Prevalence of Failure due to Adverse Reaction to Metal Debris in Modern, Medium and Large Diameter Metal-on-Metal Hip Replacements – The Effect of Novel Screening Methods: Systematic Review and Metaregression Analysis

Aleksi Reito *, Olli Lainiala, Petra Elo, Antti Eskelinen
Coxa Hospital for Joint Replacement, Biokatu 6b, 33900 Tampere, Finland
* aleksi.reito@fimnet.fi

Abstract

Metal-on-metal (MoM) hip replacements were used for almost a decade before adverse reactions to metal debris (ARMD) were found to be a true clinical problem. Currently, there is a paucity of evidence regarding the usefulness of systematic screening for ARMD. We implemented a systematic review and meta-analysis to establish the prevalence of revision confirmed ARMD stratified by the use of different screening protocols in patients with MoM hip replacements. Five levels of screening were identified: no screening (level 0), targeted blood metal ion measurement and/or cross-sectional imaging (level 1), metal ion measurement without imaging (level 2), metal ion measurement with targeted imaging (level 3) and comprehensive screening (both metal ions and imaging for all; level 4). 122 studies meeting our eligibility criteria were included in analysis. These studies included 144 study arms: 100 study arms with hip resurfacings, 33 study arms with large-diameter MoM total hip replacements (THR), and 11 study arms with medium-diameter MoM THRs. For hip resurfacing, the lowest prevalence of ARMD was seen with level 0 screening (pooled prevalence 0.13%) and the highest with level 4 screening (pooled prevalence 21.3%). Pooled prevalence of ARMD with level 0 screening was 0.29% and with level 4 screening 21.3% in the large-diameter MoM THR group. In metaregression analysis of hip resurfacings, level 4 screening was superior with regard to prevalence of ARMD when compared with other levels. In the large diameter THR group level 4 screening was superior to screening 0,2 and 3. These outcomes were irrespective of follow-up time or study publication year. With hip resurfacings, routine cross-sectional imaging regardless of clinical findings is advisable. It is clear, however, that targeted metal ion measurement and/or imaging is not sufficient in the screening for ARMD in any implant concepts. However, economic aspects should be weighed when choosing the preferred screening level.
Introduction

In the late 1990s, advances in metallurgy and tribology led to a renewed interest in the use of metal-on-metal (MoM) bearings in total hip replacements (THR) [1]. The use of large diameter (LD) femoral heads that mimic the native anatomy of the hip joint requires relatively thin, i.e., 4–8 mm acetabular components to prevent excessive acetabular bone resection. Due to the extreme hardness of the new cobalt-chrome alloy Metasul, it became possible to manufacture these thin acetabular components [1]. With improved fixation techniques, the concept of large-headed femoral components coupled with thin monoblock cups were rapidly adopted for MoM hip resurfacings. Preliminary results with these second generation MoM hip resurfacings were excellent, and the number of hip resurfacings surged in the early 2000s. Later on, LD MoM bearings for cementless stemmed THRs were adopted.

It was only after a decade of use of these contemporary MoM bearings that adverse reaction to metal debris (ARMD) came into focus [2,3]. Metal debris caused by the increased wear of the bearing and/or the corrosion in the neck-head taper in a stemmed MoM THR leads to local soft tissue reactions that include synovitis, necrosis and extra-articular cysts or solid masses, i.e., pseudotumours [4–8]. ARMD is an umbrella term proposed by Langton et al. in 2010 to describe all the microscopic and macroscopic findings that were seen in revision surgeries performed on patients with MoM hip replacements who suffered from unexplained pain [2].

Nowadays, revision surgery is considered if a large thick-walled pseudotumour is seen in MRI, or if extremely high metal ion levels (>10–20 ppb) are found in the serum or whole blood (WB). Prior to 2010, MoM hip resurfacings and modular MoM THRs produced excellent results in young and active patients. Since 2010, however, there has been a drastic decline in the use of MoM hip replacements due to the higher than anticipated prevalence of ARMD and subsequent high failure rates [9,10].

An extensive amount of research has been published on ARMD. Novel screening methods such as blood metal ion measurement and cross-sectional imaging have offered the profound possibility to investigate the etiopathogenesis, clinical history and clinical manifestation of ARMD [2,4,5,11–14]. Both blood metal ion measurement and cross-sectional imaging have been proven to be useful in the diagnostics of ARMD [4,5,15]. However, there is a paucity of current literature regarding the usefulness of systematic screening for ARMD. Current guidelines on how to follow-up patients with MoM hip replacements lack sufficient evidence [16–18]. The intensity and coverage of such screening is strongly associated with the costs related to the surveillance of patients with MoM hip replacements.

Although the number of patients receiving MoM THRs has decreased drastically in recent years, there are still a vast number of patients with MoM hip replacement still in situ. Thus, there is a clear need for sufficient evidence on how to manage patients with MoM hip replacements.

The aim of this study was to conduct a systematic review and meta-analysis of current literature to establish the prevalence of revision confirmed ARMD stratified by the use of different screening protocols. A second aim was to explore the possible confounding effects of follow-up time and year of publication of the study on the prevalence of revision confirmed ARMD by performing a meta-regression analysis.

Methods

Eligibility criteria

A study was deemed eligible for our analysis if 1) it included an original patient cohort operated on with a single disclosed implant, 2) the implant used in the study was MoM hip
resurfacing or MoM THR with a femoral head diameter of 36 mm or larger, and 3) the reasons for the revisions were clearly stated or the operative findings in the revision surgery were outlined. An original patient cohort means a clearly defined population of patients operated on with a certain implant within a certain time interval at disclosed hospital(s). A study was excluded if more than one implant was used and the number of patients for each implant was not given. Moreover, a study was excluded if 1) it included patients referred from elsewhere to the place where the study was carried out (violation of eligibility criteria 1), 2) more than one implant was used, but revisions were not stratified according to the implant used, 3) the reasons for all revisions were not given, 4) the size of a study arm for a single implant was less than 20 hips.

Furthermore, if a study included a study arm or a subcohort of a study arm, which had been included in a previous study and in both studies a similar screening method was used, the more recent study was included in our analysis. However, if the two studies included an identical study arm or a subcohort of a study arm but the more recent study implemented a different level of screening, both studies were included in our analyses since the primary aim of our study was to investigate the effect of screening levels on the prevalence of revision confirmed ARMD.

Information sources and search strategy
The review was done according to PRISMA checklist (S1 Checklist). We developed a search strategy that was implemented in the PubMed and Scopus databases. Since our objective was to establish a pooled prevalence of ARMD seen with contemporary MoM hip replacements, we started our search of these databases from the year 1995. The search was conducted in May 2015.

We performed two searches of these two databases. The following search strategy was used first: “(metal-on-metal AND hip) OR ((’hip resurfacing’ OR (’surface replacement’ AND hip) OR "large-diameter total hip") NOT (metal-on-metal))”. A second search was carried out afterwards that was combined with the first search using the Boolean operator NOT in order to remove duplicates: “((recap AND hip) OR (magnum AND hip) OR (cormet AND hip) OR (durom AND hip) OR (conserve AND hip) OR (pinnacle AND hip) OR (asr AND hip) OR (m2a AND hip) OR (birmingham AND hip) OR (mitch AND hip) OR (adept AND hip))”. The latter search phrase outlines the most commonly used MoM hip replacement brand names.

Study selection
All the records retrieved from the two databases using our search strategy were screened. An assessment of duplicate references was not performed. Abstracts of all the records were assessed. Studies that outlined the use of any “metal-on-metal” hip implant or a hip implant by a brand name along with any clinical outcome (patient reported outcome score, survival rate, failure rate, complication rate, revision rate, deaths, levels of metal ion levels, cross-sectional imaging findings) were selected for eligibility assessment. All the studies meeting our eligibility criteria were selected for both systematic review and meta-analysis that was conducted using the metaregression technique.

Data extraction
The number of hips operated on with each given implant was recorded. Implant concept and publication year of the study were also recorded. Three categories for implant concept were used: 1) hip resurfacings or surface arthroplasties, 2) LD MoM THRs (femoral diameter >44
mm), which comprise identical bearing systems as in hip resurfacings coupled with a mainly cementless stem, and 3) MoM THR with a femoral diameter of 44 mm or smaller [medium-diameter (MD) MoM THR]. The last group included two fixed-sized MoM THRs: the Pinnacle 36 mm MoM THR and the M2a-38 MoM THR with a 38 mm femoral diameter. Small-diameter (<36 mm) MoM hip replacements were not included in the present study. Two studies included patients operated on with a Birmingham Mid-Head Resection (BMHR) device. These were included in the hip-resurfacing group due to their similarity. Follow-up time was recorded. We did not differentiate between mean and median follow-up times. The use of metal ion level measurement in serum or WB was assessed as well as the use of any cross-sectional imaging modality. In short, five levels of screening were identified: no screening (level 0), targeted blood metal ion measurement and/or cross-sectional imaging (level 1), blood metal ion measurement without imaging (level 2), blood metal ion measurement with targeted imaging (level 3) and comprehensive screening (both blood metal ions and imaging for all; level 4). If neither screening method was used, the level of screening was labeled “None” (Level 0). If prerevision details that included metal ion levels and/or imaging findings were described in single patients in the results section, the use of screening was considered lacking unless there was a protocol rationale in methods section that described the use of these screening methods, i.e., patients with a complaint underwent an MRI scan. If blood metal ion measurements were performed in a subset of patients and no cross-sectional imaging was performed or if cross-sectional imaging was performed in a subset of patients without any given metal ion data, the level of screening was labeled “Targeted CoCr and/or imaging” (Level 1). Again, if prerevision imaging findings or metal ion levels were described in single patients without any protocol rationale detailed in the methods section, these screening methods were considered to be lacking. If all patients underwent a metal ion measurement without any imaging protocol outlined in the methods section, the level of screening was labeled “CoCr without imaging” (Level 2). If targeted imaging was used along with a routine (full coverage) metal ion measurement, the level of screening was labeled ”CoCr with targeted imaging” (Level 3). If all patients underwent both metal ion measurement and cross-sectional imaging, the level of screening was labeled “Comprehensive” (Level 4). The modality of the imaging was recorded. We did not differentiate between serum and WB measurements.

The number and reasons for the revisions were recorded. Detailed prerevision and perioperative findings were assessed if described. The following reasons for the revision were considered to be ARMD: “ARM(e)D”, “Adverse wear”, “adverse local tissue reaction (ALTR)”, “adverse tissue reaction (ATR)”, “metallosis”, “pseudotumour” and “synovitis”. “Elevated metal ion levels” or “component/cup malposition” as reasons for revision were not considered to be ARMD unless perioperative findings were described. The definition of ARMD was also met if perioperative findings were described, that is if the operative findings described included the terms “metallosis”, “synovitis”, “pseudotumour”, “necrotic substance/tissue” and the case(s) outlined were considered to have failed due to ARMD. Cases with ARMD as revision indication but that also included a clear statement about component loosening were not included in our analyses.

Summary measures
The primary summary measure was the prevalence of ARMD. This was calculated by dividing the total number of revisions due to ARMD by the total number of hips included in the study. Confounding variables included in the meta-regression were follow-up time, year of publication and level of screening. This information was extracted as described in the previous section.
Data synthesis

The Q-statistic was used to assess heterogeneity across the studies. If the Q-statistic suggested high heterogeneity (p-value < 0.1), a random effects model was used instead of a fixed effects model. The amount of heterogeneity was assessed using the $I^2$-measure. The DerSimonian-Laird estimator was used as a random effects model when needed. Arcsine transformation was used for the summary measure (prevalence of revision confirmed ARMD). We preferred this to logit transformation because zero prevalence was overrepresented in our study. With logit transformation we would have been obliged to choose a random increment to be added to the zero summary measures. We would not have had any reasonable value for this. Metaregression analysis was used to assess whether differences in the prevalence of revision confirmed ARMD across different levels of screening remained after adjusting for the year of publication and follow-up time. All analyses were stratified by the implant concept (HR/LD THR/MD THR). Finally, we carried out a “best case” sensitivity analysis by performing all the aforementioned analyses using only study arms with patients operated on with Birmingham Hip Resurfacing (BHR, Smith&Nephew, Warwick, United Kingdom).

Results

A PRISMA flow diagram of the study selection process is shown in Fig 1. In total, 122 studies were included. These studies comprised 145 study arms (Table 1) (S1 Datafile). The median number of hips in the study arms was 128 (range 20–3095). The most commonly used implant was BHR (Table 2). Patients in 48 study arms were operated on with BHR. In total, 100 study arms included patients operated on with a hip-resurfacing device [14,15,19–99]. Thirty-three study arms included patients with LD-THA [35,56,79,95,100–121]. The most commonly used LD THA was the articular surface replacement (ASR) XL THR (DePuy Orthopedics, Warsaw, IN, USA). In general, the stems used with LD MoM bearing couples varied greatly. MD THR was used in 11 study arms [94,112,120,122–129]. In most of the studies, a traditional or conventional follow-up protocol without metal ion measurement and cross-sectional imaging was used (Table 2). Distribution of the follow-up time and year of publication are presented in Table 2.

The total overall pooled estimate for the prevalence of revision confirmed ARMD among 145 study arms was 1.07% (CI: 0.69–1.49, $I^2 = 92.3\%$, $p_{\text{heterogeneity}} < 0.001$). In general, the amount of heterogeneity was high. Individual study arms were stratified according to the level of screening for ARMD and the implant concept. The individual weighted prevalences of ARMD in each study arm under the random effects model are shown in Figs 2–4. In the hip-resurfacing group, the overall pooled prevalence of ARMD was 0.43% (CI: 0.25–0.65). With more comprehensive screening, the higher pooled prevalence of ARMD was observed (Fig 2). In the LD THR group, the overall pooled prevalence of ARMD was 4.6% (CI: 1.94–8.32). Prevalence peaked in the study arms with Level 4 screening (Fig 3). The clear trend of higher prevalence of ARMD associated with an increased level of screening seen among resurfacing groups was not observed in this group. The overall pooled prevalence of revision confirmed ARMD in the MD THR group was 1.43% (CI: 0.21–3.70%). This group lacked study arms with Level 1 and Level 4 screening (Fig 4).

Metaregression analysis

Metaregression was performed separately for hip resurfacings and LD THRs (Table 3). Metaregression was not performed in the MD THR group since no study arms were available for screening levels 1 and 4. For hip resurfacings, comprehensive screening (Level 4) was superior when compared with other levels, i.e., the prevalence of revision confirmed ARMD was
significantly higher in level 4 studies when compared with others. An increase in follow-up time had a small, positive effect on the prevalence of ARMD. This association remained after adjusting for confounding variables. In the LD THR group, level 1 screening proved to be as good as level 4 screening. Screening levels 0.2 and 3 were inferior when compared with level 4 screening, i.e., the prevalence of ARMD was significantly lower in these levels compared with the level 4 study arms. These differences remained after adjusting for confounding variables.

Fig 1. Flow chart of the study selection.
doi:10.1371/journal.pone.0147872.g001
| Study                  | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-----------------------|----------|------|----------------|-------------|-----------------------|-------------------------|------------------|------------------|-------------------|-------------------|----------------------|-------------------|
| Bergeron et al. 2009  | 209      | 228  | ASR            | ASR         | No                    | No                      | No               | No               | 0                 | 2.9               | 0                    | 0.000             |
| Jameson et al. [51]   | 192      | 214  | ASR            | ASR         | No                    | No                      | No               | No               | 0                 | 3.6               | 6                    | 0.028             |
| Malhotra et al. 2012  | 23       | 32   | ASR            | ASR         | No                    | No                      | No               | No               | 0                 | 3.6               | 0                    | 0.000             |
| Siebel et al. 2006    | 300      | 300  | ASR            | ASR         | No                    | No                      | No               | No               | 0.56              | 0                 | 0                    | 0                 |
| Whitehouse et al. 2013| 0        | 76   | ASR            | ASR         | No                    | No                      | No               | No               | 4.9               | 4                 | 0.053                |                   |
| Kadar et al. 2013     | 125      | 139  | ASR            | ASR         | Target                | Symptoms, suboptimal cup position, small femoral size, surgeon concern | Target            | MRI              | 1                 | 3.5               | 1                    | 0.007             |
| Whitwell et al. 2012  | 0        | 21   | ASR            | ASR         | Target                | Patients with symptoms | Target            | US               | 1                 | 5.2               | 3                    | 0.143             |
| Isaac et al. 2009     | 0        | 77   | ASR            | ASR         | All                   | No                      | No               | No               | 2                 | 2.0               | 0                    | 0.000             |
| Langton 2011a (Arm 1) | 0        | 59   | ASR            | ASR         | All                   | No                      | No               | No               | 2                 | 2.6               | 2                    | 0.034             |
| Langton 2011a (Arm 4) | 0        | 430  | ASR            | ASR         | All                   | No                      | No               | No               | 2                 | 3.1               | 27                   | 0.063             |
| Shemesh et al. 2014   | 0        | 49   | ASR            | ASR         | All                   | No                      | No               | No               | 2                 | 4.1               | 0                    | 0.000             |
| Fernandez et al. 2014 | 0        | 60   | ASR            | ASR         | All                   | Target                 | CT               | MRI              | 3                 | 2.9               | 2                    | 0.033             |
| Reito et al. 2013     | 142      | 168  | ASR            | ASR         | All                   | All                    | MRI              | CT               | 4                 | 5.3               | 42                   | 0.250             |
| Aulakh et al. 2010    | 95       | 101  | BHR            | BHR         | No                    | No                      | No               | No               | 3.0               | 0                 | 0                    | 0.000             |
| Aulakh et al. 2010    | 97       | 101  | BHR            | BHR         | No                    | No                      | No               | No               | 2.0               | 0                 | 0                    | 0.000             |
| Azem et al. 2015      | 222      | 224  | BHR            | BHR         | No                    | No                      | No               | No               | 0                 | 12.1              | 4                    | 0.018             |
| Baker et al. 2011     | 0        | 63   | BHR            | BHR         | No                    | No                      | No               | No               | 9.0               | 0                 | 0                    | 0.000             |

(Continued)
| Study                          | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-------------------------------|----------|------|-----------------|--------------|-----------------------|--------------------------------|------------------------|------------------|------------------|---------------------|---------------------|-------------------|------------------|
| Bose et al. 2010 [28]         | 71       | 96   | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 0                   | 5.4                 | 0                 | 0.000            |
| Coulter et al. 2012 [29]      | 213      | 230  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 0                   | 10.4               | 3                 | 0.013            |
| De Smet 2005 [32]             | 0        | 252  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 0                   | 2.8                 | 0                 | 0.000            |
| Della Valle et al. 2009 [33]  | 0        | 537  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 0                   | 0.9                 | 0                 | 0.000            |
| Delport et al. 2011 (Arm 1) [34] | 28     | 28   | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 4.8                 | 0                   | 0.000            |
| Fink Barnes et al. 2014 [35]  | 80       | 89   | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 3.6                 | 0                   | 0.000            |
| Giannini et al. 2011 [38]     | 134      | 142  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 6.1                 | 0                   | 0.000            |
| El Hachmi et al. 2014 [43]    | 141      | 151  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 4.2                 | 0                   | 0.000            |
| Heilpern et al. 2008 [46]     | 98       | 110  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 5.9                 | 0                   | 0.000            |
| Khan et al. 2009 [54]         | 653      | 679  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 6.0                 | 1                   | 0.001            |
| Madhu et al. 2011 [55]        | 104      | 120  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 7.0                 | 0                   | 0.000            |
| Marulanda et al. 2008 [137]   | 0        | 230  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 1.30                | 0                   | 0                 |
| McAndrew et al. 2007 [52]     | 155      | 180  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 2.6                 | 0                   | 0.000            |
| McBryde et al. 2010 [53]      | 1826     | 2123 | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 3.5                 | 0                   | 0.000            |
| McMinn et al. 2011b [65]      | 0        | 3095 | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 8.0                 | 10                  | 0.003            |
| Naal et al. 2009 [136]        | 0        | 22   | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 3.6                 | 0                   | 0.000            |
| Ottovere et al. 2008 [71]     | 0        | 463  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 3.6                 | 7                   | 0.015            |
| Pailhe et al. 2013 (Arm 2) [72] | 0     | 42   | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 3.2                 | 0                   | 0.000            |
| Patel et al. 2014 [73]        | 85       | 109  | BHR             | BHR          | No                    | No                             | No                     | No               | No               | 5.2                 | 0                   | 0.000            |

(Continued)
| Study                                      | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-------------------------------------------|----------|------|-----------------|--------------|-----------------------|-------------------------------|------------------------|------------------|-----------------|-------------------|-------------------|----------------------|---------------------|
| Rahman et al. 2010 [77]                   | 302      | 329  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 5.0               | 1                 | 0.003                |
| Reito et al. 2011 [78]                    | 126      | 144  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 6.0               | 2                 | 0.014                |
| Sandiford et al. 2014 [82]                | 107      | 109  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 8.2               | 3                 | 0.028                |
| Swank et al. 2009 [87]                    | 0        | 128  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 2.0               | 0                 | 0.000                |
| Takamura et al. 2014 (Arm 1) [88]         | 0        | 115  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 2.8               | 2                 | 0.017                |
| Takamura et al. 2014 (Arm 2) [88]         | 0        | 236  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 2.2               | 1                 | 0.004                |
| Whitehouse et al. 2013 [139]              | 0        | 103  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 4.3               | 4                 | 0.039                |
| Witzleb et al. 2008                      | 263      | 300  | BHR             | BHR          | No                    | No                            | No                     | No               | 0               | 2.00              | 0                 | 0                    |
| Murray et al. 2012 [66]                  | 554      | 646  | BHR             | BHR          | No                    | Target                        | OHS<33                 | MRI             | 1               | 8.0               | 26                | 0.040                |
| Holland et al. 2012 [147]                 | 90       | 100  | BHR             | BHR          | Target               | No                            | No                     | No               | 1               | 9.6               | 2                 | 0.020                |
| Kostensalo et al. 2014 (Arm 1) [56]       | 0        | 249  | BHR             | BHR          | Target               | ns                            | No                     | No               | 1               | 6.2               | 3                 | 0.012                |
| Nam et al. 2012 (Arm 2) [89]              | 126      | 137  | BHR             | BHR          | Target               | ns                            | No                     | No               | 1               | 5.7               | 2                 | 0.015                |
| Paillie et al. 2014 [73]                  | 162      | 180  | BHR             | BHR          | Target               | Patient with symptoms         | No                     | No               | 1               | 6.0               | 1                 | 0.006                |
| Daniel et al. 2014 [31]                   | 886      | 1000 | BHR             | BHR          | Target               | Patients with longest follow-up | Target               | Patients with longest follow-up | CT                | 13.7              | 7                 | 0.007                |
| Langton 2011a (Arm 2) [14]                | 0        | 1922 | BHR             | BHR          | All                  | No                            | No                     | No               | 2               | 5.7               | 23                | 0.012                |
| Langton 2011a (Arm 3) [14]                | 0        | 180  | BHR             | BHR          | All                  | No                            | No                     | No               | 2               | 5.4               | 1                 | 0.006                |
| Langton 2011a (Arm 6) [14]                | 0        | 674  | BHR             | BHR          | All                  | No                            | No                     | No               | 2               | 5.4               | 3                 | 0.004                |
| Robinson et al. 2014 (Arm 1) [91]         | 0        | 120  | BHR             | BHR          | All                  | No                            | No                     | No               | 2               | 4.2               | 1                 | 0.008                |
| Su et al. 2014 [86]                       | 265      | 293  | BHR             | BHR          | All                  | No                            | No                     | No               | 2               | 3.6               | 1                 | 0.003                |
### Table 1. (Continued)

| Study | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-------|----------|------|-----------------|--------------|-----------------------|---------------------------------|------------------------|-----------------|-----------------|-----------------|-----------------|-------------------|------------------|
| van der Straaten et al. 2013 [89] | 232 | 250 | BHR | BHR | All | No | No | 2 | 10.8 | 4 | 0.016 |
| Hartmann et al. 2012 [45] | 95 | 100 | BHR | BHR | All | Target | Co or Cr level >10 ppb | CT | 3 | 10.0 | 3 | 0.030 |
| Neito et al. 2014 [15] | 219 | 261 | BHR | BHR | All | Target | Patients with symptoms, Co or Cr level >5 ppb | US/MRI | 3 | 10.4 | 11 | 0.042 |
| Bisschop et al. 2013 [86] | 129 | 149 | BHR | BHR | All | All | CT | 4 | 3.4 | 8 | 0.054 |
| Haddad et al. 2015 | 40 | 47 | BHR | BHR | All | All | MRI | 1 | 12.1 | 0 | 0.000 |
| Junnila et al. 2015 [52] | 32 | 42 | BHR | BHR | All | All | MRI | 4 | 6.7 | 4 | 0.095 |
| Radtke et al. 2014 [75] | 75 | 85 | Bionic | Bionic | No | No | No | 0 | 5.0 | 0 | 0.000 |
| McMinn et al. 2011a [140] | 164 | 171 | BMHR | BMHR | No | No | No | 0 | 3.5 | 0 | 0.000 |
| Rahman et al. 2011 [76] | 34 | 35 | BMHR | BMHR | No | No | No | 0 | 2.8 | 0 | 0.000 |
| Amstutz et al. 2011 | 0 | 1107 | Conserve+ | Conserve+ | No | No | No | 0 | 6.8 | 3 | 0.003 |
| Arndt et al. 2013 [20] | 0 | 55 | Conserve+ | Conserve+ | No | No | No | 0 | 4.2 | 0 | 0.000 |
| Kim et al. 2008 [29] | 0 | 200 | Conserve+ | Conserve+ | No | No | No | 0 | 2.6 | 0 | 0.000 |
| Fowble et al. 2009 [141] | 50 | 50 | Conserve+ | Conserve+ | No | No | No | 0 | 3.2 | 0 | 0.000 |
| Glyn-Jones et al. 2009 (Arm 1) [39] | 0 | 606 | Conserve+ | Conserve+ | No | No | No | 0 | 4.0 | 8 | 0.013 |
| Marker et al. 2010 [61] | 0 | 361 | Conserve+ | Conserve+ | No | No | No | 0 | 4.9 | 0 | 0.000 |
| McGath et al. 2008 (Arm 1) [64] | 0 | 42 | Conserve+ | Conserve+ | No | No | No | 0 | 3.0 | 0 | 0.000 |
| McGath et al. 2008 (Arm 2) [64] | 0 | 153 | Conserve+ | Conserve+ | No | No | No | 0 | 3.0 | 0 | 0.000 |
| Newman et al. 2008 [70] | 120 | 126 | Conserve+ | Conserve+ | No | No | No | 0 | 1.0 | 0 | 0.000 |
| Ribas et al. 2014 [80] | 450 | 486 | Conserve+ | Conserve+ | No | No | No | 0 | 7.2 | 1 | 0.002 |
| Study                          | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-------------------------------|----------|------|-----------------|--------------|-----------------------|-------------------------------|-------------------------|-----------------|-----------------|-------------------|--------------------|---------------------|---------------------|
| Wang et al. 2012              | 34       | 37   | Conserve+       | Conserve+    | No                    | No                            | No                      | No              | 0               | 5.9               | 0                  | 0.000               |
| Woon et al. 2013              | 46       | 53   | Conserve+       | Conserve+    | No                    | No                            | No                      | 0               | 8.3             | 0                 | 0.000               |
| Zylberberg et al. 2015        | 458      | 548  | Conserve+       | Conserve+    | No                    | No                            | No                      | 0               | 6.6             | 4                 | 0.007               |
| Nam et al. 2012 (Arm 1)       | 124      | 137  | Conserve+       | Conserve+    | Target                | ns                            | No                      | 1               | 5.5             | 1                 | 0.007               |
| Bisseling et al. 2015         | 32       | 38   | Conserve+       | Conserve+    | All                   | No                            | No                      | 0               | 4.8             | 2                 | 0.053               |
| Kim et al. 2011 [142]         | 97       | 97   | Conserve+       | Conserve+    | All                   | No                            | No                      | 0               | 2               | 2.0               | 0.000               |
| Langton 2011a (Arm 3) [14]    | 0        | 961  | Conserve+       | Conserve+    | All                   | No                            | No                      | 2               | 2.8             | 4                 | 0.004               |
| Yang et al. 2011              | 25       | 25   | Conserve+       | Conserve+    | All                   | No                            | No                      | 2               | 2.0             | 0                 | 0.000               |
| Stulberg et al. 2008          | 0        | 337  | Cormet Hybrid   | Cormet Hybrid | No                    | No                            | No                      | 0               | 2.0             | 0                 | 0.000               |
| Gross et al. 2012 [40]        | 329      | 373  | Cormet Uncemented | Cormet Cemented | No                    | No                            | No                      | 0               | 8.0             | 2                 | 0.005               |
| Issa et al. 2013 [55]         | 114      | 120  | Cormet Uncemented | Cormet Cemented | No                    | No                            | No                      | 0               | 3.5             | 0                 | 0.000               |
| Kordas et al. 2012            | 215      | 234  | Cormet Uncemented | Cormet Cemented | No                    | No                            | No                      | 0               | 5.0             | 0                 | 0.000               |
| Madadi et al. 2011 [58]       | 18       | 52   | Cormet Uncemented | Cormet Cemented | No                    | No                            | No                      | 0               | 3.4             | 0                 | 0.000               |
| Gross et al. 2008 [42]        | 18       | 20   | Cormet Uncemented | Cormet Uncemented | No                    | No                            | No                      | 0               | 7.4             | 0                 | 0.000               |
| Hull et al. 2011 [48]         | 131      | 135  | Cormet Uncemented | Cormet Uncemented | No                    | No                            | No                      | 0               | 2.9             | 0                 | 0.000               |
| Lederg et al. 2013 [57]       | 580      | 644  | DUROM           | DUROM        | No                    | No                            | No                      | 0               | 2.8             | 1                 | 0.002               |
| Naal et al. 2011 [67]         | 91       | 100  | DUROM           | DUROM        | No                    | No                            | No                      | 0               | 5.0             | 0                 | 0.000               |
| Paille et al. 2013 (Arm 1)    | 0        | 100  | DUROM           | DUROM        | No                    | No                            | No                      | 0               | 3.2             | 0                 | 0.000               |
| Vendittoli et al. 2013 [93]   | 0        | 112  | DUROM           | DUROM        | Target                | Patients with follow-up of >5 years | No                      | 1               | 8.0             | 1                 | 0.009               |
| Robinson et al. 2014 (Arm 2)  | 0        | 240  | DUROM           | DUROM        | All                   | No                            | No                      | 2               | 4.6             | 0                 | 0.000               |
Table 1. (Continued)

| Study | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-------|----------|------|-----------------|--------------|-----------------------|-------------------------------|------------------------|-----------------|-----------------|------------------|-------------------|---------------------|---------------------|
| van der Weegen et al. 2012 [91] | 240 | 280 | M2a-Magnum | ReCap | No | Target | Patients with symptoms | US | 1 | 3.3 | 0 | 0.000 |
| van der Weegen et al. 2014 [92] | 235 | 271 | M2a-Magnum | ReCap | All | All | MRI | 4 | 4.6 | 9 | 0.033 |
| Delport et al. 2011 (Arm 2) [34] | 28 | 28 | M2a-Magnum | ReCap | No | No | No | 0 | 1.4 | 0 | 0.000 |
| Glyn-Jones et al. 2009 (Arm 2) [99] | 0 | 128 | M2a-Magnum | ReCap | No | No | No | 0 | 4.0 | 0 | 0.000 |
| Gross et al. 2013 [91] | 0 | 2166 | M2a-Magnum | ReCap | Target | Target | CT/MRI | 1 | 4.0 | 5 | 0.002 |
| Daniel et al. 2010 [30] | 160 | 184 | McMinn | McMinn | No | No | No | 0 | 10.6 | 0 | 0.000 |
| LD THR | Bolland et al. 2011 [102] | 185 | 199 | Adept/BHR | CPT | All | No | No | 2 | 5.2 | 14 | 0.070 |
| Steele et al. 2008 [119] | 109 | 120 | ASR XL | ns | No | No | No | 0 | 1.6 | 4 | 0.033 |
| Wynn-Jones et al. 2011 [121] | 54 | 62 | ASR XL | Corail | No | All | MRI | 1 | 2.5 | 7 | 0.113 |
| Whitwell et al. 2012 (Arm 2) [95] | 0 | 100 | ASR XL | Corail | Target | Patients with symptoms | Target | Patients with symptoms | US | 1 | 4.4 | 17 | 0.170 |
| Hug et al. 2013 [108] | 0 | 149 | ASR XL | Summit | Target | Symptoms or patient willingness | Target | Patients scheduled for revision with elevated metal ion levels and suspicion for ARMD | MRI | 1 | 3.3 | 24 | 0.161 |
| Langton 2011b [110] | 0 | 87 | ASR XL | 57 S-ROM, 30 Corail | All | No | No | 2 | 4.0 | 25 | 0.287 |
| Lavigne et al. 2011 (Arm 3) [113] | 0 | 32 | ASR XL | Trilock | All | No | No | 2 | 2.0 | 0 | 0.000 |
| Fernandez et al. 2014 (Arm 2) [38] | 0 | 23 | ASR XL | Proxima | All | Target | ns | CT | 3 | 2.9 | 0 | 0.000 |
| Reito et al. 2015 [117] | 196 | 225 | ASR XL | 149 Summit, 53 Corail, 21 S-ROM, 1 Proxima | All | All | MRI | 4 | 5.4 | 73 | 0.324 |
| Reito et al. 2013 (Arm 2) [79] | 281 | 312 | ASR XL | 233 Summit, 54 Corail, 24 S-ROM, 1 Proxima | All | All | MRI | 4 | 4.6 | 96 | 0.308 |

Effect of Screening Methods on the Prevalence of ARMD
| Study                  | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|------------------------|----------|------|-----------------|--------------|----------------------|-------------------------------|-------------------------|------------------|------------------|-------------------|--------------------|---------------------|---------------------|
| Cip et al. 2014 [144]  | 88       | 99   | ASR XL          | 97 CoxaFit, 2 ARGE Geradschaft | All                  | All                             | CT                      | 4                | 3.5              | 26                | 0.263              |                     |                     |
| Kostensalo et al. 2014 (Arm 2) [56] | 0       | 39   | BHR             | Synergy       | Target ns            | No                             | No                      | 1                | 3.9              | 0                 | 0.000              |                     |                     |
| Hosny et al. 2013 [107] | 41       | 44   | BHR             | Synergy       | Target “Some patients” | Target “Patient with symptoms of elevated metal ion level (no cut-off stated)” | MRI                     | 1                | 5.0              | 2                 | 0.045              |                     |                     |
| Lavigne et al. 2011 (Arm 4) [113] | 0       | 29   | BHR             | Anthology     | All                  | No                             | No                      | 2                | 2.0              | 0                 | 0.000              |                     |                     |
| Chatth et al. 2013 [104] | 88       | 89   | Conseve+        | Profemur      | No                   | No                             | No                      | 0                | 2.5              | 3                 | 0.034              |                     |                     |
| Levy et al. 2013 [107]  | 0        | 66   | Conseve+        | Profemur      | Target “Patients with suspected failing hips” | Target “Patients with suspected failing hips” | CT/US                   | 1                | 1.3              | 7                 | 0.106              |                     |                     |
| Lardanchet et al. 2012 (Arm 3) [111] | 0       | 20   | Conseve+        | 16 Profemur L, 4 Contact Evolution | All                  | No                             | No                      | 2                | 1.0              | 0                 | 0.000              |                     |                     |
| Hasegawa et al. 2013 [106] | 98       | 108  | Cormet          | Cti II        | All                  | All                             | MRI                     | 4                | 3.8              | 5                 | 0.046              |                     |                     |
| Merh et al. 2010 [115]  | 107      | 111  | DUROM           | 78 Muller type, 28 Emeraude | No                   | No                             | No                      | 0                | 2.5              | 0                 | 0.000              |                     |                     |
| Bert et al. 2010 [101]  | 92       | 100  | DUROM           | Zweymuller SL | No                   | No                             | No                      | 0                | 4.8              | 1                 | 0.010              |                     |                     |
| Saragaglia et al. 2015 [118] | 165     | 177  | DUROM           | PF Stem       | No                   | Target “Unexplained pain, osteolysis, bone cysts” | US                      | 1                | 6.7              | 4                 | 0.023              |                     |                     |
| Lavigne et al. 2011 (Arm 1) [113] | 0        | 42   | DUROM           | GLS Spottorno | All                  | No                             | No                      | 2                | 2.0              | 1                 | 0.024              |                     |                     |
| Lardanchet et al. 2012 (Arm 1) [111] | 0        | 24   | DUROMTHA        | 20 Contact Evolution, 4 Profemur L | All                  | No                             | No                      | 2                | 1.0              | 2                 | 0.083              |                     |                     |
| Bayley et al. 2015 [100] | 215      | 258  | M2a-Magnum      | Mallory Head  | All                  | Target “Follow-up >1 year” | US                      | 3                | 4.5              | 0                 | 0.000              |                     |                     |
| Kostensalo et al. 2012 [109] | 635      | 691  | M2a-Magnum/ReCap | Bimetric     | No                   | No                             | No                      | 0                | 1.0              | 0                 | 0.000              |                     |                     |
| Latieir et al. 2011 (Arm 2) [112] | 0        | 487  | M2a-Magnum/ReCap | ns            | No                   | No                             | No                      | 0                | 5.0              | 3                 | 0.006              |                     |                     |

(Continued)
| Study                        | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-----------------------------|----------|------|-----------------|--------------|-----------------------|-------------------------------|------------------------|------------------|------------------|----------------------|-------------------|----------------------|---------------------|
| Lardanchet et al. 2012 (Arm 2) [111] | 0 23    | M2a-Magnum/ ReCap | Exception    | All          | No                   | No                            | 2                      | 1.0              | 0                | 0.000                |
| Lavigne et al. 2011 (Arm 2) [113] | 0 34    | M2a-Magnum/ ReCap | Taperloc     | All          | No                   | No                            | 2                      | 2.0              | 0                | 0.000                |
| Sturup et al. 2012 (Arm 2) [120] | 0 271   | M2a-Magnum/ ReCap | ns           | All          | Target               | Patients with symptoms        | CT                     | 3.5              | 1                | 0.004                |
| Bosker et al. 2012 [103]     | 119 120 | M2a-Magnum/ ReCap | Biometric    | All          | CT                   | 4                             | 3.6                    | 13               | 0.108             |
| Mokka et al. 2013 [119]      | 74 80   | M2a-Magnum/ ReCap | BiMetric     | All          | MRI                  | 4                             | 6.0                    | 3                | 0.038             |
| Kostensalo et al. 2014 (Arm 3) [56] | 0 41    | R3    | Synergy        | Target       | ns                   | No                            | 1                      | 2.3              | 2                | 0.049                |
| Dramis et al. 2014 [105]     | 46 50   | R3    | 30 Anthology, 18 CPCS, 2 SL Plus | All | Target | Symptomatic patients and those with "adverse investigations" | MRI | 3 | 3.8 | 12 | 0.240 |
| MD THR                      |          |      |                |              |                      |                               |                        |                  |                  |                      |
| Latteier et al. 2011 (Arm 1) [112] | 0 750   | M2a-38 | ns             | No           | No                   | No                            | 0                      | 5.0              | 11               | 0.015                |
| Sturup et al. 2012 (Arm 1) [120] | 0 85    | M2a-38 | ns             | All          | Target               | Patients with symptoms        | CT                     | 3.5              | 0                | 0.000                |
| Smeekes et al. 2015 [129]    | 351 377 | M2a-38 | Taperloc       | All          | Target               | Patients with symptoms, Co or Cr level >5 ppb | MRI | 3 | 2.5 | 51 | 0.135 |
| Barret et al. 2012 [122]     | 0 779   | Pinnacle | 310 Summit Porocat, 234 S-ROM, 139 Summit DuoFix, 47 Prodigy, 35 AML, 11 Summit Cemented, 2 Replica, 1 Endurance | No | No | No | No | 4.2 | 8 | 0.010 |
| Kindsfater et al. 2012 [125] | 0 95    | Pinnacle | 86 S-ROM, 8 Summit Cemented, 1 Summit | No | No | No | No | 6.0 | 0 | 0.000 |
| Engh et al. 2010 [124]       | 126 131 | Pinnacle | AML/Prodigy (numbers ns) | No | No | No | No | 5.6 | 0 | 0.000 |
| Study                  | Patients | Hips | Acetabular side | Femoral side | Metal ion measurement | Targeted measurement performed | Cross-sectional imaging | Targeted imaging | Imaging modality | Level of screening | Follow-up in years | Revisions due to ARMD | Prevalence of ARMD |
|-----------------------|----------|------|-----------------|--------------|------------------------|-------------------------------|------------------------|------------------|------------------|---------------------|-------------------|----------------------|---------------------|
| Whitehouse et al. 2013 [94] | 0        | 99   | Pinnacle        | Corail       | No                     | No                            | No                     | No               | 0                | 4.0                 | 3                 | 0.030                |
| Bernasek et al. 2013 [123] | 0        | 354  | Pinnacle        | Summit       | No                     | No                            | No                     | No               | 0                | 6.8                 | 0                 | 0.000                |
| Schouten et al. 2012 [128] | 0        | 34   | Pinnacle        | Corail       | All                    | No                            | No                     | No               | 2                | 1.0                 | 0                 | 0.000                |
| Matharu et al. 2014 [127]  | 511      | 578  | Pinnacle        | Corail       | All                    | Target                        | Co or Cr level >7 ppb     | MRI/US           | 3                | 5.0                 | 17                | 0.029                |
| Lainiala et al. 2014 [126] | 430      | 371  | Pinnacle System | 398 Summit, 17 Corail, 14 S-ROM, 1 Prodigy | All | Target | Patients with symptoms, Co or Cr level >5 ppb | MRI | 3 | 7.5 | 32 | 0.086 |

doi:10.1371/journal.pone.0147872.t001
Table 2. Summary data of the study arms.

| Implant used                  | Study arms |
|-------------------------------|------------|
| Hip resurfacing (HR)          |            |
| BHR                           | 48         |
| Conserve+                     | 18         |
| ASR                           | 13         |
| DUROM                         | 5          |
| Cormet                        | 5          |
| Recap—M2a-Magnum              | 5          |
| Birmingham Mid Head Resection | 2          |
| Cormet Uncemented             | 2          |
| Bionic                        | 1          |
| McMinn                        | 1          |
| Large-diameter total hip replacements (LD-THA) | |
| ASR XL—Mixed stems            | 10         |
| DUROM—Mixed stems             | 5          |
| ReCap-M2a-Magnum—Mixed stems  | 8          |
| BHR—Mixed stems               | 3          |
| R3—Mixed stems                | 2          |
| Conserve—Mixed stems          | 2          |
| Adept/BHR—CPT                 | 1          |
| Cormet—Cti II                 | 1          |
| Adept—CPT                     | 1          |
| Medium-diameter total hip replacement (MD-THA) | |
| Pinnacle—Mixed stems          | 8          |
| M2a-38—Mixed stems            | 3          |

| Screening method               | Study arms |
|-------------------------------|------------|
| Level 0                       |            |
| None                          | 76         |
| Level 1                       |            |
| Targeted blood metal ions without imaging | 8 |
| Targeted imaging without blood metal ions | 3 |
| Targeted blood metal ions with targeted imaging | 9 |
| Level 2                       |            |
| Blood metal ions without imaging | 26 |
| Cross-sectional imaging without blood metal ions | 1 |
| Level 3                       |            |
| Blood metal ions with targeted imaging | 11 |
| Level 4                       |            |
| Blood metal ions AND cross-sectional imaging | 10 |

| Year of publication | Study arms |
|---------------------|------------|
| 2005                | 1          |
| 2006                | 1          |
| 2007                | 1          |
| 2008                | 8          |
| 2009                | 12         |
| 2010                | 11         |
| 2011                | 31         |
| 2012                | 23         |

(Continued)
Sensitivity analysis

All analyses were calculated using only study arms with Birmingham Hip Resurfacing, which has been the most used implant (48 arms). A trend was observed that showed an increased prevalence of ARMD associated with an increased level of screening (Fig 5). The results of the metaregression analyses were similar to those observed with all hip resurfacings with the exception of level 3, where no inferiority to level 4 screening was observed (Table 4). Screening levels 0,1 and 2 were significantly inferior to level 4.

Discussion

Despite the marginal use of MoM hip replacements nowadays, the orthopedic community must bear the burden of a vast follow-up that has resulted from the widespread use of these devices over the past 15 years [130]. It is evident that patients with MoM hip replacements must be followed-up, at least clinically. However, there is paucity of information available regarding the optimal follow-up protocol and especially regarding the use of blood metal ion measurement and cross-sectional imaging. We must be rigorous and aim for the best possible and up-to-date evidence when constructing guidelines on how to manage patients with MoM replacements. Thus, we have performed a systematic literature review and meta-analysis to investigate the influence of the extent of the screening protocol on the prevalence of revision confirmed ARMD.

The overall pooled prevalence of confirmed prevalence ARMD was low. This is not a surprising finding considering that in most of the studies no screening was implemented other than conventional x-rays and clinical examination. The prevalence of ARMD was lowest in the study arms without screening (level 0). Moreover, these study arms also included the largest number of hips. Due to the weighting based on the sample sizes, the overall prevalence of ARMD does not, therefore, correctly highlight the current situation in patients with MoM hip replacements.

Heterogeneity between the studies was high. Firstly, there was a lot of variation in the implants used. There are many implant specific factors (clearance, hemispherity, carbon content, etc) that influence the wear of the bearing surface, and, therefore, bearing wear rates may differ greatly between different bearing systems [131,132]. Furthermore, both clinical studies and registry data show that there are major differences in the failure rates between different hip resurfacings and LD THRs [79,110,133]. These differences in failure rates are due to the modular taper-trunnion junction between the head and stem in the THRs, which is an additional source of metal debris due to corrosion and mechanical wear in the taper interface [134]. Secondly, when only study arms with the BHR implant were analyzed, high heterogeneity was still observed. The outcome variable assessed in our analysis was the revision rate for ARMD. Even

Table 2. (Continued)

| Follow-up time | Study arms |
|----------------|------------|
| ≤2 years       | 23         |
| 2–4 years      | 51         |
| 4–6 years      | 43         |
| 6–8 years      | 15         |
| >8 years       | 12         |

doi:10.1371/journal.pone.0147872.t002

Effect of Screening Methods on the Prevalence of ARMD

PLOS ONE | DOI:10.1371/journal.pone.0147872 March 1, 2016 17 / 32
Fig 2. Forest plot of prevalence of ARMD in the HR group stratified by level of screening.

doi:10.1371/journal.pone.0147872.g002
### Effect of Screening Methods on the Prevalence of ARMD

Table showing the prevalence of ARMD in the LD THA group stratified by level of screening:

| Study                  | Events | Total | Proportion | 95%-CI       | W(random) |
|------------------------|--------|-------|------------|--------------|-----------|
| **Level 0 screening**  |        |       |            |              |           |
| Berton et al. 2010     | 1      | 100   | 0.010      | [0.000; 0.054] | 3.1%      |
| Chatrath et al. 2013   | 3      | 89    | 0.034      | [0.007; 0.095] | 3.1%      |
| Koetensalo et al. 2012 | 0      | 691   | 0.000      | [0.000; 0.005] | 3.3%      |
| Lattie et al. 2011 (Arm 2) | 3   | 487   | 0.006      | [0.001; 0.018] | 3.3%      |
| Mertl et al. 2010      | 0      | 111   | 0.000      | [0.000; 0.003] | 3.1%      |
| Steels et al. 2008     | 4      | 120   | 0.033      | [0.009; 0.083] | 3.2%      |
| **Random effects model** | **11** | **1598** | **0.007** | **[0.000; 0.022]** | **19.0%** |
| *Heterogeneity: I^2 = 80.4%, tau^2 = 0.0046, p = 0.0001* |

| **Level 1 screening**  |        |       |            |              |           |
| Hosny et al. 2013      | 2      | 44    | 0.045      | [0.006; 0.155] | 2.9%      |
| Hug et al. 2013        | 24     | 149   | 0.161      | [0.106; 0.230] | 3.2%      |
| Koetensalo et al. 2014 (Arm 2) | 0   | 39    | 0.000      | [0.000; 0.090] | 2.9%      |
| Koetensalo et al. 2014 (Arm 3) | 2   | 41    | 0.049      | [0.006; 0.165] | 2.9%      |
| Levy et al. 2013       | 7      | 66    | 0.106      | [0.044; 0.208] | 3.0%      |
| Saragaglia et al. 2015 | 4      | 177   | 0.023      | [0.006; 0.057] | 3.2%      |
| Whitwell et al. 2012 (Arm 2) | 17  | 100   | 0.170      | [0.102; 0.258] | 3.1%      |
| Wynn-Jones et al. 2011 | 7      | 62    | 0.113      | [0.047; 0.219] | 3.0%      |
| **Random effects model** | **63** | **678** | **0.071** | **[0.028; 0.130]** | **24.3%** |
| *Heterogeneity: I^2 = 86.4%, tau^2 = 0.0172, p = 0.0001* |

| **Level 2 screening**  |        |       |            |              |           |
| Bolland et al. 2011    | 14     | 199   | 0.070      | [0.039; 0.115] | 3.2%      |
| Langton 2011b          | 25     | 87    | 0.287      | [0.195; 0.394] | 3.1%      |
| Lardachet et al. 2012 (Arm 1) | 2   | 24    | 0.083      | [0.010; 0.270] | 2.7%      |
| Lardachet et al. 2012 (Arm 2) | 0   | 23    | 0.000      | [0.000; 0.148] | 2.7%      |
| Lardachet et al. 2012 (Arm 3) | 0   | 20    | 0.000      | [0.000; 0.168] | 2.6%      |
| Lavigne et al. 2011 (Arm 1) | 1   | 42    | 0.024      | [0.001; 0.126] | 2.9%      |
| Lavigne et al. 2011 (Arm 2) | 0   | 34    | 0.000      | [0.000; 0.103] | 2.6%      |
| Lavigne et al. 2011 (Arm 3) | 0   | 32    | 0.000      | [0.000; 0.109] | 2.6%      |
| Lavigne et al. 2011 (Arm 4) | 0   | 29    | 0.000      | [0.000; 0.118] | 2.6%      |
| **Random effects model** | **42** | **490** | **0.023** | **[0.000; 0.085]** | **25.6%** |
| *Heterogeneity: I^2 = 86.7%, tau^2 = 0.0412, p = 0.0001* |

| **Level 3 screening**  |        |       |            |              |           |
| Bayley et al. 2015     | 0      | 256   | 0.000      | [0.000; 0.014] | 3.2%      |
| Dromis et al. 2014     | 12     | 50    | 0.240      | [0.131; 0.382] | 3.0%      |
| Fernandez et al. 2014 (Arm 2) | 0   | 23    | 0.000      | [0.000; 0.148] | 2.7%      |
| Shup et al. 2012 (Arm 2) | 1   | 271   | 0.004      | [0.000; 0.020] | 3.2%      |
| **Random effects model** | **13** | **602** | **0.020** | **[0.000; 0.090]** | **12.1%** |
| *Heterogeneity: I^2 = 63.3%, tau^2 = 0.0236, p = 0.0001* |

| **Level 4 screening**  |        |       |            |              |           |
| Boskar et al. 2012     | 13     | 120   | 0.108      | [0.059; 0.178] | 3.2%      |
| Cip et al. 2014        | 28     | 99    | 0.263      | [0.179; 0.361] | 3.1%      |
| Hisegawa et al. 2013   | 5      | 108   | 0.048      | [0.015; 0.105] | 3.1%      |
| Mokka et al. 2013      | 3      | 80    | 0.038      | [0.008; 0.106] | 3.1%      |
| Reito et al. 2013 (Arm 2) | 98  | 312   | 0.308      | [0.257; 0.362] | 3.2%      |
| Reito et al. 2015      | 73     | 225   | 0.324      | [0.264; 0.390] | 3.2%      |
| **Random effects model** | **216** | **944** | **0.164** | **[0.072; 0.283]** | **19.0%** |
| *Heterogeneity: I^2 = 84.8%, tau^2 = 0.0387, p = 0.0001* |

| **Random effects model** | **345** | **4312** | **0.046** | **[0.019; 0.083]** | **100%** |
| *Heterogeneity: I^2 = 95.9%, tau^2 = 0.0465, p = 0.0001* |

Fig 3. Forest plot of prevalence of ARMD in the LD THA group stratified by level of screening.

doi:10.1371/journal.pone.0147872.g003
if two studies implemented identical screening protocols, i.e., full coverage blood metal ion measurement and targeted cross-sectional imaging, very different prevalences of revision confirmed ARMD could still be observed. This is because indications for revision surgery can vary greatly between different surgeons and different hospitals. Some surgeons may prefer closer follow-up in cases where others would prefer revision surgery. The current literature lacks a

| Study                        | Events | Total | Proportion | 95%-CI     | W(random) |
|------------------------------|--------|-------|------------|------------|-----------|
| **Level 0 screening**        |        |       |            |            |           |
| Barret et al. 2012           | 8      | 779   | 0.010      | [0.004; 0.020] | 9.9%      |
| Bernasek et al. 2013         | 0      | 354   | 0.000      | [0.000; 0.010] | 9.7%      |
| Engh et al. 2010             | 0      | 131   | 0.000      | [0.000; 0.028] | 8.9%      |
| Kindsfater et al. 2012       | 0      | 95    | 0.000      | [0.000; 0.038] | 8.6%      |
| Lattheier et al. 2011 (Arm 1)| 11     | 750   | 0.015      | [0.007; 0.026] | 9.9%      |
| Whitehouse et al. 2013       | 3      | 99    | 0.030      | [0.006; 0.086] | 8.6%      |
| Random effects model         | 22     | 2208  | 0.005      | [0.000; 0.015] | 55.7%     |
| **Heterogeneity:**           |        |       |            | l-squared=79.8%, tau-squared=0.0031, p=0.0002 |

| Study                        | Events | Total | Proportion | 95%-CI     | W(random) |
|------------------------------|--------|-------|------------|------------|-----------|
| **Level 2 screening**        |        |       |            |            |           |
| Schouten et al. 2012         | 0      | 34    | 0.000      | [0.000; 0.103] | 6.7%      |
| Random effects model         | 0      | 34    | 0.000      | [0.000; 0.028] | 6.7%      |
| **Heterogeneity:**           |        |       |            | not applicable for a single study |

| Study                        | Events | Total | Proportion | 95%-CI     | W(random) |
|------------------------------|--------|-------|------------|------------|-----------|
| **Level 3 screening**        |        |       |            |            |           |
| Lainiala et al. 2014         | 32     | 371   | 0.086      | [0.060; 0.120] | 9.7%      |
| Matharu et al. 2014          | 17     | 578   | 0.029      | [0.017; 0.047] | 9.9%      |
| Smeekes et al. 2015          | 51     | 377   | 0.135      | [0.102; 0.174] | 9.7%      |
| Sturup et al. 2012 (Arm 1)   | 0      | 85    | 0.000      | [0.000; 0.042] | 8.4%      |
| Random effects model         | 100    | 1411  | 0.047      | [0.009; 0.114] | 37.7%     |
| **Heterogeneity:**           |        |       |            | l-squared=95.2%, tau-squared=0.0154, p<0.0001 |

| Study                        | Events | Total | Proportion | 95%-CI     | W(random) |
|------------------------------|--------|-------|------------|------------|-----------|
| Random effects model         | 122    | 3653  | 0.014      | [0.002; 0.037] | 100%      |
| **Heterogeneity:**           |        |       |            | l-squared=94.6%, tau-squared=0.014, p<0.0001 |

Fig 4. Forest plot of prevalence of ARMD in the MD THR group stratified by level of screening.

doi:10.1371/journal.pone.0147872.g004
specific definition for ARMD and especially the indications for revision. Due to these implant and inter-observer related differences, a high heterogeneity is observed.

Other confounding factors that may have influenced the observed prevalence of revision confirmed ARMD are the follow-up time and the publication year of the study. The prevalence of ARMD increases in a cumulative manner with increasing follow-up time [110]. ARMD may manifest as early as two years postoperatively and a late occurrence after ten-years of follow-up is also possible [2,15]. Thus, we included follow-up time as a confounding variable in our metaregression analysis to investigate whether prevalence of ARMD is a matter of long enough follow-up time or a matter of the screening protocol used. The follow-up time had no influence on the observed prevalence of ARMD. Therefore, our results suggests that even if the prevalence of revision confirmed ARMD would increase with increasing follow-up time, this association would not be observed due to the stronger effect of the screening protocol used.

The year of publication was also an important variable to consider as a confounder. We believe that there has been considerable publication bias in the MoM literature during recent years. As a result, there has been a strong tendency to publish as high as possible prevalences of pseudotumours and ARMD. Several extremely poorly functioning MoM hip replacements in have been in widespread use, and during the last two years numerous studies have been published that report the outcome of these poorly functioning implants. In most of the studies, the primary aim has been to elucidate the higher than anticipated failure rate due to ARMD. The “higher than anticipated” failure rate reflects the actual situation that we are facing nowadays with several MoM hip replacements, but from the perspective of the literature review we are facing publication bias. We do not have a sufficient number of studies where novel screening

Table 3. Results of the metaregression analysis in the HR and LD THR groups.

| Univariate regression analysis | Hip resurfacings | LD-THA |
|-------------------------------|-----------------|--------|
| Screening                     | Reference       | Reference |
| Blood metal ions with         | -0.117 0.051 0.022 | -0.279 0.098 0.005 |
| targeted imaging (Level 3)    |                 |        |
| Blood metal ions without      | -0.221 0.037 <0.001 | -0.259 0.082 0.002 |
| imaging (Level 2)             |                 |        |
| Targeted Blood metal ions     | -0.212 0.037 <0.001 | -0.150 0.082 0.067 |
| and/or imaging (Level 1)      |                 |        |
| No screening (Level 0)        | -0.273 0.034 <0.001 | -0.329 0.086 <0.001 |

| Multivariate regression analysis | Hip resurfacings | LD-THA |
|----------------------------------|-----------------|--------|
| Screening                        | Reference       | Reference |
| Blood metal ions with            | -0.137 0.051 0.007 | -0.264 0.108 0.014 |
| targeted imaging (Level 3)       |                 |        |
| Blood metal ions without         | -0.213 0.036 <0.001 | -0.245 0.115 0.033 |
| imaging (Level 2)                |                 |        |
| Targeted CoCr and/or             | -0.220 0.037 <0.001 | -0.141 0.090 0.12 |
| imaging (Level 1)                |                 |        |
| No screening (Level 0)           | -0.261 0.034 <0.001 | -0.320 0.117 0.006 |

| Mean FU                          | Per one year    |
|----------------------------------|-----------------|
|                                  | 0.0054 0.003 0.045 | -0.013 0.02 0.5 |

| Publication year                  | Per one year    |
|-----------------------------------|-----------------|
|                                   | 0.0034 0.003 0.3 | -0.006 0.03 0.8 |

$\beta$ = unstandardized regression coefficient, SE = standard error.

doi:10.1371/journal.pone.0147872.t003
Effect of Screening Methods on the Prevalence of ARMD

| Study | Events Total | Proportion | 95%-CI | W(random) |
|-------|--------------|------------|--------|-----------|
| Level 0 screening | | | | |
| Aushah et al. 2010 (Arm 1) | 0 101 | 0.000 [0.000; 0.000] | 1.8% |
| Aushah et al. 2010 (Arm 2) | 0 101 | 0.000 [0.000; 0.000] | 1.8% |
| Azem et al. 2015 | 4 224 | 0.018 [0.005; 0.045] | 2.3% |
| Baker et al. 2011 | 0 63 | 0.000 [0.000; 0.007] | 1.4% |
| Bose et al. 2010 | 0 98 | 0.000 [0.000; 0.008] | 1.7% |
| Coulter et al. 2012 | 3 236 | 0.013 [0.003; 0.030] | 2.3% |
| De Smit 2005 | 0 253 | 0.000 [0.000; 0.004] | 2.4% |
| Delta Valle et al. 2009 | 0 537 | 0.000 [0.000; 0.007] | 2.7% |
| Delport et al. 2011 (Arm 1) | 0 29 | 0.000 [0.000; 0.128] | 0.8% |
| Finn Barnes et al. 2014 | 0 89 | 0.000 [0.000; 0.043] | 1.7% |
| Glavridis et al. 2011 | 0 142 | 0.000 [0.000; 0.028] | 2.0% |
| Hachmi et al. 2014 | 0 151 | 0.000 [0.000; 0.024] | 2.1% |
| Heilpern et al. 2008 | 0 110 | 0.000 [0.000; 0.033] | 1.8% |
| Khan et al. 2009 | 1 677 | 0.001 [0.000; 0.006] | 2.8% |
| Mathu et al. 2011 | 0 120 | 0.000 [0.000; 0.020] | 1.8% |
| Marulanda et al. 2008 | 0 230 | 0.000 [0.000; 0.016] | 2.3% |
| McAndrew et al. 2007 | 0 180 | 0.000 [0.000; 0.020] | 2.2% |
| McBryde et al. 2010 | 0 212 | 0.000 [0.000; 0.003] | 2.0% |
| McMin et al. 2011b | 10 3063 | 0.003 [0.002; 0.008] | 3.1% |
| Naid et al. 2009 | 0 22 | 0.000 [0.000; 0.154] | 0.7% |
| Orfiere et al. 2008 | 7 463 | 0.015 [0.006; 0.031] | 2.7% |
| Palhe et al. 2013 (Arm 2) | 0 42 | 0.000 [0.000; 0.006] | 1.1% |
| Patel et al. 2014 | 0 109 | 0.000 [0.000; 0.003] | 1.8% |
| Rahman et al. 2010 | 1 329 | 0.003 [0.000; 0.017] | 2.3% |
| Rezo et al. 2011 | 2 144 | 0.014 [0.002; 0.048] | 2.0% |
| Sandford et al. 2014 | 3 109 | 0.028 [0.006; 0.076] | 1.8% |
| Swank et al. 2009 | 0 128 | 0.000 [0.000; 0.028] | 1.9% |
| Takamura et al. 2014 (Arm 1) | 2 115 | 0.017 [0.002; 0.061] | 1.8% |
| Takamura et al. 2014 (Arm 2) | 1 239 | 0.004 [0.000; 0.023] | 2.3% |
| Whitehouse et al. 2013 | 4 103 | 0.039 [0.011; 0.096] | 1.8% |
| Witsel et al. 2008 | 0 309 | 0.000 [0.000; 0.012] | 2.5% |
| Random effects model | 38 10651 | 0.002 [0.001; 0.004] | 62.9% |

Level 1 screening

| Study | Events Total | Proportion | 95%-CI | W(random) |
|-------|--------------|------------|--------|-----------|
| Daniel et al. 2014 | 7 1600 | 0.007 [0.003; 0.014] | 2.9% |
| Hadad et al. 2010 | 0 47 | 0.000 [0.000; 0.007] | 1.2% |
| Holland et al. 2012 | 2 100 | 0.020 [0.002; 0.070] | 1.7% |
| Kostansalo et al. 2014 (Arm 1) | 3 249 | 0.012 [0.002; 0.039] | 2.4% |
| Murray et al. 2012 | 26 646 | 0.040 [0.026; 0.058] | 2.6% |
| Naas et al. 2012 (Arm 2) | 2 137 | 0.015 [0.002; 0.052] | 2.6% |
| Palhe et al. 2014 | 1 180 | 0.006 [0.000; 0.031] | 2.2% |
| Random effects model | 41 2359 | 0.013 [0.004; 0.026] | 15.1% |

Level 2 screening

| Study | Events Total | Proportion | 95%-CI | W(random) |
|-------|--------------|------------|--------|-----------|
| Langton 2014 (Arm 2) | 23 1922 | 0.012 [0.008; 0.018] | 3.0% |
| Langton 2014 (Arm 5) | 1 180 | 0.006 [0.000; 0.031] | 2.2% |
| Langton 2014 (Arm 6) | 3 674 | 0.004 [0.001; 0.013] | 2.8% |
| Robinson et al. 2008 (Arm 1) | 1 120 | 0.008 [0.000; 0.046] | 1.9% |
| Su et al. 2014 | 1 293 | 0.003 [0.000; 0.019] | 2.5% |
| van der Straaten et al. 2013 | 4 250 | 0.016 [0.004; 0.040] | 2.4% |
| Random effects model | 33 3439 | 0.008 [0.006; 0.012] | 14.7% |

Level 3 screening

| Study | Events Total | Proportion | 95%-CI | W(random) |
|-------|--------------|------------|--------|-----------|
| Hartmann et al. 2012 | 3 100 | 0.030 [0.006; 0.085] | 1.7% |
| Rezo et al. 2014 | 11 261 | 0.042 [0.021; 0.074] | 2.4% |
| Random effects model | 14 361 | 0.030 [0.012; 0.06] | 4.1% |

Level 4 screening

| Study | Events Total | Proportion | 95%-CI | W(random) |
|-------|--------------|------------|--------|-----------|
| Bleichkop et al. 2013 | 8 149 | 0.056 [0.023; 0.105] | 2.5% |
| Jurnich et al. 2015 | 4 42 | 0.056 [0.007; 0.176] | 1.1% |
| Random effects model | 12 191 | 0.062 [0.032; 0.109] | 3.1% |

Random effects model | 158 17051 | 0.005 [0.003; 0.008] | 100% |

Heterogeneity: I-squared=80.7%, tau-squared=0.0033, p=0.0001

Fig 5. Forest plot of prevalence of ARMD in the BHR group stratified by level of screening.

doi:10.1371/journal.pone.0147872.g005
methods have not been used (level 0) and that report the results of the use of MoM hip replacements before the problems with MoM bearings surfaces became evident and blood metal ion measurements and cross-sectional imaging became popular. Moreover, prior to 2010, MoM hip replacements were popular and there was a trend towards positive results instead. The trend towards positive results can be observed in the numerous studies that report favorable results with the BHR device. Furthermore, to support this statement, one can see that there are no studies prior to 2010 that have reported, for example, the results of the ASR XL THR, which was eventually shown to have been disastrous [79, 110, 117]. As was the case with follow-up time, we did not observe any influence of the year of publication on the observed prevalence of ARMD. Therefore, our results reliably highlight the important role that the screening protocol has in influencing the prevalence of ARMD.

In the hip-resurfacing group, metaregression analysis suggested that level 4 screening was superior to all other screening levels and especially when compared to level 3. We consider this to be a novel finding. The main difference between these screening protocols is that when changing from level 3 to level 4, we ought to refer many patients with non-elevated metal ion levels or without complaints for cross-sectional imaging since these patients are not imaged in level 3 screening. We observed slightly higher pooled prevalence of revision confirmed ARMD in study arms with level 4 screening compared with study arms with level 3 screening. This difference in pooled estimate for the prevalence of ARMD is one benefit of screening patients without relevant clinical findings.

Our results suggest that this movement from targeted imaging to full coverage imaging is useful with regard to the prevalence of revision confirmed ARMD. However, the economical aspect and cost-effectiveness of this “transition” should be carefully assessed. When only BHR implants were analyzed, level 3 screening was not found to be inferior to level 4 screening. This would indicate that full coverage imaging would not be beneficial in patients with BHR. However, in this subgroup the analysis might be underpowered. These results should be kept in mind especially when the economics of the surveillance of patients with MoM hip
replacements are considered since cross-sectional imaging is the most expensive procedure in the screening process.

In contrast to imaging, especially MRI, metal ion measurement is a readily available, inexpensive screening modality that should be used in the surveillance of patients with MoM hip replacements [15]. Current MHRA guidelines do not give instructions on how to perform metal ion measurement in asymptomatic patients with MoM hip resurfacing [135]. In our institution, however, metal ion measurement is a routine follow-up measure in all hip-resurfacing patients. As our previous study suggests, the measurement of metal ions is beneficial in patients without complaints since ARMD is often seen in asymptomatic patients [15]. The results of our current study also imply the usefulness of routine metal ion measurement. A comparison of the non-routine metal ion measurement (level 1) with the routine measurement (level 3) would have been more sensible from this point of view, but for the sake of simplicity we used level 4 as our reference in our metaregression analysis. It should be noted, however, that confidence intervals for pooled prevalences of revision confirmed ARMD in the level 1 and level 2 screening study arms barely overlap with those seen in the level 3 study arms. Moreover, a distinct change in the prevalence of ARMD is seen when moving from screening levels 1–2 to screening levels 3–4. To conclude, our results suggest that routine metal ion measurement is useful in patients with hip resurfacing or BHR. More importantly, routine metal ion measurement should be performed along with targeted or full coverage imaging.

Results in the LD THR group were different than those in the hip-resurfacing group. Surprisingly, level 1 screening was equal to level 4 screening. Moreover, the pooled prevalence of ARMD with level 2 and 3 screening was clearly smaller than in study arms with level 1 screening. This is probably a biased result due to sample sizes since most study arms in level 2 screening included less than 40 hips, and these numbers might be too small to detect the actual failure rate. However, in study arms with level 3 screening there were two cohorts with more than 250 hips, and surprisingly a small prevalence of ARMD was observed in these study arms. For example, Bayley et al. had no revision due to ARMD after extensive screening [100].

The major issue with LD THRs is taper corrosion that may possibly release more toxic wear debris than that originating from the bearing surfaces [134]. Most probably, severe ARMD may be observed even in the presence of non-elevated (< 5 ppb) metal ion levels as a result. This would also explain why the clearly highest prevalence of ARMD was seen in the study arms with level 4 screening, i.e., in those studies where all patients were screened with cross-sectional imaging independent of blood metal ion levels. Hence, in patients with LD THRs, a low threshold for imaging is recommended even in the presence of normal metal ion levels.

Conclusions

The aims of this study were successfully achieved. Based on our systematic literature review and metaregression analysis, the overall pooled prevalence of revision confirmed ARMD represented in the current MoM literature is low. However, this seems to be a consequence of the use of the conventional follow-up protocol, namely x-rays and clinical examination, in the majority of the published studies. The implementation of the novel screening protocol results in a clearly higher prevalence of ARMD. The highest prevalence of revision confirmed ARMD was seen when all patients had undergone both blood metal ion measurement and cross-sectional imaging. These outcomes were irrespective of the follow-up time or study publication year. With regard to hip resurfacings, routine cross-sectional imaging regardless of clinical findings is advisable. Moreover, targeted metal ion measurement and/or imaging are not sufficient in the screening for ARMD in any implant concept. However, economical aspects should be considered when choosing the preferred screening level.
Supporting Information

S1 Checklist. PRISMA 2009 checklist.

S1 Datafile.

Author Contributions

Conceived and designed the experiments: AR AE PE. Performed the experiments: AR. Analyzed the data: AR. Wrote the paper: AR AE OL PE.

References

1. Grigoris P, Roberts P, Panousis K, Jin Z. Hip resurfacing arthroplasty: the evolution of contemporary designs. Proc Inst Mech Eng H. 2006; 220: 95–105. PMID: 16669379

2. Langton DJ, Jameson SS, Joyce TJ, Hallab NJ, Natu S, Nargol AV. Early failure of metal-on-metal bearings in hip resurfacing and large-diameter total hip replacement: A consequence of excess wear. J Bone Joint Surg Br. 2010; 92: 38–46. doi: 10.1302/0301-620X.92B1.22770 PMID: 20044676

3. Hart AJ, Sabah S, Henckel J, Lewis A, Cobb J, Sampson B, et al. The painful metal-on-metal hip resurfacing. J Bone Joint Surg Br. 2009; 91: 738–744. doi: 10.1302/0301-620X.91B6.21682 PMID: 19483225

4. Lainiala O, Elo P, Reito A, Pajamaki J, Puolakka T, Eskelinen A. Comparison of extracapsular pseudotumors seen in magnetic resonance imaging and in revision surgery of 167 failed metal-on-metal hip replacements. Acta Orthop. 2014; 85: 474–479. doi: 10.3109/17453674.2014.934189 PMID: 24954485

5. Lainiala O, Elo P, Reito A, Pajamaki J, Puolakka T, Eskelinen A. Good sensitivity and specificity of ultrasound for detecting pseudotumors in 83 failed metal-on-metal hip replacements. Acta Orthop. 2015: 1–6.

6. Browne JA, Bechtold CD, Berry DJ, Hanssen AD, Lewallen DG. Failed metal-on-metal hip arthroplasties: a spectrum of clinical presentations and operative findings. Clin Orthop Relat Res. 2010; 468: 2313–2320. doi: 10.1007/s11999-010-1419-0 PMID: 20559767

7. Hayter CL, Gold SL, Koff MF, Nawabi DH, Miller TT, et al. MRI findings in painful metal-on-metal hip arthroplasty. AJR Am J Roentgenol. 2012; 199: 884–893. PMID: 22997383

8. Toms AP, Marshall TJ, Cahir J, Darrah C, Nolan J, Donell ST, et al. MRI of early symptomatic metal-on-metal total hip arthroplasty: a retrospective review of radiological findings in 20 hips. Clin Radiol. 2008; 63: 49–58. PMID: 18068790

9. The NJR Editorial Board. National Joint Registry for England, Wales and Northern Ireland 11th Annual Report 2014. Available: http://www.njrreports.org.uk/Portals/0/PDFdownloads/NJR%2011th%20Annual%20Report%202014.pdf.

10. The Australian Orthopaedic Association National Joint Replacement Registry. 2014 Annual Report. Available: https://aoanjrr.dmac.adelaide.edu.au/documents/10180/172286/Annual%20Report%202014.pdf.

11. Sabah SA, Mitchell AW, Henckel J, Sandison A, Skinner JA, Hart AJ. Magnetic resonance imaging findings in painful metal-on-metal hips: a prospective study. J Arthroplasty. 2011; 26: 71–6, 76.e1-2. doi: 10.1016/j.arth.2009.11.008 PMID: 20149575

12. Siddiqui IA, Sabah SA, Satcithananda K, Lim AK, Henckel J, Skinner JA, et al. Cross-sectional imaging of the metal-on-metal hip prosthesis: the London ultrasound protocol. Clin Radiol. 2013; 68: e472–8. doi: 10.1016/j.crad.2013.02.003 PMID: 23684517

13. Natu S, Sidaginamale RP, Gandhi J, Langton DJ, Nargol AV. Adverse reactions to metal debris: histopathological features of periprosthetic soft tissue reactions seen in association with failed metal on metal hip arthroplasties. J Clin Pathol. 2012; 65: 409–418. doi: 10.1136/jclinpath-2011-200398 PMID: 22422805

14. Langton DJ, Joyce TJ, Jameson SS, Lord J, Van Orsouw M, Holland JP, et al. Adverse reaction to metal debris following hip resurfacing: THE INFLUENCE OF COMPONENT TYPE, ORIENTATION AND VOLUMETRIC WEAR. J Bone Joint Surg Br. 2011; 93: 164–171. doi: 10.1302/0301-620X.93B2.25099 PMID: 2182755
15. Reito A, Puolakka T, Elo P, Pajamaki J, Eskelinen A. Outcome of Birmingham hip resurfacing at ten years: role of routine whole blood metal ion measurements in screening for pseudotumours. Int Orthop. 2014; 38: 2251–2257. doi: 10.1007/s00264-014-2429-4 PMID: 25030963

16. Reito A, Molanen T, Puolakka T, Pajamaki J, Eskelinen A. Reply to comments on Reito et al.: Repeated metal ion measurements in patients with high risk metal-on-metal hip replacement. Int Orthop. 2015; 39: 611–612. doi: 10.1007/s00264-015-2666-1 PMID: 25592832

17. Matharu GS, Mellon SJ, Murray DW, Pandit HG. Follow-up guidance for metal-on-metal hip replacement patients should be updated. Int Orthop. 2015; 39: 609–610. doi: 10.1007/s00264-015-2667-0 PMID: 25720361

18. Matharu GS, Mellon SJ, Murray DW, Pandit HG. Follow-Up of Metal-on-Metal Hip Arthroplasty Patients Is Currently Not Evidence Based or Cost Effective. J Arthroplasty. 2015; 30: 1317–1323. doi: 10.1016/j.arth.2015.03.009 PMID: 25861918

19. Amstutz HC, Wisk LE, Le Duff MJ. Sex as a patient selection criterion for metal-on-metal hip resurfacing arthroplasty. J Arthroplasty. 2011; 26: 198–208. doi: 10.1016/j.arth.2010.03.033 PMID: 20452178

20. Arndt JM, Wera GD, Goldberg VM. An initial experience with hip resurfacing versus cementless total hip arthroplasty. HSS J. 2013; 9: 145–149. doi: 10.1017/s11420-013-9333-0 PMID: 24426860

21. Aulakh TS, Rao C, Kuiper JH, Richardson JB. Hip resurfacing and osteonecrosis: results from an independent centre. J Bone Joint Surg Br. 2012; 94: 315–163. doi: 10.1302/0301-620X.94B7.23639 PMID: 20595108

22. Panit HG. Follow-Up of Metal-on-Metal Hip Arthroplasty – a prospective study at a minimum two-year follow-up. Bull NYU Hosp Jt Dis. 2009; 67: 132–134. PMID: 19583540

23. Bisschop R, Boomsma MF, Van Raay JJ, Tiebosch AT, Maas M, Gerritsma CL. High Prevalence of Pseudotumors in Patients with a Birmingham Hip Resurfacing Prosthesis: A Prospective Cohort Study of One Hundred and Twenty-nine Patients. J Bone Joint Surg Am. 2013; 95: 1554–1560. doi: 10.2106/JBJS.L.00716 PMID: 24005195

24. Bisseling P, Smolders JM, Hol A, van Susante JL. Metal ion levels and functional results following Birmingham hip resurfacing: a 3 to 5year follow-up of a randomized controlled trial. J Arthroplasty. 2015; 30: 61–67. doi: 10.1016/j.arth.2014.07.036 PMID: 25172584

25. Bose VC, Baruah BD. Resurfacing arthroplasty of the hip for avascular necrosis of the femoral head: a minimum follow-up of four years. J Bone Joint Surg Br. 2010; 92: 922–928. doi: 10.1302/0301-620X.92B7.23639 PMID: 20595108

26. Coulter G, Young DA, Dalziel RE, Shimmin AJ. Birmingham hip resurfacing at a mean of ten years: results from an independent centre. J Bone Joint Surg Br. 2012; 94: 315–321. doi: 10.1302/0301-620X.94B3.28185 PMID: 22371536

27. Daniel J, Ziae H, Kamali A, Pradhan C, Band T, McMinn DJ. Ten-year results of a double-heat-treated metal-on-metal hip resurfacing. J Bone Joint Surg Br. 2010; 92: 20–27. doi: 10.1302/0301-620X.92B1.21530 PMID: 2004674

28. Daniel J, Pradhan C, Ziae H, Pynsent PB, McMinn DJ. Results of Birmingham hip resurfacing at 12 to 15 years: a single-surgeon series. Bone Joint J. 2014; 96-B: 1298–1306. doi: 10.1302/0301-620X.96B10.33695 PMID: 25274912

29. De Smet KA. Belgium experience with metal-on-metal surface arthroplasty. Orthop Clin North Am. 2005; 36: 203–13. ix. PMID: 15833458

30. De Smet KA. Belgium experience with metal-on-metal surface arthroplasty. Orthop Clin North Am. 2005; 36: 203–13. ix. PMID: 15833458

31. Della Valle CJ, Nunley RM, Raterman SJ, Barrack RL. Initial American experience with hip resurfacing following FDA approval. Clin Orth Relat Res. 2009; 467: 72–78. doi: 10.1007/s11999-008-0563-2 PMID: 18949528

32. De Smet KA. Belgium experience with metal-on-metal surface arthroplasty. Orthop Clin North Am. 2005; 36: 203–13. ix. PMID: 15833458

33. Delport HP, De Schepper J, Smith EJ, Nichols M, Bellemans J. Resurfacing hip arthroplasty. A 3 to 5year matched pair study of two different implant designs. Acta Orthop Belg. 2011; 77: 609–615. PMID: 22187835

34. Fernandez-Valencia J, Gallart X, Bori G, Ramiro SG, Combalia A, Riba J. Assessment of Patients with a DePuy ASR Metal-on-Metal Hip Replacement: Results of Applying the Guidelines of the Effect of Screening Methods on the Prevalence of ARMD
56. Kostensalo I, Junnila M, Mokka J, Virolainen P, Vahlberg T, Makela KT. Three metal-on-metal hip replacement devices from the same manufacturer—a short- to mid-term survival. Acta Orthop Belg. 2014; 80: 222–227. PMID:25090796

57. Leclercq S, Lavigne M, Girard J, Chiron P, Vendittoli PA. Durom hip resurfacing system: retrospective study of 644 cases with an average follow-up of 34 months. Orthop Traumatol Surg Res. 2013; 99: 273–279. doi:10.1016/j.otsr.2012.10.018 PMID:23562709

58. Madadi F, Eajazi A, Kazemi SM, Aalami Harandi A, Madadi F, Sharifzadeh SR. Total hip arthroplasty in advanced osteonecrosis: The short-term results by metal-on-metal hip resurfacing. Med Sci Monit. 2011; 17: CR78–82. PMID:21278692

59. Madhu TS, Akula MR, Raman RN, Sharma HK, Johnson VG. The Birmingham hip resurfacing prosthesis: an independent single surgeon’s experience at 7-year follow-up. J Arthroplasty. 2011; 26: 1–8.

60. Malhotra R, Kannan A, Kumar V, Nagaraj C, Marimuthu K, Khatri D. Hip resurfacing arthroplasty in inflammatory arthritis a 3- to 5-year follow-up study. J Arthroplasty. 2012; 27: 15–20. doi:10.1016/j.arth.2011.02.016 PMID: 21414743

61. Marker DR, Zywiel MG, Johnson AJ, Seyler TM, Mont MA. Are component positioning and prosthesis size associated with hip resurfacing failure? BMC Musculoskelet Disord. 2010; 11: 227. doi:10.1186/1471-2474-11-227 PMID: 20920316

62. McAndrew AR, Khaleel A, Bloomfield MD, Aweid A. A district general hospital’s experience of hip resurfacing. Hip Int. 2007; 17: 1–3. PMID:19197835

63. McBryde CW, Theivendran K, Thomas AM, Treacy RB, Pynsent PB. The influence of head size and sex on the outcome of Birmingham hip resurfacing. J Bone Joint Surg Am. 2010; 92: 105–112.

64. McGrath MS, Desser DR, Ulrich SD, Seyler TM, Marker DR, Mont MA. Total hip resurfacing in patients who are sixty years of age or older. J Bone Joint Surg Am. 2008; 90 Suppl 3: 27–31. doi:10.2106/JBJS.H.00464 PMID: 18676933

65. McMinn DJ, Daniel J, Ziaee H, Pradhan C. Indications and results of hip resurfacing. Int Orthop. 2011; 35: 231–237. doi:10.1007/s00264-010-1148-8 PMID: 21079954

66. Murray DW, Grammatopoulos G, Pandit H, Gundle R, Gill HS, McLardy-Smith P. The ten-year survival of the Birmingham hip resurfacing: an independent series. J Bone Joint Surg Br. 2012; 94: 1180–1186. doi:10.1302/0301-620X.94B9.29462 PMID: 22933488

67. Naal FD, Pilz R, Munzinger U, Hersche O, Leunig M. Does hip resurfacing require larger acetabular cups than conventional THA? Clin Orthop Relat Res. 2009; 467: 923–928. doi:10.1007/s11999-008-0689-2 PMID: 19142691

68. Naal FD, Kain MS, Hersche O, Munzinger U, Leunig M. High Revision Rate at 5 Years after Hip Resurfacing with the Durom Implant. Clin Orthop Relat Res. 2011.

69. Naal FD, Pilz R, Munzinger U, Leunig M. Does hip resurfacing require larger acetabular cups than conventional THA? Clin Orthop Relat Res. 2009; 467: 923–928. doi:10.1007/s11999-008-0689-2 PMID: 19142691

70. Newman MA, Barker KL, Pandit H, Murray DW. Outcomes after metal-on-metal hip resurfacing: could we achieve better function? Arch Phys Med Rehabil. 2008; 89: 660–666. doi:10.1016/j.apmr.2007.09.045 PMID: 18373996

71. Ollivere B, Darrah C, Barker T, Nolan J, Porteous MJ. Early clinical failure of the Birmingham metal-on-metal hip resurfacing is associated with metallosis and soft-tissue necrosis. J Bone Joint Surg Br. 2009; 91: 1025–1030. doi:10.1302/0301-620X.91B8.21701 PMID: 19651828

72. Pailhe R, Reina N, Cavaignac E, Sharma A, Lafontan V, Laffosse JM, et al. Prospective study comparing functional outcomes and revision rates between hip resurfacing and total hip arthroplasty: preliminary results for 2 years. Orthop Rev (Pavia). 2013; 5: e20.

73. Pailhe R, Matharu GS, Sharma A, Munzinger U, Leunig M. Survival and functional outcome of the Birmingham Hip Resurfacing system in patients aged 65 and older at up to ten years of follow-up. Int Orthop. 2014; 38: 1139–1145. doi:10.1007/s00264-013-2240-7 PMID: 24370976

74. Patel NK, Wright J, Sabhanwal S, Afsharapad A, Bajekal R. Hip resurfacing arthroplasty at a non-specialist centre. Ann R Coll Surg Engl. 2014; 96: 67–72. doi:10.1308/003588414X13824511649850 PMID: 24417834

75. Radtke K, Ettinger M, Heidgen H, Floerkemeier T, Noll Y, Stuenkborg-Colsman C, et al. Outcomes with cementless total hip resurfacing; 5 year follow-up. Technol Health Care. 2014; 22: 263–272. doi:10.3233/THC-140820 PMID: 24898864

76. Rahman L, Muirhead-Allwood SK. The Birmingham mid-head resection arthroplasty—minimum two year clinical and radiological follow-up: an independent single surgeon series. Hip Int. 2011; 21: 356–360. doi:10.5301/HIP.2011.8407 PMID: 21698588
77. Rahman L, Muirhead-Allwood SK, Alkinj M. What is the midterm survivorship and function after hip resurfacing? Clin Orthop Relat Res. 2010; 468: 3221–3227. doi: 10.1007/s11999-010-1438-x PMID: 20574804

78. Reito A, Puolakka T, Pajamaki J. Birmingham hip resurfacing: five to eight year results. Int Orthop. 2011; 35: 1119–1124. doi: 10.1007/s00264-010-1066-9 PMID: 20559831

79. Reito A, Puolakka T, Eio P, Pajamaki J, Eskelinen A. High Prevalence of Adverse Reactions to Metal Debris in Small-headed ASR Hips. Clin Orthop Relat Res. 2013; 471: 2954–2961. doi: 10.1007/s11999-013-3023-6 PMID: 23637059

80. Ribas M, Cardenas C, Astarita E, Moya E, Bellotti V. Hip resurfacing arthroplasty: mid-term results in 486 cases and current indication in our institution. Hip Int. 2014; 24 Suppl 10: S19–S24. doi: 10.5301/hipint.5000172 PMID: 24970031

81. Robinson PG, Wilkinson AJ, Meek RM. Metal ion levels and revision rates in metal-on-metal hip resurfacing arthroplasty: a comparative study. Hip Int. 2014; 24: 123–128. doi: 10.5301/hipint.5000113 PMID: 24500833

82. Sandiford NA, Ahmed S, Doctor C, East DJ, Miles K, Apthorp HD. Patient satisfaction and clinical results at a mean eight years following BHR arthroplasty: results from a district general hospital. Hip Int. 2014; 24: 249–255. doi: 10.5301/hipint.5000126 PMID: 24817395

83. Siebel T, Maubach S, Morlock MM. Lessons learned from early clinical experience and results of 300 ASR hip resurfacing implantations. Proc Inst Mech Eng H. 2006; 220: 345–353. PMID:16669400

84. Stulberg BN, Trier KK, Naughton M, Zadzilka JD. Results and lessons learned from a United States hip resurfacing investigational device exemption trial. J Bone Joint Surg Am. 2008; 90 Suppl 3: 21–26. doi: 10.2106/JBJS.H.00718 PMID: 18676932

85. Su EP, Housman LR, Masonis JL, Noble JW Jr, Engh CA. Five year results of the first US FDA-approved hip resurfacing device. J Arthroplasty. 2014; 29: 1571–1575. doi: 10.1016/j.arth.2014.03.021 PMID: 24780203

86. Swank ML, Alkire MR. Minimally invasive hip resurfacing compared to minimally invasive total hip arthroplasty. Bull NYU Hosp Jt Dis. 2009; 67: 113–115. PMID: 19583536

87. M Takamura K, Maher P, Nath T, Su EP. Survivorship of standard versus modified posterior surgical approaches in metal-on-metal hip resurfacing. Bone Joint Res. 2014; 3: 150–154. doi: 10.1302/2046-3758.3.2000282 PMID: 24842931

88. Van der Weegen W, Hoekstra HJ, Sijbesma T, Austen S, Poolman RW. Hip resurfacing in a district general hospital: 6-year clinical results using the ReCap hip resurfacing system. BMC Musculoskelet Disord. 2012; 13: 247-2474-13-247.

89. Wang Q, Zhang XL, Jiang Y, Chen YS, Shen H, Shao JJ. Hip resurfacing arthroplasty for secondary osteoarthritis after developmental dysplasia of hip]. Zhonghua Wai Ke Za Zhi. 2008; 46: 1293–1296. PMID: 19094556

90. Vendittoli PA, Riviere C, Roy AG, Barry J, Lusignan D, Lavigne M. Metal-on-metal hip resurfacing compared with 28-mm diameter metal-on-metal total hip replacement: a randomised study with six to nine years’ follow-up. Bone Joint J. 2013; 95-B: 1464–1473. doi: 10.1302/0301-620X.95B11.31604 PMID: 24151264

91. Whitwell GS, Shine A, Young SK. The articular surface replacement implant recall: a United Kingdom district hospital experience. Hip Int. 2012; 22: 362–370. doi: 10.5301/HIP.2012.9351 PMID: 22865254

92. Witzleb WC, Arnold M, Krummenauer F, Knecht A, Ranisch H, Gunther KP. Birmingham Hip Resurfacing arthroplasty: short-term clinical and radiographic outcome. Eur J Med Res. 2008; 13: 39–46. PMID: 18226996
Effect of Screening Methods on the Prevalence of ARMD

97. Woon RP, Johnson AJ, Amstutz HC. The results of metal-on-metal hip resurfacing in patients under 30 years of age. J Arthroplasty. 2013; 28: 1010–1014. doi: 10.1016/j.arth.2012.07.043 PMID: 23433997

98. Yang J, Shen B, Zhou Z, Pei F, Kang P. Changes in cobalt and chromium levels after metal-on-metal hip resurfacing in young, active Chinese patients. J Arthroplasty. 2011; 26: 65–70, 70.e1. doi: 10.1016/j.arth.2009.11.019 PMID: 20171050

99. Zylberberg AD, Nishiwaki T, Kim PR, Beaulé PE. Clinical results of the conserve plus metal on metal hip resurfacing: an independent series. J Arthroplasty. 2015; 30: 68–73.

100. Bayley N, Khan H, Grosso P, Hupel T, Stevens D, Snider M, et al. What are the predictors and prevalence of pseudotumour and elevated metal ions after large-diameter metal-on-metal THA? Clin Orthop Relat Res. 2015; 473: 477–484. doi: 10.1007/s11999-014-3824-2 PMID: 25085361

101. Berton C, Girard J, Krantz N, Migaud H. The Durom large diameter head acetabular component: early results with a large diameter metal-on-metal bearing. J Bone Joint Surg Br. 2010; 92: 202–208. doi: 10.1302/0301-620X.92B2.22653 PMID: 20130309

102. Bolland BJ, Culliford DJ, Langton DJ, Millington JP, Arden NK, Latham JM. High failure rates with a large-diameter hybrid metal-on-metal total hip replacement: clinical, radiological and retrieval analysis. J Bone Joint Surg Br. 2011; 93: 608–615. doi: 10.1302/0301-620X.93B5.26309 PMID: 21511925

103. Bosker BH, Ettema HB, Boomsma MF, Kollen BJ, Maas M, Verheyen CC. High incidence of pseudotumour formation after large-diameter metal-on-metal total hip replacement: A prospective cohort study. J Bone Joint Surg Br. 2012; 94: 755–761. doi: 10.1302/0301-620X.94B6.28373 PMID: 22628588

104. Chatrath V, Catelas I, Beaulé P. A prospective case series examining the use of a large-head metal-on-metal total hip system ASTM Special Technical Publication. 2013; 1560: 73–85.

105. Dramis A, Clatworthy E, Jones SA, John A. High failure rate of the R3 metal-on-metal total hip arthroplasty. Acta Orthop Belg. 2013; 79: 386–391. PMID: 22414471

106. Hasegawa M, Yoshida K, Wakabayashi S, Sudo A. Prevalence of adverse reactions to metal debris after ReCap-M2A-Magnum large-diameter-head metal-on-metal total hip arthroplasty. Acta Orthop. 2013; 84: 549–554. doi: 10.3109/17453674.2013.859419 PMID: 24171688
117. Reito A, Elo P, Puolakka T, Pajamaki J, Eskelinen A. Femoral diameter and stem type are independent risk factors for ARMD in the large-headed ASR THR group. BMC Musculoskelet Disord. 2015; 16: 118-015-0566-6.

118. Saragaglia D, Belvisi B, Rubens-Duval B, Pailhe R, Rouchy RC, Mader R. Clinical and radiological outcomes with the Durom acetabular cup for large-diameter total hip arthroplasty: 177 implants after a mean of 80 months. Orthop Traumatol Surg Res. 2015; 101: 437–441. doi: 10.1016/jotts.2015.02.008 PMID: 25899667

119. Steele GD, Fehring TK, Odum SM, Dennos AC, Nadaud MC. Early failure of articular surface replacement XL total hip arthroplasty. J Arthroplasty. 2011; 26: 14–18. doi:10.1016/j.arth.2011.03.027 PMID: 21550764

120. Sturup J, Dahl LB, Jensen KE, Larsen AB, Gebuhr P. Few adverse reactions to metal on metal articulation in total hip arthroplasty in a review study on 358 consecutive cases with 1 to 5 years follow-up. Open Orthop J. 2012; 6: 366–370. doi: 10.2174/1874325012006010366 PMID: 22930667

121. Wynn-Jones H, Macnair R, Wimhurst J, Chirodian N, Derbyshire B, Toms A, et al. Silent soft tissue pathology is common with a modern metal-on-metal hip arthroplasty. Acta Orthop. 2011; 82: 301–307. doi:10.3109/17453674.2011.579518 PMID: 21504335

122. Barrett WP, Kindsfater KA, Lesko JP. Large-diameter modular metal-on-metal total hip arthroplasty: incidence of revision for adverse reaction to metallic debris. J Arthroplasty. 2012; 27: 976–83.e1. doi: 10.1016/j.arth.2012.01.019 PMID: 22425300

123. Bernasek TL, Polikandriotis JA, Levering MF, Dalury DF, Fisher DA, Adler MJ. Five- to ten-year outcomes for modular metal-on-metal total hip arthroplasty. J Arthroplasty. 2013; 28: 1231–1234. doi: 10.1016/j.arth.2013.03.012 PMID: 23643031

124. Engh CA Jr, Ho H, Engh CA. Metal-on-metal hip arthroplasty: does early clinical outcome justify the chance of an adverse local tissue reaction? Clin Orthop Relat Res. 2010; 468: 406–412. doi:10.1007/s11999-009-1063-8 PMID: 19727991

125. Kindsfater KA, Sychterz Terefenko CJ, Gruen TA, Sherman CM. Minimum 5-year results of modular metal-on-metal total hip arthroplasty. J Arthroplasty. 2012; 27: 545–550. doi:10.1016/j.arth.2011.07.002 PMID: 21908166

126. Lainiala O, Eskelinen A, Elo P, Puolakka T, Korhonen J, Moilanen T. Adverse reaction to metal debris is more common in patients following MoM total hip replacement with a 36 mm femoral head than previously thought: results from a modern MoM follow-up programme. Bone Joint J. 2014; 96-B: 1610–1617. doi: 10.1302/0301-620X.96B12.33742 PMID: 25452362

127. Matharu GS, Theivendran K, Pynsent PB, Jeys L, Pearson AM, Dunlop DJ. Outcomes of a metal-on-metal total hip replacement system. Ann R Coll Surg Engl. 2014; 96: 530–535. doi: 10.1308/003588414X14055925058030 PMID: 25245733

128. Matthaus GS, Thevendran K, Pynsent PB, Jeys L, Pearson AM, Dunlop DJ. Outcomes of a metal-on-metal total hip replacement system. Ann R Coll Surg Engl. 2014; 96: 530–535. doi: 10.1308/003588414X14055925058030 PMID: 25245733

129. Schouten R, Malone AA, Tiffen C, Frampton CM, Hooper G. A prospective, randomised controlled trial comparing ceramic-on-metal and metal-on-metal bearing surfaces in total hip joint replacement. J Bone Joint Surg Br. 2010; 94-B: 469–471. doi: 10.1302/0301-620X.94B11.29343 PMID: 20351342

130. Matthies AK, Racasan R, Bills P, Blunt L, Cro S, Panagiotidou A, et al. Material loss at the taper junction of retrieved large head metal-on-metal total hip replacements. J Orthop Res. 2013; 31: 1677–1685. doi: 10.1002/jor.22431 PMID: 23918742

131. Medicines and Healthcare Products Regulation Agency 2012. Medical Device Alert: All metal-on-metal (MoM) hip replacements (MDA/2012/036). Available: http://www.mhra.gov.uk/home/groups/dts-bs/documents/medicaldevicealert/con155767.pdf.
136. Isaac GH, Siebel T, Oakeshott RD, McLennan-Smith R, Cobb AG, Schmalzried TP, et al. Changes in whole blood metal ion levels following resurfacing: serial measurements in a multi-centre study. Hip Int. 2009; 19:330–337. PMID: 20041379

137. Marulanda GA, Wilson MS, Edwards P, Raterman S. Early clinical experience with the use of the Birmingham hip resurfacing system. Orthopedics. 2008; 31: orthosupersite.com/view.asp?rID=37184.

138. Naal FD, Schmied M, Munzinger U, Leunig M, Hersche O. Outcome of hip resurfacing arthroplasty in patients with developmental hip dysplasia. Clin Orthop Relat Res. 2009; 467:1516–1521. doi:10.1007/s11999-008-0456-4 PMID: 18719971

139. Whitehouse MR, Aquilina AL, Patel S, Eastaugh-Waring SJ, Blom AW. Survivorship, patient reported outcome and satisfaction following resurfacing and total hip arthroplasty. J Arthroplasty. 2013; 28:842–848. doi:10.1016/j.arth.2013.01.007 PMID: 23489727

140. McMinn DJ, Pradhan C, Ziaee H, Daniel J. Is Mid-head Resection a Durable Conservative Option in the Presence of Poor Femoral Bone Quality and Distorted Anatomy? Clin Orthop Relat Res. 2010; 469:1589–97.

141. Fowble VA, dela Rosa MA, Schmalzried TP. A comparison of total hip resurfacing and total hip arthroplasty—patients and outcomes. Bull NYU Hosp Jt Dis. 2009; 67:108–112. PMID: 19583535

142. Kim PR, Beaule PE, Dunbar M, Lee JK, Birkett N, Turner MC, et al. Cobalt and chromium levels in blood and urine following hip resurfacing arthroplasty with the Conserve Plus implant. J Bone Joint Surg Am. 2011; 93 Suppl 2:107–117. doi:10.2106/JBJS.J.01721 PMID: 21543699

143. Robinson PG, Wilkinson AJ, Meek RM. Metal ion levels and revision rates in metal-on-metal hip resurfacing arthroplasty: a comparative study. Hip Int. 2014; 24:123–128. doi:10.5301/hipint.5000113 PMID: 24500833

144. Cip J, von Strempel A, Bach C, Luegmair M, Benesch T, Martin A. Implication of femoral stem on performance of articular surface replacement (ASR) XL total hip arthroplasty. J Arthroplasty. 2014; 29:2127–2135. doi:10.1016/j.arth.2014.06.025 PMID: 25108735