DePuy Orthopaedics Inc.

ULTAMET®
Metal-on-Metal Articulation

Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee

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June 27/28, 2012

PINNACLE® Acetabular Cup System

OUTER SHELLS

Titanium Alloy
Hemispherical
- Porous-coated
- Duo-Fix HA/Porocoat

Options
- No-hole
- Tri-spike

Screw fixation options
- 3-hole
- Multi-hole

LINERS

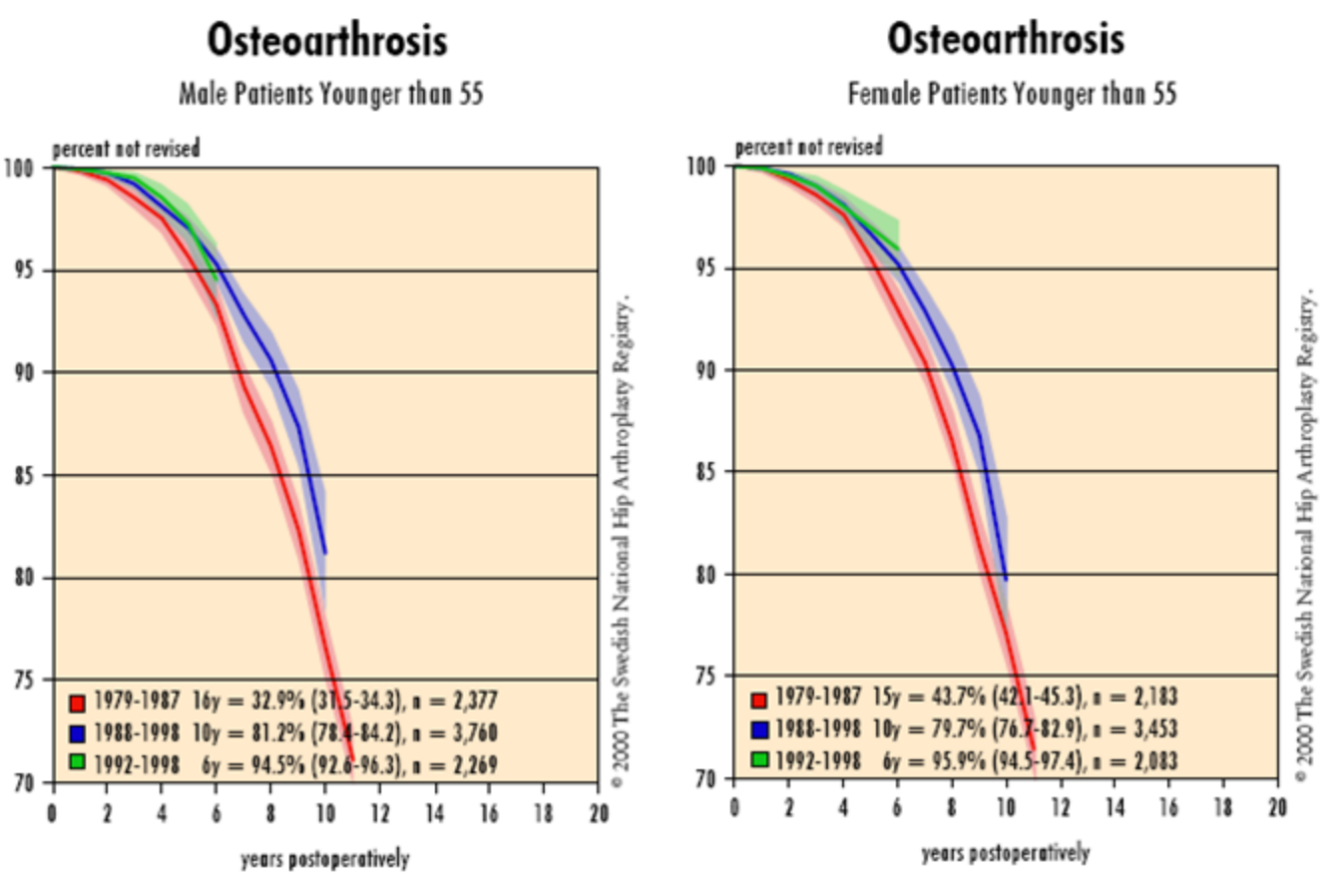
- Polyethylene
- Ceramic
- Metal

Pinnacle shell + metal liner + metal head = ULTAMET MoM

Key Takeaways

- **No single bearing surface meets the needs of all patients**
- **Not all metal-on-metal products are the same and each should be evaluated on its own merits**
- **ULTAMET Metal-on-Metal Articulation is performing consistent with or better than other metal-on-metal products: 4 to 4.5% cumulative revision rate (CCR) at five years, regardless of head size**

Metal-on-Metal Bearings: Designed to Reduce Revision Rates in Younger Patients



Source: Swedish Hip Arthroplasty Registry 2000

Registry data was showing high failure rates (≈20%) at 10 years in younger patients with metal-on-polyethylene technology. MoM was developed in response to this clinical unmet need.

Intended Benefits of ULTAMET MoM

- Low wear rates
- Increased stability to reduce postoperative dislocation
- Increased range of motion
- Reduced risk of liner chipping or fracture sometimes seen with ceramic heads

Modular Acetabular Cups Generally

- Intra-operative flexibility
- Ease of revision of modular cups (liner exchange)
- Adjunct fixation options (screws)

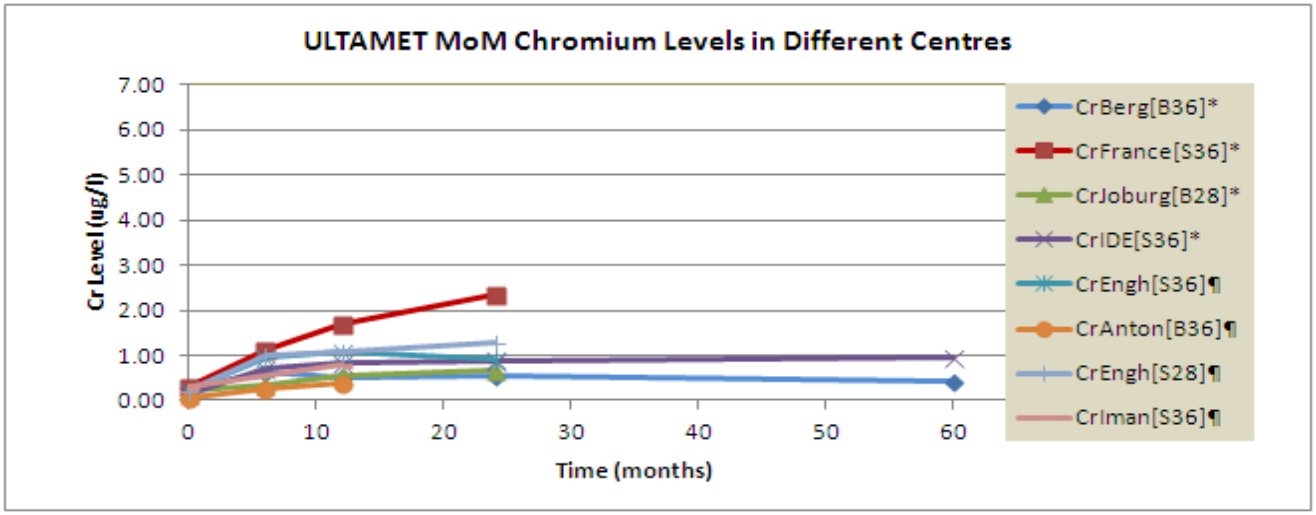
Not all MoM Articulations Are Comparable
(Head sizes >32mm)

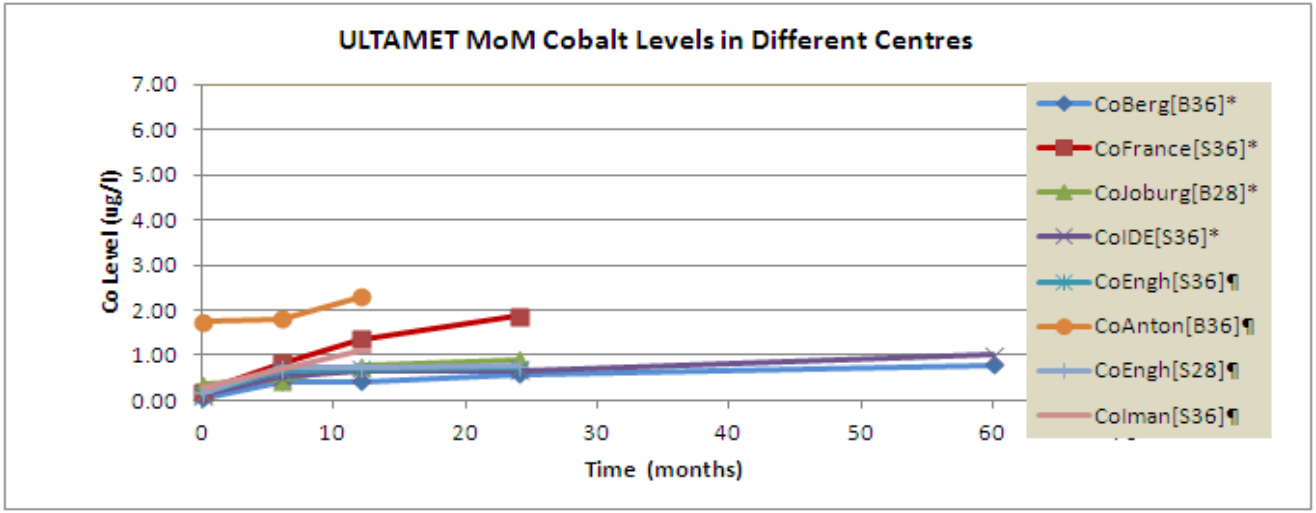
Head Surface	Acetabular Surface	1 Yr	3 Yrs	5 Yrs
ASR	ASR	1.7 (1.4, 2.2)	9.4 (8.5, 10.4)	21.9 (20.5, 23.5)
Articul/Eze	Pinnacle	1.9 (1.3, 2.7)	3.0 (2.2, 4.0)	4.2 (3.2, 5.5)
BHR	BHR	1.0 (0.7, 1.5)	3.2 (2.5, 4.1)	5.5 (4.5, 6.7)
BHR	R3	2.1 (1.2, 3.7)	5.6 (3.8, 8.1)	
BMHR	BHR	2.2 (0.9, 5.1)	2.7 (1.2, 6.0)	
Bionik	Bionik	3.7 (2.2, 6.2)	8.4 (6.0, 11.8)	15.9 (11.7, 21.3)
Cormet 2000	Cormet	1.4 (0.7, 2.7)	3.4 (2.2, 5.3)	6.0 (4.1, 8.7)
Icon	Icon	2.4 (1.2, 4.7)	6.7 (4.3, 10.2)	11.6 (8.0, 16.8)
M2a	M2a	1.8 (1.1, 3.0)	3.8 (2.6, 5.4)	5.5 (4.1, 7.4)
M2a	Recap	1.5 (0.9, 2.6)	2.2 (1.5, 3.5)	3.6 (2.4, 5.3)
Metasul	Durom	1.2 (0.7, 2.0)	3.9 (2.9, 5.3)	5.2 (3.9, 6.7)
Mitch TRH	Mitch TRH	1.7 (0.9, 3.1)	4.9 (3.4, 7.0)	
S-Rom	Pinnacle	2.1 (1.0, 4.7)	3.6 (1.9, 6.5)	4.0 (2.2, 7.0)
Other (26)		2.4 (1.4, 3.8)	5.9 (4.3, 8.2)	9.9 (7.5, 13.0)

- Cumulative revision rates vary significantly with 5-year CRR, ranging from 3.6% to 21.9%

Source AOA NJRR Data 01 Sep 1999 – Dec 2011 NB Data subject to final validation

ULTAMET Metal Ion Data (Median Values)





Legend:
B Whole blood
S Serum
* DePuy Study
¶ Independent Study

ULTAMET MoM median chromium and cobalt ion results are below 3 ppb from multiple studies with levels increasing from pre-op to 1 year post-op and levelling off thereafter.

Summary of Survival Results at 5 and 7 Years from Multiple Sources

Reference	N	5yr KM Survival % (95% CI)	7yr KM Survival % (95% CI)
UK NJR Supplier Feedback May 2012 download ULTAMET MOM	12449	95.5 (95.05, 95.96)	92.0 (90.69, 93.17)
AOA NJRR February 2012 unpublished data Pinnacle >32mm/OA MOM - Articul/eze	1621	95.8 (94.5, 96.8)	94.7 (92.9, 96.0)
AOA NJRR February 2012 unpublished data Pinnacle >32mm/OA MOM – SROM	283	96.4 (93.4, 98.1)	95.9 (92.7, 97.7)
Engh CA et al., CORR 2010; 468: 406-412 ULTAMET MoM	126	98.0 (96-100)	Not reported
Kindsfater K et al., JOA 2012; 27: 545-550 ULTAMET MOM	95	97.8 (94.8-100.0)	97.8 (94.8-100.0)
Barrett WP et al., JOA Mar 2012; e-pub ahead of print ULTAMET MoM	1076	97.0 (95.2-98.1)	Not reported

ULTAMET MoM 5 year Survival estimates range from 95.5% to 98.0% with 7 year Survival estimates from 92.0% to 97.8%

Summary of ULTAMET Performance in UK and Australian National Joint Registries

- 5-year cumulative revision rate compares favorably to other classes of articulation (less than 32 mm head size)
- CRR of ULTAMET Metal-on-Metal Articulation
  - Head size does not affect revision rates
  - Performance varies from surgical unit to surgical unit
- All PINNACLE bearing options perform within guidelines
- Approximately 1% or less of ULTAMET MoM primary cases are revised due to soft tissue reactions

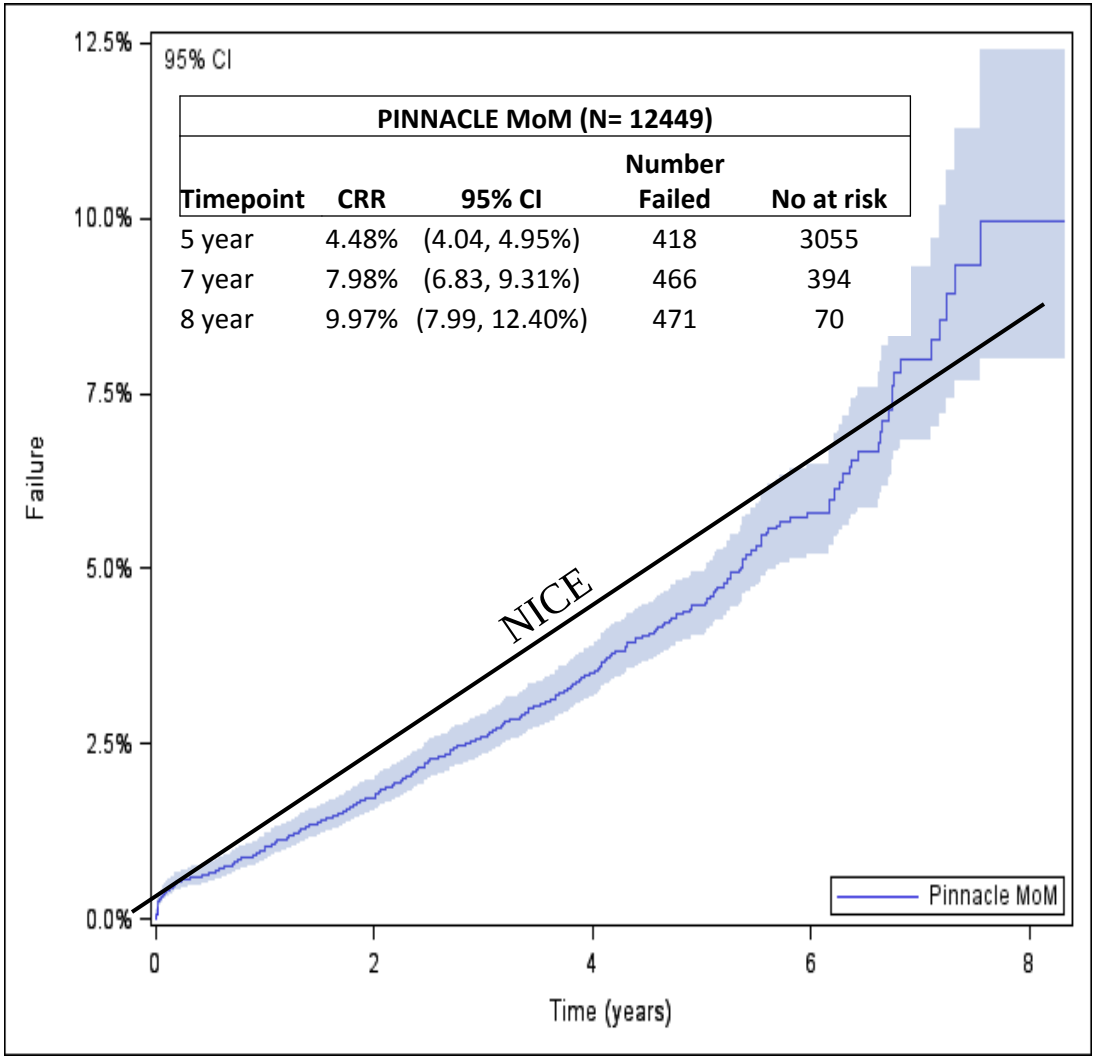
Cumulative Revision Rate:ULTAMET MoM

All head sizes, UK National Registry

ULTAMET MoM THR Revision Rate
(all head sizes & stems)

- 5 Year: 4.48%
- 7 Year: 7.98%
- 8 Year: 9.97%

- For ULTAMET MoM, revision rates are consistent with benchmarks



Source: UK NJR – May 2012 Supplier Feedback System, analyzed by DePuy

CRR of ULTAMET MoM >32mm/OA, Australian National Registry

Table HT46: Yearly Cumulative Percent Revision of Metal/Metal Primary Total Conventional Hip Replacement using Head Size >32mm by Prostheses Used (Primary Diagnosis OA)

Head Surface	Acetabular Surface	1 Yr	3 Yrs	5 Yrs	7 Yrs	10 Yrs
ASR	ASR	1.7 (1.4, 2.2)	6.6 (5.8, 7.5)	10.3 (9.0, 11.6)		
Articul/Eze	Ultamet	1.8 (1.2, 2.6)	2.8 (2.0, 3.9)	4.0 (2.9, 5.5)	4.6 (3.3, 6.3)	
BHR	BHR	0.9 (0.6, 1.4)	2.8 (2.2, 3.7)	4.9 (3.8, 6.3)	6.7 (4.8, 9.4)	
BHR	R3	2.4 (1.3, 4.2)				
Bionik	Bionik	3.5 (2.0, 5.9)	7.1 (4.7, 10.6)			
Cormet 2000	Cormet	1.2 (0.6, 2.4)	3.2 (2.0, 5.2)	6.0 (3.9, 9.1)	9.3 (5.9, 14.4)	
Icon	Icon	2.5 (1.2, 4.9)	7.4 (4.7, 11.6)			
M2a	M2a	1.8 (1.1, 3.0)	3.7 (2.6, 5.4)	5.3 (3.8, 7.2)	7.2 (5.3, 9.7)	
M2a	Recap	1.5 (0.8, 2.5)	1.9 (1.1, 3.1)	3.4 (2.1, 5.5)		
Metasul	Durom	1.3 (0.8, 2.2)	4.0 (3.0, 5.5)	5.5 (4.1, 7.3)		
Mitch TRH	Mitch TRH	1.9 (1.0, 3.3)	4.6 (3.1, 7.0)			
S-Rom	Ultamet	2.2 (1.0, 4.7)	3.3 (1.7, 6.2)	3.7 (2.0, 6.7)	3.7 (2.0, 6.7)	
Other (27)		2.3 (1.5, 3.6)	5.4 (3.9, 7.6)	10.1 (7.4, 13.6)	15.4 (11.6, 20.3)	

Table HT34: Yearly Cumulative Percent Revision of Primary Total Conventional Hip Replacement by Bearing Surface and Head Size (Primary Diagnosis OA)

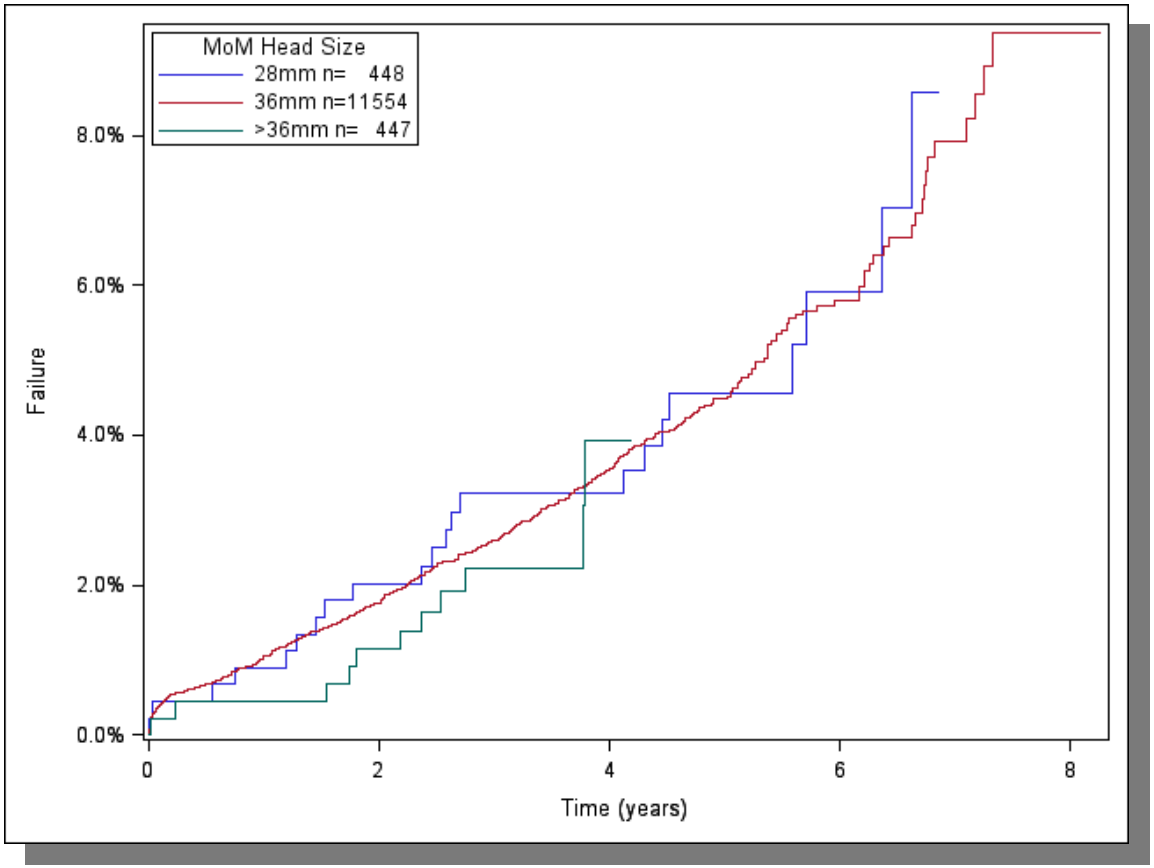
Bearing Surface	Head Size	1 Yr	3 Yrs	5 Yrs	7 Yrs	10 Yrs
Ceramic/Ceramic	≤32mm	1.6 (1.4, 1.7)	2.7 (2.4, 2.9)	3.4 (3.2, 3.7)	4.3 (4.0, 4.6)	5.6 (4.9, 6.3)
	>32mm	1.4 (1.2, 1.6)	2.4 (2.1, 2.8)	3.4 (2.9, 3.9)	3.9 (3.3, 4.6)	
Ceramic/Polyethylene	≤32mm	1.5 (1.2, 1.9)	2.4 (2.0, 2.9)	3.1 (2.6, 3.7)	4.1 (3.5, 4.9)	8.1 (6.5, 10.2)
	>32mm	3.6 (1.7, 7.6)				
Ceramic/Modified Polyethylene	≤32mm	1.4 (1.2, 1.7)	2.4 (2.1, 2.8)	2.9 (2.5, 3.3)	3.7 (3.2, 4.3)	6.2 (4.8, 8.1)
	>32mm	1.2 (0.9, 1.7)	2.6 (2.0, 3.4)	3.5 (2.4, 5.0)		
Metal/Metal	≤32mm	1.5 (1.2, 1.9)	3.0 (2.6, 3.6	3.9 (3.3, 4.5)	4.5 (3.9, 5.2)	5.2 (4.4, 6.1)
	>32mm	1.7 (1.5, 1.9)	4.6 (4.2, 5.0)	7.1 (6.6, 7.7)	9.4 (8.5, 10.4)	
Metal/Polyethylene	≤32mm	1.4 (1.3, 1.6)	2.5 (2.3, 2.7)	3.6 (3.3, 3.8)	4.8 (4.5, 5.2)	7.1 (6.5, 7.8)
	>32mm	1.7 (0.7, 3.7)	4.2 (1.9, 9.2)			
Metal/Modified Polyethylene	≤32mm	1.4 (1.3, 1.5)	2.3 (2.1, 2.4)	2.9 (2.7, 3.0)	3.6 (3.4, 3.8)	4.7 (4.3, 5.1)
	>32mm	1.5 (1.3, 1.7)	2.3 (2.0, 2.7)	3.2 (2.7, 3.8)	3.8 (3.0, 4.8)	
Ceramicised Metal/Modified Polyethylene	≤32mm	1.0 (0.8, 1.4)	1.5 (1.1, 1.9)	1.8 (1.4, 2.3)	2.2 (1.6, 2.9)	
	>32mm	1.4 (1.0, 2.0)	1.9 (1.4, 2.7)	2.1 (1.5, 2.9)		
Other (5)	≤32mm	1.9 (0.9, 4.0)	3.6 (2.0, 6.3)	4.0 (2.3, 6.8)	7.2 (4.1, 12.5)	
	>32mm	2.3 (1.4, 3.9)				

Note: More recent unpublished results from the AOA NJRR: Articul/Eze/ULTAMET and S-Rom/ULTAMET combinations showing a 5.3% and 4.1% CRR at 7 years respectively (data through December 2011)

- >32mm ULTAMET is performing well in the registries
  - ULTAMET >32mm MoM results (Table HT46) are the same as for those shown for the class of ≤32mm MoM THR at 5 and 7 years, and for CoC and MoP (Table HT34)

Table HT46 & HT34 Source: 2011 AOA NJRR Annual Report

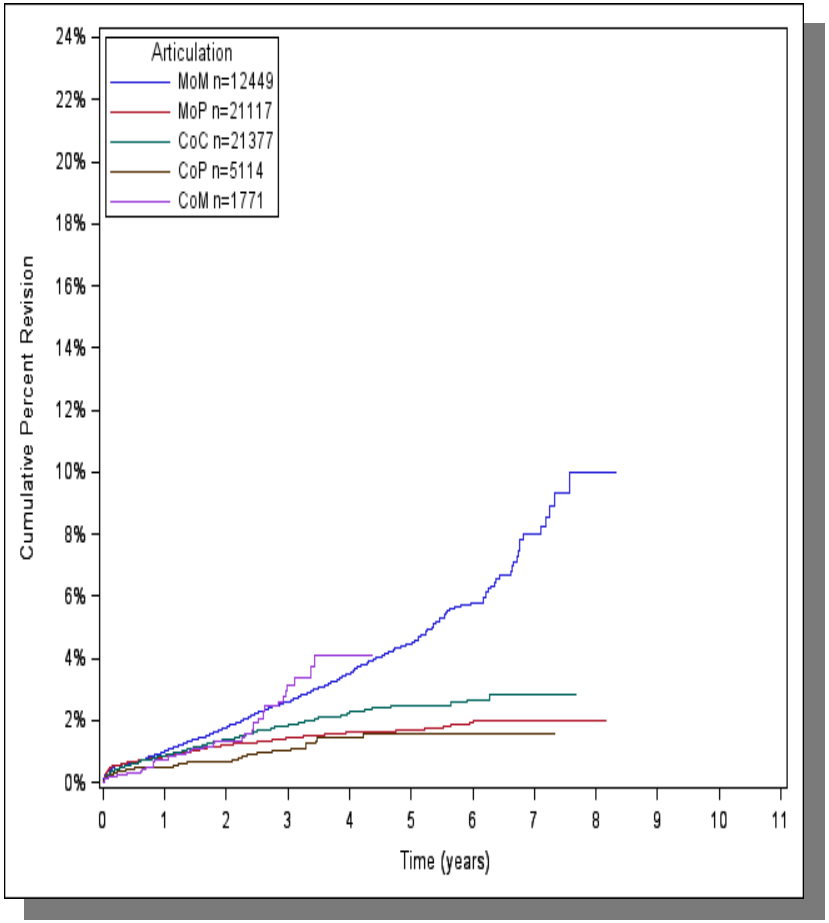
CRR is Comparable For All ULTAMET MoM Head Sizes in the UK National Joint Registry



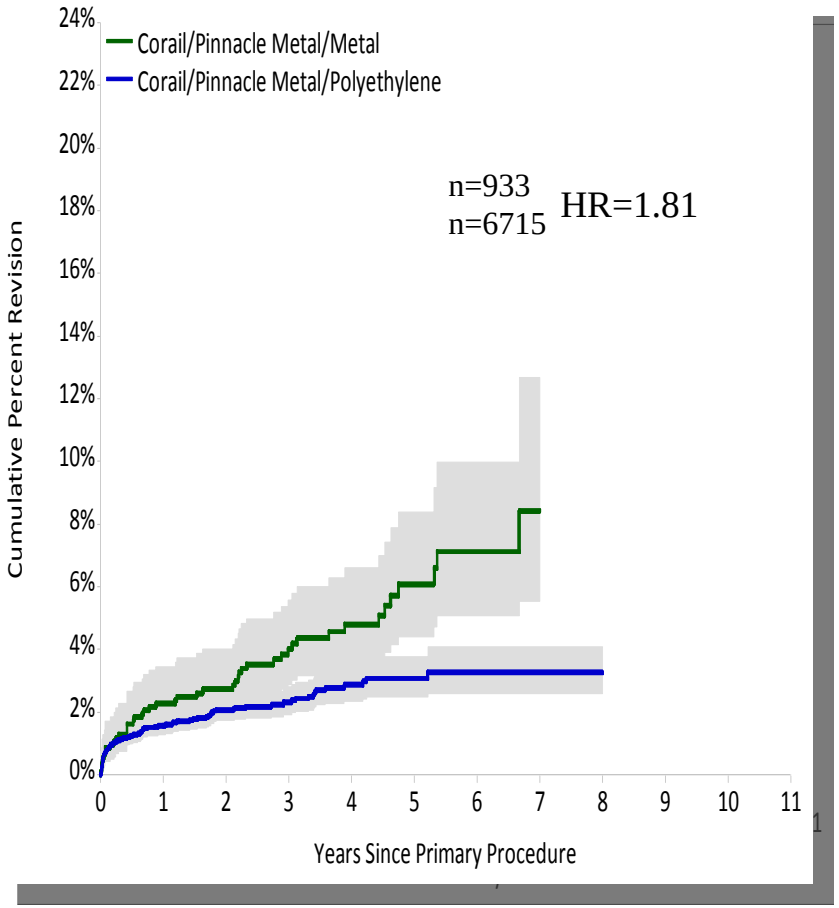
Source: UK NJR – May 2012 Supplier Feedback System, analyzed by DePuy

- ULTAMET MoM, 28mm 36mm and > 36mm heads have similar CCR

PINNACLE Performance Across All Bearing Options



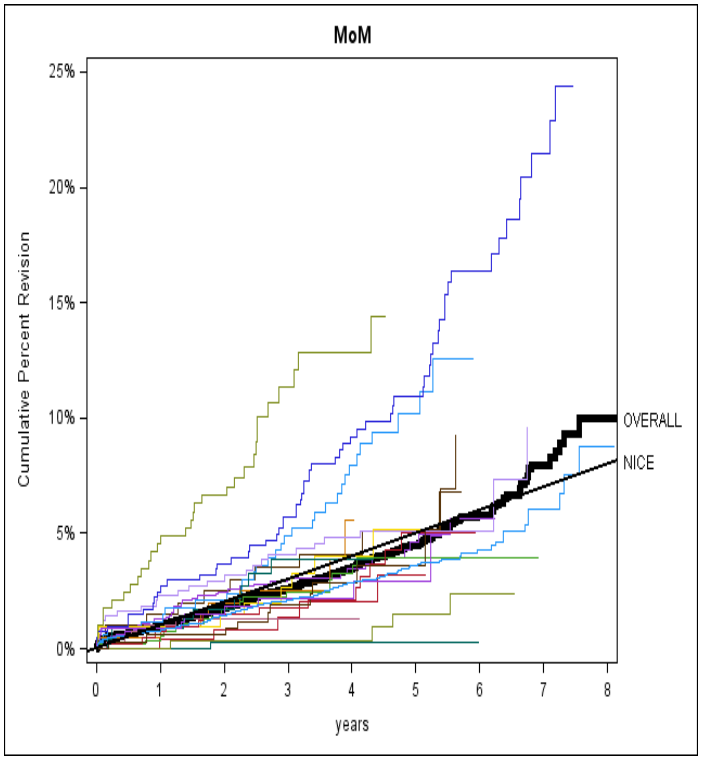
UK NJR – May 2012 Supplier Feedback System analyzed by DePuy

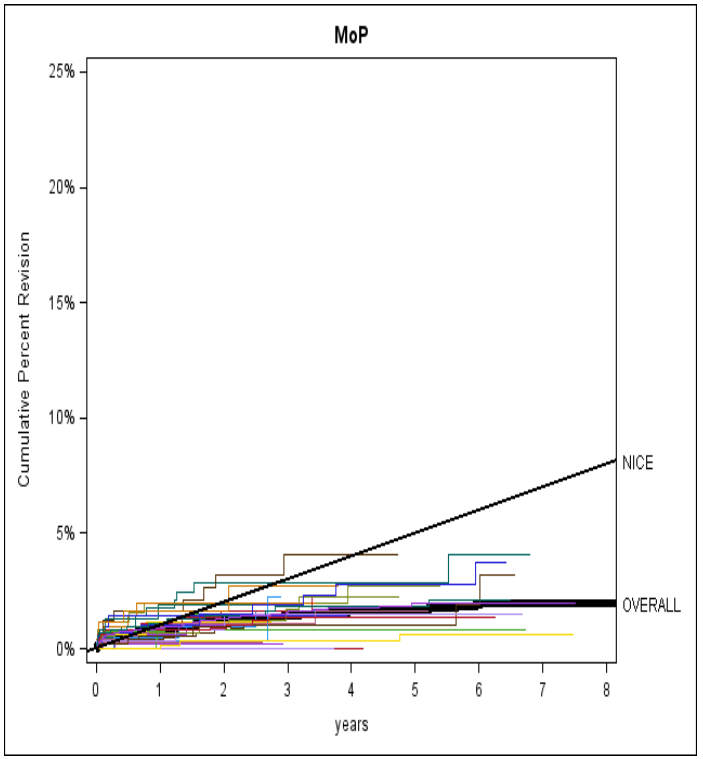


Unpublished data provided by AOA NJRR – Data through Dec. 2011

- PINNACLE MoP has performed very well in mid-term results of patients who receive it; other bearing options perform within guidelines.

CRR is Affected by Surgical Unit in UK National Joint Registry





- More variation among sites for ULTAMET MoM versus PINNACLE MoP. One MoM outlier site has long term data, which has a large influence on the 7 & 8 year overall CRR

UK NJR – May 2012 Supplier Feedback System, analyzed by DePuy

Reasons for Revision

Pinnacle MoM (≥36mm)

Revision Reason	N	% Revision Reasons	% Primaries
Soft Tissue Reaction	122	27.23%	1.02%
Pain	101	22.54%	0.84%
Other Reason	71	15.85%	0.59%
Dislocation	69	15.40%	0.57%
Aseptic Loosening Stem	69	15.40%	0.57%
Infection	59	13.17%	0.49%
Malalignment Socket	30	6.70%	0.25%
Aseptic Loosening Socket	29	6.47%	0.24%
Peri Prosthetic Fracture Stem	25	5.58%	0.21%
Malalignment Stem	17	3.79%	0.14%
Lysis of Stem	15	3.35%	0.12%
Lysis of Socket	7	1.56%	0.06%
Dissociation of Liner	5	1.12%	0.04%
Acetabular Wear	5	1.12%	0.04%
Fracture Stem	5	1.12%	0.04%
Peri Prosthetic Fracture Socket	4	0.89%	0.03%
Mismatch Head	3	0.67%	0.02%
Fracture Socket	1	0.22%	0.01%
Mismatch Socket	1	0.22%	0.01%

UK NJR supplier feedback dataset ≥36mm heads: 122 revised/12,001 **(1.02%)**

UK NJR – May 2012 Supplier Feedback System analyzed by DePuy

Table 5: Revision Diagnosis of Metal/Metal Pinnacle Primary Total Conventional Hip Replacement by Time to Revision

	<2wks		2wks-3mths		3mths-6mths		6mths-1yr		≥1yr		TOTAL	
Reason for Revision	N	Col%	N	Col%	N	Col%	N	Col%	N	Col%	N	Col%
Loosening/Lysis	3	23.1	2	15.4	1	12.5	3	20.0	16	34.0	25	26.0
Prosthesis Dislocation	1	7.7	5	38.5	2	25.0	6	40.0	5	10.6	19	19.8
Infection	.	.	3	23.1	3	37.5	3	20.0	9	19.1	18	18.8
Fracture	4	30.8	3	23.1	2	25.0	1	6.7	3	6.4	13	13.5
Metal Sensitivity	.	.	.	.	.	.	.	.	11	23.4	11	11.5
Pain	.	.	.	.	.	.	1	6.7	3	6.4	4	4.2
Malposition	2	15.4	.	.	.	.	.	.	.	.	2	2.1
Leg Length Discrepancy	2	15.4	.	.	.	.	.	.	.	.	2	2.1
Incorrect Sizing	.	.	.	.	.	.	1	6.7	.	.	1	1.0
Other	1	7.7	.	.	.	.	.	.	.	.	1	1.0
TOTAL	13	100.0	13	100.0	8	100.0	15	100.0	47	100.0	96	100.0

AOA NJRR Unpublished Analysis for ULTAMET MoM THR 11/2239 **(0.49%)** revised for metal sensitivity

NJRR Data 01 Sep 1999 – Dec 2011 NB Data subject to final validation

- Rate of ULTAMET soft tissue reaction range 0.49% to 1.02%

Key Takeaways

- Metal-on-metal implants allow for larger femoral heads to be used, which provide greater stability and lower risk of dislocation.

- Metal-on-metal products vary in their specific designs and in their clinical performance and should be evaluated on their individual merits rather than as a class.

- ULTAMET Metal-on-Metal Articulation is performing consistent with or better than other metal-on-metal products and within guidelines from the UK National Institute for Health and Clinical Excellence (NICE). Cumulative Revision rates at 5 years vary between 4.0-4.5%.

- Registry data shows that ULTAMET bearings demonstrate an acceptable revision rate regardless of head size

- Incidence of soft tissue reactions with ULTAMET is approximately 1% or less

Key Takeaways (continued)

- The ULTAMET® metal-on-metal implant has helped reduce pain and restore mobility for those patients suffering from chronic joint pain.
- DePuy continues to monitor current data about ULTAMET from a variety of sources.
- DePuy believes all patients with a joint replacement should be followed up periodically with a frequency determined by local guidance, relevant physician clinical protocol and the needs of individual patients.
  - Surgeons should contact their local orthopaedic association and/or regulatory authority for specific guidance on follow up recommendations for patients with metal-on-metal implants.

Thank You