

TABLE E-1 Summary of Studies Reporting Metal Ion Levels in Patients Treated with Metal-on-Metal Total Hip Arthroplasty*

Author(s)	Study Design	No. of Each Type of Bearing Surface, Head Diameter	Duration of Follow-up (yr)	Metal-Ion-Level Measurement Technique	Metal Ion Levels ($\mu\text{g/L}$)
Brodner et al. ¹⁰⁴ , 2003	Randomized controlled trial	50 MoM THA, 28 mm 50 CoP THA (47, 28 mm & 3, 32 mm)	5	Atomic absorption spectrometry	Median serum Co level MoM: 1 at 1 yr & 0.7 at 5 yr CoP: undetectable
Antoniou et al. ³⁶ , 2008	Prospective nonrandomized trial	18 MoP THA 28 MoM THA 28 mm 58 MoM THA 36 mm 70 MoM resurfacing	1	Inductively coupled plasma mass spectrometry	Median blood Co level MoP THA: 1.7 MoM THA, 28 mm: 2.6 MoM THA, 36 mm: 2.3 MoM resurfacing: 2.4 Median blood Cr level MoP THA: 0.05 MoM THA, 28 mm: 0.6 MoM THA, 36 mm: 0.4 MoM resurfacing: 0.5
Clarke et al. ³⁸ , 2003	Case-matched study	22 MoM THA, 28 mm 22 MoM resurfacing, 48 mm (median)	16 (median)	Inductively coupled plasma mass spectrometry	Median serum Co level MoM THA: 0.37 MoM resurfacing: 0.64 Median serum Cr level MoM THA: 0.37 MoM resurfacing: 1.02
Moroni et al. ³⁷ , 2008	Prospective nonrandomized trial	20 MoM resurfacing, 48 mm (mean) 26 MoM THA, 28 mm	24 (median)	Atomic absorption spectrometry	Median serum Co level MoM resurfacing: 0.75 MoM THA: 0.97 Median serum Cr level MoM resurfacing: 1.73 MoM THA: 1.66
Daniel et al. ³⁰ , 2006	Cross-sectional study	26 MoM resurfacing, 50 or 54 mm 20 MoM THA, 28 mm	1	Inductively coupled plasma mass spectrometry	Mean whole-blood Co level MoM resurfacing: 1.3 MoM THA: 1.7 Mean whole-blood Cr level MoM resurfacing: 2.4 MoM THA: 1.7

Grübl et al. ¹⁰⁵ , 2006	Randomized controlled trial	13 MoM THA, 28 mm 15 CoC THA, 28 mm	1	Atomic absorption spectrometry	Median serum Co level MoM: 1.4 CoC: 0.4
Lazennec et al. ⁴³ , 2009	Prospective case series	134 MoM THA, 28 mm	9 (mean)	Atomic absorption spectrometry	Median serum Co level 1 yr: 1.4 9 yr: 1.6
Lhotka et al. ⁴⁶ , 2003	Prospective case series with age & sex-matched control group	259 MoM THA (131 design A & 128 design B), 28 mm 31 controls	4 (mean)	Atomic absorption spectrometry	Mean whole-blood Co level Design A: Immediate postop. period: 3.23 ng/g 42-48 mo: 16.95 ng/g Design B: Immediate postop. period: 8.13 ng/g 42-48 mo: 27.66 ng/g Controls: 0.7 ng/g
Savarino et al. ⁴⁷ , 2003	Prospective case series	26 MoM THA, 28 mm (short-term follow-up: mean, 2 yr) 15 MoM THA, 28 mm (medium-term follow-up: mean, 4.33 yr) 22 controls (patients before surgery)	Short term: 2 (mean) Medium term: 4.33 (mean)	Atomic absorption spectrometry	Mean serum Co level Short term: 1.33 Medium term: 0.80 Mean serum Cr level Short term: 1.72 Medium term: 0.99
Savarino et al. ³¹ , 2006	Prospective case series	23 CoC THA, 28-32 mm 42 MoM THA, 28 mm 47 healthy controls	CoC: 3.33 (mean) MoM: 4.42 (mean)	Atomic absorption spectrometry	Mean serum Co level CoC: 0.18 MoM: 1.57 Mean serum Cr level CoC: 0.30 MoM: 2.10
Schaffer et al. ³⁵ , 1999	Prospective case series	76 MoM THA, 28 mm 26 controls	1	Atomic absorption spectrometry	Median serum Co level MoM at 1 yr: 1.5 Controls: 1.1 Median serum Cr level MoM at 1 yr: 2.2 Controls: 1.8
Witzleb et	Prospective case	74 MoM THA, 28 mm	2 (maximum)	Atomic absorption	Median serum Co level

al. ³⁹ , 2006	series	111 MoM resurfacing, 50 mm 130 controls		spectrometry	<p>MoM THA: 0.83 at 3 mo & 1.62 at 1 yr Unilateral: 1.70 at 2 yr Bilateral: 3.18 at 2 yr</p> <p>MoM resurfacing: 2.17 at 3 mo & 4.28 at 2 yr</p> <p>Median serum Cr level Bilateral MoM THA: 3 mo after implantation in 2nd hip: 4.42 1 yr after implantation in 2nd hip: 3.62 2 yr after implantation in 2nd hip: 2.50</p> <p>MoM resurfacing: 3 mo: 1.96 1 yr: 4.20 2 yr: 5.12</p>
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*MoM = metal-on-metal, CoP = ceramic-on-polyethylene, CoC = ceramic-on-ceramic, MoP = metal-on-polyethylene, THA = total hip arthroplasty, Co = cobalt, and Cr = chromium.

TABLE E-2 Overview of Clinical Studies on Metal-on-Metal Total Hip Arthroplasty*

Author(s), Journal, Year	Study Design	Surgery Period	No. of Centers/Surgeons	No. of Hips/Patients	Head Size (mm)	Patient-Reported Outcome Measure	Clinical Outcome Measure/Reviewer	Mean Duration of Follow-up/Patients Missing	Survivorship Analysis
Wagner and Wagner ¹⁰⁶ , Clin Orthop Relat Res, 2000	Prospective case study	Jan 1990 to Jan 1993	1/2	78/78	28	None	HHS, Merle d'Aubigné/not reported	5 yr/3 lost to follow-up	Not reported
Hilton et al. ¹⁰⁷ , Clin Orthop Relat Res, 1996, (same series as reported by Dorr et al. ⁸⁶ , 2000)	Prospective clinical review of selected case series	1991 to 1994	1/1	74/74	69 hips: 28 5 hips: 32	Modified SF-36	HHS/surgeon	2.2 yr/lost to follow-up (no. not reported)	Not reported
Dorr et al. ⁸⁶ , J Bone Joint Surg Am, 2000 (same series as reported by Hilton et al. ¹⁰⁷ , 1996)	Prospective clinical review of selected case series	1991 to 1994	1/1	70/70	66 hips: 28 4 hips: 32	Modified SF-36	HHS/surgeon	5.2 yr/9 died, 5 not reviewed (not revised)	Any failure as end-point: 94.1% (95% CI, 88.9, 99.3) at 7 yr Aseptic failure as end-point: 98.2% at 7 yr
Dastane et al. ¹⁰⁸ , Clin Orthop Relat Res, 2008 (some cases reported by Dorr et al. ⁸⁶ , 2000, & by Hilton et al. ¹⁰⁷ , 1996)	Retrospective review; osteoarthritis compared with osteonecrosis cases	1991 to 1993: 9 hips 1993 to 1998: 35 hips 1999 to 2003: 91 hips	1 center	135/129 82 hips: osteoarthritis 30 hips: osteonecrosis	28	Modified SF-36, mean function	HHS/patient reported	5.5 yr/3 died, 5 lost to follow-up, 15 revised for failed InterOp cup (Sulzer)	Not reported
Grübl et al. ⁸⁸ , J Orthop Res, 2007	Case series with minimum 10-yr follow-up	Nov 1992 to May 1994	Not reported/not reported	105/98	28	UCLA, comorbid medical conditions	HHS/not reported	10 yr/15 died, 8 lost to follow-up, 2 bedridden	98.6% (95% CI, 96, 100) at 10 yr

Sharma et al. ⁹² , Hip Int, 2007	Prospective selected case series	1993 to ?	1/1	215/193	28	None	HHS	7.33 yr/6 lost to follow-up	Revision for loosening as end point: 95.5% (95% CI, 88, 100) at 12 yr
Randle and Gordiev ¹⁰⁹ , Aust N Z J Surg, 1997	Prospective case series	1994 to 1996	2/1	57 hips	28	None	HHS/surgeon	5 to 31 mo	Not reported
Korovessis et al. ⁸⁹ , Arch Orthop Trauma Surg, 2003	Prospective study	Jan 1994 to Nov 1998	1/1	350/266	28	Satisfaction	HHS, degree of invalidity/surgeon	4.3 yr/7 lost to follow-up	Cup 99.4% & stem 96.8% at 7.6 yr
Kim et al. ¹¹⁰ , J Bone Joint Surg Am, 2004	Selected case series	Sep 1994 to Aug 1996	1/not reported	70/62	28	None	HHS/not reported	7 yr/2 revisions excluded	Not reported
Delaunay ⁴ , J Arthroplasty, 2004	Prospective case series	Jan 1994 to Mar 1999	1/1	100/89	22 femoral head sleeves 78 no femoral head sleeves	None	Merle d'Aubigné & Charnley/surgeon	6 yr	Aseptic loosening as end point Head sleeves: 81.5% at 8 yr No head sleeves: 98.7% at 8 yr P = 0.008 for difference
Milosev et al. ⁹⁰ , J Bone Joint Surg Am, 2006	Retrospective review of selected case series	Dec 1994 to Dec 2002	1/not reported	640/591	28	None	Pain, range of motion, function/not reported	7.1 yr/28 died	All revisions as end point: 91% (95% CI, 88, 95) at 10 yr Aseptic revisions as end point: 93% (95% CI, 90, 96) at 10 yr
Lombardi et al. ⁷⁹ , J Arthroplasty, 2001	Prospective multicenter randomized controlled trial	Dec 1995 to Nov 1999	8/11	194/192 95 MoM heads (78 at 2 yr) vs. 95 MoP (72 at 2 yr)	28	None	HHS/not reported	72 MoP: 3.29 yr, 78 MoM: 3.23 yr/4 (5 hips) died, 36 <2-yr review, 3 lost to follow-up	Not reported

Lombardi et al. ⁸⁰ , J Arthroplasty, 2004	As above	As above	As above	53 hips at 5 yr vs. 46 hips at 5 yr	As above	As above	As above	5.7 yr/11 (12 hips) died, 84 <5-yr review	Not reported
Migaud et al. ⁶ , J Arthroplasty, 2004	Matched-control study: MoM matched to historical controls (Zirconia CoP)	1995 to 1998	1/3	39/30 MoM vs. 39/32 CoP	MoM: 28 CoP: 28	None	HHS/independent review at 5 yr	MoM: 68.7 mo CoP: 68.6 mo	MoM: 100% at 5 yr CoP: 97% ($\pm 2\%$)
Long et al. ⁵ , J Arthroplasty, 2004	Prospective selected case series	1995 to 2002	1/1	161/154	28	Modified SF-36 pain and function	HHS/ not reported	6.5 yr/6 died, 23 lost to follow-up, 155 Sulzer recall	Not reported
Peters et al. ¹¹¹ , J Arthroplasty, 2007	Prospective selected case series	Study 1 28 mm: 1995 to 2004 38 mm: 2002 to 2004 Study 2 2001 to 2004	Study 1: 1/1 Study 2: 2/2	Study 1: 136 28-mm heads (92% MoP & 8% MoM) & 160 38-mm heads (MoM) Study 2: 469 hips	Study 1 136 hips: 28 160 hips: 38 Study 2 370 hips: 28 99 hips: 40-56	None	Study 1: HHS/not reported Study 2: HHS/not reported	Study 1 28 mm: 52 mo 38 mm: 28 mo Study 2 Not reported	Not reported
Delaunay et al. ⁸⁵ , Clin Orthop Relat Res, 2008	Retrospective review of selected case series	1995 to 2004	3/5	83/73	28	None	Merle d'Aubigné/ surgeon	7.3 yr/1 lost to follow-up	Revision as end point: 100% at 10 yr
Eswaramoorthy et al. ⁸⁷ , J Bone Joint Surg Br, 2008	Retrospective review of selected case series	Jan 1995 to June 1997	1/3	104/100 MoM vs. 372/355 MoP	MoM: 28 MoP: not reported	OHS	None	MoM: 10 yr/15 (16 hips) died, 3 lost to follow-up MoP: 11.3 yr	MoM at 10 yr: 94% for all failures & 96% for aseptic failures
Saito et al. ⁹¹ , J Arthroplasty, 2006	Retrospective review of selected case series	Feb 1996 to Aug 2004	1/2	106/90	28	None	HHS/not reported	6.4 yr/0 lost to follow-up	99.1% at 6.4 yr
Jacobs et al. ⁷⁸ , J Arthroplasty, 2004	Prospective randomized controlled trial	Mar 1997 to Jul 2000	6/not reported	171 hips (subset of 236): 95 MoM vs. 76 MoP	MoM: 28 MoP: 28	None	HHS/not reported	3.7 yr/65 <3-yr review	Not reported

Lazennec et al. ⁴³ , Acta Orthop, 2009	Prospective case series	Jan 1997 to Dec 2000	1/4	138/113	28	None	HHS/not reported	9 yr/4 lost to follow-up	At 9 yr All failures: 89% Cup failure: 91% Stem failure: 99%
MacDonald et al. ⁸¹ , Clin Orthop Relat Res, 2003	Prospective randomized controlled trial	Mar 1998 to Oct 1999	2/5	41/41: 23 MoM vs. 18 MoP	MoM: 28 MoP: 28	SF-12, WOMAC	HHS/not reported	3.2 yr/1 died	Not reported
Naudie et al. ⁸³ , J Arthroplasty, 2004	Matched case-control study of patients with revision for aseptic loosening	1988 to ?	45 centers	505 hips (82 MoM & 423 MoP) revised 1605 hips (338 MoM & 1267 MoP) unrevised	Various head sizes Analysis controlled for head size	None	International Documentation and Evaluation System/surgeon	4 yr	Not reported
Smith et al. ¹¹² , Clin Orthop Relat Res, 2005	Retrospective review of selected case series	Oct 2001 to Oct 2003	2/3	377/327	38	None	None	4 mo/0 lost to follow-up	Not reported
Cuckler et al. ³ , J Arthroplasty, 2004	FDA IDE study (28-mm heads) Case series (38-mm heads)	Not reported	Not reported/not reported	694/633: 78 28-mm heads & 616 38-mm heads	78 hips: 28 616 hips: 38	None	Range of motion/not reported	28 mm: 1.1 yr 38 mm: 5.3 yr	Not reported
Komistek et al. ¹¹³ , J Bone Joint Surg Am, 2002	Prospective selected matched cases	Not reported	1/1	20 hips: 10 randomized MoM THA (HHS > 90) vs. 10 MoP	Not reported	None	HHS, gait analysis/not reported	MoM: 19 mo MoP: 22 mo	Not reported
Zijlstra et al. ⁸² , Orthopedics, 2009	Randomized controlled trial	Not reported	1/5 (2 trainees)	200 hips	28	OHS	HHS/independent review	5.6 yr/19 died, 5 lost to follow-up, 4 revised	All failures as end point at 5 yr MoM: 97% MoP: 99%
Stuchin ¹¹⁴ , J Bone Joint Surg Am, 2008	Retrospective review of selected case series of large-diameter heads	Oct 2006 to Sep 2007	1/not reported	40/34	38-58	None	HHS/not reported	Not specified	Not reported

Lavigne et al. ⁸⁴ , Clin Orthop Relat Res, 2010	Randomized controlled trial of hip resurfacing vs. large-diameter- head THA (LDH THA)	Feb 2006 to Apr 2007	1/3	48 hips: 24 resurfacing & 24 LDH THA	Not reported	WOMAC, SF-36, UCLA, Merle d'Aubigné, patient perception of hip/not reported	Gait analysis & function/evaluator and patient blinded	14 mo/0 lost to follow-up	Not reported
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*MoM = metal-on-metal, MoP = metal-on-polyethylene, THA = total hip arthroplasty, HHS = Harris hip score, SF = Short Form, OHS = Oxford hip score, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, UCLA = University of California at Los Angeles, and CI = confidence interval.