



Trial of Acute Femoral Fracture Fixation (TrAFFix), a feasibility study
For patients with an acute, fragility fracture of the distal femur, is there a clinical and cost-effectiveness difference between locking plate fixation and retrograde intramedullary nail fixation?

Economic Analysis Plan

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1. Introduction

This document details the economic analysis plan to be performed for the TrAFFix trial. The economic analysis will investigate the feasibility of a definitive large RCT –based economic evaluation of treatment with modern intramedullary nails or anatomical locking plates for fragility fractures of the distal femur.

2 Resource use data

2.1 Collection of resource use data

The study will collect data on the use of services within the health-care system as well as on broader costs to society, in an attempt to capture relevant components that comprise the overall cost of treating fractures of the distal femur. Key items will include data completeness and the costs of the interventions under investigation.

Data will be collected from information gathered via the study participant questionnaires completed by participants, or a proxy at baseline and 4 months post randomisation.

Questionnaires will capture the frequency of use of community-based health and social care services (classified as general practitioner, practice nurse, community nurse, physiotherapist, occupational therapist), number and duration of admissions to inpatient wards, number of diagnostic tests, use of outpatient services (classified as orthopaedics (your injured bone), orthopaedics (any other bones), rehabilitation unit, physiotherapy, emergency department), medication use and equipment provided, indirect costs borne by partners and carers as a result of attending hospital visits, as well as direct non-medical costs (including travel expenses), attributable to the participants' health state.

To measure effectiveness, two multiattribute utility measures will be piloted in the study, the EuroQol EQ-5D-5L questionnaire and the DEMQoL, at baseline , 6 weeks and 4 months.

The practicalities and difficulties associated with an assessment of the cost to providers, individuals and more broadly, to society entailed by the introduction of the intervention, along with the identification of appropriate sources of unit cost data, will be addressed. A NHS and Personal Social Services perspective will be adopted for the costing component of the feasibility study.

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Data on consumables for the operation (number of screws, number of wires or cables and number of buttress plates) will be taken from the study records. Similarly, length of operation time and surgeon grade will be obtained using primary research methods (ie operation notes).

2.2 Valuation of resource-use cost data

Regarding the operative consumables for the fixation of fragility fractures of distal femur (intramedullary nails or anatomical locking plates) cost will be obtained from the NHS National Supply Catalogue (<https://www.supplychain.nhs.uk>).

The cost of the distal femur fracture surgery will be assessed using NHS reference costs (NHS Reference Costs , Department of Health 2013) and HRG code for “ Minor Knee Procedures for Non-Trauma”. Average operating time will be obtained from patient trial records. Day case cost or overnight admission cost will also be obtained from the NHS reference cost. If a patient experiences a length of stay greater than the average length of the stay reported from the trial records, then we will use the inpatient excess day cost from the NHS reference cost. Unit costs of surgeons’ time, will be obtained from the Personal Social Services Research Unit’s Unit Costs of Health and Social Care 2013 cost compendium (PSSR Unit. Unit Costs of Health and Social Care 2013, L. Curtis, Editor. Personal Social Services Research Unit: University of Kent & National Schedule of Reference Costs Year 2012-2013 DoH).

Estimation of unit costs used will follow recent guidelines on costing health and social care services as part of health economic evaluations National Institute for Health and Care Excellence. Guide to The Methods of Technology Appraisal. London: NICE; 2013 . Unit costs for hospital- and community-based health and social care services were derived from the NHS Reference Costs (2012–13) (Department of Health 2013)and the Personal Social Services Research Unit’s Unit Costs of Health and Social Care 2013 cost compendium (Curtis L. Unit Costs of Health and Social Care 2013. Canterbury: PSSRU, University of Kent; 2013).

Societal costs

Unit cost for PSS including number of meals on wheels, laundry services, and number of visit of carers will be assigned using PSSRU and Information Centre of Personal Social Services in councils (Curtis L. Unit Costs of Health and Social Care 2013. Canterbury: PSSRU, University of Kent; 2013).

2 Collection of health utilities

To measure effectiveness, two multiattribute utility measures will be piloted in the study, the EuroQol EQ-5D-5L questionnaire and the DEMQoL24, at baseline, 6 weeks and 4 months.

EQ-5D-5L (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). *Qual Life Res.* 2011;20(10):1727-36 is a validated, generalised and standardised instrument comprising a visual analogue scale (VAS) measuring self-rated health and a health status instrument, consisting of a five-level response (no problems, some problems, moderate problems, severe problems and unable) for five domains related to daily activities; (i) mobility, (ii) self-care, (iii) usual activities, (iv) pain and discomfort and (v) anxiety and depression. Responses to the health status classification system are converted into an overall score using a published utility algorithm for the UK population. A respondent's EQ-VAS gives self-rated health on a scale where the endpoints are labelled 'best imaginable health state' (100) and 'worst imaginable health state' (0). EQ-5D-5L has some important advantages in this study. It has been validated for use in patients with cognitive impairment where an appropriate proxy may respond to the questions (Sheehan BD, Lall R, Stinton C, Mitchell K, Gage H, Holland C, et al. Patient and proxy measurement of quality of life among general hospital in-patients with dementia. *Aging Ment Health.* 2012;16(5):603-7). It can be administered by mail or by telephone. Recent work has demonstrated it to have excellent measurement properties in comparison with other commonly used disease and region-specific outcome tools in the similar cohort of patients with fragility hip fracture (Stoen RO, Lofthus CM, Nordsletten L, Madsen JE, Frihagen F. Randomized trial of hemiarthroplasty versus internal fixation for femoral neck fractures: no differences at 6

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years. Clin Orthop Relat Res. 2014;472(1):360-7). EQ-5D-5L scores will be collected at baseline (for pre and post-surgery), 6-weeks post-surgery, and 4-months post-surgery.

DEMQoL score (Smith SC, Lamping DL, Banerjee S, et al. Development of a new measure of health-related quality of life for people with dementia: DEMQOL. Psychol Med 2007;37(5):737-46) is a validated questionnaire specifically designed to assess quality of life in patients with dementia. A large minority of the participants in this study are expected to have co-existing dementia. The score can be self or proxy reported and consists of 28 or 31 items respectively. These data will be collected at baseline, 6 weeks, and 4 months post-surgery in participants who have cognitive impairment. Recently preference based utility scores for a UK population have also been published (Mulhern B, Rowen D, Brazier J, et al. Development of DEMQOL-U and DEMQOLPROXY- U: generation of preference-based indices from DEMQOL and DEMQOLPROXY for use in economic evaluation. Health Technol Assess 2013;17(5):v-xv, 1- 140).

Valuation of health utilities

The utility scores for each person will be entered into a spreadsheet which will calculate the utility value for each person. Responses to the EQ-5D will be converted into multi-attribute utility scores using established algorithm [Herdman et al/, 2011]. An 'area under the curve' approach will be employed to calculate the QALY for each participant. This will be done by multiplying the time spent in that health state by the utility value for that state.

Economic analysis

If a definitive trial is feasible then **no formal** economic analysis will be undertaken and data from the feasibility study will be locked and carried over into the main (definitive) trial. No formal analysis of treatment cost and effectiveness will be undertaken in this scenario. Main drivers of treatment costs as well as reasons and patterns of any missing data, loss to follow-up and participant withdrawals will be carefully considered and reported, with particular emphasis on how these may impinge on the future trial.

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If a definitive trial is not feasible, then the economic analysis will investigate differences in cost and benefits between the two treatment groups on an intention-to-treat basis, at 4 months at the conventional way.

The main analysis will investigate differences in the primary outcome measure, EQ-5D-5L score at 4 months, between the two treatment groups (Nail and Plate) on an intention-to-treat basis. In addition as per-protocol analysis will also be reported and early EQ-5D-5L status will also be assessed and reported at 6 weeks. Differences between groups will be based on a normal approximation for EQ-5D-5L. Tests will be two-sided and considered to provide evidence for a significant difference if p-values are less than 0.05 (5% significance level). Also, DEMQoL score will be reported in a similar fashion. Mean cost and standard error (SE) will be reported for each resource category, diagnostic tests and medication by treatment allocation.

The reasons and patterns of any missing data, loss to follow-up and participant withdrawals will be carefully considered and reported, with particular emphasis on how these may impinge on any future trial.

Health Economics questionnaires Evaluation

As part of the study's qualitative process evaluation we aim to understand the clarity and acceptability of the health economics questionnaire that will be designed to acquire data on healthcare utilisation in the period following the treatment/s under investigation. Questions specific to the health economics questionnaire will be incorporated into a wider interview schedule which aims to understand participants' experience of being in a trial. Interviews with research nurses, who often assist participants in completing follow-up questionnaires, will also be conducted. Given their role, we feel that research nurses will be well placed to address

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questions relating to the clarity and acceptability of the health economics questionnaire. A sample questionnaire has been designed (Appendix 1) to enable the team to examine the clarity and acceptability of the questionnaire.

Appendix 1

Questions to be incorporated into the participant interview schedule

- As part of the study you completed several questionnaires, how did you find them?
- How did you feel about the length? -
- There were some questions about (*basic description of health economic questions,*) how did you find those questions?
- Did you have any difficulties understanding those questions?
- How comfortable were you in answering those questions?
 - *Could you easily recall the number of visits you have paid to the physiotherapist for example?*
 - *Were some of the questions too sensitive to ask? (e.g. questions about income loss)*

Questions to be incorporated into the research nurse interview schedule

- How do patients find the questionnaire?
- Do they have any difficulties understanding the questions? (Are there any questions they find particularly difficult to answer?) – How do they approach these questions? (e.g. do they just leave them blank, ask for your advice?)
- Could any of the questions be better phrased?

Clarity

Is the questionnaire self-explanatory? Do you have difficulties understanding any of the wordings? For example is it clear what inpatient/outpatient care is?

Acceptability

How confident are you in answering the questions? Can you easily recall the number of visits you have paid to the physiotherapist the last 3 months?

Do you believe that some questions are sensitive and hence should not be asked? For example question about income lost?

In case of private treatment do you know the cost paid by your medical insurance and your personal contributions?

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Interpretation

Which question have you found the most difficult to answer and why? How do you approach these question. For example do you just leave the blank? Are you willing to spend time advising your personal diary or asking your family members to help you filling it in?

Regarding the question about medication, how confident are you filling in these information? For example do you always know the drugs name, dosage, number of time you receive it and for how long? Would you rather have a list of medication for you to tick from and dosage?

Preference

How do you feel about the length of the questionnaire? How long do you need to fill it in? Do you feel it as an unnecessary burden?

Would you prefer some particular questions to be phrased on a different way? Is yes how?

Do you like the structure of the theme questionnaire? Is it easy to follow it?

Do you think there is anything substantive missing that you would like to have been asked as a patient?

Which do you think was the most interesting question to you? Why?