Cost-utility analysis of cemented hemiarthroplasty versus hydroxyapatite-coated uncemented hemiarthroplasty for the treatment of displaced intracapsular hip fractures: WHiTE5 trial

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ABSTRACT

Aims: To compare the cost-effectiveness of cemented hemiarthroplasty versus hydroxyapatite-coated uncemented hemiarthroplasty for the treatment of displaced intracapsular hip fractures in older adults.

Methods: A within-trial economic evaluation was conducted based on data collected from the World Hip Trauma Evaluation 5 (WHiTE 5) multicentre randomized controlled trial in the UK. Resource utilisation was measured over 12 months post-randomisation using trial case report forms and participant-completed questionnaires. Cost-effectiveness was reported in terms of incremental cost per quality-adjusted life year (QALY) gained from the UK National Health Service (NHS) and personal social services (PSS) perspective. Methodological uncertainty was addressed using sensitivity analysis while decision uncertainty was represented graphically using confidence ellipses and cost-effectiveness acceptability curves.

Results: The base-case analysis showed that cemented implants were cost saving (mean cost difference: -£961 (95%CI -2292 to 370)] and increased QALYs [mean QALY difference 0.010 (95%CI 0.002 to 0.017)] when compared to uncemented implants. The probability of the cemented implant being cost-effective approximated between 95% and 97% at alternative cost-effectiveness thresholds held by decision-makers and its net monetary benefit was positive. The findings remained robust to all the pre-planned sensitivity analyses.

Conclusion: This study shows that cemented hemiarthroplasty is cost-effective compared with hydroxyapatite-coated uncemented hemiarthroplasty in older adults with displaced intracapsular hip fractures.

INTRODUCTION

In the UK, hip fractures impose a significant economic burden on society with total attributable hospital costs amounting to around £1.1 billion (2012/13 prices) annually.[1] As the annual number of hip fractures in the UK increased from 64,838 in 2013[2] to 67,302 in 2019[3], attributable hospital costs will also have increased. Displaced intracapsular fractures constitute approximately half of all hip fractures, and are commonly treated with a hemiarthroplasty. The current National Institute for Health and Care Excellence (NICE) guidelines in England and Wales for the management of hip fractures recommends the use of a cemented hip hemiarthroplasty.[4] However, much of the evidence for this recommendation is based on trials comparing cemented implants with first generation uncemented implants. A Cochrane review[5] has reported a lack of evidence for contemporary hydroxyapatite-coated uncemented implants.

Cemented hemiarthroplasty has been shown to have similar or superior clinical effectiveness than contemporary hydroxyapatite-coated uncemented implants in terms of mobility, improved quality of life and lower risk of periprosthetic fracture.[6,7] However, a systematic literature review undertaken by NICE in 2016[4], showed that there were no evaluations of the cost-effectiveness of cemented versus uncemented hemiarthroplasty. The only study identified was a cost-consequences analysis, a type of economic evaluation that presents disaggregated costs and consequences for comparator interventions but does not synthesize outputs within cost-effectiveness or cost-benefit metrics tractable to health care decision making.[8] An update of this review of the literature shows one article published by Blythe et al,[9] which found that uncemented femoral components were more costly and had worse health outcomes compared to cemented stem fixation for hemiarthroplasty and total hip arthroplasty for all age groups.

The aim of this study was to evaluate the cost-effectiveness of cemented hemiarthroplasty versus hydroxyapatite-coated uncemented hemiarthroplasty for the treatment of displaced intracapsular hip fractures among older adults.

METHODS

Background of trial

World Hip Trauma Evaluation Five (WHiTE 5) is a two-arm parallel group multicentre randomized controlled trial that was approved by Wales Research Ethics Committee 5 (feasibility phase: 16/WA/0351 and main phase: 17/WA/0383) and registered (ISRCTN18393176). A detailed description of the study design is available in the published protocol[10] and the health economic analysis plan (HEAP).[11] In brief, participants aged 60 years and over with a displaced intracapsular hip fracture whose planned treatment was a hemiarthroplasty were screened for eligibility. Participants recruited from 14 trial centres were randomly allocated in a 1:1 ratio to cemented hemiarthroplasty (control) or contemporary, hydroxyapatite-coated, uncemented hemiarthroplasty between March 2017 and December 2019. The primary outcome of the trial was health-related quality of life measured using the EuroQol Group 5-Dimension five-level (EQ-5D-5L) questionnaire at 4 months after randomization[12]. The length of follow-up was 12 months post-randomisation. The main clinical results of the trial have been published elsewhere[13].

Measurement of resource use

Resource use during the first 12 months post-randomisation was collected via case report forms (CRFs) completed by trained research associates, and participant-reported questionnaires completed at four-

and 12-months post-randomisation. Baseline (pre-injury) data was collected at the time of consent into the trial in order to compare resource use before and after the intervention. Participants with cognitive impairment had their participant-reported questionnaires completed by their main carer. The 4-month follow-up questionnaire captured NHS, personal social services (PSS) i.e. social care paid for by the state, and broader societal resource use such as informal (or unpaid) care received by the participants. The 12-month questionnaire only captured resource use from the NHS perspective, for the period between four and 12 months, to estimate the costs of managing complications related to the hip fracture or its treatment. The CRFs captured the type of implant (manufacturer and model) used and the duration of the surgery while the participant-reported questionnaires captured resource use from both the NHS and Personal Social Services perspective (PSS) related to the hip fracture, such as the frequency of use of inpatient care (further treatment due to wound infection or complications), physiotherapy provided in hospital outpatient or community base contexts and formal (or paid) social care in the community. Broader resource use, such as home adaptations and informal care received by the participants, was also captured using the participant-reported questionnaires and was included in the economic evaluation that adopts a societal perspective.

Valuation of costs

The unit cost for each resource item (Supplementary Table 1) was sourced from the latest national resources during the time of analysis such as the NHS Electronic Drug Tariff[14], NHS Supply Chain Catalogue[15], NHS Reference Costs 2018/19[16], and Personal Social Services Research Unit (PSSRU) Costs of Health and Social Care compendium[17] as appropriate. A detailed description of the valuation of costs of each resource item listed is available in the published HEAP[11].

The compound NHS and PSS cost for each trial participant was computed by multiplying the reported frequency of each NHS and PSS resource input by its unit cost and summing across all NHS and PSS resource categories. Participants with fragility hip fracture represent a frail elderly population, therefore participant-facing questionnaire were kept short in order to reduce respondent fatigue. The following assumptions, which is similar to that of the WHITE cohort study[18], were made for the cost estimation for each participant: (1) participants who reported staying in residential care facilities following hospital discharge did not have any home adaptations; (2) participants who reported having formal full-time care did not receive any informal care; (3) participants who reported staying in residential care facilities/hospitals or had formal full-time care did not have any physiotherapy; (4) the duration of each physiotherapy session was assumed to be one hour; (5) if one category of resource use within a participant questionnaire was completed (e.g. home adaptations) and if the others were not completed, values for resource use, and therefore economic costs, for incomplete resource categories were zero; and (6) 37.5 working hours per week was assumed.

The base currency of all costs was UK pounds sterling and the unit costs were adjusted, where necessary, to 2019/20 prices using the NHS Cost Inflation Index that supersedes the Hospital and Community Health Services Index.[19]

Valuation of health outcomes

The health-related quality of life of trial participants was measured using the EQ-5D-5L[12] at baseline (retrospectively assessed pre-injury status), and at four- and 12-months post-randomisation. The EQ-5D-5L contains a health status classification system delineated by five 'dimensions' of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The participant identifies one of five levels of response for each dimension: no problems, slight problems, moderate problems, severe problems or extreme problems. These responses were then converted into a single health utility score using an established mapping algorithm. The EuroQol-5 Dimensions, three-level (EQ-5D-3L) algorithm[20] is currently recommended by NICE,[21] and valued using the UK EQ-5D-3L time trade-off tariff.[22] (The conversion from the EQ-5D-5L responses to the EQ-5D-3L value set is needed because NICE does not currently recommend using the EQ-5D-5L value set, pending further validation work and recommends this mapping approach[21]). Quality-adjusted life years (QALYs) were calculated by combining the health utility data with time spent in a particular health state; a higher utility value indicates a better health-related quality of life. More specifically, QALYs were computed using the area under the utility curve across the baseline and 4-month data under the trapezoidal rule.[23]

Estimates of mean QALYs were adjusted using regression methods with the baseline EQ-5D utility score as the independent variable[24]. Utilities were set to zero at the studied time-point (four or 12 months) if the participant had died in the period since the last data collection timepoint.[25]

Data analysis

Resource use items were summarized by treatment group (cemented or uncemented hemiarthroplasty) and follow-up period and differences between groups were analysed using t-tests for continuous variables and Pearson chi-squared (χ^2) test for categorical variables. Means and standard errors for values of each cost category were estimated by treatment group and follow-up period. Differences in mean costs were assessed using t-tests. The bootstrap 95% confidence interval (CI) surrounding differences in mean costs was computed based on 10,000 replications. A two-sided significance level of 0.05 was used throughout. No discounting for costs and QALYs was applied because the time horizon was only 12 months.

Missing data

Under the missing at random (MAR) assumption, multiple imputation analysis (performed using Amelia II in R[26]) was used to impute missing costs and QALYs. This was done using chained regression equations predicting missing values from the observed baseline covariates (observed responses of participant), namely age, sex, baseline EQ-5D utility and VAS scores when imputing QALYs, and baseline costs of hospital stay, theatre time and implants when imputing compound total cost. Sets of multiple datasets containing possible values for missing observations were then created[27] and estimates were pooled using Rubin's rules[28] to obtain overall estimates for costs and QALYs. This imputation was run 50 times according to the 'rule of thumb', which suggests that the number of imputations should be similar to the percentage of incomplete cases.[29]

Cost-utility analysis

For the base case (or primary) analysis, a within-trial cost-utility analysis was conducted from the NHS and PSS perspective, where the cost of self-funded home adaptations and informal care were excluded,

using the multiple imputed trial data over a follow-up period of four months. The analysis adopted an intention-to-treat ("as randomized" with imputation of missing data) approach and an incremental cost-effectiveness ratio (ICER) was calculated as the difference in mean costs divided by the difference in mean QALYs between the interventions.

The NICE cost-effectiveness thresholds of £20,000 per additional QALY[30] and £30,000 per additional QALY[30] were used to determine the cost-effectiveness of cemented versus contemporary uncemented hemiarthroplasty. An intervention with an ICER below this cost-effectiveness threshold was considered to be cost-effective. The net monetary benefit (NMB) of cemented versus contemporary uncemented hemiarthroplasty was computed across different cost-effectiveness thresholds. A positive incremental NMB would indicate that cemented hemiarthroplasty is cost-effective compared with uncemented hemiarthroplasty at the given cost-effectiveness threshold.

Non-parametric bootstrapping was also performed to assess the uncertainty surrounding the ICERs. The probability that cemented hemiarthroplasty is cost-effective compared with contemporary uncemented hemiarthroplasty was plotted at varying levels of cost-effectiveness thresholds for an additional QALY and presented using cost-effectiveness acceptability curves. The cost-effectiveness plane was drawn based on bootstrap estimates of the difference in cost and difference in effectiveness and the confidence ellipses (computed based on the methods described by Nixon et al[31]) represented a 50%, 75% and 95% confidence region around the ICER for the cemented hemiarthroplasty compared to contemporary uncemented hemiarthroplasty. The exact position of the confidence ellipse shows how confident we are in our results; for example, a 95% confidence ellipse that is found entirely in the south-east quadrant indicates that cemented hemiarthroplasty is clearly preferable to contemporary uncemented hemiarthroplasty as it improves health and reduces costs [31].

Sensitivity analyses

One-way sensitivity analyses were performed to explore the effects of (1) extending the study perspective to a societal perspective that additionally encompassed the cost of self-funded home adaptations and valuation of informal care; (2) extending the time horizon from 4 months post-injury to 12 months post-injury and including the costs of managing complications related to the hip fracture or its treatment; (3) restricting the analysis to participants with complete data; and (4) including an additional £15,000 per QALY cost-effectiveness threshold[32] to reflect recent trends in healthcare decision-making. No subgroup analysis was performed, as pre-specified in the HEAP.[11]

RESULTS

There were 1225 participants randomly allocated to receive hydroxyapatite-coated uncemented hemiarthroplasty (n=615) or cemented hemiarthroplasty (n=610) for a displaced intracapsular hip fracture. Baseline characteristics of these participants are summarized in Table 1. The mean age of study participants was 85 years, and the majority were female.

A complete set of EQ-5D-5L and resource use values (from the NHS and PSS perspective) from baseline to four months post-randomisation were collected from 647 out of 1225 participants (52.8%). Completion rates of individual resource items at each time point, by treatment group, are presented in Supplementary Table 2.

Descriptive statistics for resource use values are presented in Supplementary Table 3 by treatment group and by follow-up time point. There were no significant differences in resource utilisation rates between the treatment groups except for descriptors of the index hospitalisation where the mean number of days spent in the hospital by participants in the cemented group (14.2 days, SE 0.5 days) were marginally significantly lower than those for the uncemented group (15.7 days, SE 0.6 days; t-test, p=0.05; difference = -1.5 days, 95% CI -3.0 to -0.006).

Mean costs by trial group are summarized in Table 2 for each resource category. There were no statistically significant differences in the unadjusted mean costs between treatment groups other than for the intervention cost, which consisted of the sum of cost of the implant and theatre time. Those in the cemented group (£1421, SE £14) incurred a lower mean intervention cost than the uncemented group (£2005, SE £25; t-test, p<0.001; 95%CI difference = -£584, 95% CI -£642 to -£528).

In terms of health-related quality of life outcomes, the unadjusted mean QALYs were 0.127 (SE 0.005) for the cemented implant group, which was significantly higher than that for the uncemented implant group (0.110 [SE 0.005]; t-test, p-value = 0.011; difference = 0.017, 95%CI 0.004 to 0.030).

The incremental cost-effectiveness analysis results are presented in Table 3 for the base-case analysis and for each of the sensitivity analyses. The probabilities that cemented implant is cost-effective at cost-effectiveness thresholds of £15,000, £20,000 and £30,000 per QALY gained are also presented. Figure 1 shows the cost-effectiveness planes with the confidence ellipses of the base-case analysis. The net monetary benefit statistics and cost-effectiveness acceptability curves for the base-case analysis and each of the sensitivity analyses, as well as the cost-effectiveness planes with the confidence ellipses for each of the sensitivity analyses, are presented in Supplementary Figures S1-S9. In general, the confidence ellipses mainly lie under the cost-effectiveness threshold, net monetary benefit was positive and the cost-effectiveness acceptability curve was above 0.5; these Supplementary Figures indicate that the cemented implant is highly likely to be cost-effective relative to uncemented implants.

The base-case analysis showed that cemented implant was cost saving (lower cost [-£961 (95%CI -2292 to 370)] from the NHS and PSS perspective and resulted in increased QALYs [0.010 (95%CI 0.002 to 0.017)] when compared to uncemented implant. The probability of cemented implant being cost-effective ranged between 95% and 97% depending on the assumed cost-effectiveness thresholds of £15,000, £20,000 and £30,000 per QALY, while its net monetary benefit was positive. Therefore, the base-case analysis indicated that cemented implant is highly likely to be cost-effective relative to uncemented implant in the study population.

All sensitivity analyses (societal perspective, extension of studied time frame to 12 months, and complete-case analysis) showed similar results that supported the base-case finding that cemented implants were cost saving at all the specified cost-effectiveness thresholds. The net monetary benefit of cemented implants was consistently positive.

DISCUSSION

This study shows that cemented implants are cost-saving relative to contemporary, hydroxyapatite-coated, uncemented implants for older adults who have sustained displaced intracapsular hip fracture from both a UK NHS and PSS perspective, and a broader societal perspective which includes, for example, adaptations to the home and unpaid care in the community. This finding remained robust to all the pre-planned sensitivity analyses; the base case cost-effectiveness outcomes remained robust following separate analyses that tested alternative missing data mechanisms and alternative model specifications that varied the explanatory variables incorporated. Further evidence that cemented implants are cost saving comes from the sensitivity analysis that extended the time horizon to 12 months. This analysis only compared the cost of treating further complications and showed a higher probability of cemented implant being cost-effective relative to uncemented implant than the base case analysis over four months.

This is the first economic evaluation embedded within a randomized trial that investigates the cost effectiveness of hydroxyapatite-coated uncemented hemiarthroplasty versus cemented hemiarthroplasty for displaced intracapsular hip fractures. Blythe et al,[9] conducted a population-level cost-effectiveness analysis of cemented and uncemented hemiarthroplasty and total hip arthroplasty in Australia and recommended that cemented fixation of the femoral stem be given for patients receiving both hemiarthroplasty and total hip arthroplasty for fractured neck of femur. Their results are consistent with our findings.

The analysis presented here differs from our pre-specified health-economic analysis plan[11] in one respect. The computation of costs associated with informal care in the published plan was to be based upon the median wage of the UK population, but our trial participant questionnaires were updated during the trial to allow us to attribute gender-specific median wage values to informal care time inputs.

A key strength of the study lies in its capture of informal care inputs as a result of hip fracture, as this key cost driver was not captured in studies conducted prior to the WHiTE cohort study.[33] Limitations of this study include the restricted number of resource items we could capture in this group of frail, older individuals. In order to increase the completion rate of the resource use questionnaire, we concentrated on collecting the most important information such as rehabilitation (i.e. physiotherapy), which is the second highest cost contributor of care (after inpatient care)[34]. Another limitation was that participants had difficulty reporting their use of informal care and tended to report 'care availability'; hence the cost of informal care could have been overestimated[35].

In conclusion, cemented hemiarthroplasty is cost-effective compared with hydroxyapatite-coated, uncemented hemiarthroplasty in older adults with displaced intracapsular hip fractures.

TAKE-HOME MESSAGE

- Cemented hemiarthroplasty is a cost-effective treatment compared with hydroxyapatite-coated uncemented hemiarthroplasty in older adults with displaced intracapsular hip fractures from both a UK NHS and PSS perspective, and a broader societal perspective.

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CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTION

ME Png: Investigation, Formal analysis, Methodology, Writing - Original Draft, Writing - Review & Editing.

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REFERENCES

1. **Leal J, Gray AM, Prieto-Alhambra D, Arden NK, Cooper C, Javaid MK, et al.** Impact of hip fracture on hospital care costs: a population-based study. *Osteoporosis International* 2016;27:549–558.

2. **Boulton C, Burgon V, Cromwell D, Johansen A, Stanley R, Tsang C, et al.** Falls and Fragility Fracture Audit Programme (FFFAP): National Hip Fracture Database (NHFD) extended report 2014. https://www.nhfd.co.uk/20/hipfractureR.nsf/vwcontent/2014reportPDFs/$file/NHFD2014ExtendedReport.pdf?OpenElement , (date last accessed 22 October 2021).

3. **National Hip Fracture Database**. The challenge of the next decade: are hip fracture services ready? A review of data from the National Hip Fracture Database (January–December 2019). https://www.hqip.org.uk/wp-content/uploads/2021/01/NHFD-Annual-Report-14-January.pdf , (date last accessed 6 October 2021).

4. **National Institute for Health and Care Excellence**. Hip Fracture: management. https://www.nice.org.uk/guidance/cg124 , (date last accessed 24 October 2019).

5. **Parker MJ, Gurusamy KS, Azegami S**. Arthroplasties (with and without bone cement) for proximal femoral fractures in adults. *Cochrane Database of Systematic Reviews* 2010;(6).

6. **Parker MJ, Cawley S**. Cemented or uncemented hemiarthroplasty for displaced intracapsular fractures of the hip: A randomized trial of 400 patients. *Bone and Joint Journal* [Internet] British Editorial Society of Bone and Joint Surgery, 2020 [cited 24 May 2022];102 B(1):11–16.

7. **Fernandez MA, Achten J, Parsons N, Griffin XL, Png M-E, Gould J, et al.** Cemented or Uncemented Hemiarthroplasty for Intracapsular Hip Fracture. *The New England Journal of Medicine* 2022;386(6).

8. **Santini S, Rebeccato A, Bolgan I, Turi G**. Hip fractures in elderly patients treated with bipolar hemiarthroplasty: comparison between cemented and cementless implants. *Journal of Orthopaedics and Traumatology* 2005;6(2):80–7.

9. **Blythe R, O'Gorman P, Crawford R, Feenan R, Hatton A, Whitehouse S, et al.** Fixation method for hip arthroplasty stem following hip fracture: A population-level cost-effectiveness analysis. *Journal of Arthroplasty* 2020;35(6):1614–21.

10. **Fernandez MA, Achten J, Lerner RG, Mironov K, Parsons N, Dritsaki M, et al.** Randomised controlled trial comparing hydroxyapatite coated uncemented hemiarthroplasty with cemented hemiarthroplasty for the treatment of displaced intracapsular hip fractures: a protocol for the WHITE 5 study. *BMJ Open* 2019;9(12):e033957.

11. **Png M, Fernandez M, Achten J, Parsons N, McGibbon A, Gould J, et al.** Economic evaluation plan of a RCT of hydroxyapatite-coated uncemented hemiarthroplasty versus cemented hemiarthroplasty for the treatment of displaced intracapsular hip fractures: the WHiTE5 trial. *Bone and Joint Open* 2020;1(3):13–8.

12. **Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al.** Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research* 2011;20(10):1727–1736.

13. **Fernandez M, Achten J, Parsons N, Griffin X, Png M, Gould J, et al.** Cemented or uncemented hemiarthroplasty for intracapsular hip fracture. *New England Journal Medicine* 2022;In Press.

14. **National Health Service**. NHS Electronic Drug Tariff. http://www.drugtariff.nhsbsa.nhs.uk/#/00770298-DC/DC00770293/Home , (date last accessed 9 January 2020).

15. **NHS Business Services Authority**. NHS Supply Chain Catalogue. https://my.supplychain.nhs.uk/catalogue , (date last accessed 22 October 2021).

16. **National Health Service**. 2018/19 National Cost Collection Data Publication. https://www.england.nhs.uk/publication/2018-19-national-cost-collection-data-publication/ , (date last accessed 7 October 2021).

17. **Curtis L, Beecham J, Burns A**. Unit Costs of Health and Social Care. https://www.pssru.ac.uk/research/354/ , (date last accessed 23 April 2021).

18. **Png ME, Griffin XL, Costa ML, Achten J, Pinedo-Villanueva R**. Utilization and costs of formal and informal care, home adaptations, and physiotherapy among older patients with hip fracture. *Bone and Joint Research* British Editorial Society of Bone and Joint Surgery, 2020;9(5):250–257.

19. **Curtis L, Burns A**. Unit Costs of Health and Social Care 2019. https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2019/ , (date last accessed 8 April 2022).

20. **Hout B van, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, et al.** Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value in Health* 2012;15(5):708–715.

21. **National Institute for Health and Care Excellence**. Position statement on use of the EQ-5D-5L value set for England. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/eq-5d-5l , (date last accessed 14 September 2021).

22. **Dolan P**. Modeling Valuations for EuroQol Health States. *Medical Care* 1997;35:1095–1108.

23. **Drummond MF, Sculpher MJ, Torrance GW, O'Brien, Stoddart BJ and GL**. *Methods for the economic evaluation of health care programmes*. Oxford University Press, 2005.

24. **Franklin M, Hunter RM, Enrique A, Palacios J, Richards D**. Estimating Cost-Effectiveness Using Alternative Preference-Based Scores and Within-Trial Methods: Exploring the Dynamics of the Quality-Adjusted Life-Year Using the EQ-5D 5-Level Version and Recovering Quality of Life Utility Index. *Value in Health* Elsevier, 2022;

25. **Parsons N, Griffin XL, Achten J, Chesser TJ, Lamb SE, Costa ML**. Modelling and estimation of health-related quality of life after hip fracture: A re-analysis of data from a prospective cohort study. *Bone and Joint Research* 2018;7(1):1–5.

26. **Honaker J, King G, Blackwell M**. Amelia II: A Program for Missing Data. 2018.

27. **Rubin D**. *Multiple imputation for nonresponse in surveys*. New York: John Wiley & Sons, Ltd, 1987.

28. **Faria R, Gomes M, Epstein D, White IR**. A Guide to Handling Missing Data in Cost-Effectiveness Analysis Conducted Within Randomised Controlled Trials. *Pharmacoeconomics* 2014;32(12):1157–1170.

29. **White IR, Royston P, Wood AM**. Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in Medicine* John Wiley & Sons, Ltd, 2011;30(4):377–399.

30. **National Institute for Health and Care Excellence**. Guide to the methods of technology appraisal 2013. https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781 , (date last accessed 3 October 2019).

31. **Nixon R, Wonderling D, Grieve R**. How to estimate cost-effectiveness acceptability curves, confidence ellipses and incremental net benefits alongside randomised controlled trials. *Health Economics* 2010;19(3):316–33.

32. **National Institute for Health and Care Excellence**. The social care guidance manual. https://www.nice.org.uk/process/pmg10/resources/ : NICE, (date last accessed 8 April 2022).

33. **Costa ML, Griffin XL, Achten J, Metcalfe D, Judge A, Pinedo-Villanueva R, et al.** World Hip Trauma Evaluation (WHiTE): Framework for embedded comprehensive cohort studies. *BMJ Open* 2016;6(10):e011679.

34. **Williamson S, Landeiro F, McConnell T, Fulford-Smith L, Javaid MK, Judge A, et al.** Costs of fragility hip fractures globally: a systematic review and meta-regression analysis. *Osteoporosis International* 2017;28(10):2791–2800.

35. **Png M, Griffin X, Costa M, Achten J, Pinedo-Villanueva R**. Utilization and costs of formal and informal care, home adaptations, and physiotherapy among older patients with hip fracture. *Bone and Joint Research* 2020;9(5):250–7.

TABLES

Table 1. Baseline characteristics of WHiTE5 participants

	Cemented (n=610)	Uncemented (n=615)
Mean age at randomisation, years (SE)	85.0 (0.3)	84.8 (0.3)
Female (n, %)	421 (69.0)	411 (66.8)
Diabetes (n, %)	100 (16.4)	95 (15.4)
Chronic renal failure (n, %)	52 (8.5)	53 (8.6)
Regular smoker (n, %)	50 (8.2)	38 (6.2)
Alcohol use per week (n, %)		
0-7 units	494 (81.0)	515 (83.7)
8-14 units	28 (4.6)	22 (3.6)
15-21 units	10 (1.6)	9 (1.5)
More than 21 units	13 (2.1)	9 (1.5)
Mean pre-injury EQ-5D-5L utility score (SE)	0.56 (0.01)	0.54 (0.01)
Mean pre-injury EQ-5D-5L VAS score (SE)	61.9 (0.9)	62.6 (0.9)

Table 2. Unadjusted mean costs (SE) by treatment group, resource category at each time point (£, 2019-20 prices); available cases

	Cemented (n=610)		Uncemented (n=615)		Mean difference	p-value*	Bootstrap 95% CI
Baseline to discharge	**n=601**		**n=606**				
Intervention cost**	1421	(14)	2005	(25)	-584	<0.001	-642 to -528
Index hospitalisation	3278	(170)	3759	(185)	-480	0.056	-967 to 15
Discharge to 1 month	**n=467**		**n=472**				
Further treatment due to complications	34	(11)	40	(13)	-6	0.747	-41 to 28
1 month to 4 months	**n=421**		**n=416**				
Further treatment due to complications	9	(4)	20	(8)	-10	0.270	-30 to 6
Physiotherapy, NHS	91	(15)	67	(13)	24	0.244	-16 to 63
Residential care and subsequent inpatient care	6596	(506)	6415	(487)	181	0.797	-1180 to 1522
Home adaptations, council	509	(88)	441	(86)	69	0.577	-169 to 310
Formal care: full-time, council	423	(108)	532	(120)	-109	0.497	-418 to 200
Formal care: part-time, council	491	(72)	361	(57)	130	0.158	-49 to 309
Physiotherapy, private	8	(3)	5	(3)	3	0.475	-5 to 10
Home adaptations, out-of-pocket	307	(80)	205	(56)	102	0.291	-79 to 301
Formal care: part-time, out-of-pocket	342	(65)	374	(111)	-32	0.802	-305 to 202
Informal care	1172	(342)	659	(223)	513	0.209	-254 to 1361
4 months to 12 months	**n=373**		**n=363**				
Further treatment due to complications	2	(2)	6	(3)	-3	0.370	-11 to 3

* Computed using t-tests; ** Intervention cost is the sum of implant (which includes two bone cement mixes and bone cement mixing disposables) and theatre time

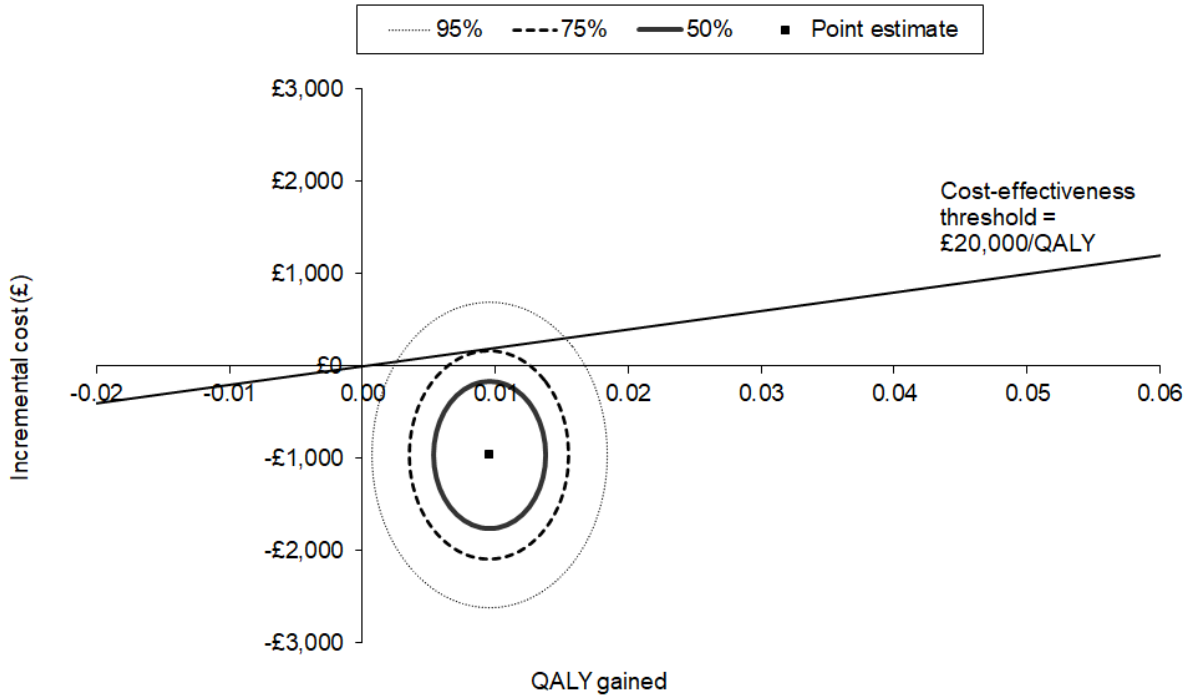
Table 3. Incremental cost effectiveness of cemented versus uncemented implant

	Incremental cost, £ (95% CI)		Incremental QALY (95% CI)		ICER, £/QALY	Probability of cemented implant being cost-effectiveness at specified cost-effectiveness threshold		
						£15,000	£20,000	£30,000
Base case analysis								
Baseline to 4 months, NHS and PSS perspective: imputed costs and QALYs, covariate adjusted	-961	(-2292 to 370)	0.010	(0.002 to 0.017)	-100,717 (SE quadrant)	0.95	0.95	0.97
Sensitivity analysis								
(1) Baseline to 4 months, Societal perspective: imputed costs and QALYs, covariate adjusted	-531	(-2143 to 1080)	0.010	(0.002 to 0.017)	-55,662 (SE quadrant)	0.79	0.81	0.84
(2) Baseline to 4 months, NHS and PSS perspective: complete case costs and QALYs, covariate adjusted	-214	(-1883 to 1456)	0.012	(0.001 to 0.022)	-18,046 (SE quadrant)	0.68	0.70	0.74
(3) Baseline to 12 months, NHS and PSS perspective: imputed costs and QALYs, covariate adjusted	-964	(-2295 to 368)	0.024	(0.001 to 0.048)	-39,785 (SE quadrant)	0.97	0.98	0.99

PSS: personal social services, QALY: Quality-adjusted life-years, SE: south-east

FIGURES

Figure 1. Base-case analysis of cemented versus uncemented implant: Confidence ellipse on the cost-effectiveness plane



SUPPLEMENTARY MATERIALS

Supplementary Tables

Supplementary Table 1. Unit cost of resource items (£, 2019-20 prices)

Resource item	Unit	Unit cost	Source
Theatre time*	hour	620.43	Foundation Trust Network[1]
Implant			
Accolade II (Stryker, Newbury, UK)	each	1687.99	NHS Supply Chain Catalogue[2]
Articul/Eze head (DePuy, Leeds, UK)	each	68.40	NHS Supply Chain Catalogue[2]
Bipolar head (Stryker, Newbury, UK)	each	312.48	NHS Supply Chain Catalogue[2]
Bipolar head (DePuy, Leeds, UK)	each	439.20	NHS Supply Chain Catalogue[2]
Cathcart head (DePuy, Leeds, UK)	each	412.80	NHS Supply Chain Catalogue[2]
Corail stem (DePuy, Leeds, UK)	each	686.40	NHS Supply Chain Catalogue[2]
Corin head (DePuy, Leeds, UK)	each	427.20	NHS Supply Chain Catalogue[2]
Exeter trauma stem (Stryker, Newbury, UK)	each	382.20	NHS Supply Chain Catalogue[2]
Exeter v40 stem (Stryker, Newbury, UK	each	670.32	NHS Supply Chain Catalogue[2]
Metafix stem (Corin Medical, Cirencester, UK)	each	1584.00	NHS Supply Chain Catalogue[2]
Thompson (DePuy, Leeds, UK)	each	229.32	NHS Supply Chain Catalogue[2]
Unitrax head (Stryker, Newbury, UK)	each	267.12	NHS Supply Chain Catalogue[2]
Average price for most common cemented implants*	each	440.79	NICE, 2017[3]
Average price for most common uncemented implants*	each	906.18	NICE, 2017[3]
Bone cement*	each	51.67	NICE, 2017[3]
Bone cement mixing disposables*	each	40.19	NICE, 2017[3]
Hospital stay			
Orthopaedics: Hip	day	179.39	NHS Reference Costs 2019/20[4]
Day case	day	341.29	NHS Reference Costs 2019/20[4]
Excess bed day*	day	361.82	NHS Reference Costs 2017/18[5]
Rehabilitation care	day	406.13	NHS Reference Costs 2019/20[4]
Acute care	day	418.99	NHS Reference Costs 2019/20[4]
Further treatment due to wound infections/ complications			
Antibiotics	dose	6.70	NHS Electronic Drug Tariff[6]
Surgery			
Reduction of dislocation	day	1091.93	NHS Reference Costs 2019/20[4]
Washout or debridement	day	1062.35	NHS Reference Costs 2019/20[4]
Implant removal	day	1091.93	NHS Reference Costs 2019/20[4]
Revision of internal fixation	day	761.32	NHS Reference Costs 2019/20[4]
Revision of arthroplasty	day	994.65	NHS Reference Costs 2019/20[4]
Conversion to hemiarthroplasty	day	870.80	NHS Reference Costs 2019/20[4]
Conversion to total hip replacement	day	761.32	NHS Reference Costs 2019/20[4]
Excision arthroplasty	day	1091.93	NHS Reference Costs 2019/20[4]
Surgery for peri-prosthetic fracture	day	1091.93	NHS Reference Costs 2019/20[4]

Resource item	Unit	Unit cost	Source
Outpatient care			
Physiotherapy	hour	38.00	PSSRU 2020[7]
Community care			
Physiotherapy	hour	36.00	PSSRU 2020[7]
Personal social services			
Residential home	week	712.00	PSSRU 2020[7]
Nursing home	week	856.00	PSSRU 2020[7]
Full-time paid care	hour	20.69	UKHCA, 2020[8]
Part-time paid care	hour	30.00	PSSRU 2020[7]
Home adaptations			
Bathroom*	each	8156.02	Garrett, 2016[9]
Bedroom	each	47.00	PSSRU 2020[7]
Fixed hoist*	each	3402.84	Garrett, 2016[9]
Grab rails	each	33.00	PSSRU 2020[7]
Level-access shower	each	5599.00	PSSRU 2020[7]
Outdoor rails	each	49.00	PSSRU 2020[7]
Ramp	each	370.00	PSSRU 2020[7]
Stair lift	each	2256.00	PSSRU 2020[7]
Steps	each	563.00	PSSRU 2020[7]
Toilet*	each	2700.67	Garrett, 2016[9]
Informal care			
Median wage: all	week	586.00	Office for National Statistics[10]
Median wage: women*	hour	20.53	Imperial College London[11]
Median wage: men*	hour	22.32	Imperial College London[11]

* Unit cost has been inflated to 2019/20 prices

Supplementary Table 2. Completion rates of health resource use data

	Cemented (n=610)		Uncemented (n=615)	
	n	(%)	n	(%)
Baseline to 4 months (NHS and PSS perspective)				
Health resource use only	417	(68.4)	414	(67.3)
Health resource use and EQ5D	334	(54.8)	313	(50.9)
Baseline	**601**	**(98.5)**	**606**	**(98.5)**
Implant type	590	(96.7)	596	(96.9)
Surgery duration	572	(93.8)	578	(94.0)
Index hospitalisation	585	(95.9)	596	(96.9)
1 month	**467**	**(76.6)**	**472**	**(76.7)**
Further treatment due to complications	440	(72.1)	439	(71.4)
4 months	**421**	**(69.0)**	**416**	**(67.6)**
Further treatment due to complications	400	(65.6)	388	(63.1)
Physiotherapy: NHS	468	(76.7)	470	(76.4)
Physiotherapy: Private	468	(76.7)	470	(76.4)
Residential care and subsequent inpatient care	462	(75.7)	459	(74.6)
Home adaptations	380	(62.3)	366	(59.5)
Formal care: full-time	380	(62.3)	367	(59.7)
Formal care: part-time	380	(62.3)	366	(59.5)
Informal care	467	(76.6)	469	(76.3)
12 months	**373**	**(61.1)**	**363**	**(59.0)**
Further treatment due to complications	342	(56.1)	334	(54.3)

Supplementary Table 3. Health resource utilisation rate at each time point by treatment group

	Cemented (n=610)		Uncemented (n=615)		p-value	Bootstrap 95% CI
Baseline to discharge	**n=601**		**n=606**			
Index hospitalisation, mean number of days (SE)	14.2	(0.5)	15.7	(0.6)	0.050	-3.0 to -0.006
Discharge to 1 month	**n=467**		**n=472**			
Further treatment due to complications, number (%)*						
Surgery	9	(1.9)	11	(2.3)	0.901	
Antibiotics	17	(3.6)	11	(2.3)	0.254	
1 month to 4 months	**n=421**		**n=416**			
Further treatment due to complications, number (%)*						
Surgery	3	(0.7)	6	(1.4)	0.909	
Antibiotics	10	(2.4)	6	(1.4)	0.347	
Physiotherapy, mean number of sessions (SE)						
Outpatient	2.9	(0.5)	2.3	(0.5)	0.312	-0.6 to 2.0
Private	0.3	(0.1)	0.2	(0.1)	0.520	-0.2 to 0.3
Residential care and subsequent inpatient care, mean number of weeks (SE)						
Residential home	2.8	(0.3)	3.6	(0.4)	0.095	-1.7 to 0.1
Nursing home	2.4	(0.3)	2.2	(0.3)	0.536	-0.5 to 1.1
Acute ward	1.1	(0.2)	1.0	(0.2)	0.604	-0.4 to 0.6
Rehabilitation ward	0.3	(0.1)	0.4	(0.1)	0.637	-0.4 to 0.2

	Cemented (n=610)		Uncemented (n=615)		p-value	Bootstrap 95% CI
Home adaptations, number (%)*						
Bathroom	27	(6.4)	24	(5.8)	0.674	
Fixed hoist	3	(0.7)	1	(0.2)	0.317	
Grab rails	71	(16.9)	73	(17.5)	0.868	
Level-access shower	13	(3.1)	7	(1.7)	0.180	
Outdoor rails	21	(5.0)	15	(3.6)	0.317	
Ramp	9	(2.1)	6	(1.4)	0.439	
Stair lift	18	(4.3)	15	(3.6)	0.602	
Toilet	14	(3.3)	12	(2.9)	0.695	
Step	7	(1.7)	3	(0.7)	0.206	
Bedroom	8	(1.9)	10	(2.4)	0.637	
Formal care: full-time, number (%)*	15	(3.6)	19	(4.6)	0.420	
Formal care: part-time, mean hours per week (SE)	2.9	(0.3)	3.0	(0.4)	0.919	-1.0 to 0.8
Formal care: part-time, mean number of weeks (SE)	3.8	(0.3)	3.3	(0.3)	0.216	-0.3 to 1.5
Informal care, mean hours per week (SE)	42.8	(3.6)	38.6	(3.5)	0.406	-5.7 to 13.9
Informal care, mean number of weeks (SE)	8.5	(0.4)	7.3	(0.4)	0.050	0 to 2.4
4 months to 12 months	**n=373**		**n=363**			
Further treatment due to complications, number (%)*						
Surgery	1	(0.3)	2	(0.6)	0.181	

	Cemented (n=610)		Uncemented (n=615)		p-value	Bootstrap 95% CI
Antibiotics	3	(0.8)	3	(0.8)	0.932	

* p-values were computed using t-tests except for the ones indicated here which used chi-square tests. SE: Standard error

Supplementary Figures

Figure 1. Base-case analysis of cemented versus uncemented implant: Net monetary benefit

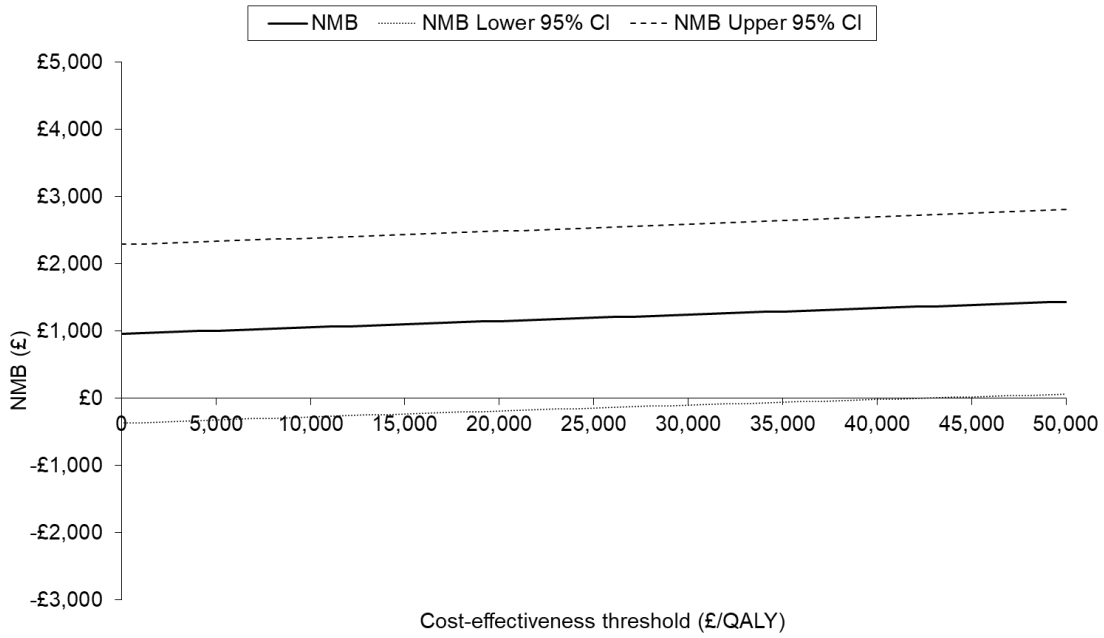


Figure 2. Base-case analysis of cemented versus uncemented implant: Cost-effectiveness acceptability curve

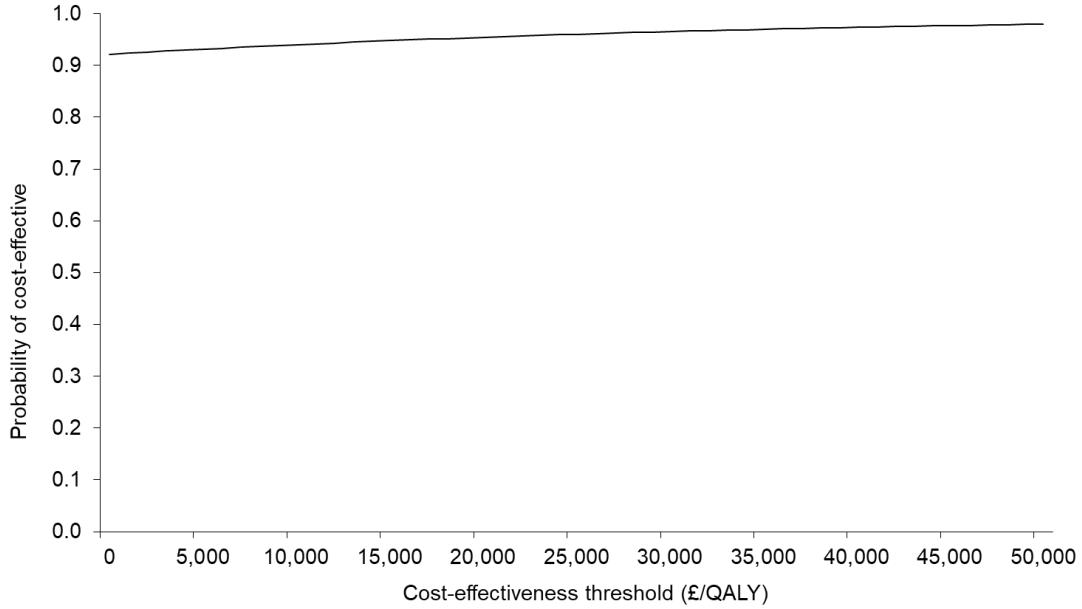


Figure 3. Sensitivity analysis (societal perspective) of cemented versus uncemented implant: Confidence ellipse on the cost-effectiveness plane

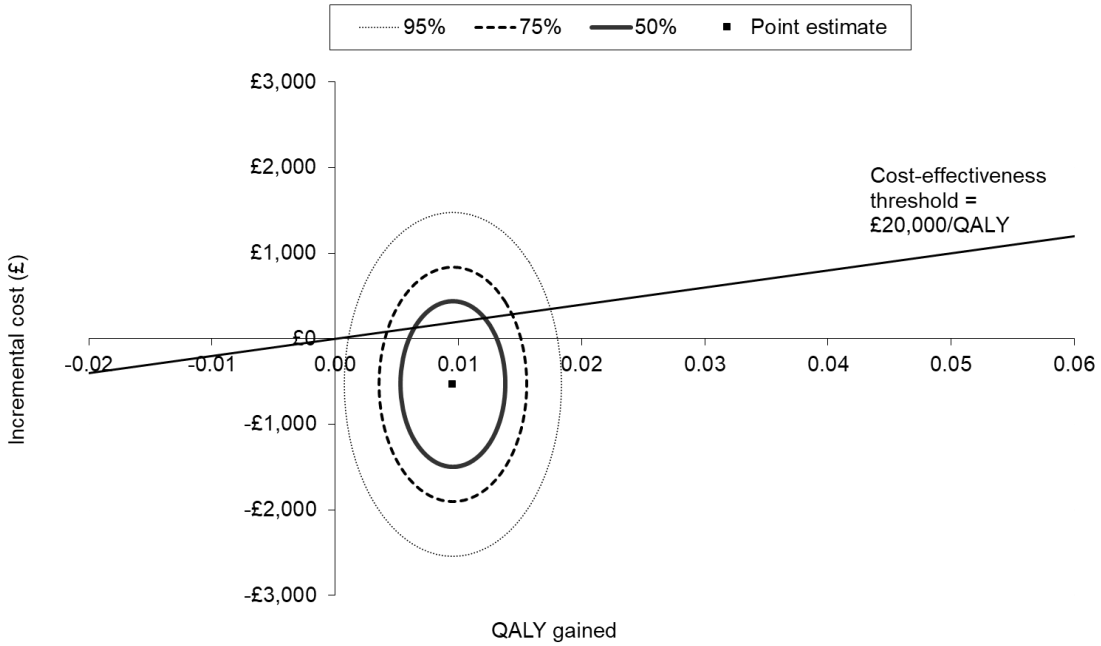


Figure 4. Sensitivity analysis (societal perspective) of cemented versus uncemented implant: Net monetary benefit

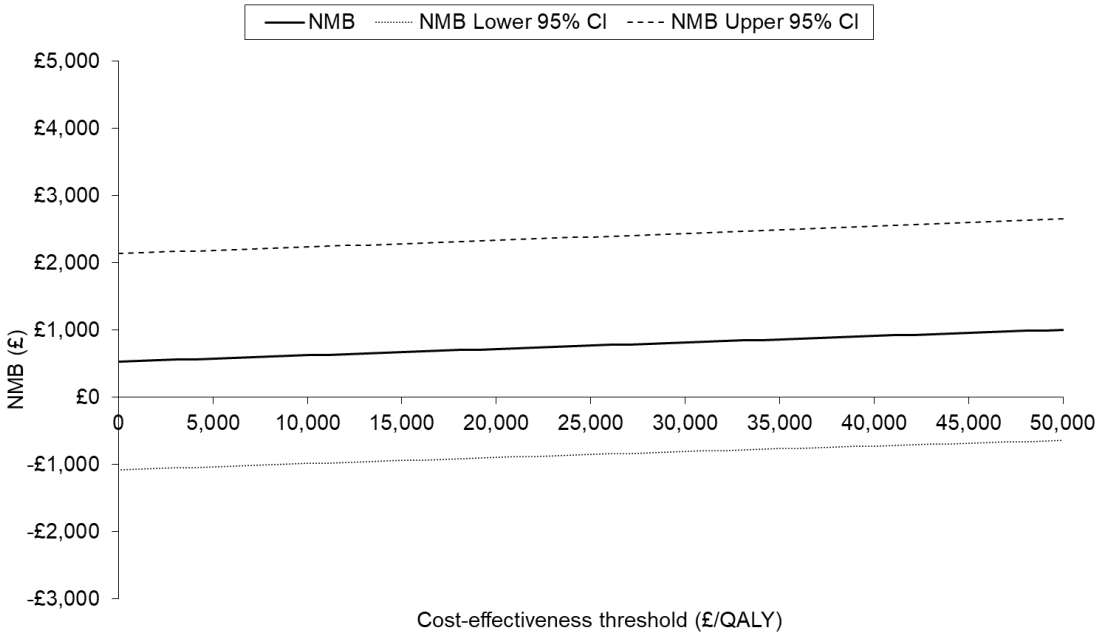


Figure 5. Sensitivity analysis (societal perspective) of cemented versus uncemented implant: Cost-effectiveness acceptability curve

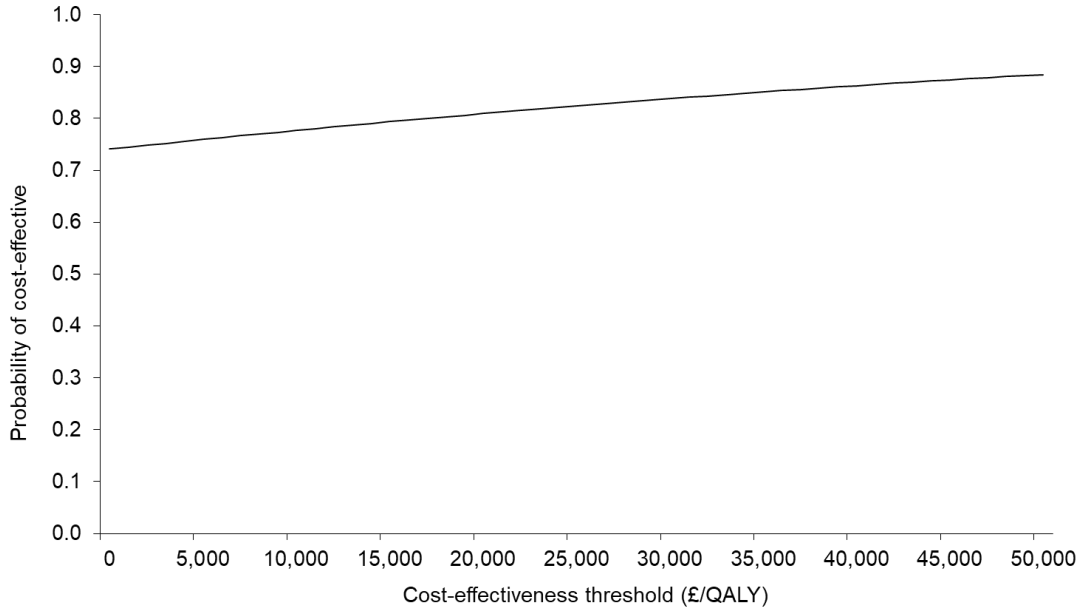


Figure 6. Sensitivity analysis (complete case) of cemented versus uncemented implant: Confidence ellipse on the cost-effectiveness plane

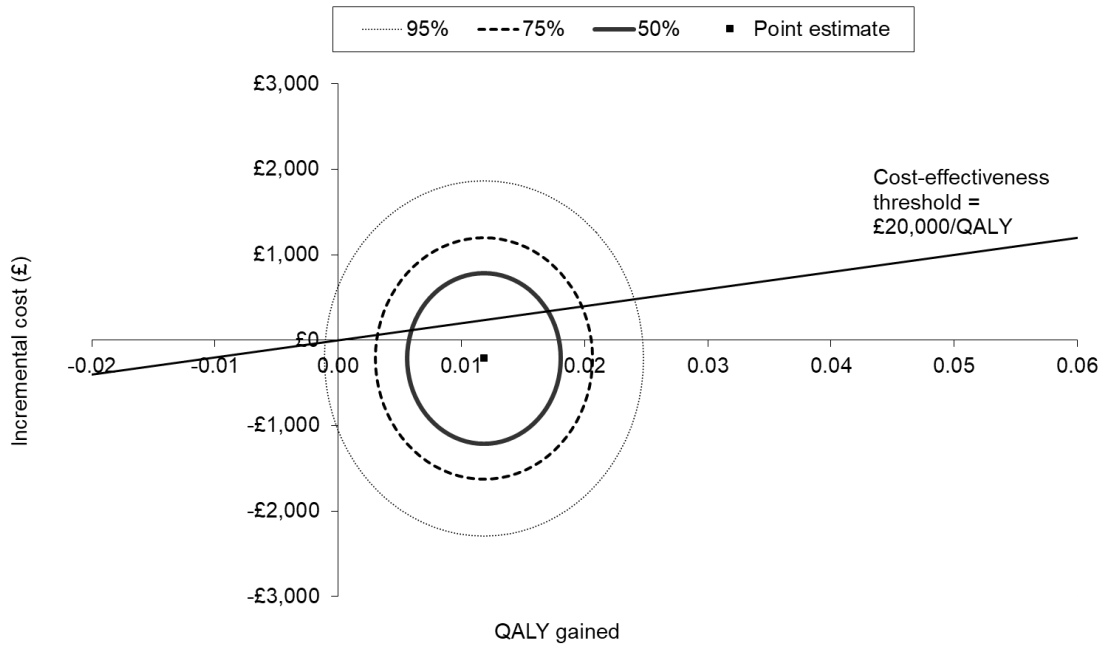


Figure 7. Sensitivity analysis (complete case) of cemented versus uncemented implant: Net monetary benefit

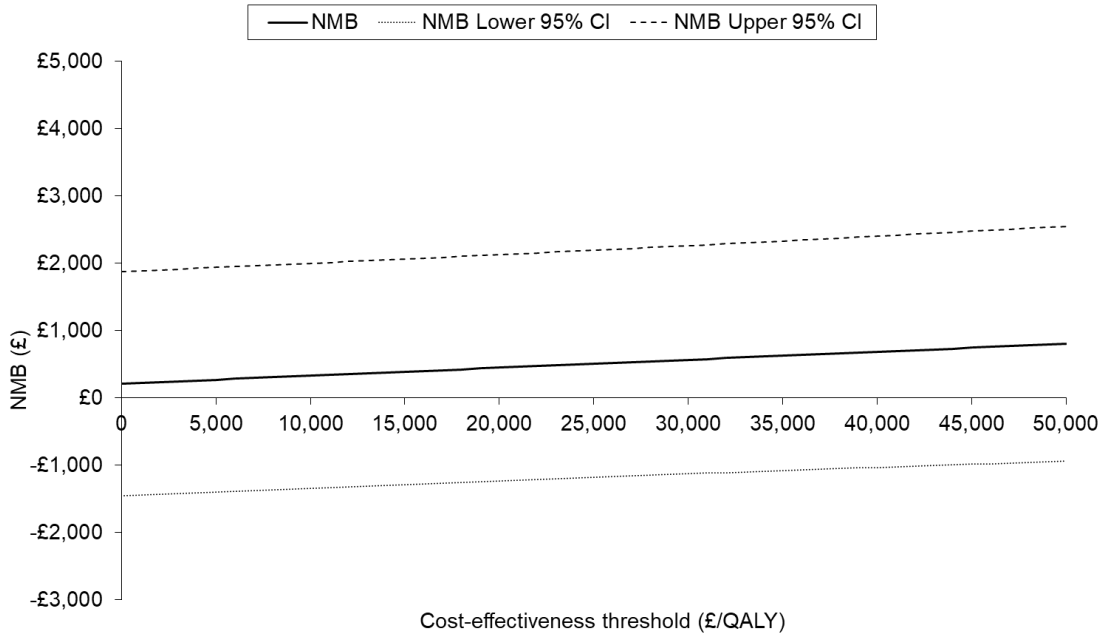


Figure 8. Sensitivity analysis (complete case) of cemented versus uncemented implant: Cost-effectiveness acceptability curve

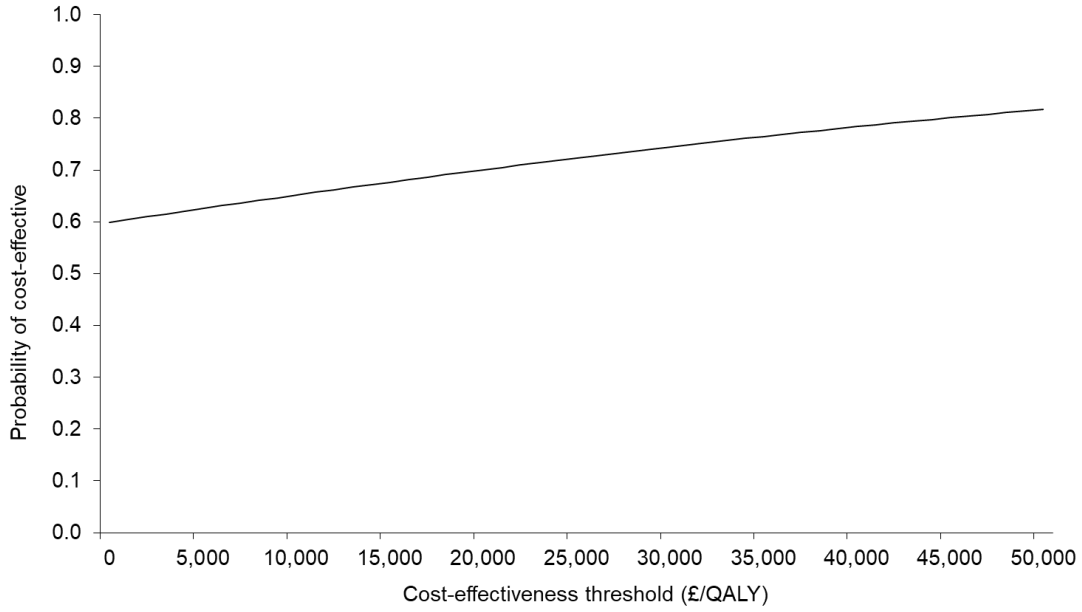


Figure 9. Sensitivity analysis (baseline to 12 months) of cemented versus uncemented implant: Confidence ellipse on the cost-effectiveness plane

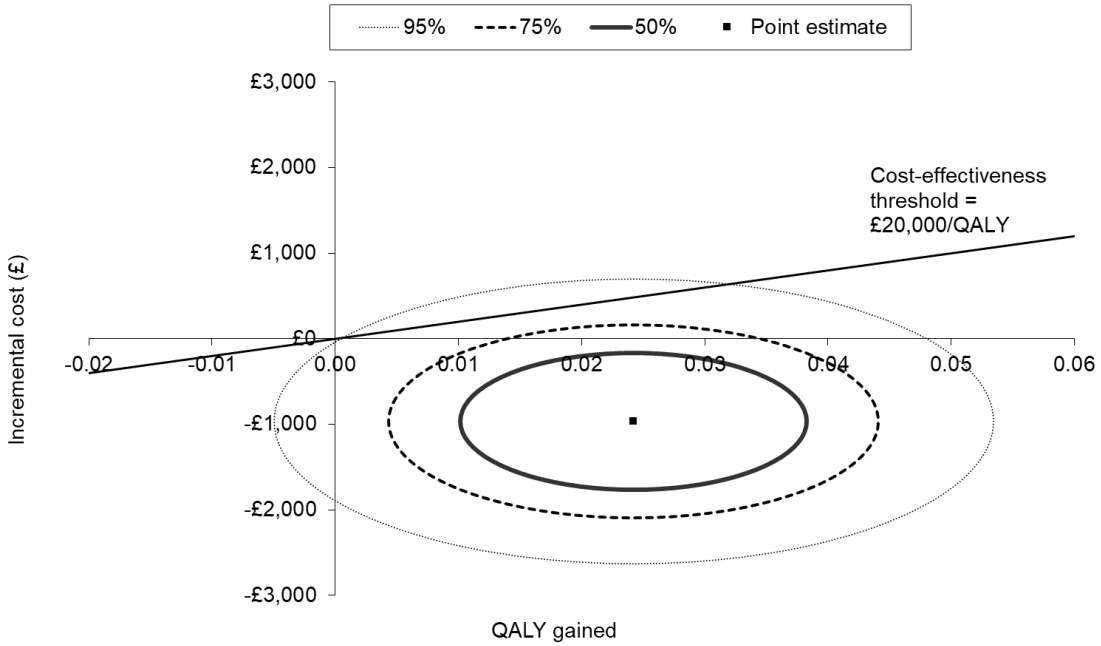


Figure 10. Sensitivity analysis (baseline to 12 months) of cemented versus uncemented implant: Net monetary benefit

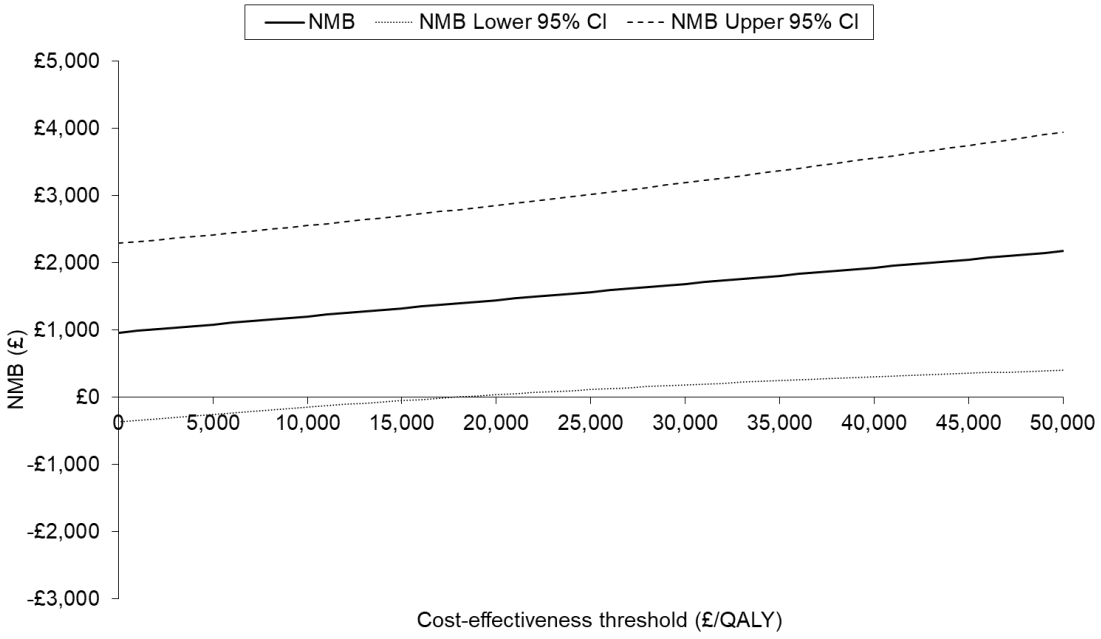
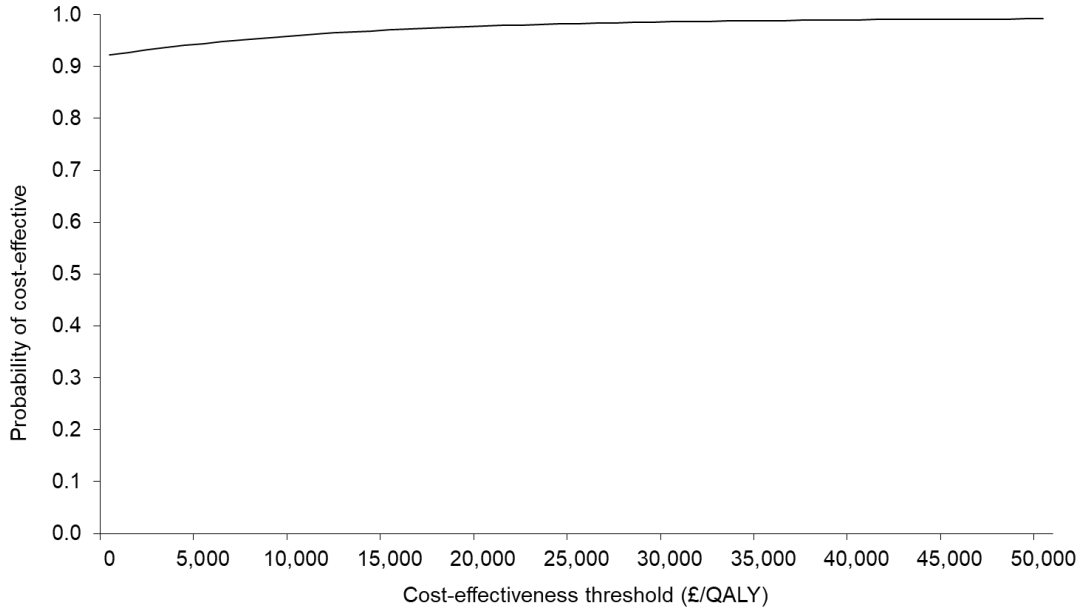


Figure 11. Sensitivity analysis (baseline to 12 months) of cemented versus uncemented implant: Cost-effectiveness acceptability curve



References

1. **Foundation Trust Network**. Operating theatres - maximising a valuable resource. https://nhsproviders.org/media/1128/operating-theatres-final.pdf , (date last accessed 24 October 2019).

2. **NHS Business Services Authority**. NHS Supply Chain Catalogue. https://my.supplychain.nhs.uk/catalogue , (date last accessed 22 October 2021).

3. **National Clinical Guideline Centre**. The management of hip fracture in adults. https://www.nice.org.uk/guidance/cg124/evidence/full-guideline-pdf-183081997 , (date last accessed 7 October 2021).

4. **National Health Service**. 2018/19 National Cost Collection Data Publication. https://www.england.nhs.uk/publication/2018-19-national-cost-collection-data-publication/ , (date last accessed 7 October 2021).

5. **National Health Service**. Archived Reference Costs. https://improvement.nhs.uk/resources/reference-costs/ , (date last accessed 24 March 2020).

6. **National Health Service**. NHS Electronic Drug Tariff. http://www.drugtariff.nhsbsa.nhs.uk/#/00770298-DC/DC00770293/Home , (date last accessed 9 January 2020).

7. **Curtis L, Beecham J, Burns A**. Unit Costs of Health and Social Care. https://www.pssru.ac.uk/research/354/ , (date last accessed 23 April 2021).

8. **United Kingdom Homecare Association**. Getting the price right: Calculating the cost of homecare in 2019. https://www.ukhca.co.uk/CostOfHomecare2019.aspx , (date last accessed 19 November 2019).

9. **Garrett H, Roys M, Burris S, Nicol S**. *The cost-benefit to the NHS arising from preventative housing interventions*. BRE FB 82. Bracknell: IHS BRE Press, 2016.

10. **Office for National Statistics**. Employee earnings in the UK: 2020. https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2020 , (date last accessed 7 October 2021).

11. **Imperial College London**. 2020 Gender Pay Gap Report. https://www.imperial.ac.uk/human-resources/pay-and-pensions/pay-initiatives/2020-gender-pay-gap-report/ , (date last accessed 7 October 2021).