroplasty: a minimum 18.5-year follow-up study. *J. Bone Joint Surg. Am.* 84-A, 69-77
- 15 D'Antonio,J. *et al.* (2005) Alumina ceramic bearings for total hip arthroplasty: five-year results of a prospective randomized study. *Clin. Orthop. Relat Res.*, 164-171
- 16 DiCapria M,H.M.K.J.e.a. (2002) Ceramic-on-ceramic articulation in cementless THAs done in young patients: a 10-year follow-up study (69th Annual Meeting edn) p. p. 170
- 17 Yoon,T.R. *et al.* (1998) Osteolysis in association with a total hip arthroplasty with ceramic bearing surfaces. *J. Bone Joint Surg. Am.* 80, 1459-1468
- 18 Clarke,M.T. *et al.* (2003) Levels of metal ions after small- and large-diameter metal-on-metal hip arthroplasty. *J. Bone Joint Surg. Br.* 85, 913-917
- 19 Howie,D.W. (1990) Tissue response in relation to type of wear particles around failed hip arthroplasties. *J. Arthroplasty* 5, 337-348
- 20 Howie,D.W. (1990) Tissue response in relation to type of wear particles around failed hip arthroplasties. *J. Arthroplasty* 5, 337-348
- 21 Isaac,G.H. *et al.* (2006) Development rationale for an articular surface replacement: a science-based evolution. *Proc. Inst. Mech. Eng [H. J]* 220, 253-268
- 22 Roberts P *et al.* (2005) Resurfacing arthroplasty of the hip (19 edn) pp. 263-279
- 23 Charnley,J. (1961) Arthroplasty of the hip. A new operation. *Lancet* 1, 1129-1132
- 24 Charnley J (1963) Tissue reactions to polytetrafluorethylene. *Lancet*, 1379
- 25 Townley,C.O. (1982) Hemi and total articular replacement arthroplasty of the hip with the fixed femoral cup. *Orthop. Clin. North Am.* 13, 869-894
- 26 Trentani,C. and Vaccarino,F. (1978) The Paltrinieri-Trentani hip joint resurface arthroplasty. *Clin. Orthop. Relat Res.*, 36-40
- 27 Freeman,M.A. *et al.* (1978) Cemented double cup arthroplasty of the hip: a 5 year experience with the ICLH prosthesis. *Clin. Orthop. Relat Res.*, 45-52
- 28 Wagner,H. (1978) Surface replacement arthroplasty of the hip. *Clin. Orthop. Relat Res.*, 102-130



- 29 Salzer, M. *et al.* (1978) Cement-free bioceramic double-cup endoprosthesis of the hip-joint. *Clin. Orthop. Relat Res.*, 80-86
- 30 Amstutz, H.C. and Grigoris, P. (1996) Metal on metal bearings in hip arthroplasty. *Clin. Orthop. Relat Res.*, S11-S34
- 31 Wagner, M. and Wagner, H. (1996) Preliminary results of uncemented metal on metal stemmed and resurfacing hip replacement arthroplasty. *Clin. Orthop. Relat Res.*, S78-S88
- 32 Grigoris, P. *et al.* (2005) The evolution of hip resurfacing arthroplasty. *Orthop. Clin. North Am.* 36, 125-34, vii
- 33 Vale, L. *et al.* (2002) A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease. *Health Technol. Assess.* 6, 1-109
- 34 Wyness, L. *et al.* (2004) The effectiveness of metal on metal hip resurfacing: a systematic review of the available evidence published before 2002. *BMC. Health Serv. Res.* 4, 39
- 35 Alberta Heritage Foundation for Medical Research (2002) Metal-on-metal hip resurfacing for young, active adults with degenerative hip disease (Technote 33 edn)
- 36 Medical Advisory Secretariat, f.t.M.o.H.a.L.-T.C.O.C. (2006) Metal-on-Metal Total Hip Resurfacing Arthroplasty, Ministry of Health and Long-Term Care, Ontario, Canada
- 37 Howie, D.W. *et al.* (2005) Metal-on-metal resurfacing versus total hip replacement-the value of a randomized clinical trial. *Orthop. Clin. North Am.* 36, 195-201, ix
- 38 Schmalzried, T.P. *et al.* (1996) Metal on metal surface replacement of the hip. Technique, fixation, and early results. *Clin. Orthop. Relat Res.*, S106-S114
- 39 Vendittoli, P.A. *et al.* (2006) A prospective randomized clinical trial comparing metal-on-metal total hip arthroplasty and metal-on-metal total hip resurfacing in patients less than 65 years old. *Hip International.* 16, S73-S81
- 40 Beaulé, P.E. *et al.* (2004) Risk factors affecting outcome of metal-on-metal surface arthroplasty of the hip. *Clin. Orthop. Relat Res.*, 87-93
- 41 Beaulé, P.E. *et al.* (2004) Metal-on-metal surface arthroplasty with a cemented femoral component: a 7-10 year follow-up study. *J. Arthroplasty* 19, 17-22
- 42 Treacy, R.B. *et al.* (2005) Birmingham hip resurfacing arthroplasty. A minimum follow-up of five years. *J. Bone Joint Surg. Br.* 87, 167-170
- 43 Amstutz, H.C. *et al.* (2004) Metal-on-metal hybrid surface arthroplasty: two to six-year follow-up study. *J. Bone Joint Surg. Am.* 86-A, 28-39
- 44 Pollard, T.C. *et al.* (2006) Treatment of the young active patient with osteoarthritis of the hip. A five- to seven-year comparison of hybrid total hip arthroplasty and metal-on-metal resurfacing. *J. Bone Joint Surg. Br.* 88, 592-600
- 45 Back, D.L. *et al.* (2005) Early results of primary Birmingham hip resurfacings. An independent prospective study of the first 230 hips. *J. Bone Joint Surg. Br.* 87, 324-329
- 46 Daniel, J. *et al.* (2004) Metal-on-metal resurfacing of the hip in patients under the age of 55 years with osteoarthritis. *J. Bone Joint Surg. Br.* 86, 177-184
- 47 Lilikakis, A.K. *et al.* (2005) Hydroxyapatite-coated femoral implant in metal-on-metal resurfacing hip arthroplasty: minimum of two years follow-up. *Orthop. Clin. North Am.* 36, 215-22, ix
- 48 Vail, T.P. *et al.* (2006) Metal-on-Metal Hip Resurfacing Compares Favorably with THA at 2 Years Followup. *Clin. Orthop. Relat Res.*
- 49 De Smet, K.A. (2005) Belgium experience with metal-on-metal surface arthroplasty. *Orthop. Clin. North Am.* 36, 203-13, ix
- 50 Schmalzried, T.P. *et al.* (2005) Optimizing patient selection and outcomes with total hip resurfacing. *Clin. Orthop. Relat Res.* 441, 200-204
- 51 Siebel, T. *et al.* (2006) Lessons learned from early clinical experience and results of 300 ASR hip resurfacing implantations. *Proc. Inst. Mech. Eng [H.]* 220, 345-353
- 52 Beaulé, P.E. *et al.* (2004) Metal-on-metal surface arthroplasty with a cemented femoral component: a 7-10 year follow-up study. *J. Arthroplasty* 19, 17-22
- 53 Roberts, J. *et al.* (2005) Metal-on-metal hip resurfacing. *Scott. Med. J.* 50, 10-12
- 54 Joshi, A.B. *et al.* (1993) Long-term results of Charnley low-friction arthroplasty in young patients. *J. Bone Joint Surg. Br.* 75, 616-623



- 55 Fitzpatrick,R. *et al.* (1998) Primary total hip replacement surgery: a systematic review of outcomes and modelling of cost-effectiveness associated with different prostheses. *Health Technol. Assess.* 2, 1-64
- 56 Vail,T.P. *et al.* (2006) Metal-on-Metal Hip Resurfacing Compares Favorably with THA at 2 Years Followup. *Clin. Orthop. Relat Res.*
- 57 Daniel,J. *et al.* (2004) Metal-on-metal resurfacing of the hip in patients under the age of 55 years with osteoarthritis. *J. Bone Joint Surg. Br.* 86, 177-184
- 58 Zichner,L.P. and Willert,H.G. (1992) Comparison of alumina-polyethylene and metal-polyethylene in clinical trials. *Clin. Orthop. Relat Res.*, 86-94
- 59 Wan,Z. and Dorr,L.D. (1996) Natural history of femoral focal osteolysis with proximal ingrowth smooth stem implant. *J. Arthroplasty* 11, 718-725
- 60 Schmalzried,T.P. *et al.* (1996) Metal on metal surface replacement of the hip. Technique, fixation, and early results. *Clin. Orthop. Relat Res.*, S106-S114
- 61 Doorn,P.F. *et al.* (1996) Tissue reaction to metal on metal total hip prostheses. *Clin. Orthop. Relat Res.*, S187-S205
- 62 Shimmin,A.J. *et al.* (2005) Complications associated with hip resurfacing arthroplasty. *Orthop. Clin. North Am.* 36, 187-93, ix
- 63 Shimmin,A.J. and Back,D. (2005) Femoral neck fractures following Birmingham hip resurfacing: a national review of 50 cases. *J. Bone Joint Surg. Br.* 87, 463-464
- 64 Amstutz,H.C. *et al.* (2004) Fracture of the neck of the femur after surface arthroplasty of the hip. *J. Bone Joint Surg. Am.* 86-A, 1874-1877
- 65 De Smet,K.A. (2005) Belgium experience with metal-on-metal surface arthroplasty. *Orthop. Clin. North Am.* 36, 203-13, ix
- 66 Hopman,W.M. *et al.* (2000) Canadian normative data for the SF-36 health survey. Canadian Multicentre Osteoporosis Study Research Group. *CMAJ.* 163, 265-271
- 67 Roberts,J. *et al.* (2005) Metal-on-metal hip resurfacing. *Scott. Med. J.* 50, 10-12
- 68 Duijsens,A.W. *et al.* (2005) Resurfacing hip prostheses revisited: failure analysis during a 16-year follow-up. *Int. Orthop.* 29, 224-228
- 69 Schmalzried,T.P. *et al.* (1996) Long-duration metal-on-metal total hip arthroplasties with low wear of the articulating surfaces. *J. Arthroplasty* 11, 322-331
- 70 Clarke,M.T. *et al.* (2003) Levels of metal ions after small- and large-diameter metal-on-metal hip arthroplasty. *J. Bone Joint Surg. Br.* 85, 913-917
- 71 Back,D.L. *et al.* (2005) How do serum cobalt and chromium levels change after metal-on-metal hip resurfacing? *Clin. Orthop. Relat Res.* 438, 177-181
- 72 Ellis,E.N. *et al.* (1982) Effects of hemodialysis and dimercaprol in acute dichromate poisoning. *J. Toxicol. Clin. Toxicol.* 19, 249-258
- 73 Kaufman,D.B. *et al.* (1970) Acute potassium dichromate poisoning. Treated by peritoneal dialysis. *Am. J. Dis. Child* 119, 374-376
- 74 Huo,M.H. *et al.* (1992) Metallic debris in femoral endosteolysis in failed cemented total hip arthroplasties. *Clin. Orthop. Relat Res.*, 157-168
- 75 Visuri,T. *et al.* (1996) Cancer risk after metal on metal and polyethylene on metal total hip arthroplasty. *Clin. Orthop. Relat Res.*, S280-S289
- 76 Signorello,L.B. *et al.* (2001) Nationwide study of cancer risk among hip replacement patients in Sweden. *J. Natl. Cancer Inst.* 93, 1405-1410
- 77 Brodner,W. *et al.* (2003) Serum cobalt levels after metal-on-metal total hip arthroplasty. *J. Bone Joint Surg. Am.* 85-A, 2168-2173
- 78 Skipor,A.K. *et al.* (2002) Serum and urine metal levels in patients with metal-on-metal surface arthroplasty. *J. Mater. Sci. Mater. Med.* 13, 1227-1234
- 79 Harkness J and Daniels A (2003) Chapter introduction and overview. In *Campbell's Operative Orthopedics* (10th edn) (S.Terry Canale, ed), Mosby
- 80 Elbetieha,A. and Al-Hamood,M.H. (1997) Long-term exposure of male and female mice to trivalent and hexavalent chromium compounds: effect on fertility. *Toxicology* 116, 39-47
- 81 Pedersen,R.S. and Morch,P.T. (1978) Chromic acid poisoning treated with acute hemodialysis. *Nephron* 22, 592-595



- 82 Mont,M.A. *et al.* (2006) Hip resurfacing arthroplasty. *J. Am. Acad. Orthop. Surg.* 14, 454-463
- 83 Siebel,T. *et al.* (2006) Lessons learned from early clinical experience and results of 300 ASR hip resurfacing implantations. *Proc. Inst. Mech. Eng [H.]* 220, 345-353
- 84 Chandler,H.P. *et al.* (1981) Total hip replacement in patients younger than thirty years old. A five-year follow-up study. *J. Bone Joint Surg. Am.* 63, 1426-1434
- 85 Amstutz,H.C. *et al.* (2004) Metal-on-metal hybrid surface arthroplasty: two to six-year follow-up study. *J. Bone Joint Surg. Am.* 86-A, 28-39
- 86 Clark,D.O. *et al.* (1995) A chronic disease score with empirically derived weights. *Med. Care* 33, 783-795
- 87 Sun,J. *et al.* (2006) Estimating Osteoarthritis Incidence From Population-Based Administrative Health Care Databases. *Ann. Epidemiol.*
- 88 Bellamy,N. *et al.* (1988) Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J. Rheumatol.* 15, 1833-1840
- 89 Ware,J.E., Jr. (2000) SF-36 health survey update. *Spine* 25, 3130-3139
- 90 Horsman,J. *et al.* (2003) The Health Utilities Index (HUI(R)): concepts, measurement properties and applications. *Health Qual. Life Outcomes.* 1, 54
- 91 Marra,C.A. *et al.* (2005) A comparison of generic, indirect utility measures (the HUI2, HUI3, SF-6D, and the EQ-5D) and disease-specific instruments (the RAQoL and the HAQ) in rheumatoid arthritis. *Soc. Sci. Med.* 60, 1571-1582
- 92 Feeny,D. *et al.* (1993) The comprehensive assessment of health status in survivors of childhood cancer: application to high-risk acute lymphoblastic leukaemia. *Br. J. Cancer* 67, 1047-1052
- 93 Feeny,D. *et al.* (1995) Multi-attribute health status classification systems. Health Utilities Index. *Pharmacoeconomics.* 7, 490-502
- 94 Laupacis,A. *et al.* (2003) Gaps in the evaluation and monitoring of new pharmaceuticals: proposal for a different approach. *CMAJ.* 169, 1167-1170

Our vision

is a standard of bone and joint health and health care that is the best in the world – a standard others will want to emulate.

Our mission

is to be the leading agent for continuous improvement in bone and joint health and health care.

About the Alberta Bone & Joint Health Institute:

The ABJHI is a not-for-profit organization dedicated to creating and maintaining a standard of bone and joint health and health care that is the best in the world. In pursuing this standard, the ABJHI creates knowledge through excellent research and evaluation, and translates this knowledge by interpreting it for and sharing it with health care providers and the public. This publication is a product of knowledge translation.

Article Distribution:

This publication is available at www.albertaboneandjoint.com in Portable Document Format (PDF).

Disclaimer:

This publication has not been peer-reviewed and may not reflect all available literature findings on the subject.

The work and conclusions expressed in this publication are the product of the author(s) and do not necessarily reflect the views of the members or the Board of Directors of the ABJHI.

Copyright:

Copyright © 2006 Alberta Bone and Joint Health Institute. All rights reserved. The contents of this article are copyrighted by ABJHI. No part of this article may be used for any purpose other than personal use. Therefore, reproduction, modification, storage or retransmission, in any form or by any means, electronic, mechanical or otherwise, for reasons other than personal use, is strictly prohibited without prior written permission.

Enquiries and Contact Information:

Kathy Gooch, Chief Operating Officer
Email: kgooch@albertaboneandjoint.com

