

Design Features and Clinical Performance of Biomet MoM Total Hip Arthroplasty Systems

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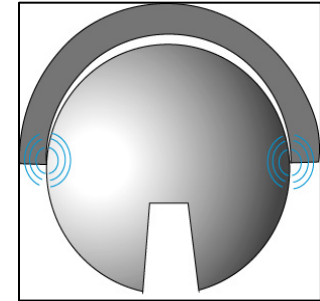
Topics

- **Design Features of Biomet Metal on Metal Total Hip Arthroplasty Systems (MoM THA)**
- **Design Impact on Outcomes of MoM THA – Review of Publications**
 - Metal Ion Level
 - Performance of MoM THA based on NJRs
- **Global Experience on Biomet MoM THA Clinical Performance**
- **Recent Medical Literature**
- **Questions for the Panel**

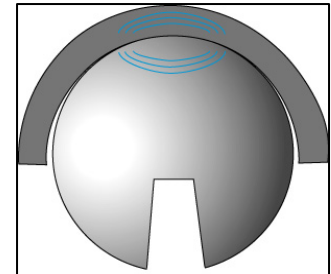
Design Features of MoM THA

- Important to consider design features in combination, not just independently.
- Design Features of MoM include:
 - Diameter
 - Surface Roughness
 - Clearance
 - Sphericity
 - Metallurgy
 - Microstructure
 - Carbon content
 - Coverage angle of cup on head
 - Functional arc coverage or Cup Articular Arc Angle (CAAA)
 - Thickness of shell
 - Deformation
 - Range of motion
 - Taper(s)
 - Taper adaptors
 - Design
 - Material
 - Monobloc or modular cup
 - Cup fixation

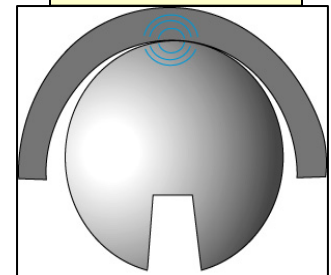
Too Little Clearance



Optimum Clearance

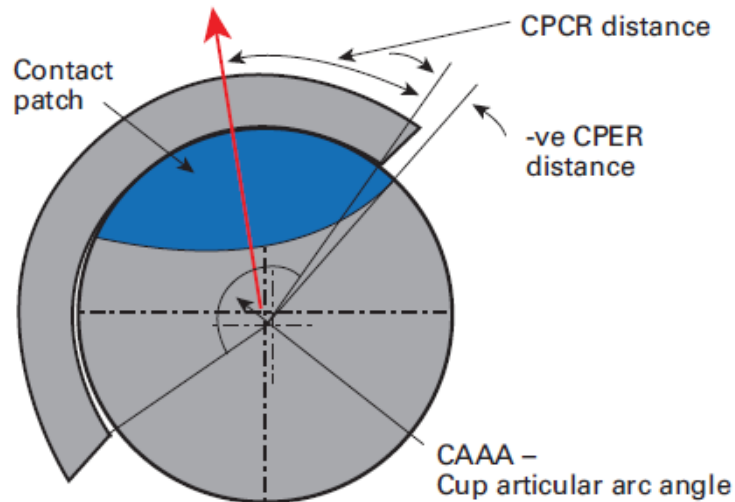


Too Much Clearance

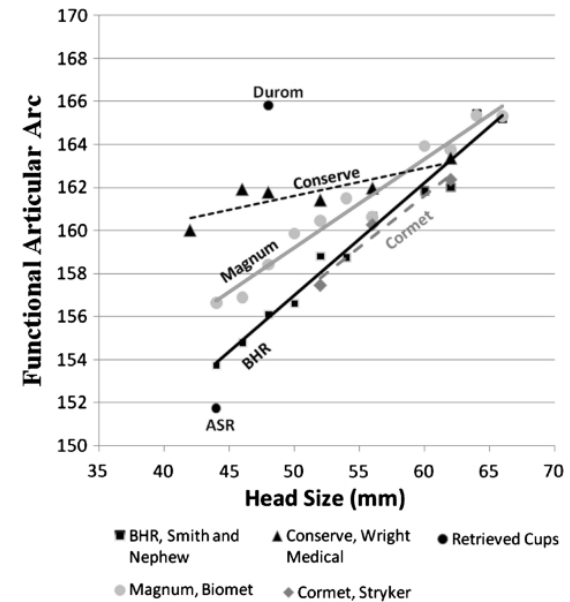


Design Features of Biomet M2a-Magnum

- To minimize possible edge loading, the M2a-Magnum design controls:
 - Diameter
 - Clearance
 - Functional articular arc



{Underwood et.al. ,JBJS-Br 2011, 93-B: 1169-77}



{Griffin et.al., CORR 2010, 468; 2328-2332}

Design, Patient Factors, and Positioning affect Edge Loading

- **Matthies et.al. showed that “edge-loaded MoM hips are higher wearing”** {JBJS-Br 2011, 93-B: 307-14}
 - Positive correlation to inclination angle
 - Adverse acetabular version may be more important than inclination angle
- **Underwood et.al.** {JBJS-Br 2011, 93-B: 1169-77}
 - Designs with reduced cup articular arc angle (CAAA) increase risk of edge contact
- **Underwood et.al.** {J. Eng. In Med., 2012, vol 226, no 3, 217-226}
 - “Low clearance hips, which have a more conformal contact, have a larger diameter contact patch and thus are more at risk of edge loading for similarly positioned hips.”
- **Glyn-Jones et.al.** {JBJS-Br 2009, 91-B: 1566-74}
 - Gender, age, and dysplasia factors in revision rate

Design Features of Biomet M2a-Magnum

- To minimize wear and Co & Cr metal ions, the M2a- Magnum design controls:

- Diameter
- Clearance
- Surface roughness
- Microstructure
- **Titanium** taper adaptor
 - Smooth taper profile



- Taper Corrosion is an area of current investigation
 - Recent publications
 - **Metal-on-Metal Local Tissue Reaction Is Associated With Corrosion of the Head Taper Junction**; Fricka et.al, J Arthroplasty, 2012 May 2
 - **Mixing and matching causing taper wear: corrosion associated with pseudotumour formation**; Chana et.al., JBJS-Br, 2012; 94(2)
 - **Taper junction failure in large-diameter metal-on-metal bearings**; Langton et.al., Bone Joint Res 2012; 1: 56-63

Clinical Publications on the Impact of Design on Metal Ion Levels

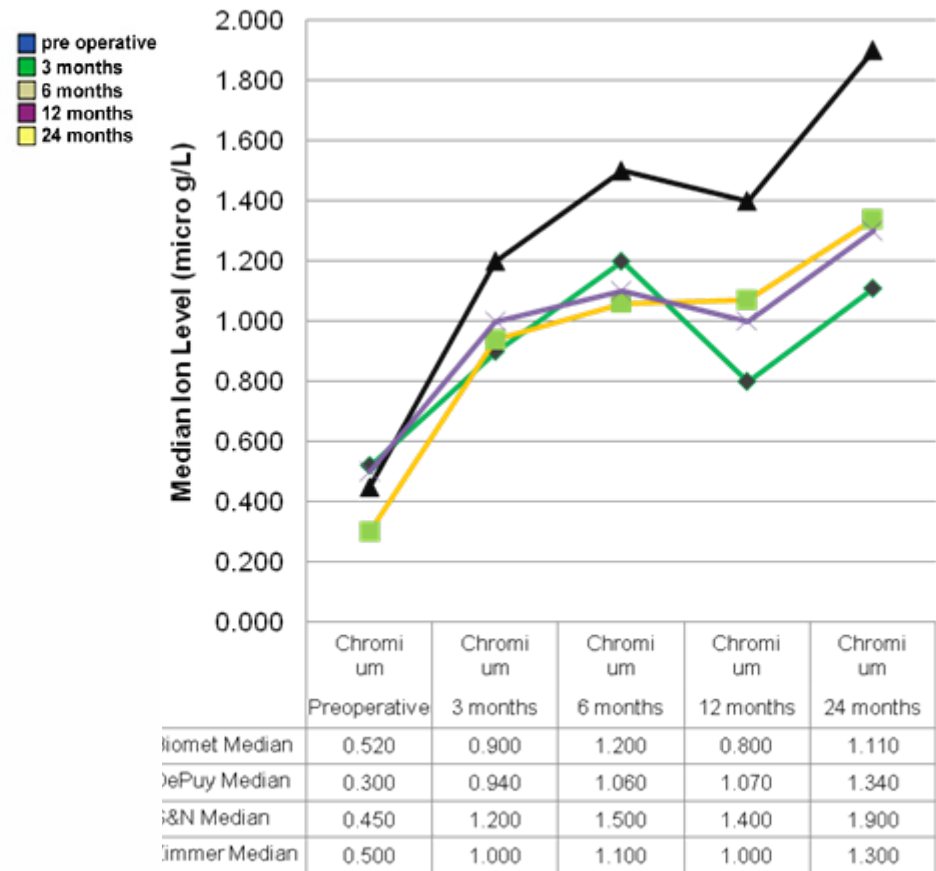
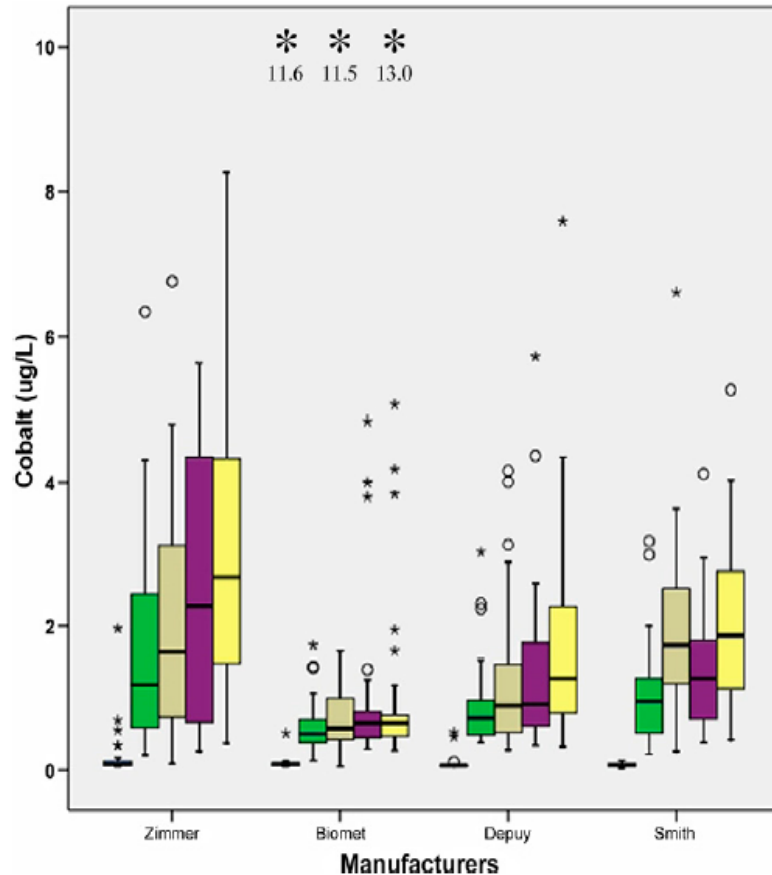
**Lavigne M. et al, JBJS-Am, 2011;
93:128-136.**

- **Prospective cohort study**
- **144 hips assigned to one of four MoM THA**
 - **Biomet M2a Magnum**
 - **Zimmer Durom LDH**
 - **Smith & Nephew**
 - **DePuy ASR**
- **Metal ion in whole blood**

**Lardanchet JF. et al, Orthop Traumatol
Surg Res. 2012 May;98(3):265-74**

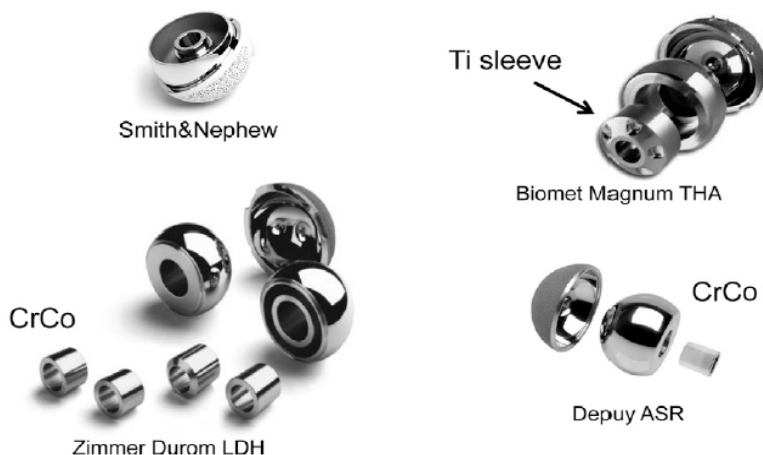
- Prospective cohort study**
- **24 Durom Cup**
 - **20 M2a Magnum**
 - **23 Conserve Total**
- **Metal ion in Serum**

Lavigne M. et al. - Significant Variation in Co and Cr Levels among 4 MoM Hips



Design Impact on Metal Ion Level – Author Conclusions

Although better wear characteristics of the Biomet bearing surface or other design characteristics of the Biomet large-diameter-head total hip arthroplasty implants may be responsible for the low levels of cobalt ions, one may hypothesize that the design of the taper adapter sleeve is likely one important factor to explain the lower ion levels in the Biomet design. The Biomet large-diameter-head total hip arthroplasty system is the only system that possesses an adapter sleeve made of titanium, and it possesses design characteristics that differ substantially from other large-diameter-head total hip arthroplasty systems.



Several hypotheses may explain the differences across cup types. First, the M2a Magnum™ adapter sleeve is made of titanium and therefore limits the chrome-cobalt surface area on which passive corrosion can occur, thereby diminishing the release of chromium and cobalt ions at this interface. This factor has been suggested by Lavigne et al. [36] as a cause of differences across cups. In addition, the larger diameter of the Magnum™ adapter sleeve probably decreases rotational friction of the head on the adapter sleeve.

Design Impact on MoM Outcome

Graves et al (JBJS Am. Dec. 2011) - A Multinational assessment of MoM hip performance based on Australia, England and Wales and New Zealand NJRs

Abstract: There is emerging evidence that many metal-on-metal (MoM) bearings, when used with large femoral heads in conventional hip replacement and some resurfacing prostheses, are associated with increased rates of revision arthroplasty. Registries are the main sources of data on MoM prostheses. At the recent International Consortium of Orthopaedic Registries (ICOR) meeting, data were presented from the Australian, England and Wales, and New Zealand registries. All registries reported an increased rate of revision for large femoral head MoM prostheses when prostheses were aggregated compared with the aggregated data of hip prostheses with other bearing surfaces. There was also evidence, however, that the outcome varied, depending on the type of prostheses used, in both large femoral head MoM conventional hip replacement as well as resurfacing hip replacement.

Femoral Head†	Acetabular Prosthesis†	Cumulative Percent of Revised Prostheses		
		1 Yr	3 Yr	5 Yr
ASR	ASR	1.6 (1.3, 2.1)	5.9 (5.0, 6.8)	7.8 (6.4, 9.6)
Articul/Eze	Ultamet	1.8 (1.2, 2.8)	2.7 (1.9, 3.8)	3.5 (2.4, 5.1)
BHR	BHR	0.7 (0.4, 1.2)	2.6 (1.9, 3.6)	4.9 (3.4, 7.1)
BHR	R3	2.4 (1.2, 4.8)		
Bionik	Bionik	3.4 (2.0, 5.9)	8.0 (5.1, 12.5)	
Cormet 2000	Cormet	1.4 (0.7, 2.9)	3.4 (2.0, 5.7)	7.1 (4.4, 11.5)
Icon	Icon	2.5 (1.2, 5.2)	6.5 (3.5, 11.7)	
M2a*	M2a	1.9 (1.1, 3.1)	4.0 (2.8, 5.7)	5.5 (4.0, 7.6)
M2a*	ReCap	1.6 (0.9, 2.8)	2.2 (1.3, 3.6)	
Metasul	Durom	1.3 (0.8, 2.2)	4.0 (2.9, 5.5)	4.6 (3.3, 6.4)
Mitch TRH	Mitch TRH	1.5 (0.8, 3.1)		
S-Rom	Ultamet	2.2 (1.0, 4.7)	3.3 (1.7, 6.2)	3.8 (2.0, 6.9)
Other (24)		2.6 (1.6, 4.2)	6.4 (4.5, 9.1)	11.7 (8.5, 15.9)

* M2a-ReCap same as Biomet M2a Magnum; M2a-M2a same as Biomet M2a 38

Critique of Smith, et al: Analysis should be Specific Design

Smith et al, Failure Rates of Stemmed metal-on-metal Hip Replacement: Analysis of Data from the National Joint Registry of England and Wales, March 13, 2012, The Lancet

- Analyzed the National Joint Registry of England and Wales for primary hip replacements undertaken between 2003 and 2011.
- Analyzed 402,051 procedures of which 31,171 used stemmed metal-on-metal (MoM) hip products.
- The primary measures analyzed were cumulative incidence of revision, hazard ratio and a person-time incidence rate for revision.

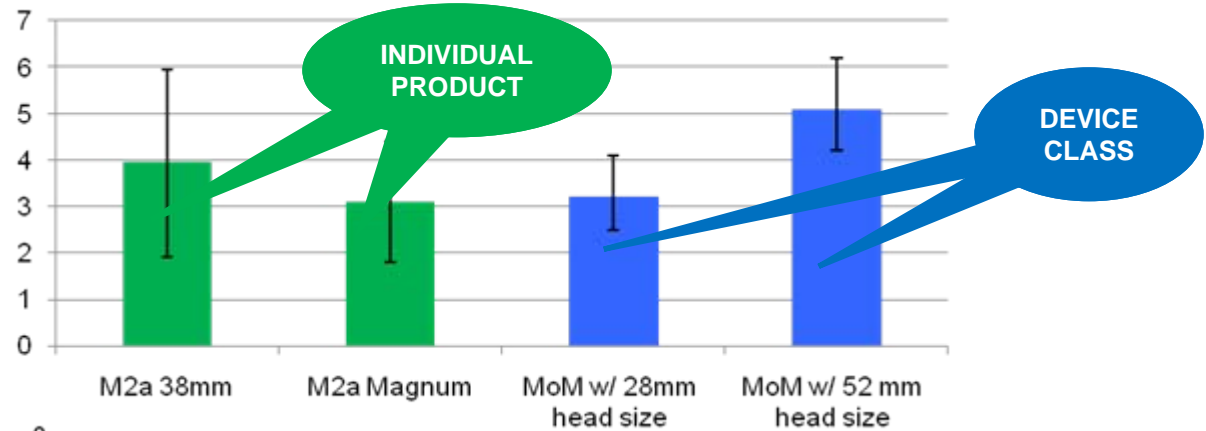
Biommet Analysis

- Case level data extract on Biommet MoM THAs from the England and Wales NJR via supplier feedback.
- Parameters include de-identified patient information (age, gender), primary diagnosis, date of surgery, components used, revision etc.
- M2a 38 and M2a Magnum identified with sufficient data
- Only England and Wales NJR mined and analyzed to reduce variability of patient baseline and other variables.
- Cox model to determine cumulative revision rate in men & women of age 60 years

Findings by Smith et al. on MoM THA CLASS NOT Observed in Biomet MoM THAs

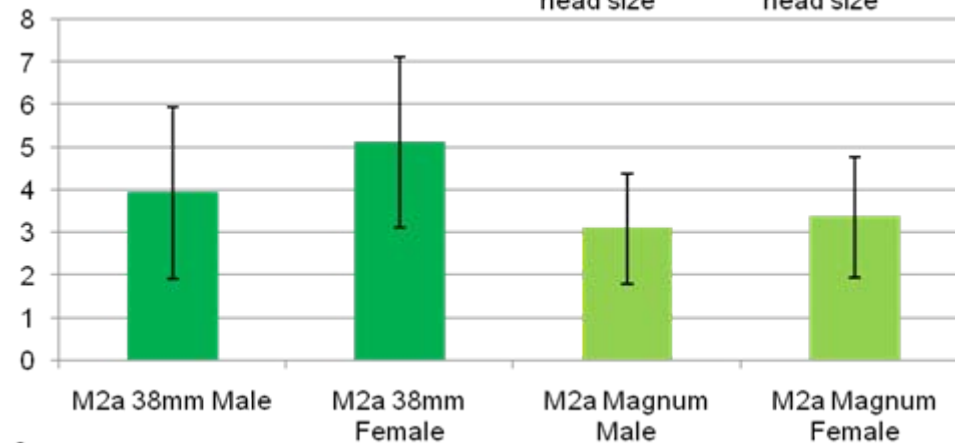
Head size was an independent predictor of revision

NOT Observed in Biomet MoM THAs



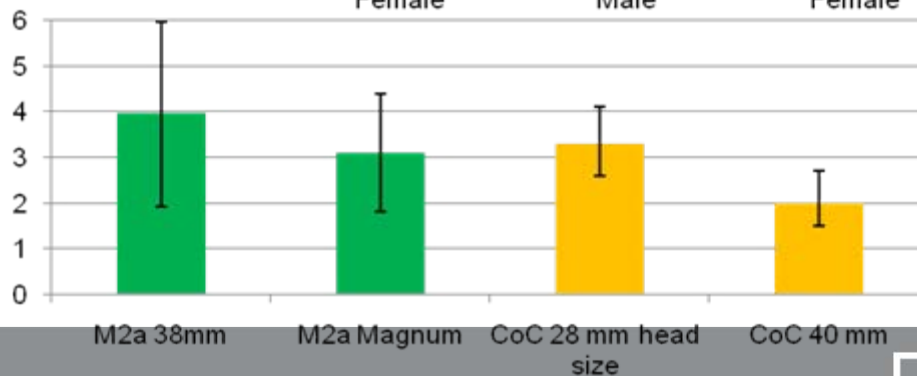
MoM revision rates for women were higher than for men

NOT Observed in Biomet MoM THAs



Higher failure rates in MoM compared with other bearing surfaces

NOT Observed in Biomet MoM THAs



Global Experience of Biomet MoM THA Clinical Performance

- Biomet is committed to ongoing post-market surveillance of its products, including its MoM THAs.
- Biomet has diligently conducted periodic clinical evaluations based on worldwide data from National Joint Registries, pre- and post-market studies, licensed clinical databases and published clinical results.
- Updated clinical data submitted to FDA as 515i Supplements in September 2010, March 2011, August 2011 and March 2012
 - Post-market surveillance protocol submitted in December 2010
 - Biomet first company to receive FDA approval of Section 522 study protocol
 - Biomet moving forward with study
- Survivorship and revision rates per 100 OCY in most recent were also communicated to multiple other Regulatory bodies and surgeons worldwide

Biomet MoM Products

Implant Name	Head Sizes	Year of 1 st Global Introduction
<u>M2a-Taper</u>	28 & 32 mm	2000 An IDE was conducted before obtaining 510K clearance
<u>M2a-RingLoc</u>	28 mm	2000
<u>M2a-38</u>	38 mm	2001
<u>M2a-Magnum</u>	38 - 60mm, 2mm increments	2004

Global Experience on Biomet MoM THA

Survivorship and Revision Rate

Brands	# of Hips with Required Data for Survival Analysis	Kaplan-Meier Survivorship		Revision Rate per 100 OCY	
		Year	KM Survivorship (95% CI)	Mean Survival in Years	Revision Rate per 100 CY (95%CI)
M2a-Magnum	6759	5	95.1 (89.0, 100)	2.75	0.72 (0.60,0.85)
M2a-38	4313	7	90.9** (84.9,96.9)	4.23	0.96 (0.82,1.11)
M2a –Taper	865	7	97.5 (96.8,98.2)	5.70	0.39 (0.23,0.60)

Benchmark Comparison – Australian, England and Wales and New Zealand NJRs

Meta-Analysis: Revision Rate per 100 OCY									
Biomet MoM	(95% CI)	New Zealand NJR ALL THA	New Zealand NJR ALL MoP THA	New Zealand NJR ALL MoM THA	Australia NJR ALL THA*	Australia NJR ALL MoP** THA*	Australia NJR ALL MoM THA*	The England & Wales NJR ALL THA	The England & Wales NJR ALL MoM THA
M2a-Magnum	0.72 (0.60,0.85)	0.66 (0.63, 0.69)	0.63 (0.56 0.63)	0.86 (0.73, 1.01)	0.74 (0.72, 0.76)	0.67 (0.64, 0.69)	1.23 (1.15, 1.31)	0.74 (0.72, 0.76)	1.73 (1.64,1.83)
M2a-Taper	0.39 (0.23,0.60)								
M2a- 38	0.96*** (0.82,1.11)								
*Primary diagnosis of osteoarthritis reported by AOANJRR **Combines Metal on Poly and Metal on Modified Poly ***Will discuss during gender analysis									

Benchmark Comparison – Australian, England and Wales NJRs

Kaplan Meier Survivorship			
Data Sources	3yr - Survival rate (%)	5yr - Survival rate (%)	7yr - Survival rate % (yr)
M2a-Taper	99.38 (98.13,100.00)	98.66 (96.72,100.00)	97.49 (96.76,98.23)
M2a-Magnum	98.10(96.71, 99.48)	95.07 (88.98, 100)	Not Sufficient Data for Analysis
M2a-38	97.77 (95.98,99.55)	95.90 (92.86,98.94)	90.93 (84.94,96.91)
All MoM UKNJR**	95.9 (95.6,96.2)	92.7 (92.1, 93.4)	86.4(83.0, 89.1)
All THA AOANJR *,**	97.4 (97.3, 97.5)	96.6 (96.7, 96.5)	95.6 (95.5, 95.8)
All MoM AOANJR *,**	95.8 (95.5, 96.1)	94.0 (93.5, 94.4)	92.7 (92.1, 93.2)

*Primary diagnosis of osteoarthritis reported by AOANJRR

** 2011 Annual Reports

Gender Analysis

- The impact of Gender on risk of revision is NOT statistically significant for M2a-Taper and M2a-Magnum
- There is a statistically significant impact of Gender on risk of revision for overall M2a-38 due to a single US center

M2a-38	All Male	All Female Including the single US center	Female Excluding the single US center	Australian NJR All MoM (OA)	Australian NJR All THA (OA)	England and Wales NJR All MoM	England and Wales NJR All THA
Kaplan-Meier survivorship – 7 yr	95.1 (93.2, 96.5)	89.5 (86.1, 92.1)	92.2 (89.0, 94.6)	92.7 (92.1, 93.2)*	95.6 (95.5, 95.8)*	86.4 (83.0, 89.1)	-
Revision rate per 100 OCY	0.67 (0.49, 0.89)	1.15 (0.91, 1.42)	0.91 (0.68, 1.18)	1.23 (1.15, 1.31)	0.74 (0.72, 0.76)**	1.73 (1.64, 1.83)	0.74 (0.72, 0.76)**
<p>*Biomet results in females including the single US center is statistically/marginally statistically significantly lower than benchmarks per confidence intervals.</p> <p>**Biomet results in females including the single US center is statistically significantly higher than benchmarks per confidence intervals.</p>							

Recent Medical Literature

Bosker et al (JBJS Br. June 2012) - High incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement

- Observational study on 108 hips implanted with M2a Magnum
- All screened for pseudotumor using CT; confirmed with MRI and/or Ultrasound
- 42 hips with pseudotumor (defined as (semi)-solid or cystic peri-prosthetic soft-tissue mass with a diameter $\geq 2\text{cm}$)
 - 13 hips revised (No specific criteria reported; “Symptoms warranted a revision procedure...”)
- 66 hips without pseudotumor
 - No Revisions
- Authors reported correlation between Co level and incidence of pseudotumor
 - patients with serum cobalt levels $> 5 \text{ ug/L}$ had a fourfold increased risk of developing a pseudotumour.

Bosker, et al: Pseudotumor vs. Symptoms

	Pseudotumor Group	Non Pseudotumor Group	Total
No. of Symptomatic	?	14	?
No. of Asymptomatic	?	52	?
Total	42	66	108

Authors concluded -

Because most revisions in symptomatic patients were identified only after applying a comprehensive screening protocol, we recommend close monitoring of all patients with a MoM hip arthroplasty.

Questions for the Panel

➤ New Questions:

- What are the criteria for revision?
- Should asymptomatic patients be revised?
- To what degree, if any, do pseudotumors progress in certain patients? If so, are there particular factors that impact the rate of progression?
- How do the results for MoM compare to other bearings with the same treatment protocol?