FLARE

A randomised trial to determine the clinical and cost effectiveness of repairing flexor digitorum profundus (FDP) alone versus repair of both FDP and flexor digitorum superficialis (FDS) for treatment of complete zone 2 flexor tendon injuries: the FLexor repAir and REhabilitation (FLARE) Trial

STATISTICAL ANALYSIS PLAN

Version 1.0

ISRCTN: 10918157

York Trials Unit
Department of Health Sciences
University of York
York, YO10 5DD

Version date: 28/04/2025

Authors: Fraser Wiggins, Laura Mandefield and Kalpita Baird
Co-Chief Investigators: Mr Matthew Gardiner and Ms Emma Reay
Trial Manager: Liz Cook

Contents

1. Document scope and relevant SOPs and guidance documents

This statistical analysis plan (SAP) deals only with the statistical analysis of clinical effectiveness, the cost-effectiveness analysis will be detailed in a separate plan. This SAP was written prior to the completion of recruitment.

This SAP was prepared according to York Trials Unit (YTU) standard operating procedures (SOPs) and guidance documents. Data and documents relevant to the statistician will be kept in a Statistical Master File following the directory structure detailed in the YTU SOP entitled “DS01 Directory structure and version control”.

2. Definition of terms/acronyms

AE	Adverse event
BSSH	British Society for Surgery of the Hand
CACE	Complier average causal effect
CI	Confidence interval
CONSORT	Consolidated standards of reporting trials
CRF	Case Report Form
DIPJ	Distal interphalangeal joint
EQ-5D-5L	EuroQol 5 Dimensions 5 Levels
FDP	Flexor digitorum profundus
FDS	Flexor digitorum superficialis
HTA	Health Technology Assessment
ISRCTN	International Standard Randomised Controlled Trial Number
ITT	Intention-to-treat
MCPJ	Metacarpophalangeal joint
NIHR	National Institute for Health and Care Research
PEM	Patient evaluation measure
PIPJ	Proximal interphalangeal joint
PROM	Patient Reported Outcome Measure
PRWHE	Patient reported wrist/hand evaluation
RCT	Randomised Controlled Trial
REDCap	Research Electronic Data Capture
ROM	Total Range of Motion
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard deviation
SOP	Standard Operating Procedure
TAM	Total Active Movement
YTU	York Trials Unit

3. Design

FLARE is a pragmatic, multi-centre, two-armed, blinded, parallel group, non-inferiority randomised controlled trial (RCT) with an eight-month internal pilot. Randomisation will take place at the participant level. The two trial arms are: repair of both Flexor Digitorum Profundus (FDP) and Flexor Digitorum Superficialis (FDS) and repair of FDP only for the treatment of recent complete zone 2 flexor tendon injuries in adult patients.

Full details of the background and design of the trial are presented in the protocol (version 1.1).

4. Trial Objectives

The overarching objective of the FLARE trial is to undertake a multi-centre, two-arm, blinded, parallel group, non-inferiority RCT to determine the clinical and cost effectiveness of whether FDP repair alone is *not inferior* to both FDP and FDS repair, for the treatment of recent complete zone 2 flexor tendon injuries in adult patients.

4.1 Primary objective

The primary objective of this trial is to undertake a multi-centre RCT to determine whether repair of FDP alone is not inferior to repair of both FDP and FDS for the treatment of recent complete zone 2 flexor tendon injuries in adult patients measured using the Patient Evaluation Measure (PEM) at six-months post-randomisation.

4.2 Secondary objectives

The secondary objectives of the FLARE trial are:

a) To undertake an eight-month internal pilot to obtain robust estimates of recruitment and confirm trial feasibility against pre-specified stop/go pilot progression criteria.
b) To assess and compare range of motion between treatment groups
c) To assess and compare grip strength between treatment groups
d) To assess and compare the complications of both types of repair (FDP and FDS; FDP alone)
e) To assess and compare hand pain and disability using the patient self-reported Patient Related Wrist/Hand Evaluation (PRWHE) measure
f) To compare the costs, quality adjusted life years and cost effectiveness of repairing both FDP and FDS to repairing FDP alone. (This analysis is detailed elsewhere and not within the scope of this SAP)
g) To undertake an embedded qualitative study. (This analysis is detailed elsewhere and not within the scope of this SAP)

5. Follow-up

Following randomisation and treatment, all participants will be followed up for six-months. The main data collection timepoints are baseline, within one-week, six-weeks, three-months and six-months post-randomisation. This includes three clinic visits (one-week, six-weeks and three-months) where trial follow up visits should coincide with clinical visits that occur as part of routine care, and a patient medical record review six-months post-randomisation.

If unable to attend the clinic in person, participants can opt to complete the six-week and three-month visits remotely. However, participants will be encouraged to visit the clinic to obtain measurements regarding grip strength and range of motion.

Participants will be asked to complete follow-up outcome data via self-reported questionnaires at baseline, six-week, three-months and six-months post-randomisation.

A schedule of upcoming assessments and the outcome data collected at each timepoint (baseline, within one-week, six-weeks, three-months and six-months) are given in **Table 1**.

Table 1: Schedule of Assessments

Assessment	**Baseline**[1] *(face-to-face)*	**Randomisation / Surgery**	**Clinic Visit** *(Within 7 days of Surgical Intervention)*	**6 Week Clinic Visit**[2] *(face-to-face or remote)*	**3 Month Clinic Visit**[2] *(face-to-face or remote)*	**6 Month Remote** *(Participant Questionnaire by Email/Post/Telephone)*
Allowed variation in days				+/- 7 days	+/- 14 days	+/- 14 days
Eligibility Screen	X					
Informed Consent	X					
Demographics	X					
Randomisation		X				
Surgical Data *(including Epitendinous Suture Use)*		X				
Confirmation of Treatment			X			
Hand Therapy Review			X			
PEM	X			X	X	X
PRWHE	X[3]			X	X	X
EQ-5D-5L	X[3]			X	X	X
Total Range of Motion				X	X	
Work Outcomes				X	X	X
Treatment and Outcome Satisfaction				X	X	X
Healthcare Resource Use	X	X	X	X	X	X
Adherence to therapy Regimen				X	X	
Splint Adherence				X		
Grip Strength					X	
Complications			X	X	X	X

[1]Baseline measurements will be collected prior to randomisation.

[2]The 6-week clinic appointment may be virtual as part of routine practice.

[3]Pre- and post-injury.

6. Internal Pilot Outcomes

The first eight-months of recruitment constitutes an internal pilot. A traffic-light stop/go progression criteria system has been developed and pre-specified for the eight-month internal pilot phase and is provided in **Table 2**. The pilot phase will be assessed against these criteria.

Table 2: Pre-specified stop/go pilot progression criteria

Domain	**Target at end of internal pilot**	**Green**	**Amber**	**Red**
Participant recruitment	80	100%	75%-99%	<75%
Centres open	10	10	7-9	<7

Randomisation rate/centre/month	1	1	0.7-1	<0.7
Primary outcome data available	7	100%	85%-100%	<85%

7. Main Trial Outcomes

7.1 Primary outcome

The primary outcome measure is the Patient Evaluation Measure (PEM) Hand Health Profile completed at baseline, six-weeks, three-months and six-months post-randomisation. The pre-specified primary timepoint of interest is six-months post-randomisation.

The PEM is widely used in National Institute for Health and Care Research (NIHR) funded hand trauma studies and is the main patient reported outcome measure (PROM) used for flexor tendon injuries in the British Society for Surgery of the Hand (BSSH) United Kingdom National Hand Registry. The PEM comprises 19 items and three subscales; Treatment (5-items); Hand Health Profile (11-items) and Overall assessment (3-items). The 11-items which make up the Hand Health Profile subscale will be the primary outcome measure for the FLARE trial.

Items on the PEM Hand Health Profile subscale are measured on seven-point Likert scale such as 1 = Never and 7 = All the time, for example, with questions relating to symptoms, satisfaction and general disability. Scores across the 11-items are summed and used to generate a 0%-100% score to determine an overall disability score, with higher scores indicating greater levels of disability. At baseline the PEM will be collected twice: the first determining the patients Hand Health Profile before they sustained their injury and the second after their injury occurred.

The 11-item PEM Hand Health Profile will not be scored if more than two items are missing. If up to two items are missing, the missing items will be replaced with the mean of the remaining non-missing items.

7.2 Secondary outcomes

Most secondary outcome measures will be collected at baseline, within one-week, six-weeks, three-months and six-months post-randomisation. Where this is not the case this is outlined below and given in the study assessment schedule (**Table 2**).

7.2.1 Patient Evaluation Measure (Hand Health Profile)

The PEM Hand Health Profile as described in Section 7.1 above will be measured at six-weeks and three-months post randomisation.

7.2.2 Patient Evaluation Measure (Treatment subscale)

The PEM Treatment subscale comprises five-items relating to their treatment. Items are scored on a seven-point Likert scale ranging from one to seven. Scores are summed to generate a total score from 5 – 35 with higher scores indicating receipt of poorer treatment. The PEM Treatment subscale is collected at six-weeks, three-months and six-months post-randomisation, but not at baseline as the

items are unsuitable prior to receiving treatment/surgery. The PEM treatment subscale will not be scored if more than one of the five items are missing. If only one item is missing, the missing item will be imputed with the mean of the four non-missing items.

7.2.3 Patient Evaluation Measure (Overall Assessment subscale)

The PEM Overall Assessment subscale comprises three-items relating to overall treatment and hand health. Items are scored on a seven-point Likert scale ranging from one to seven. Scores are summed to generate a total score from 3 – 21. The PEM Overall Assessment subscale is collected at six-weeks, three-months and six-months post-randomisation, but not at baseline as the items are unsuitable prior to receiving treatment/surgery.

7.2.4 Patient Reported Wrist Hand Evaluation (PRWHE)

The PRWHE is a 15-item self-reported questionnaire used to assess the pain and function in the wrist and/or hand when carrying out day-to-day activities. There are five-items assessing pain in the wrist and/or hand and ten-items assessing function. The ten function items are further divided into specific activities (six-items) and usual activities (four-items). Each item is scored on a 0 to 10 scale, ranging from 0 (no pain) to 10 (worst possible pain) for the five pain related items and 0 (no difficulty) to 10 (unable to do so) for the ten function related items. A total score is generated by summing the five-pain items to generate a score from 0 – 50, and summing the ten function items to generate a score between 0 – 100. The score from the ten function items is then divided by two, to produce a score ranging from 0 – 50. This then weights pain and function equally. The pain and function scores are then summed to produce a score ranging from 0-100, with a higher score indicating more pain and functional disability. We can calculate PRWHE scores if no more than half of the items are missing. Missing items are replaced by the rounded mean of the relevant subscale. Missing items will be replaced by the mean for relevant subscales if no more than half of the items are missing. This means that up to two missing items for the pain subscale and up to five missing items for the function subscale can be imputed by the remaining items of the corresponding subscale.

7.2.5 Total Range of Motion

Total range of motion (ROM) will be clinically measured using a goniometer and will assess the degree of movement at a joint. ROM will be assessed either in person or remotely at six-weeks and three-months post-randomisation only. Due to the nature of the injury, it is not possible to collect ROM at baseline. The assessment measures both extension ROM and flexion ROM for each of the three joints. The joints of the affected finger are measured first, measuring the metacarpophalangeal joint (MCPJ) first, then the proximal interphalangeal joint (PIPJ) and finally the distal interphalangeal joint (DIPJ) in extension and flexion. This process is then repeated taking measurements for the same finger on the contralateral (opposite) hand. If measurements for the same finger on the contralateral hand are unable to be taken, measurements of the neighbouring finger on the contralateral hand will be taken as a surrogate. Measurements range from 0 to 260 degrees and can be negative in value. The three flexion measurements are then totalled, and the extension lag is deducted from the total sum to provide a Total Active Motion (TAM) for the injured digit. The same process is then used to calculate TAM for the contralateral digit. The TAM for the injured digit and contralateral digit are then

compared with the following rating; ‘excellent’ where the TAM of the injured and contralateral digit are equal; ‘good’ for >75%; ‘fair’ for >50%; and ‘poor’ for <50%.

7.2.6 Grip Strength (Clinical measurement)

Grip strength will be clinically measured with a JAMAR dynamometer, at three-months post-randomisation only. The three-month assessment is encouraged to take place in clinic, where possible. Both hands will be measured during the assessment, with the unaffected hand being measured first. The score (to the nearest kilogram) is recorded. After the initial grip strength recording, the same assessment process will be undertaken on the opposite hand. Maximum grip strength will be reported. Grip strength is reported a percentage of the grip strength of the opposite hand to account for normal variation in strength during the day. A higher score indicates a stronger grip strength.

7.2.7 Grip Strength (subjective measurement)

A self-reported subjective measurement of grip strength will be assessed using a global question, captured at three-months post-randomisation only. The item is measured on a four-point Likert scale ranging from 0 (much worse now than before my injury), 1 (slightly worse now than before my injury), 2 (almost the same now than before my injury), 3 (the same now or better than before my injury).

7.2.8 Adherence to splint regimen

The adherence to the splint regimen is assessed at six-weeks post-randomisation only and is self-reported by participants. Splint adherence is captured with five discrete questions: If the participant continues to wear the splint, measured with a yes/no response; how many weeks did the participant wear the splint, ranging from 0 to 5 weeks; how often, per day, did the participant wear the splint, measured on a four point Likert scale from constantly (except when bathing, dressing, etc), to not at all; which activities did the participants take their splint off for and how restricted the participant was while carrying out daily activities when wearing their splint measured on a 0-10 scale. These questions are discrete and are not combined to create an overall adherence score.

7.2.9 Treatment and outcome satisfaction

Treatment and outcome satisfaction is measured at six-weeks, three-months and six-months post-randomisation. Four questions measure treatment satisfaction by asking participants how likely they would be to recommend the treatments they received to a friend or relative with the same injury. The four items are scored on a 0-10 scale, ranging from 0 (not likely at all) to 10 (extremely likely).

7.2.10 Adherence to therapy regimen

Adherence to the hand therapy regimen is measured at six-weeks and three-months post-randomisation. Four items, self-reported by participants capture the following: was information regarding home exercises provided, measured using a yes/no response; if yes, how useful was the information they were provided, measured on a four-point Likert scale from extremely helpful to not very helpful at all; for how many weeks has the participant completed these exercises ranging from never to six weeks and continuing and has the pain and/or discomfort in the affected area stopped the

participant from carrying out the home exercises measured on five-point Likert scale from never to always. These questions are discrete and are not combined to create an overall adherence score.

7.2.11 Complications

Expected complications associated with the flexor tendon repair surgery will be collected at all follow-up time points. Complications are categorised into four areas: general surgical complications, anaesthetic-related complications, complications specific to flexor tendon repair surgery and hand therapy-related complications. Examples of expected complications include deep wound infection, rehospitalisation, nerve and skin problems. The full list of expected complications for each category is provided within the trial protocol.

Other collected outcome measures include the EQ-5D-5L, work outcomes and healthcare resource use but are pertinent to the economic evaluation and outside the scope of this document.

7.3 Other collected variables

7.3.1 Patient Reported Baseline Data

Participant reported demographic data will be collected at baseline. Participants will be asked to report the level of qualifications they hold, their employment status, their role within their occupation, living arrangements, smoking status, alcohol assumption and questions regarding their treatment preferences.

7.3.2 Clinician Reported Baseline Data

Clinician reported baseline data includes participant date of birth, which is the affected hand, if this is the participant's dominant hand, which digit is being treated, where the injury occurred and what was the injury caused by.

7.3.3 Primary Surgery Details

Data on the surgery that the participant underwent will be collected. The surgical details captured include: grade of the primary operating surgeon, background specialty, date of operation, subzone of injury, digital nerve injury, which nerve was damaged (if applicable), if the digital nerve was repaired, location of the surgical procedure, time the anaesthetic was administered, start and end time of the surgery, if the surgery was a day case, date of admission, date of discharge, type of anaesthetic used, tourniquet use, tourniquet placement, length of time tourniquet applied, antibiotic use.

7.3.4 Adverse events

Adverse events data will be collected (further details of this can be found in the study protocol).

7.3.5 Withdrawals

Data on withdrawals, such as date and timing of withdrawal, level of withdrawal (fully or from follow-up) and reasons for withdrawal (where given) will be collected.

8. Data

8.1 Data collection via REDCap

Data will be collected at baseline, within one-week, six-weeks, three-months and six-months post-randomisation. A secure online Research Electronic Data Capture (REDCap) system has been specifically developed for the FLARE trial.

Baseline data will be collected at recruiting sites by a member of the clinical/research staff and the patient. The data will be entered directly into REDCap by the clinical/research staff or returned electronically by the patient.

Clinical data collected at follow-up visits (one-week, six-weeks, three-months and six-months) post-randomisation will be collected via delegated blinded hand therapists or research staff and entered directly into REDCap. When data cannot be entered directly into REDCap, it may be entered onto paper copies first and then entered into REDCap by appropriately delegated site staff.

Participants can choose to complete questionnaires online and will be sent links to complete case report forms (CRFs) online at baseline, six-weeks, three-months and six-months post-randomisation, if this is their preferred method of data collection. If participants choose to complete follow-up data via post or telephone, this will be entered into REDCap by YTU staff.

REDCap is the default data collection method for the FLARE trial and will be used to electronically complete the following CRFs:

- Screening and initial eligibility form
- Consent status form
- Baseline investigator form
- Participant baseline form
- Eligibility and randomisation form
- Primary surgery form
- Investigator Form- 1week
- Investigator Form- 6weeks
- Participant 6weeks Follow Up Questionnaire form
- Investigator Form- 3months
- Participant 3Month Follow Up Questionnaire form
- Participant 6 Month Follow Up Questionnaire form
- Additional surgery form
- (S)AE form
- Adverse Events form
- Change of Status form

Data will be entered directly onto REDCap online. A copy of the CRFs and REDCap specifications are saved securely here: Y:\Project -- FLARE – Shared.

Trial management data such as the date the CRF is due, sent and returned, date of randomisation, setting and participant ID will also be stored in REDCap. Contact details including patient names and

addresses are stored in REDCap, however no identifiable data will be made available to the statisticians conducting the analysis.

8.2 Data collected via paper

Participants will be given the option to complete consent forms, baseline, and follow-up postal questionnaires on paper, if required. Paper consent forms and baseline questionnaires will be returned to sites to be recorded into the REDCap study management system. Paper follow-up questionnaires will be returned to YTU where data will be transferred into the REDCap study management system. Paper copies will be stored in a locked filing cabinet in a room with restricted access at the University of York.

9. Sample Size

A six-point difference on the PEM represents the threshold at which treatment differences become important (based on observational data from patients with Dupuytren's contracture for the DISC trial (HTA 15/102/04)). However, recent analysis within a flexor tendon population has found a seven-point difference on the PEM to be important and thus represents an appropriate non-inferiority margin to be used in this population. For 90% power and alpha=0.025, 310 participants are required to establish noninferiority within a margin of seven points on the PEM (SD=17; upper 80% confidence limit), based on the lower limit of a 95% two-sided confidence interval (equivalent to a one-sided 97.5% CI) and 20% attrition.

10. Randomisation

Eligible patients will be randomly allocated in a 1:1 ratio to receive either repair of both FDS and FDP or repair of FDP only using block randomisation stratified by study site with randomly varying block sizes. An independent statistician at YTU, who is not involved in the recruitment of participants, will generate the allocation schedule. The allocation schedule will be generated in Stata v17 or later.

Randomisation will be carried out using REDCap and be completed in theatre with treatment allocated on an individual patient basis.

11. Blinding

Patients will be blinded to treatment allocation and will not be told which type of tendon repair they have received. The resulting scar will not disclose the allocated intervention. A code break procedure for clinical care or safety reporting will be in place.

The operating surgeon and theatre staff will not be blinded and will be informed of the randomisation result in order to complete the treatment. Site clinical and research team staff will be blinded to the allocation. Outcome assessments will be performed wherever possible by assessors unaware of treatment allocation. Post-operative rehabilitation and exercises will be according to standard of care at the participating site in both groups, which means therapists can remain blinded.

To assess the success of participant blinding, six months after randomisation, participants will be asked which surgical treatment they think they received. Participants will be given opportunity to find

out which treatment they have received once the primary outcome has been collected and their participation in the trial has ended. At this point, the research team will send the participant a letter/email to inform them of the treatment they received where requested.

12. Analysis of internal pilot trial

The first eight-months of recruitment constitutes an internal pilot phase. Analyses at the end of the pilot trial will focus on descriptive summaries of primary and secondary outcomes, by trial arm as well as overall, with no formal hypothesis testing.

A Consolidated Standards of Reporting Trials (CONSORT) diagram will be presented to show the flow of participants through the trial. The number of sites open to recruitment will be presented. The number of patients screened, eligible, approached, consented and recruited will be presented. Reasons for ineligibility (before and during surgery), non-approach and non-consent will be summarised, where available.

The overall recruitment rate and 95% confidence interval (CI) will be estimated and reported from the data collected.

The number and proportion of participants randomised who do not receive the randomly allocated treatment will be presented, alongside reasons for non-compliance where possible.

The number and proportion of participants for whom scorable primary outcome (PEM Hand Health Profile) is available will be reported by trial arm and overall.

Results of the pilot trial analysis will be compared against the trial's internal pilot stop/go progression criteria.

Whilst not a formal pilot stop/go progression criterion, response rates to the clinician and participant reported CRFs will be presented by trial arm, and overall. Additionally, the number of who withdraw from follow-up or the trial will be presented, alongside the timing and reasons for withdrawal (where given).

The full final analysis will only be performed if the trial passes the pilot stage. If the trial does not meet the target sample size in pilot stage, the sample size will not be sufficiently powered for a full statistical analysis. The primary analysis results based on an insufficient sample are likely to be biased and we believe that presenting such results would mislead audience. Therefore, in the case of the trial stops at the pilot stage, we will present descriptive statistics of outcomes by randomised groups, as we will have done for a standalone feasibility study.

13. Main Trial analysis

13.1 Analysis software

All analyses will be conducted in Stata v18 (StataCorp, 2023), or later (to be confirmed in final report).

13.2 Analysis principles and populations

Analyses will follow the principles of intention-to-treat (ITT) with participant's outcomes analysed according to their original, randomised group, where data are available, irrespective of deviations

based on non-compliance. One-sided 97.5% confidence limits (equivalent to the upper bound of the two-sided 95% confidence interval) will be reported for the primary analysis. There will be no pre-defined non-inferiority margins for the remaining secondary outcomes, these will be compared for evidence of superiority and two-sided tests at the 5% significance level will be used.

13.3 Screening, eligibility, recruitment and follow-up data

This trial will be reported according to the CONSORT guidelines for a parallel group RCT (Schulz et al., 2010). The flow of participants through each stage of the trial will be presented in a CONSORT diagram (see **Appendix A** for an example).

The number of individuals screened, eligible, consented, and randomised will be presented. Reasons for ineligibility (before and during surgery) and non-consent will be provided, where available.

The number of sites recruited and patient recruitment by site will be summarised. The average recruitment rate per month, and per site per month, will be presented. Recruitment graphs presenting the overall recruitment by month and the actual vs target recruitment will be produced.

Response rates to the clinician and participant reported completed questionnaires will be presented by treatment arm, and overall, at each follow-up timepoint (one week, six-weeks, three-months and six months).
The type (from the trial or from follow-up) and timing of withdrawals will be presented by randomised group, and overall, with reasons for withdrawal where available.

13.4 Baseline data

All baseline data will be summarised descriptively by treatment group, as randomised and as included in the primary analysis. The baseline demographics, clinical characteristics and treatment preference of the participant will be reported. No formal statistical comparisons for baseline imbalance will be undertaken, but any noteworthy difference will be descriptively reported. Continuous data will be presenting using a mean and standard deviation and categorical data will be present using a count and a percentage.

A separate table of patients who consented but were not randomised will also be presented.

13.5 Primary analysis

The primary outcome measure (PEM Hand Health Profile) will be reported descriptively, by trial arm and overall, for all data collection timepoints (baseline, six-weeks, three-months and six-months post-randomisation).

The primary analysis will compare PEM Hand Health Profile scores between treatment groups using a covariance pattern mixed effect linear model, incorporating data from all post-randomisation time points (six-weeks, three-months and six-months). The model will adjust for digital nerve injury, anaesthetic type, baseline PEM Hand Health Profile score (both pre and post-injury), time, treatment arm, treatment-by-time interaction as fixed effects, with site and participant as random effects to account for clustering by site and repeated observations per participant.

The correlation of observations within participants over time will be modelled by a covariance structure. The different covariance structures for repeated measurements that are available as part of the analysis software will be applied to the model. The Akaike information criterion will be used to compare models specifying different covariance structures with smaller values preferred. Model assumptions will be checked as follows: the normality of the standardised residuals will be assessed using a QQ plot, and homoscedasticity will be assessed by means of a scatter plot of the standardised residuals against fitted values. One possible violation of the assumptions may be the normality of the residuals due to a potential ceiling or floor effect where a lot of patients have a score of zero. In this instance, we will carry out an additional sensitivity analysis using a semi-parametric approach based on an ordinal regression model using the 'glm' Stata command with a logit link function.

Participants will only be included in the model if they have complete data for the baseline covariates and a valid PEM Hand Health Profile score for at least one post-randomisation timepoint.

The treatment effect at all time points (six-weeks, three-months and six-months) and overall will be extracted in the form of an adjusted mean difference, two-sided 95% CIs (equivalent to a one-sided 97.5% CI) and p-value. The primary timepoint of interest is six-months post-randomisation. A detailed description of how we will interpret the treatment effect estimate is included in Appendix A.

Analysis of the primary outcome will be checked by a second statistician according to YTU SOPs and Guidance and a copy of F16: Primary Analysis Sign Off Form will be completed, signed and stored in the Trial Master File.

13.6 Analysis of secondary outcomes

All outcomes will be reported descriptively for all data collection timepoints.

The PEM Hand Health Profile subscale will be extracted from the primary analysis model at six-weeks and three-months post-randomisation.

Continuous outcome measures will be analysed in a similar way to the primary outcome, swapping baseline PEM Hand Health Profile score with the baseline value of the outcome as a covariate. If the measure was not completed at baseline (PEM treatment subscale, PEM Overall assessment, ROM and Grip strength) no adjustment will be made.

Adherence to the splint regimen at six-weeks post-randomisation will be summarised descriptively, by trial arm and overall, using counts and percentages for items one to four, and a mean and standard deviation for item five.

Adherence to the therapy regimen at six-weeks and three-months post-randomisation will be summarised descriptively, by trial arm and overall, using counts and percentages.

Treatment and outcome satisfaction will be analysed descriptively.

Complications (including deep wound infection (Yes/No), tendon rupture (Y/N), superficial infection (Yes/No) and rehospitalisation (Yes/No)) and further surgical procedures (Y/N) will be analysed using

a separate logistic regression models including similar covariates as the primary analysis model providing there are a minimum number of events (at least 5 per arm).

13.7 Sensitivity analysis of the primary outcome

13.7.1 CACE analysis

In non-inferiority comparisons the ITT analysis could bias towards the null, which may lead to false claims of non-inferiority. For this reason a CACE (complier average causal effect) analysis will also be undertaken in addition to the ITT analysis.

A CACE analysis for the primary outcome will be conducted to obtain unbiased estimates of the intervention effectiveness in the presence of full compliance with the intervention for those allocated to the intervention i.e. outcomes analysed with participants in the treatment group for the treatment which they received, rather than were randomised to.

A two-stage least squares instrumental variable approach will be used (with treatment assignment as the instrumental variable) using the `ivregress` command in Stata, with the `2sls` option (Dunn et al., 2005). This analysis will use a linear regression model for the PEM Hand Health Profile score at six-months, adjusting for baseline score, and with robust standard errors to account for clustering within site.

Data from the Primary surgery form will be used to define a ‘complier’ (based on the question ‘Which treatment did the participant receive?’.

13.7.2 Missing Data

Mixed-effect models assume that data is missing at random (MAR) and uses the correlation of within-subject observations to adjust for any missing outcome data. Therefore, participants will be included in the primary analysis model if they have completed the PEM Hand Health Profile for at least one follow-up timepoint and they have data for all baseline covariates within the model.

If the overall proportion of participants not included within the primary model, due to missing outcome data at all time points or missing baseline covariates, is greater than 5%, the impact of missing data on the primary analysis will be assessed using multiple imputation by chained equations. The imputation model will include key baseline variables (age, sex, digital nerve injury, anaesthetic type, baseline PEM Hand Health Profile score and baseline EQ5D-5L score).

A ‘burn –in’ of 150 will be used and 50 imputed datasets will be created. The primary analysis will then be rerun within the imputed datasets and Rubin's rules will be used to combine the multiply imputed estimates.

13.8 Adverse events

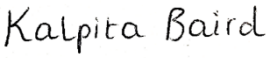
Adverse events (AEs) and Serious Adverse Events (SAEs) will be summarised descriptively, by trial arm, and overall. The number of AEs and SAEs per participant will be presented, by treatment group and overall. The event type, expectedness and relatedness to the study treatment of the AEs and SAEs will be summarised similarly.

14. SAP amendment log

Please note all changes that are made to the SAP following initial sign-off in the box below. Include details of the changes made, any notes/justification for these changes, the new version number if applicable, who the changes were made by, and the date.

Amendment/addition to SAP and reason for change	New version number, name and date

15. Signatures of approval

Name	Trial Role	Signature	Date
Matthew Gardiner	Co-Chief Investigator		28.04.2025
Emma Reay	Co-Chief Investigator		28.04.2025
Liz Cook	Trial Manager		28.04.2025
Kalpita Baird	Statistician		28.04.2025
Fraser Wiggins	Statistician		28.04.2025
Laura Mandefield	Senior Statistician		28.04.2025

16. References

Dunn, G., Maracy, M., & Tomenson, B. (2005). Estimating treatment effects from randomized clinical trials with noncompliance and loss to follow-up: The role of instrumental variable methods. In *Statistical Methods in Medical Research*. https://doi.org/10.1191/0962280205sm403oa

Schulz, K. F., Altman, D. G., & Moher, D. (2010). CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. *Journal of Clinical Epidemiology*, *63*(8), 834–840. https://doi.org/10.1016/j.jclinepi.2010.02.005

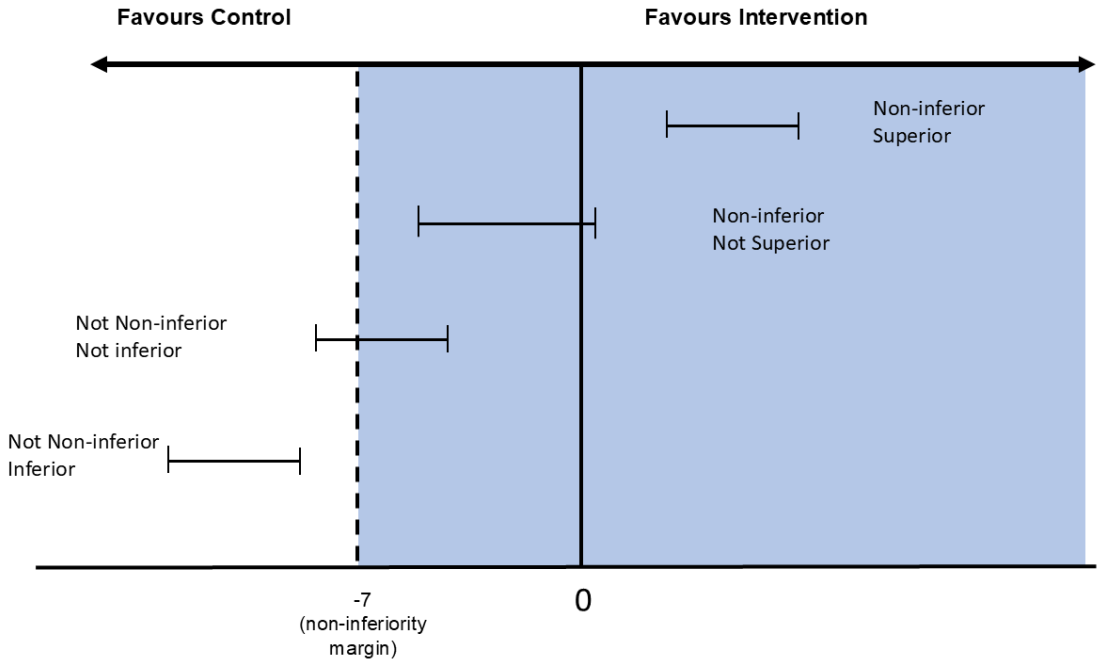
StataCorp. (2023). *Stata Statistical Software: Release 18* (18). Stata Press.

17. Appendices

17.1 Appendix A Accepting non-inferiority

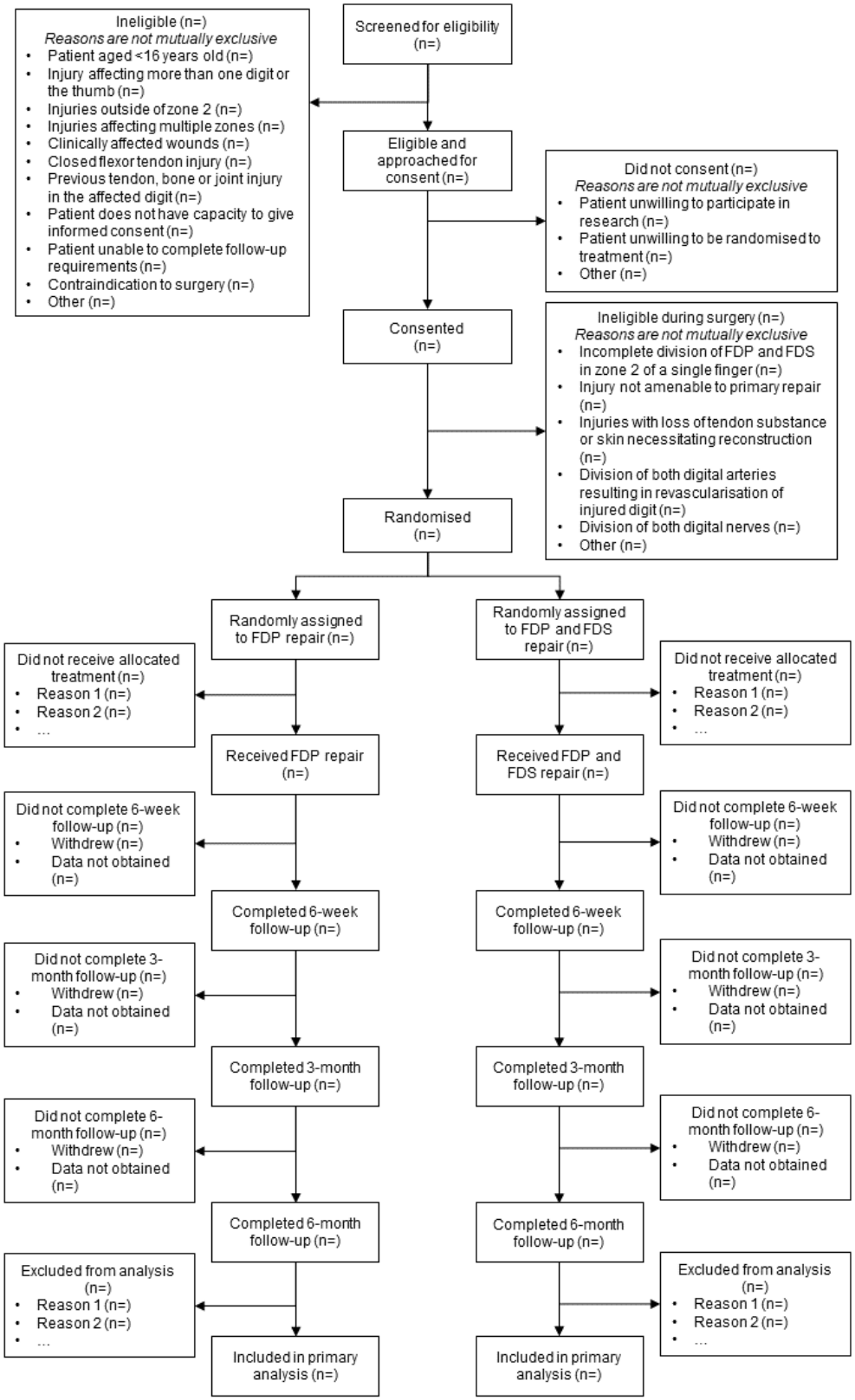
Section 13.5 outlines how we will determine whether repair of FDP only is non-inferior to repair of both FDS and FDP. The primary endpoint is the PEM score at six months. The desired direction of effect is an increase in PEM scores (higher PEM scores are more favourable). When modelling the treatment effect, the treatment allocations will be coded as 1= intervention (repair of FDP only) and 0= control (repair of both FDS and FDP). Therefore, a positive effect will mean the treatment difference will be positive. The non-inferiority margin has been specified as six points and non-inferiority will be accepted if the lower bound of the of the one-sided 97.5% confidence interval for the treatment difference at six months is greater than the non-inferiority margin of -7 points (a 7-point reduction). Figure 1 shows how we will interpret different possible results.

Figure 1: Example scenarios of non-inferiority in the FLARE trial



17.2 Appendix B – Trial Progression

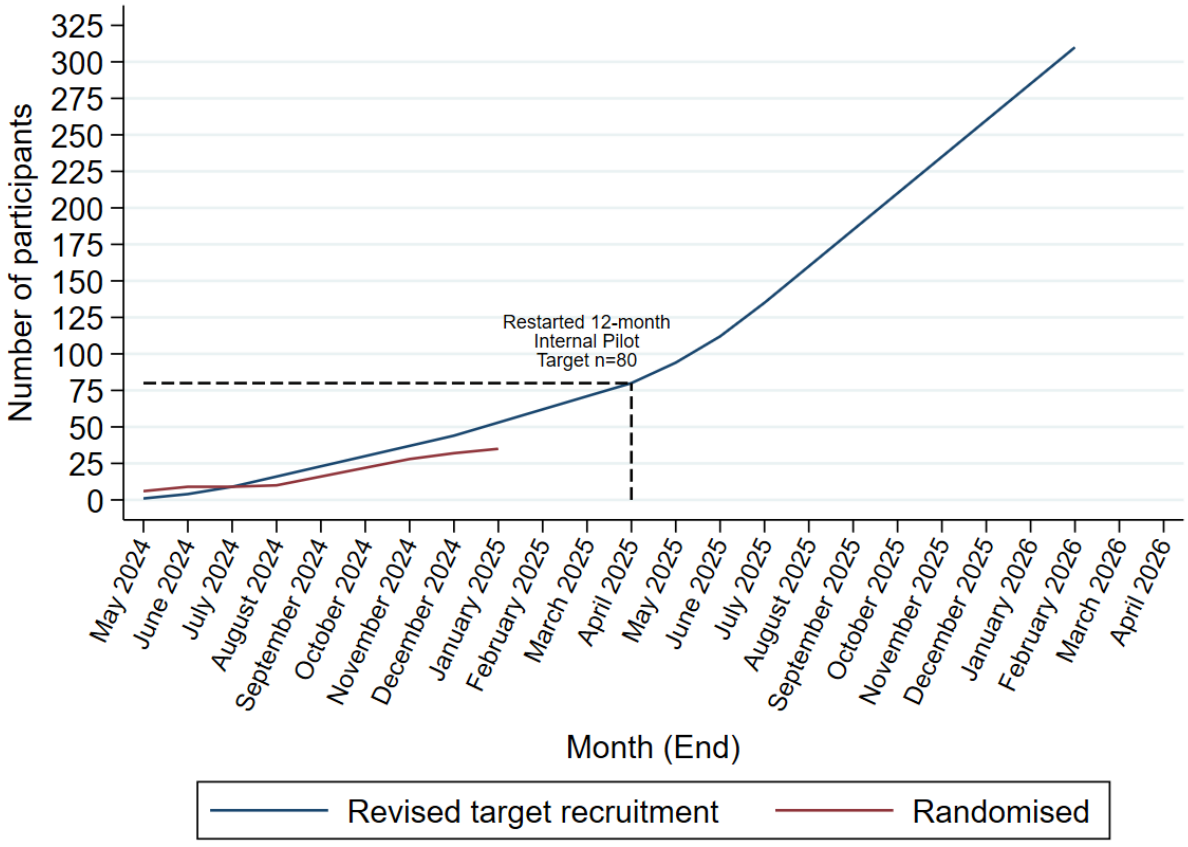
Figure 2: A CONSORT diagram outlining the progression of the trial.


Screened for eligibility (n=)
Ineligible (n=)
Reasons are not mutually exclusive
Patient aged <16 years old (n=)
Injury affecting more than one digit or the thumb (n=)
Injuries outside of zone 2 (n=)
Injuries affecting multiple zones (n=)
Clinically affected wounds (n=)
Closed flexor tendon injury (n=)
Previous tendon, bone or joint injury in the affected digit (n=)
Patient does not have capacity to give informed consent (n=)
Patient unable to complete follow-up requirements (n=)
Contraindication to surgery (n=)
Other (n=)
Eligible and approached for consent (n=)
Did not consent (n=)
Reasons are not mutually exclusive
Patient unwilling to participate in research (n=)
Patient unwilling to be randomised to treatment (n=)
Other (n=)
Consented (n=)
Ineligible during surgery (n=)
Reasons are not mutually exclusive
Incomplete division of FDP and FDS in zone 2 of a single finger (n=)
Injury not amenable to primary repair (n=)
Injuries with loss of tendon substance or skin necessitating reconstruction (n=)
Division of both digital arteries resulting in revascularisation of injured digit (n=)
Division of both digital nerves (n=)
Other (n=)
Randomised (n=)
Randomly assigned to FDP repair (n=)
Randomly assigned to FDP and FDS repair (n=)
Did not receive allocated treatment (n=)
Reason 1 (n=)
Reason 2 (n=)
…
Did not receive allocated treatment (n=)
Reason 1 (n=)
Reason 2 (n=)
…
Received FDP repair (n=)
Received FDP and FDS repair (n=)
Did not complete 6-week follow-up (n=)
Withdrew (n=)
Data not obtained (n=)
Did not complete 6-week follow-up (n=)
Withdrew (n=)
Data not obtained (n=)
Completed 6-week follow-up (n=)
Completed 6-week follow-up (n=)
Did not complete 3-month follow-up (n=)
Withdrew (n=)
Data not obtained (n=)
Did not complete 3-month follow-up (n=)
Withdrew (n=)
Data not obtained (n=)
Completed 3-month follow-up (n=)
Completed 3-month follow-up (n=)
Did not complete 6-month follow-up (n=)
Withdrew (n=)
Data not obtained (n=)
Did not complete 6-month follow-up (n=)
Withdrew (n=)
Data not obtained (n=)
Completed 6-month follow-up (n=)
Completed 6-month follow-up (n=)
Excluded from analysis (n=)
Reason 1 (n=)
Reason 2 (n=)
…
Excluded from analysis (n=)
Reason 1 (n=)
Reason 2 (n=)
…
Included in primary analysis (n=)
Included in primary analysis (n=)

17.3 Appendix C- Example tables

17.3.1 Screening, eligibility, recruitment and follow-up

Figure 3: Recruitment progress against target* (up to 17/01/2025)



*The internal pilot restarted at the beginning of May 2024 and was agreed to run for a 12-month period until the end of April 2025. The revised target recruitment figures for each month are included in Table 1 below (these are suggested targets based on the same n=80 recruited to be achieved by the end of the internal pilot period).

Table 3: Monthly recruitment to the FLARE trial

Month	Screened, N	Eligible at screening, N (% screened)	Approached, N (% eligible at screening)	Consented, N (% approached)	Eligible at surgery, N (% consented)	Randomised, N (% consented)
Total						

Figure 4: Monthly recruitment to the FLARE trial (as of 17/01/2025)

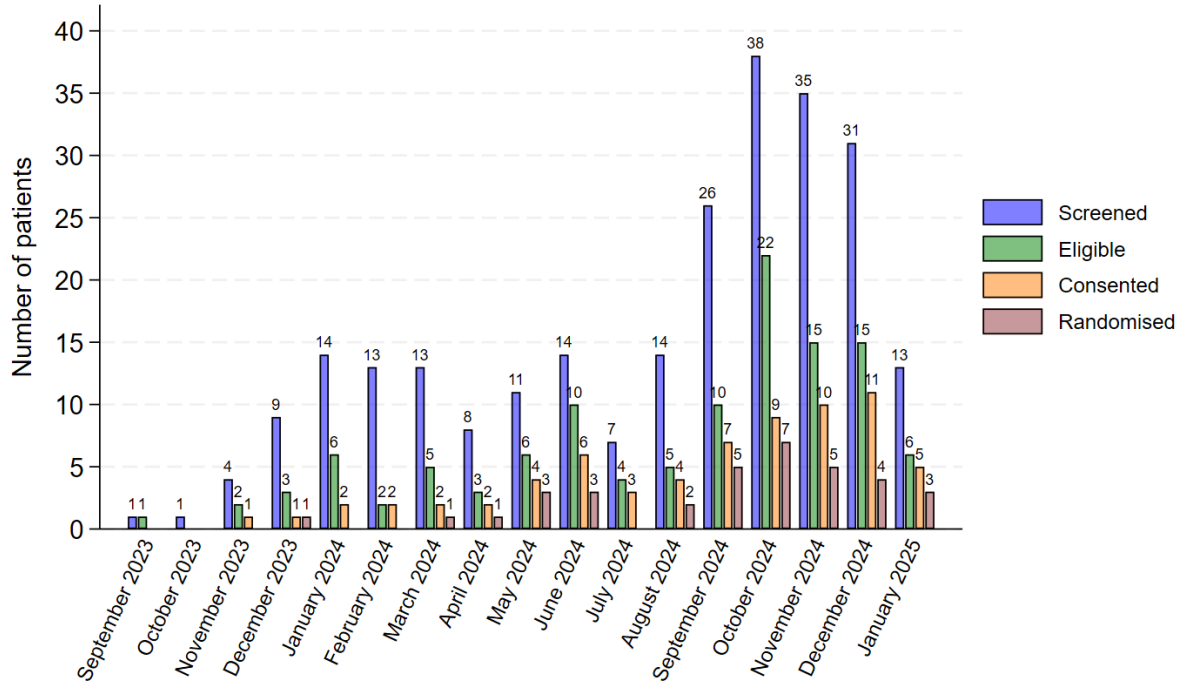


Table 4: Recruitment by site

Site ID	Site Name	Open to recruitment	Recruitment Period (months open)	Recruited, N	Avg. Randomised per month
Total					

Table 5: Screening by site

Site ID	Site Name	Screened, N	Eligible at screening, N (% screened)	Approached, N (% eligible at screening)	Consented, N (% approached)	Recruited, N (% consented)
Total						

Table 6: Reasons for ineligibility (pre-surgery). Reasons not mutually exclusive.

Ineligible Reason (Pre-surgery)	N	% of N who are ineligible
Aged less than 16 or no suspected division of both FDP and FDS tendons		
Injuries affecting more than one digit or the thumb		
Injuries outside of zone 2		
Injuries affecting multiple zones		
Clinically infected wounds		
Closed flexor tendon injury		
Previous tendon, bone or joint injury in the affected digit		
Patient does not have capacity to give informed consent		
Patient unable to complete follow up requirements		
Contraindication to surgery		
Other		
Unknown/Missing data		

Table 7: Reasons for non-consent. Reasons not mutually exclusive.

Reason for non-consent	N	% of N approached who did not give consent
Patient unwilling to participate in research		
Participant unwilling to be randomised to treatment		
No reason given		
Other		

Table 8: Reasons for ineligibility (during surgery). Reasons not mutually exclusive.

Ineligible Reason (During surgery)	N	% of N who are ineligible
No complete division of FDP and FDS in zone 2 of a single finger		
Injury not amenable to primary repair		
Injuries with loss of tendon substance		
Injuries with loss of skin necessitating reconstruction		
Division of both digital arteries resulting in revascularisation of injured digit		
Division of both digital nerves		
Other		
Unknown/Missing data		

Table 9: Information on the collection of the primary outcome and the return of participant questionnaires

	Intervention (n=)	Control (n=)	Overall
Primary outcome obtained, n (%) Yes No			
6-week questionnaire returned, n (%) Yes No			
3-month questionnaire returned, n (%) Yes No			
6-month questionnaire returned, n (%) Yes No			

Table 10: Information on the collection of the primary outcome and the return of clinician questionnaires (investigator forms)

	Intervention (n=)	Control (n=)	Overall
Baseline Investigator form, n (%) Yes No			
Primary Surgery form, n (%) Yes No			
Week 1 Investigator form, n (%) Yes No			
Week 6 Investigator form, n (%) Yes No			
Month 3 Investigator form, n (%) Yes No			

17.3.2 Withdrawals

Table 11: Withdrawals reasons by type and site

ID	Type of Withdrawal	Site	Date Randomised	Date Withdrawn	Reason for withdrawal (if provided)

Table 12: Information on withdrawals presented overall and by site.

	Intervention (n=)	Control (n=)	Overall (n=)
Withdrew, n (%) Yes No			
Time between randomisation and withdrawal, n (%) n (%) Mean (SD) Median (IQR) Min, Max			
Type of withdrawal, n (%) Treatment only Follow-up only Full withdrawal Deceased			

17.3.3 Baseline demographic and hand injury characteristics

Table 13: Patient reported demographic and baseline characteristics presented by treatment allocation for the 'as randomised' and 'as analysed' participants for the ITT population.

	As randomised (n=)		As analysed (n=)		Overall (n=)
	Intervention (n=)	Control (n=)	Intervention (n=)	Control (n=)	
Demographics					
Sex, n (%) Male Female Other Rather not say Missing					
Age at randomisation (years) n (%) Mean (SD) Median (IQR) Min, Max					
Age (Grouped), N (%) 16 - 25 years 26 - 35 years 36 - 45 years 46 - 55 years 56 - 65 years 66- 75 years 76 -85 years					
Ethnicity, n (%) White - British White - Irish White - Any other White background Mixed - White and Black Caribbean Mixed - White and Black African Mixed - White and Asian Mixed - Any other mixed background Asian or Asian British - Indian Asian or Asian British - Pakistani Asian or Asian British - Bangladeshi Asian or Asian British - Any other Asian background Black or Black British - Caribbean Black or Black British - African Black or Black British - Any other Black background Other Ethnic Groups - Chinese Other Ethnic Groups - Any other ethnic group Missing					

Highest level of qualification, n (%) No qualifications Apprenticeships or equivalent GCSE or equivalent A and AS Level or equivalent qualifications Degree-level or higher qualification Other					
Employment Status (past 7-days), n (%) Working as an employee Self-employed or freelance Temporarily away from work, ill, on holiday or laid off On maternity or paternity Doing other paid work Retired Studying Looking after home or family Long term sick or disabled Other					
Role in occupation (if employed), n (%) Managers Professional Technicians and associate professionals Clerical support workers Service and sales workers Skilled agricultural, forestry and fishery workers Craft related trades workers Plant and machine operators, and assemblers Elementary occupations (cleaning, labouring, food preparation) Armed forces occupations Other					
Living arrangements, n (%) Live alone Live alone but with support Live with wife/husband/partner Live with friends Live with relatives Other Missing					
Currently a smoker, n (%) Yes No					
Drinks alcohol 3 days or more a week, n (%) Yes No					
Injury Details (Pre-surgery)					
Hand with injury, N (%)					

Left Right					
Injury affecting dominant hand, N (%) Yes No					
Location of injury, N (%) At work - job related activity At work – not job related At home - household activity Leisure activity Other					
Cause of injury, N (%) Glass Knife or other kitchen equipment - Accidental Knife or Offensive Equipment - Violent Incident Sports equipment Working with machinery Gardening equipment Bitten Traffic accident Fall Self Harm Other					
Treatment preference, n (%) One flexor tendon repaired Both flexor tendons repaired No preference Missing					
Anaesthetic preference, n (%) Awake, with just numb finger or hand Awake, whole arm numb Asleep or sedated No preference Missing					

Table 14: Patient reported demographic and baseline characteristics presented for consenting participants that were not randomised (due to ineligibility during surgery or other reasons).

	Overall
	N=
Demographics	
Sex, n (%)	
Male	
Female	
Other	
Rather not say	
Missing	
Age at randomisation (years)	
n (%)	
Mean (SD)	
Median (IQR)	
Min, Max	
Age (Grouped), N (%)	
16 - 25 years	
26 - 35 years	
36 - 45 years	
46 - 55 years	
56 - 65 years	
66- 75 years	
76 -85 years	
Ethnicity, n (%)	
White - British	
White - Irish	
White - Any other White background	
Mixed - White and Black Caribbean	
Mixed - White and Black African	
Mixed - White and Asian	
Mixed - Any other mixed background	
Asian or Asian British - Indian	
Asian or Asian British - Pakistani	
Asian or Asian British - Bangladeshi	
Asian or Asian British - Any other Asian background	
Black or Black British - Caribbean	
Black or Black British - African	
Black or Black British - Any other Black background	
Other Ethnic Groups - Chinese	
Other Ethnic Groups - Any other ethnic group	
Missing	
Highest level of qualification, n (%)	
No qualifications	
Apprenticeships or equivalent	
GCSE or equivalent	
A and AS Level or equivalent qualifications	
Degree-level or higher qualification	
Other	

Employment Status (past 7-days), n (%) Working as an employee Self-employed or freelance Temporarily away from work, ill, on holiday or laid off On maternity or paternity Doing other paid work Retired Studying Looking after home or family Long term sick or disabled Other	
Role in occupation (if employed), n (%) Managers Professional Technicians and associate professionals Clerical support workers Service and sales workers Skilled agricultural, forestry and fishery workers Craft related trades workers Plant and machine operators, and assemblers Elementary occupations (cleaning, labouring, food preparation) Armed forces occupations Other	
Living arrangements, n (%) Live alone Live alone but with support Live with wife/husband/partner Live with friends Live with relatives Other Missing	
Currently a smoker, n (%) Yes No	
Drinks alcohol 3 days or more a week, n (%) Yes No	
Injury Details (Pre-surgery)	
Hand with injury, N (%) Left Right	
Injury affecting dominant hand, N (%) Yes No	
Location of injury, N (%) At work - job related activity At work – not job related At home - household activity Leisure activity Other	
Cause of injury, N (%) Glass	

Knife or other kitchen equipment - Accidental Knife or Offensive Equipment - Violent Incident Sports equipment Working with machinery Gardening equipment Bitten Traffic accident Fall Self Harm Other	
Treatment preference, n (%) One flexor tendon repaired Both flexor tendons repaired No preference Missing	
Anaesthetic preference, n (%) Awake, with just numb finger or hand Awake, whole arm numb Asleep or sedated No preference Missing	

17.3.4 Treatment delivery

Table 15: Treatment received presented by randomised treatment group

	Randomised treatment	
	Intervention (n=)	**Control (n=)**
Treatment received Intervention Control Other		

Table 16: Primary surgery data presented by randomised treatment group

	Intervention (n=)	**Control (n=)**	**Overall (n=)**
Injury Details			
Sub zone of injury, n (%) 2A 2B 2C 2D			
Digital nerve injury, n (%) Partial Complete No nerve injury			
Nerve damaged, n (% of partial or complete injury) Ulnar Radial			
Digital nerve repaired, n (% of partial or complete injury) Nerve suture repaired			

Nerve ends laid inline but not sutured No repair Other			
Theatre Logistics			
Physical location of procedure, n (%) Main operating theatre with laminar flow Main operating theatre with air changes Minor operating room/procedure room Trauma clinic / outpatient room Emergency department room Other			
Duration of operation (mins) N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Type of anaesthetic, n (%) Local anaesthetic alone (without adrenaline) Local anaesthetic with adrenaline Upper limb block alone General anaesthetic and upper limb block General anaesthetic and local anaesthetic General anaesthetic alone			
Tourniquet used, n (%) Yes No			
Tourniquet placed, n (%) Arm Forearm			
Length of time tourniquet applied (mins) N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Prophylactic antibiotics at induction, n (%) Yes No			
Surgical Repair of FDP			
Core suture technique of FDP, n (%) Adelaide Modified Kessler Cruciate M-Tang Other			
Core suture number of strands of FDP, n (%) 2 4 6 8			
Core type of suture of FDP, n (%) Prolene Polydioxanone suture (PDS)			

Fibrewire Ti Cron Other			
Core suture size of FDP, n (%) 2-0 3-0 4-0 5-0 Other			
Epitendinous suture for FDP, n(%) Yes No			
Epitendinous suture technique for FDP, n (%) Simple continuous Silverskold Other			
Epitendinous type of suture for FDP, n (%) Prolene Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Epitendinous suture size for FDP, n (%) 2-0 3-0 4-0 5-0 6-0			
Pulleys surgically vented, n (%) Yes - A1 Yes - A2 Yes - A3 Yes - A4 No Other			
Surgical Repair of FDS			
Core tendon repaired Yes No			
Core suture technique of FDS, n (%) Adelaide Modified Kessler Cruciate M-Tang Other			
Core suture number of strands of FDS, n (%) 2 4 6 8			
Core type of suture of FDS, n (%) Prolene			

Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Core suture size of FDS, n (%) 2-0 3-0 4-0 5-0 Other			
Epitendinous suture for FDS, n(%) Yes No			
Epitendinous suture technique for FDS, n (%) Simple continuous Silverskold Other			
Epitendinous type of suture for FDS, n (%) Prolene Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Epitendinous suture size for FDS, n (%) 2-0 3-0 4-0 5-0 6-0			
Pulleys surgically vented (Core FDS), n (%) Yes - A1 Yes - A2 Yes - A3 Yes - A4 No Other			
Ulnar slip of FDS repaired Yes No			
Core suture technique of ulnar slip, n (%) Adelaide Modified Kessler Cruciate M-Tang Other			
Core suture number of strands of ulnar slip, n (%) 2 4 6 8			
Core type of suture of ulnar slip, n (%) Prolene			

Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Core suture size of ulnar slip, n (%) 2-0 3-0 4-0 5-0 Other			
Epitendinous suture for ulnar slip, n(%) Yes No			
Epitendinous suture technique for ulnar slip, n (%) Simple continuous Silverskold Other			
Epitendinous type of suture for ulnar slip, n (%) Prolene Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Epitendinous suture size for ulnar slip, n (%) 2-0 3-0 4-0 5-0 6-0			
Pulleys surgically vented (ulnar slip), n (%) Yes - A1 Yes - A2 Yes - A3 Yes - A4 No Other			
Unrepaired ulnar slip excised, n (%) Yes No			
Radial slip of FDS repaired Yes No			
Core suture technique of radial slip, n (%) Adelaide Modified Kessler Cruciate M-Tang Other			
Core suture number of strands of radial slip, n (%) 2 4 6			

8			
Core type of suture of radial slip, n (%) Prolene Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Core suture size of radial slip, n (%) 2-0 3-0 4-0 5-0 Other			
Epitendinous suture for radial slip, n(%) Yes No			
Epitendinous suture technique for radial slip, n (%) Simple continuous Silverskold Other			
Epitendinous type of suture for radial slip, n (%) Prolene Polydioxanone suture (PDS) Fibrewire Ti Cron Other			
Epitendinous suture size for radial slip, n (%) 2-0 3-0 4-0 5-0 6-0			
Pulleys surgically vented (radial slip), n (%) Yes - A1 Yes - A2 Yes - A3 Yes - A4 No Other			
Unrepaired radial slip excised, n (%) Yes No			
Both ulnar and radial slip not repaired, n (%) Yes No			
Immediate post-operative management			
Wound closure suture, n (%) Absorbable Non-absorbable			
Primary splint applied, n (%) Long dorsal-blocking splint (modified Belfast) Short dorsal-blocking splint (Manchester short splint)			

Relative motion flexion splint and wrist splint Other			
Inadvertent unblinding of participant, n (%) Yes No			

17.3.5 Primary Analysis

Table 17: Unadjusted PEM Hand Health Profile presented by treatment group

	Intervention (n=)	Control (n=)	Overall (n=)
Baseline N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Weeks N (% data available) Mean (SD) Median (IQR) (Min, Max)			
3 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			

Table 18: PEM Hand Health Profile score at 6-months presented descriptively by treatment group for the ITT population. Adjusted mean differences alongside corresponding 95% confidence intervals are presented.

	Mean estimates		Adjusted Mean Difference (95% CI)	p-value
	Intervention	Control		
PEM HHP Score				
Number of participants analysed 6 Months				

17.3.6 Analysis of Secondary Outcomes

Table 19: Unadjusted secondary outcomes presented by treatment group

	Intervention (n=)	Control (n=)	Overall (n=)
PEM Treatment Score			
Baseline N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Weeks N (% data available) Mean (SD) Median (IQR) (Min, Max)			
3 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			
PEM Overall Score			
Baseline N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Weeks N (% data available) Mean (SD) Median (IQR) (Min, Max)			
3 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			
PHRWE Score			
Baseline N (% data available) Mean (SD) Median (IQR)			

(Min, Max)			
6 Weeks N (% data available) Mean (SD) Median (IQR) (Min, Max)			
3 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			
6 Months N (% data available) Mean (SD) Median (IQR) (Min, Max)			

Table 20: Range of motion at 6 weeks and 3 months of the affected digit, presented by treatment group

	Intervention	**Control**	**Overall**
6 Weeks	**N=**	**N=**	**N=**
Extension (°)			
MCPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
PIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
DIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Flexion (°)			
MCPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
PIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
DIPJ N (% data available)			

Mean (SD) Median (IQR) (Min, Max)			
Total Active Motion			
Combined measurement (°) N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Percentage comparison with contralateral digit N (% data available) Mean (SD) Median (IQR) (Min, Max)			
3 months	**N=**	**N=**	**N=**
Extension (°)			
MCPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
PIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
DIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Flexion (°)			
MCPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
PIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
DIPJ N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Total Active Motion			
Combined measurement (°) N (% data available) Mean (SD)			

Median (IQR) (Min, Max)			
Percentage comparison with contralateral digit N (% data available) Mean (SD) Median (IQR) (Min, Max)			

Table 21: Clinical and subjective grip strength measurements at 3 months of the affected hand, presented by treatment group

	Intervention (n=)	**Control (n=)**	**Overall (n=)**
Clinical measure			
Affected hand (kg) N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Unaffected hand (kg) N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Percentage comparison with contralateral hand N (% data available) Mean (SD) Median (IQR) (Min, Max)			
Subjective measure			
Grip strength compared with before the injury 0 – Much worse now 1 – Slightly worse 2 – Almost the same now 3 – The same now or better			

Table 22: Secondary outcomes presented by treatment group. Adjusted mean differences alongside corresponding 95% confidence intervals are presented.

	Mean estimates		Adjusted Mean Difference (95% CI)	p-value
	Intervention	Control		
PEM HHP score				
Number of participants analysed 6 weeks 3 months				
PEM Treatment Score				
Number of participants analysed 6 weeks 3 months 6 months				
PEM Overall Score				
Number of participants analysed 6 weeks 3 months 6 months				
PRWHE Score				
Number of participants analysed 6 weeks 3 months 6 months				
Total range of motion				
Number of participants analysed 6 weeks 3 months				
Grip Strength (Clinical measure)				
Number of participants analysed 3 months				

Table 23: Adherence to splint and therapy regimen

	Intervention (n=)	Control (n=)	Overall (n=)
Splint Regimen (6 weeks)			
Still continue to wear splint as part of your hand therapy, n (%) Yes No			
Number of weeks the splint was worn, n (%) 0 weeks 1 week 2 weeks 3 weeks 4 weeks 5 weeks			

Frequency of wearing splint per day, n (%) Constantly, except when bathing, dressing etc. Most of the day Less than half the day Not at all			
Activities that resulted in splint removal (Not mutually exclusive), n (%) Whilst I was dressing or undressing The splint became too uncomfortable To wash my hand Whilst I was showering I wanted to see my hand I became frustrated only using one hand I did not really understand why it was so important to wear the splint all of the time Other			
Splint restriction for daily activities, n (%) 0 – Not restricted at all 1 . . . 10 – Very restricted			
Hand Therapy Regimen (6 weeks)			
Home exercise information provided, n (%) Yes No			
Helpfulness of the information, n (% of those who had information provided) Extremely helpful Somewhat helpful Not very helpful Not very helpful at all			
Number of weeks completing home exercises, n (%) Never Up to 1 week 2-3 weeks 4-5 weeks 6 weeks and still continuing the exercises			
Pain or discomfort stopping home exercises, n (%) Never Rarely Sometimes Often Always			
Hand Therapy Regimen (3 months)			
Home exercise information provided, n (%) Yes No			

Helpfulness of the information, n (% of those who had information provided) Extremely helpful Somewhat helpful Not very helpful Not very helpful at all			
Number of weeks completing home exercises, n (%) Never Up to 1 week 2-3 weeks 4-5 weeks 6 weeks and still continuing the exercises			
Pain or discomfort stopping home exercises, n (%) Never Rarely Sometimes Often Always			

Table 24: Treatment and outcome satisfaction

	Intervention (n=)	**Control (n=)**	**Overall (n=)**
6 weeks post-randomisation			
Likelihood to recommend the treatment to a friend/relative with the same injury in relation to the surgery, n (%) 0 – Not likely at all 1 . . . 10 – Extremely likely			
Reasons given for recommendation in relation to the surgery, n (%) Reason 1 . . . Reason n			
Likelihood to recommend the treatment to a friend/relative with the same injury in relation to the hand therapy, n (%) 0 – Not likely at all 1 . . . 10 – Extremely likely			

Reasons given for recommendation in relation to the hand therapy, n (%) Reason 1 . . . Reason n			
3 months post-randomisation			
Likelihood to recommend the treatment to a friend/relative with the same injury in relation to the surgery, n (%) 0 – Not likely at all 1 . . . 10 – Extremely likely			
Reasons given for recommendation in relation to the surgery, n (%) Reason 1 . . . Reason n			
Likelihood to recommend the treatment to a friend/relative with the same injury in relation to the hand therapy, n (%) 0 – Not likely at all 1 . . . 10 – Extremely likely			
Reasons given for recommendation in relation to the hand therapy, n (%) Reason 1 . . . Reason n			
6 months post-randomisation			
Likelihood to recommend the treatment to a friend/relative with the same injury in relation to the surgery, n (%) 0 – Not likely at all 1 . . . 10 – Extremely likely			
Reasons given for recommendation in relation to the surgery, n (%)			

Reason 1 . . . Reason n			
Likelihood to recommend the treatment to a friend/relative with the same injury in relation to the hand therapy, n (%) 0 – Not likely at all 1 . . . 10 – Extremely likely			
Reasons given for recommendation in relation to the hand therapy, n (%) Reason 1 . . . Reason n			

Table 25: Frequency of intra-operative and post-operative complications for each follow-up time point, presented by treatment group.

	Intervention	**Control**	**Total**
Intra-operative complications			
Type of complication, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Intraoperative failure of tendon repair			
Reaction to anaesthetic			
Post-operative general complications			
1 week, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Deep wound infection			
Superficial infection			
Bleeding / haematoma			
Suture abscess			
Surgical site infection			
…(all complications will be reported)			
6 weeks, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Deep wound infection			
Superficial infection			
Bleeding / haematoma			
Suture abscess			
Surgical site infection			
…(all complications will be reported)			

3 months, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Deep wound infection			
Superficial infection			
Bleeding / haematoma			
Suture abscess			
Surgical site infection			
…(all complications will be reported)			
6 months, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Deep wound infection			
Superficial infection			
Bleeding / haematoma			
Suture abscess			
Surgical site infection			
…(all complications will be reported)			
Post-operative anaesthetic-related complications			
1 week, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Myocardial infarction (MI)			
Block related nerve lesion			
Cerebrovascular accident (CVA)			
Venous thromboembolism (VTE)			
Local anaesthetic toxicity			
…(all complications will be reported)			
6 weeks, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Myocardial infarction (MI)			
Block related nerve lesion			
Cerebrovascular accident (CVA)			
Venous thromboembolism (VTE)			
Local anaesthetic toxicity			
…(all complications will be reported)			
3 months, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Myocardial infarction (MI)			
Block related nerve lesion			
Cerebrovascular accident (CVA)			
Venous thromboembolism (VTE)			
Local anaesthetic toxicity			
…(all complications will be reported)			
6 months, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Myocardial infarction (MI)			
Block related nerve lesion			

Cerebrovascular accident (CVA)			
Venous thromboembolism (VTE)			
Local anaesthetic toxicity			
…(all complications will be reported)			
Post-operative flexor tendon related complications			
1 week, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Digital nerve injury/ neuroma/ numbness/ altered sensation			
Tendon adhesions			
Re-rupture of tendon repair			
Bow stringing			
Cold intolerance			
…(all complications will be reported)			
6 weeks, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Digital nerve injury/ neuroma/ numbness/ altered sensation			
Tendon adhesions			
Re-rupture of tendon repair			
Bow stringing			
Cold intolerance			
…(all complications will be reported)			
3 months, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Digital nerve injury/ neuroma/ numbness/ altered sensation			
Tendon adhesions			
Re-rupture of tendon repair			
Bow stringing			
Cold intolerance			
…(all complications will be reported)			
6 months, n (%)	**n=xxx**	**n=xxx**	**n=xxx**
Digital nerve injury/ neuroma/ numbness/ altered sensation			
Tendon adhesions			
Re-rupture of tendon repair			
Bow stringing			
Cold intolerance			
…(all complications will be reported)			
Hand therapy related complications			
6 weeks, n (%)	**n=xxx**	**n=xxx**	**n=xxx**

Skin problems due to splint fitting			
Other			
…(all complications will be reported)			

17.3.7 Adverse Events

Table 26: Number of non-serious adverse events per participant presented overall and by treatment group.

	Intervention	Control	Overall
	N=	N=	N=
One or more NSAEs, N (%) Yes No			
Number of NSAEs per participant, N (%) 0 1			
Days between randomisation and onset of NSAE N Mean (SD) Median Min, Max			
Study action taken, N (%) None Study treatment halted Discontinued study			
Relationship to study treatment, N (%) Not related Unlikely to be related Possibly related Probably related Related			
Expectedness, n (% of those possibly, probably or definitely related) Yes No			

Table 27: Number of serious adverse events per participant presented overall and by treatment group.

	Intervention	Control	Overall
	N=	N=	N=
One or more SAEs, N (%) Yes No			
Number of SAEs per participant, N (%) 0 1 2 3			

Days between randomisation and onset of SAE N (% data available) Mean (SD) Median Min, Max			
Study action taken, N (%) Study treatment interrupted/halted Discontinued study None			
Relationship to study treatment, N (%) Not related Unlikely to be related Possibly related Probably related Related			
Expectedness, n (% of those possibly, probably or definitely related) Yes No			

Table 28: Non-serious adverse event details by site and allocation.

Participant ID	Site ID	Allocation	Onset date	Action Taken	Related	Outcome	Description

Table 29: Serious adverse event details by site and allocation

Participant ID	Site ID	Allocation	Onset date	Action Taken	Related	Outcome	Description