HEALTH ECONOMICS ANALYSIS PLAN

Suture fixation versus tension band wiring for simple olecranon fracture fixation: a multi-centre randomised controlled trial (SOFFT)

Version 1.0

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Contents

1. Document scope

This health economics analysis plan (HEAP) outlines the key steps and methods that will be used to investigate the cost-effectiveness of suture fixation repair compared to tension band wiring for surgical fixation of Mayo Grade IIA fractures of the olecranon.

This analysis will be conducted based on the Simple Olecranon Fracture Fixation Trial (SOFFT).

2. Abbreviations

AE	Adverse Event
CCA	Complete Case Analysis
CEA	Cost Effectiveness Analysis
CEAC	Cost Effectiveness Acceptability Curve
CEP	Cost Effectiveness Plane
CI	Confidence Interval
GP	General Practice
HEAP	Health Economics Analysis Plan
ICER	Incremental Cost-Effectiveness Ratio
ITT	Intention-to-Treat
LY	Life Year
MAR	Missing At Random
MCAR	Missing Completely At Random
MI	Multiple Imputation
MICE	Multiple Imputation by Chained Equations
MID	Minimally Important Difference
MNAR	Missing Not At Random
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OWSA	One-way Sensitivity Analysis
PSA	Probabilistic Sensitivity Analysis
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
QALY	Quality-adjusted Life Year
RCT	Randomised Controlled Trial
SD	Standard Deviation
SE	Standard Error
TBW	Tension Band Wiring
TSR	Tension Suture Repair

WTP	Willingness To Pay

3. Overview

3.1 Trial design

SOFFT is a multi-centre, parallel group, non-inferiority RCT within Major Trauma Centres and Trauma Units across up to 44 trial sites in the UK. The trial investigates whether suture fixation repair is at least as effective as traditional tension band wiring for the internal surgical fixation of Mayo Grade IIA fractures of the olecranon in adult patients (≥16 years old).

The study has a total 27-month recruitment period, including an internal pilot phase of 9 months at the start followed by the main recruitment period. Following treatment, all participants will be followed up for 18 months including a follow-up visit at 4 months post treatment then remote questionnaire to be completed by the participant at 12 months and 18 months. Those patients that reach 24 months within the planned follow-up period will be asked to complete an additional remote questionnaire at 24 months.

The primary outcome will be the Disabilities of the Arm Shoulder and Hand (DASH) score at 4-months, the point at which the patient should have recovered from the initial intervention and bony union should be complete. The secondary outcomes will be collected at 4, 12 and 18 months post-treatment for the whole population (and at 24 months post-treatment only for those who reach that follow-up point), including DASH (at 12, 18, and 24 months), pain using a Visual Analog Scale (VAS), net promotor score (an overarching measure of patient satisfaction), EQ-5D-5L, and resource use (1).

For further details (e.g. trial inclusion/exclusion criteria), please refer to the trial protocol (1).

3.2 Economic analysis

3.2.1 Aim and objectives

The aim of the economic analysis is to investigate the cost-effectiveness of tension suture repair (TSR) compared to tension band wiring (TBW) for surgical fixation of Mayo Grade IIA fractures of the olecranon.

The evaluation consists of the within-trial cost-effectiveness analysis (CEA) and model-based CEA, which addresses the short-term and life-time cost-effectiveness, respectively:

- Within-trial CEA: It will be conducted alongside the SOFFT trial, based on the health outcomes and resource use collected from the trial.
- Model-based CEA: A health economic model will be used to project cost-effectiveness beyond the trial period based on the SOFFT trial data and published secondary data sources.

3.2.2 Perspective

Both within-trial and model-based CEA will be conducted from the perspective of NHS and personal social services (PSS) as recommended by the National Institute for Health and Care Excellence (NICE) (2).

3.2.3 Time horizon

The time horizon for the within-trial CEA will be 18 months, during which period all participants will be followed up. The data collected from participants who reach the 24th month timepoint will be used for subgroup analysis.

The model-based CEA will adopt a life-time horizon to capture the costs and benefits until the death of all participants in the model.

3.2.4 Discounting rates for costs and benefits

For the within-trial CEA, no discounting will be accounted for given the limited time horizon. For model-based CEA, future costs and benefits (beyond 12-month time frame) will be discounted at 3.5% per year as recommended by NICE (2).

3.2.5 Cost-effectiveness threshold(s)

A cost-effectiveness threshold of £20,000 to £30,000 per QALY will be used in the economic evaluation to determine whether the tension suture repair represents a good use of NHS resources (2).

4. Methods

4.1 Within-trial CEA

The within-trial CEA will be conducted in Stata (version 15 or later; Stata Corp LLC; College Station, TX).

4.1.1 Measurement and valuation of resource use

The valuation of the resource use will be conducted by multiplying the quantities of resource use with the unit costs of the resources.

All costs will be presented in 2022/2023 pounds sterling (£). When the unit costs derived from data sources are not 2022/2023 prices, inflation indices (the Health Services index using the CPI) will be applied to inflate the costs to 2022/2023 (3).

Please refer to **Table 1** in **Dummy tables for the analysis** for the list of resource use and corresponding unit costs and data sources.

Missing data will be dealt with appropriate imputation methods following pre-defined procedures, which will be discussed in detail in section 4.1.3.

4.1.1.1 Training-related resource use and unit costs

In order to standardise delivery of interventions across all participating sites, all Principal Investigator surgeons will be required to attend a training course to learn the correct suture technique and to revise the standard technique of tension band wiring. The training includes three components:

- Online video demonstrations followed by group discussion
- Assessments of understanding with a structured questionnaire

The cost of training is potentially relevant for inclusion as part of the intervention in the analysis. However, considering that the participant surgeons for both treatment arms are equally required to attend the training, the training costs would be cancelled out in the incremental analysis. Hence, the cost of training will not be considered in the analysis.

4.1.1.2 Surgery-related resource use and unit costs

The types and quantities of resource use for the olecranon fracture surgery, as well as the operation time will be collected via the designed surgical form.

The surgical form collects the procedures of surgery with tension band wiring and tension suture repair technique, as well as potential intra operative complications, including fracture, nerve injury, vascular injury, loss of fixation and others.

The materials/staff required for the surgeries include but are not limited to:

- Tension band wiring surgery
  - K-wires
  - Cerclage wires
  - Surgeons and other professional staff (e.g., nurse)

- Suture fixation repair surgery
    - Cerclage suture material
    - Surgeons and other professional staff

The unit costs of the staff for the surgeries will be derived from the salary data from PSSRU Unit Costs of Health and Social Care (3). Due to the fact that the staff's time in theatre during the surgery was not collected in the surgical form, it will be derived from literature and validated with clinical experts. The time required for undertaking the surgery, as recorded on the surgical form, will be multiplied by the operation room's unit cost to calculate the cost of conducting the surgery. The unit costs for the consumables and procedures for the surgeries will be derived from NHS purchase price, published literature and national costing source such as National Cost Collection data for the NHS (4). Regarding the complications, the unit costs of management of complications will be derived from National Cost Collection data for the NHS (4) or published literature.

4.1.1.3 Routine care-related resource use and unit costs

The resource use for routine care will be collected based on case report form (CRF) and patient-reported questionnaire at 4, 12, 18 and 24 months (only for those participants who reach 24 months). The CRF will be completed by the local principal investigators or a delegated member of staff, whilst the questionnaire will be completed by patients.

The CRF collects the following clinical events that might incur cost relevant to the within-trial CEA:

- Surgical complications related to the affected arm
    - whether they resulted in secondary procedure
    - duration of hospital admissions

- Medical complications and duration of hospital admissions due to the complications
- Secondary procedures and duration of hospital admissions
- Physiotherapy received, and associated number/average duration of sessions

The patient-reported questionnaire collects the information about the types of health care services received by the patient, provided by NHS within and without the hospital and the frequency of these services being used for routine care. The services collected include the following:

- Care from the NHS not in the hospital
  - GP visit at GP practice
  - Practice nurse at GP practice
  - Occupational therapist
  - Physiotherapist
- Care from the NHS in the hospital
  - Outpatient visit with a surgeon for a follow-up appointment about the elbow
  - Outpatient visit with a surgeon for a surgical procedure of the injured arm
  - Outpatient visit with a nurse about the elbow
  - Outpatient visit with a physiotherapist for physiotherapy about the elbow
  - Outpatient visit to a pain clinic about the elbow
  - Outpatient visit with an occupational therapist about the elbow
- Visit to Accident and Emergency about the elbow
- Inpatient
  - Admitted to hospital as an inpatient for further surgery to the elbow

  - Admitted to hospital as an inpatient for any other treatment to the elbow
- Day case
  - Admitted to hospital as a day case about the elbow

The unit costs of the health services provided by the NHS will be derived from the latest versions of the national costing sources such as National Cost Collection data for the NHS and the PSSRU Unit Costs of Health and Social Care (3, 4). For any drug to be prescribed for the trial participants, the unit cost will be derived from the British National Formulary (5). When there is no evidence from these latest national costing sources, previous versions of national costing sources and published literature will be reviewed as a supplementary source.

4.1.2 Measurement and valuation of health outcomes

The primary health outcome measure for the within-trial economic evaluation is quality-adjusted life year (QALY), which will be calculated by using the utility values of each patient collected over the trial follow-up with the "area under curve" (trapezoidal) method by assuming linear interpolation between measurements over time (6).

The utility of patients will be estimated by firstly measuring the health condition of each patient with the EQ-5D-5L, then mapping the EQ-5D-5L data to EQ-5D-3L and applying UK-specific EQ-5D-3L value set to derive the utility values. This recommendation was made in the latest manual of NICE health technology evaluations (2).

EQ-5D-5L data will be collected at baseline (once to assess patient health related QoL after the injury and once with regard to the week before injury), 4, 12, 18, and 24 months (only those who reach 24

months will complete the questionnaire at 24 months). The EQ-5D-5L will be collected according to the official User Guide (7).

Similar to measurement of health care resource use, missing health outcomes data will be dealt with appropriate imputation methods following pre-defined procedures, which will be discussed in detail in section 4.1.3.

4.1.3 Handling missing data

4.1.3.1 Mechanism of missing data

Trial data will be examined for any missingness. The optimal method for handling the missing data will be decided based on the likely mechanism of missingness. Following the Rubin's framework, the mechanism of missing data could be classified as missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR) (8).

The following steps will be taken to decide the missingness mechanism (8):

- Firstly, descriptive analysis will be conducted to present the missing pattern:
  - The amount of missing data across treatment arms at each follow-up time point will be summarised. If the proportion of participants with missing data varies significantly by treatment allocation, MCAR will be ruled out. Please refer to **Table 2** in the **Dummy tables for the analysis** as an example summary table on the missing pattern.
- Secondly, the association between missingness and baseline covariates/previous observed outcomes will be investigated via logistic regression. Based on the statistical significance and clinical

plausibility, if any baseline covariate or previous observed outcomes are shown to be predictor of missingness, MCAR will be ruled out. MAR could be plausible reasons for missingness.

Due to the fact that we will not know the unobserved data, it is usually impossible to investigate whether the probability that data are missing depends on the unobserved data. Hence, the assumption of MNAR and the implications will be tested in sensitivity analysis (8).

4.1.3.2 Methods for handling missing data

For the missing baseline values, mean imputation, which impute missing values of the baseline covariate with the mean of the observed baseline values, will be used. This would ensure the imputed values are independent of the treatment allocation (8).

- Under the assumption of MCAR, complete case analysis (CCA) will be performed by only including trial participants with complete data on all variables at any follow-up points.
- Assuming MAR, multiple imputation (MI) will be used, which follows three main steps:
    - Firstly, regression models will be used to predict the plausible values for the missing data based on regression parameters. Such process will be repeated *m* times, creating *m* different datasets. As a rule of thumb, *m* will be set to be similar to the percentage of incomplete cases (9).
    - Secondly, each dataset will be independently analysed to estimate the costs and utilities in each treatment group at each time point throughout the trial.
    - Lastly, the estimates from each dataset will be synthesised following Rubin's rules to generate an overall mean estimate of costs and utilities and its standard error (10).

Chained equations (MICE) will be used to implement MI. MICE specifies one imputation model for each variable. Imputed values in one variable will be used to predict missing values in other variables iteratively until model convergence.

- MNAR will be tested in sensitivity analysis. Pattern mixture model will be used, in which costs and health outcomes will firstly be imputed under MAR and then shifted under several scenarios that are considered of most interest after future discussions with clinical experts (8). The probability of tension suture repair being cost-effective at WTP threshold under these scenarios will be compared to assess the impact of MNAR on cost-effectiveness.

Costs and QALYs information for patients who died will be replaced with zero after the date of death.

4.1.4 Descriptive analysis of the baseline characteristics

After the missing data is handled with appropriate method, the descriptive analysis of baseline characteristics of treatment arms will be performed based on the imputed dataset (base case) and complete case, respectively. Please refer to **Table 3** in **Dummy tables for the analysis** as an example summary table of the descriptive baseline characteristics.

4.1.5 Primary analysis

The primary analysis is to calculate the incremental cost-effectiveness ratio (ICER) based on the costs and the QALYs calculated from EQ-5D-5L utilities. The analysis will be conducted by adopting an intention-to-treat (ITT) approach, in line with the trial protocol.

Firstly, the arithmetic mean and 95% CI for the costs and utilities at each follow-up time point will be generated and tabulated for each arm.

Please refer to **Table 4** and **Table 5** in the **Dummy tables for the analysis** for an example summary table of mean costs and utilities of each arm.

Furthermore, to account for potential correlation between costs and utility, and control for the baseline covariates across treatment arms (utility, cost, age, gender, and other covariates), seemingly unrelated regression equations (SURE) will be used to estimate the adjusted incremental mean costs and QALYs.

The equation for computing ICER is written as:

$$ICER = \frac{Cost(suture\ repair\ fixation) - Cost(tension\ band\ wiring)}{QALY(suture\ repair\ fixation) - QALY\ (tension\ band\ wiring)}$$

Sampling uncertainty will be explored by non-parametric bootstrapping. The process will be iterated for 1,000 times. For each bootstrapped dataset, SURE will be used to estimate the adjusted incremental mean costs and QALYs to compute the ICER. The uncertainty around the ICER will be presented graphically in cost-effectiveness plane (CEP). The probability of tension suture repair being cost-effective under various WTP thresholds will be presented in cost-effectiveness acceptability curve (CEAC).

4.1.6 Consideration on non-inferiority design of SOFFT

SOFFT is a non-inferiority clinical trial, where a pre-defined margin was established based on the primary endpoint (DASH score) at 4 months to determine the clinical non-inferiority of TSR to TBW. However, it is worth noting that although previous study by Bosmans has proposed methods specifically for economic evaluation alongside equivalence or non-inferiority trials (11), the methods are only applicable in a trial that tests the hypothesis of non-inferiority from both economic and clinical

perspective, whilst non-inferiority of cost is out of the scope of SOFFT. Moreover, non-inferiority study design does not justify replacing cost-effectiveness analysis with cost-minimisation analysis, as the joint distribution of costs and effects in CEA is still recommended to represent uncertainty even with the presence of non-inferiority in primary clinical outcome.

Hence, the non-inferiority study design will not change the methods being used to analyse the trial data and interpret the cost-effectiveness results.

4.1.7 Sensitivity analysis

To test the robustness of the cost-effectiveness findings, assuming data are MAR, within-trial CEA will also be conducted based on the complete cases of the trial participants as sensitivity analysis, in addition to the primary analysis based on the dataset imputed with MICE.

In addition, as mentioned in section 4.1.3, the assumption of data are MNAR will also be tested using pattern mixture model in sensitivity analysis.

The steps are identical to beforementioned methods in section **4.1.5 Primary analysis.**

4.1.8 Subgroup analysis

The within-trial CEA will also be conducted solely based on the trial data collected from those participants who reach 24 months to test the robustness of the cost-effectiveness findings.

The steps are identical to beforementioned methods in section **4.1.5 Primary analysis.**

4.2 Model-based CEA

It should be noted that the following considerations might justify omitting the long-term model:

- Diminishing long-term treatment effect: if the benefits of using tension suture repair (e.g., lower risk of complications) is unlikely to last beyond the end of trial follow-up.
- Stable disease states with well-understood long-term progression: if trial data indicates the progression patterns and outcomes stablise when approaching the end of trial, and published literature/clinical experts inform that such patterns remain unchanged beyond the trial.
- Availability of reliable published literature to parameterise the model: if there is lack of data, the model results will be highly uncertain and unreliable.

On the other hand, if it is deemed feasible and clinically relevant to extrapolate the long-term cost-effectiveness, the model-based CEA will be conducted in Microsoft Excel®. The proposed model design and associated parameters and assumptions are as follows.

4.2.1 Literature review on previous economic modelling studies

In order to understand whether there are any previous model-based CEAs that have adequately addressed the long-term cost-effectiveness of the tension suture repair versus traditional band wire for simple olecranon fracture fixation, a pragmatic literature review was conducted. The review also informed us on whether there are any existing models that could be adapted, as well as the potential model design that is informative to construct a de novo model in our study. Full details of literature search strategy are given in **Literature review search strategy**.

4.2.2 Findings from literature review

47 articles were identified for title/abstract screening. The review found no previous model-based CEA for simple olecranon fracture fixation. Only one study (Dias 2020) comparing the clinical effectiveness and cost-effectiveness of surgical fixation for adults with a bicortical fracture of the scaphoid waist (SWIFFT) was considered relevant to our model design (13).

After the first 52 weeks from treatment initiation, according to the fracture recovery status patients, patients are divided into two groups, fracture union and non-union. A Markov model was used to simulate the downstream disease progression of the two groups respectively in SWIFFT:

- For the patients with fracture union, they were placed in one of two states in the Markov model: "no osteoarthritis (OA) or other adverse events (AEs)" or "no OA but long-term AEs". Those in "No OA or other AEs" are subject to the risk of developing "OA with symptoms" or "OA without any symptoms". Death is the absorbing health state.
- For patients failing to achieve fracture union, they entered the "no scaphoid non-union advanced collapse (SNAC)" health state and throughout their lifetime face a risk of progressing to SNAC or dying from unrelated causes. Patients in SNAC could either remain in the state or die at each cycle. The reason why SNAC was chosen as the health state for patients with fracture non-union is SNAC represents a serious AE that results from non-union.

For the detailed model structure in SWIFFT, please refer to Dias 2020 (13).

4.2.3 Model design

Considering that the model developed in Dias 2020 was for scaphoid waist fracture, which differs from olecranon fracture in terms of the long-term disease progression, it needs to be adapted so that it could accurately reflect the disease progression of patients with simple olecranon fracture after they receive the surgery using tension band wiring or tension suture repair. The adaptation will be based on the long-term disease trajectory of olecranon fracture and major clinical events that might occur during the lifespan of patients.

After consulting with the Chief Investigator regarding the model design, it has been taken into consideration that patients might develop chronic complications in the long-run, which might require re-operation. The success/failure of re-operation would further decide the future health status of patients throughout the lifetime.

As shown in **Figure 1** below, a cohort Markov model was designed to reflect the possibility of chronic complications and associated re-operation to be experienced by the patients beyond 18 months.

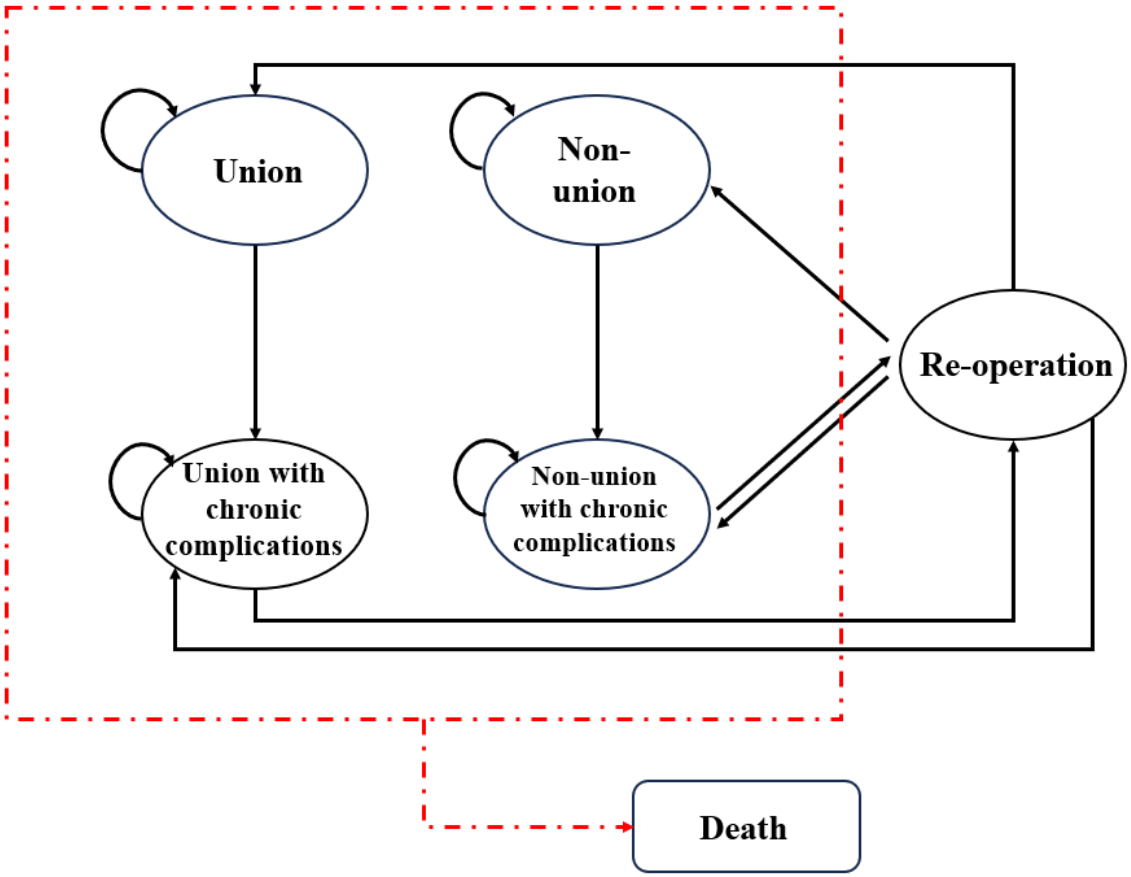

Figure 1 Proposed Markov model structure

4.2.3.1 Health states

The health states defined in the Markov model encompass:

- **Union (U)**: Patients have healed fractures without any chronic complications.
- **Non-Union (NU)**: Fractures have not healed, and patients are not experiencing any chronic complications.
- **Union with Chronic complications (UwC)**: Patients have healed fractures but are experiencing chronic complications.
- **Non-Union with Chronic complications (NUwC)**: Fractures have not healed, and patients are experiencing chronic complications.

- **Re-operation (RO)**: A temporary tunnel state representing the surgical intervention to treat the chronic complications
- **Death (D)**: Representing mortality, which could potentially occur from any state at each model cycle.

At the beginning of the long-term model, patients will reside in either U or NU health states:

- From U, patients might either remain U, or develop chronic complications (UwC), which require re-operation (RO). Patients who chose not to receive re-operation are assumed to remain UwC. Patients with U are not allowed to transition back to NU/NUwC. The successful re-operation will bring patients back to U, whilst the failure of re-operation will result in patients remaining in UwC. Once UwC patients do not respond to re-operation, they are assumed to stay in UwC until death.
- On the other hand, from NU, patients might either remain NU without chronic complications or have chronic complications (NUwC). NUwC patients require re-operation, and those NUwC patients who chose not to be treated are assumed to remain NUwC. Similarly to the case among U patients, successful re-operation would resolve complications and bring them back to (NU), or even lead to fracture union (U). Instead, unsuccessful re-operation will keep patients in NUwC. Once NUwC patients do not respond to re-operation, they are assumed to stay in NUwC until death.

Of note, RO is a temporary tunnel state, meaning patients can only stay in this state for one cycle, after which they will transition to other various health states, dictated by the success/failure of the operation.

4.2.3.2 Time horizon

As previously mentioned, a lifetime Horizon will be adopted to fully capture the costs and benefits of using tension band wiring and tension suture repair.

4.2.3.3 Cycle length

6-month cycle length was adopted as it provides a compromise between detail and computational efficiency and aligns with the granularity of the available 18-month clinical trial data.

4.2.4 Key model parameters and data source

The proposed list of model parameters is summarised in **Table 6 Proposed list of key parameters for the long-term model**. The parameters by category are presented below.

Initial proportion of union and non-union patients

According to the SOFFT trial protocol (1), patients will undergo radiological assessment at the 4 month from the baseline to document the status of their fracture union or non-union and there will be no further radiological assessment for all patients, although a proportion of patients might be assessed subsequently. Hence, the long-term Markov will adopt the proportion of union/non-union patients at 4 months as a proxy of that at 18 months. It is possible that during the 14 months window between 4 and 18 months, non-union patients might achieve union and it is likely that the proportion of union patients at 18 months will be underestimated. However, due to the lack of data, this seems to be the best available and most reliable data. Additionally, as addressed in the trial protocol, by 4-months the patient should have recovered from the initial intervention and bony union should be complete, which justifies our method. However, in order to test the robustness of the model results to the proportion of union and non-union patients at 18

months, we will increase the proportion of union patients at 4 months by 5%/10%/15%/20% in scenario analysis.

Risk of chronic complications

Patients in both fracture U/NU health state are subjective to the risk of chronic complications. The risk and type of chronic complications will be informed by published literature and validated by clinical experts.

Transition probability after re-operation

Due to the treatment efficacy of re-operation, patients who receive the re-operation might experience transition to various potential health states, which include:

- From UwC to U
- From UwC to UwC
- From NUwC to NUwC
- From NUwC to NU
- From NUwC to U

The transition probabilities will be informed by published literature and validated by clinical experts.

Mortality

Patients in any non-death health states of the model are subject to the risk of death at each cycle. For patients in U health state, it is assumed that the mortality is equal to the age-sex adjusted mortality of the general population in the UK, according to the latest UK national life tables (14). The excess mortality associated with residence in health state such as UwC, NU, NUwC, as well as the instant excess mortality due to re-operation will be informed by the published literature and validated by the clinical experts.

Cost and healthcare resource use

The costs to be considered in the model include:

- The cost of residing in the fracture U/NU/UwC/NUwC health state
- Cost of re-operation

For costing parameters, when the lump-sum costs (for example, the cost of re-operation) are unavailable from the literature, micro-costing approach will be adopted to estimate the types and quantities of health services required for re-operation by multiplying the unit costs of these health services with the quantities to derive the total costs. The data source for these unit costs will be the same as those used in within-trial CEA (3-5).

Heath-related quality of life

The QoL of patients to be considered in the model include:

- Health state utility value of U/NU
- Utility decrements due to chronic complications
- QALY loss due to re-operation

The QoL data will be informed by SOFFT trial data and published literature.

4.2.5 Model uncertainty

The model uncertainty will be explored via one-way sensitivity analysis (OWSA), probabilistic sensitivity analysis (PSA) and scenario analysis.

OWSA will be conducted to assess the impact of varying key model parameters (probabilities of developing chronic complications, treatment efficacy of re-operation, utilities, and costs) on the model output once in a time by taking the lower and upper bound of the value

range. 95% CI, if available, will be used as the value range. If not, an estimated interval that represents beliefs about the parameter's plausible range will be used (the range of all candidate values for this parameter derived from the literature) (15). Tornado diagrams will be plotted to present the extent to which each tested parameter impacts the model outputs (costs, QALYs and ICER).

PSA will be conducted to explore the parameter uncertainty by sampling estimates from a range of possible values (characterised by a parametric distribution) for key model parameters simultaneously as inputs into the models. CEP will be used to demonstrate the robustness of the cost-effectiveness to the parameter uncertainty of the model.

Scenario analyses will be used to test the structural uncertainty of the models, by changing model assumptions or model structure to explore the impact of such uncertainty on the model results.

4.2.6 Model validation

The face validity of the model will be assured by presentation of the model structure, assumptions, key parameters and data sources, and results to experts. The internal validity of the model will be assured through code checking and extreme value testing within the model. The cross-validation will be conducted by comparing the model results with other relevant studies (either clinical or economic evaluation) that analyse the same disease. Finally, the external validity of the model will be assured by comparing the model outcomes (costs, QALYs and other intermediate outcomes of the model) to real-world results (16).

5. Signatures of approval

Sign-off of the final approved version of the Health Economics Analysis Plan.

Name	**Trial Role**	**Signature**	**Date**
Qian Zhao	Health Economist		18/06/2024
Professor Adam C Watts	Chief Investigator		21/05/2024
Liz Cook	Trial Manager		20/05/2024

6. Appendix

5.1 Dummy tables for the analysis

Table 1 List of resource use and data source for unit costs

Category	Components	Unit cost (£)	Source of unit cost
Surgery-related costs			
Tension band wiring	K-wires	xxx.xx	NHS purchase price
	Cerclage wires	xxx.xx	
	Surgeons and other professional staff's salary for surgery	xxx.xx	PSSRU Unit Costs of Health and Social Care (3)
	Unit cost of operation room	xxx.xx	Published literature National Cost Collection data for the NHS (4)
	Other miscellaneous resource use (anaesthesia, diathermy, antibiotics, analgesics, tourniquet, tranexamic acid, pharmacological VTE prophylaxis)	xxx.xx	Published literature National Cost Collection data for the NHS (4)

Suture fixation repair	Cerclage suture material (to be determined based on the surgical form)	xxx.xx	NHS purchase price
	Surgeons and other professional staff's salary for surgery	xxx.xx	PSSRU Unit Costs of Health and Social Care (3)
	Unit cost of operation room	xxx.xx	Published literature National Cost Collection data for the NHS (4)
	Other miscellaneous resource use (anaesthesia, diathermy, antibiotics, analgesics, tourniquet, tranexamic acid, pharmacological VTE prophylaxis)	xxx.xx	Published literature National Cost Collection data for the NHS (4)
Intra operative complications (by treatment arm)	Fracture	xxx.xx	Published literature National Cost Collection data for the NHS (4)
	Nerve injury	xxx.xx	
	Vascular injury	xxx.xx	
	Loss of fixation	xxx.xx	

	Others	xxx.xx	
Routine care-related costs			
Data collected from CRF			
Surgical complications related to the affected arm	Cost of managing complications	xxx.xx	Published literature National Cost Collection data for the NHS (4)
	Hospital admissions due to the complications	xxx.xx	
Medical complications	Cost of managing complications	xxx.xx	Published literature National Cost Collection data for the NHS (4)
	Hospital admissions due to the complications	xxx.xx	
Secondary procedures	Cost of secondary procedures	xxx.xx	Published literature National Cost Collection data for the NHS (4)
	Hospital admissions due to secondary procedures	xxx.xx	
Physiotherapy	Physiotherapy received	xxx.xx	National Cost Collection data for the NHS (4)
Data collected from patient-reported questionnaire			

Care from the NHS not in the hospital	GP visit at GP practice	xxx.xx	PSSRU Unit Costs of Health and Social Care (3)
	Practice nurse at GP practice	xxx.xx	
	Occupational therapist	xxx.xx	National Cost Collection data for the NHS (4)
	Physiotherapist	xxx.xx	
Care from the NHS in the hospital	Outpatient visit with a surgeon for a follow-up appointment about the elbow	xxx.xx	
	Outpatient visit with a surgeon for a surgical procedure of the injured arm	xxx.xx	
	Outpatient visit with a nurse about the elbow	xxx.xx	
	Outpatient visit with a physiotherapist for physiotherapy about the elbow	xxx.xx	

	Outpatient visit with a physiotherapist about the elbow	xxx.xx	
	Outpatient visit to a pain clinic about the elbow	xxx.xx	
	Outpatient visit with an occupational therapist about the elbow	xxx.xx	
Accident and Emergency	Visit to Accident and Emergency about the elbow	xxx.xx	
Inpatient	Admitted to hospital as an inpatient for surgery	xxx.xx	
	Admitted to hospital as an inpatient for any other treatment	xxx.xx	
Day case	Admitted to hospital as a day case about the elbow	xxx.xx	

Table 2 Number and proportion of individuals with complete data (resource use and EQ-5D-5L) by treatment allocation at each time point

Time point	**Baseline**			**4 months**			**12 months***		
Questionnaire	**Total (N=xxx) n (%)**	**TBW (N=xxx) n (%)**	**TSR (N=xxx) n (%)**	**Total (N=xxx) n (%)**	**TBW (N=xxx) n (%)**	**TSR (N=xxx) n (%)**	**Total (N=xxx) n (%)**	**TBW (N=xxx) n (%)**	**TSR (N=xxx) n (%)**
EQ-5D-5L and resource use questionnaire									
Completed both									
Resource use only									
EQ-5D-5L only									
Completed none of both									
EQ-5D-5L									
No missing									

Resource use questionnaire									
No missing									
Abbreviations: TBW, tension band wiring; TSR, tension suture repair *The table only presents baseline, 4 months, and 12 months follow-up time point. The missing pattern at 18 months, as well as throughout the whole follow-up period will also be analysed.									

Table 3 Baseline characteristics by trial arm

	Base case (n= xxx)		**Complete case (n= xxx)**	
Baseline characteristics	**Tension band wiring (n=xxx)**	**Suture fixation repair (n=xxx)**	**Tension band wiring (n=xxx)**	**Suture fixation repair (n=xxx)**
Gender, n (%)				
Male				
Age (years), n (%)				
xx-xx				

xx-xx				
xx-xx				
Mean (SD)				
EQ-5D-5L utility				
Mean (SD)				
DASH score				
Mean (SD)				
VAS (pain)				
Mean (SD)				

Table 4 Average costs to the NHS and PSS by trial arm

Cost by category	**Base case**		**Complete case**	
	Tension band	**Suture fixation**	**Tension band**	**Suture fixation**

	(n=xx), £ (95% CI)	**(n=xx), £ (95% CI)**	**(n=xx), £ (95% CI)**	**(n=xx), £ (95% CI)**
Surgical-related costs				
Surgery for olecranon fracture				
Intra operative complications				
Routine care-related costs				
Surgical complications related to the affected arm				
Medical complications				
Secondary procedures				
Care from the NHS not in the hospital				
GP visit at GP practice				
Practice nurse at GP practice				
Occupational therapist				

Physiotherapist				
Care from the NHS in the hospital				
Outpatient visit with a surgeon for a follow-up appointment about the elbow				
Outpatient visit with a surgeon for a surgical procedure of the injured arm				
Outpatient visit with a nurse about the elbow				
Outpatient visit with a physiotherapist for physiotherapy about the elbow				
Outpatient visit to a pain clinic about the elbow				
Outpatient visit with an occupational therapist about the elbow				
Accident and Emergency				
Visit to Accident and Emergency about the elbow				
Inpatient				

Admitted to hospital as an inpatient for surgery to the elbow				
Admitted to hospital as an inpatient for other treatment to the elbow				
Day case				
Admitted to hospital as a day case about the elbow				
Total costs				

Table 5 Average EQ-5D-5L utilities by trial arm

EQ-5D-5L utilities by time point	**Base case**		**Complete case**	
	Tension band (n=xx), mean (95% CI)	**Suture fixation (n=xx), mean (95% CI)**	**Tension band (n=xx), mean (95% CI)**	**Suture fixation (n=xx), mean (95% CI)**

Baseline				
4 months				
12 months				
18 months				

Table 6 Proposed list of key parameters for the long-term model

List of model parameters	**Data source**
Proportion of union and non-union	
Tension band wiring	SOFFT trial data
Suture fixation repair	
Risk of chronic complications	
Tension band wiring	Published literature SOFFT trial data
Risk of long-term complications for union patients	
Risk of long-term complications for non-union patients	
Suture fixation repair	
Same category as tension band wiring arm with potentially different values	

Transition probability after re-operation	
Tension band wiring	Published literature SOFFT trial data
From UwC to U	
From UwC to UwC	
From NUwC to NUwC	
From NUwC to NU	
From NUwC to U	
Tension band wiring	
Same category as tension band wiring arm with potentially different values	
Mortality	
Mortality of U population	UK life tables
Excess mortality associated with UwC/NU/NUwC/re-operation	Published literature
Cost and resource use	

Cost of residing in U/UwC/NU/NUwC health states	Published literature SOFFT trial data National Cost Collection data PSSRU Unit Costs of Health and Social Care
Cost of re-operation (one-off)	
Health-related quality of life	
State-specific utility of fracture U/NU	Published literature SOFFT trial data
Utility decrements due to chronic complications	
QALY loss due to re-operation	

5.2 Literature review search strategy

This appendix details the literature review conducted to determine if there are any model-based economic analyses that could answer the long-term cost-effectiveness of tension suture repair compared with traditional band wire for simple olecranon fracture fixation. In addition, we aim to find if there are any previous cost-effectiveness model(s) that could be adapted to avoid developing a de novo model.

Our search strategy was not designed to limit any treatment for simple olecranon fracture fixation, so as to include as many relevant studies as possible for our review. Since this is not a systematic review, the strategy request was only submitted to PubMed in May 2023, supplemented by a search of grey literature consisting of iterative investigations of the information using Google and official websites such as NICE. The review was conducted by a single reviewer, but the findings are discussed in group.

Search strategy

The search was conducted in PubMed on 08 Jun 2023, with only English publications included. There are no restrictions on the publication date or types of studies. 45 studies were identified for title/abstract screening. Relevant papers will be reviewed in full-text.

1. "economic evaluation"[Title/Abstract] (12,357 hits)
2. "cost effectiveness"[Title/Abstract] (72,160 hits)
3. "cost utility"[Title/Abstract] (6,084 hits)
4. "cost benefit"[Title/Abstract] (11,929 hits)
5. 1 or 2 or 3 or 4 (89,096 hits)
6. elbow*[Title/Abstract] (35,879 hits)
7. olecranon*[Title/Abstract] (2,158 hits)
8. ulna*[Title/Abstract] (26,559 hits)
9. 6 or 7 or 8 (57,844 hits)

10. fracture*[Title/Abstract] (260,226 hits)
11. break*[Title/Abstract] (277,261 hits)
12. broken[Title/Abstract] (27,633 hits)
13. injur*[Title/Abstract] (905,411 hits)
14. 10 or 11 or 12 or 13 (1,185,219 hits)
15. 5 and 9 and 14 (45 hits)

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