

Title: Protocol for Follow up of Hip arthroplasty long term: Effect on revision (WHISTLER study)

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Abstract

Total hip arthroplasty (THA) is highly successful for reducing pain and improving function, providing health related quality of life benefit. Demand for THA is increasing with associated increase in revision hip surgery. Hip arthroplasty surveillance (long term follow up) can identify asymptotically failing THA to prepare for revision surgery, reducing potential for complications or complexity of surgery. But, it is unknown whether the surveillance of THA can be shown to improve the patient outcomes or reduce costs around revision surgery. With the current need to reduce unnecessary health consultations and to show the economic advantages of any service, the purpose of this study is to consider the relative effectiveness of hip arthroplasty surveillance on revision hip arthroplasty.

This is a single centre, observational study in which consecutive patients undergoing aseptic revision of THA over twelve months in a large orthopaedic unit will be considered for participation. Primary outcome measures will be change in each of three valid patient reported scores from pre-operatively to 12 months post-surgery. Secondary outcomes will be the costs of treatment calculated using data obtained from the participants' hospital records and a self-report questionnaire

An exploratory approach will be used to investigate the effect of surveillance on the outcomes of interest. A linear mixed method model will be used to study the change in scores between baseline and 12months. The economic evaluation will be a cost-utility analysis, which compares the value of alternative interventions by attaching costs to the quality adjusted life years produced by each intervention.

250 words

Protocol for the Follow up of hip arthroplasty long term: Effect on revision (WHISTLER study)

Introduction

Total hip arthroplasty has been shown to be a surgical procedure which decreases pain and improves function for the patient, and has significant health related quality of life benefit when compared with other procedures (Patel, Pavlou et al. 2015). The National Joint Registry for England, Wales and Northern Ireland shows a steady increase in the number of procedures undertaken each year (National Joint Registry 2016). Revision of a hip replacement is necessary when the primary arthroplasty fails, which can be for one of a number of reasons. Early failure of a joint replacement may be the result of infection in the joint (septic) or an aseptic cause such as dislocation, component failure or adverse response of the host body to the implanted material, particularly in metal on metal articulations. These conditions will be accompanied by symptoms that will prompt the patient to seek medical help. Mid-term and late failure occur five years or more from the primary surgery and may be due to late infection, which will be accompanied by symptoms, but more often are aseptic in nature and asymptomatic until the later stages. The causes include debonding of the components from the host bone with subsequent instability, or wear of the components with production of wear debris. This wear debris can disrupt bone metabolism leading to destruction of bone around the hip replacement (osteolysis), predisposing the patient to periprosthetic fracture (Harris 2004, Katz, Wright et al. 2014).

As the demand for hip arthroplasty increases due to presentation of patients at a younger age, increased life expectancy and a prevalence of obesity, the burden of revision is predicted to rise 31% by 2030 (Patel, Pavlou et al. 2015). This is associated with significant costs as revision surgery is more expensive to the health service than a primary procedure, the cost being determined by the indication for the surgery. In 2014, 4% of revision hip surgeries in England, Wales and Northern Ireland were undertaken for infection and 57% for aseptic loosening or lysis (National Joint Registry 2016). Vanhegan et al (2012) calculated that the average cost of revision for infection was £21,937, for peri-prosthetic fracture was £18,185 and for aseptic loosening was £11,897 (Vanhegan, Malik et al. 2012). Although peri-prosthetic fracture can be classified as an aseptic revision, the cost of revision for peri-prosthetic fracture is one third higher than for aseptic loosening without fracture due to the technical demands, the additional components required and the associated high rate of complications which may affect recovery (da Assunção, Pollard et al. 2015).

The advantage of hip arthroplasty surveillance (long term follow up) is that it provides screening by specialists who can identify failing joints. Failure of hip replacements due to wear and loosening is radiologically evident but often asymptomatic, meaning that the patient is unaware of change until significant bone loss has occurred. Routine surveillance offers the opportunity to identify asymptotically failing hip replacements and plan for revision surgery, thus reducing the potential for peri-prosthetic fracture or other complications. In addition to any cost saving at the time of surgery, this is thought to benefit the patient and

the orthopaedic surgeon, who would otherwise be faced with a more complex reconstructive process and rehabilitation (Howard 2009).

Long term follow up of hip arthroplasty is recommended by many in the orthopaedic community in order to monitor in vivo responses and to identify failure (British Orthopaedic Association, British Hip Society et al. 2014, Hart, Sabah et al. 2015). Current guidelines include the use of the ODEP rating, which is a measure of the revision rating of a component based on data supplied by the manufacturing company (Orthopaedic Data Evaluation Panel 2015). There is a letter and a number, the former denoting the strength of the evidence and the latter the number of years to which it relates. For instance, an acetabular cup with an ODEP 10A rating means that evidence exists that at least 90% of that specific component are still in situ (in the patient) at 10 years. For a component with an ODEP rating of 10A, it is recommended that a follow up is offered by the orthopaedic team at one year, seven years and three yearly thereafter, with review of x-ray images by a health professional with the required specialist knowledge. For a component that has not achieved the 10A rating, it is recommended that there is annual follow up for the first five years, then two yearly up to ten years and three yearly thereafter (British Orthopaedic Association, British Hip Society et al. 2014).

The interpretation of the guidelines for follow up does, however, have some complications. A hip replacement incorporates both an acetabular and a femoral component, and each is rated independently. The latest report from the National Joint Registry for England, Wales and Northern Ireland shows that, of the components used in 2014, 89% of cemented femoral stems, 69% of cementless femoral stems and 43% of acetabular cups had a 10A rating. But, the same report shows that, in 13% of hip replacements, the surgeon had used a femoral component from one manufacturer and an acetabular component from another manufacturer, known as 'mix and match' (National Joint Registry 2016). Finally, the results of a recent survey suggest that there is a variety of follow up practice across the UK with only 43% of orthopaedic units offering any form of follow up five years after primary surgery (Smith 2014).

In the present economic climate, there is a need to reduce unnecessary health consultations and a growing requirement to show the economic advantage of any service that is provided in order to develop a 'leaner' health care system (Corbacho 2015, Fillingham 2008). Many members of the orthopaedic community consider that some follow up is of value for hip arthroplasty patients although this is threatened by lack of funding. However, it is still unknown whether or not routine surveillance of this group of patients has any benefit through improving the patient outcomes at the time of revision surgery or through reduction of the associated costs. The purpose of this study is to consider the relative effectiveness of hip arthroplasty surveillance: *Does revision with surveillance have a different outcome to revision without surveillance?*

Objectives

The primary objective is to investigate if there is a difference in the health related quality of life after hip revision surgery between patients diagnosed through routine surveillance and those who have not had any form of long term follow up.

The secondary objective is to determine if there is a difference in the costs of revision hip surgery and early postoperative care between patients diagnosed through routine surveillance and those who have not had any form of long term follow up.

Materials and methods

Study design and duration

This study is a designed to inform a larger study at a later date and will take place at a single centre. It will be an observational study over a twelve month period to compare the relative effectiveness of surveillance or lack of surveillance on revision hip arthroplasty.

Participants

The criteria that will be applied to the selection of possible participants are shown in Table 1.

Table 1. Criteria for selection of study participants

Inclusion	Exclusion
<ul style="list-style-type: none">Adults listed for revision of a primary hip arthroplastyRevision of acetabular or femoral or both components of a hip arthroplasty	<ul style="list-style-type: none">Less than five years from primary operationRevision for infection of the hip arthroplastyUnable to complete postal questionnaires e.g. dementia

Comparators

Revision with surveillance

For the purposes of this study, hip arthroplasty surveillance will be considered as planned orthopaedic review of the hip implant that now requires revision surgery. The review(s) will have taken place at any time in the period that commences five years after the primary operation and continues to the present day, and will include an x-ray image of the affected hip. As there are currently a variety of review intervals in use, all intervals will be included (Smith 2014). The patients in this group will be considered as those **with** surveillance.

Revision without surveillance

The comparator group will be those patients who are scheduled for revision surgery following an emergency admission, or following a GP referral for problems with the hip implant. They will be considered to be those with no orthopaedic long term follow up of their hip arthroplasty and, therefore, **without** surveillance.

In some units, patients are selected for review based on their type of implant or associated research funding. It is beyond the scope of this study to consider sub groups of selective follow up, and a pragmatic approach will be adopted of surveillance versus no surveillance.

Recruitment

Patients will be recruited to this study by one of two routes (see Figure 1). The first is for those whose revision hip surgery is planned in advance. The date of surgery will be obtained from Southmead Hospital approximately one month in advance of the date of operation, and the medical record will be screened for inclusion criteria by the principal investigator. Any patient that is deemed to be eligible will subsequently be sent an invitation letter and information leaflet to read at home. When they attend the pre-operative assessment clinic, they will be asked about participation in the study by a designated, named research nurse. If they consent to participate, they will be given the first questionnaire at that time and asked to complete and return it prior to their surgery using the pre-paid envelope which will be supplied.

The second route of recruitment is for those patients who are in hospital and awaiting revision hip surgery following an emergency admission. The names of prospective participants will be obtained by the designated research nurse through liaison with co-researchers who are present in the daily trauma meeting, and she/he will review the medical records (present on the ward) for eligibility. No information will be extracted or recorded if the patient is ineligible. She/he will visit any eligible patient on the ward to describe the study and to leave an information leaflet with the patient. She/he will return at a pre-agreed time to take consent if the patient is willing and able to participate. The pre-operative questionnaire will be completed by the patient any time preceding their surgery, either in paper form with return by pre-paid envelope or by the research nurse recording their verbal responses to the questionnaire. The patient will be offered this option to minimise the burden of participation while awaiting surgery.

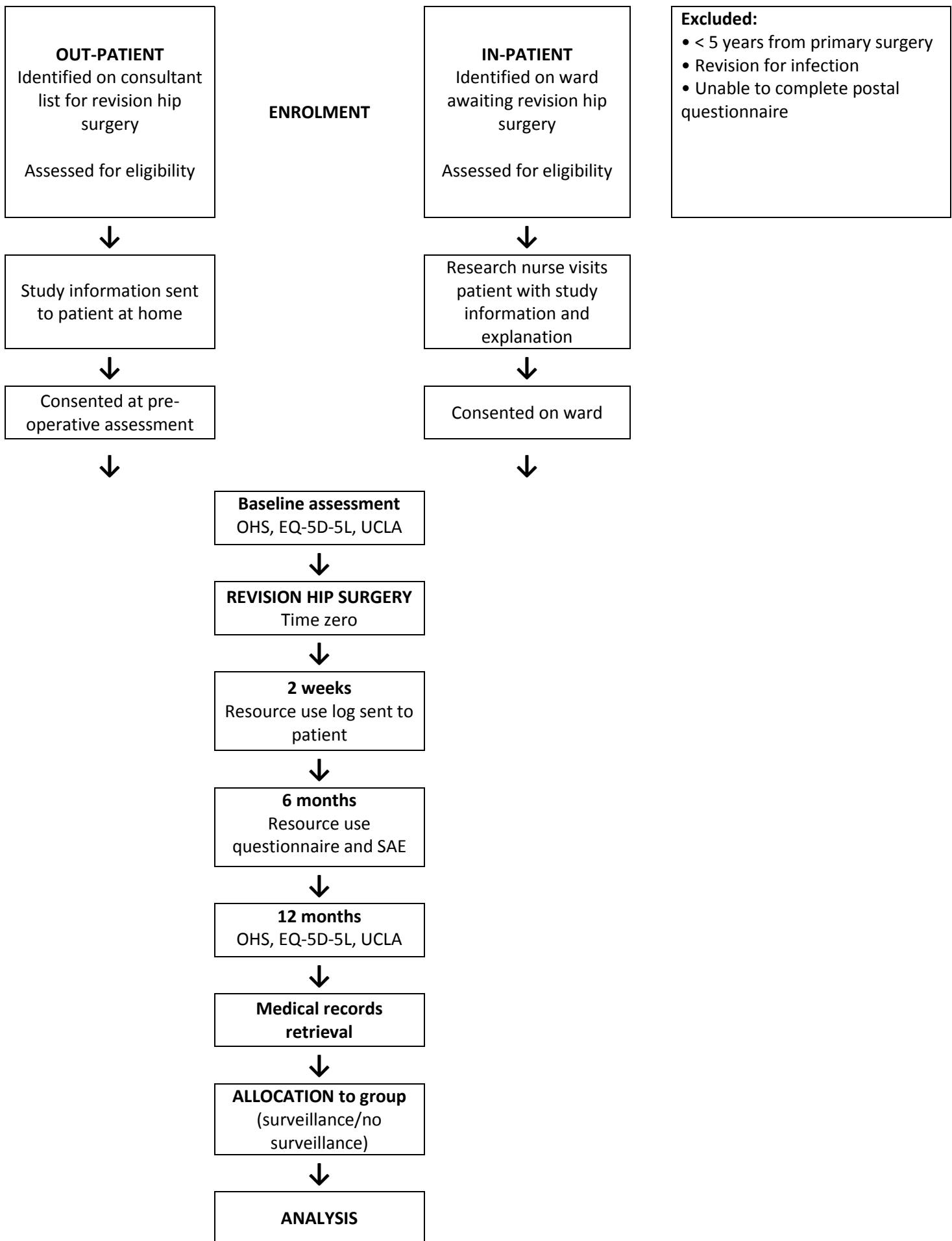


Figure 1. Participant flow through Whistler study

Key: OHS = Oxford Hip Score, EQ-5D = EuroQol 5D-5L health questionnaire, UCLA = University of Southern California at Los Angeles activity score

Assignment

The assignment of each patient to one of the two groups will be retrospective, twelve months after their revision hip surgery, and will be based on their medical records. Any uncertainty will be clarified directly with the patient by the principal investigator.

Intervention

The intervention will consist of questionnaires administered at three time points. The first will be a pre-operative questionnaire; the second will be a health resource use questionnaire at six months post-operatively; the final questionnaire, a repeat of the first questionnaire, will be at 12 months post-operatively.

At the time of completion of the pre-operative questionnaire, details of the participant's name, age, diagnosis and comorbidities will be collected and stored electronically in a spreadsheet within a hospital trust electronic clinical folder. Each participant will be allocated a unique number which will be used for further data collection. Questionnaire response will be recorded against the unique number of each participant on an encrypted laptop computer. No patient identifiable information will leave the hospital site at any time. If any questionnaire is not returned by a participant, a reminder letter will be issued two weeks after the anticipated return date of the questionnaire. If there is still no response, an attempt will be made to telephone the patient to request the return of the questionnaire.

The final data will be collected from participant's medical records 12 months after the revision hip surgery and will take place on hospital premises. These details include the surgical procedure, any additional in-patient costs, length of stay and out-patient visits before and after the revision surgery. The medical records will be retrieved by an NHS administrator and reviewed by the primary researcher or research nurse. The unique identifier of each participant will be used to record the data on an encrypted computer.

Concomitant care

The medical care of the patient will be unaffected by this study which is purely observational.

Study outcomes

Primary outcome measures

Primary outcome measures will be the change on each of three valid scores, measuring pain and function, activity and quality of life, from pre-operatively to 12 months post-surgery.

The Oxford Hip Score (OHS) is a widely used score consisting of twelve questions (score range from zero which is poor to 48, best outcome) and has been shown to be valid and reliable for use in revision hip surgery (Dawson, Fitzpatrick et al. 2001). Pain and

function (six questions for each) will be analysed separately as it has been shown to be reliable when used in this way and it has been suggested that pain may be more sensitive to change than other measures in the two years following revision hip arthroplasty (Harris, Price et al. 2014, Zampelis, Ornstein et al. 2014).

The EuroQol-5D (EQ-5D-5L) is a widely used score of general health consisting of five questions with five levels each and a visual analogue scale to record health state (EuroQol Group 2010). It can be used to calculate the quality adjusted life years for a given condition and is widely used with hip arthroplasty as part of the PROMS programme from the Health and Social Care Information centre (Health and Social Care Information Centre 2013). The five level score is converted to a value between -1.0 to 1.0 where zero represents a state equivalent to death and 1.0 equates to perfect health. There is a reference set of data for a UK population which is useful for interpretation of results and calculation of cost.

The University of Southern California at Los Angeles (UCLA) activity score will be used to measure the change in activity level of each patient. It has been shown to be a simple and reliable measure to use at the time of hip arthroplasty and is freely available for use (Naal, Impellizzeri et al. 2009). It consists of ten levels of activity described in words and the patient selects one level to best describe their current state (range from one to 10 with a high value representing a more active lifestyle).

In order to avoid undue patient burden, these questionnaires will not be repeated six months post-surgery as the patient will be asked to complete postal versions of two of them (OHS and EQ-5D-3L) at that time for the national PROMS programme. Our preparatory work with patients and the public has highlighted that a repeat of these questionnaires for study purposes at six months often causes confusion and patient overload.

Permission to use each of the scores was obtained from the appropriate organisation, prior to commencement of the study.

Secondary outcome measures

The secondary outcome measure will be the costs of treatment, as shown in Table 2. The health costs will be calculated using data obtained from the participants' hospital records and from a self-report questionnaire. The participants will each be given a log book to keep a record of their use of resources over the six months after discharge from hospital. A questionnaire will then be sent to their home for completion using the log book at six months after surgery. The self-report questionnaire will also be used to collect data that indicate any personal costs (non-prescribed medication and time off work).

Table 2. Cost data to be collected

Costs	Duration	Data source
Initial operation including prostheses, length of stay, additional procedures, return to theatre	Time zero to 12 months post-surgery	Hospital records of patient
Inpatient care post-discharge	Time zero to 12 months post-surgery	Hospital records of patient
Outpatient care	Time zero to 12 months post-surgery	Hospital records of patient
Primary/community care	Time zero to 6 months post-op	Self-report questionnaire
Medications	Time zero to 6 months post-op	Self-report questionnaire
Aids/Adaptations	Time zero to 6 months post-op	Self-report questionnaire

The self-report data will only be collected for six months for two reasons: a) it is the time period in which there will be the greatest effect on the participant's lifestyle, and b) compliance with completion of self-report data will be improved by limiting the time period and reducing the patient burden.

Statistical analysis

This is an observational study and we intend to use an exploratory approach to investigate the effect of surveillance or lack of surveillance on the outcomes of interest.

Primary outcomes

The study of the change in patient reported outcome scores between baseline and 12 months assessment will be performed with a linear mixed method model to account for repeated measurements within patients. For each outcome score, the main analysis will regress the baseline and 12 month assessment on long term follow up status, the indicator of assessment time (zero or 12 months) and their interaction. The confidence intervals and p-value related to this interaction will provide the quantitative findings to determine if there is a difference in the change of recovery between participants with and without surveillance. The analyses will be adjusted for potential confounders including the type of hip replacement.

Depending on the size of the study sample, we will investigate further the impact of both observed and unobserved confounders using a matching technique such as a propensity score method.

Secondary outcomes

The economic evaluation of health benefits will be performed with a cost-utility analysis, which compares the value of alternative interventions by attaching costs to the quality adjusted life years (QALY) produced by each intervention (costs/QALYs) (McCabe 2009). A ratio is then constructed from the differences in costs and QALYs of each of the interventions,

the incremental cost-effectiveness ratio (ICER). This can be compared with a threshold ICER for the NHS to indicate the likelihood of funding the intervention and has been applied in a similar research study comparing the cost-effectiveness of resurfacing arthroplasty with total hip replacement (Edlin, Tubeuf et al. 2012). Although this technique is known to have some disadvantages, such as the inability to capture the patient experience, the results will be considered in conjunction with planned simultaneous qualitative research study.

Sample size

This is an observational pilot study and all eligible patients will be included. The group allocation will be retrospective, determined from medical records and patient corroboration. No sample size will be determined in advance as it is unknown what proportion of patients will be eligible and available for each group although existing local data suggests that approximately 180 patients may be eligible in a twelve month period.

Organisation

Monitoring

This study forms one part of a research plan in the NIHR five year clinical lectureship awarded to the primary researcher. It will be sponsored by the hosting NHS Trust and monitored with reference to the team of experts already in existence for the duration of the research fellowship. Data monitoring will be conducted through bi-monthly meetings between the statistician and the primary researcher, with reference to two of the professors with expertise in this area (health economics and musculoskeletal rehabilitation). In addition, the two patient partners will continue to be invited to comment on all aspects of the study. Due to the combined expertise available from this group, no additional data monitoring committee will be required for this single-centre observational study.

No harm will be caused from participation in this study but withdrawal for any reason, including participant burden, will be recorded, summarised and presented with the results.

Ethics

Research ethics approval for this study was granted from the NHS Health Research Authority (London - Camden and King's Cross Research Ethics Committee) on 19 April 2016: 16/LO/0650.

Dissemination

The dissemination of the results from this study will include a short written summary for participants (prepared with patient partners), an abstract and poster presentation to be displayed at regional and national conferences of orthopaedic health professionals and researchers, and a paper submitted to an international orthopaedic journal. In addition, social media will be used to support publications and presentations with the support of research administration at the University of the West of England.

Study status

This study commenced on 11 July 2016 on completion of all statutory requirements.

Discussion

Many of the orthopaedic community advocate long term follow up but the effect of hip arthroplasty surveillance on health related quality of life and health economics at the time of revision hip surgery is unknown at present. It is anticipated that the results of this study will provide information to support the design of a larger, multi-centre study which can investigate the use of surveillance following hip arthroplasty.

Although this is a simple observational study, the burden on patients to complete questionnaires can be significant. The questionnaires in this study have been constructed to minimise this burden and the research nurse will be available to assist participants who are in hospital following an emergency admission and may require help to complete their questionnaires in order to maximise the response rate. This group of patients are important to the outcome of the study but may be asked to participate in more than one research study; consequently, provision has been made to assist them if required.

References

- British Orthopaedic Association, British Hip Society and Royal College of Surgeons (2014) Commissioning guide 2013: Pain arising from the hip in adults. V1.1. London: Royal College of Surgeons of England.
- Corbacho, B. (2015) Orthopaedic research in the UK: current state of the art. London: British Orthopaedic Association. <http://www.boa.ac.uk/publications/jto-vol-3-issue-3/> edn. [24 November 2015]
- Da Assunção, R.E., Pollard, T.C.B., Hrycaiczuk, A., Curry, J., Glyn-Jones, S. and Taylor, A. (2015) Revision arthroplasty for periprosthetic femoral fracture using an uncemented modular tapered conical stem. *Bone & Joint Journal* 97-B: 1031-1037. DOI:10.1302/0301-620X.97B8.
- Dawson, J., Fitzpatrick, R., Frost, S., Gundle, R., McLardySmith, P. and Murray, D. (2001) Evidence for the validity of a patient-based instrument for assessment of outcome after revision hip replacement. *Bone & Joint Journal* 83-B: 1125-1129. DOI: 10.1302/0301-620X.83B8.11643
- Edlin, R., Tubeuf, S., Achten, J., Parsons, N. and Costa, M. (2012) Cost-effectiveness of total hip arthroplasty versus resurfacing arthroplasty: Economic evaluation alongside a clinical trial. *BMJ Open* 2 (5) , 2012. DOI:10.1136/bmjopen-2012-001162
- EuroQol Group Association (2016). EQ-5D: A standardised instrument for use as a measure of health outcome. <http://www.euroqol.org/> [21 March 2016].
- Fillingham, D. (2008) *Lean Healthcare. Improving the patient's experience.* Chichester, UK: Kingsham Press.
- Harris, W.H. (2004) Conquest of a worldwide human disease: particle-induced periprosthetic osteolysis. *Clinical orthopaedics and related research* 429: 39-42.
- Harris, K.K., Price, A.J., Beard, D.J., Fitzpatrick, R., Jenkinson, C. and Dawson, J. (2014) Can pain and function be distinguished in the Oxford Hip Score in a meaningful way?: an exploratory and confirmatory factor analysis. *Bone and Joint Research* 3(11): 305-309. DOI: 10.1302/2046-3758.311.2000313
- Hart, A.J., Sabah, S.A., Henckel, J., Lloyd, G. and Skinner, J.A. (2015) Lessons learnt from metal-on-metal hip arthroplasties will lead to safer innovation for all medical devices. *Hip International* 25(4): 347-354. DOI: 10.5301/hipint.5000275
- Health and Social Care Information Centre (2013) Patient Reported Outcome Measures. <http://www.hscic.gov.uk/proms> [22 March 2016].
- Howard, P.W. (2009) Reconstruction/revision of acetabular failure in revision hip replacement. *Orthopaedics and Trauma* 23(5): 322-326. DOI: [10.1016/j.mporth.2009.08.007](https://doi.org/10.1016/j.mporth.2009.08.007)
- Katz, J.N., Wright, E.A., Polaris, J.J.Z., Harris, M.B., and Losina, E. (2014) Prevalence and risk factors for periprosthetic fracture in older recipients of total hip replacement: a cohort study. *BMC Musculoskeletal Disorders* 15: 168. DOI: 10.1186/1471-2474-15-168
- McCabe, C. (2009) What is cost-utility analysis? Hayward Medical Communications. http://www.medicine.ox.ac.uk/bandolier/painres/download/whatis/What_is_cost-util.pdf [25 January 2016].
- Naal, F.D., Impellizzeri, F.M. and Leunig, M. (2009) Which is the best activity rating scale for patients undergoing total joint arthroplasty? *Clinical Orthopaedics & Related Research* 467(4): 958-965. DOI: 10.1007/s11999-008-0358-5
- National Joint Registry (2016) 13th Annual Report. <http://www.njrcentre.org.uk> [23 November 2016].
- Orthopaedic Data Evaluation Panel (2015) Northgate Public Services (UK) Ltd. <http://www.odep.org.uk> [24 November 2015].
- Patel, A., Pavlou, G., Mujica-Mota, R.E. and Toms, A.D. (2015) The epidemiology of revision total knee and hip arthroplasty in England and Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset. *Bone & Joint Journal* 97-B: 1076-1081. DOI: 10.1302/0301-620X.97B8.

Smith, L.K. (2014) Assessment of the current state of hip arthroplasty surveillance in the UK. *Musculoskeletal Care* 12, 4: 232. DOI: 10.1002/msc.1077

Vanhegan, I.S., Malik, A.K., Jayakumar, P., Ul Islam, S. and Haddad, F.S. (2012) A financial analysis of revision hip arthroplasty. *Bone & Joint Journal* 94-B: 619-623. DOI: 10.1302/0301-620X.94B5.

Zampelis, V., Ornstein, E., Franzen, H. and Atroshi, I. (2014) A simple visual analog scale for pain is as responsive as the WOMAC, the SF-36, and the EQ-5D in measuring outcomes of revision hip arthroplasty. *Acta Orthopaedica* 85(2): 128-132. DOI: 10.3109/17453674.2014.887951