# Retrograde intramedullary nail fixation compared with fixed-angle plate fixation for fracture of the distal femur: the TrAFFix feasibility RCT

Xavier L Griffin,[1,2]* Matthew L Costa,[1,2] Emma Phelps,[1] Nicholas Parsons,[3] Melina Dritsaki,[4] May Ee Png,[4] Juul Achten,[1] Elizabeth Tutton,[2,5] Robin Lerner,[1] Alwin McGibbon[6] and Janis Baird[7,8]

[1]Oxford Trauma, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), Kadoorie Centre, University of Oxford, Oxford, UK
[2]Oxford University Hospitals NHS Foundation Trust, John Radcliffe Hospital, Oxford, UK
[3]Statistics and Epidemiology Unit, Warwick Medical School, University of Warwick, Coventry, UK
[4]Oxford Clinical Trials Research Unit, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford, Oxford, UK
[5]Warwick Research in Nursing, Warwick Medical School, University of Warwick, Coventry, UK
[6]Patient and public representative, Coventry, UK
[7]Medical Research Council Lifecourse Epidemiology Unit, Southampton General Hospital, University of Southampton, Southampton, UK
[8]National Institute for Health Research Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK

*Corresponding author xavier.griffin@ndorms.ox.ac.uk

**Declared competing interests of authors:** Matthew L Costa is a member of the UK National Institute for Health Research Health Technology Assessment General Board.

Published September 2019
DOI: 10.3310/hta23510

# Scientific summary

## The TrAFFix feasibility RCT

Health Technology Assessment 2019; Vol. 23: No. 51
DOI: 10.3310/hta23510

NIHR Journals Library www.journalslibrary.nihr.ac.uk

# Scientific summary

## Background

Fractures of the distal femur are increasingly common injuries. They account for 5% of all fractures of the femur with an estimated incidence of 10 per 100,000. The majority, and those of interest in this study, are fragility fractures sustained by patients after a fall from a standing height.

Fragility fractures of the distal femur occur in the same population as hip fractures. As with hip fractures, these are significant injuries in a vulnerable group of patients, causing considerable morbidity and mortality as well as placing a major financial burden on the NHS.

It is current practice to manage these fractures with operative fixation if the patient is medically fit enough to undergo surgery. Surgery reduces the substantial complications associated with non-operative treatment, such as prolonged immobilisation and bed rest. However, there has been very little research comparing operative technologies for treating distal femoral fractures in this population. A recent Cochrane review found few trials in this area, most of which compared outdated implants, such as non-anatomical, non-locking plating systems or earlier-generation nails (Griffin XL, Parsons N, Zbaeda MM, McArthur J. Interventions for treating fractures of the distal femur in adults. *Cochrane Database Syst Rev* 2015;**8**:CD010606). The two interventions most commonly used in contemporary UK practice are intramedullary fixation with a locked retrograde nail and extramedullary fixation with an anatomical locking plate. There are few clinical data available to guide clinicians and it is clear that there is no current consensus concerning the best management of these injuries.

## Objectives

The objectives of this feasibility study were to:

1. estimate the number of eligible patients in the UK population and the proportion of those eligible who were willing to consent to take part in the study
2. optimise the protocol, procedures and clinical reporting forms in preparation for a future definitive trial
3. perform a process evaluation to better understand the implementation, mechanisms of impact and context of the interventions and the generalisability and likely success of any future definitive trial
4. explore the validity of self and proxy reporting of the primary outcome measure in this specific population.

## Methods

This feasibility study was a multicentre randomised controlled trial, stratified by centre and cognitive impairment with balanced 1 : 1 allocation. In parallel with the feasibility study, we also performed a process evaluation in line with the recommendations of the Medical Research Council (MRC). The evaluation focused on investigating the fidelity and quality of implementation, clarifying the causal mechanisms and identifying the contextual factors that might be important in understanding the circumstances under which the interventions will be effective and the variation of outcome. The study was approved by the Wales Research Ethics Committee (REC) (reference number 16/WA/0225), and study-wide NHS approval was given by the Health Research Authority (Integrated Research Application System 206745).

The study was conducted across seven participating NHS hospitals. The sample was recruited between 29 September 2016 and 3 July 2017. Patients aged ≥ 18 years, including those with chronic cognitive

impairment, with a fracture of the distal femur involving the distal two 'Müller' squares, who the attending surgeon believed would benefit from internal fixation were potentially eligible. Patients were excluded if they had a loose, ipsilateral hip or knee arthroplasty requiring revision, or a femoral deformity or arthroplasty that precluded nail fixation.

No formal sample size calculation was conducted for a test of effectiveness in this feasibility study. However, assuming that the recruitment rate was 1.0 participant per month per centre, then a recruitment period of 52 centre.months would allow us to estimate the recruitment rate with a 95% confidence interval of 0.73 to 1.28 participant per month per centre.

Participants were randomly allocated to fixation using either intramedullary nailing or locking plate fixation. A regional or general anaesthesia technique was used and routine analgesia provided in accordance with local practice. Appropriate preparation, positioning and fracture reduction were left to the discretion of the operating surgeon, as per their normal clinical practice. Participants received the same standardised, written physiotherapy advice; weight-bearing status was decided by the treating surgeon, with a preference for early weight-bearing mobilisation immediately or as soon as the surgeon felt appropriate.

The primary outcome measures for this study were the participant recruitment rate and the completion rate of the EuroQol-5 Dimensions, five-level version (EQ-5D-5L), instrument at 4 months post surgery. Additional measurements collected included baseline characteristics, measures of social support and self-efficacy, Disability Rating Index (DRI), dementia quality-of-life measures and a radiographic assessment of any malunion.

The overall monthly recruitment rate was estimated using Poisson regression analysis, with 95% confidence intervals to assess the likely range of rates in a future main study. Data completeness for the primary EQ-5D-5L outcome was calculated as the percentage of randomised participants completing the instrument at baseline and at 6 weeks and 4 months after operation. The main analysis of the effects of the intervention investigated differences in the EQ-5D-5L score at 4 months between the two treatment groups on an intention-to-treat basis. In addition, a per-protocol analysis was reported and early EQ-5D-5L status assessed and reported at 6 weeks. Tests were two-sided and considered to provide evidence for a significant difference if $p$-values were $< 0.05$. A secondary analysis was performed using a mixed-effects model, incorporating random effects for recruiting centres and fixed effects for the treatment groups, cognitive impairment, age and sex.

An economic analysis investigated the feasibility of a definitive economic evaluation within a large randomised controlled trial (RCT) of treatment with modern intramedullary nails or anatomical locking plates for fragility fractures of the distal femur. A NHS and Personal Social Services perspective was adopted for the costing component of the feasibility study. The main analysis reports the practicalities and difficulties associated with an assessment of the cost to providers, to individuals and, more broadly, to society consequent on the intervention, along with the identification of appropriate sources of unit cost data.

We evaluated intervention implementation, mechanisms of impact and context in line with the MRC guidance on process evaluation of complex interventions using a mixed methodology approach. Process evaluation enables us to understand how the interventions work and under what circumstances effectiveness is achieved.

A number of data sources were used to inform the process evaluation. Screening logs were kept at each site to determine the number of patients assessed for eligibility. We requested admissions data from the Trauma Audit and Research Network in order to monitor the accuracy of the screening logs. We used data from NHS Digital, NHS England Statistics and the annual reports of the participating NHS trusts to describe the context for each participating hospital. A brief questionnaire, formed of six questions, was used to assess surgical expertise and preference. The questionnaire was sent to consultant trauma and orthopaedic surgeons by e-mail using the distribution lists of the Orthopaedic Trauma Society and to principal investigators at each of the participating centres. We held a 1-day workshop with patient and

public involvement representatives to learn about the factors other than surgery that influence patients' recovery from this injury. In addition, semistructured interviews were conducted by an experienced qualitative researcher with participants and members of the research and clinical teams. Interviews were audio-recorded and transcribed verbatim. Interviews were analysed inductively using thematic analysis. Data saturation occurred when the team agreed that no new elements were arising from the interviews or within the themes.

Qualitative and quantitative data relating to each aspect of the process evaluation were integrated within the process evaluation framework. The themes and categories identified from the thematic analysis were also mapped onto the process evaluation framework to demonstrate how they relate to each aspect of the process evaluation.

## Results

A total of 173 patients were screened during the course of the feasibility study, 85 of whom were eligible for inclusion in the study. This very closely matched our estimate of approximately 1.5 eligible patients per centre per month. Of these, only 23 participants were recruited into the study (11 and 12 were allocated to the nail and plate groups, respectively). The most important barriers to recruitment were surgeon related, accounting for 39 out of the 60 missed patients.

The screening data demonstrated very marked variation in practice across the centres. This was most apparent in the variation in surgical decision-making. For example, in one centre 18 patients were managed non-operatively, whereas in another there were none; in two centres, surgeons had strong preferences, whereas in another two centres three patients or fewer were excluded because of surgeon preference.

The process evaluation showed that surgeon-related factors were the principal barrier to recruitment. Surgeons perceived the operative treatment of these patients to be complex and were often more confident using one technology over the other. Some surgeons reported that a lack of individual equipoise inhibited their participation in the study. However, our data suggest that there was community equipoise among surgeons. Our findings also suggest that in some centres recruitment was facilitated by a strong research culture, in which research was part of everyday clinical practice, supported by integrated research teams and good communication.

The interviews with participants and staff, and the workshop with patient and public involvement representatives, gave insights into factors that influence outcomes and impede recovery in this group of patients. These included limited mobility prior to fracture, a loss of confidence after the fracture had occurred and limited access to physiotherapy. It was clear that a patient's home circumstances could aid recovery: some participants reported that support from relatives or carers helped them to manage at home.

Taken together, recruitment for the study took place over 54.8 centre.months. Fitting a Poisson model to the monthly count data provided a reasonable model to the observed numbers and gave an estimated recruitment rate of 0.42 (95% CI 0.27 to 0.62) participants per site per month. Out of the 23 study participants, 20, 15 and 14 participants completed the EQ-5D-5L assessment at baseline, 6 weeks and 4 months, respectively, and the proportion of patients who completed the EQ-5D-5L at each of these time points was 87% (95% CI 65% to 97%), 65% (95% CI 43% to 83%) and 61% (95% CI 39% to 80%), respectively.

The response rate to health economics questionnaires at 4 months was a little more than 50%, which may have been related to the difficulty in completing questionnaires before participants have completed recovery and are discharged from acute or intermediary services. There were no difficulties in relation to accessing

information to evaluate the interventions under investigation. Item completeness for questionnaires that were returned was good, but participants reported that the number of questionnaires was too great a burden during follow-up. Other than the direct medical cost of the trial interventions, the main cost driver was loss of work productivity.

## Conclusions

This feasibility study has challenged many of the assumptions that underpinned the development of proposed definitive trial protocol. We propose a modified protocol that would be feasible given the recruitment rate observed here, which is equal to that reported in the similar FixDT trial [Health Technology Assessment (HTA) 11/136/04: Costa ML, Achten J, Hennings S, Boota N, Griffin J, Petrou S, *et al.* Intramedullary nail fixation versus locking plate fixation for adults with a fracture of the distal tibia: the UK FixDT RCT. *Health Technol Assess* 2018;**22**(25)], which delivered to target and budget.

## Recommendations for further research

A modified protocol could successfully deliver a trial to answer this research question. We recommend a definitive trial, with an embedded internal pilot to test the assumptions found in this feasibility study. The study design would be a randomised trial reporting a two-sided test for superiority between treatments for adult patients with fragility fracture of the distal femur with an integrated qualitative recruitment intervention based on the theme of community equipoise. The primary outcome should be the DRI, a patient-reported global lower limb functional measure. Explicit stop–go criteria for the internal pilot should be defined against which to make an assessment of the likely success of the definitive trial recruitment phase. A recruitment target of 0.5 participants per centre per month would mean that across 28 centres over 2.5 years a sufficient sample of 422 participants could be recruited.

## Registration

This trial is registered as ISRCTN92089567.

## Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research. Funding was also supported by NIHR Oxford Biomedical Research Centre.

# Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.819

*Health Technology Assessment* is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

### Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

### HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

### This report

The research reported in this issue of the journal was funded by the HTA programme as project number 15/59/22. The contractual start date was in June 2016. The draft report began editorial review in March 2018 and was accepted for publication in June 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.



Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).