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By email and post

February 2, 2013

RE:
Total hip replacement and surface replacement for the treatment of pain resulting from end stage arthritis of the hip (review of technology appraisal guidance 2 and 44, ID540)

In response to the announcement by the National Institute for Health and Clinical Excellence (NICE) of the review of technology appraisal guidance 2 and 44, to appraise the clinical and cost effectiveness of total hip replacement and surface replacement within their CE marked indications for the treatment of pain resulting from end stage arthritis of the hip, Smith & Nephew Orthopaedics Ltd ("Smith & Nephew") is providing comments to NICE on Total Hip Replacement.

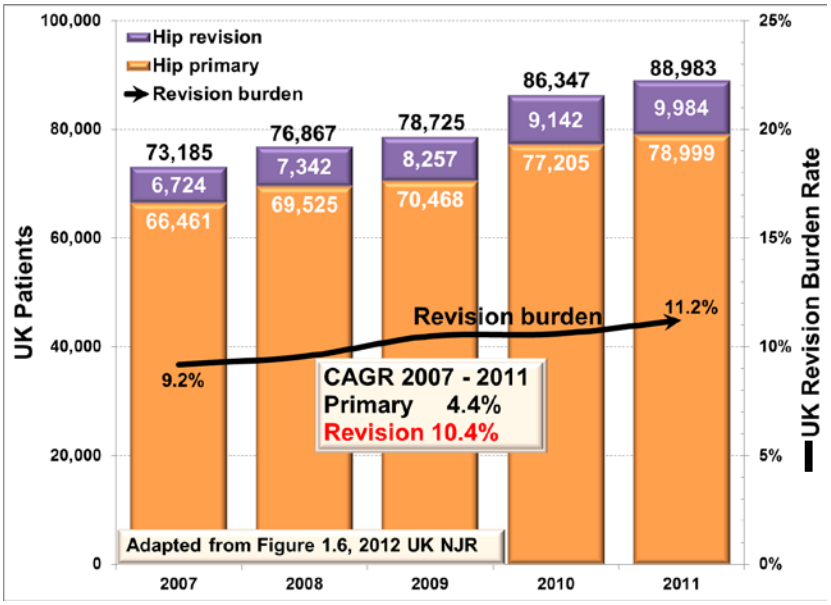
THR burden in the UK

The growth of total hip replacement (THR) in the United Kingdom is placing increasing burden on the National Health Service (NHS).[1] Culliford and colleagues reported that in the UK the "mortality-adjusted lifetime risk of THR at age 50 was estimated at 8.3% for women and 5.2% for men."[2] They note that the risk had risen between 1991 and 2006 and state the finding is important because the gender specific risk for THR is lower than that for osteoarthritis. They discuss that some may attribute this difference to "unmet need." [2]

According to the 2012 National Joint Registry for England and Wales (NJR) 88,983 hip replacement procedures were performed in 2011, including 9,984 revision procedures. Between 2007 and 2011, the compound annual growth rate (CAGR) of primary THR was 4.4 percent. However, the CAGR of revision procedures has increased over twice as fast, at 10.4 percent over this same period. The revision burden in 2011 of 11.2 percent compares to 9.2 percent in 2007. [3] See **Figure 1**.

The increasing number and proportion of revision THR's are of high concern because revision THR is well accepted to be substantially more costly than primary THR.[4-7] A just published analysis of arthroplasty costs in the UK identified that the net cost of revision THR is about 38 percent higher than the cost of primary THR.[8] The report stated that during the period of data collection primary THR cost £7137 while aseptic revision THR and septic revision THR cost £9048 and £14441, respectively. Septic revision was proposed to be 15 percent of all THR revisions.[8] This cost applied to the UK THR population growth rate discounted three percent per annum against the 2010 index costs for primary and revision surgery suggests a probable CAGR for the THR budget of 8.8 percent during the 2004 to 2011 period. A budget that is expanding at twice the growth rate of the primary THR population is likely to be unsustainable.

Figure 1. Revision THA is Increasing Faster Than Primary THA in the UK



THR evidence base

A previous NHS Research & Development Health Technology Assessment had concluded that "There is overwhelming evidence that overall THR is a successful form of surgery."[9] Many other works support this conclusion. Prospective economic analyses of clinical evaluations[10-14], cost-effectiveness evaluation decision models[6;8;9;15-19], and systematic reviews[20;21] universally conclude that THR is a cost-effective procedure for end-stage osteoarthritis in broad patient populations across numerous global jurisdictions that consistently falls well under the threshold generally adopted by NICE as an indicator that an evaluated entity is cost-effective.

Cost-effectiveness analysis design – key import of revision rate

Recognizing that NICE will conduct its own cost-effectiveness appraisal of THA, we address evidence on the factors that should be included as possible sensitivity elements within the cost-effectiveness model to be developed. In addition, there has been much discussion in the literature on how to apply cost-effectiveness analyses to prospectively evaluate new technology implants in the context of estimating whether they provide sufficient value for their often incremental cost. These considerations are critical to appropriate cost-effectiveness analysis (CEA) of THA because the extent of cost-effectiveness may be significantly influenced by modifiable and non-modifiable differentiating factors not obvious from existing literature. At the time many of the available cost-effectiveness evaluations were developed, mid- and long-term outcome data from registries such as the NJR and the Australian Orthopaedic Association's National Joint Replacement Registry (AOA NJRR) were not available so estimates for sensitive variables were frequently applied to transition probabilities.

Age and gender are typically the principle non-modifiable factors included in any such analysis. Some early CEAs suggested that procurement cost of joint implants is an important variable when assessing the cost-effectiveness of joint implants.[9;12;22;23] However, one early clinical study with a CEA evaluating cemented to cementless implants provided insight by concluding, "These data clearly indicate that

comparing the cost of cemented and cementless hip prostheses will only differ significantly if there is a difference in the rate of revision surgery.[10]

Subsequently, several CEAs were published demonstrating that revision rate following primary THR would have significant impact on a patient's lifetime care costs and therefore on the overall cost-effectiveness of a primary THA.[9;11;14;17;18;24] Drummond and Sorenson identify that for orthopaedic implants, maximum value is delivered when revision rates are minimized.[25]

Several CEAs looked to identify what incremental reduction in revision risk would be necessary for a new technology implant to justify a given incremental price premium.[9;16;18;24] Two separate reports originating from the same group using the same analytic method reported a different magnitude of results seemingly from the same data.[9;16] Both evaluations calculated the necessary revision rate reduction over a patient's remaining lifetime adjusted for gender and age at implant under assumptions comparing a new technology implant to a standard implant, at cost neutrality, a £6500 per quality adjusted life year (QALY) threshold or a £10000 per QALY threshold. The reports basically agreed that if a new implant placed in a male under 50 years old had a 300 percent cost premium but reduced the revision risk by about 27 percent, it would be considered cost-effective at a threshold of £6500 per QALY. However, if the revision risk was only 22 percent, its cost-effectiveness threshold would increase to £10000. Contrasting this to a cost premium of 150 percent, they showed that the respective revision reductions needed to get to the same QALY thresholds were seven percent and six percent. The most conservative of the reports found that even in men over 70 years old, an implant with a 150 percent price premium compared to a standard cost implant was cost-effective at a threshold of £6500 per QALY if it reduced revision risk by 35 percent.[16]

Bozic etal identified age at time of implant, implant procurement cost and change in revision risk as factors that when comparing alternative bearings could strongly influence the cost effectiveness of a particular bearing surface.[24] They reported that a bearing surface with a US$2000 price premium must deliver an 18.7 percent risk reduction over a 20 year period for revision to be considered cost-effective. They further report that a US$2000 cost premium in a 63 year-old patient would not be cost-effective for any level of risk reduction concluding, "The cost-effectiveness of alternative bearings will ultimately be determined by their ability to reduce wear, prolong implant longevity, and therefore delay and in some cases prevent the need for revision surgery."[24]

In the UK, Briggs and colleagues applied a probabilistic decision model to evaluate two prostheses.[18] An "All-Poly Cup and a Spectron EF or EF Primary Stem (Smith & Nephew, Memphis, TN, USA)" was compared to a Charnley prosthesis. Revision probabilities were taken from the Swedish THA Register and costing showed a 36 percent price premium for the former prostheses. The hazard ratios for Spectron compared to Charnley, respectively were 0.669 for early revision risk and 0.261 for late revision risk. They concluded, "based on mean costs and QALYs, and compared with the Charnley prostheses, the Spectron has cost savings in younger patients, and generates an incremental cost-effectiveness ratio of between £1000 and £16000 in older patient groups."[18]

Prosthesis design features modify revision risk

In an early report comparing 10 hip prostheses, it was identified that the revision rate following a primary THR performed with a particular prosthesis among the ten was much lower than the others.[26] However, subsequent unrelated reports over the following years suggested that new prosthesis design features did not influence revision risk.[27-29] These reports evaluated new technology implants as a category rather than evaluating them individually. When category evaluations are performed, distinctions that might be attributed to low volume comparators may sometimes not be found. In these evaluations, data was either not available or not investigated at a granular enough level to separately evaluate the impact of individual prostheses or design elements on revision rate following THR.

[redacted]

The AOA NJRR does report that level of granularity. Using the 2012 and 2011 registry reports, we review seven to 10 year data reporting the "Yearly cumulative percent revision of primary total conventional hip replacement by bearing surface."[30;31] Ceramicized metal is a bearing surface manufactured by Smith and Nephew. Because the published 2011 AOA NJRR reported 7 year data but the published 2012 AOA NJRR did not, we performed a regression extrapolation of the data to 11 years by combining the 2012 data with the year 7 data from the 2011 report to allow comparison to other bearing surfaces as reported in 2012. **Figure 2** displays the results. This shows the extrapolated 11 year cumulative revision rate for ceramicized metal is the lowest among reported surfaces at [redacted] percent. A limitation of this data is that the published data does not allow for risk adjustment.

Figure 3 demonstrates that ceramicized metal revision rates when extrapolated to 10 years are nearly [redacted] percent lower than the index bearing surface, metal on modified polyethylene. It is the only bearing surface to demonstrate a lower revision risk than the index bearing surface.

[redacted]

Table 1 is taken from Table HT31 of the AOA NJRR and reports the data by revisions per 100 observed years.[30] Ceramicized metal was reported to have the lowest reported revisions per 100 observed years in the [redacted] observed years reported. The index bearing surface reported [redacted] observed years.[30]

Confidential data to be redacted

The UK NJR does not publically report similar analyses at this time. However, under an agreement with the NJR, manufacturers may confidentially request data on their own devices but may not publish the data. We share such confidential data here in **Table 1a** and **Figure 4**. These data should be redacted from any public release of this comment letter. This report from [redacted] observed patient years over a period of nearly [redacted] years shows that ceramicized metal with highly cross-linked polyethylene liners demonstrates a rate of [redacted] revisions per 100 observed years. Thus, the UK revision rate data in patients receiving THR with a ceramicized metal bearing surface not only appears consistent with the data reported in the AOA NJRR but results in a hazard ratio of [redacted] compared to the NICE 10 year revision target for THR

prostheses of 0.95 revisions per 100 observed years (which is equivalent to a 10 year revision rate of 10 percent).
Based on the work cited previously, revision rate reductions of the magnitude reported in the AOA NJRR for any prostheses may be expected to have favorable impact on the cost-effectiveness of THR if their incremental cost is within the described ranges. One could expect that as use of prostheses associated with reductions in the risk of future revision THRs increases in a given jurisdiction, an associated reduction in revisions may be expected based on the AOA NJRR data when modeled forward with cost data for primary and revision THR. Beyond improving the cost-effectiveness of THR, increased use of any hip prosthesis associated with a revision rate reduction could also result in a favorable NHS budget impact for THR procedures.

The magnitude of reduction in revision rate in the provided extrapolated example, nearly [redacted]%, taken from the Australian data, combined with the comparable data from the UK NJR suggests that any cost-effectiveness model prepared to evaluate the cost-effectiveness of THR in the UK at this time should include detail beyond a generic revision rate reduction variable. A more detailed analysis that includes factors now known to modify the rate of THR revisions, including specific bearing surface, should be designed. Because the volume of ceramicized metal used at this time in the UK is low compared to other bearing surfaces, any benefit conferred by its use may not be apparent in a pooled analysis of newer bearing surfaces on revision rates following a primary THR.

In conclusion, several evaluations have found that implant price and the rate of revision THR following primary THR are two important factors that influence the cost-effectiveness of THR when assessed over patients' lifetimes. Therefore, it is important to include in any CEA of THR, modifiable and non-modifiable factors that influence implant price and revision rate. We have presented evidence that bearing surface is among known factors that impacts revision rates following primary THR.

Sincerely,

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4 February, 2013

Dear Mr Powell,

RE: **Total hip replacement and surface replacement for the treatment of pain resulting from end stage arthritis of the hip (review of technology appraisal guidance 2 and 44, ID540)**

In response to the announcement by the National Institute for Health and Clinical Excellence (NICE) of the review of technology appraisal guidance 2 and 44, to appraise the clinical and cost effectiveness of total hip replacement and surface replacement within their CE marked indications for the treatment of pain resulting from end stage arthritis of the hip, Smith & Nephew Orthopaedics Limited ("Smith & Nephew") is providing comments to NICE on metal-on-metal (MoM) hip resurfacing systems. Our comments focus in particular on the BIRMINGHAM HIP™ Resurfacing System (BHR), which Smith & Nephew manufactures here in the UK.

It is important to address the differences in design, material and biomechanical characteristics between MoM resurfacing systems and MoM THA systems, as well as the differences in clinical performance among the currently marketed MoM devices. Recent evidence has drawn critical attention to the design and material characteristics of certain competitor MoM resurfacing systems, highlighting the potential for accelerated wear, metal ion generation, and failure in patients implanted with these devices. Such outcomes have been widely reported by the news media, though the majority of publications and alerts cited by the media fail to differentiate between devices. This has provoked contentious debate within the orthopaedic community and degraded public opinion about a treatment option – resurfacing – that has, in general, provided real benefits for many younger, more active patients for whom traditional metal-on-polyethylene (MoP) devices may be less suitable and for whom MoM THA may be a less bone-conserving option and may present other disadvantages (see below).

We welcome NICE's request for public comment and expert scientific and clinical opinion on the risks and benefits of these types of devices, and how the risks can be mitigated. We agree that all available hip resurfacing clinical evidence should be subject to diligent evaluation and scrutiny. To this end, we are providing NICE with the following information relative to the design and clinical performance of the Smith & Nephew BHR System.

The BIRMINGHAM HIP™ Resurfacing System (BHR)

Smith & Nephew currently markets the BHR system in the European Union (including the UK), the US and in 18 other countries. This device consists of a stemmed femoral head resurfacing component designed for cemented fixation and a hemispherical acetabular cup designed for cementless, press-fit, fixation. The BHR is a "resurfacing" prosthesis because only the surface of the femoral head is removed to implant the femoral head resurfacing component. In contrast to conventional Total Hip Arthroplasty (THA), BHR is considered a bone conserving system.

MoP bearings may be appropriate for THA patients who are more elderly and less active. By contrast, the use of MoM technology for resurfacing has significant advantages, especially for younger, more active patients. These advantages include the following: [1-4]

- Elimination of proximal femoral stress shielding
- Elimination of polyethylene induced osteolysis
- Reduced risk of dislocation, as compared to traditional THA
- Reduced risk of postoperative leg length discrepancy
- Physiological restoration of hip offset, supporting normal function

Clinical Evidence

Many publications that have raised concerns about MoM devices have failed to differentiate between devices. The long term clinical performance of the BHR system continues to support its high level of safety and effectiveness when implanted in accordance with the operative technique and in indicated patients. In such cases, the survival of BHR is equivalent to the best performing THA systems currently on the market.

Clinical Literature

A list of peer-reviewed publications reporting mid- to long-term survivorship data for the BHR system is provided in Table 1. In summary, a total of 13,789 BHR implants and 128,617 observed component years are reported. Weighted average follow-up among these study populations is 9.3 years, with a weighted average survivorship of 95.6 %. A total of 9,287 patients and 102,453 observed component years are reported at a minimum of 10 years follow-up with a weighted average survivorship of 95.5%.

Table 1: Literature summary for the BHR system

Reference	*N*	*Survival %*	*Years*
De Smet[5]	*200*	*99.5*	*15*
Daniel[6]	*446*	*99.8*	*4*
Treacy[7]	*144*	*99.0*	*5*
Hing[8]	*230*	*99.1*	*5*
McBryde[9]	*2,123*	*97.5*	*5*
Nishii[10]	*50*	*96.0*	*5*
Reito[11]	*144*	*96.7*	*6*
Heilpern[12]	*110*	*96.3*	*6*
Pollard[13]	*54*	*94.0*	*6*
Steffen[14]	*610*	*95.1*	*7*
Madhu[15]	*117*	*91.5*	*7*
Khan[16]	*653*	*95.7*	*8*
Witzleb[4]	*100*	*95.0*	*8*
Seppänen[17]	*111*	*95.0*	*8*
Robinson, Oswestry Report	*569*	*95.2*	*10*
Carrothers[18]	*5,000*	*95.3*	*10*
Treacy[19]	*144*	*93.5*	*10*
Holland[20]	*100*	*92.0*	*10*
Coulter[21]	*230*	*94.5*	*10*
De Smet	*149*	*93.1*	*12*
McMinn[22]	*3,095*	*96.0*	*13*

In each of these long term survivorship studies, the reported annual rate of revision falls below the benchmark revision rate for the best performing THA devices set out in guidance published by the UK National Institute for Health and Clinical Excellence (NICE)[23].

Arthroplasty Registry Revision Data

Revision data for the BHR system are reported by the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR)[24] and the National Joint Registry for England and Wales (NJREW)[25] including all patient subpopulations. Survival from the AOANJRR and the NJREW is plotted in Figure 1. Following [redacted] procedures, the AOANJRR reports a revision rate of [redacted] (CI [redacted]) at 10 years. The NJREW, following 17,519 patients, reports a revision rate of 5.09% (CI 4.64-5.57) at 7 years.

Figure 1: Registry cumulative revision rates for BHR[24, 25]

[redacted]

These annual revision rates fall within (below) the NICE benchmark referred to above.

The AOANJRR 2012 Annual Report[24] provides comparative revision information for the different MoM hip resurfacing systems available in Australia (Table 2). Of the [redacted] resurfacing devices tracked in the registry, [redacted] are BHR. None of the other 16 systems represented individually exceeds [redacted] of the cohort.

The AOANJRR expresses implant survivorship as revisions per 100 observed component years (OCY). For BHR it reports [redacted] OCY, [redacted] of the [redacted] resurfacing OCY reported. BHR is the best represented device in the class data set at over [redacted] times OCY of the nearest competitor device and the only resurfacing device with 10 year follow-up. BHR shows [redacted] revisions per 100 OCY (CI [redacted]), below the resurfacing class average of [redacted] revisions per 100 OCY (CI [redacted]). The other devices below the class average for revisions per 100 OCY are [redacted], all of which have a limited presence in the cohort. [redacted] has stopped selling the [redacted] devices.

Table 2: Table [redacted] from the AOANJRR 2012 report[24]

[redacted]

The AOANJRR also reports annual cumulative percent revision data for the hip resurfacing devices available in Australia (Table 3).

Table 3: Table [redacted] from the AOANJRR 2012 report[24]

[redacted]

Of the five systems with data tabulated to seven years, BHR is the only one showing a yearly cumulative revision rate within (below) the NICE benchmark, at [redacted] (CI [redacted]).

Furthermore, the BHR system is the only hip resurfacing device with annual cumulative revision rates out to, and beyond, ten years. Following [redacted] procedures, the AOANJRR reports a revision rate of [redacted] (CI [redacted]) at 10 years, making it the only hip resurfacing to satisfy the NICE benchmark. In the text of its 2012 Annual Report it offers the further BHR datum point of [redacted] at eleven years.

The NJREW 2012 Annual Report[25] also provides comparative revision information for the different MoM hip resurfacing systems, tracking those available in England and Wales (Table 4). Of the 31,671 resurfacing patients tracked in the registry, 55.4% are BHR. None of the other six systems tracked individually exceeds 11.2% of the cohort.

Table 4: Table 3.10 from the NJREW 2012 report[25]

Table 3.10 Revision rates (all-cause) for main hip resurfacing brands (95% confidence intervals).

Resurfacing brand	Number of patients	Year 1	Year 3	Year 5	Year 7
Adept Resurfacing	3,137	1.22% (0.88-1.68)	2.48% (1.95-3.17)	4.41% (3.39-5.73)	-
ASR Resurfacing	2,982	1.53% (1.15-2.05)	5.97% (5.14-6.94)	13.77% (12.29-15.42)	24.22% (21.31-27.52)
BHR Resurfacing	17,519	1.07% (0.93-1.24)	2.41% (2.18-2.67)	3.67% (3.36-4.01)	5.09% (4.64-5.57)
Conserve Plus	1,275	2.00% (1.35-2.97)	5.16% (3.99-6.67)	8.52% (6.76-10.73)	-
Cormet 2000	3,532	1.35% (1.01-1.79)	3.61% (3.02-4.32)	7.13% (6.15-8.25)	10.38% (8.86-12.15)
Durom Resurfacing	1,608	1.46% (0.97-2.20)	3.77% (2.90-4.90)	5.99% (4.74-7.58)	-
Recap Resurfacing	1,618	1.82% (1.26-2.61)	3.63% (2.75-4.79)	5.96% (4.35-8.16)	-

Note: Revision rates are only shown where at least 100 patients have been observed for at least that period of time.

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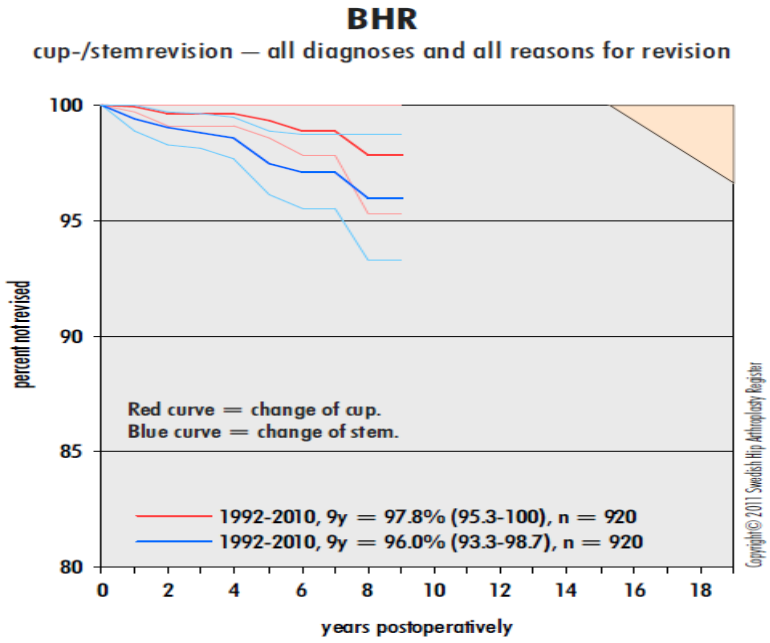
Of the three systems with data tabulated to seven years, BHR is the only one showing a yearly cumulative revision rate below the NICE benchmark, at 5.09% (CI 4.64-5.77), mirroring almost exactly the performance in the AOANJRR.

While the Australian and UK registry reports are most prominent, additional survival data are reported by the Swedish Hip Arthroplasty Register.[26] A total of 920 BHR procedures are reported in the Swedish register. At an average follow-up of 9 years, cup and stem revision rates of 2.2% and 4%, respectively, have been observed (Figure 2).

Figure 2: Swedish registry results for the BHR system



The Swedish register applied a Cox regression analysis adjusted for age, gender and diagnosis to report that BHR performs better than other within class resurfacing devices.[26] There was no statistically significant increase in risk between BHR and a control group (BHR 1.34 CI: 0.82-2.17), but, the class, when compared with a THA control group, demonstrated an increased risk (2.39 CI: 1.80-3.18). However, in a gender breakdown, the risk of revision with the BHR system is greater for women (2.43 CI: 1.20-4.98), but still about half the class rate 4.88 (CI: 3.27-7.24). Revision risk for men was about equal to control (1.02 CI: 0.51-2.04), while that for the class was significantly higher 1.60 (CI: 1.06-2.39).[26]

In summary, these Swedish data show that the BHR system performs equally as well as a control group of proven THA devices, better than all other MoM resurfacing devices and better than all MoM THA devices.

Analysis of Causes of BHR Revision Rates

The failure of any hip prosthesis is multifactorial. Table 5, taken from a confidential *ad hoc* report requested by Smith & Nephew from the Australian National Joint Replacement Registry,[27] analyzing data collected from September 1999 to December 2010, lists the reasons for revision, and their incidence, for BHR and primary total conventional hip arthroplasty (THA). Overall, the revision rate for any cause is slightly lower in the BHR cohort ([redacted]) than that for conventional primary THA ([redacted]).

Table 5: Revision Diagnosis of BHR and Primary Total Conventional Hip Replacement[27]

[redacted]

Of the six main reasons for revision, BHR revision rates for loosening/lysis and prosthesis dislocation ([redacted] and [redacted] respectively) are below the rates reported for other conventional THA devices ([redacted] and [redacted] respectively). BHR revision rate for infection ([redacted]) is slightly above the rate for THA ([redacted], while fracture and pain are reported at equivalent revision rates for BHR and THA devices. Metal sensitivity is recorded at a higher revision rate for BHR ([redacted]) than for all THA devices ([redacted]), although both rates are low.

According to MDA/2012/036 issued by the MHRA in June 2012,[28] as well as more recent pronouncements from the FDA, elevated metal ion concentration alone is not a reason for revision for MoM hip prostheses.

Causes of Resurfacing Revision: Loosening/Lysis

Loosening of components can be caused by high levels of activity and impact on the implant shortly after the surgery. An association with wear particles has also been reported; these may trigger an autoimmune reaction leading to lysis (absorption of bone tissue).[29] The absorption of bone tissue around the implant can cause the implant to loosen and so require revision surgery.

Causes of Resurfacing Revision: Prosthesis Dislocation

Dislocation is a complication commonly associated with all hip implants, including resurfacing. Recurrent dislocations can lead to the need for revision surgery. It has been reported that the rate of dislocation for MoM hip devices is much lower than the rate of dislocation for ceramic-on-polyethylene.[30]

Causes of Resurfacing Revision: Infection

Infection is a risk for any surgical intervention. Infections in hip arthroplasty may occur where bacteria adopt a biofilm mode of growth on the surface of the implant.[31] This increases the antibiotic resistance, which makes treatment extremely difficult.[32] Where this is the case, the appropriate course will often be to remove and replace the implant.[33]

Causes of Resurfacing Revision: Fracture

Causes of femoral neck fracture include poorly positioned femoral devices, notched lateral neck cortex, and poor bone quality. Because of the fact that the BHR, by nature, preserves more bone structure in the femoral neck, fracture is a predominant cause of revision surgery for the BHR device. For THA, periprosthetic fracture is also a significant failure mode (see Table 5).

Causes of Resurfacing Revision: Pain

Pain is a symptom of failure modes across the range of hip implants and is not unique to BHR patients. However, there are also instances in which pain is unexplained and becomes a failure mode in itself (see Table 5).[29]

Causes of Resurfacing Revision: Metal Sensitivity

Some patients may develop hypersensitive reactions to metal components of any prosthesis. This is a phenomenon that affects conventional MoP devices as well as MoM. In such cases, it has been suggested that

metal ions released from the metal implant combine with proteins and activate the immune system as antigens and elicit hypersensitivity reactions. The incidence of this hypersensitivity has been reported to be about 1 per 5,000 patients.[34] Metal hypersensitivity can result in secondary reactions, including Aseptic Lymphocytic Vasculitis-Associated Lesions (ALVAL) and extensive necrosis and granuloma formation. The associated soft tissue mass that can form has been termed a pseudotumour.[35] While preoperative screening techniques for metal sensitivity are not yet fully validated, we are aware of encouraging results using lymphocyte transformation testing to identify the small number of metal sensitive patients prior to surgery.

BHR risk factors and contraindications

Apart from poor device positioning by surgeons, which (as described above) may lead to edge loading and, in turn, to excessive wear of the device, certain factors have been identified which may increase the risk of device failure and, ultimately, revision.

Femoral head size

It is well understood that femoral component head size can affect patient outcomes and that there is an elevated revision risk for patients with a component size smaller than 48mm, particularly in female patients (see Table 6 below). For 44mm heads in both the AOANJRR and the NJREW, in addition to 46mm heads in the AOANJRR, the observed annual revision rate exceeds the NICE benchmark.

Table 6: Revision risk by size[27,36]

[redacted]

Gender

It is understood that patients who are female have a greater revision risk than other patients. Following a recent study published in the Lancet,[37] attention has been focused on the specific issue of the performance of MoM resurfacing in female patients. We are actively reviewing the question of how well BHR performs in female patients and whether there is a confounding effect for head size (above), as part of our post-market surveillance obligations.

Pathologies

The most successful clinical indication for BHR is osteoarthrosis. Certain other pathologies have been identified as having an influence on the survivorship of BHR implants. More specifically, patients who have been diagnosed with avascular necrosis or developmental dysplasia of the hip have a greater risk of device failure than other patients if they are implanted with a BHR implant.

BHR is contraindicated in the case of infection and sepsis and relative contraindications include osteoporosis, metabolic disorders such as partial renal failure, vascular insufficiency, muscular atrophy, or neuromuscular disease, inadequate bone stock, distant foci of infection (which may cause hematogenous spread to the implant site), and incompetent or deficient soft tissue surrounding the joint. The use of metal-on-metal prostheses is contraindicated in further patients with chronic renal failure and in pregnancy.

Smith & Nephew has also informed surgeons and the patient community of the inflammatory tissue response to high levels of wear debris resulting in peri-prosthetic lesions (ALVAL), fluid collection, or soft tissue masses (pseudotumours) which have been linked to MoM implants.

Conclusions

The BHR system is distinguished by over 14 years superior clinical performance, as evidenced by independently published clinical studies, multi-national registry data, and Smith & Nephew's post-approval clinical studies.

Smith & Nephew will continue to recommend the use of the BHR system for appropriate patients. Typically, these are active male osteoarthritis patients under the age of 65, who have no bone or biomechanical contra-indications and require a head size 48 mm or larger. BHR can bring significant advantages to appropriate patients when compared with conventional THA.

Patients who are female; who require a smaller component size (≤46mm); have the device implanted at a high abduction angle; have a high combined anteversion angle; are obese; or who have a diagnosis of avascular necrosis or developmental dysplasia of the hip, have a greater risk of revision than other patients. The more risk factors a patient has, the greater the risk of procedure failure and revision.

Smith & Nephew appreciates the opportunity to provide NICE with this information showing that MoM hip resurfacing devices differ substantially in design and clinical performance. Generic alerts and advisories broadly communicated by regulatory agencies, the surgeon community and the media that fail to distinguish between hip resurfacing devices are neither warranted nor in the best interest of public health.

Yours sincerely,

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