

BJO



## ■ HIP

# Survivorship and risk factors for revision of metal-on-metal hip resurfacing

A LONG-TERM FOLLOW-UP STUDY

H. Subbiah Ponniah,  
K. Logishetty,  
T. C. Edwards,  
G. C. Singer

From Frimley Health  
NHS Foundation Trust,  
Slough, UK

## Aims

Metal-on-metal hip resurfacing (MoM-HR) has seen decreased usage due to safety and longevity concerns. Joint registries have highlighted the risks in females, smaller hips, and hip dysplasia. This study aimed to identify if reported risk factors are linked to revision in a long-term follow-up of MoM-HR performed by a non-designer surgeon.

## Methods

A retrospective review of consecutive MoM hip arthroplasties (MoM-HRAs) using Birmingham Hip Resurfacing was conducted. Data on procedure side, indication, implant sizes and orientation, highest blood cobalt and chromium ion concentrations, and all-cause revision were collected from local and UK National Joint Registry records.

## Results

A total of 243 hips (205 patients (163 male, 80 female; mean age at surgery 55.3 years (range 25.7 to 75.3)) with MoM-HRA performed between April 2003 and October 2020 were included. Mean follow-up was 11.2 years (range 0.3 to 17.8). Osteoarthritis was the most common indication (93.8%), and 13 hips (5.3%; 7M:6F) showed dysplasia (lateral centre-edge angle < 25°). Acetabular cups were implanted at a median of 45.4° abduction (interquartile range 41.9° - 48.3°) and stems neutral or valgus to the native neck-shaft angle. In all, 11 hips (4.5%; one male, ten females) in ten patients underwent revision surgery at a mean of 7.4 years (range 2.8 to 14.2), giving a cumulative survival rate of 94.8% (95% confidence interval (CI) 91.6% to 98.0%) at ten years, and 93.4% (95% CI 89.3% to 97.6%) at 17 years. For aseptic revision, male survivorship was 100% at 17 years, and 89.6% (95% CI 83.1% to 96.7%) at ten and 17 years for females. Increased metal ion levels were implicated in 50% of female revisions, with the remaining being revised for unexplained pain or avascular necrosis.

## Conclusion

The Birmingham MoM-HR showed 100% survivorship in males, exceeding the National Institute for Health and Care Excellence '5% at ten years' threshold. Female sex and small component sizes are independent risk factors. Dysplasia alone is not a contraindication to resurfacing.

Cite this article: *Bone Jt Open* 2023;4-11:853–858.

Keywords: Arthroplasty, Hip Resurfacing, Metal on Metal

## Introduction

Metal-on-metal hip resurfacing arthroplasty (MoM-HRA) is an alternative to conventional total hip arthroplasty, especially for younger patients requiring hip arthroplasty, with benefits including high range of motion, more physiological loading of the proximal

femur, a more normal gait, and simplicity of revision surgery due to preservation of the femoral canal.<sup>1,2</sup>

Current National Joint Registry for England, Wales and Northern Ireland (NJR) data shows only 3.1% of all primary hip arthroplasties performed are MoM-HRAs,

Correspondence should be sent to  
Kartik Logishetty; email:  
k.logishetty@imperial.ac.uk

doi: 10.1302/2633-1462.411.BJO-  
2023-0084.R1

*Bone Jt Open* 2023;4-11:853–858.

following the decline in its popularity in the mid 2000s due to adverse reactions to metal debris and poor performance of specific implants resulting in their withdrawal.<sup>3-5</sup> Despite this, several studies have reported positive findings of survivorship of the Birmingham Hip Resurfacing (BHR) (Smith & Nephew Orthopaedics, USA) at five, ten, and up to 15 years.<sup>2,4,6-11</sup> Studies by both designer and non-designer surgeons advocate for careful patient selection for the optimal survival of BHRs, with studies showing females, hip dysplasia, and smaller implant sizes to have higher risk of revisions.<sup>2,6,7,12,13</sup>

The aim of the current study was to report the outcomes of a series of BHR cases performed by a single, non-designer surgeon at up to 17 years of follow-up.

## Methods

This study was ethically approved and registered locally. All consecutive patients aged  $\geq 18$  years who underwent BHR performed by one non-designer surgeon at a single centre between April 2003 and October 2020 were reviewed. Data regarding patient demographics, procedure side, implant sizes, primary indication for BHR, and highest blood cobalt and chromium ion concentrations were collected from the centre's electronic medical records and the NJR. If a patient had undergone a revision procedure, this was cross-checked with medical notes, and details of the revision surgery, including date and indication of revision, were collected. The earliest available standardized position of postoperative antero-posterior (AP) pelvic radiographs was analyzed using the open access DICOM viewer, OsiriX (OsiriX, Switzerland). Cup inclination using methods previously described by De Haan et al,<sup>14</sup> and lateral centre-edge angle (LCEA) was measured using the methods described by Ogata et al.<sup>15</sup> LCEA was measured on the contralateral native hip where available and an acetabular coverage  $< 25^\circ$  was deemed dysplastic.

**Statistical analysis.** All analyses were performed using R3.6.3 (R Foundation for Statistical Computing, Austria) with the use of "tidyverse", "survival" and "ggsurvfit" packages. Cumulative BHR survival was calculated using the Kaplan-Meier method. The endpoint for survival analysis was revision, defined as the removal or exchange of either the femoral or acetabular component, or both. A Cox proportional hazards model was used to compare BHR survival distributions for the covariates of patient age, sex, dysplasia, and femoral component size. Each covariate was individually assessed. Variables deemed to have a significant association during the univariate analysis were then chosen to create a multivariable model. Data were assessed for normality using histograms and the Shapiro-Wilk test or Kolmogorov-Smirnov depending on the sample size. Quantitative variables are expressed as mean (range) if parametric or median (interquartile range, IQR) otherwise. Categorical variables are

**Table I.** Summary of the study cohort.

Variable	Data (243 hips)
Male	163 (67.1)
Female	80 (32.9)
Mean age at surgery, yrs (range)	55.3 (25.7 to 75.3)
<b>Primary diagnosis, n (%)</b>	
Osteoarthritis	228 (93.8)
Avascular necrosis	4 (1.65)
Slipped upper femoral epiphysis	2 (0.82)
Chronic trauma	2 (0.82)
Congenital dislocation dysplasia of hip	2 (0.82)
Neck of femur fracture	1 (0.41)
Perthes' disease	1 (0.41)
Failed Internal fixation	1 (0.41)
Other inflammatory arthropathy	1 (0.41)
Other Indication	1 (0.41)
Mean follow-up time, yrs (range)	11.2 (0.3 to 17.8)
<b>Size of femoral component, mm (males:females), n (%)</b>	
38 (0:1)	1 (0.41)
40 (1:0)	1 (0.41)
42 (2:32)	34 (14.0)
44 (0:4)	4 (1.65)
46 (17:37)	54 (22.2)
48 (27:1)	28 (11.5)
50 (71:2)	73 (30.0)
52 (16:1)	17 (7.00)
54 (26:2)	28 (11.5)
56 (1:0)	1 (0.41)
58 (2:0)	2 (0.82)

expressed as counts (percentages). The Mann-Whitney U test was used to compare differences between groups with a non-parametric distribution of data. Statistical significance was set at p-value  $< 0.05$ . Confidence intervals (CIs) were reported at the 95% confidence level.

## Results

Overall, 370 BHRs were performed between April 2003 and October 2020. A total of 127 BHRs were subsequently excluded: 108 patients with no blood concentrations of cobalt and chromium, and 19 BHRs for lack of implant sizes. Following all exclusions, 243 BHRs (65.7%) performed on 205 patients were available for analysis. Four patients died (four hips) during the study period, all unrelated to the primary BHR, and none underwent revision surgery. A summary of the study cohort is presented in Table I. Of 243 hips, 163 (67.1%) were performed in males and 80 (32.9%) in females. The mean age of the patients at surgery was 55.3 years (25.7 to 75.3); osteoarthritis (93.8%) was the most common primary diagnosis. The LCEA was measured in 134 contralateral hips, and 13 hips were found to be dysplastic (5.3%; seven males, six females). The mean follow-up time for BHRs was 11.2 years (0.3 to 17.8). A total of 11 BHRs (4.5%) in ten patients underwent revision surgery at a mean of

**Table II.** Clinical details of 11 Birmingham Hip Resurfacing of 11 hips requiring revision surgery in ten patients (hips three and five were in the same patients).

Hip	Sex	Patient age, yrs	Primary diagnosis	Femoral component size, mm	Time to revision, yrs	Indication for revision
1	F	65.9	Osteoarthritis	46	2.8	Infection
2	F	55.4	Osteoarthritis	42	4.0	Persistent hip pain
3*	F	71.1	Osteoarthritis	42	4.9	Metal sensitivity reaction
4	F	63.9	Osteoarthritis	42	5.8	Infection
5*	F	71.1	Osteoarthritis	42	6.8	Metal sensitivity reaction
6	F	66.8	Osteoarthritis	46	7.4	High metal ion levels
7	F	75.6	Osteoarthritis	44	7.8	Pain of unknown cause
8	F	61.1	Osteoarthritis	46	8.6	Avascular necrosis
9	F	66.4	Osteoarthritis	46	9.2	Thick walled fluid collection
10	F	68.0	Osteoarthritis	46	9.8	ALVAL
11	M	49.4	Other inflammatory arthropathy	54	14.2	Septic arthritis

\*Denotes same patient.

ALVAL, aseptic lymphocyte-dominant vasculitis-associated lesion.

7.4 years (2.8 to 14.2) from the primary procedure and are shown in Table II. The indication for revision in three of the 11 patients was infection. Increased metal ion levels were implicated in 50% (5/10) of female revisions, with the remainder reporting unexplained pain or AVN. The median femoral implant sizes were 50 mm (interquartile range (IQR) 48 to 42) and 46 mm (IQR 42 to 46) in males and females, respectively; this difference was statistically significant ( $p < 0.001$ ). The majority (92.5%) of the femoral implant sizes used in females were 46 mm or less. The majority of BHRs in females were performed before 2010, while all BHRs performed from 2016 onwards were exclusively in males with a minimum femoral head implant size of 48 mm (Figure 1).

The cumulative survival rate for all BHRs ( $n = 243$ ) in the study at five years was 98.6% (95% CI 97.1% to 100.0%; 205 hips at risk), at ten years was 94.8% (95% CI 91.6% to 98.0%; 163 hips at risk), at 15 years was 93.4% (95% CI 89.3% to 97.6%; 53 hips at risk), and at 17 years was 93.4% (95% CI 89.3% to 97.6%; 16 hips at risk) (Figure 2). When aseptic revision was used at the endpoint, the cumulative survival for 163 BHRs performed in males with a primary indication of osteoarthritis was 100% (95% CI 100% to 100%; ten hips at risk) at 17 years (Figure 3). When the same endpoint was used in females with primary indication of osteoarthritis, the cumulative survival for 78 BHRs was 97.4% (95% CI 94.0% to 100.0%; 76 hips at risk) at five years, 89.6% (95% CI 83.1% to 96.7%; 69 hips at risk) at ten years, and 89.6% (95% CI 83.1% to 96.7%; six hips at risk) at 17 years (Figure 3). When Cox proportional hazard models were applied to each covariate individually, only femoral component size ( $p = 0.021$ ) and sex ( $p = 0.009$ ) were significantly associated with BHR survival. When adjusting for these two variables in a multivariate model, only sex ( $p = 0.026$ ) had a significant independent effect on survival, with females 14.8-times more likely to undergo revision than males. The size of the

femoral component did not have a significant independent effect on BHR survival, despite all cases undergoing aseptic revision with a femoral head size of 46 mm or less.

Across the 205 patients, median blood cobalt and chromium ion concentration were 24.0 nmol/l (IQR 16.941.6) and 35.85 nmol/l (IQR 25.9 to 57.0), respectively. Both blood cobalt and chromium ion concentration were significantly greater in patients who underwent revision surgery (115.0 nmol/l; IQR 30.0 to 284.0) vs 23.7 nmol/l (IQR 16.4 to 39.4;  $p = 0.009$ ) and 95.0 nmol/l (IQR 34.0 to 175.0) vs 35.35 nmol/l (IQR 25.9 to 53.5);  $p = 0.027$ ) respectively. Across the 243 BHRs, the median acetabular component inclination angle for the cohort was 45.4° (IQR 41.9–48.3). Postoperative AP radiographs for three BHRs that underwent revision were not available. There was no significant difference in the inclination angle between revised and non-revised BHRs (44.5°: IQR 40.9 to 45.9) in revised BHRs vs 45.5° (IQR 42.0 to 48.3) in non-revised BHRs;  $p = 0.562$ ).

## Discussion

The principal finding of this case series was the cumulative survival of BHRs at 17 years was 93.4% (95% CI 89.3% to 97.6%; 16 hips at risk) for revisions following any indication. When aseptic revision was used as the endpoint, BHRs performed in males had 100% survivorship, while in females it was 89.6% (95% CI 83.1% to 96.7%; six hips at risk).

The distribution of BHRs performed in males and females in this study period reflects the changes in national guidance made during this study period. The decline in cases observed in both sexes in 2010 aligns with the timeframe during which a series of medical device alerts issued by the Medicines and Healthcare products Regulatory Agency (MHRA), prompted the removal of the DePuy Orthopaedics' Articular Surface Arthroplasty (ASR) hip system from the market in the UK.<sup>16</sup> The pattern

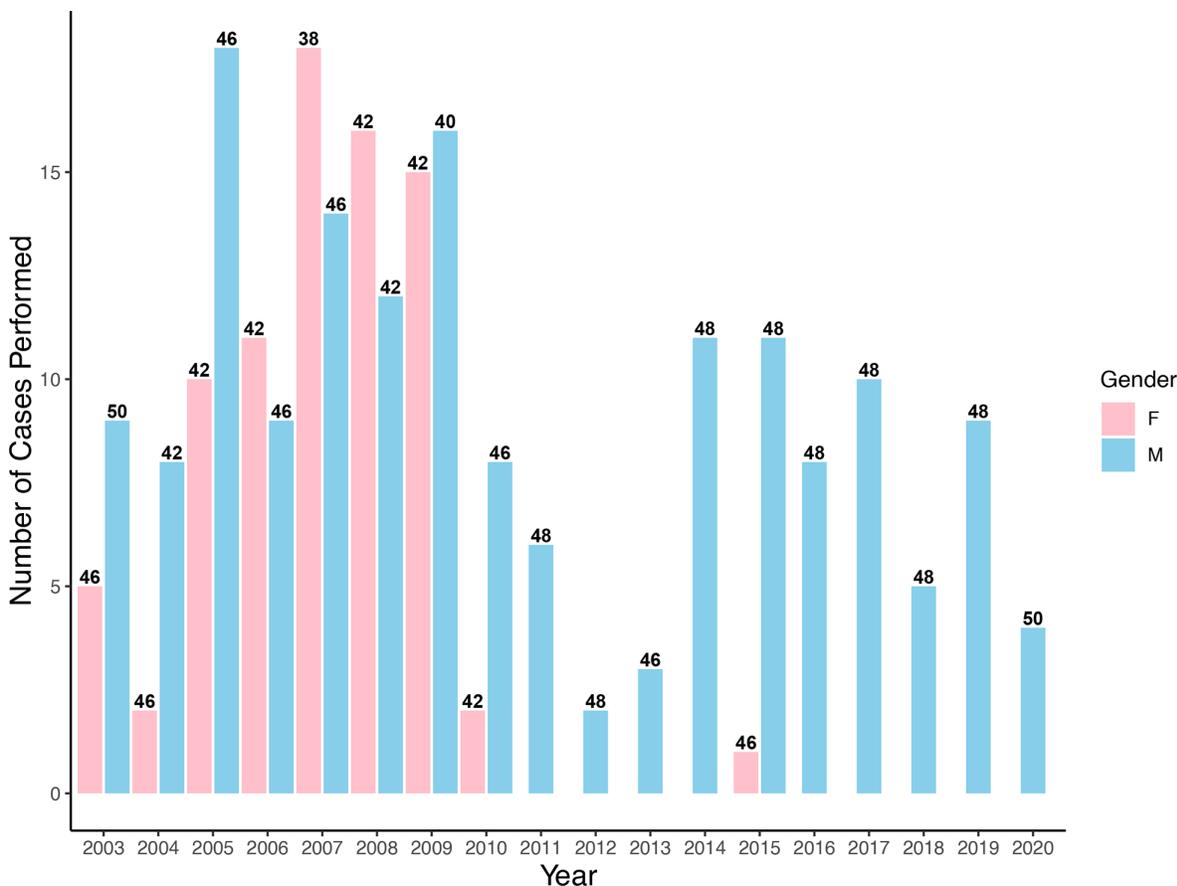


Fig. 1

Distribution of Birmingham Hip Resurfacing conducted across sexes during the study duration. Number on top of each bar represents the minimum femoral head size employed.

observed in the distribution of BHR cases after 2015 aligns with the introduction of the MHRA's 2015 guidance specific for the BHR implant.<sup>17</sup> This discouraged its usage in females and in individuals with femoral head sizes of 46 mm or less. In our study, the singular instance of a female BHR conducted in 2015 occurred before the release of this MHRA guidance; following this alert, our study exclusively included male patients with femoral head sizes of at least 48 mm.

Our findings of survivorship at ten years for any indication of revision are consistent with the current literature, with previous case series from both designer and non-designer surgeons demonstrating survival rates between 91% to 97.4%.<sup>5,6,18</sup> Survivorship reported at 15 years for any indication of revision in our study was also similar to the 95.8% (95% CI 95.1% to 96.5%) rate reported by Daniel et al.<sup>6</sup> While BHRs performed in males with a primary indication of osteoarthritis had a survival of 100% in our study, survival for women in the same criteria was 89.6% - outside the revised acceptable limits by National Institute for Health and Clinical Excellence (revision rate  $\leq$  5% at ten years).<sup>19</sup>

Several studies have reported better survivorship of BHRs in males compared to females. Murray et al<sup>13</sup> observed a ten-year survival of BHRs in males to be 95% (95% CI 92.0% to 97.4%) compared to 74% (95% CI 83% to 91%), and recommended against the use of MoM implants in females. Matharau et al<sup>7</sup> also reported a significantly greater risk of revision in females when investigating the survival of BHRs in young (aged  $\leq$  50 years) patients. While our study found only sex to have a significant association with implant survival, the clear interaction between sex and implant size in patients is obvious, with females generally receiving smaller implants. It was noted in our study that the majority of the femoral implants that underwent revision were 46 mm or smaller, reflecting the findings of Hunter et al,<sup>4</sup> Azam et al,<sup>10</sup> and Coulter et al;<sup>11</sup> thus, further reinforcing the idea of size rather than sex being the dominant factor for implant survival as demonstrated by Matharau et al.<sup>7</sup> Careful patient selection, with an emphasis on implant size, should provide reliable outcomes. Our study also found that the presence of hip dysplasia alone had no effect on implant survival. Registry reports and case series

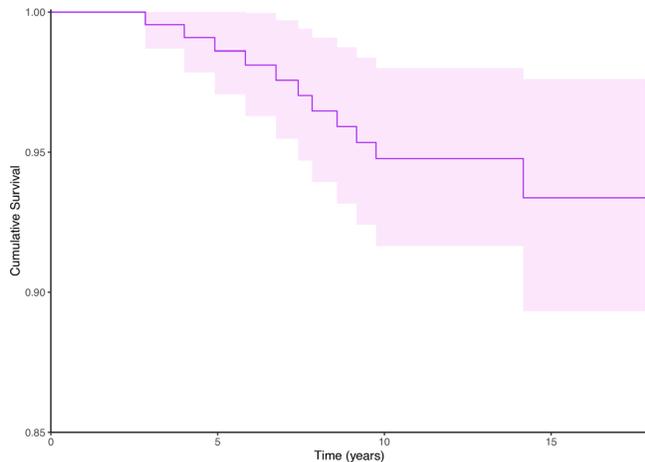


Fig. 2

Kaplan-Meier survival curve for all Birmingham Hip Resurfacings (n = 243). Revision following any indication was used as the endpoint for survival, with 11 hips revised in total. Shaded area represents the upper and lower limits of the 95% confidence intervals.

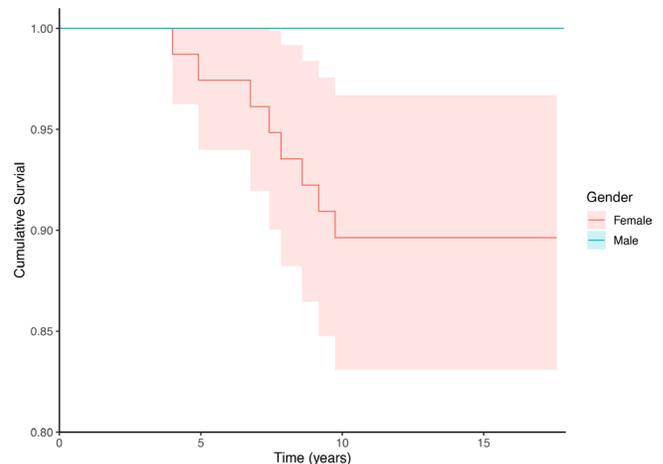


Fig. 3

Kaplan-Meier survival curve for all Birmingham Hip Resurfacings with patients with primary indication of osteoarthritis (n = 240). Revision with aseptic revision used as the endpoint for survival. All aseptic revisions performed were in females. Shaded area represents the upper and lower limits of the 95% confidence intervals.

have reported dysplasia as a significant risk factor for revision of MoM-HR,<sup>6,20</sup> but this correlation is of course confounded by sex. Male patients with hip dysplasia in our study were not at risk of revision. Furthermore, it was observed that every implant failure in the females occurred within the initial ten years. With the majority of successful BHRs in this cohort being followed up for a minimum of ten years, this implies that a BHR in females surpassing the ten-year mark is less susceptible to subsequent long-term failure. A comprehensive study of the differences between early failures and successful implants could reveal more factors behind poor performance of the implant in females. No study to date has exclusively investigated this in an all-female cohort, highlighting the need for future research in this area.

This study has some limitations. While we were able to compare performance from a survival perspective, we were unable to obtain data on patient satisfaction scores. Furthermore, while it is recognized that hip resurfacing is a technically challenging procedure, the patients who underwent revision had components with appropriate orientation and sizing, and were not performed early in the study period, suggesting no effect of a learning curve. A total of 127/370 hips (34.3%) were lost to follow-up. It is possible that our findings would differ had these data been available. In our experience, patients with problems with their hip resurfacing tend to return to their surgeon; the NJR also retrospectively alerts surgeons when their individual patients undergo revision, including at another site. As a single-surgeon single-centre study, we are reassured that our sample reflects the population. Finally, while the inclination angle was measured – as excessive inclination results in edge loading and early failure – the

degree of anteversion was not measured, thus limiting the interpretation of acetabular implant positioning.<sup>21</sup>

In conclusion, this study reported the survival rate of BHRs to be 93.4% (95% CI 89.3% to 97.6%) at a maximum of 17 years in patients of all ages. The long-term outcomes of MoM resurfacing using the BHR device, when performed accurately in males and with larger implant sizes, is excellent, and is thus a safe and predictable solution for patients with end-stage hip arthritis. While registries have noted that dysplasia is a risk factor for revision, we note that this should not be a contraindication when diagnosed in male patients.



#### Take home message

- The long-term survivorship of Birmingham metal-on-metal resurfacing in males in this series is excellent.
- Female sex and smaller components are independent risk factors for revision, while dysplasia alone is not.

#### Twitter

Follow H. Subbiah Ponniah @Hari\_SubPon7  
Follow K. Logishetty @klogishetty  
Follow T. C. Edwards @edwards\_tomc

#### References

1. Amstutz HC, Le Duff MJ. Hip resurfacing: A 40-year perspective. *HSS J.* 2012;8(3):275–282.
2. Treacy RBC, McBryde CW, Shears E, Pynsent PB. Birmingham Hip Resurfacing: a minimum follow-up of ten years. *J Bone Joint Surg Br.* 2011;93-B(1):27–33.
3. Brittain R, Howard P, Lawrence S, Stonadge J, Wilkinson M, Wilton T, et al. National Joint Registry 20th annual report. [www.njrcentre.org.uk](http://www.njrcentre.org.uk) (date last accessed 18 October 2023).
4. Hunter TJA, Moores TS, Morley D, Manoharan G, Collier SG, Shaylor PJ. 10-year results of the Birmingham Hip Resurfacing: a non-designer case series. *HIP Int.* 2018;28(1):50–52.
5. Uemura K, Takao M, Hamada H, Sakai T, Ohzono K, Sugano N. Long-term results of Birmingham hip resurfacing arthroplasty in Asian patients. *J Artif Organs.* 2018;21(1):117–123.

6. **Daniel J, Pradhan C, Ziaee H, Pynsent PB, McMinn DJW.** Results of Birmingham Hip Resurfacing at 12 to 15 years. *Bone Joint J.* 2014;96-B(10):1298–1306.
7. **Matharu GS, McBryde CW, Pynsent WB, Pynsent RB, Treacy RBC.** The outcome of the Birmingham Hip Resurfacing in patients aged < 50 years up to 14 years post-operatively. *Bone Joint J.* 2013;95-B(9):1172–1177.
8. **Mehra A, Berryman F, Matharu GS, Pynsent PB, Isbister ES.** Birmingham Hip Resurfacing: A Single Surgeon Series Reported at A Minimum of 10 Years Follow-Up. *J Arthroplasty.* 2015;30(7):1160–1166.
9. **Pailhe R, Matharu GS, Sharma A, Pynsent PB, Treacy RB.** 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(6):1139–1145.
10. **Azam Q, McMahon S, Hawdon G.** Survivorship and clinical Outcome of Birmingham Hip Resurfacing: a minimum ten years. *Int Orthop.* ;40(1):1–7. 2016
11. **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-B(3):315–321.
12. **McMinn DJW, Daniel J, Ziaee H, Pradhan C.** Indications and results of hip resurfacing. *Int Orthop.* 2011;35(2):231–237.
13. **Murray DW, Grammatopoulos G, Pandit H, Gundle R, Gill HS, McLardy-Smith P.** The ten-year survival of the Birmingham hip resurfacing. *J Bone Joint Surg Br.* 2012;94-B(9):1180–1186.
14. **De Haan R, Pattyn C, Gill HS, Murray DW, Campbell PA, De Smet K.** Correlation between inclination of the acetabular component and metal ion levels in metal-on-metal hip resurfacing replacement. *J Bone Joint Surg Br.* 2008;90-B(10):1291–1297.
15. **Ogata S, Moriya H, Tsuchiya K, Akita T, Kamegaya M, Someya M.** Acetabular cover in congenital dislocation of the hip. *J Bone Joint Surg Br.* 1990;72-B(2):190–196.
16. **Wienroth M, McCormack P, Joyce TJ.** Precaution, governance and the failure of medical implants: the ASR(TM) hip in the UK. *Life Sci Soc Policy.* 2014;10(1):19.
17. **MHRA.** Metal-on-metal (MoM) hip replacements: Birmingham HipTM Resurfacing (BHR) system (Smith & Nephew Orthopaedics). 2023. <https://assets.publishing.service.gov.uk/media/558bf580e5274a1559000002/MDA-2015-024.pdf> (date last accessed 18 October 2023).
18. **Reito A, Puolakka T, Elo P, Pajamäki 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(11):2251–2257.
19. **No authors listed.** Total hip replacement and resurfacing arthroplasty for end-stage arthritis of the hip. National Institute for Health and Clinical Excellence. 2014. [www.nice.org.uk/guidance/ta304](http://www.nice.org.uk/guidance/ta304) (date last accessed 18 October 2023).
20. **No authors listed.** Hip, Knee & Shoulder Arthroplasty Annual Report. Australian Orthopaedic Association. 2018. <https://aoanjrr.sahmri.com/documents/10180/576950/Hip%20Knee%20Shoulder%20Arthroplasty> (date last accessed 18 October 2023).
21. **Mellon SJ, Kwon Y-M, Glyn-Jones S, Murray DW, Gill HS.** The effect of motion patterns on edge-loading of metal-on-metal hip resurfacing. *Med Eng Phys.* 2011;33(10):1212–1220.

#### Author information:

- H. Subbiah Ponniah, BSc (Hons), Medical Student
- K. Logishetty, PhD, FRCS (T&O), NIHR Clinical Lecturer
- T. C. Edwards, BSc (Hons), MRCS, Clinical Research Fellow MSK lab, Imperial College London, London, UK.
- G. C. Singer, FRCS (T&O), Consultant Trauma and Orthopaedic Surgeon, Frimley Health NHS Foundation Trust, Slough, UK.

#### Author contributions:

- H. Subbiah Ponniah: Conceptualization, Writing – original draft, Writing – review & editing.
- K. Logishetty: Conceptualization, Writing – original draft, Writing – review & editing.
- T. C. Edwards: Writing – original draft, Writing – review & editing.
- G. C. Singer: Conceptualization, Supervision.

- H. Subbiah Ponniah and K. Logishetty are joint first authors.

#### Funding statement:

- The authors received no financial or material support for the research, authorship, and/or publication of this article.

#### ICMJE COI statement:

- The authors have no conflicts of interest to declare.

#### Data sharing:

- The datasets generated and analyzed in the current study are not publicly available due to data protection regulations. Access to data is limited to the researchers who have obtained permission for data processing. Further inquiries can be made to the corresponding author.

#### Ethical review statement:

- This project was registered locally at Frimley Health NHS Trust. Ethics approval was not required by our institution for analysis of retrospective anonymized data.

#### Open access funding:

- The authors report that they received open access funding for this manuscript from Imperial College London, UK.

© 2023 Logishetty et al. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (CC BY-NC-ND 4.0) licence, which permits the copying and redistribution of the work only, and provided the original author and source are credited. See <https://creativecommons.org/licenses/by-nc-nd/4.0/>