

Dutch advice not to use large head metal-on-metal hip arthroplasties justifiable - results from the Dutch Arthroplasty Register

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Background: In 2012, the Netherlands Orthopaedic Association advised against the use of all large femoral head (≥ 36 mm) metal-on-metal (MoM) hip arthroplasties, including resurfacing hip arthroplasties (RHA). We examined mid-term revision rates of MoM THA and RHA and evaluated the use of these prostheses.

Methods: We selected total hip arthroplasties (THA) and RHA performed in 2007-2016 ($n=211,002$) from the LROI. Hip arthroplasties were divided into RHA, large head MoM THA, small head (≤ 32 mm) MoM THA, and non-MoM THA. The use of these types of hip prostheses was examined over time. Cumulative incidence of revision using competing risk analyses and multivariable Cox regression analyses were performed.

Results: In males, large head MoM THA had an 8-year revision rate of 15.9% (95%CI: 13.8-18.4); for RHA this was 7.4% (95%CI: 6.3-8.8), which were both significantly higher than for non-MoM THA (4.0% (95%CI: 3.8-4.2)). In females the 8-year revision rate of large head MoM THA was 22.7% (95% CI: 20.6-25.0) and 17.7% (95%CI: 15.3-20.3) for RHA compared to 3.5% (95%CI: 3.4-3.7) for non-MoM THA. Multivariable survival analyses showed an elevated hazard ratio (HR) for large head MoM THA and RHA for both males and females. In females, the risk of revision for small head MoM THA was also increased (HR 1.58 (95%CI: 1.33-1.88)). The use of either large and small head MoM THA and RHA decreased over time to almost none in 2012-2016.

Conclusion: Large head MoM THA and RHA performed significantly worse than conventional non-MoM THA in Dutch patients. The Dutch advice not to use large head MoM THA and RHA was justifiable and the use of MoM THA and RHA decreased to almost none after the advice.

Introduction

Hip arthroplasty is one of the most successful elective surgical procedures in modern medicine, restoring mobility and quality of life to many patients.¹ Due to an aging population and the increasing vitality of elderly people in the western world, as well as the good performance of total hip arthroplasty (THA), the incidence of THA is increasing.^{2,3} In 2016 a total of 29,520 THAs were performed in the Netherlands, which is a 27% increase compared to 2010. The number of younger patients receiving a THA is expected to increase.⁴ These patients are generally more active and thus have higher revision

rates due to wear of the prosthesis. Therefore, hip prostheses claiming low wear characteristics based on laboratory tests were designed, like metal-on-metal (MoM) hip arthroplasties.⁵ Even more, in this younger population, large femoral heads were advocated in this more demanding younger patient population, since these larger heads claimed to have an improved range of motion⁶ and lower dislocation rates.⁷ Short-term results of large head THA showed promising results.⁸ Additionally, the resurfacing hip arthroplasty (RHA) claimed to have less bone stock damage, and would thus be a good option in younger patients if revision surgery was indicated. However, after larger scale use, large head MoM bearings showed a variety of unexpected complications, like early aseptic loosening,^{9,10} raised metal ion levels,^{6,11-14} adverse local periprosthetic tissue reactions,^{15,16} aseptic vasculitis associated lesions,¹² and increased mortality.¹⁷ Population-based registry studies increasingly reported that large head MoM THA and RHA resulted in higher revision rates than conventional non-MoM THA.^{13,18-23} However, some studies showed promising results for RHA in young male patients,²⁴ especially for the Birmingham Hip Resurfacing prosthesis.^{25,26} Based on this evidence, the Netherlands Orthopaedic Association (NOV), the scientific association of Dutch orthopaedic surgeons and allied health professionals, published a moratorium to be cautious with respect to the use of MoM hip prostheses in

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Table 1. Descriptive statistics of all patients who received a THA or RHA in 2007-2016 in the Netherlands (n=211,002).

	RHA (n=2,863)		Large head MoM THA (n=2,663)		Small head MoM THA (n=3,941)		Non MoM THA (n=201,535)	
	n	(%)	n	(%)	n	(%)	n	(%)
Age (years)								
<60	2,227	78	942	36	883	22	33,571	17*
60-74	623	22	1,303	49	2,251	57	103,528	51
≥75	7	0	411	15	805	20	64,277	32
Gender (%)								
Male	1896	66	1098	41	1,261	32	66,958	33*
Female	967	34	1565	59	2,680	68	134,577	67
ASA score (%)								
I	1,723	74	955	43	1,137	31	44,923	23*
II	565	24	1103	49	2,182	60	122,053	63
III-IV	37	2	177	8	318	9	26,609	14
Diagnosis (%)								
Osteoarthritis	2,422	92	2335	89	3,452	88	174,399	87*
Non-osteoarthritis	218	8	285	11	468	12	25,030	13
Period (%)								
2007-2009	2,001	70	1868	70	2,256	57	35,848	18*
2010-2011	821	29	775	29	1,056	27	40,243	20
2012-2016	41	1	20	1	629	16	125,444	62

THA: Total Hip Arthroplasty; MoM: metal-on-metal; RHA: Resurfacing Hip Arthroplasty; * $p < 0.0001$
 NB. Numbers do not add up to total due to missing data

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mid-2011. In January 2012, the NOV was the first national orthopaedic association to advise against the use of all large head (≥ 36 mm) MoM hip implants, including RHA, until the safety and long-term effectiveness of these implants had been established conclusively.^{27,28} Our goal was to compare mid-term (8-year) revision rates of MoM THA and RHA to conventional non-MoM THA since 2007 and evaluate the effect of this de-implementation advice in 2012 using data of the Dutch Arthroplasty Register. We hypothesized that large head MoM THA and RHA have higher revision rates compared to non-MoM THA and that the de-implementation of large head MoM THA and RHA was almost accomplished in the Netherlands.

Materials and methods

Dutch Arthroplasty Register

The Dutch Arthroplasty Register (LROI) is a nationwide population-based register that includes information about joint arthroplasties in the Netherlands since 2007. The LROI is initiated by the NOV, with nearly all Dutch orthopaedic surgeons being a member of this society. The LROI is very well sup-

ported by these members on a voluntary basis, resulting in a coverage of 100% of Dutch hospitals and a completeness of over 95% for primary THAs and 88% for hip revision arthroplasty.^{2,29} Registration is performed at the hospital of surgery. Privacy of all patients is secured by using a trusted third party (ZorgTTP) to encrypt the personal identification number, a number given by the Dutch government to each individual inhabitant in the Netherlands.

Data collection

The LROI database contains information on patient, procedure, and prosthetic characteristics.² For each component a product number is registered to identify the characteristics of the prosthesis. A primary hip arthroplasty is defined as the first implantation of a total or resurfacing hip prosthesis, to replace a (part of a) hip joint. Hip revision arthroplasty is defined as any exchange (placement, replacement or removal) of one or more components of the hip prosthesis, including head or liner exchanges.² Vital status of all patients was obtained actively on a regular basis from Vektis, the national insurance database on health care in the Netherlands, which records all

deaths of Dutch citizens.³⁰ The LROI uses the opt-out system to require informed consent of patients.

For the present study, all cases who underwent a primary THA or RHA in the period 2007-2016 in a Dutch hospital were included (n=211,002). Patients were excluded if the type of hip arthroplasty or gender was missing (n=2,859). Age was divided into three groups: <60, 60-74, and ≥75 years. Overall physical condition of the patient was scored using the ASA score (I-IV). Diagnosis was categorized as osteoarthritis or non-osteoarthritis (e.g. hip fractures, osteonecrosis, dysplasia, and late posttraumatic). Since the MoM awareness on unexpected problems occurred in 2010, periods of evaluation were divided into: 2007-2009, 2010-2011, and 2012-2016. The median follow-up was 3.8 years with a maximum of 10 years.

Hip arthroplasty articulation was divided based on the bearing surface of the head, the inlay or the monoblock cup and categorized as metal-on-metal (MoM) and non-MoM. Non-MoM THA consisted of mainly ceramic-on-PE, metal-on-PE, and ceramic-on-ceramic. Femoral head size was categorized as small (≤32 mm) and large (≥36mm) for hip arthroplasties. Hip arthroplasties were divided for this research as (large head MoM) RHA, large head MoM THA, small head MoM THA, and conventional non-MoM THA.

Statistics

RHA, large head MoM THA, small head MoM THA, and conventional non-MoM THA, were described separately and compared using a Chi-square test to test differences in patient characteristics. The differences in the proportion of RHA, large head MoM THA, and small head MoM THA were described in the three periods on MoM problem awareness. Survival time was calculated as the time from primary hip arthroplasty to first revision arthroplasty for any reason, death of the patient, or the end of the study follow-up (January 1, 2017). Survival analyses were stratified by gender. Cumulative crude incidence of revision was calculated using competing risk analysis, where death was considered to be a competing risk.^{31,32} Multivariable Cox regression analyses were performed stratified by gender to compare adjusted revision rates between the types of hip arthroplasties. Adjustments were made for age at surgery, ASA score, diagnosis (osteoarthritis versus non-osteoarthritis), and period of surgery to discriminate independent risk factors for revision arthroplasty. Reasons for revision were described per type of hip arthroplasty and compared using a Chi-square test to test differences between types of hip arthroplasty (SAS 7.1 and SPSS 24). P-values below 0.05 were considered statistically significant.

Results

In the period 2007-2016 2,863 RHAs, 2,663 large head MoM THAs, 3,941 small head MoM THAs and 201,535 non-MoM THAs were registered in the LROI. The proportion of RHA patients aged under 60 years was 78% compared to 17% of non-MoM THA patients. Two-thirds of RHA patients were males compared to one-third of conventional non-MoM THA patients; 74% of RHA patients had ASA score I compared to 33% of non-MoM THA patients. Patients with a large head MoM THA were generally younger and had a lower ASA score than patients who received a non-MoM THA (Table 1). Seventy percent of all registered large head MoM RHA or THA were performed before 2010. In 2007-2009, RHA and MoM THA were used in 4-5% of procedures; in 2010-2011 this was 2% of procedures and in 2012-2016 <0.1% of procedures were large head MoM THA or RHA and 0.5% for small head MoM THA in 2012-2016 (Figure 1).

Crude revision rates of hip arthroplasty

Among males, RHA had a crude 8-year revision rate of 7.4% (95%CI: 6.3-8.8) and large head MoM THA had a crude 8-year revision rate of 15.9% (95%CI: 13.8-18.4), which are both significantly higher than the crude 8-year revision rate for non-MoM THA (4.0% (95%CI: 3.8-4.2) (Table 2). Small head MoM THA had a similar 8-year revision rate compared to non-MoM THA among males (Figure 2A). Among females, RHA had a crude 8-year revision rate of 17.7 (95%CI: 15.3-20.3); for large head MoM THA this was 22.7% (95%CI: 20.6-25.0), which are both significantly higher than for non-MoM THA (3.5% (95%CI: 3.4-3.7). Small head

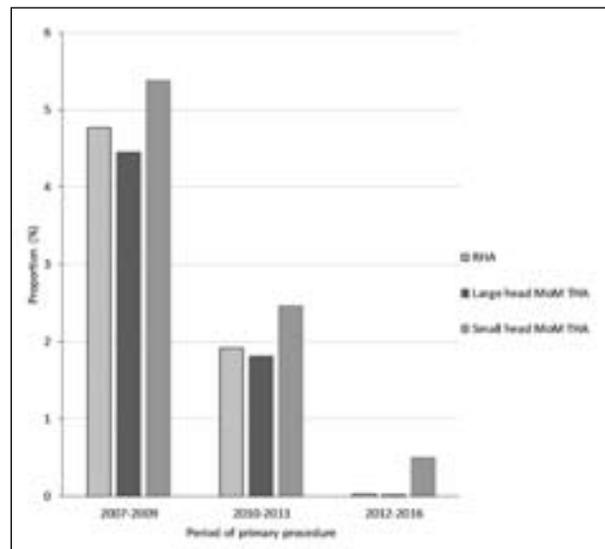


Figure 1. Use of (primary) large head MoM RHA, large head MoM THA and small head MoM THA per period in the Netherlands. RHA: Resurfacing Hip Arthroplasty; THA: Total Hip Arthroplasty

Table 2. Cumulative revision rate of THA or RHA in the period 2007-2016 in the Netherlands according to gender (n=211,002).

	Males (n=71,213)		Females (n=139,789)	
	n	Crude 8-year cumulative revision rate (%) (95%CI)	n	Crude 8-year cumulative revision rate (%) (95%CI)
Hip arthroplasty				
RHA	1896	7.4 (6.3-8.8)	967	17.7 (15.3-20.3)
Large head MoM THA	1098	15.9 (13.8-18.4)	1565	22.7 (20.6-25.0)
Small head MoM THA	1261	5.0 (3.8-6.5)	2680	5.9 (5.0-7.1)
Non-MoM THA	66,958	4.0 (3.8-4.2)	134,577	3.5 (3.4-3.7)

CI: confidence interval; RHA: Resurfacing Hip Arthroplasty; THA: Total Hip Arthroplasty; MoM: metal-on-metal

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MoM THA had a crude 8-year revision rate of 5.9% (95%CI: 5.0-7.1), which is significantly higher compared to non-MoM THA among females (Figure 2B).

Casemix adjusted revision rates of hip arthroplasty

Multivariable survival analyses adjusted for age, ASA score, diagnosis, and period of surgery showed that among males the risk of revision arthroplasty (hazard ratio) for RHA was 1.87 (95%CI: 1.54-2.26) and for large head MoM THA this was 4.22 (95%CI: 3.56-4.99) compared to conventional non-MoM THA (Table 3). Small head MoM THA had a similar risk of revision compared to conventional non-MoM THA among males (Table 3). Among females, mul-

tivariable survival analyses adjusted for age, ASA score, diagnosis, and period of surgery showed that the hazard ratio was 4.38 (95%CI: 3.69-5.20) for RHA and 6.46 (95%CI: 5.73-7.28) for large head MoM THA compared to conventional non-MoM THA. The hazard ratio for small head MoM THA among females was 1.58 (95%CI: 1.33-1.88) compared to conventional non-MoM THA (Table 3). A large head non-MoM THA had a slightly higher risk of revision compared to small head non-MoM THAs (HR 1.07 (95%CI: 1.01-1.15)). The adjusted hazard ratio for THAs with a large (≥ 36 mm) ceramic head showed a similar risk for revision compared to non-MoM THA (data not shown).

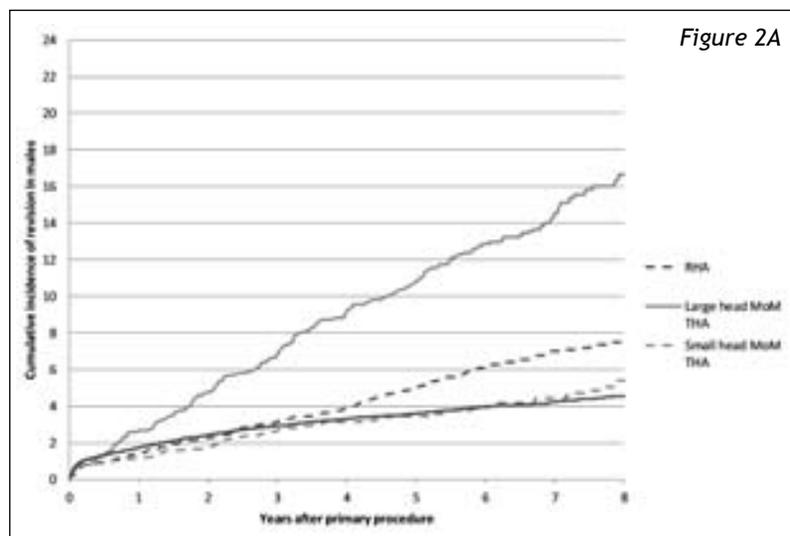


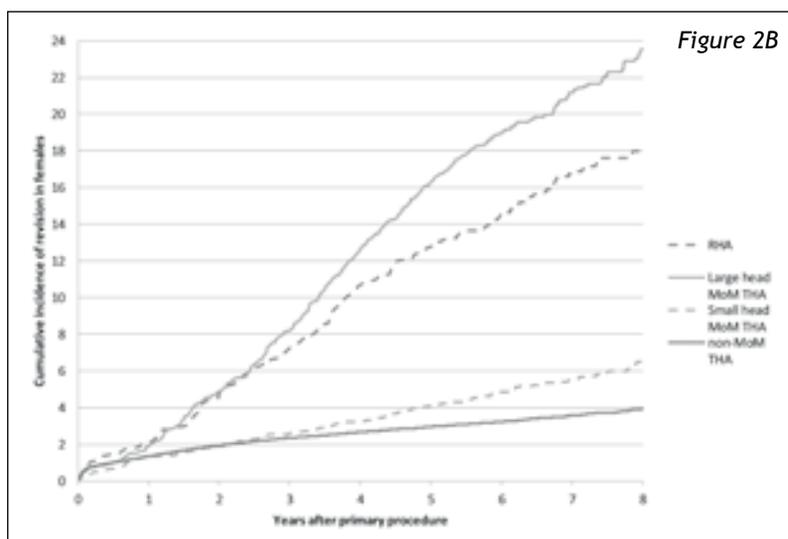
Figure 2A

Characteristics of revision

The most frequent reasons for revision in the first ten years after primary hip arthroplasty were dislocation and loosening of the femoral component, with dislocation being the most frequent reason for revision (30%) of non MoM THAs. In patients with an RHA or large head MoM THA 47% to 58% of revisions were due to symptomatic MoM bearing. In these groups dislocation and periprosthetic fractures were less common. Furthermore, symptomatic MoM bearing was registered in 13% of small head MoM THAs (Table 4). In the large majority (91-96%) of revised large head MoM THA and RHA at least the cup and/or femur were revised during the revision procedure. For small

Figure 2A and B. Cumulative incidence of revision according to hip arthroplasty type in the Netherlands in the period 2007-2016 for males (n=71,213) and females (n=139,789).

RHA: Resurfacing Hip Arthroplasty; THA: Total Hip Arthroplasty



like the NOV has no sanction possibilities. Furthermore, about 95% of Dutch orthopaedic surgeons work in private practice, and still this quality measurement was highly adopted. However, as a consequence of the NOV advice, there might be a selected group of patients, especially young active males,^{24,25} that is withheld the opportunity of a potentially well-functioning hip prosthesis. Generally, orthopaedic surgeons are balancing the risks and benefits of their arthroplasties, and over time better alternatives have become available, making a MoM THA or RHA less 'worth the risk'.

head MoM THAs and non-MoM THAs around 20% of revision procedures consisted of partial revisions where the femoral head and/or the inlay was revised only (data not shown).

Discussion

Based on population-based registry data we found that the 8-year revision rates for large head MoM THA and RHA were largely elevated compared to non-MoM THA, especially among females with an 8-year revision rate of 23% for large head MoM THA and 18% for RHA. The use of MoM THA and RHA decreased to almost none after the advice.

Based on worrisome and disappointing outcomes in literature, the NOV published mid-2011 instructions to orthopaedic surgeons to be cautious with respect to the use of MoM hip prostheses. In January 2012, the NOV advised against the use of all MoM ≥ 36 mm head hip implants, including RHA, until the safety and long-term effectiveness were established conclusively.^{27,28} Given the outcome of the current study based on national 'real-world' data, the 2012 advice was justifiable: large head MoM hip prostheses, both THA and RHA, showed significantly higher revision rates than conventional non-MoM THA in both males and females. However, the EFORT guideline concerning MoM hip prostheses advises to use MoM hip prosthesis in selected patients only and the procedure should be performed by a very experienced surgeon to minimize the risks.³³ We showed that hardly any MoM THAs and RHAs were placed after the advice of the NOV. This indicates that Dutch orthopaedic surgeons were highly compliant with the advice of their scientific association. Some believe that medical specialists can only change a policy if sanctioned, but a scientific association

Our results, stating that RHA and large head MoM THA had a higher revision rate compared to conventional non-MoM THA, especially in females, is in line with results from other registries^{19-23,34,35} and other literature.^{36,37} Our finding that small head MoM THAs had a higher risk of revision in females is contrary to results from the Australian registry¹⁹ and a Dutch RCT with a follow-up of 10 years.³⁸ This stresses the value of studies with larger numbers; it makes it possible to correct for case mix factors and still have enough data points for analysis and differences between countries. The higher risk of revision for MoM THA in females in the Netherlands might also be due to an increased susceptibility of both patients and surgeons by media for MoM problems like the development of pseudo tumors in females.³⁹

The NOV advice from mid-2011 also included an active follow-up on all patients who received MoM hip prostheses, including measurements of serum metal ion concentration, as well as giving detailed information to these patients on potential risks of MoM. The awareness and fear of both orthopaedic surgeons and patients as well as the active follow-up may have resulted in an earlier revision of MoM hip prostheses. This increased revision rates of large head MoM THA and RHA, but most likely also resulted in a collateral increase of revisions of the small head MoM THA. Therefore, the increased revision rate of MoM THA could very well be the consequence of increased awareness due to e.g. media attention and the risk of lawsuits and thorough follow-up of all MoM prostheses, and may not solely reflect a device related problem. Furthermore, symptomatic MoM bearing as a reason for revision was only added as an option to the database in 2012. In the period before 2012, 'symptomatic MoM bearing' was registered as free text in the option 'other reason for

Table 3. Multivariate survival analyses of patients with a THA or RHA in the period 2007-2016 in the Netherlands according to gender (n=211,002).

	Males (n=71,213)	Females (n=139,789)
	Adjusted hazard ratio ¹ (95% CI)	Adjusted hazard ratio ¹ (95% CI)
Hip arthroplasty		
RHA	1.87 (1.54-2.26)*	4.38 (3.69-5.20)*
Large head MoM THA	4.22 (3.56-4.99)*	6.46 (5.73-7.28)*
Small head MoM THA	1.17 (0.89-1.54)	1.58 (1.33-1.88)*
Non-MoM THA	1.0	1.0
Age at surgery (years)		
<60	1.09 (0.99-1.21)	1.31 (1.20-1.42)*
60-74	1.0	1.0
≥75	0.89 (0.80-1.00)#	0.83 (0.77-0.89)*
ASA score		
I	1.0	1.0
II	1.05 (0.95-1.15)	1.11 (1.03-1.20) [§]
III-IV	1.27 (1.10-1.45)*	1.40 (1.26-1.57)*
Diagnosis		
Osteoarthritis	1.0	1.0
Non-osteoarthritis	1.32 (1.18-1.47)*	1.25 (1.14-1.36)*
Period		
2007-2009	1.03 (0.91-1.16)	1.07 (0.98-1.17)
2010-2011	1.0	1.0
2012-2016	1.31 (1.17-1.46)*	1.27 (1.17-1.39)*

¹ Adjusted for age at surgery, ASA score, diagnosis, and period of surgery.
 * $p < 0.0001$; # $p = 0.04$; [§] $p = 0.0050$
 CI: confidence interval; RHA: Resurfacing Hip Arthroplasty; THA: Total Hip Arthroplasty;
 MoM: metal-on-metal

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revision', which could have resulted in under registration of this reason for revision.

The use of large head MoM THA and RHA decreased sharply in primary hip arthroplasty, but parallel to this, the use of small head MoM THA also decreased. Although, the latter was not intended by the NOV advice. Nevertheless, in female patients the risk of revision for these small head MoM THAs was also elevated. Around 26,500 primary hip arthroplasties were performed annually since 2010.² Therefore, the total number of registered hip arthroplasties is large, allowing subgroup analyses. However, the number of revised hip arthroplasties is still relatively small due to the overall good performance at long term follow-up of hip prostheses. A limitation is that the first years (2007 until 2009) of the LROI registration was the run-in phase and therefore, the completeness of the LROI was suboptimal (completeness in 2009 was 88%).²⁹ This results in

a significant proportion of hip arthroplasties that were not registered, especially RHA and MoM THA, which were regularly used in these first years of the registration.

Furthermore, causality cannot be inferred from observational data since patients are not randomly allocated between treatment groups. Therefore, our results may have been influenced by confounding. These problems were adjusted for as far as possible by the use of multivariable regression models. However, unmeasured confounding, such as bone quality, physical activity, the surgeons technique and the preferences of the patient and surgeon will certainly also influence the results. The latter might have resulted in a decreased threshold for revision arthroplasty in presence of (subjective) symptoms. Furthermore, revision rates from registry data are generally somewhat higher compared to expert data. Apart from patient selection, this

Table 4. Reasons for revision expressed as proportion (%) of THA and RHA performed in 2007-2016 in the Netherlands (n=6,269).

	RHA (%) (n=302)	Large head MoM THA (%) (n=508)	Small head MoM THA (%) (n=195)	Non MoM THA (%) (n=5,264)	Total (%) (n=6,269)
Dislocation	3	4	23	30*	26
Loosening femoral component	12	9	23	21*	20
Loosening acetabular component	13	15	11	13 [#]	13
Periprosthetic fracture	6	4	11	14*	13
Infection	3	3	11	17*	15
Symptomatic MoM bearing	47	58	13	0*	8
Dissolve girdlestone situation	1	2	6	3 [@]	3
Cup/liner wear	2	2	4	2 [§]	2
Peri-articular ossification	2	0	4	2 ^â	2
Other	42	39	18	17*	20

NB. A patient can have several reasons for revision, therefore the total proportion is >100%.

CI: confidence interval; **RHA:** Resurfacing Hip Arthroplasty; **THA:** Total Hip Arthroplasty;

MoM: metal-on-metal; * $p < 0.0001$; # $p = 0.0012$; @ $p = 0.0003$; § $p = 0.1399$; â $p = 0.0042$.

might be the result of the learning curve of each surgeon. On the other hand, registries have the advantage of reporting on the entire population receiving the treatment rather than a selected sample in a trial, thus reducing sampling bias. The relatively large sample size and the diversity of surgeons, patients and prostheses included, means the results have good generalizability and external validity. Registry data from other countries confirm that patient demographics and disease profile are similar.^{18,40}

In conclusion, large head MoM THA and RHA, performed significantly worse than conventional non-MoM THA in Dutch patients. The Dutch advice not to use large head MoM THA and RHA was justifiable and the use of MoM THA and RHA decreased to almost none after the advice. Further research is warranted, especially for RHA in young males patients.

Contribution of authors

LS, GD, BS, WZ, HK and RN planned the study. LS, GD, HK and RN were responsible for the dataset. LS and GD performed the analyses. LS wrote the manuscript with substantial contribution from all authors, who also participated in interpretation of the results.

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