Derivation of utility payoffs

Pre-operative values, measured by the Euro-Qol 5-Dimension Questionnaire (EQ-5D [27]), were adopted for the states before and after progression under Medical Therapy, and are consistent with values previously used to represent ACR III and ACR IV [1]. The corresponding 12-month post-operative values were used for Successful primary THR [28]. The Successful Delayed THR state was also assigned this value but with a decrement for the utility loss due to delayed surgery [29]. The utility loss was calculated by the formula:

\[
\text{Utility loss} = \beta (u_{IV} - u_{III})
\]

where \( \beta \) is the regression to the mean coefficient between post-operative and pre-operative utility scores and \( u_{IV}-u_{III} \) is the mean difference in pre-operative scores between delayed and early THR (i.e. -0.22, the utility change from ACR class III to ACR IV class). In the base case the utility loss was -0.0528, which corresponded to an estimate for \( \beta \) that was obtained from linear regression analysis of pre-operative EQ-5D scores and post-operative scores recorded at a minimum 6 months after unilateral Hip Replacement operations, involving both primary and revision total and partial procedures [30], from a Patient Reported Outcome Measures (PROM) individual patient dataset for episodes of hospitalisation starting in the period April 1-December 31 2011 (n=14475 operations at 240 sites, available from the Hospital Episode Statistics website, HES online, http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=1632 last accessed 18 May 2012).

The length of follow-up in the PROMs data was shorter than the one-year end point typical from observational studies. However, in analysis of individual data [29], the regression to the mean coefficient of 6 months utility scores approximated that for 12 month scores: 0.58 vs. 0.60 (further details available upon request). Despite the limitation of not being able to separate primary THR operations from revision and partial operation, the \( \beta=0.24 \) estimated from these data was used in the base case because it served as conservative value and was estimated from individual observations as opposed to mean estimates in the alternative source [27]. In the latter study a regression to the mean coefficient of 0.478 was calculated by the formula: 1 + the ratio of the difference in mean 12 month post-operative gains to the difference in
mean pre-operative utility in high and low pre-operative utility primary THR patients. The base case values for the need of Revision Surgery and Successful Revision states were taken from preoperative and postoperative revision hip replacement EQ-5D values [31].

A range of optimistic utility values was considered in sensitivity analysis [32, 33, 34, 35, 36, 37]. The preferred set of values for this analysis were those measured by TTO in a group of OA patients seeing a surgeon for primary and revision operation TTO [35]. This source did not report pre-operative values for distinct disease severity levels of OA, but a single value for ‘chronic OA’. This value, 0.60, was assumed to apply to the state before disease progression and a reduction of 36% was applied to it to derive the value for the state after disease progression, which corresponded to the ratio of the utility of the predetermined ‘moderate’ OA (i.e. experiencing ‘moderate pain and stiffness upon exertion’, the ‘need to use a cane to walk for more than 1 city block’, ‘occasional’ need to take painkillers, ‘sometimes’ night pain relieved by change of position/painkillers, and ‘you can only do light housework or chores’, and ‘socialise with family and friends but more than 1 hour is painful and tiring’ [32]) to ‘severe’ OA (i.e. ‘constant pain and stiffness’, ‘you must use a walker at all times’, ‘regularly use pain pills’, ‘sleep poorly at night’, ‘unable to do any housework and/or chores’ and ‘it is very difficult for you to socialize with family and friends for even a few minutes’ [32]) states, i.e. 0.39/0.61.

Conservative utility gains with surgery were estimated using individual patient data on disease status measured by the Harris Hip Score (HHS) and utility outcomes [29], recorded with the 15D instrument [38], provided by primary study authors (P. Rasanen, Personal Communication March, 2011). Dividing primary THR patients between those with HHS 40-70 (n=57) and < 40 (n=14), to represent those with ACR III and IV [1], resulted in parameter values in the Low benefit column of Table 3, which imply overall, 12-month gains of 0.064, for ACR III (early THR) and 0.050 for ACR IV (Delayed THR), and 0.011 for revision patients (n=24) (although a decline with age was observed in utility gains from primary surgery, the numbers of the age≥75 group (n=8) were too small to permit reliable estimation of differences across age groups).
Since the average utility value during the first year after operation is likely to be lower than the mean value at 12 months after operation due to the lower utility values experienced during the rehabilitation period, the literature was searched for evidence of the evolution of utility in the first year after surgery. Only one study was identified that measured utility outcomes for at least 12 months postoperatively which also reported utilities earlier than 3 months after surgery (Brunenberg et al., 2007). It reported the results of an RCT of an experimental rehabilitation programme in the US that measured EQ-5D utility scores of primary THR patients 1 day pre-operatively, and at 7, 12, 26 and 52 weeks after operation. In the standard rehabilitation practice arm (n=50; mean age, 65 years; 25% females), the estimated area under the utility curve was 0.65, equal to 97% of the reported 0.67 utility value at 12-months. Therefore, we applied a 3% discount on the 12-month utility mean estimate to account for the average utility in the year after primary and revision hip replacement and assumed the 12-month values to be maintained over the remaining lifetime in the absence of further hip surgery. A disutility value was calculated for NSAIDs use (in both arms) given its associated risk of bleeding ulcer (Silversten et al., 2000) and amount of drug consumed (Bolland et al., 2011), resulting in an annual disutility effect of 0.001 and 0.002 for the states before and after progression.

Costs
One study alone has reported the cost of primary THR in Italy; this study compared the costs of THR across nine EU countries using vignettes to estimate the cost of uncomplicated THR [41]. Its estimates for Italy were obtained from a purposive sample of five general hospitals, including independent hospitals (Hospital Trusts) and hospitals managed by Local Health Units from two Italian regions, using a bottom-up micro-costing approach. Data on quantity of resources used during admission, intervention, hospital stay and discharge by an uncomplicated, hypothetical THR patient were gathered using questionnaires administered to clinicians and administrative staff in those hospitals. Costs included per diem, personnel costs, procedure (time and operating theatre unit costs), implant and consumables, medications, laboratory tests and imaging, and overheads, calculated from information provided by Hospital Accounting Departments, and complemented with regional tariffs for laboratory exams and imaging. The range of hospital length of stay (LOS) for primary THR in the sample was 5-11 days, resulting in hospital
costs, excluding prosthesis and fixation materials, of €3370. The cost of prosthesis and materials was €3272, a weighted average of four hospitals using cementless devices in at least 90% of cases, and one hospital using them for 60% of cases (see Table 3 for further details).

In the absence of evidence, the cost of RHR was estimated relative to the costs of primary THR on the basis of the economic costs reported by Bozic, et al.[42], which found RHR to cost 30% more than primary THR. This study included 14% of operations due to sepsis, which have been reported to cost 176% more than revisions due to aseptic loosening, the most common cause for revision [43]. Multiplying the primary THR (including prosthesis) cost estimates in Table 3 by 1.30 yields a cost of RHR of €8612 (range €5816 - €11408), which is below the only available estimates for Italy, of €27194 for aseptic loosening revision and €60394, for septic revision [44]. Lack of methodological information required to obtain these figures, prevents using them for the base case. They are adopted as the upper bound for sensitivity analysis, combined into a weighted average of €29983, where 8.1% of revisions are assumed to be due to sepsis and the rest to aseptic causes, as reported for all revisions in the Hip Arthroplasty Register in 2008 [18].

The costs of a ‘Successful’ THR outcome, is differentiated between the first year after operation and subsequent years. For the first year, it included the costs of routine discharge, follow-up and the costs of complications due to PE and wound infection post discharge. The quantities of resources used during routine discharge and follow-up, including rehabilitation, were based on guidelines by the National Association of Orthopaedics Surgeons (Società Italiana Ortopedia Traumatologica, SIOT). Costs of NSAID use and treating and preventing its severe adverse effects (including medications, and diagnostic tests) were also accounted for the first year and subsequent years, in proportion to the frequency of use [13] and the ratio of gastro-protective drug to NSAIDs costs [51]. Costs of hospitalisations in the second year after surgery were derived from the product of unpublished estimates for hip OA patients in the year 2000 (Leardini, unpublished data), and the ratio of costs estimates of ACR class II (representing mild OA) to ACR class III (OA before disease progression) documented in Leardini et al. [52].
The annual cost of medication use by severe OA (before progression to functional dependency; applicable to patients who did not undergo OA and those requiring revision) was derived from estimated NSAIDs consumption (prescriptions) in primary care during the year before hip replacement, as reported for the UK [13], at prices of cyclo-oxygenase 2 (COX-2) inhibitors and nonselective NSAIDs prescribed in Italy [53;54;55] (see Table 3). The UK study had no information available on the quantities of prescriptions; the dataset only recorded whether a) an individual had no anti-inflammatory medication prescriptions in the year and b) whether the person had received prescriptions >80% of the year. The relative frequencies for a, b and the remainder (i.e. neither a nor b) were used to calculate a weighted average of their imputed number of days of drug prescription, which in the case of a was by definition zero, b was assigned the mid-point number of days in the range, that is 0.9*365 and the remaining case (i.e. receiving prescription ≤80% of the year) was assigned 0.4*365 days. Since the reported figures for the year before THR were 39% for a and 21% for b, the number of days of prescription was (1-0.39-0.21)*0.40*365 + 0.21*0.9*365 = 127 days per year. Given that the relative frequencies for the discrete measures of drug prescription quantities were not available according to severity of disease, the quantities reported for the year before the operation [13] were assumed to apply to the functionally independent state, and the quantities of drug consumption for the disease progression state were approximated by the same algorithm but assuming that a was 0%, and b was 50%. Quantities were also available for the first two years post-THR [13] and the corresponding cost pay-offs were calculated likewise. These assumptions had little effect on sensitivity analysis due to the low costs of NSAIDs (see Table 3). Costs of treatment and prevention of adverse events due to NSAIDs use, including medications, and tests were derived in proportion of the cost of NSAIDs, by applying the iatrogenic cost factor of 2.3 as reported for patients with OA in Italy [51]. Costs of other drugs (i.e., corticosteroids, analgesics, etc.) were derived from their reported share in drug costs [51]. The cost of routine and emergency hospitalisations before disease progression under the non-surgical strategy were obtained from unpublished data for the subgroup of hip OA patients studied by Leardini, et al.[51]; for the post progression state, the ratio of hospitalisation costs in ACR IV to ACR III among RA patients in Italy [52] was multiplied by the costs for the before progression state. The large uncertainty due to heterogeneity of sources and measures was
reflected by considering plausible ranges of relative variation between these estimates in sensitivity analyses. Hospital costs were reflated to 2010 using the Consumer Price Index for the Health Sector in Italy.

The cost of primary and revision hip replacement was adjusted to reflect the additional cost of deep wound infection complications by including the additional LOS associated with deep-incisional surgical site infections, as reported by Monge-Jodra, et al., [47], in 11 case-control THR pairs, matched for age, sex and the National Nosocomial Infection Surveillance System risk index. The median additional LOS and postoperative LOS of patients with deep wound incisional surgical site infections were reported to be 49 (p<0.13) and 43 (p<0.001), respectively. Thus the additional costs of deep wound infections in primary and revision hip replacement were calculated as the additional postoperative LOS valued at the cost per day in hospital, including all costs except for prosthesis, that is, €27.28 and €109.13 in the base case (43 days in hospital at €423 per day times an incidence rate of 0.15% and 0.60%; see Table 1), respectively. The cost of PE complications in primary and revision surgery was equal to their incidence (0.008 and 0.012) times the cost of pharmacological treatment with anticoagulants [48] in Italy (€256; [49]), that is, €2.05 and €3.28, respectively.

The expected cost of treatment of dislocations in the immediate postoperative period was added to the cost of primary and revision operations. It included the cost of closed reduction (€642), imputed on the basis of its magnitude relative to the cost of uncomplicated primary (18.9%) and revision (17.7%) surgery as reported in the literature [50]; this was converted to a per patient basis by multiplying it by the probability of dislocation in males (primary: 0.039 and revision: 0.086) and females (primary: 0.027 and revision: 0.082; [15] - authors’ calculations, see Table 1).

Analysis of declining utility after the first year post-THR in the ‘Successful’ state

The scenario consisted on applying a 5% declining rate for 12 years. That is, extrapolating the 7-year average rate documented in the study by Laupacis et al [36] for 5 years after its study end. In order to maintain the model compatibility with incentives to accept THR, the utility values for the revision and
successful revision states were reduced by 39% percent. This ensured that the expected utilities of the revision state and the successful revision state were lower than the expected utility in the successful primary THR state the year prior to the time of implant failure.

It must be noted that the values of the scenario depicted by Figure 3 in the main text were obtained by applying base case values with three exceptions: 1) the declining annual utility in the successful THR state for 12 years following the end of the first year post primary THR; 2) women’s utilities were set to the base case values of men’s in Table 2; 3) the reduction of 39% on the base case revision and successful revision states described before; and 4) the low progression to functional dependency rate of 4%. It is proposed that these values may be interpreted as depicting a hypothetical situation where patient management for women and men is analysed at the same time point in the disease course. Further, the low utilities of revision and successful revision may reflect ex-ante subjective assessments of decision makers, say the surgeon who decided whether to recommend surgery to a patient. This interpretation deviates from the standard ex post health technology assessment approach but may correspond with the way in which actual decision making occurs [3]. Further, the finding of delayed THR being more economically appealing in young women than men of the same age, which was explained by the longer life expectancy and prospect of low utility later in life (similar to optimization arguments made by other authors [8]) may help to rationalise the empirical regularity that women undergo primary surgery at a later time than that of men’s primary operation [3,26].