STATISTICAL ANALYSIS PLAN

Ankle Injury Rehabilitation - A multi-centre randomised controlled trial to assess the difference between plaster cast and functional bracing in the management of ankle fractures

ISRCTN:	ISRCTN15537280
Funding Body:	NIHR Career Development Fellowship Ref CDF-2016-09-009
Ethics Approval:	17/WM/0239; 4 Jul 2017
SAP version number:	2
Date:	25 March 19
Stage:	Final
Protocol version:	6.0; 6 March 2019

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2 Administrative information

2.1 List of abbreviations

Abbreviation	Explanation
AE	Adverse Event
CI	Chief Investigator
CONSORT	*Con*solidated *S*tandards *o*f *R*eporting *T*rials
CRF	Case Report Form
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
DVT	Deep Vein Thrombosis
FARO	Fixed Angle Removable Orthotic
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
ISRCTN	International Standard Randomised Controlled Trial Number
HEAP	Health Economics Analysis Plan
MHRA	Medicines and Healthcare products Regulatory Agency
MOXFQ	The Manchester-Oxford Foot Questionnaire
MRC	Medical Research Council
MREC	Multicentre Research Ethics Committee
OMAS	Olerud and Molander Ankle Score
PE	Pulmonary Embolism
PI	Principal Investigator
PROM	Patient Reported Outcome Measure
QoL	Quality of Life
RCT	Randomised Controlled Trial
R&D	Research and Development
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
TSC	Trial Steering Committee
WCTU	Warwick Clinical Trials Unit

2.2 SAP amendments

SAP version no.	Protocol version	Section(s) changed	Details of SAP changes	Date of update
0.1	1	-	First draft	-
-	2	-	None	-
1	3	All	Additional details added at the request of DMC: clarification of primary analysis. Formatting updated and some additional sections also added to be in line with new UKCTU guidance.	23 Aug 18
2	6	2.3; 3.2; 4; 5; 6.2 and 8	Amendments at the request of the DMC including addition of detail of per protocol, details of complications/SAEs and imputation analyses. Small changes to layout and removal of typos	25 Mar 19

2.3 Supporting documents

This Statistical Analysis Plan (SAP) should be read in conjunction with the study protocol and WCTU Standard Operating Procedures:

- SOP 8: Statistical Considerations
- SOP 9: Randomisation and Blinding
- SOP 15: Information Handling
- SOP 21: Statistical Analysis Plan

The Trial Master File, including the Data management Plan can be found in the AIR Trial Manager's office: Warwick Clinical Trials Unit, Clinical Sciences Building, Clinical Sciences Research Laboratories, University Hospitals Coventry and Warwickshire, Clifford Bridge Road, Coventry, CV2 2DX

2.4 Study oversight

As described in the protocol, the procedures in place for oversight of this study include both a Trial Steering Committee (TSC) and Data Monitoring Committee (DMC). The DMC is advisory to the TSC and write to the TSC and recommend any alterations to the study to ensure the safety of participants and the integrity of the data.

2.5 Roles and responsibilities

Details of all AIR co-applicants can be found in the protocol.

Role	**Name, address, telephone, email**
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3 Introduction

3.1 Background and rationale

Ankle fractures represent 9% of the trauma workload and demand is increasing. The increasing frequency of this injury is a growing burden on the NHS year on year. After ankle fracture, the immediate management has traditionally been plaster cast immobilisation for several weeks, whilst the bone heals. A cast provides maximum support; however, there are potential problems. Firstly, there is the immediate impact on mobility for a period of around six weeks. Secondly, there are the risks associated with prolonged immobilisation: muscle atrophy, deep vein thrombosis and joint stiffness. Finally, there are the long-term consequences, which include prolonged gait abnormalities, persistent calf muscle weakness and an inability to return to previous activity levels. Alternative functional bracing may potentially address these issues. However, it does not provide the same degree of support to the healing bones. Hence there exists uncertainty about the optimum management of ankle fractures.

The CI has successfully completed a feasibility RCT funded by NIHR RfPB comparing cast with fixed angle removable orthotic (FARO) for the management of operative and non-operative ankle fractures. The trial ran from August 2015 and completed May 2017, successfully recruiting 50 participants. This has informed this (main) study, also funded by NIHR.

More details about the background to the trial can be found in the study protocol.

3.2 Trial aims and objectives

This study proposes to answer the question: In adults with an ankle fracture suitable for cast immobilisation, does a fixed angle removable orthotic (FARO) improve OMAS 16 weeks post randomisation when compared to cast immobilisation?

3.2.1 Primary objective

To quantify and draw inferences on observed differences in the OMAS between FARO and cast treatment groups at sixteen weeks after randomisation.

3.2.2 Secondary objectives

1) To quantify and draw inferences on observed differences in ankle function assessed using the OMAS score at 6 weeks, 10 weeks, 24 weeks and 24 months and the MOXFQ 16 weeks after randomisation.
2) To quantify and draw inferences on observed differences in health related quality of life (EQ5D-5L) between trial treatment groups At 6 weeks, 10 weeks, 16 weeks, 24 weeks and 24 months after randomisation.
3) To quantify and draw inferences on observed differences in disability rating (DRI) between trial treatment groups at 6 weeks, 10 weeks, 16 weeks, 24 weeks and 24 months after randomisation.
4) To quantify and draw inferences on observed differences on complication rates between trial treatment groups at 6 weeks, 10 weeks, 16 weeks, 24 weeks and 24 months after randomisation.
5) To estimate comparative cost-utility of the two trial treatment groups and collect resource use data at 6 weeks, 10 weeks, 16 weeks, 24 weeks, 12 months, 18 months and 24 months after randomisation.

4 Study Methods

4.1 Trial Design

This study is a UK multi-centre, randomised controlled trial of two parallel treatment arms.

4.2 Trial interventions

A full description can be found in the protocol. Briefly; after ankle fracture, patients may require ankle fixation surgery prior to being fitted with a cast or brace:

- All participants who require ankle fixation will have this performed according to the preferred technique of the operating surgeon. All participants will then receive normal local care until satisfactory clinical wound check, at which point randomization will occur.
- All participants not receiving surgery will be approached to take part in the trial on first presentation to the trauma team fracture clinic, and will be eligible for randomization up to a maximum of 3 weeks from injury.

4.2.1 Control Group - Standard Plaster Cast

All participants in the control arm will be fitted with cast immobilisation for a minimum of three weeks. It is expected that the control intervention will not exceed eight weeks.

4.2.2 Active Intervention Group – Functional Bracing

All participants in the intervention arm will be fitted with a FARO for a minimum of three weeks. It is expected that the intervention will not exceed eight weeks and the participant will remove the brace and perform short exercises.

4.3 Inclusion and exclusion criteria

Full descriptions of the inclusion and exclusion criteria can be found in the protocol. A brief summary only is provide here.

4.3.1 Inclusion criteria

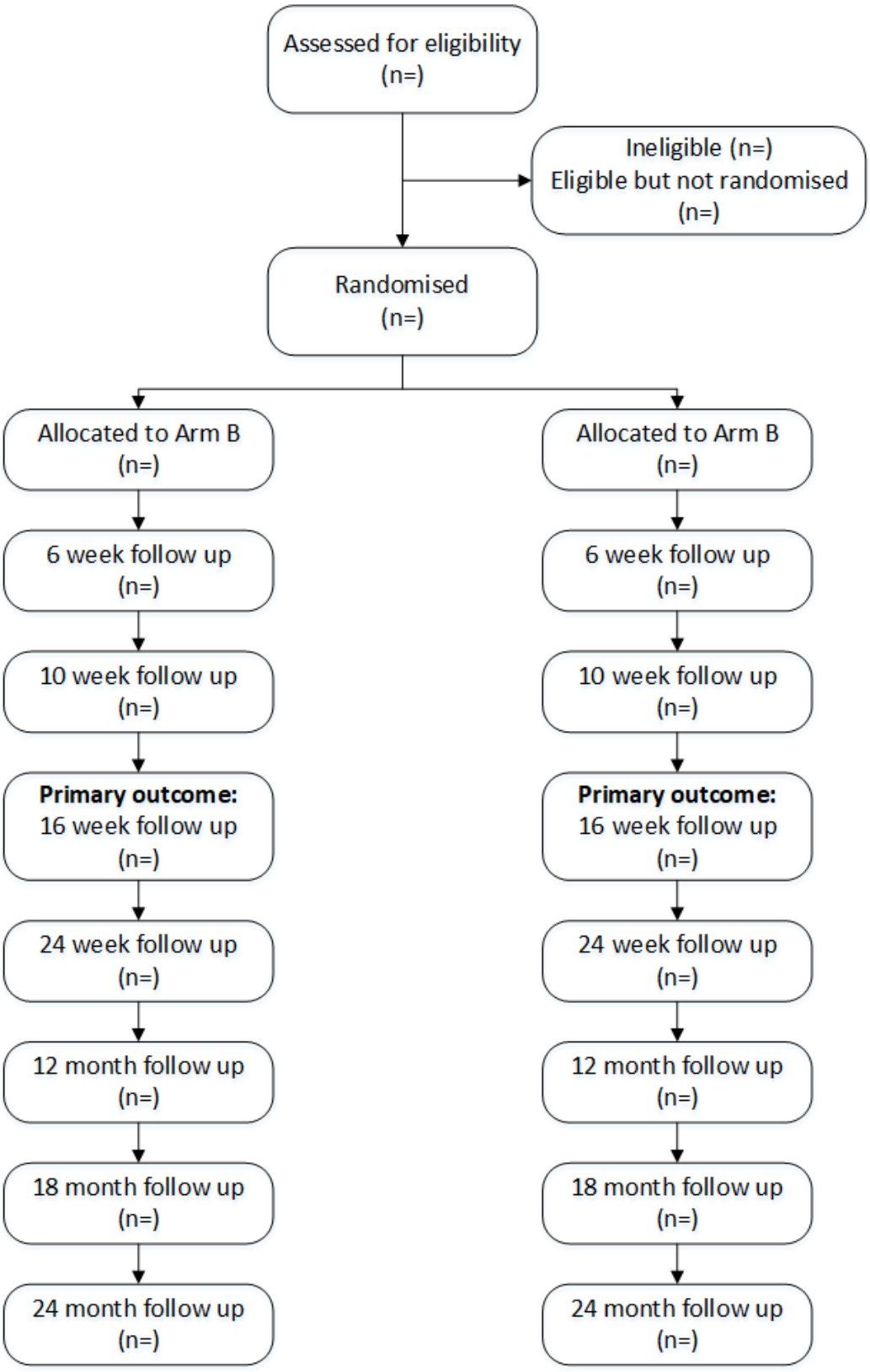
1) Provision of written informed consent.
2) Aged 18 years or over.
3) A closed ankle fracture where a plaster cast is a management option.
4) Within 3 weeks of operative management or injury if non-operative.

4.3.2 Exclusion criteria

1) Ankle fracture secondary to known metastatic disease.
2) Complex intra-articular fracture.
3) The patient would require manipulation and close contact casting.
4) In the opinion of the surgeon the patient would require manipulation and moulded cast.
5) Wound complications following surgical management contraindicating FARO intervention.
6) Previous ankle fracture randomised in the present trial.
7) The patient is unable to adhere to trial procedures or complete postal questionnaires.
8) Known pre-existing neuropathic joint disease contraindicating FARO intervention

4.4 Trial flow chart

Figure 1: CONSORT chart



4.5 Schedule of assessments

Table 1: Trial assessments

Visit no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Visit Window (Scheduled time ± allowance)	**Pre - Consent**	**Baseline (0)**	**6wk (± 2wk) after V2**	**10wk (± 2wk) after V2**	**16 wk (± 4 wk) after V2**	**24 wk (± 4 wk) after V2**	**12 m (± 1m) after V2**	**18 m (± 1m) after V2**	**24 m (± 1m) after V2**
Eligibility Check	✓								
Written and verbal information provided	✓								
Written informed consent		✓							
Baseline CRFs (Pre and Post injury)		✓							
Randomisation		✓							
Intervention delivery		✓							
OMAS (Critical data item)		✓	✓	✓	✓	✓			✓
MOXFQ		✓			✓				✓
DRI		✓	✓	✓	✓	✓			✓
EQ5D5L (Critical data item)		✓	✓	✓	✓	✓	✓	✓	✓
Resource use questionnaires			✓	✓	✓	✓	✓	✓	✓
Complications (Critical data item)			✓	✓	✓	✓			✓
Global Impression of Change (Critical data item)					✓				

4.6 Randomisation and blinding

Pre-randomisation eligibility checks will be carried out to ensure that potential participants meet the eligibility criteria and are not randomised in error. Written informed consent for entry into the trial and baseline assessment must be obtained prior to randomisation. Subjects will be randomised strictly sequentially, as they become registered as eligible for randomisation on the web based system. Allocation concealment will be maintained by an independent randomisation team who will be responsible for generation of the sequence and will have no role in the allocation of participants.

The treatment group will be allocated by computer using a minimisation algorithm with a random element and stratification by centre, age (<50 *vs* ≥50) and operative/non operative management following use of a secure web based randomisation service.

No blinding of participants or clinical staff is possible due to the nature of the intervention arms. Furthermore, outcome data to be entered onto the trial database will contain treatment identifying variables, making blinding of the trial team impracticable; however, blinding of the trial team will be maintained where possible.

4.7 Sample size

The primary outcome for this study is the OMAS 16 weeks post injury. The minimum clinically important difference (MCID), or smallest between group difference that is likely to be clinically meaningful beyond measurement error for foot and ankle conditions is a change of 10 points. This is consistent with the AIM study [1], which set the OMAS equivalence margin between groups to be 6 points. It is also consistent with other similar outcome measures such as the Foot and Ankle Outcome Score [2], and visual analogue pain scores in acute injury; that report MCIDs of approximately 10 points on a 100 point scale.

The standard deviation (SD) of the OMAS at six months after injury from previous feasibility work was approximately 28 points. To account for any variation arising from recruiting from multiple study centres and to allow that the primary outcome has been moved from this time point, we have selected a conservative estimation of the trial SD of 30 points. This corresponds to a moderate standardised effect size of 0.33. Hence, the total trial sample size required to detect a difference of 10 points given a SD of 30 points with two-sided significance set at 5% and 90% power is 382 participants.

Allowing a margin of 20% loss during follow-up (whilst striving to keep this below 10%), this gives a figure of 478 participants in total. Therefore, a **minimum of 239 participants** randomised to each group will provide 90% power to detect a difference of 10 points in OMAS at sixteen weeks at the 5% level.

5 Outcomes

5.1 Primary outcome measure

The primary outcome for the AIR study is the **Olerud and Molander Ankle Score** (OMAS). The OMAS a self-administered questionnaire which is suitable for assessing symptoms after an ankle fracture. The OMAS is measured on a scale between 0 and 100, where higher scores denote better function. The score will be calculated as standard [3] and is based on nine different items: pain, stiffness, swelling, stair climbing, running, jumping, squatting, supports and work/activities of daily living.

For responses which contain missing items, the OMAS will be calculated by assuming that the missing item scores were zero for those responses where the sum of the maximum missing scores does not exceed 25 (inclusive) points. Instances where the maximum missing score is greater than 25 will be assumed to be missing and treated as described in section 6.3.

5.2 Secondary outcome measures

The following secondary outcome measures will also be collected:

EQ-5D: Is a validated, generic health-related quality of life measure consisting of five items each with a 5 possible responses. These are then converted into a health utility score. EQ-5D-5L responses will be used to generate health preference values using the UK time-trade-off (TTO) value set recommended [4], or those recommended for use by the Health Economic Team.

MOXFQ: The Manchester-Oxford Foot Questionnaire (MOXFQ) [5] is a validated questionnaire which is self-reported. It contains 16 items, each with 5 response options comprising 3 separate underlying dimensions: Walking/standing problems (7 items), foot pain (5 items) and issues related to social interaction (4 items). Item responses are each scored from 0 to 4, with 4 representing the most severe state. The scale scores representing each dimension are produced by summing the responses to each item within that dimension. Raw scale scores are then converted to a metric (0-100; 100=most severe).

DRI: The Disability Rating Index (DRI) is a self-administered questionnaire. It consists of 12 items specifically related to function of the lower limb. Each item is a visual analogue scale with anchor points of 0 and 100 and the summary score is simply the mean of all items [6].

Complications: All complications will be recorded, including mal-union, delayed/non-union, infection, wound complications after surgery, vascular injury, neurological injury, and venous thromboembolism. A record will also be kept of any other surgery required in relation to the index fracture.

Radiology: All baseline X-Ray/radiographs and also the last X-Ray/radiograph taken before the primary outcome point of 16 weeks will be collected. As very little evidence of an association between ankle function and radiology outcomes were found from the feasibility study [7] (paper in preparation), it was decided that while the radiology outcomes would be collected, they would not constitute part of the main trial analysis. It will, however, be possible to carry out exploratory analysis using relevant radiology outcomes, if deemed appropriate, at a later date.

Resource use: details of resource use have been collected to inform the economic analysis. Hence, further details can be found in the protocol and Health Economics Analysis Plan (HEAP).

5.3 Adherence and compliance

Compliance with the intervention is captured on patient completed CRFs. This consists of asking the participant to report at 6, 10 and 16 weeks if:

- They are still wearing cast or FARO given at randomisation
- If they have had a replacement cast or FARO, and if so when was and what was the replacement

The time the participant wore the cast or FARO will be calculated and the participant will be considered to have not adhered if this time is 21 days or fewer. If the participant reports multiple dates which they discontinued the intervention, the smallest time to discontinuation will be used.

The effect of compliance on the primary outcome will be assessed by carrying out per-protocol analysis as a secondary analysis and comparing the results of this to the primary analysis (intention to treat). The per-protocol approach will follow the methods set out for the primary analysis (see section 6.1), but only include those participants who have worn their treatment (cast or FARO) for at least three weeks. Participants who change their intervention after three weeks (>21 days) will therefore still be classified as wearing their intervention for this analysis.

Further protocol deviations and violations observed in the study can be dealt with as appropriate, dependent on the observed data. For example, if a large number of participants are observed to wear a single intervention for less than three weeks, a “dose delivered” analysis will be considered.

5.4 Minimal data set

The following outcomes are considered the core outcome set to be collected if the entirety of the CRF cannot be collected. For example; by telephone follow up after non-return of postal questionnaire

1. OMAS (all time points)
2. Complications (all time points)
3. EQ5D (all time points)
4. Global impression of change (16 week time point only)

6 Analysis strategy

The routine statistical analysis will mainly be carried out using R [8] or Stata (StataCorp. 2017. *Stata Statistical Software:* College Station, TX: StataCorp LP).

All data will be analysed and reported in accordance with the CONSORT statement. [9] Treatment effects will be presented, with appropriate 95% confidence intervals, for both the unadjusted and adjusted analyses. Tests will be two-sided and considered to provide evidence for a significant difference if p-values are less than 0.05 (5% significance level). All analyses will be conducted as intention to treat unless otherwise specified.

Standard descriptive summaries will be provided for the primary outcome measure (OMAS) and all secondary outcome measures. Baseline data will be summarised to check comparability between treatment arms, and screening data will be checked to highlight any characteristic differences between those individuals in the study, those ineligible, and those eligible but withholding consent. Patient reported outcome measure (PROM) data, such as the OMAS scores, will be assumed to be

normally distributed during modelling, but subsidiary analyses may also be undertaken after appropriate variance-stabilising transformation if assumptions of normality prove to be unsustainable.

6.1 Primary analysis

The main analysis will investigate differences in the primary outcome measure, sixteen weeks after randomisation, between the two treatment groups. The differences between treatment groups will initially be assessed using a t-test, based on a normal approximation for the OMAS score at 16 weeks. In addition, regression analyses to adjust for any imbalance between test treatment groups as well as pre-injury function, patient age, gender and operative treatment (Yes or No) will also be carried out.

This fixed effects model will also be generalised by adding a random effect for recruiting centre to allow for possible heterogeneity in patient outcomes due more generally to the recruiting centre. Since individual clinicians will treat only a small number patients enrolled in the trial, we do not expect clinician specific effects to be important in this study and hence these will not be modelled. This adjusted mixed-effects linear regression analysis will be reported as the primary analysis, and will be used to assess evidence for differences in outcomes between intervention arms.

6.2 Secondary analyses

The primary analysis will also be conducted on a per protocol basis based on patient reported adherence to their intervention group and will also be conducted as a sensitivity analysis. Further details on how per-protocol is being defined for the purposes of this trial have been given in section 5.3.

Descriptive statistics of PROM data (OMAS, MOSFQ, EQ5D and DRI) at each time point collected (6 weeks, 10 weeks, 16 weeks, 24 weeks 12 months, 18 months and 24 months after randomisation) will be constructed with between group analyses following the method set out for the primary analysis above.

Complications will be summarised with between groups comparisons evaluated using chi-squared tests. Temporal patterns of any complications will be presented graphically and if appropriate, a time-to-event analysis (e.g. Kaplan-Meier survival analysis) will be used to assess the overall risk and risk within individual classes of important complications (e.g. non-union).

Other outcomes (e.g. Physiotherapy outcomes, weight bearing status) will be summarised and compared between groups using appropriate tests for the outcome (e.g. proportions and chi-squared tests for binary outcomes, means and t-tests for continuous data).

6.3 Missing data

It seems likely that some data may not be available due to voluntary withdrawal of patients, lack of completion of individual data items or general loss to follow-up. Where possible the reasons for data 'missingness' will be ascertained and reported. The nature and pattern of the missingness will be carefully considered, including whether data can be treated as missing completely at random (MCAR). Little's test will be used to assess whether the data can be considered MCAR or missing at random (MAR) and/or missing not at random (MNAR). An assessment between MAR and MNAR is

subjective, so cannot be tested [10]. Variables that will be checked for their impact on missingness rates will include: the intervention received, site of randomisation, age (<50 *vs* ≥50) and whether the participant received operative or non-operative management

If judged appropriate, missing data will be imputed using multiple imputation. Any imputed analyses will be considered as secondary analyses and will be reported along with the primary analysis.

If imputation is undertaken, the resulting imputed datasets will be analysed, together with appropriate sensitivity analyses. Any imputation methods used for scores and other derived variables will be carefully considered and justified. In particular the model used for the multiple imputation will be assessed along with the plausibility of any imputed values. Reasons for ineligibility, non-compliance, withdrawal or other protocol violations will be stated and any patterns summarised. More formal analysis, for example using logistic regression with 'protocol violation' as a response, may also be appropriate and aid interpretation.

6.4 Subgroup analyses

Two pre-specified sub-group analyses will be undertaken to assess whether there is evidence that the intervention effect differs between whether:

i. The study participants receives operative or non-operative treatment prior to the study intervention
ii. The study participants are aged 50 or over at study randomisation

The subgroup analyses will follow the methods described for the primary analysis, with additional interaction terms incorporated into the mixed-effects regression model to assess the level of support for these hypotheses. The study is not powered to formally test these hypotheses, so they will be reported as exploratory analyses only, and as subsidiary to the analysis reporting the main effects of the intervention in the full study population at the 16 week primary endpoint.

7 Interim analyses

No interim analyses are planned, and will be carried out only at the direction of the DMC.

8 Safety and adverse event reporting

Safety monitoring will be conducted primarily through the participant self-reporting. At each follow up point, participants will be asked if they have had any adverse events and how these were managed using a postal questionnaire.

Complications deemed serious will be reported separately as SAEs. The number and nature will be reported and assessed by intervention arm, as shown in Table 12 of the dummy tables.

9 References

[1] K. Willett et al, "Close Contact Casting vs Surgery for Initial Treatment of Unstable Ankle Fractures in Older Adults: A Randomized Clinical Trial," *JAMA,* vol. 316, no. 14, pp. 1455-1463., 2016.

[2] S. Lamb et al, "Mechanical supports for acute, severe ankle sprain: a pragmatic, multicentre, randomised controlled trial.," *Lancet,* vol. 373, no. 9663, pp. 575-81, 2009.

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[4] N. Devlin, K. Shah, Y. Feng, B. Mulhern and B. van Hout, "Valuing Health-Related Quality of Life: An EQ-5D-5L Value Set for England.," *Office of Health Economics,* p. Research Paper 16/01., 2016.

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[6] B. Salen, E. Spangfort, A. Nygren and R. Nordemar, "The Disability Rating Index: An instrument for the assessment of disability in clinical settings," *J Clin Epidemiol,* vol. 47, no. 12, pp. 1423-34, 1994.

[7] AIR feasibility radiology paper, in preperation.

[8] R Core Team, "R: A language and environment for statistical computing," R Foundation for Statistical Computing, Vienna, Austria, [Online]. Available: https://www.R-project.org/.

[9] K. F. Schulz, D. G. Altman and D. Moher, "CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials," *BMJ,* p. 340:c332, 2010.

[10] I. R. White, P. Royston and A. M. Wood, Multiple imputation using chained equations:Issues and guidance for practice, Statistics in medicine, 2011.

10 Dummy tables

The following tables fill form the basis for the final statistical report. For brevity, some tables which have are reported at multiple time points are shown once; with variables noted when reported where necessary. Note also that variable level missingness is not reported here, but will be marked in the final report as appropriate.

Table 2: Participant flow from screening data

Reason not recruited		n
Ineligible	Known metastatic disease	
	Complex, intra-articular fracture	
	Requires manipulation and close contact casting	
	Requires manipulation and moulded cast	
	Wound complication contraindicates FARO	
	Previous entry in trial	
	Patient unable to adhere to trial procedures	
	Neuropathic joint disease contraindicates FARO	
Eligible, patient unwilling	Prefer plaster cast	
	Prefer functional brace	
	Does not want to take part in research	
	Other	
Other	Patient missed	
	Clinician unwilling	
	Other	

Table 3: Summary of screened participant characteristics. Values reported are means and standard deviations unless otherwise stated

	Randomised (n=)	**Eligible, not randomised (n=)**
Gender: Male (n, %)		
Age (years)		

Table 4: Recruitment by site

Code	Site name	Plaster cast (n)	Functional brace (n)	Total (n)
UHC	University Hospitals Coventry and Warwickshire			
NBT	North Bristol Southmead			
RLH	Royal London Hospital			
NTH	North Tees and Hartlepool			
NGH	Sheffield Northern General Hospital			
KCH	Kings College Hospital			
RVI	Royal Victoria Newcastle upon Tyne			
MKH	Milton Keynes University Hospital			
TNH	Tayside Ninewells Hospital Dundee			
SHK	St Helens and Knowsley			
LDH	Luton and Dunstable			
RNT	Rotherham NHS Trust			
UHL	United Lincolnshire Hospital			
ELH	East Lancashire			
RBH	Royal Berkshire Hospital			
LHS	Lister Hospital Stevenage			
UHS	Uni Hospitals Southampton			
STH	South Tees Hospital			
BHN	Bedford Hospitals NHS Trust			
LRI	Leicester Royal Infirmary			
Total				

Table 5: Withdrawal and loss to follow up

Trial status	Time point	Plaster cast (n)	Functional brace (n)	Total (n)
Withdrawn from study (n, %)	Baseline			
	6 weeks			
	10 weeks			
	16 weeks			
	24 weeks			
	12 months			
	18 months			
	24 months			
Questionnaire not returned (n, %)	Baseline			
	6 weeks			
	10 weeks			
	16 weeks			
	24 weeks			
	12 months			
	18 months			
	24 months			

Table 6: Baseline data. Values reported are means and standard deviations unless otherwise stated

		Plaster cast (n=)	Functional brace (n=)	Total (n=)
Age (years)				
Age group: 49 years or under (n, %)				
Gender: Male (n, %)				
BMI (kg/m^2)				
Diabetic: Yes (n, %)				
Leg fracture in last 12 months (n, %)				
Tendon/nerve injury in last 12 months (n, %)				
Currently taking steroids (n, %)				
Other medications: Yes (n, %)				
Smokes: Yes (n, %)				
Alcohol per week (n, %)	0 – 7 units			
	8 – 14 units			
	15 – 21 units			
	More than 21 units			
Ethnicity (n, %)	White			
	Asian/Asian British			
	Mixed/multiple ethnic groups			
	Black/ African/ Caribbean/ Black British			
	Other ethnic group			
Employment status (n, %)	Full-time employed			
	Part time employed			
	Self-employed			
	Retired/looking after home			
	Unpaid work			
	Unemployed			
	Full time student			
Employment category (n, %)	Unskilled manual			
	Skilled manual			
	Unskilled non-manual			
	Skilled non-manual			
	Professional			
	Other			
Interventional preference (n, %)	Plaster cast			
	Functional brace			
	No preference			

Table 7: Injury data. Values reported are numbers and percentages unless otherwise stated

		Plaster cast (n=)	**Functional brace (n=)**	**Total (n=)**
Injury CRF completed				
Side of fracture: Left				
Mechanism of injury* (n, %)	Low energy fall			
	High energy fall			
	Road traffic accident			
	Crush injury			
	Contact sports injury			
	Other			
Lateral malleolus affected: Yes				
Lateral malleolus affected: Weber A				
Lateral malleolus affected: Weber B				
Lateral malleolus affected: Weber C				
Medial malleolus affected: Yes				
Posterior malleolus affected: Yes				
Ankle fracture treatment: Operative				
Advised weight bearing status	Fully			
	Partial			
	None			
Concurrent injuries* (Yes)	Head			
	Chest			
	Abdomen			
	Pelvis			
	Spine			
	Shoulders/arms			
	Opposite leg			
	Same leg			

**Participant can be included in multiple categories*

Table 8: Operation data. Values reported are numbers and percentages unless otherwise stated

			Plaster cast (n=)	Functional brace (n=)	Total (n=)
CRF returned					
Length of operation, mins (mean, SD)					
Lead surgeon grade	Consultant				
	Specialist Trainee				
	Staff grade/associate specialist				
	Other				
Number of years at this grade (mean, SD)					
Other surgeons present: Consultant (mean, SD)					
Other surgeons present: Specialist Trainee (mean, SD)					
Other surgeons present: Staff grade/ associate specialist (mean, SD)					
Intra-operative complications: Yes					
Intra-operative complications: Nerve Injury					
Intra-operative complications: Vascular Injury					
Intra-operative complications: Tendon Injury					
Intra-operative complications: Other					
Lateral malleolus fixed: Yes					
Lateral malleolus fixed: No. of fibula screws (mean, SD)					
Lateral malleolus fixed: plate used		Locking			
		Non locking			
		No plate			
No. of syndesmosis screws used (mean, SD)					
Syndesmosis tightrope used: Yes					
Medial malleolus fixed: Yes					
Medial malleolus fixed: No. of screws (mean, SD)					
Medial malleolus fixed: Plate used					
Medial malleolus fixed: Tension band used					
Posterior malleolus fixed: Yes					
Posterior malleolus fixed: No. of screws (mean, SD)					
Posterior malleolus fixed: Plate used					

Table 9: Patient reported outcome measures. Values reported are means and standard deviations unless otherwise stated

PROM	Time point	Plaster cast (n=)	Functional brace (n=)	Total (n=)
OMAS	Pre injury			
	Post injury			
	6 weeks			
	10 weeks			
	16 weeks			
	24 weeks			
	24 months			
MOXFQ	Pre injury			
	Post injury			
	16 weeks			
	24 months			
DRI	Pre injury			
	Post injury			
	6 weeks			
	10 weeks			
	16 weeks			
	24 weeks			
	24 months			
EQ5D	Pre injury			
	Post injury			
	6 weeks			
	10 weeks			
	16 weeks			
	24 weeks			
	12 months			
	18 months			
	24 months			
Global impression of change (16 weeks only)				

Table 10: Patient reported wound complications post-surgery at specified time points for participants who had surgical fracture management. Values reported are numbers and percentages unless otherwise stated

Time point	Wound complication	Plaster cast (n=)	Functional brace (n=)	Total (n=)	No. deemed serious
6 weeks; 10 weeks; 16 weeks; 24 weeks; 24 months	Issues with wound healing: Yes				
	Discharge from wound: Any				
	Discharge from wound: Clear or blood stained				
	Discharge from wound: Yellow/green pus				
	Increased pain: Yes				
	Become swollen				
	Edges of wound separated				
	Lab sample taken				

Table 11: Patient reported complications at specified time points. Values reported are numbers and percentages unless otherwise stated

Time point	Complication	Plaster cast (n=)	Functional brace (n=)	Total (n=)	No. deemed serious
6 weeks; 10 weeks; 16 weeks; 24 weeks; 24 months	Pressure sore/ulcer				
	Numbness at side of foot				
	Problems with fracture healing				

Table 12: Expected Serious Adverse Events (SAEs)

SAE	Plaster cast (n=)	Functional brace (n=)	Total (n=)
All expected SAEs			
Participant experienced any expected SAE			
Further surgery for ankle fracture			
Ankle surgery: Removal of metalwork			
Ankle surgery: Fixed with metalwork			
Ankle surgery: Metalwork replaced			
Ankle surgery: Wound washout			
Ankle surgery: Other			
Ankle surgery: Not sure why			
Deep Vein Thrombosis (DVT)			
DVT: confirmed with ultrasound			
DVT: prescribed medicine			
Pulmonary Embolism (PE)			
PE: confirmed by CT Pulmonary Angiogram			
PE: prescribed medicine			

Table 13: Unexpected, unrelated Serious Adverse Events (SAEs)

SAE	Plaster cast (n=)	Functional brace (n=)	Total (n=)
All SAEs (n)			
Participant experienced any SAE (n, %)			
SAE: death (n, %)			
SAE: life threatening (n, %)			
SAE: requires/extends hospitalisation (n, %)			
SAE: persistent or significant disability or incapacity (n, %)			
SAE: Requires medical intervention to prevent one of the above, or otherwise significant (n, %)			

Table 14: Unexpected, related Serious Adverse Events (SAEs)

SAE	Plaster cast (n=)	Functional brace (n=)	Total (n=)
All SAEs (n)			
Participant experienced any SAE (n, %)			
SAE: death (n, %)			
SAE: life threatening (n, %)			
SAE: requires/extends hospitalisation (n, %)			
SAE: persistent or significant disability or incapacity (n, %)			
SAE: Requires medical intervention to prevent one of the above, or otherwise significant (n, %)			

Table 15: Fracture management at specified time points. Values reported are numbers and percentages unless otherwise stated

Time point	Wound complication		Plaster cast (n=)	Functional brace (n=)	Total (n=)
6 weeks only	Patient reported allocation: Functional Brace				
	Received allocated treatment	Yes			
		No, patient choice			
		No, clinician choice			
		No, other			
	Received VTE prophylaxis: Yes				
	Received VTE prophylaxis: No. of weeks (mean, SD)				
6 weeks; 10 weeks	Patient reported weight bearing status	Full weight			
		Some weight			
		No weight			
	Weight bearing same as instructed: Yes				
6 weeks; 10 weeks; 16 weeks	Still wearing brace/cast				
	Changed intervention: Yes				
	Intervention change to:	Plaster cast			
		Functional brace			

Table 16: Physiotherapy at specified time points. Values reported are numbers and percentages unless otherwise stated

Time point	Physiotherapy outcome		Plaster cast (n=)	Functional brace (n=)	Total (n=)
6 weeks; 10 weeks; 16 weeks; 24 weeks	Referred to physiotherapy: Yes				
	Referred to foot and ankle class	Yes			
		No			
		Unknown			
	Referred to individual physiotherapy	Yes			
		No			
		Unknown			
6 weeks; 10 weeks; 16 weeks; 24 weeks; 24 months	Received physiotherapy: Yes				
	If received physio: No. of appointments (mean, SD)				
6 weeks; 10 weeks	If received brace: completing daily exercises				
10 weeks 16 weeks 24 weeks 24 months	Received physio: discharged				

Table 17: Fidelity and adherence outcomes

	Plaster cast (n=)	**Functional brace (n=)**	**Total (n=)**
Intervention not worn for 3 weeks (n, %)			
Protocol deviations (n)			