Rehabilitation strategy after non-surgical treatment of Achilles tendon rupture: UKSTAR, a multicentre RCT

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Competing interests: Declared competing interests of authors: Prof. Matthew Cota is NIHR Senior Investigator and member of the NIHR HTA General Board. Dr Juul Achten reports grants from Department of Health during the conduct of the study. Mrs. Susan Dutton reports grants from UK NIHR Health Technology Assessment (HTA), during the conduct of the study. Dr Kearney is a member of the UK NIHR HTA CET board, NIHR ICA Doctoral panel and NIHR RfPB board. Dr. Petrou reports grants from UK National Institute for Health Research HTA Programme (project no 13/115/62), during the conduct of the study.Professor Sarah Lamb reports grants from the NIHR Health technology Assessment Programme during the conduct of the study and was a member of the following Boards: HTA Additional Capacity Funding Board 2012-2015; HTA Clinical Trials Board 2010-2015; HTA End of Life Care and Add on Studies 2015-2015; HTA Funding Boards Policy Group (formerly CSG) 2010-2015; HTA MNCH Methods Group 2013-2015; HTA Post-board funding teleconference (PG members to attend) 2010 – 2015; HTA Primary Care Themed Call board 2013 – 2014; HTA Prioritisation Group 2012-2015; NIHR CTU Standing Advisory Committee 2012-2016.

Keywords: ankle, Achilles, tendon, rupture, rehabilitation

Abstract

Background: Achilles tendon rupture affects over 11,000 people each year in the UK, leading to prolonged periods away from work, sports and social activities. Traditionally, after a ruptured tendon, the foot and ankle is held still in a plaster cast for eight weeks or more. Functional bracing is an alternative treatment which allows patients to mobilise sooner, but there is little evidence about how it affects overall recovery.

Objectives: To measure the Achilles Tendon Rupture Score (ATRS), quality of life, complications including re-rupture, and resource use in patients having non-operative treatment for an Achilles tendon rupture, treated with plaster cast versus functional bracing.

Design: A pragmatic, multicentre randomised controlled trial.

Setting: Thirty-nine NHS hospitals

Participants: 542 adult patients treated non-operatively for an Achilles tendon rupture were recruited from July 2016 through May 2018. Exclusion criteria included presentation after 14 days, previous rupture and unable to complete questionnaires.

Interventions: 266 participants had a plaster cast applied in the position that the foot naturally adopts when unsupported. The cast was changed over an 8-week period to bring the foot up to a position allowing walking before the cast was then removed. 274 patients had a functional brace which also held the foot with the toes pointing down, using wedge inserts, therefore allowing immediate weight-bearing. The foot position was adjusted within the brace over the same 8-week period.

Main outcome measures: ATRS is patient-reported and consists of 10 items assessing symptoms and physical activity related to the Achilles tendon to give a score between 0 and 100 (100, best possible outcome). Secondary outcomes were: health-related quality of life, complications including re-rupture and resource use at 8 weeks and 3, 6 and 9 months.

Results: Participants had a mean age of 48.7 years, were predominantly male (79%) and ruptured their tendon during sports (70%). Over 93% of participants completed follow-up. There was no statistically significant difference in the ATRS at 9 months post-injury (-1.38; 95% CI -4.9 to 2.1). There was a statistically significant difference in the ATRS at 8 weeks post-injury in favour of the Functional Brace group (5.75; 95% CI 2.2 to 9.3), but not at 3 or 6 months post-injury. Health-related quality of life showed the same pattern with a

statistically significant difference at 8 weeks post-injury but not at later time-points. Complication profiles were similar between the groups. There were 17 cases of re-rupture in the Plaster Cast and 13 in the Functional Brace group. There was no difference in resource use.

Conclusions: This trial provides strong evidence that early weight-bearing in a functional brace provides similar outcomes to traditional plaster casting and is safe for patients having non-operative treatment of an Achilles tendon rupture. The use of functional bracing is very likely to be cost-effective.

Future work: While the UKSTAR trial provides guidance with regard to the early management of patients, rehabilitation following an Achilles tendon rupture is prolonged and further research is required to define the optimal mode of rehabilitation after the initial cast/brace is removed.

Study registration: Current Controlled Trials ISRCTN12726986

Funding details: This study was funded by the NIHR Health Technology Assessment programme.

Word count: 498

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List of abbreviations

AE	Adverse event
ARUK	Arthritis Research UK
ATRS	Achilles Tendon Rupture Score
AUC	Area Under the Curve
BMI	Body Mass Index
CACE	Complier Average Causal Effect
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DSMC	Data and Safety Monitoring Committee
DVT	Deep vein thrombosis
GCP	Good Clinical Practice
GP	General Practitioner
HRG	Healthcare Resource Group
HTA	Health Technology Assessment
IQR	Interquartile Range
ITT	Intention-To-Treat
MAR	Missing at Random
MCAR	Missing Completely at Random
MCID	Minimum Clinically Important Difference
MNAR	Missing Not At Random
NHS	National Health Service
NICE	National Institute for Health and Care Excellence

OCTRU	Oxford Clinical Trials Research Unit
PE	Pulmonary embolism
PPI	Patient and Public Involvement
PRO	Patient Reported Outcome
PROM	Patient Reported Outcome Measure
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
QALY	Quality Adjusted Life-Year
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SD	Standard deviation
SMS	Short Message Text
TMG	Trial Management Group
TSC	Trial Steering Committee
UNTRAP	University/User Teaching and Research Action Partnership
UKSTAR	UK Study of tendo Achilles Rehabilitation
VAS	Visual analogue scale
VTE	Venous thromboembolism

Plain English Summary

Achilles tendon rupture affects over 11,000 people each year in the UK, leading to prolonged periods away from work, sports and social activities. Traditionally, after a ruptured tendon, the foot and ankle is held still in a plaster cast for eight weeks or more. Functional bracing is an alternative treatment which allows patients to mobilise sooner, but there is little evidence about how it affects later recovery.

This study was to compare traditional plaster casting to functional bracing for adult patients with an Achilles tendon rupture. The participants reported their own recovery using the Achilles Tendon Rupture Score (ATRS) which consists of 10 questions about symptoms and physical activity, where 100 is the best possible outcome. We also recorded quality of life, complications including re-rupture of the tendon, and costs from both the NHS and patients' perspective.

542 patients, treated at 39 hospitals, agreed to take part and were assigned by chance to either plaster casting or functional bracing. Patients reported their recovery at 8 weeks and 3,6 and 9 months.

What did the trial find?

Patients recovered steadily after their injury but were still not back to normal at nine months. The average ATRS score rose from 38/100 at 8 weeks to 73/100 at nine months.

Patents who had the functional brace reported that their recovery was a little better at 8 weeks than the patients having the plaster cast, but there was no evidence of a difference after that. There were 17 cases of re-rupture of the Achilles tendon in the Plaster Cast group and 13 in the Functional Brace group. There was no evidence of a difference in costs.

In conclusion, this study provides strong evidence that early weight-bearing in a functional brace provides similar outcomes to traditional plaster casting and is safe for patients having treatment for an Achilles tendon rupture.

Word count: 305

Scientific Summary

Background: Achilles tendon rupture affects over 11,000 people each year in the UK, leading to prolonged periods away from work, sports and social activities. Traditionally, after a ruptured tendon, the foot and ankle are immobilised in a plaster cast for eight weeks or more. Functional bracing is an alternative treatment which allows patients to mobilise sooner, but there is little evidence about how it affects overall recovery.

Objectives: To measure the Achilles Tendon Rupture Score (ATRS), quality of life, complications including re-rupture, and resource use in patients having non-operative treatment for an acute Achilles tendon rupture, treated with plaster cast versus functional bracing.

Design: A pragmatic, multicentre randomised controlled trial.

Setting: Thirty-nine hospitals in the UK NHS

Participants: 542 adult patients treated non-operatively for an Achilles tendon rupture were recruited from July 2016 through May 2018. Patients were excluded if they presented more 14 days after their injury, had suffered a previous rupture of the same Achilles tendon, or were unable to complete questionnaires.

Interventions: 266 participants were randomised to a below-knee plaster cast applied in the 'gravity equinus' position, i.e. the position that the foot naturally adopts when unsupported. In this position, with the toes pointing down towards the floor, the ends of the ruptured tendon are roughly approximated. The participants were permitted to mobilise with crutches immediately using their toes for balance (toe-touch) but were not able to bear weight on the injured hindfoot. Over the first eight weeks, as the tendon was healing, the participants returned to the hospital and the position of the plaster cast was gradually changed until the foot achieved plantigrade, i.e. the foot flat to the floor. At this point the patient was permitted to start to bear weight in the plaster cast. The number of changes of plaster cast and the time to weight-bearing was left to the discretion of the treating clinician, as per their usual practice. The cast was removed at eight weeks. The plaster cast provided maximum protection for the healing tendon; specifically restricting upward movement (dorsiflexion) of the ankle which may stretch the healing tendon, but it did not allow the patient to bear weight on the foot immediately or to move their ankle.

274 patients were randomised to the Functional Brace group. Initially, two solid heel wedges (or equivalent) inserted inside the brace to replicate the 'gravity equinus' position of the foot. However, because the bottom of the brace was flat to the floor, the participant was able to mobilise with immediate full weight-bearing within the functional brace. The brace also permitted some movement at the ankle joint. The number of wedges and foot position were reduced over eight weeks until the patient reached plantigrade. Again, the timing of the removal of wedges and change in foot position were left to the discretion of the treating clinician, as per their usual practice. The brace was removed at eight weeks, as per routine clinical care.

Outcome measures: The primary outcome measure was the Achilles Tendon Rupture Score (ATRS). ATRS is patient-reported and consists of 10 items assessing symptoms and physical activity related to the Achilles tendon to give a score between 0 and 100, where 100 is the best possible outcome. Secondary outcomes were health-related quality of life (EQ-5D), and complications including re-rupture. Outcomes were collected at 8 weeks and 3, 6 and 9 months post injury.

We also collected resource use from the perspective of the National Health Service (NHS) and personal social services (PSS). A societal perspective for costs was adopted for the sensitivity analysis and this included private costs incurred by trial participants and their families, as well as productivity losses and loss of earnings as a result of work absences.

Results: Participants had a mean age of 48.7 years, were predominantly male (79%) and ruptured their tendon during sports (70%). Over 93% of participants completed follow-up.

There was no statistically significant difference in the ATRS at 9 months post injury (-1.38; 95% confidence interval (CI) -4.9 to 2.1). There was a statistically significant difference in the ATRS at 8 weeks post injury in favour of the Functional Brace group (5.75; 95% CI 2.2 to 9.3), but not at 3 or 6 months post injury. Health-related quality of life showed the same pattern with a statistically significant difference at 8 weeks post injury but not at later time-points. Complication profiles were similar between the groups. There were 17 (6.4%) cases of re-rupture of the tendon in the Plaster Cast group and 13 (4.7%) in the Functional Brace group.

The mean direct intervention costs were £36 for the Plaster Cast group compared with £109 for the Functional Brace group; the mean difference of £73 was statistically significant.

However, by 8 weeks this difference had reversed such that the mean total NHS and PSS costs were significantly lower in the Functional Brace group. The difference at 8 weeks post injury was mostly driven by the cost of extra outpatient appointments in the Plaster Cast group.

The mean total NHS and PSS cost throughout the entire follow-up period was £1183 for the Plaster Cast group and £1018 for the Functional Brace group. Although the functional bracing was marginally cheaper, the mean between-group cost difference of £164 was not statistically significant.

In terms of health-related quality of life, the mean quality adjusted life-year (QALY) value was, on average, marginally higher for the Functional Brace group amongst complete cases and in the sensitivity analyses, although this mean QALY difference was not statistically significant.

Therefore, since the Functional Brace group incurred slightly lower costs and achieved slightly better quality of life over the course of the study, in health economic terms, functional bracing is the dominant intervention.

Conclusions: This trial provides strong evidence that early weight-bearing in a functional brace provides similar outcomes to traditional plaster casting and is safe for patients having non-operative treatment of an Achilles tendon rupture. The use of functional bracing is very likely to be cost-effective.

Future work: While the UKSTAR trial provides guidance with regard to the early management of patients, rehabilitation following an Achilles tendon rupture is prolonged and further research is required to define the optimal mode of rehabilitation after the initial cast/brace is removed.

Study registration: Current Controlled Trials ISRCTN62639639

Funding: This study was funded by the NIHR Health Technology Assessment programme.

Scientific summary word count: 1050

1. Introduction

1.1 Background

The Achilles tendon is the largest tendon in the human body and transmits the powerful contractions of the calf muscles that are required for walking and running. When the tendon ruptures, it is painful and has an immediate and serious detrimental impact on daily activities of living [1]. In the longer-term, tendon rupture results in prolonged periods off work and time away from sporting activity: average time away from work is between four and eight weeks and time away from sport is between 26 and 39 weeks [1]. This results in lost income and restricted daily activities in the early phase and reduced physical activity, with associated negative health and social consequences, in the long-term. For high-level sportsmen it is frequently a 'career-ending' injury.

Achilles tendon rupture affects over 11,000 people each year in the UK, and the incidence is increasing as the population remains more active into older age [2]. It affects all age groups in a bi-modal distribution; with the first peak in patients aged 30-40 years and the second 60-80 years [2]. The first peak in incidence is often associated with participation in sport, such as football and racquet sports, whereas the second peak often occurs during normal daily activities such as climbing stairs [2, 3]. However, all Achilles tendon ruptures are associated with a pre-existing 'tendinopathy' which is attributed to failures in the protective/regenerative functions which respond to repeated microscopic injury [4, 5].

Historically, the main question in relation to the management of patients with a rupture of the Achilles tendon has been whether or not to perform a surgical repair of the tendon. In 1981, Nistor *et al* [6] designed and published the first Randomised Controlled Trial (RCT) to address this clinical question.; this study was followed by a series of RCTs that were pooled in a meta-analysis by the Cochrane review group in 2004 [7]. The results suggested that surgical repair reduced the risk of re-rupture but came with an increased cost and a greatly increased risk of other complications, most of which were associated with infection and wound healing. There was little data on functional outcome at the time of this review. More recent trials comparing surgical repair and non-operative treatment have found no difference in functional outcome [8, 9]. Since surgery carries considerable costs, and carries considerable risks to the patient in terms of complications [7], there is an increasing trend towards non-operative

treatment. However, some surgeons have been reluctant to advocate non-operative treatment because of concerns about the lack of evidence to guide early rehabilitation for this group of patients [10]; specifically whether functional bracing is safe and effective if the tendon is not surgically repaired.

Traditionally, patients have been treated in plaster casts after rupture of the Achilles tendon; with the cast immobilising the foot and ankle while the tendon heals. [11] However, there are potential problems with this approach. Firstly, there is the immediate impact on mobility for a period of around eight weeks, affecting activities of daily life. Secondly, there are the complications and risks associated with prolonged immobilization: muscle atrophy, deep vein thrombosis (DVT) and joint stiffness [12, 13]. Finally, there are the potential long-term consequences which include prolonged gait abnormalities, persistent calf muscle weakness and an inability to return to previous activity levels [14]. Functional bracing, involving immediate, protected weight-bearing in a brace, was designed to address these issues.

In patients having a surgical repair, seven RCTs [15-21] directly comparing plaster casts with early movement and/or weight-bearing in a 'functional brace' had been conducted at the time that the protocol was developed for the UK Study of tendo Achilles Rehabilitation (UKSTAR) trial. The results favour functional bracing in terms of re-rupture rate, functional outcome and quality of life measures. Therefore, in the first guideline (2009) produced on this topic, the American Academy of Orthopaedic Surgeons recommended functional bracing for patients having surgical repair of their tendon [22].

What about patients managed non-operatively?

Whilst there is clear guidelines for rehabilitation for patients who have a surgical repair, there is no clarity with regards the use of functional bracing in non-operatively managed patients. Does functional bracing provide improved function and quality of life if the tendon is not surgically repaired? Or, in the context of a tendon that has not been stitched together, does a plaster cast provide greater protection and therefore improved healing compared with a brace? Does functional bracing facilitate faster return to work and is this cost effective? Or, is the tendon more vulnerable to re-rupture in a brace with the subsequent risk and cost of reconstructive surgery?

At the time that UKSTAR was developed, we supplemented the 2004 Cochrane review [7] with an updated literature search and found that in total only 2 additional studies [23, 24] had been performed comparing the use of functional bracing with plaster casts for patients managed non-operatively following a rupture of the Achilles tendon. Both studies suggested potential benefits from bracing. However, the data from the studies should be interpreted with caution due small patient numbers (90 in total), patients having received different functional bracing regimes, and minimal reporting of outcomes.

The gap in the evidence was recognized in the American Academy of Orthopaedic Surgeons Guideline 2009 [22], which concluded that "*For patients treated non-operatively, we are unable to recommend for or against the use of immediate functional bracing for patients with acute Achilles tendon rupture*". With the incidence of Achilles tendon rupture on the rise, and in light of the large personal and societal cost associated with the injury, this gap in the evidence is a clear priority. A Versus Arthritis (formerly known as Arthritis Research UK (ARUK)) multidisciplinary 'Think Tank' (ARUK Birmingham 2013) on tendon injuries reported that rehabilitation following non-operative treatment of acute Achilles tendon injury was "the top research priority" in this area.

Since the start of the UKSTAR trial, there have been a number of small randomised trials investigating both the mechanistic and functional effects of early weight-bearing in a brace versus cast immobilisation. In terms of tendon healing, a trial of 56 patients indicated that healing at a molecular level may be enhanced through early mobilisation but, given the small number of participants, there was no difference in objective functional outcome (heel-raise testing in this study) [25]. A second trial investigated the biomechanical properties of the healing tendon in patients randomised to early weightbearing versus delayed weightbearing [26]. The investigators noted that there was less tendon stiffness in the group treated with early weightbearing. However, in terms of functional outcomes, the authors reported no evidence of a difference in Achilles Tendon Rupture Score (ATRS), although they did report a statistically significant improvement in health-related quality of life at one year in the group treated with early weight-bearing [26]. Another trial included forty-seven patients who were treated non-operatively for an acute Achilles tendon rupture. Half of the patients were treated

with partial weight bearing beginning on the first day of treatment and the other half with non-weight bearing for the first four weeks [27]. The authors concluded that early weight-bearing was 'safe', in terms of the incidence of re-rupture, but there was no evidence of a difference in functional outcome (ATRS or Physical Activity Scale) in the first 12 months after the rupture. Finally, another trial compared two types of cast immobilisation of the Achilles tendon rupture [28]. Half of the patients wore a traditional cast, which restricted weightbearing, while the other group wore a modified cast which included a heel 'iron' to facilitate weight-bearing. The authors found no evidence of a difference in functional outcome (Leppilahti Score), but there were only 84 patients in the trial. One further protocol has been published for a larger randomised trial of 130 patients at single centre, but results are not yet available [29].

1.2 Pre-pilot data

Before the UKSTAR trial, we completed four phases of pilot and preparatory work to establish the following:

1. External pilot study [18]. We randomised 48 patients having non-operative treatment for an acute rupture of the Achilles tendon to either functional bracing or plaster cast. This trial showed that patients and clinicians had equipoise for this question and were happy to take part. However, the trial identified that while plaster casting was a mature intervention, the important facets of the complex intervention which is functional bracing were inadequately defined, and that this needed to be addressed before a larger trial was performed.

2. Defining the functional bracing intervention. In keeping with MRC framework for developing complex interventions, our group and collaborators performed a UK survey of current practice, a systematic review of published rehabilitation methods, gait analysis experiments using different functional brace and heel wedge combinations and qualitative interviews to define the optimal functional bracing regime and refine the trial design. [30, 31] The rehabilitation strategy proposed in UKSTAR was the summation of that work which identified: the optimal type of orthosis (brace), the optimal foot position within the orthosis and the duration of application of the orthosis.

3. The acceptability and safety of this newly defined regime was tested in a further single-centre pilot RCT and qualitative recruitment investigation (ISRCTN68273773).

4. To investigate the number of patients potentially eligible for UKSTAR, we performed a UK-wide survey of orthopaedic trauma clinicians [10]. This clearly showed that clinicians were enthusiastic about the study and that the number of eligible patients was large enough for a full trial.

1.3 Research objectives

The primary objective is:

To quantify and draw inferences on observed differences in ATRS between the trial treatment groups at nine months post injury.

The secondary objectives are:

1. To quantify and draw inferences on observed differences in ATRS between the trial treatment groups at eight weeks, three and six months post injury.

2. To identify any differences in health-related quality of life between the trial treatment groups in the first nine months post injury.

3. To determine the complication rate between the trial treatment groups in the first nine months post injury.

4. To investigate, using appropriate statistical and economic analytical methods, the resource use, costs and comparative cost effectiveness between the trial treatment groups in the nine months post injury.

1.4 Patient and public involvement

We have been working with and listening to the views of patients with Achilles tendon injuries for many years. However, as well as this informal contribution, a series of formal qualitative interviews with patients and clinicians were performed in the development of the STAR trial (ISRCTN68273773). [11] The views of patients were used to inform and refine the trial interventions, processes and in particular the development of the trial information/materials. The patient perspective was key in the development of the trial protocol to ensure the acceptability of the interventions and participation.

Two of the patients who contributed during our development work, agreed to act as lay representatives on the Trial Management Group (TMG) and co-applicants on the research grant award. Mrs Richmond later had to leave the research team for personal reasons, but Mr

Grant attended trial management meetings throughout the trial and contributed to all trial process and paperwork, with particular reference to Patient Information Leaflets. Mr Grant will be crucially involved in the dissemination of the findings of this study to the wider public. He will lead in the development of any materials, leaflets, website information, to be used for this purpose. Mr Grant has reviewed the plain English summary section of this report.

Mr Grant was supported by the Chief Investigator and the trial coordination team. He had peer-support from the UK Musculoskeletal Trauma Patient and Public Involvement (PPI) Group, hosted in Oxford. He also had access to and support from the UNTRAP (University/User Teaching and Research Action Partnership) network through Warwick University, an organisation which promotes the engagement and involvement of service users and carers from the local community in research and teaching in Health and Social Care.

2. Clinical Trial Methods

2.1 Summary of study design

The UKSTAR trial was a multicentre, randomised, pragmatic, two-group superiority trial. Patients presenting at 39 NHS hospitals in England and Scotland with an acute, primary Achilles tendon rupture for non-surgical treatment were randomised 1:1 to receive either functional bracing or plaster cast.

2.2 Settings and locations

The thirty-nine NHS hospital orthopaedic or trauma clinics in England and Scotland screened and recruited participants for this trial were:

- King's College Hospital NHS Foundation Trust, London
- Nottingham University Hospitals NHS Trust
- Royal Berkshire Hospital, Royal Berkshire NHS Foundation Trust
- Aberdeen Royal Infirmary, NHS Grampian
- Ninewells Hospital and Medical School, NHS Tayside, Dundee
- Glasgow Royal Infirmary, NHS Greater Glasgow and Clyde
- Pilgrim Hospital, Boston, United Lincolnshire Hospitals NHS Trust
- University Hospital of North Tees, North Tees and Hartlepool NHS Foundation Trust, Stockton-on-Tees
- Airedale NHS Foundation Trust, Keighley
- Salisbury District Hospital, Salisbury NHS Foundation Trust
- The Rotherham NHS Foundation Trust
- George Eliot Hospital NHS Foundation Trust, Nuneaton
- James Paget University Hospital NHS Foundation Trust, Great Yarmouth
- Southampton General Hospital, University Hospital Southampton NHS Foundation Trust
- Lister Hospital, East and North Herts NHS Foundation Trust
- Royal Cornwall Hospital, Truro, Royal Cornwall Hospitals NHS Trust
- Tunbridge Wells Hospital, Maidstone & Tunbridge Wells NHS Trust

- Addenbrookes Hospital, Cambridge University Hospital NHS Foundation Trust
- Derriford Hospital, University Hospitals Plymouth NHS Trust
- Hull Royal Infirmary, Hull and East Yorkshire Hospitals NHS Trust
- Luton and Dunstable University Hospital
- Salford Royal NHS Foundation Trust
- Scunthorpe General Hospital, Northern Lincolnshire and Goole NHS Foundation Trust
- Pinderfields Hospital, Mid Yorkshire NHS Trust
- Leeds General Infirmary, The Leeds Teaching Hospitals NHS Trust
- Worcestershire Royal Hospital, Worcester Acute Hospitals NHS Trust
- Doncaster Royal Infirmary, Doncaster & Bassetlaw Hospitals NHS Foundation Trust
- St Helier Hospital, Epsom and St Helier University Hospitals NHS Trust
- St Mary's Hospital, Imperial College Healthcare NHS Trust London
- Raigmore Hospital, Inverness, NHS Highland
- Whiston Hospital, Warrington, St Helens & Knowsley Teaching Hospital NHS Trust
- Milton Keynes University Hospital NHS Foundation Trust
- Warwick Hospital, South Warwickshire NHS Foundation Trust
- Queen's Hospital, Burton Hospitals NHS Foundation Trust
- Hereford County Hospital, Wye Valley NHS Trust
- Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust
- John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust
- University Hospital of South Manchester NHS Foundation Trust
- Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust

2.3 Participants

2.3.1 Participant screening and eligibility

All adult patients presenting at the trial centres with a primary (first-time) rupture of the Achilles tendon were screened. The patient, in conjunction with their surgeon, decided whether non-surgical treatment was appropriate, as per normal clinical practice. If they decided not to have surgery, they were potentially eligible to take part in the trial.

2.3.2 Eligibility

In order that the trial findings would be generalisable to a UK-wide population, eligibility criteria were broad. Patients with acute rupture of the Achilles tendon were eligible if they met all of the inclusion criteria and none of the exclusion criteria.

The inclusion criteria were:

- Patient is aged 16 years or older.
- Patient has a primary rupture of the Achilles tendon.
- Patient has decided to have non-operative treatment.

The exclusion criteria were:

- Patient presented to the treating hospital more than 14 days after injury.
- There was evidence that the patient would be unable to adhere to trial procedures or complete questionnaires.
- Patient had a previous rupture of the Achilles tendon.

The first exclusion criterion related to patients with late presentation, which is not uncommon after this injury. Patients who present late may have problems with chronic tendon lengthening irrespective of treatment and are frequently offered surgical intervention. The limit of 14 days since injury has been widely used to define ‘acute’ rupture.

If a patient taking part in the study sustained a contralateral rupture during the trial period, the second rupture was not included in the study because the result of this intervention would not be independent from the first injury. However, the patient remained in the trial, with both previous and future data related to the initial rupture included in the final analysis.

Screening logs were completed at recruiting centres and collected by the UKSTAR trial office throughout the trial to assess the main reasons for patient exclusion at each recruitment centre and the number of patients who were unwilling to participate.

Members of the local research team informed the patient of the study, and carried out the informed consent process, baseline data collection and randomisation.

2.4 Baseline Assessment

Potential participants were allowed as much time as they needed to consider the trial information and had the opportunity to ask questions of the attending clinical team and a member of the research team. The trial information was delivered verbally and in writing detailing the exact nature of the study; the implications and constraints of the protocol; what

to expect as a participant; and any risks involved in taking part. It was clearly stated that the participant was free to withdraw from the study at any time, for any reason, without prejudice to future care, and with no obligation to give the reason for withdrawal. If the patient was happy to participate, they were asked to personally sign and date a consent form, which was also signed and dated by the person who obtained consent. Consent was obtained by an appropriately trained member of the research team who had been delegated to obtain consent by the local Principal Investigator

A copy of the signed consent form was given to the participant, and one copy was sent to the study coordinating team in Oxford to facilitate central monitoring. The original signed consent form was retained in the medical notes, and a copy was held in the Investigator Site File. Consent forms were held in a secure location separately from study data. Permission was obtained to inform the participant's general practitioner (GP) of study participation.

Consent was asked for name and contact details (including address, mobile, phone and email) to be collected to facilitate follow-up, data collection and reporting of results and for a copy of the contact details to be sent to the UKSTAR central office team in Oxford. These details were used by the study team to contact the participant for follow-up at the three, six and nine month time-points, to resolve queries, and to send a thank you letter at the end of the participant's involvement in the trial.

Permission was sought to allow access to participant data by responsible members of the University of Oxford or the NHS Trust for monitoring or audit of the study to ensure that regulations were complied with.

Following consent, baseline data was collected and the participant was randomised. The treatment took place on the same visit. A Good Clinical Practice (GCP) trained member of the local research team oversaw the participant's completion of the paper Baseline Questionnaire, which included:

- Date, mechanism and side of injury;
- Baseline demographics: height, weight, smoking and alcohol status, employment status;
- Current medication;
- Previous medical history: diabetes, rheumatoid arthritis, lower limb fracture, ligament, tendon or nerve injury to lower limb in last 12 months, arthritis, Achilles tendinopathy

or other relevant conditions.

2.5 Randomisation

Participants were randomly allocated (1:1) to either functional bracing or plaster cast using a computer-generated allocation sequence stratified by recruitment centre via a secure, centralised web-based randomisation service provided by the Oxford Clinical Trials Research Unit (OCTRU). The Research Associate informed the treating clinical team of the allocated treatment.

Stratification by recruitment centre helped to ensure any cluster effect related to the recruitment centre itself was equally distributed in the trial groups. The catchment area was similar for all of the recruitment centres; each recruitment centre was a trauma unit dealing with these injuries on a daily basis. All of the recruitment centres were familiar with both techniques i.e. the clinical staff used both plaster casts and functional bracing on a regular basis as part of their routine clinical practice.

2.6 Post randomisation withdrawals

Participants were free to decline consent or withdraw from the trial at any time without prejudice and without affecting the standard of care that they received. Participants had two options for withdrawal:

- To withdraw from completing further questionnaires but allow the trial team to view and record de-identified data that is recorded as part of the normal standard of care;
- To withdraw wholly from the study and only permit data obtained up to the point of withdrawal to be included in the final analysis.

Withdrawn participants were not replaced, as the target sample size allowed for losses to follow-up.

2.7 Interventions

Participants received their allocated treatment (plaster cast or functional bracing) following randomisation.

Although the principles of application of both plaster casts and functional bracing are inherent in the technique, there are different types of plaster cast material and functional brace design. Each patient underwent the allocated intervention as specified below, but the

details of application and materials used for the plaster and brace were left to the discretion of the treating clinician, as per their usual practice. This was intended to ensure that the results can be generalised across the NHS.

2.7.1 Plaster cast

Participants randomised to Plaster Cast received a cast in the 'gravity equinus' position, i.e. the position that the foot naturally adopts when unsupported. In this position, with the toes pointing down towards the floor, the ends of the ruptured tendon are roughly approximated. Use of ultrasound to assess the approximation of the tendon ends is not routine in the NHS [10] and was left to the discretion of the treating clinician. The participant was permitted to mobilise with crutches immediately using their toes for balance (toe-touch) but was advised not to bear weight on the injured hindfoot. Over the first eight weeks, as the tendon was healing, the position of the plaster cast was changed until the foot achieved plantigrade, i.e. the foot flat to the floor. At this point the patient was permitted to start to bear weight in the plaster cast. The number of changes of plaster cast and the time to weight-bearing was left to the discretion of the treating clinician, as per their usual practice. The cast was removed at eight weeks.

The plaster cast provided maximum protection for the healing tendon; specifically restricting upward movement (dorsiflexion) of the ankle which may stretch the healing tendon, but it did not allow the patient to bear weight on the foot immediately or to move the ankle.

2.7.2 Functional bracing

Participants randomised to Functional Brace received a rigid brace, as opposed to a flexible brace [30]. Initially, two solid heel wedges (or equivalent) were inserted into the brace to replicate the 'gravity equinus' position of the foot [30]. The patient was able to mobilise with immediate full weight-bearing within the functional brace. The brace also permitted some movement at the ankle joint. The number of wedges and foot position were reduced over eight weeks until the patient reached plantigrade. Again, the timing of the removal of wedges and change in foot position were left to the discretion of the treating clinician, as per their usual practice. The brace was removed at eight weeks, as per routine clinical care.

2.7.3 Monitoring intervention delivery and compliance

Clinic staff recorded the participant's treatment in clinic records as per usual practice. At the 8 week follow-up visit research staff recorded on the 8-week trial case report form (CRF):

- the intervention the patient was randomised to;
- the intervention they received;
- the date of the 8-week follow-up appointment;
- for participants treated in a functional brace, irrespective of their randomisation allocation:
    - the number of heel wedges inserted into the heel of the functional brace at baseline (date of treatment), and at two, four, six and eight weeks after treatment;
    - the number of weeks after treatment when the patient was allowed to fully weight bear;
    - the number of weeks after treatment when the functional bracing was removed;
    - the brand of functional bracing.
- for participants treated in a plaster cast, irrespective of their randomisation allocation:
    - the number of plaster cast changes over the eight weeks since treatment;
    - the number of weeks after treatment when the patient was allowed to fully weight bear;
    - the number of weeks after treatment when the plaster cast was removed;
- whether the patient switched to another intervention during the eight weeks after treatment, the date of switching and the reason for switching.
- Whether the participant received treatment with venous thromboembolism (VTE) prophylaxis, type and duration.

2.8 Rehabilitation

At the patient's 8-week clinic appointment the plaster cast or functional brace was removed, unless the clinical team directed otherwise. All participants were provided with the same standardised, written physiotherapy advice detailing the exercises they need to perform for rehabilitation following their injury. This standardised rehabilitation advice was based on a published systematic review of current rehabilitation protocols[32]. All the participants were advised to move their toes, ankle and knee joints fully within the limits of their comfort, and walking was encouraged. In this pragmatic trial, any other rehabilitation input beyond the written physiotherapy advice (including a formal referral to physiotherapy) was left to the discretion of the treating clinicians. A record of any rehabilitation input (type and number of

additional appointments) as well as other investigations or interventions was collected as part of the 8-week, 3-month, 6-month and 9-month follow-up questionnaires.

2.9 Outcome measures

2.9.1 Primary outcome

The primary outcome measure for this study was the ATRS [33] at nine months post injury. The ATRS is a validated questionnaire[34] which is self-reported (completed by the participant). It consists of 10 items assessing symptoms and physical activity specifically related to the Achilles tendon. It measures: strength, fatigue, stiffness, pain, activities of daily living, walking on uneven surfaces, walking upstairs or uphill, running, jumping and physical labour. Each ATRS item varies from 0 (major limitations/symptoms) to 10 (no limitations/symptoms) on an 11 point scale. The final ATRS is derived from the sum of the 10 questions with a total possible score range between 0 and 100, where 100 is the best possible score.

2.10 Secondary outcome measures

The secondary outcome measures were:

- The ATRS collected at eight weeks, three months and six months post injury.
- EQ-5D; The EQ-5D-5L is a validated, generic health-related quality of life measure consisting of 5 dimensions each with a 5-level answer possibility and a visual analogue scale (VAS) [35]. The EQ-5D can be used to report health-related quality of life in each of the five dimensions and each combination of answers can be converted into a health utility score where 1 represents perfect health and 0 indicates death. The EQ-5D VAS takes values between 0 and 100, where 0 represents worst imaginable health and 100 best imaginable health. It has good test-retest reliability, is simple for patients to use, and gives a single preference-based index value for health status that can be used for broader cost-effectiveness comparative purposes.
- Complications; all complications were recorded, from the medical records at the 8 week review and self-reported by the patient thereafter, including: re-rupture, blood clots/emboli, pressure areas/hindfoot pain, falls and neurological symptoms in the foot. The 3-, 6- and 9-month follow-up questionnaires sent to the participant included questions on complications.

2.11 Adverse events

Adverse events (AEs) are defined as any untoward medical occurrence in a clinical trial subject and do not necessarily have a causal relationship with the treatment. All AEs were listed on the CRF for routine return to the UKSTAR central office.

Serious adverse events are defined as any untoward and unexpected medical occurrence that:

- results in death;
- is life-threatening;
- requires hospitalisation or prolongation of existing inpatients´ hospitalisation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect;
- is any other important medical condition which, although not included in the above, may require medical or surgical intervention to prevent one of the outcomes listed.

All serious adverse events (SAEs) were recorded by recruitment centre staff on the trial SAE reporting form and emailed to a secure NHS.net account accessed only by the research team within 24 hours of the investigator becoming aware of them. Once received, causality and expectedness were confirmed by the Chief Investigator. SAEs that were deemed to be unexpected and related to the trial were notified to the Research Ethics Committee within 15 days. All such events were reported to the Trial Steering Committee (TSC) and Data and Safety Monitoring Committee (DSMC) at their next meetings.

Some AEs were foreseeable as part of the proposed treatment – including those which met the definition of "serious" as described above – and did not require reporting immediately to the UKSTAR central office, provided they were recorded in the 'Complications' section of the CRFs or participant questionnaires. These events were: re-rupture, blood clots/emboli, pressure areas/hindfoot pain, falls and neurological symptoms in the foot.

All participants experiencing SAEs were followed up as per protocol until the end of the trial.

All unexpected SAEs or suspected unexpected SAEs that occurred between date of consent and the date of the 9-month follow-up time-point were reported.

2.12 Blinding

As the type of rehabilitation used was clearly visible, participants could not be blinded to their treatment. In addition, the treating clinician was also not blinded to the treatment but

took no part in the post injury assessment of the participants. The outcome data was collected and entered onto the trial central database via questionnaire, by a research assistant or data entry clerk in the trial central office to reduce the risk of assessment bias.

2.13 Follow-up

UKSTAR Trial office staff contacted the participants directly for follow-up at three, six and nine months using the contact details that had been supplied by the participant. Participants were contacted by post, by email or by short message text (SMS) text message according to their preference and, if no response was received, they were telephoned. All follow-up contacts and attempted contacts were logged without personal identifying details in a contact log.

Participants who had supplied an email address were sent a link by email to complete an online questionnaire. Participants who had supplied a mobile telephone number were sent the same link by SMS text message. Participants who had supplied both email address and mobile number were sent the link via both mechanisms. If participants did not respond to any of these initial approaches, they were sent a reminder one week later. If there was still no response after a further week, the participants were sent a paper questionnaire. If the paper questionnaire was not returned within two weeks, UKSTAR office staff telephoned the participants. If the participant was uncontactable during working hours, attempts were made to phone them during the evening, as many participants were of working age.

Participants who had specified that they preferred to be contacted by post, or who had not supplied an email address or mobile number, were sent a questionnaire in the post, and a second postal questionnaire if no response was received within two weeks. UKSTAR office staff attempted to phone the participant for follow-up if the second postal questionnaire was not returned within two weeks.

DVTs, pulmonary embolisms (PEs) and re-ruptures were reported by participants through completion of a questionnaire, or by participants directly to the study office, or by recruitment centre staff after participants had returned to their recruitment centre for further treatment. These reports underwent validation, as follows. In the case of a patient-reported DVT or PE, recruitment centres were requested to complete a DVT/PE form, which detailed symptoms, results of any ultrasound imaging, results of any computed tomography pulmonary angiogram imaging, treatment received and treatment duration. In the case of a

patient reported re-rupture, recruitment centres were requested to provide details of diagnosis and treatment. If the patient underwent surgery for a re-rupture, an operation note was requested. All information submitted in connection with a re-rupture was reviewed by the Chief Investigator, blind to the treatment allocation, in order to confirm the diagnosis.

2.14 Sample size

The minimum clinically important difference (MCID) for the primary outcome ATRS was 8 points. At an individual patient level, a difference of 8 points represents the ability to walk upstairs or run with 'some difficulty' versus with 'great difficulty'. At a population level, 8 points represents the difference between a 'healthy patient' and a 'patient with a minor disability' [34].

In previous work, the standard deviation (SD) of the ATRS at nine months post injury was 20 points [36] Assuming a likely population variability of 20, MCID value of 8 and 90% power to detect the selected MCID, there was a requirement of 264 total participants to be randomised. Allowing a margin of 20% loss of primary outcome data to include patients who would cross over between interventions and those lost to follow-up, led to a requirement of 330 participants. We intended to recruit a minimum of 330 patients from at least 22 centres over a period of 16 months. The trial reached its primary recruitment target of 330 participants before the end of the proposed recruitment window and therefore the sample size was recalculated based on a larger population variability equivalent to a SD of 25 points following a blinded review of the variability by the DSMC. As per Table 1 calculations for SD 25, MCID 8, 5% two-sided tests and 20% loss to follow-up 516 participants were required. The maximum number of participants to be recruited for the trial was set at 550.

Table 1: Sample size

	80% Power			90% Power		
MCID	6	8	10	6	8	10
SD						
15	198	112	72	264	150	96
20	350	198	128	468	**264**	170
25	548	308	198	732	412	264

2.15 Statistical analysis

2.15.1 Software employed

All analyses outlined here were undertaken using Stata version 15.0 (StataCorp, College Station, TX).

2.15.2 Blinded analysis

The distribution of variables, missing data distributions and outliers was assessed as part of a blinded analysis of data (not separated by treatment group) prior to the final data lock. This analysis was also used to help identify key prognostic variables to be included in the adjusted analysis. The treatment code was added to the database after the data cleaning had been completed and all subsequent analyses described were conducted on an unblinded dataset. The Statistical Analysis Plan was updated to incorporate necessary changes.

2.15.3 Data validation

To ensure consistency, validation checks of the data were conducted. This included checking for duplicate records, checking the range of variable values or missing items and validating potential outliers by comparing with CRFs and referring back to recruitment centres when necessary. Calculations for derived variables such as the ATRS were checked by hand calculations on 20 randomly selected participants from the dataset. These checks confirmed that the data had been imported into the statistical software correctly, calculation of derived variables had been performed correctly and merging of different data to form an analysis dataset was verified.

2.15.4 Study populations

Two populations were considered for analysis, the intention-to-treat (ITT) population and the Complier Average Causal Effect (CACE) population [37]. The ITT population included all participants in their randomised groups and the CACE population included all randomised participants compliant with treatment. Participants were considered compliant with the intervention if they wore their allocated treatment for a period of six weeks or more without any change of treatment within this period.

2.15.5 Descriptive analysis

All available data from both treatment groups (Functional Brace and Plaster Cast) was used in descriptive analysis. The flow of participants through each stage of the trial, including numbers of participants eligible for randomisation, those randomised, receiving intended treatment, completing the study protocol, and analysed for the primary outcome was assessed. Reporting of the results was in accordance with the Consolidated Standards of Reporting Trials (CONSORT) for Patient Reported Outcomes (PRO) statement using the extension for non-pharmacologic treatment interventions and patient reported outcomes [38]. Any protocol deviations and violations were investigated.

Participant baseline characteristics were reported by treatment group and overall, and included recruitment centre stratification, demographic variables age, gender, side of injury and mechanism of injury, body mass index (BMI), smoking status, alcohol consumption, medication, diagnoses, employment status and baseline values for ATRS and EQ-5D-5L before and after the injury. Numbers (with percentages) for categorical variables and mean (and SD), or medians (with interquartile range (IQR)) for continuous variables were presented for each treatment group and overall. There were no tests of statistical significance nor confidence intervals (CIs) for differences between randomised groups on any baseline variable.

Data collected at the 8-week, 3-, 6- and 9- months post injury follow-ups was summarised and the proportion of missing items from completed questionnaires examined. The patterns of data availability for primary and secondary outcomes from baseline to end of follow-up, were summarised for the two treatment groups as well as reasons for missingness where known. The nature and pattern of missing data (missing completely at random (MCAR); missing at random (MAR); or missing not at random (MNAR)) was explored. Differentiation was made between partially completed and fully missing outcome data. Validation rules for the primary outcome ATRS ensured that data was entered in the correct format, within valid ranges, minimising the chance of missing data. Where ATRS item responses were missing and at least half of the items were present, a pro-rata estimation of the ATRS score was imputed based on the average of the available ATRS item responses.

Withdrawals and losses to follow-up were compared between the Functional Brace and Plaster Cast groups at each time-point and the reasons reported where known. Absolute risk differences (with 95% CIs) between the two groups were calculated, and the importance of differences identified using Chi-squared tests or Fisher's exact test if appropriate. Where

participants were identified with tendon re-ruptures followed by surgery, the participant was not treated as loss to follow-up. Deaths and their causes were reported separately.

Quality assurance and the compliance with treatment was assessed. Treatment received was reported by intervention group and summarised with reasons for not receiving the assigned treatment where this was possible.

For all analyses tests were two sided and considered to provide evidence for a significant statistical difference if p-values to three decimal places were less than 0.05 (5% significance level) and any reported treatment estimates will be presented with their associated 95% CI.

2.15.6 Analysis of primary outcome

The primary outcome ATRS at nine months post injury was reported for each of the two treatment groups, Functional Brace and Plaster Cast. The main findings of the trial show the difference in the ATRS between the two treatment groups, estimated with a linear mixed effects regression model, including outcome information from all follow-up points and adjusting for recruitment centre, age, gender and baseline ATRS. An additional fully adjusted model included centre, age, gender, baseline ATRS, smoking status and diabetic condition as prognostic variables. Important clinician-specific effects were not expected as individual clinicians only treated a small number of patients, but recruitment centre was included in the model as a random effect factor to adjust for potential cluster differences. Estimates of treatment effects were presented with 95% CIs. Histograms and residual checks were used to assess an approximate normal distribution of the ATRS and where relevant the medians and IQRs reported for each treatment group.

An unadjusted analysis was also undertaken to assess the differences between treatment groups using a Student t-test, based on a Normal approximation for the ATRS score. Estimates of treatment effects were presented with 95% CIs for both unadjusted and adjusted analyses. The ITT adjusted analysis of the primary outcome ATRS was used to determine the success or otherwise of the trial.

Sensitivity analyses to examine the robustness of conclusions to different assumptions were conducted for the CACE population. Compliance was defined as using the allocated intervention for a minimum of six weeks and further sensitivity analysis was undertaken using different definitions of compliance, minimum of four weeks and minimum of two weeks.

Supplementary analysis

In order to explore recovery in the two treatment groups over time, a further analysis of the ATRS was conducted. This summarised longitudinal data collected at all four time-points to a single value, the area under the curve (AUC) [39] in order to facilitate comparison of the ATRS between treatment groups over time. Parameter estimates from the mixed effects models were used to calculate AUCs for each treatment group from baseline to the 9-month post injury follow-up. This provided an overall estimate of recovery over time in each group. Larger ATRS scores were associated with fewer limitations/difficulties related to the injured Achilles tendon, therefore larger AUCs were suggestive of improved function. AUCs for each treatment group and their difference calculated using a t-test were presented together with their associated 95% CI. The *lincom* command in Stata was used to calculate AUC for each group. This analysis was also conducted for the EQ-5D utility score and the EQ-5D VAS.

2.15.7 Analysis of secondary outcome

Continuous secondary outcomes ATRS at 8 weeks, 3 and 6 months post injury follow-up and EQ-5D-5L were evaluated and analysed for the ITT population using the methodology described for the primary outcome. Histograms and residual checks were used to assess whether these variables were approximately normally distributed. Means and SDs were reported at the 8-weeks, 3-, 6- and 9-month post-injury follow-up time-points and medians and IQRs where appropriate. A linear mixed effects regression model including outcome information from all time-points and adjusting for recruitment centre, age, gender and baseline pre-injury outcome values was used to examine the difference between the treatment groups.

Complications in each of the treatment groups were reported as numbers (with percentages) and compared over the nine months study period using Chi-squared tests or Fisher's exact test. The results were reported with their associated 95% CI and p-values for comparison between the two treatment groups. The population for this analysis was ITT. Complications were further grouped for to identify the number of patients with one or more complications at each time-point.

Sensitivity analyses were also conducted for the secondary outcome EQ-5D-5L analysis using the CACE population.

2.16 Health economics methods

2.16.1 Overview

The main objective of the health economic evaluation was to assess the comparative cost-effectiveness of the two non-surgical treatment options (plaster cast versus functional bracing) for patients with a primary (first-time) rupture of the Achilles tendon. To achieve this, a systematic comparison of the cost of resource inputs used by participants in the two arms of the trial and consequences associated with the interventions was conducted. The primary analysis adopted a NHS and PSS perspective, in accordance with National Institute for Health and Care Excellence (NICE) recommendations [40]. A societal perspective for costs was adopted for the sensitivity analysis and this included private costs incurred by trial participants and their families, as well as productivity losses and loss of earnings as a result of work absences.

The economic evaluation took the form of a cost–utility analysis, expressed in terms of incremental cost per QALY gained. The time horizon covered the period from randomisation to end of follow-up at 9 months post injury. Costs and outcomes were not discounted due to the short, 9-month, time horizon adopted for this within-trial evaluation.

2.16.2 Measurement of resource use and costs

Data were collected on:

i) Resource use and costs associated with delivery of the interventions (direct intervention costs)
ii) Broader health and social care service use during the 9 months of follow-up
iii) Broader societal resource use and costs – this encompassed private medical costs and lost productivity costs such as lost income over the 9 months of follow-up.

All costs were expressed in pounds sterling and valued in 2017-18 prices. When appropriate, costs were inflated or deflated to 2017–18 prices using the Hospital and Community Health Services (HCHS) Pay and Price Inflation Index [41].

Direct intervention costs

Direct intervention costs comprised costs associated with the application of the two interventions. This included cost of the walking boot and wedges, materials used for plaster cast, the cost associated with fitting the interventions to patients (hospital staff time), and the costs associated with any changes required to either plaster cast or functional bracing (Table 2). Information on how long it takes to deliver each intervention and type and volume of materials used was collected at each recruitment centre, through a questionnaire completed by recruitment centre staff in consultation with staff responsible for fitting the functional brace or applying the plaster cast. Unit costs for staff were obtained from the Personal Social Services Research Unit (PSSRU) Unit Costs of Health and Social Care 2018 compendium [42] and were multiplied by the median time it takes to deliver each intervention. The median time for fitting a functional brace was 10, 11 and 17.5 minutes for a plaster technician, nurse and other staff (included physiotherapists, orthotists and occupational therapists) respectively. The median time to change wedges was 5 minutes for a plaster technician and nurse and 10 minutes for 'other' staff. The median time for changing a plaster cast was 15 minutes for a plaster technician and 17.5 minutes for a nurse. The base case analysis assumed costs of a plaster technician. Unit costs of plaster cast materials, walking boots and wedges were obtained from the 2018 NHS Supply chain catalogue. The total direct intervention cost for each patient was calculated by combining the resource inputs with their respective unit cost values.

Table 2: Unit costs associated with direct intervention costs for plaster cast and functional bracing

Resource item	**Unit cost**	**Unit of analysis**	**Source of unit cost**
Direct intervention costs			
Functional brace:			
Walking boot[1] cost by brand:			
Samson walking boot Donjoy walking boot Airstep walking boot	£15.00 £19.24 £68.66	Per walking boot	John Radcliffe finance department;

			NHS Supply Chain Catalogue 2018
Plaster cast:			
Plaster cast materials [2]			
2 x 7.5cm poly rolls 2x 10 cm poly rolls	£2.83 £6.69	Per roll	NHS Supply Chain Catalogue 2018
Fibreglass casting tape 5 inch x3.6m	£11.48	Per roll	NHS Supply Chain Catalogue 2018
1m stockinette	£3.23	Per roll	NHS Supply Chain Catalogue 2018
2 x rolls of 5inch wool bandage	£3.00	Per roll	NHS Supply Chain Catalogue 2018

[1] Unit costs for all other walking boot brands that patients received (not pre-specified in case report forms) were individually-derived from the NHS Supply Chain Catalogue.

[2] Unit costs for any other plaster cast materials that sites use (not pre-specified in site-specific questionnaire) were individually-derived from the NHS Supply Chain Catalogue 2018.

2.16.3 Measuring broader resource use

Broader resource use data were collected using follow-up questionnaires completed by trial participants at the four follow-up assessment points: 8 weeks, 3 months, 6 months and 9 months post injury. The questionnaires captured details of inpatient and day case admissions, outpatient and emergency care attendances, encounters with primary or community health and social care services, medication use and walking aids provided/self-purchased, as well adaptations to home environments. In addition, the questionnaires captured the direct non-medical costs (including travel expenses) incurred by patients and their carers, as well as number of days off work and gross loss of earnings attributable to the trial participant's health state or contacts with care providers.

2.16.4 Valuation of resource use

Resource inputs were valued by attaching unit costs derived from national compendia in accordance with NICE's Guide to the Methods of Technology Appraisal 2013 [40]. The key databases for deriving unit cost data included the Department of Health and Social Care's Reference Costs 2016–17 schedules [43], the PSSRU's Unit Costs of Health and Social Care 2018 compendium [42], the 2018 NHS Prescription Cost Analysis database for England [44], 2018 volumes of the British National Formulary [45], and the NHS Supply Chain Catalogue 2018 [46]. Table 27 (Appendix 4) gives a summary of the unit costs values and data sources for broader resource use categories identified within the follow-up questionnaires.

Per diem costs for hospital inpatient admissions during the follow-up period were calculated individually as a weighted average of Healthcare Resource Group (HRG) codes of related procedures and/or clinical diagnoses. For example, the average cost per day for an inpatient stay in a medical ward to treat a PE was calculated as the sum total of weighted average HRG codes (DZ09J – DZ09Q; PE with or without interventions) divided by average length of stay across elective and non-elective inpatient services. The individual HRG codes were derived using the NHS HRG4 2017/18 Reference Cost Grouper software version RC1718 (NHS Digital, Leeds, UK). The Department of Health and Social Care's *Reference Costs 2017–18* [43] schedule was used to assign the costs for each of the derived HRG codes.

Costs for community-based health and social care services were calculated by applying unit costs extracted from national tariffs, primarily extracted from the PSSRU Unit Costs of Health and Social Care 2018 compendium [42], to resource volumes. Costs of medications for individual participants were estimated based on their reported doses and frequencies, when these were available, or based on an assumed daily doses using *British National Formulary* [45] recommendations. When a dose range was reported as 'as required' or when the quantities were not recorded, we assumed a mean cost for that medication item based on the prescription cost analysis values (net ingredient cost per item). In cases where medication dosages were missing, we conservatively assumed that the patient received the same dosage as other trial participants who reported taking the same medication.

The costs of walking aids and adaptations (equipment participants receive to manage their injury and make daily lives easier) were derived by combining data on number and type of items received with their unit cost values. Unit cost values were derived from the NHS supply chain catalogue [46] if equipment was provided by a health provider during the trial follow-up period. Where aids and adaptations were self-financed, the costs were provided by participants themselves.

We used data on sex and employment status-specific median earnings from the UK national annual survey of hours and earnings [47] to derive the costs of time taken off work. The employment status of trial participants was derived from self-reported work status information. Broader societal costs were calculated by combining the productivity losses and income losses attributable to work absences.

Summary statistics were generated for resource use variables by treatment allocation and assessment point. Between treatment-group differences in resource use and costs at each assessment point were compared using the two sample t-test. Statistical significance was assessed at the 5% significance level. Standard errors are reported for treatment group means and bootstrap 95% confidence intervals for the between-group differences in mean resource use and cost estimates.

2.16.5 Measurement of outcomes

In accordance with NICE guidelines, the primary health outcome for the health economic evaluation was the QALY metric. [48] QALYs are a measure that combines quantity and preference-based health-related quality of life (HRQoL) into a single metric. To calculate QALYs, it is imperative to obtain health state values for participants within the trial. Health-related quality of life of trial participants was assessed at baseline (both pre and post injury), and 8 weeks, 3 months, 6 months and 9 months post injury using the EuroQoL EQ-5D-5L instrument. [49] The EQ-5D-5L instrument defines health-related quality of life in terms of five dimensions: (1) mobility, (2) self-care, (3) usual activities, (4) pain/discomfort and (5) anxiety/depression. Responses in each dimension are divided into five ordinal levels coded: (1) no problems, (2) slight problems, (3) moderate problems, (4) severe problems, and (5)

extreme problems. Responses to each health dimension were categorised as optimal or sub-optimal with respect to function where optimal level of function indicates no impairment (for example “no problems in walking about” for the mobility dimension) and sub-optimal function refers to any functional (below level 1) impairment. Between-group differences in optimal versus sub-optimal level of function for each health dimension were compared at each time-point using chi-squared ($\chi 2$) tests.

Responses to the EQ-5D-5L instrument were converted into health utility scores using the EQ-5D-5L Crosswalk Index Value Calculator currently recommended by NICE, [50] which maps the EQ-5D-5L descriptive system data onto the EQ-5D-3L valuation set. Detailed description on the mapping methodology is described elsewhere. [50] QALYs were generated for each patient using the area under the baseline-adjusted utility curve, assuming linear interpolation between health utility measurements across assessment points.

Health utility values and QALYs accrued over the 9-month follow-up period were summarised by treatment group and assessment point and presented as means and associated standard errors; between group differences were compared using the two-sample t-test, similar to the descriptive analyses of resource inputs and costs.

2.16.6 Cost-effectiveness analysis methods

Missing data

Missing data are a common occurrence within randomised controlled trials: participants may be lost to follow-up, questionnaires unreturned or responses to individual questionnaire items may be missing. [51] Because costs and outcomes of individuals with missing data may differ systematically to those with fully observed data, it is important to handle missing data using a principled approach that is justified by, amongst other factors, the missing data mechanism. Missing costs and health utility data were imputed at each time-point using fully conditional multiple imputation by chain equations, implemented through the MICE package, under the missing at random (MAR) assumption. Appropriateness of the MAR assumption was assessed by: (i) investigating the missing data patterns (monotonic vs. non-monotonic), and (ii) comparing attributes of participants with and without missing costs and health-related quality of life data at each follow-up time-point.

The multiple imputation model used baseline covariates (age, gender), costs and health utility values at each follow-up time-point to impute unobserved costs and health utility values, such that, for example, missing costs at 9 months were imputed using data on baseline covariates, costs at 8 week, 3 months and 6 months and health utility values at each follow-up time-point. The imputations were implemented separately by treatment allocation in line with best practice. [52] The imputation was run 50 times, following the rule of thumb that the number of imputations should be at least greater than the proportion of missing data. [52]

Bivariate regressions using a seemingly unrelated regression model (Sureg) were used to independently analyse the multiply imputed datasets so as to estimate the costs and QALYs in each treatment group over the 9-month trial horizon. Joint distributions of costs and outcomes from the original data set were generated through non-parametric bootstrapping and changes in costs and QALYs were calculated for each sample. A total of 1000 bootstrap samples were drawn and means for both incremental costs and incremental QALYs (with associated 95% CIs) were calculated. Estimates from each imputed dataset were combined using Rubin's rule [53] to generate overall mean estimates of costs and QALYs and their standard errors (SE). The latter reflects the variability within and across imputations. The imputation model was validated by assessing the distributions of imputed and observed values. A mixed model with adjustment for baseline pre-injury EQ-5D health utility scores is also presented for comparison.

Presentation of cost-effectiveness results

Cost-effectiveness results are expressed in terms of the incremental cost-effectiveness ratio (ICER) and calculated as the difference between treatments in mean total costs divided by mean total QALYs. Given the pattern of results, plaster cast has been selected as the referent and functional brace as the comparator, i.e. functional brace minus plaster cast, for the estimation of ICER values. The bootstrap replicates generated by the non-parametric bootstrapping, described in the sub-section 'Missing data', were used to populate cost-effectiveness scatterplots. Cost-effectiveness acceptability curves, which showed the probability that functional brace is cost-effective relative to plaster cast across a range of

cost-effectiveness thresholds, were also generated based on the proportion of bootstrap replicates with positive incremental net benefits. The net monetary benefit (NMB) of using functional brace versus plaster cast was also calculated across three pre-specified cost-effectiveness thresholds, namely £15,000 per QALY , [54] £20,000 per QALY and £30,000 per QALY. [55] A positive incremental NMB indicates that the functional brace is cost-effective compared with the plaster cast at the given cost-effectiveness threshold. For the purpose of the secondary analysis that adopted the ATRS as the health outcome measure of interest, the NMB was estimated at cost-effectiveness thresholds of £100 - £500 per unit change in ATRS score. We failed to identify any external evidence on economic values for changes in ATRS score and therefore a range of arbitrary threshold values had to be selected for this analysis.

Sensitivity and secondary outcomes analyses

Several sensitivity analyses were conducted to test the robustness of the cost-effectiveness estimates. These involved re-estimating the main cost-effectiveness outcomes under the following scenarios: (1) restricting the analyses to complete cases (i.e. those with complete cost and outcome data over the 9-month follow-up period); (2) adopting a wider societal perspective that included private costs incurred by trial participants and their families, as well as economic losses placed on attributable work absences; and (3) Estimating incremental cost-effectiveness using a CACE population. In addition, as a secondary analysis, cost-effectiveness was estimated using the ATRS, rather than the QALY, as the health outcome measure of interest.

Longer-term economic modelling

The study protocol also allowed for decision-analytic modelling to estimate longer-term cost-effectiveness of functional bracing or plaster cast provided the costs and health outcomes did not converge at the end of the 9-month post injury follow-up period.

2.17 Data management

According to the standard operating procedures of the OCTRU, data management procedures were defined in a Data Management Plan. This covered trial databases and data handling,

definition of critical data fields, forms and questionnaires used, data collection, how protocol deviations were recorded, data rulings, handling data deviations, data security and confidentiality, dataset closure, archiving and data sharing. Each Data Management Plan version was signed off by the Chief Investigator and Trial Statistician.

The Monitoring Plan determined the need for central and on-site data monitoring. All recruitment centres were monitored centrally. The monitoring plan specified that on-site monitoring was not required for this trial and no monitoring visits were conducted.

Statistics on data collection, data entry and query management were presented to each TMG meeting for oversight.

UK legislation requires data to be anonymised as soon as it is practical to do so. Participants were identified only by initials and a participant number on UKSTAR questionnaires and in the study database. All documents were stored securely and only accessible by study staff and authorised personnel. Personal data and sensitive information required for the study were collected directly from trial participants and hospital notes. All personal information received in paper format for the trial was held securely and treated as strictly confidential. Personal data was stored separately from study outcomes, in lockable cabinets in secure keycard accessed rooms in the Kadoorie Centre in the John Radcliffe Hospital and in the Botnar Research Centre, University of Oxford, in Oxford. All paper and electronic data will be retained for at least five years after completion of the trial.

2.18 Patient and public involvement

The UKSTAR TSC and TMG both included a patient representative as a PPI member. Mrs S Webb was TSC PPI representative and attended meetings from the initial meeting and Mr R Grant was PPI representative at TMG meetings from September 2017.

2.19 Ethical approval and monitoring

2.19.1 Ethical approval

The study was given a favourable opinion by the South Central - Oxford B Research Ethics Committee on 07 April 2016 (Research Ethics Committee reference 16/SC/0109) and each recruitment centre was granted site-specific approval from its NHS Trust Research and Development department before trial commencement.

2.19.2 Data and Safety Monitoring Committee

The DSMC was a group of independent experts external to the trial who assessed the progress, conduct, participant safety and critical endpoints of the trial. The UKSTAR DSMC adopted a DAMOCLES charter [56] which defined its terms of reference and operation in relation to oversight of the trial. They reviewed copies of data accrued to date including information on allocation balance, data quality and participant safety summarised by treatment group, and assessed the screening algorithm against the eligibility criteria. No formal interim analysis of the outcome data was requested for review by the DSMC. During the period of recruitment to the trial, all information supplied to the DSMC members was done in strict confidence. They also considered emerging evidence from other related trials or research and reviewed related SAEs that have been reported. They were able to advise the chair of the TSC at any time if, in their view, the trial should be stopped for ethical reasons, including concerns about participant safety. DSMC meetings were held at least annually during the recruitment phase of the study.

2.19.3 Trial Steering Committee

The TSC, which included independent members, and had an independent Chair, provided overall supervision of the trial on behalf of the funder. Its terms of reference were defined in a TSC Charter, agreed with The Health Technology Assessment (HTA) Programme, who also approved the appointment of TSC members. The TSC's remit was to:

- monitor and supervise the progress of the trial towards its interim and overall objectives;
- review at regular intervals relevant information from other sources;
- consider the recommendations of the DSMC;
- inform the funding body of the progress of the trial.

TSC meetings were held at least annually during the recruitment phase of the study.

2.19.4 Trial Management Group

The TMG was made up of the Study Investigators and staff working on the project. This group oversaw the day-to-day running of the trial and met regularly throughout the lifetime of the study.

2.20 Summary of changes to the trial protocol

All protocol versions can be found on the NIHR journals library website at [URL to be provided].

The changes to the project protocol are summarised in Table 3.

Table 3: Changes to the protocol during the study by version number

Protocol Version No.	**Date**	**Details of Changes made**
1	27 January 2016	The first version.
2	18 August 2016	References to fax removed; replaced with description of sending confidential documents to a secure nhs.net email. Addition of resource use questionnaire at eight weeks Clarification of data collection roles of recruitment centre staff and UKSTAR office staff. Update to the statistical analysis section of the protocol so that it reflects the statistical analysis plan for the trial. Clarification regarding the consent process. Correction of typographical errors and clarifications.
3	10 July 2017	Clarification that questionnaires at the 3, 6 or 9 month time-points may be sent electronically to patients via email or text, as an alternative to by post.
4	19 September 2017 (not issued)	Update of sample size to a maximum of 550 patients.
5	23 October 2017	Correction of protocol version number from 4.1 to 5.0.
6	16 May 2018	Addition of Study Within a Trial to assess the effect of thank you emails on follow-up rates. Updates to Study personnel, Trial Steering Committee membership and sponsor address details. Correction of minor typographical errors.
7	13 November 2018	Removal of Study Within a Trial. Addition of thank you letter to participants after final follow-up.

3. Clinical trial results

3.1 Study participants

Patients with an Achilles tendon rupture typically attend the Emergency Department at their local hospital and, following their diagnosis, are referred to the next available fracture/trauma clinic to discuss the management of their injury.

The flow of participants through the study is summarised in

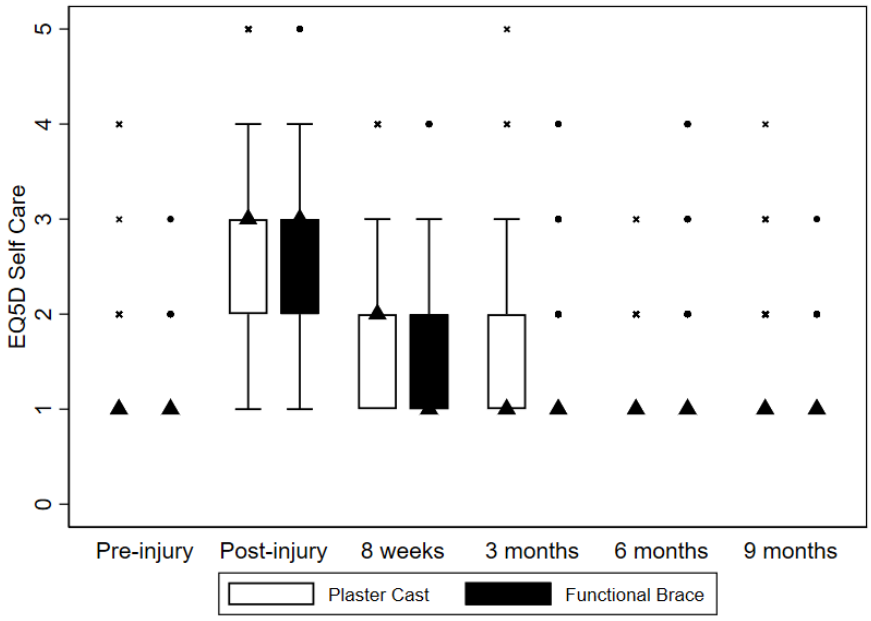

Figure 16: EQ-5D Self Care from baseline pre-injury to 9 months. EQ-5D Self Care values range from 1 to 5 with 1 indicating no problems

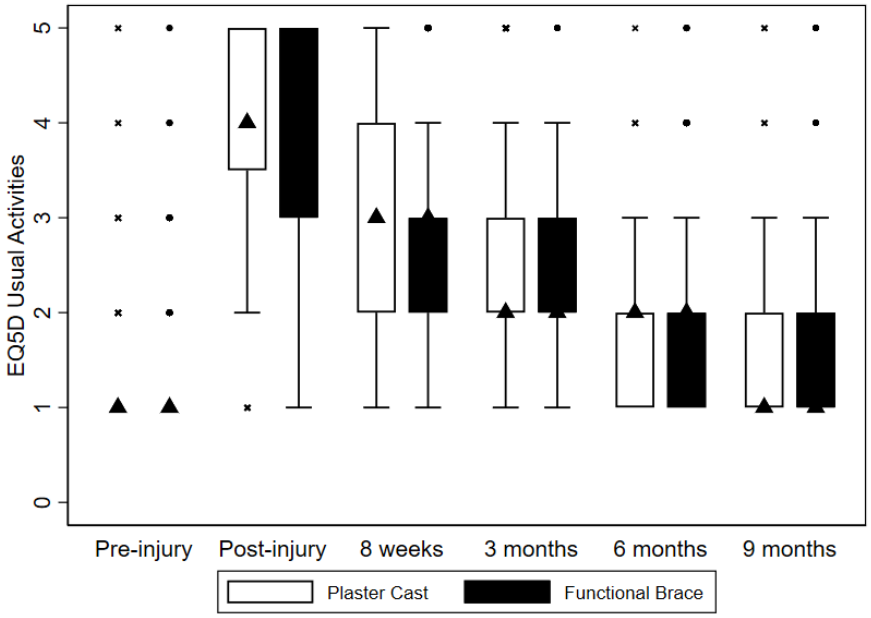

Figure 17: EQ-5D Usual Activities from baseline pre-injury to 9 months. EQ-5D Usual Activities values range from 1 to 5 with 1 indicating no problems

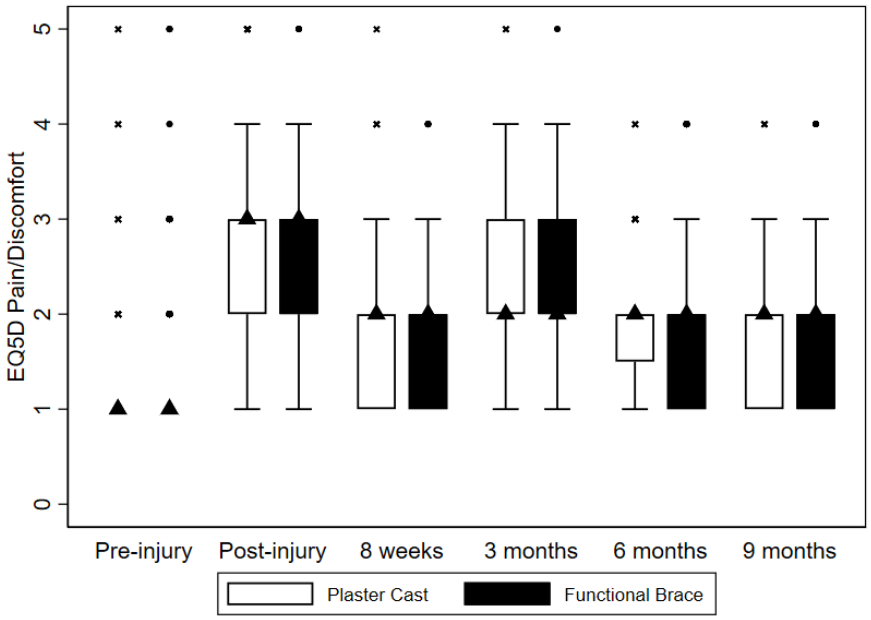

Figure 18: EQ-5D Pain Discomfort from baseline pre-injury to 9 months. EQ-5D Pain Discomfort values range from 1 to 5 with 1 indicating no problems

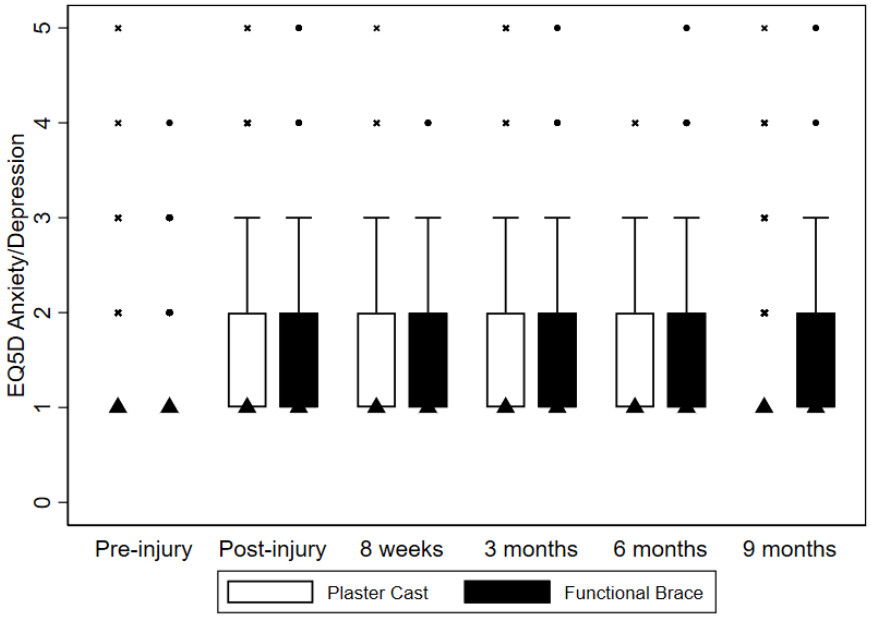

Figure 19: EQ-5D Anxiety Depression from baseline pre-injury to 9 months. EQ-5D Anxiety Depression values range from 1 to 5 with 1 indicating no problems

. This includes details on the total number of patients referred to the trauma clinic with an Achilles tendon rupture and those randomised. The availability of the primary outcome for analysis is also reported by intervention group as well as the total number excluded from the primary outcome analysis.

3.2 Recruitment

One thousand and seventy-six eligible participants were screened from July 2016 to May 2018 from 39 NHS hospitals in across England and Wales (

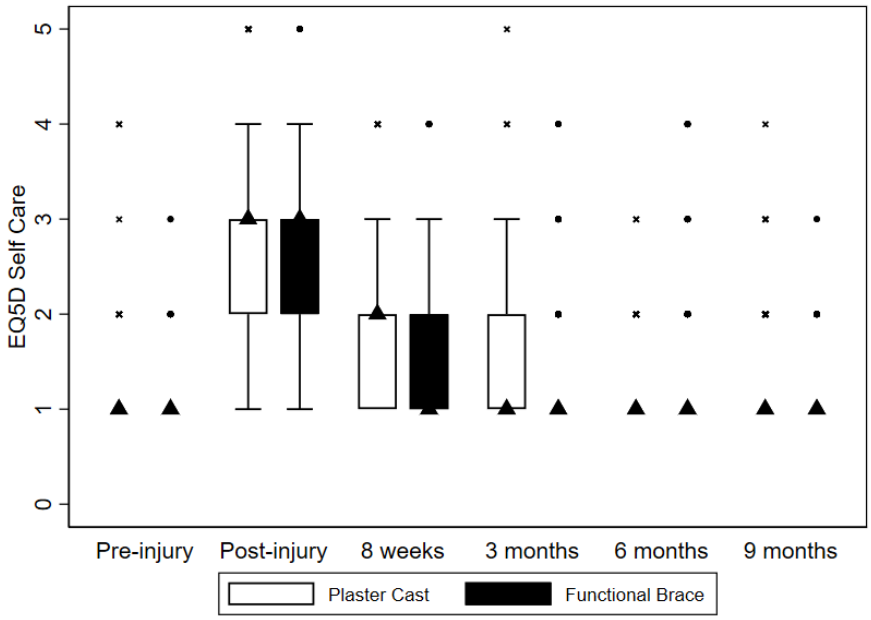

Figure 16: EQ-5D Self Care from baseline pre-injury to 9 months. EQ-5D Self Care values range from 1 to 5 with 1 indicating no problems

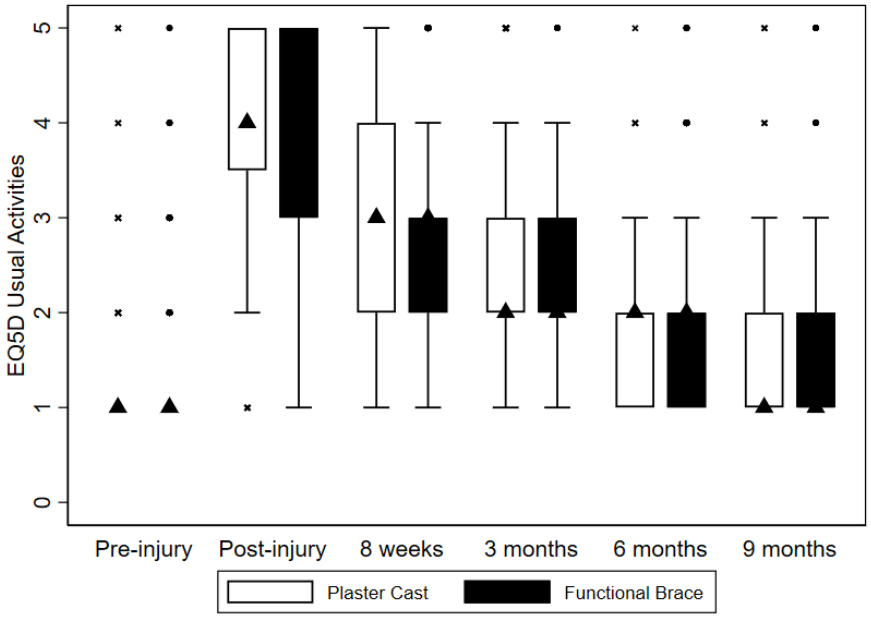

Figure 17: EQ-5D Usual Activities from baseline pre-injury to 9 months. EQ-5D Usual Activities values range from 1 to 5 with 1 indicating no problems

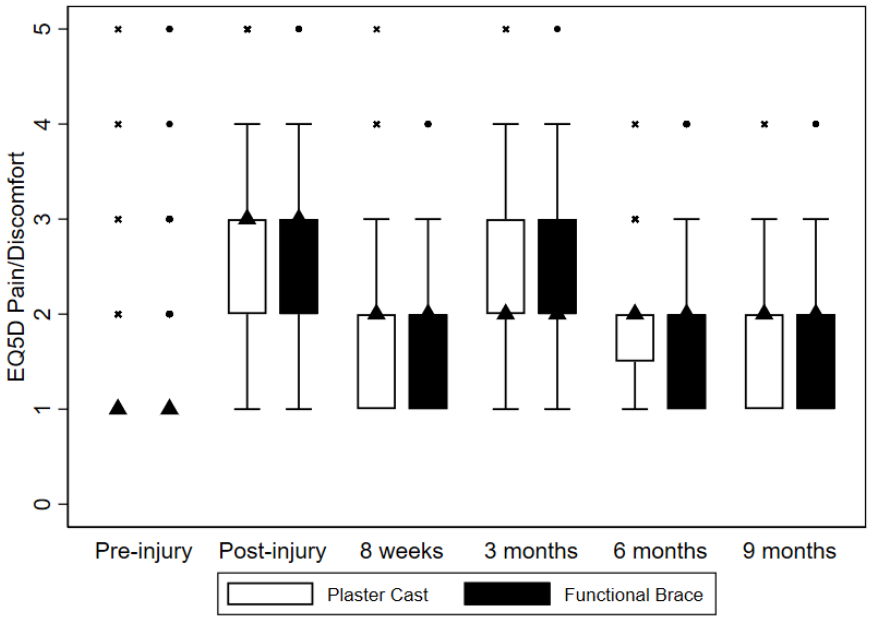

Figure 18: EQ-5D Pain Discomfort from baseline pre-injury to 9 months. EQ-5D Pain Discomfort values range from 1 to 5 with 1 indicating no problems

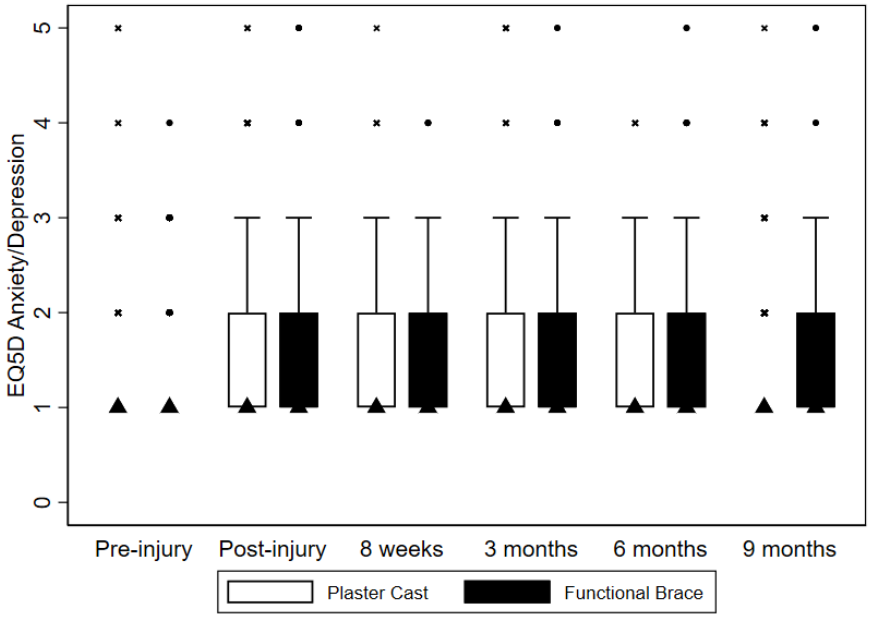

Figure 19: EQ-5D Anxiety Depression from baseline pre-injury to 9 months. EQ-5D Anxiety Depression values range from 1 to 5 with 1 indicating no problems

). Of these, five hundred and forty participants consented to taking part in the trial. Reasons why patients were not included in the trial are presented. Participants attended clinic visits at the time of randomisation (baseline) and at the 8-week follow-up. Participants were additionally contacted by the trial team via post, email or telephone to complete follow-up questionnaires at 3, 6 and 9 month post injury. Two participants were randomised in error before consenting and are therefore not included in the numbers allocated to each treatment group.

3.3 Baseline characteristics

The randomisation was stratified by centre and the allocation of participants to the intervention groups in each centre and the overall numbers is given in Table 4. The descriptive characteristics of the participants included in the ITT population are summarised by intervention group and overall in Table 5. These values are presented as numbers and percentages for categorical factors and means and SD or medians and IQR as appropriate for continuous variables. These variables all appear well balanced across the two treatment groups. The distribution of participant ages by gender at enrolment is shown in **Error! Reference source not found.** This distribution has a peak in male patients aged 30-40 years and in female patients aged 40-60 years. Baseline values of Patient Reported Outcomes Measures (PROMs);

ATRS and EQ-5D-5L) are summarised by intervention group in Table 6. ATRS, values range from 0 to 100 with lower scores indicating more functional limitations; EQ-5D utility scores range from -0.511 to 1 with higher scores indicating better quality of life, 0 is equivalent to death; EQ-5D VAS scores range from 0 to 100 with higher scores indicating better quality of life. The values reported are similar in the two treatment groups.

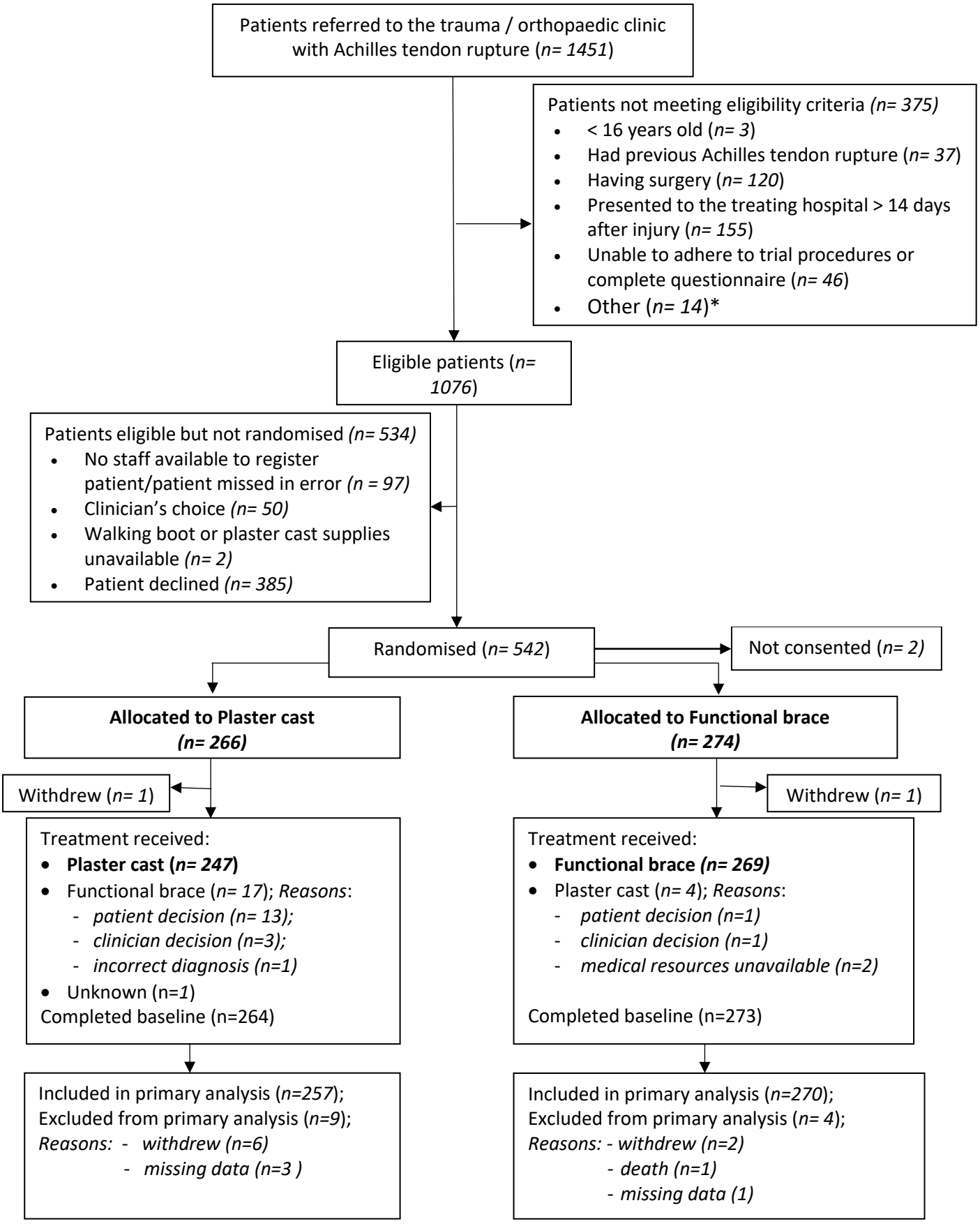

Figure 1: UKSTAR Consort Flow Diagram

Table 4: Stratification factor (recruitment centre) according to intervention group and overall

	Plaster Cast (n = 266)		**Functional Brace (n = 274)**		**Overall (n = 540)**	
	n	%	n	%	n	%
Trial centre [a]						
ABD	31	11.7%	33	12.0%	64	11.9%
AIR	11	4.1%	12	4.4%	23	4.3%
BRT	4	1.5%	4	1.5%	8	1.5%
CHX	1	0.4%	1	0.4%	2	0.4%
CUH	12	4.5%	14	5.1%	26	4.8%
DBH	7	2.6%	6	2.2%	13	2.4%
DUN	9	3.4%	10	3.6%	19	3.5%
ENH	17	6.4%	18	6.6%	35	6.5%
GEH	11	4.1%	12	4.4%	23	4.3%
GLA	3	1.1%	5	1.8%	8	1.5%
HCH	2	0.8%	3	1.1%	5	0.9%
HEY	3	1.1%	2	0.7%	5	0.9%
INV	6	2.3%	5	1.8%	11	2.0%
KCH	1	0.4%	0	0.0%	1	0.2%
LDH	4	1.5%	4	1.5%	8	1.5%
LDS	13	4.9%	14	5.1%	27	5.0%
MKN	12	4.5%	12	4.4%	24	4.4%
MPH	6	2.3%	6	2.2%	12	2.2%
MTW	6	2.3%	7	2.6%	13	2.4%
MYH	2	0.8%	1	0.4%	3	0.6%
NLG	5	1.9%	6	2.2%	11	2.0%
NTE	1	0.4%	3	1.1%	4	0.7%
NUH	9	3.4%	8	2.9%	17	3.1%
OUH	3	1.1%	3	1.1%	6	1.1%
PLY	10	3.8%	9	3.3%	19	3.5%
QEH	13	4.9%	12	4.4%	25	4.6%
RBK	4	1.5%	3	1.1%	7	1.3%

RCH	6	2.3%	6	2.2%	12	2.2%
RED	5	1.9%	5	1.8%	10	1.9%
RTH	5	1.9%	5	1.8%	10	1.9%
SAL	6	2.3%	7	2.6%	13	2.4%
SHC	5	1.9%	4	1.5%	9	1.7%
SLF	8	3.0%	7	2.6%	15	2.8%
UHS	6	2.3%	6	2.2%	12	2.2%
ULH	11	4.1%	10	3.6%	21	3.9%
WAR	1	0.4%	3	1.1%	4	0.7%
WHI	6	2.3%	6	2.2%	12	2.2%
WYT	1	0.4%	2	0.7%	3	0.6%

[a] See Appendix 2 for full NHS Trust Hospital name

Table 5: Descriptive characteristics of ITT population by treatment group at baseline. Values are n (%) for categorical variables, and mean (SD) or median (IQR) for continuous outcomes.

	Plaster Cast	**Functional Brace**	**Overall**
	(n = 264)	**(n = 274)**	**(n = 538)**
Gender, N (%)			
Male	213 (80.7%)	213 (77.7%)	426 (79.2%)
Female	51 (19.3%)	61 (22.3%)	112 (20.8%)
Age, mean (SD)	49.0 (13.9)	48.3 (13.8)	48.7 (13.8)
BMI, kg/m^2, mean (SD), N	27.5 (4.5), 255	27.8 (5), 265	27.7 (4.8), 520
Days since injury, median (IQR)	5.0 (2.5, 8)	5.0 (2, 8)	5.0 (2, 8)
Mechanism of injury, N (%)			
Fall from height	3 (1.2%)	8 (3%)	11 (2%)
Fall on steps/stairs	22 (8.4%)	14 (5.1%)	36 (6.7%)
Fall/trip from standing height	6 (2.4%)	11 (3.9%)	17 (3.2%)
Sports	187 (70.8%)	192 (70.2%)	379 (70.4%)
Walking	14 (5.4%)	28 (10.2%)	42 (7.8%)
Other	14 (5.4%)	6 (2.1%)	20 (3.7%)

Side of injury, N (%)			
Right	122 (46.2%)	138 (50.4%)	260 (48.3%)
Left	142 (53.7%)	136 (49.5%)	278 (51.7%)
Regular smoker, N (%)			
No	225 (85.2%)	234 (85.5%)	459 (85.2%)
Yes	39 (14.7%)	39 (14.1%)	78 (14.4%)
Missing	0 (0%)	1 (0.3%)	1 (0.2%)
Cigarettes (per day), median (IQR), N	10.0 (5, 15), 39	10.0 (5, 15), 39	10.0 (5, 15), 78
Smoking duration (years), median (IQR), N	20.0 (10, 25), 38	20.5 (13, 30), 38	20.0 (10, 30), 76
Alcohol units (per week), N (%)			
0-7 units	162 (61.5%)	161 (58.8%)	323 (60%)
8-14 units	49 (18.6%)	65 (23.7%)	114 (21.3%)
15-21 units	40 (15.3%)	35 (12.9%)	75 (13.8%)
>21 units	12 (4.5%)	10 (3.6%)	22 (4.2%)
Missing	1 (0.3%)	3 (1.2%)	4 (0.6%)
Taking the following medication, N (%)			
Fluoroquinolone Antibiotics	5 (1.9%)	4 (1.5%)	9 (1.7%)
Steroids	7 (2.7%)	14 (5.1%)	21 (3.9%)
DMARDs	2 (0.8%)	1 (0.4%)	3 (0.6%)
Diabetic Medication	5 (1.9%)	14 (5.1%)	19 (3.5%)
Regular Analgesia	23 (8.7%)	14 (5.1%)	37 (6.9%)
Anticoagulant Medication	66 (25%)	78 (28.5%)	144 (26.8%)
Diagnosis prior to injury, N (%)			
Diabetes	5 (1.9%)	18 (6.6%)	23 (4.3%)
Rheumatoid Arthritis	0 (0%)	3 (1.1%)	3 (0.6%)
Lower Limb Fracture (last 12 months)	1 (0.4%)	4 (1.5%)	5 (0.9%)
Ligament, tendon or nerve injury to lower limb (last 12 months)	5 (1.9%)	8 (2.9%)	13 (2.4%)
Arthritis	21 (8%)	21 (7.7%)	42 (7.8%)
Achilles tendinopathy	10 (3.8%)	10 (3.6%)	20 (3.7%)
Employment status			
Full-time employed	160 (60.6%)	168 (61.3%)	328 (61%)

Part-time employed	18 (6.8%)	15 (5.5%)	33 (6.1%)
Self-employed	39 (14.8%)	29 (10.6%)	68 (12.6%)
Retired/looking after home/inactive	35 (13.3%)	41 (15%)	76 (14.1%)
Unpaid work	1 (0.4%)	2 (0.7%)	3 (0.6%)
Unemployed	8 (3%)	8 (2.9%)	16 (3%)
Full time student	3 (1.1%)	9 (3.3%)	12 (2.2%)
Missing	0.0 (0%)	2.0 (0.7%)	2.0 (0.4%)
Employment category			
Unskilled manual	11 (4.2%)	11 (4%)	22 (4.1%)
Skilled manual	62 (23.5%)	64 (23.4%)	126 (23.4%)
Unskilled non-manual	6 (2.3%)	7 (2.6%)	13 (2.4%)
Skilled non-manual	29 (11%)	21 (7.7%)	50 (9.3%)
Professional	109 (41.3%)	108 (39.4%)	217 (40.3%)
Missing	0.0 (0%)	3.0 (1%)	3.0 (0.6%)

BMI: Body mass index; DMARDs: Disease-modifying antirheumatic drugs; SD: Standard deviation; IQR: Inter-quartile range.

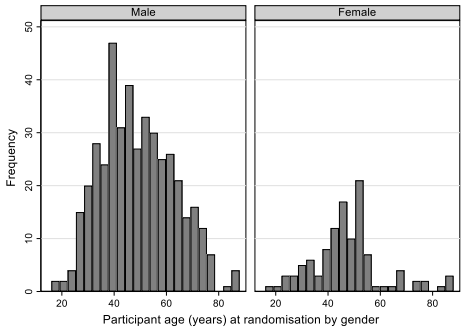

Figure 2: Participant age (years) at randomisation by gender

Table 6: PROMs by intervention group for ITT population at baseline. Values are median (IQR) unless otherwise specified.

	Plaster Cast (n = 264)	**Functional Brace (n = 274)**	**Overall (n = 538)**
ATRS pre injury	100 (96.5, 100), 264	100 (94, 100), 273	100 (96, 100), 537
EQ-5D VAS pre injury	90 (80, 95), 263	90 (80, 95), 273	90 (80, 95), 536
EQ-5D VAS post injury, mean (SD), N	57.6 (21.1), 262	58.3 (21.5), 273	58.0 (21.3), 535
EQ-5D Utility pre injury	1 (1, 1), 262	1 (1, 1), 273	1 (1, 1), 535
EQ-5D Utility post injury, mean (SD), N	0.2 (0.3), 262	0.3 (0.3), 273	0.3 (0.3), 535

PROM: patient reported outcome measure; IQR: inter-quartile range; ATRS = Achilles Tendon Rupture Score; VAS: Visual Analogue Scale ; SD: standard deviation

3.4 Compliance

Participants were considered compliant if they wore their allocated treatment following randomisation for a period of 6 weeks or more without any cross-over at baseline or treatment change within this period (

Table 7). The population compliant with treatment for 6 weeks or more was made up of 477 (88.2%) participants overall, 212 (79.7%) of whom were in the Plaster Cast group and 265 (96.7%) of whom were in the Functional Brace group. The number of patients compliant with treatment for 4 weeks or more and 2 weeks or more are also listed in

Table 7.

Table 7: Number of patients compliant to treatment

	Plaster Cast (n = 266)		Functional Brace (n = 274)	
	n	**%**	**n**	**%**
Compliance with treatment [a]				
6 weeks or more	212	79.7%	265	96.7%
4 weeks or more	223	83.8%	268	97.8%
2 weeks or more	240	90.2%	268	97.8%

[a] Compliance starts at randomisation. Each time point includes the period following the time point specified.

Details of the treatment intervention received following randomisation are listed in Table 8. There were 247 (92.9%) participants in the Plaster Cast group and 269 (98.2%) who received their allocated treatment immediately at baseline. Those who did not receive the allocated treatment at baseline, *received the opposite treatment* instead or *withdrew*. A further 35 participants (13.2%) in the Plaster Cast and 4 (1.5%) in the Functional Brace group changed from the treatment they were randomised to within the first six weeks and received the *opposite treatment* or *surgery* instead. The reasons why participants changed from their allocated treatment are listed in Table 9 and include *patient decision, clinician decision, medical resources unavailable, incorrect Achilles tendon rupture diagnosis, surgery or withdrawal.*

Table 8: Details of the intervention received by treatment group

	Plaster Cast (n = 266)		Functional Brace (n = 274)	
	n	%	n	%
Received allocated treatment at baseline	247	92.9%	269	98.2%
Changed treatment at baseline	19	7.1%	5	1.8%
Received opposite treatment	17	6.4%	4	1.5%
Withdrew	1	0.4%	1	0.4%
Unknown	1	0.4%	0	0.0%

Changed treatment within 6 weeks excluding changes at baseline	35	13.2%	4	1.5%
Received opposite treatment	30	11.3%	1	0.4%
Received surgery	5	1.9%	3	1.1%

Table 9: Reasons for changing allocated treatment in each intervention group

	Plaster Cast (n = 54)		**Functional Brace (n = 9)**	
	n	%	**n**	%
Reason for treatment change at baseline				
Patient requested	13	24.1%	1	11.1%
Clinician decision	3	5.6%	1	11.1%
Medical resource unavailable	0	0.0%	2	22.2%
Incorrect Achilles tendon rupture diagnosis	1	1.9%	0	0.0%
Withdrew	1	1.9%	1	11.1%
Unknown	1	1.9%	0	0.0%
Reason for treatment change within 6 weeks after baseline				
Patient requested	18	33.3%	1	11.1%
Clinician decision	12	22.2%	0	0.0%
Surgery	5	9.3%	3	33.3%

Details of the treatment received in each treatment group including time-point when the patient was allowed to fully bear weight, time-point when cast/brace was removed, number of cast changes, type of brace used, number of heel wedges and venous thromboembolism (VTE) prophylaxis are listed in Table 10**.** Data collected shows that the number of participants allowed to bear weight early was higher in the Functional Brace than in the Plaster Cast group. Proportions for these patients are described for each treatment group and are restricted to

patients who did not change from their allocated treatment in the first six weeks following randomisation.

There were no differences between the two treatment groups in the time-point when the plaster cast/functional brace was removed. On average, patients in the Plaster Cast group changed their plaster cast three times throughout the treatment period. The most frequently used functional brace make was Aircast (44.5%) and the median number of heel wedges was 3, although this varied from zero to five, depending on time-point. VTE prophylaxis was offered to more patients in the Plaster Cast group (187, 70.3%) than in the Functional Brace group (158, 57.7%). The type of VTE treatment used was Low Molecular Weight Heparin (LMWH) and oral anticoagulant in similar proportions across the two groups.

Table 10. Details of treatment received for each treatment group

	Plaster Cast (n = 266)		**Functional Brace (n = 274)**	
	n	**%**	**n**	**%**
Time point when patient is allowed to fully bear weight[a]				
Baseline	6	2.8%	121	45.7%
2 weeks	7	3.3%	24	9.1%
4 weeks	15	7.1%	26	9.8%
6 weeks	99	46.7%	30	11.3%
8 weeks or more	81	38.2%	57	21.5%
Unknown	0	0.0%	1	0.4%
Missing	4	1.9%	6	2.3%
Time point when brace/cast is removed				
Before 2 weeks	1	0.4%	1	0.4%
2 weeks	1	0.4%	2	0.7%
4 weeks	4	1.5%	1	0.4%
6 weeks	25	9.4%	10	3.6%
8 weeks	164	61.7%	167	60.9%
Still not removed	12	4.5%	76	27.7%
Number of plaster cast changes over 8 weeks[b]	3.0	(1, 6), 241	N/A	N/A

Functional brace make at baseline				
Donjoy	N/A	N/A	15	5.5%
Samson	N/A	N/A	10	3.6%
Aircast	N/A	N/A	122	44.5%
Ossur	N/A	N/A	64	23.4%
VACOped	N/A	N/A	25	9.1%
Promedics	N/A	N/A	23	8.4%
Not known	N/A	N/A	5	1.8%
Number of heel wedges in functional brace			Median	Range, N
Baseline	N/A	N/A	3.0	(0, 5), 263
2 weeks	N/A	N/A	3.0	(0, 4), 258
4 weeks	N/A	N/A	2.0	(0, 4), 258
6 weeks	N/A	N/A	1.0	(0, 4), 260
8 weeks	N/A	N/A	0.0	(0, 4), 258
VTE prophylaxis	187	70.3%	158	57.7%
VTE treatment				
Low Molecular Weight Heparin	148	79.1%	120	75.9%
Oral Anticoagulant	39	20.9%	38	24.1%
VTE treatment duration (weeks)[b]	8.0	(0, 12), 181	8.0	(1, 12), 156

[a] Not included are patients who changed their treatment in the first 6 weeks

[b] Median (Range), N

VTE: venous thromboembolism

3.5 Numbers analysed

The *ITT population* included all patients who were randomised and gave consent to participate in the trial. These patients were analysed in the groups they were allocated to and was used in the analysis of PROMs. Data for the two randomised participants who did not give their consent was excluded from the analysis. This population was made up of 540 participants overall, 266 of whom were in the Plaster Cast group and 274 of whom were in the Functional Brace group. Analyses of all primary and secondary outcomes were performed for this population.

The *CACE population* [37] included all randomised participants compliant with treatment for 6 weeks or more.

3.6 Withdrawals

Table 11 provides details on the available data at each follow-up time-point, including the number of CRFs and PROs, the number of participants who withdrew or died, according to treatment group. There was a good completion rate of CRFs and PROs across both treatment groups throughout the study period. In total 10 patients withdrew, 7 from Plaster Cast group and 3 from the Functional Brace group. There were 2 deaths, both in the Functional Brace group. Reasons for withdrawal are listed in

Table **12** and these include *clinician decision*, *patient decision* and *private treatment*.

Table 11: Details of available data at each follow-up time-point

	Plaster Cast (n = 266)		**Functional Brace (n = 274)**		**Total (n = 540)**	
	n	**%**	**n**	**%**	**n**	**%**
8 weeks						
CRF Completed	264	99.2%	273	99.6%	537	99.4%
PRO Completed	234	88.0%	241	88.0%	475	88.0%
Withdrawn[a]	6	2.3%	2	0.7%	8	1.5%
Died	0	0.0%	1	0.4%	1	0.2%
CRF Not Completed	1	0.4%	0	0.0%	1	0.2%
PRO Not Completed	26	9.8%	30	10.9%	56	10.4%
3 month						
PRO Completed	229	86.1%	245	89.4%	474	87.8%
Withdrawn[a]	7	2.6%	3	1.1%	10	1.9%
Died	0	0.0%	1	0.4%	1	0.2%
PRO Not Completed	30	11.3%	25	9.1%	55	10.2%
6 month						
PRO Completed	225	84.6%	238	86.9%	463	85.7%

Withdrawn[a]	7	2.6%	3	1.1%	10	1.9%
Died	0	0.0%	2	0.7%	2	0.4%
PRO Not Completed	34	12.8%	31	11.3%	65	12.0%
9 month						
PRO Completed	244	91.7%	260	94.9%	504	93.3%
Withdrawn[a]	7	2.6%	3	1.1%	10	1.9%
Died	0	0.0%	2	0.7%	2	0.4%
PRO Not Completed	15	5.6%	9	3.3%	24	4.4%

[a] Withdrawn participants and those who died are reported cumulatively and include the two participants who withdrew before receiving their treatment at baseline. See CONSORT flow diagram in

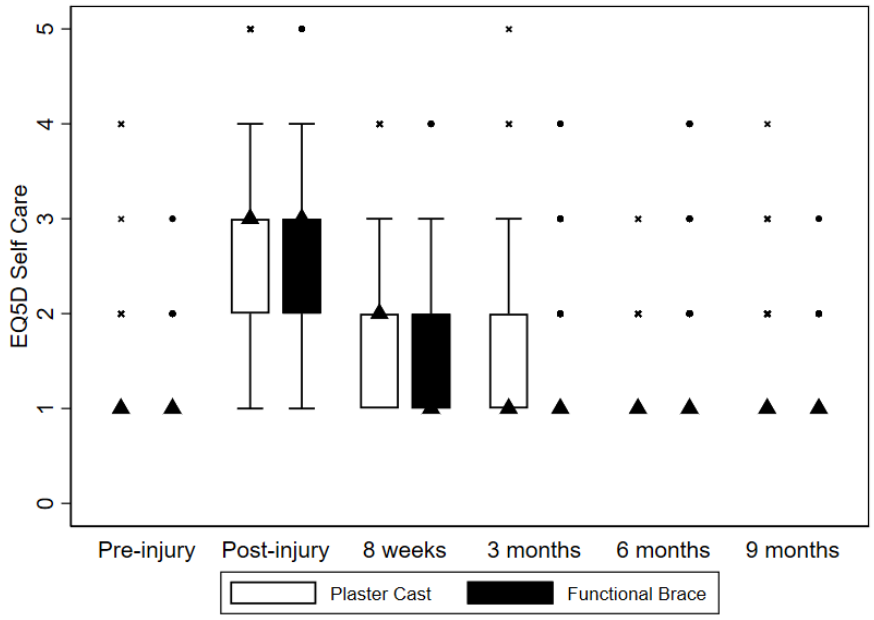

Figure 16: EQ-5D Self Care from baseline pre-injury to 9 months. EQ-5D Self Care values range from 1 to 5 with 1 indicating no problems

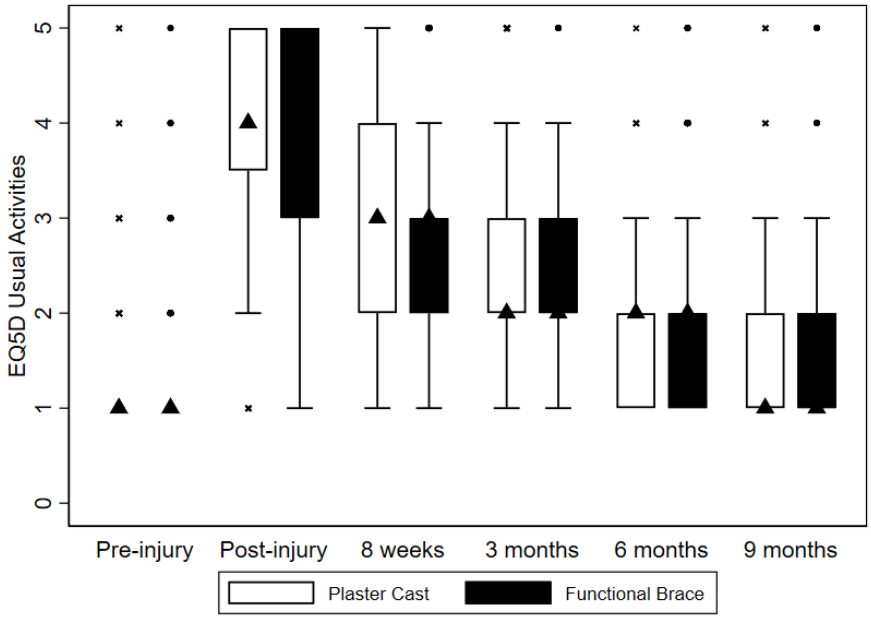

Figure 17: EQ-5D Usual Activities from baseline pre-injury to 9 months. EQ-5D Usual Activities values range from 1 to 5 with 1 indicating no problems

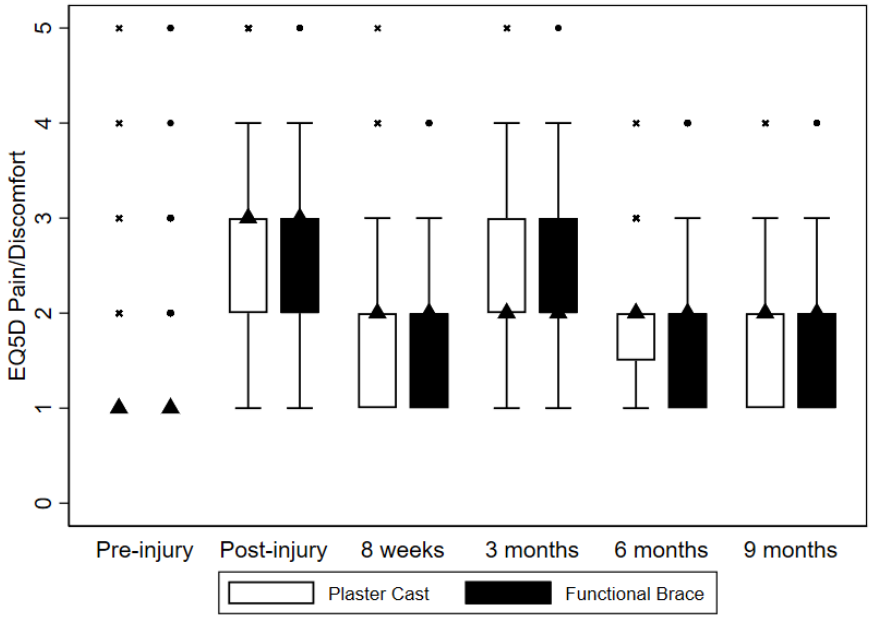

Figure 18: EQ-5D Pain Discomfort from baseline pre-injury to 9 months. EQ-5D Pain Discomfort values range from 1 to 5 with 1 indicating no problems

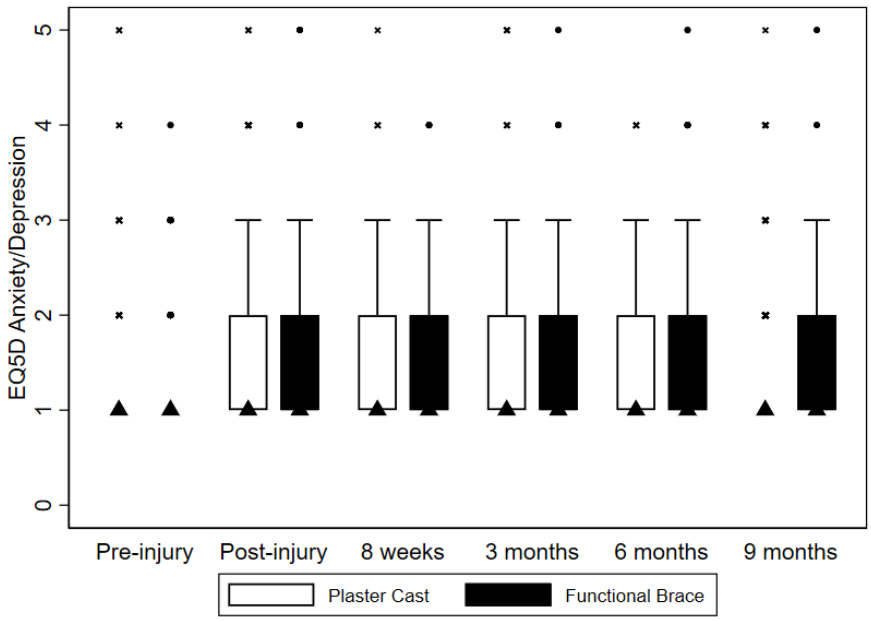

Figure 19: EQ-5D Anxiety Depression from baseline pre-injury to 9 months. EQ-5D Anxiety Depression values range from 1 to 5 with 1 indicating no problems

.

CRF: case report form; PRO: patient reported outcome

Table 12: Number of withdrawals and reasons for withdrawal at follow-up time-points[a].

	Plaster Cast (n = 266)		Functional Brace (n = 274)		Total (n = 540)	
	n	%	n	%	n	%
8 weeks						
Withdrawn	6	2.3%	2	0.7%	8	1.5%
Withdrawal Reason						
Clinician decision	1	0.4%	0	0.0%	1	0.2%
Patient decision	4	1.5%	1	0.4%	5	0.9%
Private treatment	1	0.4%	1	0.4%	2	0.4%
3 month						
Withdrawn	1	0.4%	1	0.4%	2	0.4%
Withdrawal Reason						
Patient decision	0	0.0%	1	0.4%	1	0.2%

Private treatment	1	0.4%	0	0.0%	1	0.2%

[a] Percentages are calculated out of total withdrawals.

3.7 Analyses to address primary aims

The primary outcome in this study is the ATRS measured at 9 months post injury as described in the Statistical Analysis Plan.

ATRS was assessed at baseline (pre-injury), 8 weeks, 3 months, 6 months and 9 months after the tendon rupture. The mean ATRS score and SD for each treatment group at each time-point is provided in Table 13. The mean ATRS differences between the two treatment groups was estimated based on a linear mixed effects regression model both unadjusted and adjusted for the stratification factor recruitment centre, age, gender and baseline ATRS. The adjusted analysis was pre-specified as the principal analysis of the trial results.

The adjusted analysis showed no statistically significant difference in ATRS between the two treatment groups at 9 months (-1.38; 95% CI -4.9 to 2.1). The 8-week follow up results show a statistically significant difference in the ATRS in favor of the Functional Brace group (5.75; 95% CI 2.2 to 9.3), however this effect fades during the 9-month follow up. The ATRS adjusted mean difference between the two treatment groups is presented across time from the 8-week to the 9-month follow-up in **Error! Reference source not found.**.

Supplementary fully adjusted analyses were carried out accounting for further pre-defined prognostic variables and included recruitment centre, age, gender, baseline ATRS, diabetes and smoking status and are included in Table 14. These results showed a similar between-group difference compared to the primary analysis at 9 month post injury (-1.15; 95% CI -4.7 to 2.4).

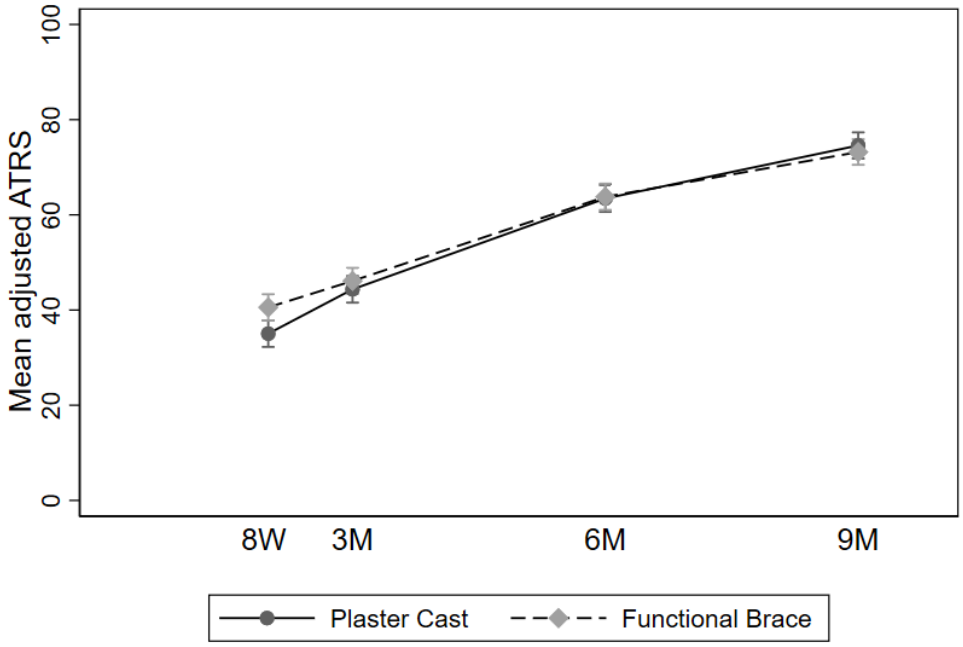

Figure 3: ATRS adjusted mean difference between treatment groups pre-injury to 9 months post injury. ATRS range from 0 to 100 with higher scores indicating better outcome

Table 13: ATRS analysis at each time-point (ITT population)

	Plaster Cast		Functional Brace		Between - Group Difference (95% CI)		
	Mean (SD)	**n**	**Mean (SD)**	**n**	**Unadjusted**	**Adjusted[b]**	**p-value**
Baseline	100.0 (96.5, 100)[a]	264	100.0 (94, 100)[a]	273			
8 week	35.3 (20.1)	234	40.3 (17.8)	240	4.98 (1.3, 8.7)	5.53 (2, 9.1)	0.002
3 month	44.4 (21.1)	229	45.6 (20.4)	244	1.23 (-2.5, 4.9)	1.76 (-1.8, 5.3)	0.335
6 month	63.9 (21.4)	224	63.5 (23)	235	-0.44 (-4.2, 3.3)	0.35 (-3.3, 4)	0.850
9 month	74.4 (19.8)	244	72.8 (20.4)	259	-1.65 (-5.2, 1.9)	-1.38 (-4.9, 2.1)	0.439

[a] Median and Interquartile Range

[b] Achilles Tendon Rupture Score (ATRS) analysis adjusted for recruitment centre, age, gender and baseline ATRS

CI: Confidence Interval; SD: standard deviation

Sensitivity Analyses

Complier Average Causal Effect Analysis

Sensitivity analyses were conducted to explore the definition of compliance with treatment and to assess whether the primary analysis results were robust. Adherence to allocated treatment can affect the interpretation of the impact of what was offered to patients. This may be a particular issue in an ITT analysis as this includes all patients as they were expected to be treated and does not account for whether patients received or adhered to the intervention allocated to them.

The number of participants compliant with the allocated treatment for the different periods from 6 weeks or more, 4 weeks or more and 2 weeks or more was shown in

Table 7 in Section 0. A CACE analysis was conducted to estimate the mean effect of treatment in compliers with treatment for 6 weeks or more (265, 96.7% in the Functional Brace group). The number of participants compliant with treatment for 4 weeks or more and 2 weeks or more were identical in the Functional Brace group (268, 97.8%) and hence CACE analysis was only conducted including patients compliant for 4 weeks or more.

We estimated the CACE using the *xtivreg* and *xtset* commands in Stata software. The unadjusted and the adjusted analyses estimating the ITT effect and the CACE analysis effect are shown in Table 14. The unadjusted CACE estimate was marginally greater in modulus compared to the ITT (-1.70, 95% CI -5.3, 1.9), but this difference was small given the ATRS scoring scale. The adjusted CACE analysis showed similar results to the ITT population analysis (-1.17, 95% CI -4.5 to 2.1).

Area Under the Curve

A further analysis of the ATRS was conducted in order to explore recovery in the two treatment groups over time. This analysis shows a summary of the longitudinal data collected at all four time-points to a single value, the AUC. [39] Parameter estimates from the mixed effects models were used to calculate AUC from 8 week to the 9-month follow-up for a male participant of mean age (48.65 years). Results showing an overall estimate of recovery over time and a t-test comparison of the two treatment groups is presented in Table 14. Higher AUCs indicate better overall functionality. Functional Brace group shows a better overall functionality than the Plaster Cast group, however the difference (-5.26; 95% CI -24.66 to 14.14) was not statistically significant.

Table 14: ATRS supplementary analyses

Analysis (population)	**Time point**	**Between - Group Difference (95% CI)**	**p-value**
Unadjusted (ITT)[b]	9 month	-1.65 (-5.2, 1.9)	0.367
Adjusted (ITT) [c]	9 month	-1.38 (-4.9, 2.1)	0.439
Fully adjusted (ITT) [d]	9 month	-1.15 (-4.7, 2.4)	0.520
Unadjusted (CACE) [b]	9 month	-1.70 (-5.3, 1.9)	0.349
Adjusted (CACE) [c]	9 month	-1.18 (-4.5, 2.1)	0.486
AUC adjusted (ITT) [c]	8 week to 9 month	-5.26 (-24.66, 14.14)	0.595

[b] Based on a mixed effects model analysis

[c] Based on a mixed effects model adjusted for site, age, gender and baseline ATRS

[d] Based on a mixed effects model adjusted for site, age, gender, baseline ATRS, diabetes and smoking status

CI: confidence interval; CACE: Complier Average Causal Effect; AUC = Area Under the Curve; ITT: Intention-To-Treat

Pre-specified subgroup analysis

There were no pre-specified subgroups and therefore no subgroup analyses were conducted.

3.8 Analyses to address secondary outcomes

The secondary outcomes collected and analysed in the UKSTAR trial were EQ-5D-5L and complications evaluated at 8 weeks, 3, 6 and 9 months after the injury.

EQ-5D-5L

EQ-5D-5L was analysed as a continuous outcome using the utility score values from the 5-level questions and based on the reported EQ VAS. Summary results for the EQ-5D utility score are reported in the Health Economics 4.1.3 and EQ-5D VAS are reported for each intervention group at each time point in Table 15 together with the unadjusted and adjusted mixed effects model estimates**.** The analysis for both EQ-5D utility score and EQ-5D VAS was adjusted for recruitment centre, age, gender and baseline EQ-5D pre-injury value and is presented graphically in

Figure **4** and

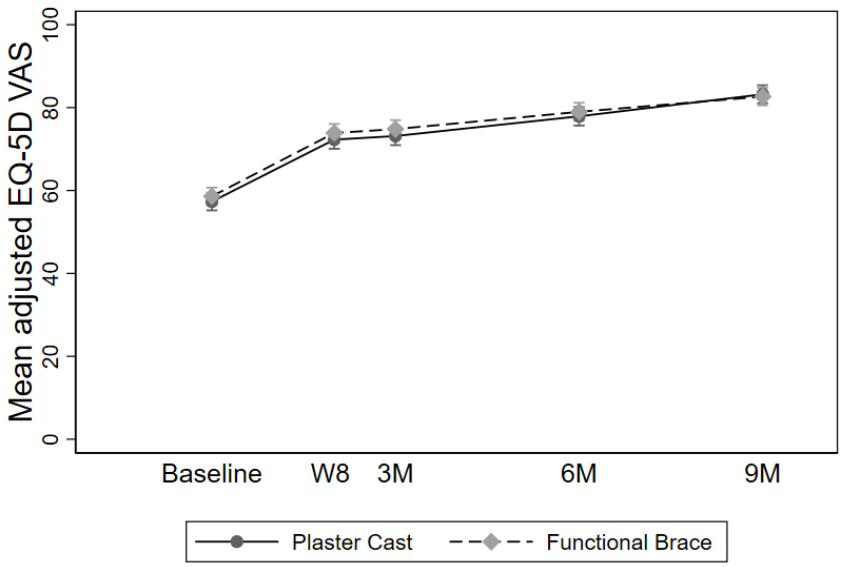

Figure 5. Both EQ-5D scores present a trend of improvement over time. The EQ-5D utility score analysis showed a statistically significant difference between the two treatment groups at the 8-week follow-up in favour of the Functional Brace group (0.069; 95% CI 0.03 to 0.1) but this difference was no longer present by the 9-month post injury follow-up.

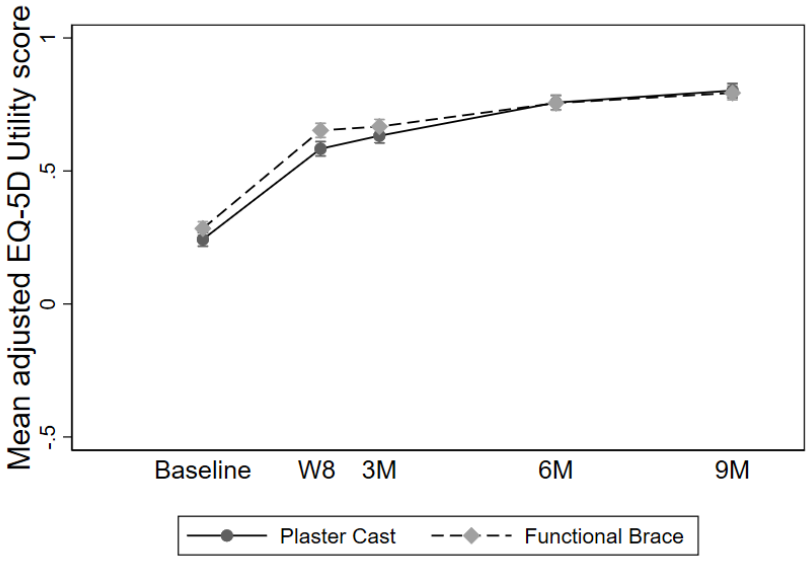

Figure 4: EQ-5D utility adjusted difference between treatment groups post injury baseline to 9 months.

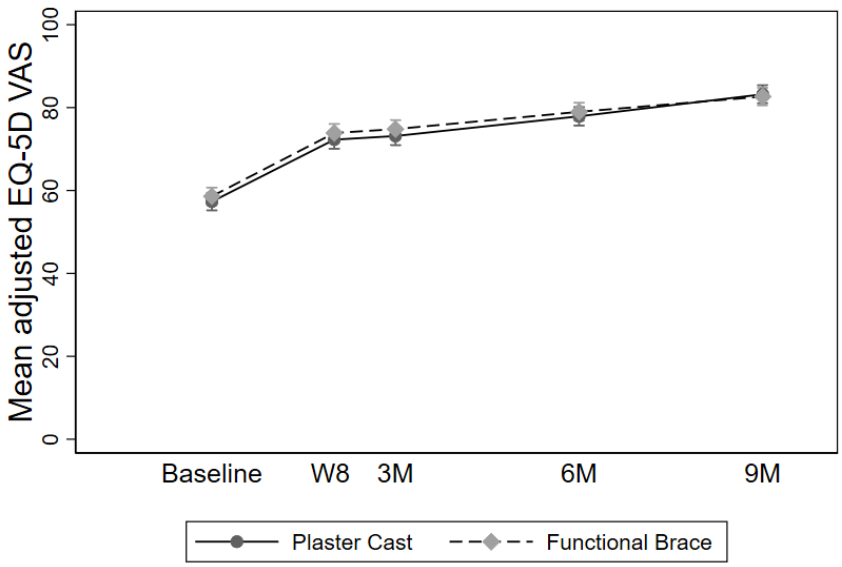

Figure 5: EQ-5D VAS adjusted difference between treatment groups post injury baseline to 9 months post injury.

Table 15: EQ-5D Utility and VAS results at 8, 3, 6 and 9 months post injury (ITT population)

	Plaster Cast (n = 266)		Functional Brace (n = 274)		Between - Group Difference (95% CI)		
	Mean (SD)	**n**	**Mean (SD)**	**n**	**Unadjusted**	**Adjusted[b]**	**p-value**
EQ-5D VAS[c]							
Baseline post injury	90.0 (80, 95)[a]	263	90.0 (80, 95)[a]	273	0.77 (-2.18, 3.72)	1.28 (-1.4, 3.97)	0.349
8 week	75.0 (60, 85)[a]	234	75.0 (65, 85)[a]	240	1.08 (-2.05, 4.2)	1.61 (-1.21, 4.43)	0.264
3 month	80.0 (65, 85)[a]	229	80.0 (65, 90)[a]	245	1.29 (-1.84, 4.42)	1.66 (-1.16, 4.48)	0.249
6 month	81.5 (70, 90)[a]	224	80.0 (70, 90)[a]	236	0.49 (-2.69, 3.66)	1.08 (-1.77, 3.93)	0.458
9 month	86.0 (80, 92)[a]	242	85.0 (75, 91)[a]	259	-0.76 (-3.8, 2.28)	-0.56 (-3.32, 2.2)	0.693

[a]Median (Interquartile Range); [b]Analysis adjusted for site, age, gender and EQ-5D baseline pre-injury equivalent

VAS: Visual Analogue Scale; CI: Confidence Interval; SD: standard deviation

Sensitivity analyses

Sensitivity analyses were performed for the EQ-5D utility and VAS outcomes using CACE analysis and the AUC (**Error! Reference source not found.**). CACE was conducted using a similar approach as for the primary outcome ATRS and showed similar results to the EQ-5D ITT population analysis. The AUC summary statistics were estimated for a male participant of mean age (48.65 years) calculated from baseline post injury to the 9 months post injury, with higher AUCs indicating better quality of life.

Table 16: EQ-5D-5L sensitivity analyses

Analysis (population)	Time point	Between - Group Difference (95% CI)	p-value
EQ-5D Utility			
Adjusted (ITT) [a]	9 month	-0.009 (-0.04, 0.03)	0.623
Adjusted (CACE) [a]	9 month	-0.008 (-0.03, 0.02)	0.502
AUC adjusted (ITT) [a]	8 week to 9 month	-0.20 (-0.4, 0.01)	0.056
EQ-5D VAS			
Adjusted (ITT) [a]	9 month	-0.56 (-3.3, 2.2)	0.693
Adjusted (CACE) [a]	9 month	-0.53 (-2.7, 1.7)	0.637
AUC adjusted (ITT) [a b]	8 week to 9 month	-9.42 (-26.9, 8.1)	0.292

[a] Based on a mixed effects model adjusted for site, age, gender and baseline ATRS

[b] AUC: Area Under the Curve, higher AUC indicates better overall quality of life

CACE: Complier Average Causal Effect; CI: Confidence Interval; ITT: Intention-To-Treat; VAS: visual analogue scale

3.9 Complications

Complications were recorded from medical notes at the 8-week review and were patient-reported at the 3-, 6- and 9-month follow up. The predefined complication categories were *tendon re-rupture, DVT, PE, non-injurious falls, injurious falls, pain under the heel, numbness around the foot, pressure sores* and additionally three categories were created based on the recorded text and included *skin condition requiring medication, surgery related to Achilles rupture* and *fractured toe.*

The rate of individual complications and the number of participants with one or more complications in each treatment group is presented overall from baseline to 9 months in Table 17 and at every time point for the ITT population in Table 18. Fisher's exact and chi-squared tests showed no statistically significant results when testing for associations between the treatment groups and each type of complication across time.

Table 17: Analysis of secondary outcome complications from baseline to 9 months (ITT population)[a]

	Plaster Cast (n = 266)		**Functional Brace (n = 274)**		
	n	**%**	**n**	**%**	**p-value**
Tendon re-rupture	17	6.4%	13	4.7%	0.404
Deep Vein Thrombosis	3	1.1%	6	2.2%	0.505
Pulmonary Embolism	0	0.0%	2	0.7%	0.499
Fall - no injury	60	22.6%	53	19.3%	0.359
Fall - injury sustained	21	7.9%	24	8.8%	0.716
Pain under the heel	158	59.4%	180	65.7%	0.131
Numbness around the foot	108	40.6%	130	47.4%	0.109
Pressure sores	39	14.7%	51	18.6%	0.218

[a] Numbers shown are complications reported at least once per participant

Table 18: Complications recorded at the 8-week, 3-, 6- and 9-month follow-up (ITT population)

	Plaster Cast (n = 266)		**Functional Brace (n = 274)**	
	n	**%**	**n**	**%**
8 weeks				

Tendon re-rupture	3	1.1%	3	1.1%
Deep Vein Thrombosis	2	0.8%	6	2.2%
Pulmonary Embolism	0	0.0%	2	0.7%
Fall - no injury	26	9.8%	12	4.4%
Fall - injury	3	1.1%	6	2.2%
Pain under the heel	33	12.4%	48	17.5%
Numbness around the foot	24	9.0%	32	11.7%
Pressure sores	9	3.4%	9	3.3%
Skin condition requiring medication	0	0.0%	4	1.5%
Surgery related to Achilles rupture	0	0.0%	3	1.1%
Fractured toe	1	0.4%	0	0.0%
3 month				
Tendon re-rupture	8	3.0%	4	1.5%
Deep Vein Thrombosis	2	0.8%	1	0.4%
Pulmonary Embolism	0	0.0%	2	0.7%
Fall	20	7.5%	15	5.5%
Fall - injury	7	2.6%	9	3.3%
Pain under the heel	125	47.0%	137	50.0%
Numbness around the foot	59	22.2%	79	28.8%
Pressure sores	23	8.6%	35	12.8%
6 month				
Tendon re-rupture	6	2.3%	6	2.2%
Deep Vein Thrombosis	0	0.0%	0	0.0%
Pulmonary Embolism	0	0.0%	2	0.7%

Fall	19	7.1%	23	8.4%
Fall - injury	6	2.3%	11	4.0%
Pain under the heel	78	29.3%	82	29.9%
Numbness around the foot	54	20.3%	66	24.1%
Pressure sores	9	3.4%	15	5.5%
9 month				
Tendon re-rupture	0	0.0%	0	0.0%
Deep Vein Thrombosis	0	0.0%	0	0.0%
Pulmonary Embolism	0	0.0%	0	0.0%
Fall	16	6.0%	11	4.0%
Fall - injury	10	3.8%	5	1.8%
Pain under the heel	48	18.0%	66	24.1%
Numbness around the foot	51	19.2%	50	18.2%
Pressure sores	2	0.8%	8	2.9%

3.10 Ancillary analyses

Following a presentation of the preliminary results, the Trial Steering Committee wished to explore where the apparent differences at 8 weeks in EQ-5D utility score came from. The individual domains in EQ-5D were explored using box-plots in Figure 15: EQ-5D Mobility from baseline pre-injury to 9 months. EQ-5D Mobility values range from 1 to 5 with 1 indicating no problems

to Figure 19: EQ-5D Anxiety Depression from baseline pre-injury to 9 months. EQ-5D Anxiety Depression values range from 1 to 5 with 1 indicating no problems

as part of Appendix 3. The median score is marked with a triangle, whiskers are interquartile ranges and the individual dots and crosses mark the outliers. The differences at 8 weeks appear to lie in the *ability to self-care* and *usual activities* only.

3.11 Adverse Events

Foreseeable Adverse Events (AEs) were reported as complications in **Section 3.8.**

Two deaths were reported in this study, one of which was a SAE. The SAE was due to a known lung cancer condition and was unrelated to the Achilles injury. The second death was due to a cardiac arrest following a bilateral PE and as judged by the investigators, was potentially related but not unexpected. Both deaths were reported for participants in the Functional Brace group.

4. Health Economics

This section presents the results for the health economic analyses comparing plaster cast to functional bracing. We compare: (i) missing data by treatment group; (ii) resource use and economic costs for different health and social care categories; (iii) distribution of the responses to the EQ-5D-5L questionnaires and EQ-5D-5L utility scores and; (iv) cost-effectiveness results for the base-case and sensitivity analyses.

4.1 Results of economic analysis

Table 19 shows the degree of missing health economic data by treatment allocation and follow-up time point. The missing data pattern is non-monotonic, as individuals with missing data at one follow-up time point may return to the trial subsequently. For example, there are more missing EQ-5D data at 6 months than at 9 months post injury. A similar pattern can be observed for economic costs. It is worth noting that the lower number of participants with complete data for the entire duration of follow-up (baseline to 9 months post-injury) was due to a strict application of the term missing i.e. we considered a participant as having incomplete data if, for example, they responded positively to vising a GP surgery at 3 months but did not specify number of consultations, despite all other resource use items being completed. However, for the cost-effectiveness analysis, imputation was not done at the aggregate level such that most of the data used for the analysis was based on actual participant responses.

Table 19: Number and proportion of individuals with missing health economic data by treatment allocation

Variable	**Description**	**Treatment group, missing values, *n* (%)**		**Total, missing values, *n (%)***
		Plaster cast (n=266)	**Functional brace (n = 274)**	
eq5db	EQ-5D index score pre injury	2 (0.75)	2 (0.73)	4 (0.74)
eq5d0	EQ-5D index score post injury	2 (0.75)	1 (0.36)	3 (0.56)
eq5d1	EQ-5D at 8 weeks	32 (12.06)	33 (12.04)	65 (12.04)
eq5d2	EQ-5D at 3 months	37 (13.91)	29 (10.58)	66 (12.22)
eq5d3	EQ-5D at 6 months	42 (15.79)	37 (13.5)	79 (14.63)
eq5d4	EQ-5D at 9 months	22 (26)	15 (5.47)	37 (8.27)
QALY	QALYs generated from EQ-5D utility scores	76 (28.57)	74 (27.01)	149 (27.78)

c0	Total resource use between baseline and 8 weeks post injury	66 (24.8)	59 (21.53)	125 (23.15)
c1	Total resource use between 8 weeks and 3 months post injury	59 (22.18)	47 (17.15)	106 (19.63)
c2	Total resource use between 3 and 6 months post injury	56 (21.05)	48 (8.89)	104 (19.26)
c3	Total resource use between 6 and 9 months post injury	31 (11.65)	18 (6.57)	49 (9.07)
c4	Total resource use between baseline and 9 months post injury	132 (49.62)	116 (42.34)	248 (45.93)

QALY: quality adjusted life-year

4.1.1 Health and social care resource use

Table 28 (Appendix 4) shows resource use values for participants by trial group allocation, resource use category and follow-up period for complete cases. The resource values are presented for subcategories of resource use, including hospital inpatient and outpatient care, community health and social care, prescribed medications, equipment and aids, and productivity losses.

In terms of specific resource use for plaster cast versus functional brace for all participants at the 8 week follow-up (Table 28, Appendix 4), notable differences were observed for: proportion prescribed anticoagulant as VTE prophylaxis treatment (0.72 vs 0.59; p=0.003), mean number of NHS outpatient orthopaedic visits (2.63 vs 1.80; p<0.001), mean number of NHS outpatient physiotherapy visits (0.23 vs 0.46; p=0.003), mean number of GP surgery visits (0.10 vs 0.19; p=0.028), and mean number of grab rail installations (0.05 vs 0; p=0.019). For all other resource use items, there were no noticeable differences between the trial groups.

Between 8 week and 3 months post injury, for all participants (Table 28, Appendix 4) there were differences in resource use for plaster cast versus functional brace observed for: proportion of participants prescribed analgesics (0.11 vs 0.05; p=0.015) and proportion of participants prescribed other medications (0.02 vs 0; p=0.038). For all other resource use items, there were no noticeable differences between the trial groups.

There were no significant differences in resource use for the Plaster Cast versus Functional Brace trial groups at 6 months and 9 months post injury.

4.1.2 Economic costs

Table 20 summarises the total NHS and PSS costs associated with resource use during the trial period among complete cases, by cost category and follow-up period. The mean direct intervention costs were £35.71 for the Plaster Cast group compared with £108.64 for the Functional Brace group; the mean difference of £72.93 was statistically significant at the 5% level. The mean total NHS and PSS costs were significantly lower in the Functional Brace group between randomisation and 8-week post injury and between 8 weeks and 3 months post injury with mean between-group cost differences of £107.73 and £92.95, respectively. The mean total NHS and PSS cost throughout the entire follow-up period was £1182.64 for the Plaster Cast group and £1018.26 for the Functional Brace group; the mean between-group cost difference of £164.39 was not statistically significant at the 5% level.

Table 20: NHS and personal social services costs for cases with complete resource use data by trial allocation, study period and cost category (£, 2017-18 prices)

Cost category by period	**Treatment group, mean (SE) Cost**		**Mean difference**	**p-value[a]**	**Bootstrap 95% CI[b]**
	Plaster Cast	**Functional Brace**			
Baseline to 8 weeks post injury – direct intervention costs[c] (total , n = 497: Plaster Cast group; n = 256; Functional Brace group, n =256)					
Total direct intervention costs	35.71 (0.492)	108.64 (3.114)	-72.93	<0.0001	-79.22 to (-66.64)
Baseline to 8 weeks post injury – NHS PSS resource use (total , *n* = 432: Plaster cast group; *n* = 210; Functional brace group, *n* =222)					
Inpatient care	55.8 (28.382)	39.3 (22.163)	16.51	0.647	(-53.48 to 86.49)
Outpatient care	370.2 (15.114)	282.6 (15.078)	87.59	<0.0001	45.97 to 129.21)
Community care	9.66 (2.521)	28.94 (14.493)	-19.28	0.191	(-47.64 to 9.07)
Medications	151.35 (9.334)	106.45 (8.701)	44.9	0	20.34 to 69)
Aids and adaptations	9.51 (0.842)	7.32 (0.568)	2.19	0.032	(0.20 to 4.19)
PSS	0.15 (0.151)	0 (0)	0.15	0.318	(-0.45 to 0.14)
Total NHS and PSS cost	596.67 (36.596)	464.61 (32.946)	-132.06	0.008	(-230.78 to -33.35)
Total Costs throughout first 8 weeks (including direct intervention costs)[d]	***647.88 (37.99)***	***540.15 (26.10)***	***107.73***	***0.02***	***(-199.31 to -16.15)***

Cost category by period	Treatment group, mean (SE) Cost		Mean difference	p-value[a]	Bootstrap 95% CI[b]
	Plaster Cast	Functional Brace			
8 weeks – 3months post injury (total , n = 434: Plaster Cast group; n = 207; Functional Brace group, n =227)					
Inpatient care	61.69 (27.278)	4.74 (4.74)	56.95	0.041	(4.33 to 109.57)
Outpatient care	118.74 (9.948)	98.76 (7.608)	19.98	0.111	(-5.07 to 45.03)
Community care	31.96 (15.86)	19.89 (4.77)	12.07	0.339	(-20.69 to 44.83)
Medications	5.95 (3.359)	2.86 (2.133)	3.1	0.437	(-4.56 to 10.75)
Aids and adaptations	1.65 (0.359)	0.75 (0.261)	0.9	0.044	(0.014 to 1.78)
PSS	0 (0)	0.04 (0.04)	-0.04	0.318	(-0.12 to 0.039)
Total NHS and PSS cost	**220.00 (36.662)**	**127.04 (12.333)**	**92.95**	**0.017**	**(14.80 to 171.11)**
3 – 6 months post injury (total , n = 436: Plaster Cast group; n = 210; Functional Brace group, n =226)					
Inpatient care	21.08 (16.736)	43.94 (22.392)	-22.86	0.414	(-80.61 to 34.90)
Outpatient care	128.56 (11.731)	142.56 (13.215)	-14	0.429	(-47.66 to 19.67)
Community care	33.56 (2.617)	27.75 (5.679)	5.812	0.376	(-19.98 to 31.60)
Medications	0 (0)	1.51 (1.015)	-1.51	0.138	(-3.56 to 0.54)
Aids and adaptations	1.02 (0.472)	1.03 (0.534)	-0.01	0.989	(-1.38 to 1.36)
PSS	0.49 (0.491)	0 (0)	0.49	0.318	(-0.42 to 1.40)
Total NHS and PSS cost	**184.70 (26.350)**	**216.78 (29.988)**	**-32.07**	**0.422**	**(-108.74 to 44.58)**
6 – 9 months post injury (total , n = 491: Plaster Cast group; n = 235; Functional Brace group, n =256)					
Inpatient care	5.94 (4.771)	45.45 (45.45)	-39.51	0.388	(-133.06 to 54.05)
Outpatient care	76.44 (22.253)	65.98 (9.884)	10.46	0.668	(-39.34 to 60.26)
Community care	14.03 (4.022)	17.302 (7.197)	-3.27	0.691	(-19.78 to 13.24)
Medications	0.33 (0.228)	0.13 (0.058)	0.2	0.396	(-0.26 to 0.66)
Aids and adaptations	0.36 (0.217)	0.08 (0.052)	0.28	0.214	(-0.15 to 0.71)
PSS	0.11 (0.11)	0 (0)	0.11	0.318	(-0.10 to 0.32)
Total NHS and PSS cost	**97.21 (23.666)**	**128.94 (46.80)**	**-31.73**	**0.543**	**(-127.40 to 63.94)**
0 – 9 months post injury (total , n = 292: Plaster Cast group; n = 134; Functional Brace group, n =158)					

Cost category by period	Treatment group, mean (SE) Cost		Mean difference	p-value[a]	Bootstrap 95% CI[b]
	Plaster Cast	Functional Brace			
Total direct intervention costs	35.96 (0.646)	106.46 (4.08)	-70.5		(-78.30 to -62.69)
Inpatient care	162.29 (85.042)	45.43 (24.373)	116.86	0.188	(-62.66 to 296.38)
Outpatient care	722.78 (39.326)	653.42 (40.288)	69.36	0.219	(-38.61 to 177.33)
Community care	103.22 (33.32)	91.18 (22.809)	12.04	0.766	(-67.72 to 91.80)
Medications	146.41 (11.364)	112.61 (10.884)	33.8	0.033	(-2.66 to 64.94)
Aids and adaptations	11.75 (1.331)	9.16 (1.127)	2.59	0.139	(-0.71 to 5.88)
PSS	0.24 (0.236)	0 (0)	0.24	0.319	(-0.22 to 0.70)
Total NHS and PSS costs throughout first 9 months	**1182.64 (114.696)**	**1018.26 (58.143)**	**164.39**	**0.203**	**(-95.75 to 424.52)**

[a] *p*-value calculated using the student's t-test, two-tail unequal variance

[b] Non-parametric bootstrap estimation suing 1000 replications

[c] Time horizon for calculating total direct intervention costs was 8 weeks in order to capture costs associated with any changes required to either plaster cast or functional bracing (e.g. plaster cast changes)

[d] Total costs throughout first 8 weeks calculated based on total sample size of 415: Plaster cast, n=200; Functional brace, n=215) i.e. cases with complete intervention and resource use costs at 8 weeks.

PSS: Personal social services

4.1.3 Health outcomes

The distribution of the responses to the EQ-5D-5L questionnaires by trial group and assessment point is presented in Table 21 and Table 22 for all participants. Table 21 shows that there were no significant differences in the proportions of individuals reporting suboptimal health (i.e. any functional (below level 1) impairment) within dimensions between the two treatment groups at each time point. The mean EQ-5D utility score was significantly lower at 8 weeks post injury in the Functional Brace group (0.588 versus 0.655; $p<0.0001$) amongst complete cases. However, there were no statistically significant differences in EQ-5D utility scores between the treatment groups at any other follow-up time-point. There were no statistically significant differences in the Visual Analogue Scale scores between the comparator groups (Table 22).

Table 21: Distribution of EQ-5D-5L responses by trial group

			Pre-injury Baseline		***Post injury Baseline***		***8-week post- injury***		***3-months post injury***		***6-months post injury***		***9-months post injury***	
			Plaster Cast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)	Plaste rcast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)
EQ-5D-5L dimension, n(%)	*Mobility*	Level 1	243 (91.4%)	247 (90.2%)	1 (0.4%)	1 (0.4%)	24 (9.0%)	34 (12.4%)	24 (9.0%)	34 (12.4%)	94 (35.3%)	103 (37.6%)	143 (53.8%)	148 (54.0%)
		Level 2	10 (3.8%)	14 (5.1%)	10 (3.8%)	11 (4.0%)	63 (23.7%)	88 (32.1%)	90 (33.8%)	101 (36.9%)	89 (33.5%)	85 (31.0%)	74 (27.8%)	80 (29.2%)
		Level 3	6 (2.3%)	8 (2.9%)	51 (19.2%)	64 (23.4%)	92 (34.6%)	100 (36.5%)	89 (33.5%)	90 (32.9%)	40 (15.0%)	40 (14.6%)	22 (8.3%)	28 (10.2%)
		Level 4	3 (1.1%)	3 (1.1%)	103 (38.7%)	108 (39.4%)	41 (15.4%)	22 (8.0%)	19 (7.1%)	17 (6.2%)	1 (0.4%)	9 (3.3%)	4 (1.5%)	3 (1.1%)
		Level 5	2 (0.8%)	0	99 (37.2%)	88 (32.1 %)	14 (5.3%)	1 (0.4%)	7 (2.6%)	3 (1.1 %)	0		1 (0.4%)	0
		Missing	2 (0.8%)	2 (0.7%)	2 (0.8)	1 (0.4%)	32 (12.0%)	33 (12.0%)	37 (13.9%)	29 (10.6%)	42 (15.8%)	37 (13.5%)	22 (8.3%)	15 (5.5%)
		Sub-optimal	21 (7.9%)	25 (9.1%)	264 (99.25%)	273 (99.6 %)	210 (78.9%)	207 (75.5%)	205 (77.1%)	211 (77.0%)	130 (48.9%)	134 (48.9%)	101 (38.0%)	111 (40.5%)
		P-value[1]	0.877		0.981		0.20		0.264		0.715		0.414	
	Self-care	Level 1	254 (95.5%)	265 (96.7%)	35 (13.2%)	45 (16.4%)	114 (42.9%)	131 (47.8%)	169 (63.5%)	192 (70.1%)	204 (76.7%)	207 (75.6%)	230 (86.5%)	242 (88.3%)
		Level 2	7 (2.6%)	6 (2.2%)	68 (25.6%)	51 (18.6%)	74 (27.8%)	81 (29.6%)	38 (14.3%)	36 (13.1%)	18 (6.8%)	23 (8.4%)	10 (3.8%)	17 (6.2%)
		Level 3	1 (0.4%)	1 (0.4%)	107 (40.2%)	117 (42.7)	41 (15.4%)	26 (9.5%)	19 (7.1%)	15 (5.5%)	2 (0.8%)	4 (1.5%)	3 (1.1%)	1 (0.4%)
		Level 4	2 (0.8%)	0	49 (18.4%)	55 (20.1%)	5 (1.9%)	3 (1.1%)	2 (0.8%)	2 (0.7%)	0	3 (1.1%)	1 (0.4%)	0
		Level 5	0	0	5 (1.9%)	5 (1.8%)	0	0	1 (0.4%)	0	0	0	0	0
		Missing	2 (0.8%)	2 (0.7%)	2 (0.8%)	1 (0.4%)	32 (12.0%)	33 (12.0%)	37 (13.9%)	29 (10.6%)	42 (15.8%)	37 (13.5%)	22 (8.3%)	14 (5.1%)
		Sub-optimal	10 (3.8%)	7 (2.6%)	229 (86.1%)	227 (82.9%)	120 (45.1%)	110 (40.1%)	60 (22.6%)	53 (19.3%)	20 (7.5%)	30 (11.0%)	14 (5.3%)	18 (6.6%)
		P-value[1]	0.725		0.294		0.219		0.253		0.330		0.292	
	Usual Activities	Level 1	245 (92.1%)	253 (92.3%)	3 (1.1%)	1 (0.4%)	18 (6.8%)	19 (6.9%)	26 (9.8%)	40 (14.6%)	80 (30.1%)	96 (35.0%)	141 (53.0%)	134 (48.9%)
		Level 2	10 (3.8%)	10 (3.7%)	13 (4.9%)	13 (4.7%)	59 (22.2%)	89 (32.5%)	92 (34.6%)	100 (36.5%)	132 (38.4%)	91 (33.2%)	80 (30.1%)	85 (31.0%)
		Level 3	5 (1.9%)	6 (2.2%)	50 (18.8%)	73 (26.6%)	83 (31.2%)	85 (31.0%)	74 (27.8%)	76 (27.7%)	38 (14.3%)	34 (12.4%)	19 (7.1%)	33 (12.0%)
		Level 4	2 (0.8%)	2 (0.7%)	100 (37.6%)	102 (37.2%)	51 (19.2%)	30 (10.9%)	25 (9.4%)	17 (6.2%)	3 (1.1%)	13 (4.7%)	2 (0.8%)	3 (1.1%)
		Level 5	2 (0.8%)	1 (0.4%)	98 (36.8%)	84 (30.7%)	23 (8.6%)	18 (6.6%)	12 (4.5%)	12 (4.4%)	1 (0.4%)	3 (1.1%)	2 (0.8%)	5 (1.8%)

			Pre-injury Baseline		***Post injury Baseline***		***8-week post- injury***		***3-months post injury***		***6-months post injury***		***9-months post injury***	
			Plaster Cast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)	Plaste rcast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)	Plaster Cast (n=266)	Functional Brace (n=274)
		Missing	2 (0.8%)	2 (0.7%)	2 (0.8%)	1 (0.7%)	32 (12.0%)	33 (12.0%)	37 (13.9%)	29 (10.6%)	42 (15.8%)	37 (13.5%)	22 (8.3%)	14 (5.1%)
		Sub-optimal	19 (7.1%)	19 (7.1%)	261 (98.1%)	273 (99.3%)	216 (81.2%)	222 (81.0%)	203 (76.3%)	205 (74.8%)	144 (54.1%)	141 (51.5%)	103 (38.7%)	126 (46.0%)
		P-value[1]	0.995		0.299		0.938		0.147		0.431		0.126	
	Pain/Discomfort	Level 1	226 (85.0%)	226 (82.5%)	18 (6.8%)	13 (4.7%)	63 (23.7%)	74 (27.0%)	23 (8.7%)	33 (12.0%)	56 (21.1%)	61 (22.3%)	87 (32.7%)	86 (31.3%)
		Level 2	24 (9.0%)	33 (12.0%)	86 (32.3%)	98 (35.8%)	125 (47.0%)	112 (40.9%)	139 (52.3%)	139 (50.7%)	126 (47.4%)	134 (48.9%)	124 (46.6%)	140 (51.1%)
		Level 3	7 (2.6%)	10 (3.7%)	102 (38.4%)	113 (41.2%)	38 (14.3%)	52 (19.0%)	61 (22.9%)	68 (24.8%)	38 (14.3%)	35 (12.8%)	29 (10.9%)	29 (10.6%)
		Level 4	4 (1.5%)	1 (0.4%)	46 (17.3%)	40 (14.6%)	6 (2.3%)	3 (1.1%)	3 (1.1%)	4 (1.5%)	4 (1.5%)	7 (2.6%)	4 (1.5%)	5 (1.8%)
		Level 5	3 (1.1%)	2 (0.7%)	12 (4.5%)	9 (3.3%)	2 (0.8%)	0	3 (1.1%)	1 (0.4%)	0	0	0	0
		Missing	2 (0.8%)	2 (0.7%)	2 (0.8%)	1 (0.4%)	32 (12.0%)	33 (12.0%)	37 (13.9%)	29 (10.6%)	42 (15.8%)	37 (13.5%)	22 (8.3%)	14 (5.1%)
		Sub-optimal	38 (14.3%)	46 (16.8%)	246 (92.5%)	260 (94.9%)	171 (64.3%)	167 (60.9%)	206 (77.4%)	212 (77.4%)	168 (63.2%)	176 (64.2%)	157 (59.0%)	174 (63.5%)
		P-value[1]	0.725		0.307		0.363		0.256		0.742		0.281	
	Anxiety/Depression	Level 1	231 (86.8%)	240 (87.6%)	145 (54.5%)	158 (57.7%)	141 (53.0%)	158 (57.7%)	138 (51.9%)	149 (54.4%)	155 (58.3%)	174 (63.5%)	190 (71.4%)	190 (69.3%)
		Level 2	20 (7.5%)	20 (7.3%)	69 (25.9%)	70 (25.5%)	57 (21.4%)	59 (21.5%)	59 (22.2%)	69 (25.2%)	49 (18.4%)	38 (13.9%)	41 (15.4%)	55 (20.1%)
		Level 3	9 (3.4%)	11 (4.0%)	39 (14.7%)	38 (13.9%)	32 (12.0%)	22 (8.0%)	26 (9.8%)	23 (8.4%)	17 (6.4%)	21 (7.7%)	7 (2.6%)	13 (4.7%)
		Level 4	2 (0.8%)	1 (0.4%)	9 (3.4%)	5 (1.8%)	3 (1.1%)	2 (0.7%)	3 (1.1%)	3 (1.1%)	3 (1.1%)	3 (1.1%)	5 (1.9%)	1 (0.4%)
		Level 5	2 (0.8%)	0	2 (0.8%)	2 (0.7%)	1 (0.4%)	0	3 (1.1%)	1 (0.4%)	0	1 (0.4%)	1 (0.4%)	1 (0.4%)
		Missing	2 (0.8%)	2 (0.7%)	2 (0.8%)	2 (0.7%)	32 (12.0%)	33 (12.0%)	37 (13.9%)	29 (10.6%)	42 (15.8%)	37 (13.5%)	22 (8.3%)	14 (5.1%)
		Sub-optimal	33 (12.4%)	32 (11.7%)	119 (44.7%)	115 (42.0%)			91 (34.2%)	96 (35.0%)	69 (25.9%)	63 (23.0%)	54 (20.3%)	70 (25.6%)
		P-value[1]	0.966		0.761		0.231		0.495		0.457		0.155	

[1]Comparisons of plaster cast vs functional brace groups carried out using χ^2 test for categorical variables.

Table 22: Patient-reported EQ-5D-5L utility scores and VAS results by treatment group and time-point

	Plaster Cast (n=266)		**Functional Brace (n=274)**		**Plaster Cast versus Functional Brace**	**Between - Group Difference (95% CI[a])**	
Assessment period	**Participants with complete data (n)**	**Mean (SE)**	**Participants with complete data (n)**	**Mean (SE)**	**Mean unadjusted difference (bootstrap 95% CI)**	**Adjusted[b]**	**P-value**
EQ-5D-5L utility scores							
Baseline post injury	264	0.243 (0.017)	273	0.285 (0.017)	-0.042 (-0.09 to 0.006)	0.041 (0.01, 0.07)	0.017
8 weeks	234	0.588 (0.015)	241	0.655 (0.012)	-0.066 (-0.102 to -0.031)	0.069 (0.03, 0.1)	<0.0001
3 months	229	0.638 (0.014)	245	0.669 (0.012)	-0.031 (-0.070 to 0.002)	0.035 (0, 0.07)	0.056
6 months	224	0.766 (0.010)	237	0.757 (0.011)	0.009 (-0.021 to 0.039)	-0.002 (-0.04, 0.03)	0.916
9 months	244	0.806 (0.011)	259	0.796 (0.010)	0.010 (-0.019 to 0.038)	-0.009 (-0.04, 0.03)	0.623
VAS[d]							
Baseline post injury	263	90.0 (80, 95)[b]	263	90.0 (80, 95)[c]	0.77 (-2.18, 3.72)	1.28 (-1.4, 3.97)	0.349
8 weeks	234	75.0 (60, 85)[b]	234	75.0 (65, 85)[c]	1.08 (-2.05, 4.2)	1.61 (-1.21, 4.43)	0.264
3 months	229	80.0 (65, 85)[b]	229	80.0 (65, 90)[c]	1.29 (-1.84, 4.42)	1.66 (-1.16, 4.48)	0.249
6 months	224	81.5 (70, 90)[b]	224	80.0 (70, 90)[c]	0.49 (-2.69, 3.66)	1.08 (-1.77, 3.93)	0.458
9 months	242	86.0 (80, 92)[b]	242	85.0 (75, 91)[c]	-0.76 (-3.8, 2.28)	-0.56 (-3.32, 2.2)	0.693

[a] CI: confidence interval

[b] Analysis adjusted for site, age, gender and EQ-5D baseline pre-injury equivalent. Given the pattern of results, Plaster Cast has been selected as the referent and Functional Brace as the comparator in the estimation of adjusted values.

[c] Median (Interquartile Range)

[d] VAS: Visual Analogue Scale

4.1.4 Cost-effectiveness results

The cost-effectiveness results are presented in Table 23 with Plaster Cast selected as the referent and Functional Brace as the comparator, i.e. functional brace minus plaster cast, for the estimation of ICER values. The analytic time horizon covers the entire 9-month post-injury follow-up period of the trial. The joint distribution of costs and outcomes for the base-case analysis and sensitivity analyses are graphically represented in Figure 6 to Figure 13.

Base case analysis

Patients in the Functional Brace group experienced a non-statistically significant increase in QALYs in the base case (0.015 QALYs, 95% CI: -0.0013 to 0.030) over the 9-month follow-up period. Mean NHS and PSS costs were also lower in the Functional Brace group [mean cost difference: -£103 (95% CI: -289 to 84)]. The ICER for the base-case analysis indicates that functional bracing is the dominant procedure as average costs for this intervention were lower whilst average benefits were greater than those for plaster cast.

Assuming cost-effectiveness thresholds of £15000 per QALY, £20000 per QALY and £30000 per QALY, respectively, the probability of cost-effectiveness for functional bracing ranged from 0.96 to 0.97, whilst the NMB associated with functional bracing was positive (Table 23).

Sensitivity analyses

Comparing mean costs and QALY estimates using different analytical scenarios (complete case, societal perspective and CACE population) revealed that the cost-effectiveness results generally supported the base case finding, with the exception of the sensitivity analysis that adopted a societal perspective. For the societal perspective, mean costs were higher in the Functional Brace group (£248, 94% CI: -476 to 972). However, the QALY results followed the same pattern as that for the base case analysis and indicated that participants in the Functional Brace group experienced a non-statistically significant increase in QALYs over the 9-month follow-up period (0.015 QALYs, 95%CI: -0.0042 to 0.031). The probability of cost-effectiveness of functional brace declined to a range of 0.50 to 0.69 at cost-effectiveness thresholds of £15000 per QALY, £20000 per QALY and £30000 per QALY. The results of

the mixed effects model followed a similar pattern to that of the base case (imputed) model: Patients in the Functional Brace group experienced a non-statistically significant increase in QALYs (0.014 QALYs, 95% CI: -0.0018 to 0.031) over the 9-month follow-up period. Mean NHS and PSS costs were also lower in the Functional Brace group [mean cost difference: -£135 (95% CI: -342 to 71)].

4.1.5 Long-term economic modelling

The protocol allowed for decision-analytic modelling to estimate the longer-term cost-effectiveness of functional bracing or plaster cast. However, we note that cost and health utility values started to converge from the 3-month follow-up time-point and converged at subsequent time points, even though functional brace was cost-effective over the entire follow-up period. It was therefore concluded that longer-term extrapolation of cost-effectiveness of functional is highly unlikely to be meaningful. Furthermore, we did not identify external studies that compared differences in economic costs, functional outcomes or health-related quality of life beyond 9 months post injury in non-surgical patients treated with a plaster cast or functional brace. This lack of data needed to parameterize a model further challenged any efforts to conduct longer-term decision modelling.

Table 23: Cost-effectiveness, cost/QALY (£, 2017): functional brace compared to plaster cast

Scenario	**Treatment group, mean (SE) Cost**		**Incremental cost (95% CI)**	**Treatment group, mean (SE) QALY**		**Incremental QALYs (95% CI)**	**ICER***	**Probability of cost-effectiveness**			**Net monetary benefits**		
	Functional Brace	**Plaster Cast**		**Functional Brace**	**Plaster Cast**			**P[1]**	**P[2]**	**P[3]**	**NMB[1] (95% CI[6])**	**NMB[2] (95% CI[6])**	**NMB[3](95% CI[6])**
Base case analysis													
Imputed attributable costs and QALYs, covariate adjusted	1078.16 (83.42)	1180.72 (89.63)	-102.56 (-289.28 to 84.16)	0.506 (0.0064)	0.492 (0.0066)	0.015 (-0.0013 to 0.030)	Dominant	0.963	0.965	0.966	312.28 (-31.26 to 655)	383.82 (-32.67 to 793.80)	526.90 (-42.50 to 1076.87)
Sensitivity analyses													
Complete case attributable costs and QALYs, covariate adjusted	948.77 (53.91)	1117.28 (110.66)	-168.51 (-458.01 to 32.88)	0.513 (0.00642)	0.497 (0.0064)	0.017 (-0.0035 to 0.037)	Dominant	0.976	0.976	0.972	443.54 (19.83 to 933.22)	527.26 (9.11 to 1094.07)	694.70 (-17.56 to 1406.23)
Societal perspective	4362.15 (348.71)	4114.54 (292.18)	247.61 (-476.44 to 971.66)	0.506 (0.0063)	0.502 (0.007)	0.015 (-0.0042 to 0.031)	16510	0.501	0.576	0.688	-29.65 (-991.50 to 874.93)	44.36 (-964.19 to 991.46)	192.39 (-926.97 to 1244.53)
CACE [4] population	1038.6 (62.89)	1169.44 (78.48)	-130.84 (-335.38 to 90.36)	0.510 (0.00609)	0.488 (0.00688)	0.022 (0.0051 to 0.038)	Dominant	0.992	0.993	0.994	44.52 (89.86 to 852.63)	57.36 (127.50 to 1030.39)	818.02 (199.26 to 1434.03)

Secondary cost-effectiveness analysis using ATRS[4] as outcome measure	1057.22 (71.91)	1149.44 (79.25)	-92.21 (-273.86 to 89.44)	45.09 (0.72)	44.30 (0.73)	0.78 (-1.12 to 2.69)	Dominant	0.875	0.839	0.822	174.03 (-117.37 to 463.44)	328.84 (-306 to 970.91)	406.25 (-403.75 to 1218.76)

*ICER: Incremental cost-effectiveness ratio. Given the pattern of results, Plaster Cast has been selected as the referent and Functional Brace as the comparator, i.e. functional brace minus plaster cast, for the estimation of ICER values. Dominance indicates average costs were less and average benefit greater for functional brace vs. plaster cast

P^1, P^2, P^3: probability cost-effective if cost-effectiveness threshold set at £15,000/QALY, £20,000/QALY or £30,000/QALY, respectively with the exception of the sensitivity analysis using ATRS as the health outcome measure of interest. In the latter case P^1, P^2, P^3 refer to probability of cost-effectiveness if cost-effectiveness threshold arbitrarily set at £100; £300 and £500 per unit gain in ATRS score

NMB^1, NMB^2,NMB^3: net monetary benefit if cost-effectiveness threshold set at £15,000/QALY, £20,000/QALY or £30,000/QALY, respectively with the exception of the sensitivity analysis using ATRS as the health outcome measure of interest. In the latter case NMB^1, NMB^2,NMB^3 refer to net monetary benefit if cost-effectiveness threshold arbitrarily set at £100; £300 and £500 per unit gain in ATRS score

[4] CACE Complier Average Causal Effect

[5] ATRS (Achilles Tendon Rupture Score) range from 0 to 100 with higher scores indicating better outcome

[6] CI: confidence interval

QALY: quality adjusted life-year

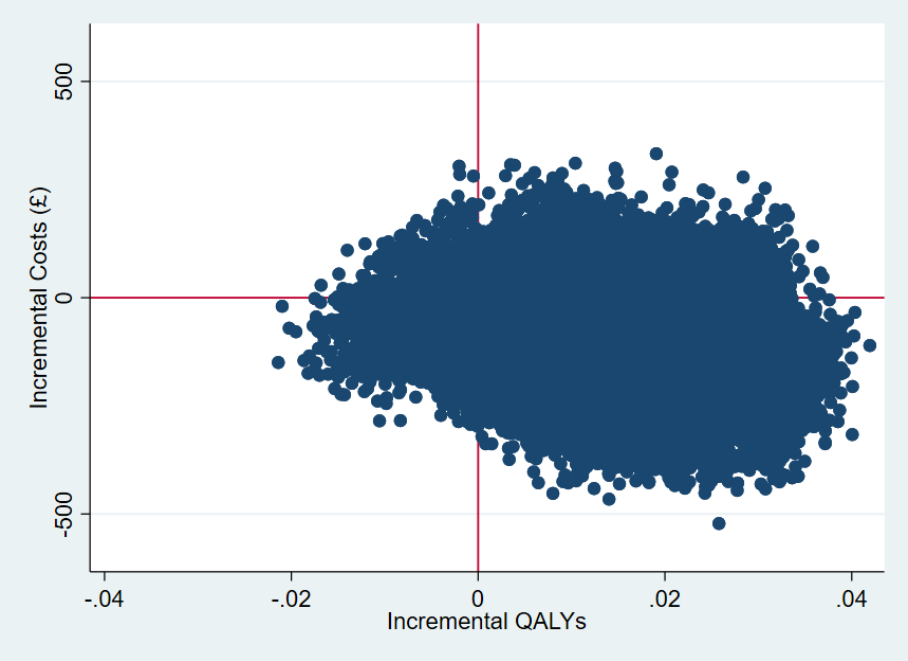

Figure 6: Cost-effectiveness scatterplot at 9 months for base case analysis (NHS and personal social service perspective, imputed- additionally controlled for pre-injury utility, intention-to-treat analysis)

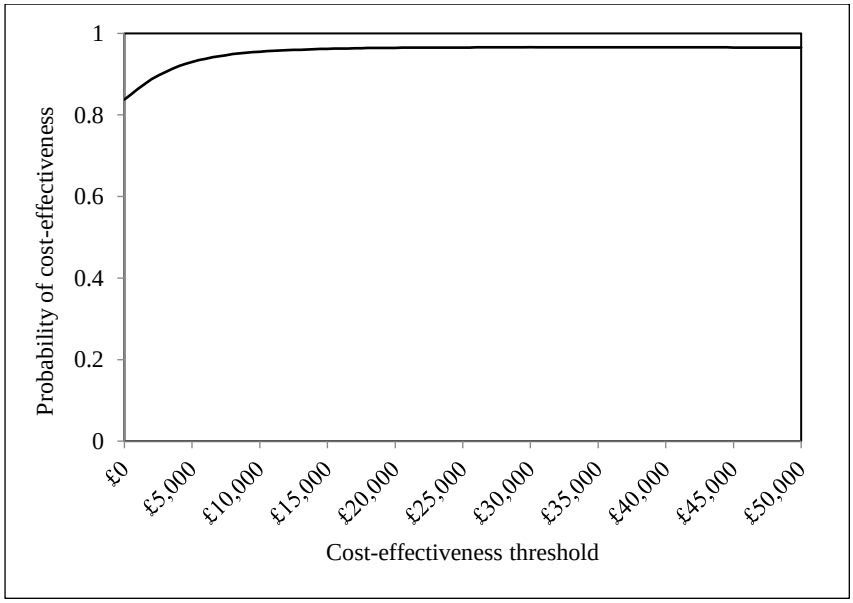

Figure 7: Cost-effectiveness acceptability curve at 9 months for base case analysis (NHS and personal social service perspective, imputed- additionally controlled for pre-injury utility, intention-to-treat analysis)

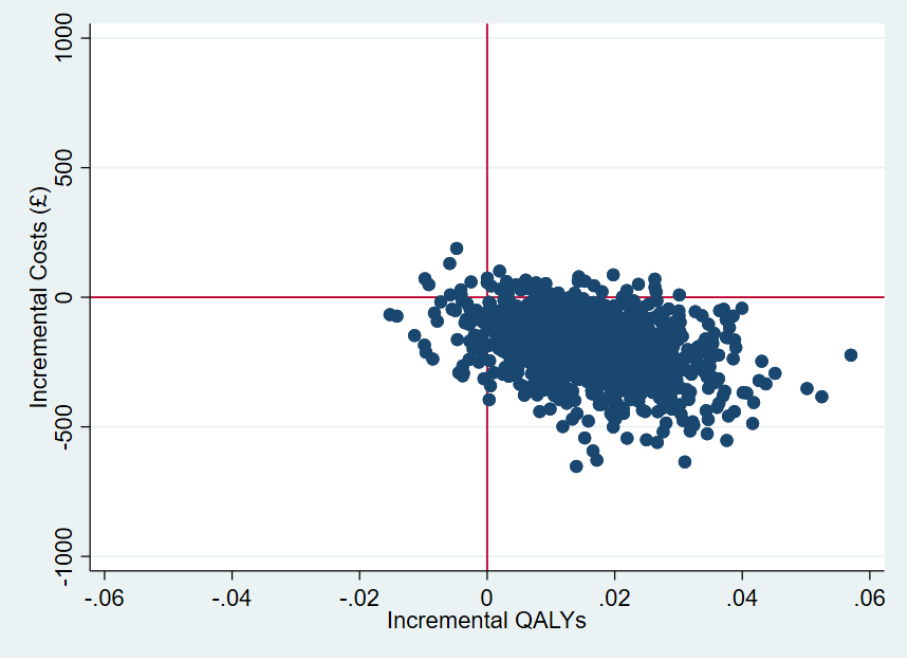

Figure 8: Cost-effectiveness scatterplot at 9months for complete cases (NHS and personal social perspective, intention-to-treat analysis)

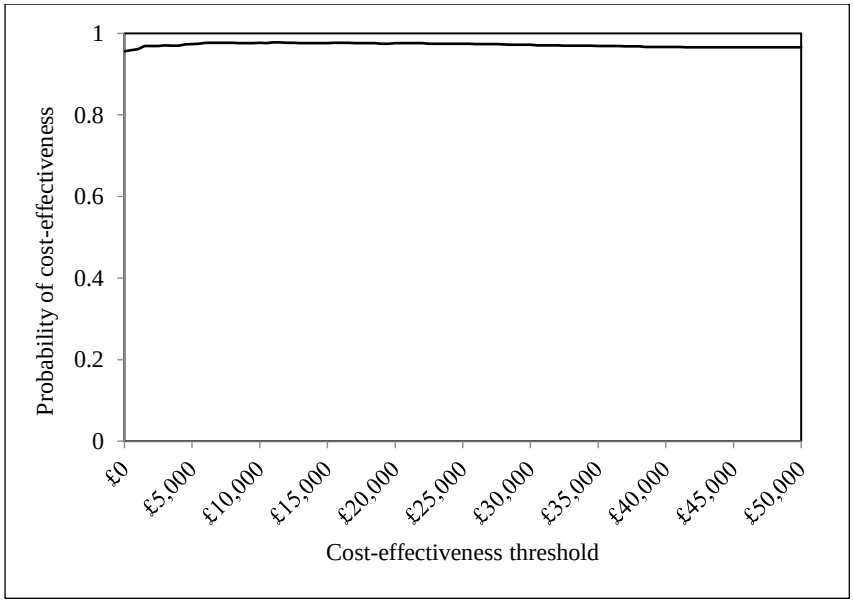

Figure 9: Cost-effectiveness acceptability curve for complete cases (NHS and personal social perspective, intention-to-treat analysis)

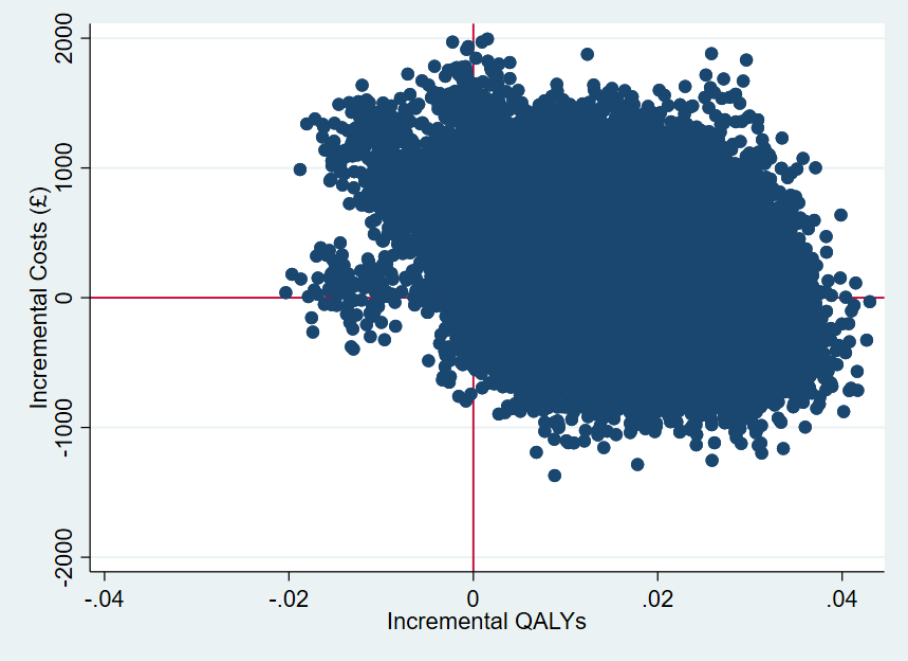

Figure 10: Cost-effectiveness scatterplot for societal perspective (imputed, intention-to-treat analysis)

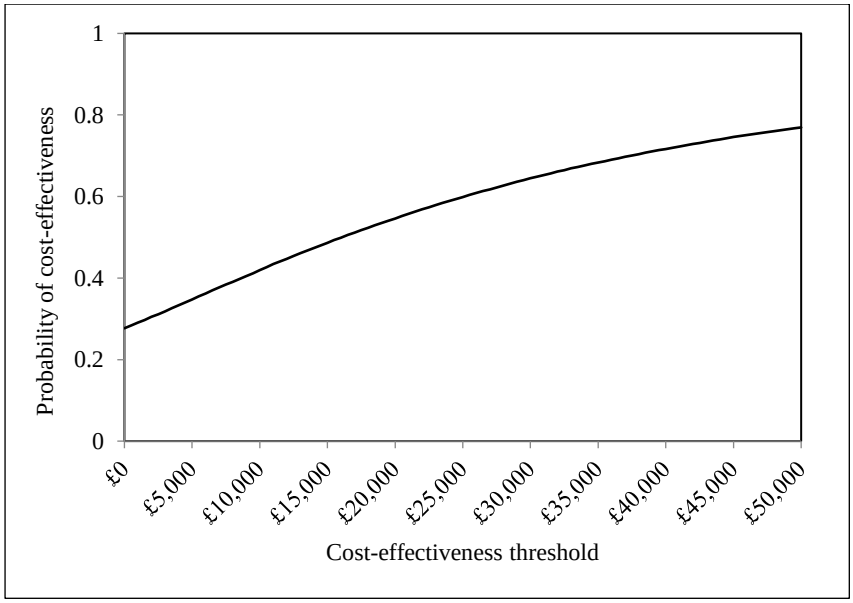

Figure 11: Cost-effectiveness acceptability curve for societal perspective (imputed, intention-to-treat analysis)

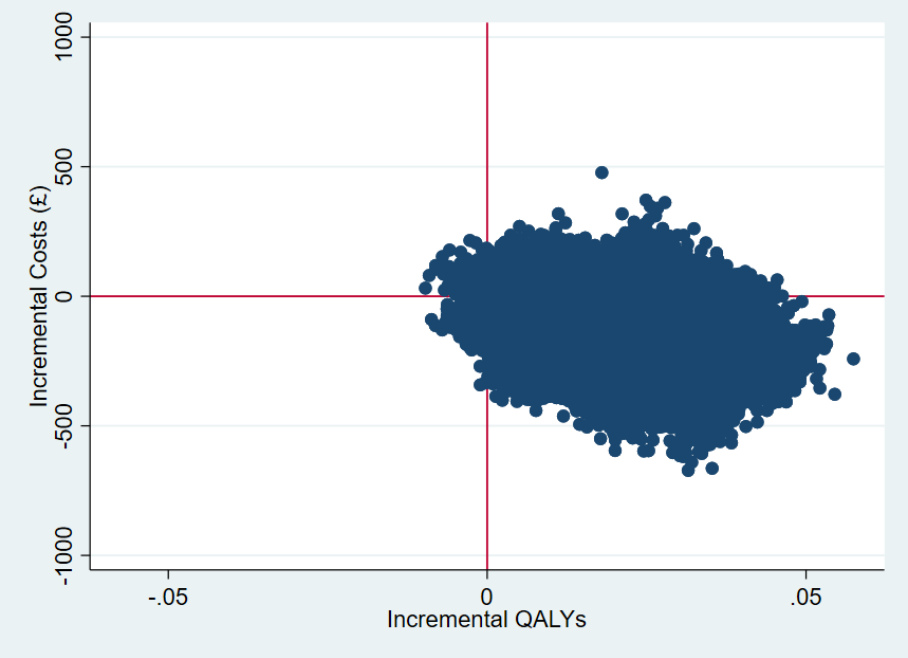

Figure 12: Cost-effectiveness scatterplot for complier average causal effect population, imputed, NHS and personal social service perspective

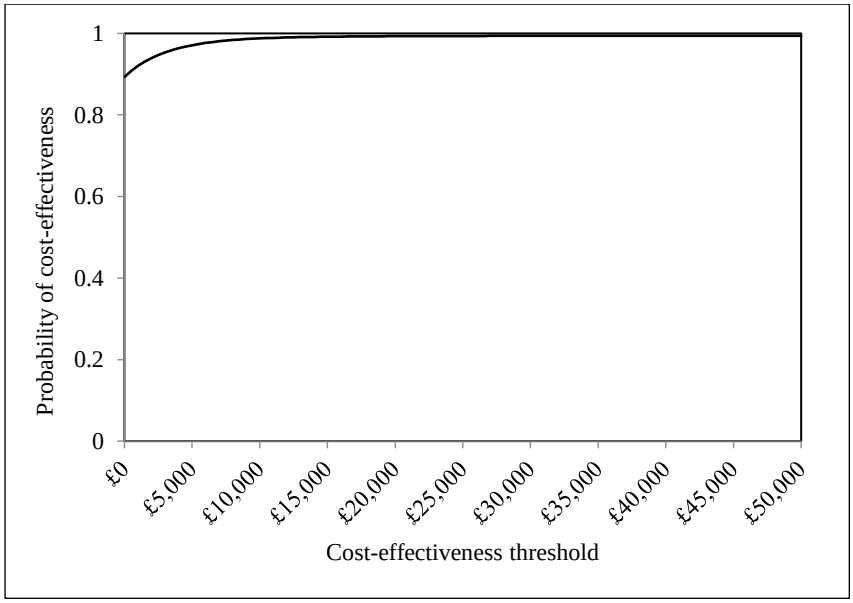

Figure 13: Cost-effectiveness acceptability curve for complier average causal effect population, imputed, NHS and personal social service perspective, covariate adjusted

5. Discussion

5.1 Recruitment

A total of 375 patients were screened but found to be ineligible for the trial. The most common reason for patients being ineligible (n=155) was that they presented more than 14 days after their Achilles tendon injury. Late presentation after an Achilles tendon rupture is not uncommon. Although the patient may have severe pain when the tendon ruptures, this acute pain usually settles quickly and the patient can often put weight through their leg, albeit without being able to walk normally. Some patients feel that they would not be able to walk at all if they had suffered a 'serious' injury and therefore continue to try to mobilise on their leg before eventually seeking treatment some time later, when their limp has not improved. The cut-off of 14 days used to define an 'acute' rupture is somewhat arbitrary, but in keeping with definitions used in previous research into this injury. Patients presenting at later times may have partial or complete healing of the tendon, but often with tendon lengthening which restricts their function. The treatment of late presentation injuries is not straightforward and often requires surgical intervention, therefore these patients were excluded from this trial of acute non-operative management.

The second common reason for patients being ineligible (n=120) was that they chose to have surgery. This is perhaps fewer than was anticipated when the UKSTAR trial was designed and, to some degree, accounts for the faster than expected rate of recruitment. However, it is in keeping with the worldwide trend towards non-operative treatment of acute rupture of the Achilles tendon, as per the recent evidence base which suggests little functional advantage to surgery. [8, 9]

Only 46 patients were excluded because they were unable to adhere to trial procedures or complete questionnaires, most commonly because they could not read written English, as used in the follow-up questionnaires. Thirty-seven patients were excluded because they had suffered a previous Achilles tendon injury, which was likely to have affected their baseline, pre-injury function. Achilles tendon rupture is very rare in children and hence it is not surprising that only three patients were excluded as being less than 16 years of age. The

remaining 14 patients were excluded by recruitment centres under the heading of ‘other’; we did not record details of these individual cases.

Of the 1076 potentially eligible patients screened across the 39 recruitment centres, 540 consented to enter the trial. Ninety nine patients were not approached about the trial because there was no research associate available to discuss the trial (n=97), usually because the patient presented at the weekend, or because there was no functional brace available at the time of presentation (n=2). A further 50 patients were not offered the opportunity to take part in the trial due to a clinician decision. In some cases, there were specific reasons given for this decision, for example “active treatment of a local skin lesions precluding the use of a cast”, but in other cases the clinician did not provide a reason. Therefore, a total of 149 potentially eligible patients were never offered the opportunity to take part in the trial. This reduced the number of participants but is unlikely to have caused a selection bias.

Of the 927 patients who had the opportunity to take part, 385 declined. Patients may decline to take part in a trial for various reasons. Those who do not want to be part of any research – often because of the perception, of indeed the reality, of filling out extra, onerous questionnaires – are unlikely to adversely affect the trial in terms of the difference between treatment groups. However, those who decline because of a preference for one treatment over another do create a selection bias. In this trial, it is reassuring that 542 of the 927 patients who were offered the opportunity to take part in the trial (58%) agreed to participate.

5.2 Participants and interventions

The two groups of participants were well balanced in terms of baseline, pre-injury characteristics.

In keeping with the epidemiology of Achilles tendon rupture, there were more men aged 30-40 years, whereas women were a little older at the time of their injury, being 40-60 years most commonly. Sports accounted for the great majority of ruptures (70.4%) and relatively few patients declared pre-disposing risk factors; only 4.3% of participants had diabetes and

3.9% were taking steroids, these being associated with an increased risk of tendon rupture. Only 3.7% declared a pre-existing Achilles tendinopathy, which also fits with the literature in that most patients do not have symptoms before their tendon rupture. This is despite the fact that histological studies indicate that there are almost always degenerative changes present in biopsies taken from tendons immediately after injury. [4, 5]

The median pre-injury ATRS score was 100 in both groups, indicating normal Achilles function. Similarly, the median EQ-5D utility score was 1, indicting perfect health. This, and the fact that the large majority of participants were employed or self-employed, suggests that most Achilles ruptures affect working-age people with good pre-injury health. However, the characteristics of the participants reflects the epidemiology in that Achilles rupture affects all age groups with both men and women in their 80's represented within the trial. Overall the participants in the trial are representative of the previously reported demographics of patients with this injury.

We anticipated some cross-over between treatment groups following the random allocation, but in fact this was relatively uncommon. Only one participant decided to have a cast, having been allocated a functional brace. Thirteen participants decided to change to a functional brace, having been allocated a cast, which may reflect the perception that the brace made mobilisation easier. However, the numbers were small and we did not formally investigate the qualitative aspects of the decision to change treatment. Two further participants withdrew from the trial immediately after randomisation and seven others crossed over treatment groups for what were described as clinical or unknown reasons. Given the small number of cross-overs at baseline, these are very unlikely to have influenced the results of the trial.

In terms of compliance with treatment once implemented, the trial protocol stipulated that patients would be deemed compliant if they maintained their allocated treatment for a minimum of six weeks. The choice of six weeks reflects the fact that this was the time at which weight-bearing would usually be permitted for those patients in a cast, those in a functional brace generally being fully weight-bearing from the outset. Overall, 88% of participants were fully compliant. However, compliance was higher in the Functional Brace group (97%) compared to the Plaster Cast group (80%). This may reflect the participants desire to have the cast removed as soon as possible (most of these participants then using a functional brace for a further two weeks or more) but we did not interview participants regarding the reasons why they changed treatment after six weeks.

Some patients did of course change treatment before six weeks, having initially accepted their allocated intervention. This was more common in the plaster cast group where 11.3% changed to a functional brace, versus 0.4% allocated a functional brace who changed to a plaster cast. This may also suggest that the functional brace was preferred but, although we asked these participants if they or the clinician treating them chose/recommended changing treatment, we were not able to formally explore the reasons behind the decision to change treatment. An additional 3% of participants chose to have surgery before six weeks; 1.9% in the plaster cast group and 1.1% in the functional brace group. In some cases, these participants described a further fall/injury to their tendon. However, we have not reported these as 're-ruptures' of the tendon on the basis that the tendon was unlikely to be healed in the first place, before six weeks.

One other notable element of the participants' treatment beyond the allocation to functional brace or cast, was the use of VTE prophylaxis. Patients with Achilles tendon rupture are at increased risk of VTE, as the injury defunctions the triceps surae muscles which are an important part calf muscle pump which helps return of venous blood to the heart. In the Plaster Cast group, 70% of patients had VTE prophylaxis, most commonly with self-administered low molecular weight heparin injections. Fewer patients (58%) had VTE prophylaxis in the Functional Brace group. This difference may reflect the belief that patients who are able to fully weight-bear in a functional brace are at lower risk of VTE than those with restricted weight-bearing in a cast, but this trial was not designed to address questions related to the management of VTE.

5.3 Results

In total, 93.3% of participants completed the primary outcome measure at 9 months after their Achilles tendon rupture. This included 91.7% in the Plaster Cast group and 94.9% in the Functional Brace group. Therefore, loss to follow-up was considerably less than the 20% accounted for in the trial design which, alongside the fact that the trial was able to recruit more patients than the minimum of 330 required by the sample size calculation, ensures that the trial had considerably greater than 90% power.

Follow-up was also good at other time-points with 88%, 88% and 86% of participants completing questionnaires at 8 weeks, 3 months and 6 months respectively.

5.3.1 Primary Outcome

The adjusted ITT analysis showed no statistically significant difference in ATRS between the two treatment groups at the primary end-point of 9-month post injury (-1.38; 95% CI -4.9 to 2.1).

There was a statistically significant difference in the ATRS at 8 week in favour of the Functional Brace group (5.75; 95% CI 2.2 to 9.3), although this difference is of borderline clinical importance. However, any benefit to functional bracing was not evident later in the participants' recovery with very similar ATRS scores at three and six, as well as nine months.

As expected, given the relatively small number of patients who were non-compliant with treatment, the secondary sensitivity analysis, using adjusted Complier Average Causal Effect, showed the same pattern. There was no evidence of a difference at 9 months post injury (-1.17, 95% CI -4.5 to 2.1). Nor was there any evidence of a difference on the other pre-specified analysis of overall ATRS scores (AUC) over the full period of follow-up.

5.3.2 Secondary Outcomes

The analysis of patient-reported health-related quality of life (EQ-5D utility score) provides powerful corroborating evidence in support of the findings using the ATRS. There was a statistically significant and clinically relevant difference in favour of functional bracing at 8 weeks (0.069; 95% CI 0.03 to 0.1). A breakdown of the EQ-5D by domain of health showed that this differences at 8 weeks lies in the ability to 'self-care' and 'usual activities'. This difference in EQ-5D utility scores was of borderline statistical significance (0.035 95% CI 0 to 0.07) at 3 months but there was no evidence of a difference at any subsequent time-point. There was no evidence of a difference in EQ-5D VAS scores.

The trial was designed to compare patient-centred outcomes between participants randomly allocated to a plaster cast versus a functional brace. However, the safety profile of the functional brace was another important consideration. Specifically, if the risk of re-rupture of the tendon was higher in those patients allowed to fully weight-bear in a functional brace, this would influence decision-making in this area, even when patient-reported outcomes were similar. Interestingly, the risk of re-rupture was generally lower than reported in the literature, with a total of 17 (6.4%) cases in the Plaster Cast group and 13 (4.7%) in the Functional Brace group. None of the re-ruptures occurred more than six months after the injury.

There was no evidence of associations between treatment group and any other type of complication, with the exception of *non-injurious falls*, which were more common in the Plaster Cast group (p=0.015)

5.4 Health economic evaluation

The mean direct intervention costs were £36 for the Plaster Cast group compared with £109 for the Functional Brace group. The greater up-front cost of the functional brace (mean difference £73) was statistically significant. However, by 8 weeks this difference had reversed such that the mean total NHS and PSS costs were significantly lower in the Functional Brace group. The difference being driven mostly by the increased number of outpatient appointments required in the Plaster Cast group.

This is an important finding as it will reassure the finance teams in Trauma and Orthopaedic Departments that, despite the extra initial cost of a functional brace, they will reduce their overall costs when treating patients with an Achilles tendon rupture.

The mean total NHS and PSS cost throughout the entire follow-up period was £1183 for the Plaster Cast group and £1018 for the Functional Brace group. Although the functional bracing was marginally cheaper, the mean between-group cost difference of £164 was not statistically significant.

In terms of health-related quality of life, the mean QALY value was, on average, marginally higher for the Functional Brace group amongst complete cases and in the sensitivity analyses, although this mean QALY difference was not statistically significant.

Therefore, since the Functional Brace group incurred slightly lower costs and achieved slightly better quality of life over the course of the study, in health economic terms, functional bracing is the dominant intervention.

In summary, the health economic evaluation indicates that functional bracing is very likely to be cost-effective.

5.5 Limitations

A concern at the start of the study was that patients would not be willing to take part in a trial comparing two distinct interventions which needed to be worn for a prolonged period of time. Some of the 385 patients who declined did so because they did not wish to be part of a

research project. These patients, whilst undoubtedly affecting the external validity of the trial, are unlikely to create a selection bias when comparing the two interventions. By contrast, those who declined because of a preference for one treatment over another do create a selection bias. However, in total, 542 of the 927 patients who were offered the opportunity to take part in the trial (58%) agreed to participate, so we can be confident that the participants in the trial are broadly representative of the population of patients having non-operative treatment for an acute rupture of the Achilles tendon.

A further anticipated limitation was cross-over from the allocated trial treatment, and indeed 14 patients did not receive their allocated intervention after being randomised. There were also some cases of incomplete compliance with treatment. The ability to bear weight immediately within a functional brace may have triggered the desire to change treatment, given that the majority changed from the Plaster Cast group to the Functional Bracing group. However, the overall number is small in a trial of this size and the CACE analysis, that is the analysis adjusted for incomplete compliance, confirmed the result of the primary analysis i.e. there was no evidence of a difference between the two groups of participants at nine months post injury.

Loss to follow-up is another potential limitation. However, over 93% of participants provided primary outcome data at nine months, which is considerably higher than the 80% assumed in the trial design. Therefore, given that the trial also exceeded the minimum sample size by some margin, we can be confident that the conclusions are robust and the risk of type II error is very low.

6. Conclusions

This trial provides strong evidence that early weight-bearing in a functional brace provides similar outcomes to traditional plaster casting and is safe for patients having non-operative treatment of an Achilles tendon rupture. The use of functional bracing is very likely to be cost-effective.

While the UKSTAR trial provides guidance with regard to the early management of patients, rehabilitation following an Achilles tendon rupture is prolonged and further research is required to define the optimal mode of rehabilitation after the initial cast/brace is removed.

7. Acknowledgements

7.1 Contribution of authors

Matthew Costa was Chief Investigator, led the funding application, study conception and design, development of interventions, provided overall study supervision, and wrote and reviewed the report.

Juul Achten prepared the funding application, provided overall study supervision, developed the study, developed the intervention, designed the study and wrote and reviewed the report.

Susan Wagland managed and supervised the study, wrote and reviewed the report.

Ioana Marian was trial statistician, conducted the statistical analysis and wrote the report.

Mandy Maredza was trial health economist, designed the study, conducted the health economics analysis and wrote the report.

Michael Maia Schlüssel was trial statistician, conducted the statistical analysis and wrote the report.

Anna Liew managed and supervised the study, developed the study, developed the intervention, designed the study and reviewed the report.

Nick Parsons developed the study, developed the intervention, designed the study and reviewed the report.

Susan Dutton was lead statistician, designed the study, conducted the statistical analysis and wrote and reviewed the report.

Rebecca Kearney developed the study, developed the intervention, designed the study and reviewed the report.

Sarah Lamb developed study conception and design and reviewed the report.

Benjamin Ollivere developed the study, developed the intervention, designed the study and reviewed the report.

Stavros Petrou oversaw the health economics analysis and wrote and reviewed the report.

7.2 UKSTAR study team

Chief Investigator: Matthew Costa.

Co-investigators: Matthew Costa, Juul Achten, Rebecca Kearney, Sarah Lamb, Nick Parsons, Stavros Petrou, Ben Ollivere, Malvenia Richmond, Richard Grant.

Study Lead: Juul Achten.

Trial Managers: Susan Wagland, Anna Liew.

Senior Trial Managers: Juul Achten, Damian Haywood.

Study co-ordinators and administrators: Catherine Thompsett, Ramona Barbu, Kylea Draper, Hugo Strachwitz, Hasina Mangal, Alice Brealy.

Health Economists: Stavros Petrou, Mandy Maredza.

Study statisticians: Michael Maia Schlüssel, Ioana Marian, Susan Dutton.

7.3 Recruitment Centres

Table 24: Principal Investigators by recruitment centre

NHS Trust name	**Principal Investigator**
King's College Hospital	Ines Reichert
Nottingham University Hospitals- Queen's Medical centre	Ben Ollivere
Royal Berkshire Hospital	Andrew McAndrew
Aberdeen Royal Infirmary	Alan Johnstone
NHS Tayside - Dundee	Fraser Harrold
Glasgow Royal Infirmary	Jane Madeley
Pilgrim Hospital, Boston, United Lincolnshire Hospitals NHS Trust	Harish Kurup
University Hospital of North Tees	Rajesh Nanda
Airedale General Hospital	Avijeet Ghosh
Salisbury District Hospital	Sridhar Sampalli

Rotherham Hospital	Sandeep Kapoor
George Eliot Hospital NHS Trust	Asterios Dramis
James Paget University Hospital NHS Foundation Trust	Nitin Modi
University Hospital Southampton NHS Foundation Trust	Nicholas Hancock
Lister Hospital, East and North Herts NHS Trust	Rupe Deol
Royal Cornwall Hospital	Richard Walter
Maidstone and Tunbridge Wells NHS Trust	Justin Forder
Cambridge University Hospitals - Addenbrookes	Peter Hull
Derriford Hospital, Plymouth	Mark Westwood
Hull Royal Infirmary	Viren Mishra
Luton and Dunstable Hospital	Simon Burtt
Salford Royal NHS Foundation Trust	Victoria Lyle
Northern Lincolnshire & Goole	Nikos Reissis
Mid Yorkshire NHS Trust	Jason Eyre
Leeds General Infirmary	Paul Harwood
Alexandra Hospital, Redditch	Abhijit Guha
Doncaster and Bassetlaw Hospitals NHS Foundation Trust	Sanjeev Madan
Epsom and St Helier University Hospitals NHS Trust	Andrea Sott
Imperial College Healthcare NHS Trust	Rajarshi Bhattacharya
Raigmore Hospital, Inverness	James Beastall
Whiston Hospital	Jordi Ballester
Milton Keynes University Hospital	Atif Malik
Warwick Hospital	Sameh El-Kawy

Burton Hospitals NHS Foundation Trust	Babis Karagkevrekis
Hereford County Hospital	Amr Abdallah
Queen Elizabeth Hospital, Birmingham	Ansar Mahmood
John Radcliffe, Oxford University Hospitals	Mark Deakin
Musgrove Park Hospital, Taunton	Moez Ballal, Nasser Kurdy
Musgrove Park Hospital, Taunton	Andrew Kelly

7.4 Study Steering Committee

The TSC comprised:

Independent members:

- Mr Paul Baker (Orthopaedic Surgeon) - Chair
- Mrs Sarah Webb (Patient Representative)
- Dr Dylan Morrissey (Consultant Physiotherapist)
- Dr Anne-Marie Hutchison (Consultant Physiotherapist)

Non-independent members:

- Prof Matthew Costa (Chief Investigator)
- Dr Susan Wagland (Trial Manager)
- Susan Dutton (OCTRU Lead Statistician)
- Ioana Marian (Trial Statistician)

7.5 Funding

The Health Technology Assessment Programme, a NIHR funding stream (reference 13/115/62).

7.6 Data sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to available anonymised data may be granted following review.

7.7 Publications

Achten J, Parsons NR, Kearney RL, et al. Cast versus functional brace in the rehabilitation of patients treated non-operatively for a rupture of the Achilles tendon: protocol for the UK study of tendo achilles rehabilitation (UK STAR) multi-centre randomised trial. *BMJ Open* 2017;7:e019628. doi: 10.1136/bmjopen-2017-019628.

Marian, I, Costa, M. L., Dutton, S. Cast versus functional brace in the rehabilitation of patients with a rupture of the Achilles tendon: statistical analysis plan for the UK study of tendo Achilles rehabilitation (UK STAR) multi-centre randomised controlled trial. *Trials*. (manuscript accepted for publication).

Word Count 16,658 words

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Appendix 1: Trial management

Introduction

The UKSTAR Trial completed recruitment on schedule (Figure 14), recruiting 540 participants.

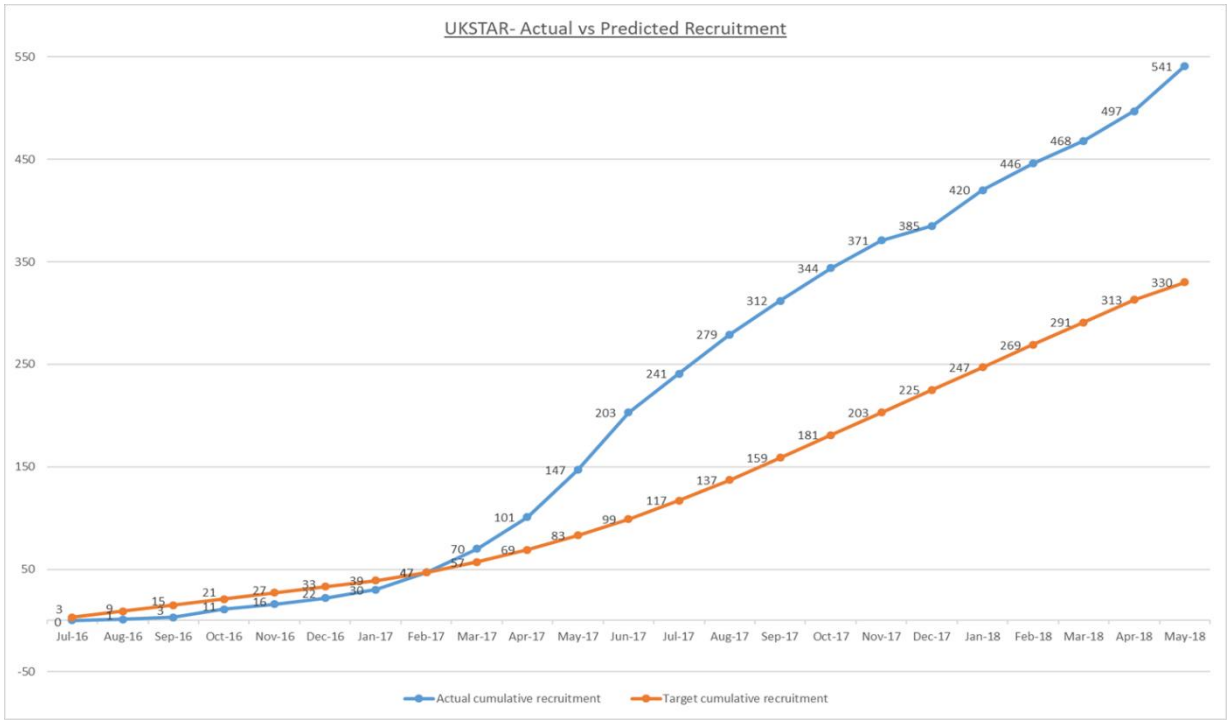

Figure 14: UKSTAR actual and predicted recruitment

Completeness of baseline and 8-week data, and rates of follow-up at all time-points were excellent, thanks to the dedication of clinicians and researchers at the recruitment centres and an experienced, dedicated, central trial management team.

Management milestones

Table 25 shows the dates when milestones in the Project Management Plan were achieved.

Table 25: Progress against milestones in Project Management Plan

Event	Planned date	Actual date
Grant activation	1st April 2016	1st April 2016
Trial open	16th August 2016	16th August 2016
First DSMC[a]/TSC[b] meeting	6th July 2016	6th July 2016
Expected end of recruitment	31st May 2018	31st May 2018
Expected end of follow-up	31st March 2019	12th March 2019
Expected start of data cleaning	January 2019	January 2019
Expected start of final analysis	March 2019	March 2019
End of Grant	31st May 2019	31st May 2019

[a] DSMC: Data Safety and Monitoring Committee; [b] TSC: Trial Steering Committee

Recruitment target and recruitment centre selection

Principal Investigators at potential recruitment centres were approached through the NIHR/Orthopaedic Trauma Society Research Network and British Foot and Ankle Society. We included sites from regions across England and Scotland, of all sizes from Major Trauma Centres to Local Emergency Hospitals.

Each potential recruitment centre completed a Site Feasibility Questionnaire, which was reviewed by the Chief Investigator. Sites were asked to declare how many patients presented at their site with Achilles tendon rupture and were treated non-operatively, and their expected recruitment rate, which needed to be at least 1 participant per month. Some sites declined on the grounds that their patients were already all put into a functional brace, or were all treated with a plaster cast. Sites which were actively recruiting for another Achilles trial in our research group, the PATH-2 study, were not opened to UKSTAR until after recruitment for PATH-2 was complete, to avoid competition between trials for the same patients and potential recruitment bias.

The UKSTAR trial opened to recruitment on 16th August 2016, one month later than planned due to contractual delays at recruitment centres. The original application predicted a recruitment rate of 1 participant per month per centre, which led to the conclusion that a minimum of 22 centres was required. However, during the first six months, although more recruitment centres were opened than planned (nine as opposed to six), recruitment in most was slower than expected (27 participants in total) and weighted towards a single, high-recruiting recruitment centre (15 participants at Aberdeen). We decided therefore to expand the number of recruitment centres and were successful in opening 39 recruitment centres, including some whose Trauma departments were new to trials.

One recruitment centre (James Paget, Norfolk) closed to recruitment early due to lack of research staff, having recruited no participants. All other recruitment centres recruited at least one participant.

The trial reached its original recruitment target of 330 participants in October 2017, seven months ahead of target. For 90% power in the primary outcome (ATRS at 9 months) and allowing for 20% loss to follow-up and crossovers, a sample size of 330 participants was required. In September 2017, when it became apparent that the target would soon be reached, there was doubt over the quantity and quality of data being collected. Some patients were unhappy with their allocation and crossed over to the other group of the trial. In addition, as few participants by then had reached the nine month time-point, which was the primary outcome, we could not be sure how many of the cohort would remain engaged with the trial up to the nine month time-point. To avoid the power of the trial being compromised by high numbers of crossovers and loss to follow-up at nine months, we submitted a substantial amendment to increase the sample size to a maximum of 550, and to recruit up to the original recruitment end date (31 May 2018). The chairs of the DSMC and TSC ratified this approach and the Research Ethics Committee gave a favourable opinion. The trial continued recruiting until its original planned end date, recruiting 540 participants (Figure 14: UKSTAR actual and predicted recruitment

).

Monitoring of trial recruitment

Recruitment centres were trained in recruitment procedures at Site Initiation Visits, which were performed in person, or by conference call. It was not necessary for trial staff to travel to distant

recruitment centres when staff were experienced in trial recruitment. Recruitment centres completed a monthly Screening Log, declaring all patients who had presented to the Emergency Department or specialist Fracture Clinic or Foot and Ankle Clinic with Achilles tendon rupture. We monitored the reasons for non-recruitment, looking for trends at particular recruitment centres, and addressed them on a centre-by-centre basis. Recruitment centres were informed of how their recruitment rate compared to that of other recruitment centres in a monthly newsletter.

Data management

The Data Management Plan (DMP) defined the trial's data management procedures, in accordance with the Trials Unit's Standard Operating Procedures. The DMP identified databases and IT systems used by the trial, defined data types, data sharing and access, the critical data items, questionnaires and events, and the location of the trial data matrix; and described confidentiality, how protocol deviations were defined and what action to take, how source data was collected and entered at each time-point, and how follow-up was managed. It recorded decisions on follow-up time windows made by TMG, data rulings made by Chief Investigator, Statistician, Health Economist or Trial Manager, how data queries were handled and how data would be processed at the end of the trial.

The trial Monitoring Plan described procedures for central monitoring, and stated that no site monitoring would take place unless triggered by concerns. All recruitment centres were monitored centrally and none generated concerns sufficient to merit a monitoring visit.

Trial promotion

Promotion to patients and the public

A public-facing web page hosted within the OCTRU trials unit web pages held trial information, current recruitment figures and news.

Promotion within the Trauma and scientific communities

The UKSTAR trial was featured on a poster at the 7th NIHR OTS Musculoskeletal Trauma Trials Annual Meeting on 9th January 2019. The Kadoorie Centre newsletter, sent to recruitment centres participating in Oxford Trauma trials, highlighted the end of follow-up and excellent retention rate in its March 2019 issue. A regular monthly newsletter was sent to

recruitment centres during recruitment to help maintain engagement and to acknowledge and thank recruitment centres that recruited well.

Appendix 2: Site Names by NHS Trust

Table 26. Site Names by NHS Trust

Trial center	Trust Name
ABD	Aberdeen Royal Infirmary, NHS Grampian
AIR	Airedale NHS Foundation Trust, Keighley
BRT	Queen's Hospital, Burton Hospitals NHS Foundation Trust
CHX	St Mary's Hospital, Imperial College Healthcare NHS Trust London
CUH	Addenbrookes Hospital, Cambridge University Hospital NHS Foundation Trust
DBH	Doncaster Royal Infirmary, Doncaster & Bassetlaw Hospitals NHS Foundation Trust
DUN	Ninewells Hospital and Medical School, NHS Tayside, Dundee
ENH	Lister Hospital, East and North Herts NHS Foundation Trust
GEH	George Eliot Hospital NHS Foundation Trust, Nuneaton
GLA	Glasgow Royal Infirmary, NHS Greater Glasgow and Clyde
HCH	Hereford County Hospital, Wye Valley NHS Trust
HEY	Hull Royal Infirmary, Hull and East Yorkshire Hospitals NHS Trust
INV	Raigmore Hospital, Inverness, NHS Highland
KCH	King's College Hospital NHS Foundation Trust, London
LDH	Luton and Dunstable University Hospital
LDS	Leeds General Infirmary, The Leeds Teaching Hospitals NHS Trust
MKN	Milton Keynes University Hospital NHS Foundation Trust
MPH	Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust
MTW	Tunbridge Wells Hospital, Maidstone & Tunbridge Wells NHS Trust
MYH	Pinderfields Hospital, Mid Yorkshire NHS Trust
NLG	Scunthorpe General Hospital, Northern Lincolnshire and Goole NHS Foundation Trust
NTE	University Hospital of North Tees, North Tees and Hartlepool NHS Foundation Trust, Stockton-on-Tees

NUH	Nottingham University Hospitals NHS Trust
OUH	John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust
PLY	Derriford Hospital, University Hospitals Plymouth NHS Trust
QEH	Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust
RBK	Royal Berkshire Hospital, Royal Berkshire NHS Foundation Trust
RCH	Royal Cornwall Hospital, Truro, Royal Cornwall Hospitals NHS Trust
RED	Worcestershire Royal Hospital, Worcester Acute Hospitals NHS Trust
RTH	The Rotherham NHS Foundation Trust
SAL	Salisbury District Hospital, Salisbury NHS Foundation Trust
SHC	St Helier Hospital, Epsom and St Helier University Hospitals NHS Trust
SLF	Salford Royal NHS Foundation Trust
UHS	Southampton General Hospital, University Hospital Southampton NHS Foundation Trust
ULH	Pilgrim Hospital, Boston, United Lincolnshire Hospitals NHS Trust
WAR	Warwick Hospital, South Warwickshire NHS Foundation Trust
WHI	Whiston Hospital, Warrington, St Helens & Knowsley Teaching Hospital NHS Trust
WYT	University Hospital of South Manchester NHS Foundation Trust

Appendix 3: EQ-5D Individual Level Items

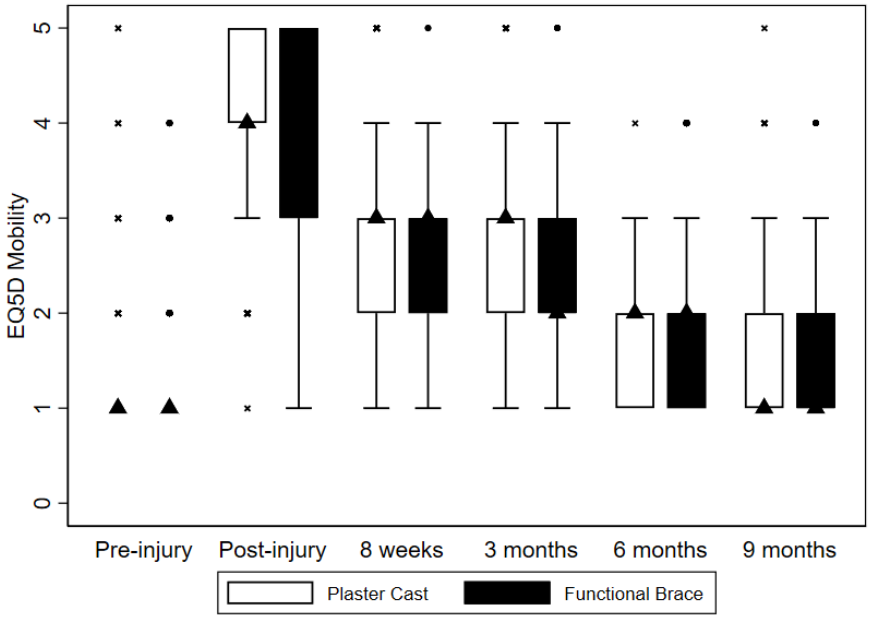

Figure 15: EQ-5D Mobility from baseline pre-injury to 9 months. EQ-5D Mobility values range from 1 to 5 with 1 indicating no problems

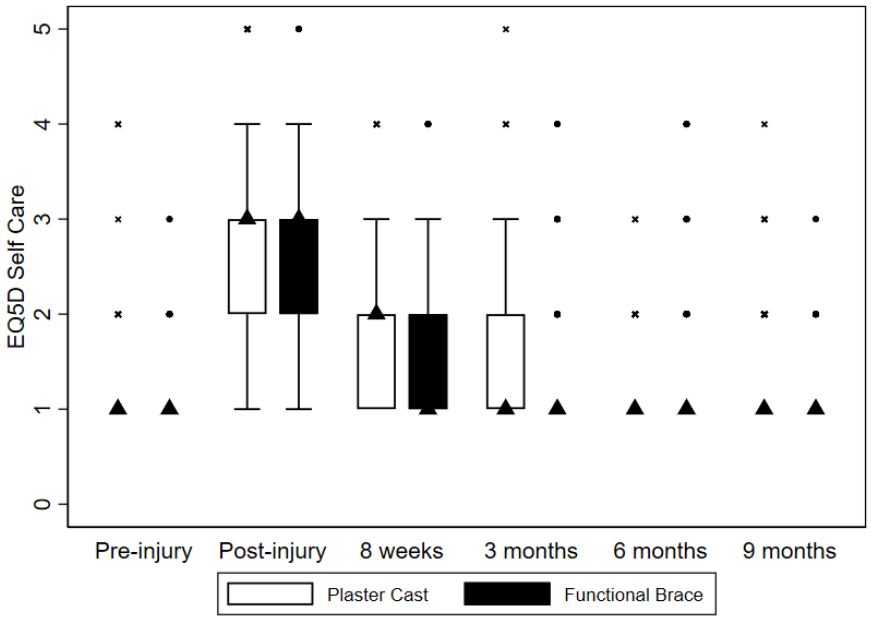

Figure 16: EQ-5D Self Care from baseline pre-injury to 9 months. EQ-5D Self Care values range from 1 to 5 with 1 indicating no problems

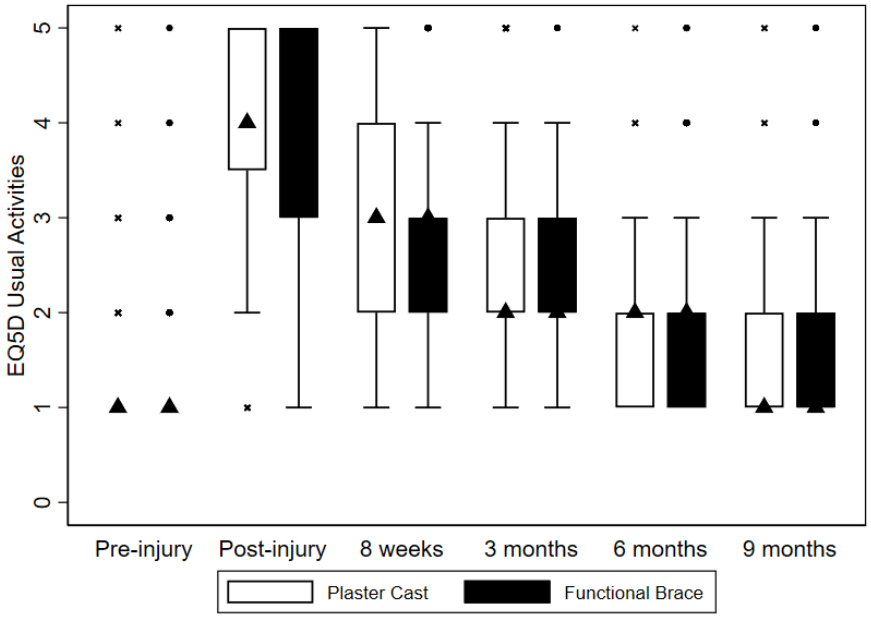

Figure 17: EQ-5D Usual Activities from baseline pre-injury to 9 months. EQ-5D Usual Activities values range from 1 to 5 with 1 indicating no problems

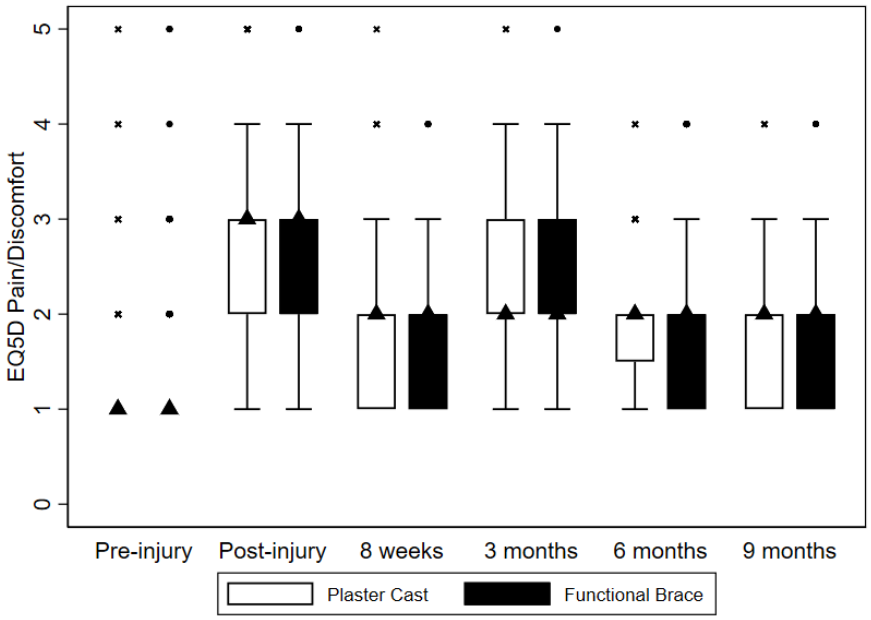

Figure 18: EQ-5D Pain Discomfort from baseline pre-injury to 9 months. EQ-5D Pain Discomfort values range from 1 to 5 with 1 indicating no problems

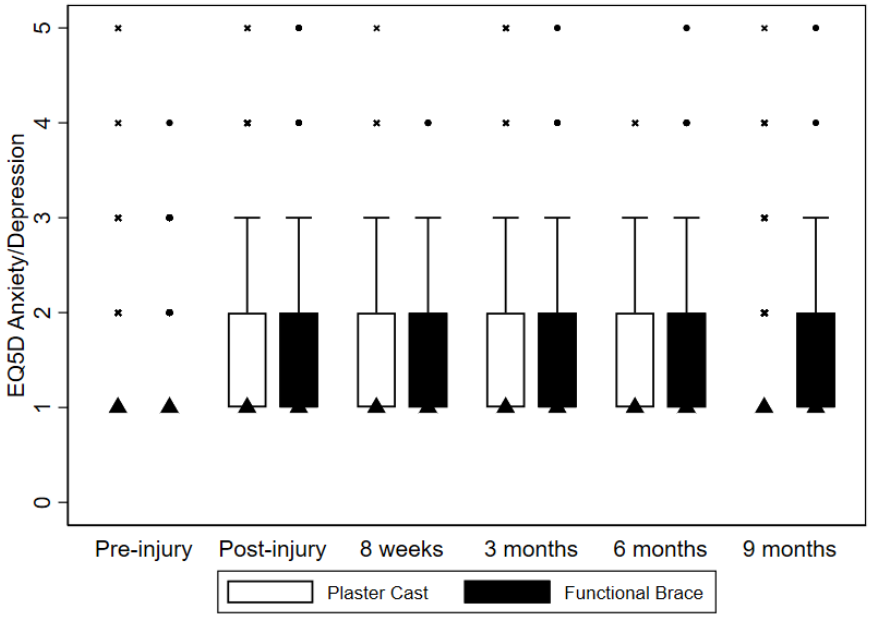

Figure 19: EQ-5D Anxiety Depression from baseline pre-injury to 9 months. EQ-5D Anxiety Depression values range from 1 to 5 with 1 indicating no problems

Appendix 4: Health Economics

Table 27: Summary of unit cost data and data sources

Resource item	Unit cost[1]	Unit of analysis	Source of unit cost
Outpatient care			
Speciality: Orthopaedics	£121.30	per visit	NHS reference costs 2016-17 [51]
Speciality: Pathology	£114.03	per visit	NHS reference costs 2016-17 [51]
Speciality: Radiology	£47.78	per visit	NHS reference costs 2016-17 [51]
Speciality: Physiotherapy (NHS)	£48.81	per visit	NHS reference costs 2016-17 [51]
Speciality: Physiotherapy (Private)	£82.00	per visit	https://www.capitalphysio.com/fees-and-payment/
Speciality: Emergency department	£147.80	per visit	NHS reference costs 2016-17 [51]
Primary and community care			
General practitioner consultations in surgery	£4.00	per minute contact	PSSRU 2018 [42]
General practitioner home visits	£4.00	per minute contact	PSSRU 2018 [42]
General practitioner telephone contacts	£3.80	per 1min telephone consultation lasting 7.1 min	PSSRU 2015 [57]
Practice nurse contacts	£0.53	minute	PSSRU 2018 [42]
District nurse contacts	£0.97	per minute of patient-related work	PSSRU 2018 [42]
Community physiotherapy contacts	£0.87	Per minute of patient-related work	PSSRU 2018 [42]
Calls to NHS direct/111	£8.00	per call	Turner et al. 2012 [58]
Calls for an ambulance or paramedic	£7.21	per call	
Occupational therapy contacts	£0.70	per min	PSSRU 2017 [59]

Personal Social Services			
Meals on wheels (frozen, daily)	£3.60	per meal	Meals on wheels survey, 2018 (http://costsectorcatering.co.uk/sites/default/files/attachment/nacc_-_meals_on_wheels_report_2018.pdf, last accessed 5 June 2019)
Meals on wheels (hot daily)	£3.60	per meal	Meals on wheels survey, 2018 (http://costsectorcatering.co.uk/sites/default/files/attachment/nacc_-_meals_on_wheels_report_2018.pdf, last accessed 5 June 2019)
Laundry services	£4.52	per load	North Yorkshire social care
Social worker contacts	£48.00	per visit	PSSRU 2017, pg 94 [59]
Care worker contacts including help at home	£0.43	per min	PSSRU 2017, pg 125 [59]
Other:			
Aids and Adaptations			
Crutches	£5.61	per item	NHS Catalogue 2018 [46]
Stick	£3.98	per item	NHS Catalogue 2018 [46]
Zimmer frame	£37.70	per item	NHS Catalogue 2018 [46]
Grab rail	£5.03	per item	NHS Catalogue 2018 [46]
Dressing aids	£4.42	per item	NHS Catalogue 2018 [46]
Long-handle shoe horn	£1.78	per item	NHS Catalogue 2018 [46]
Productivity losses			
Days off work	£90.90	per day	Office for National Statistics [47]

[1]When appropriate, costs were inflated or deflated to 2017–18 prices using the Hospital and Community Health Services (HCHS) Pay and Price Inflation

PSSRU: Personal Social Services Research Unit

Table 28: Use of health and social care resources related to two non-surgical treatment options for patients with a primary (first-time) rupture of the Achilles tendon by each follow-up period and treatment arm (complete cases)

	Plaster Cast (N=266)	**Functional brace (N=274)**	**Mean difference (Bootstrapped 95% CI)**	**p-value[1]**
8-week follow-up				
Inpatient Care	**Mean length of stay in days (SE)**			
Hospital stay	0.035 (0.018)	0.071 (0.032)	-0.036 (-0.110 to 0.028)	0.323
	Proportion of participants prescribed anticoagulant as VTE prophylaxis treatment (SE)			
Anticoagulant treatment	0.716 (0.028)	0.594 (0.030)	0.122 (0.032 to 0.200)	0.003
Outpatient care	**Mean no. of visits (SE)**			
Orthopaedics	2.627 (0.107)	1.800 (0.097)	0.827 (0.574 to 1.119)	P<0.001
Pathology	0.041 (0.014)	0.068 (0.023)	-0.027 (-0.084 to 0.025)	0.325
Radiology	0.150 (0.023)	0.146 (0.029)	0.004 (-0.070 to 0.074)	0.907
Physiotherapy NHS	0.228 (0.042)	0.460 (0.064)	-0.232 (-0.397 to -0.095)	0.003
Physiotherapy Private	0.091 (0.037)	0.184 (0.160)	-0.093 (-0.575 to 0.117)	0.576
Emergency Department (Injury –related)	0.104 (0.023)	0.096 (0.021)	0.008 (-0.051 to 0.070)	0.804
Emergency Department (other reasons)	0.029 (0.012)	0.016 (0.008)	0.013 (-0.012 to 0.044)	0.371
Other	0.111 (0.037)	0.168 (0.045)	-0.058 (-0.162 to 0.062)	0.326
Community health care	**Mean no. of contacts (SE)**			

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
GP Visits (surgery)	0.100 (0.024)	0.188 (0.032)	-0.088 (-0.176 to -0.012)	0.028
GP (home visits)	0.008 (0.006)	0 (0)	0.008 (0 to 0.024)	0.148
GP (telephone contacts)	0.084 (0.025)	0.108 (0.031)	-0.024 (-0.103 to 0.049)	0.542
Practice nurse contacts	0.008 (0.006)	0.008 (0.006)	0 (-0.015 to 0.018)	0.964
District nurse contacts	0.151 (0.146)	0 (0)	0.151 (0 to 0.553)	0.293
Community physiotherapy contacts	0.021 (0.013)	0.040 (0.020)	-0.019 (-0.074 to 0.020)	0.429
Calls to NHS direct	0.017 (0.010)	0.008 (0.008)	0.009 (-0.012 to 0.039)	0.499
Calls for an ambulance or paramedic	0.004 (0.004)	0 (0)	0.004 (0 to 0.017)	0.307
Occupational therapy contacts	0.013 (0.009)	0.008 (0.006)	0.005 (-0.012 to 0.034)	0.673
Other	0.216 (0.146)	0.034 (0.015)	0.183 (-0.010 to 0.580)	0.206
Medicines	**Proportion of participants prescribed each class of drug (SE)**			
Analgesics	0.388 (0.055)	0.330 (0.050)	0.058 (-0.083 to 0.213)	0.434
Anti-inflammatories	0.042 (0.013)	0.076 (0.017)	-0.034 (-0.081 to 0.004)	0.110
Anti-coagulant	0.151 (0.023)	0.112 (0.020)	0.039 (-0.026 to 0.093)	0.206
Other	0.017 (0.008)	0.048 (0.014)	-0.031 (-0.064 to -0.001)	0.052
Aids and adaptations	**Mean count (SE)**			
Crutches	1.290 (0.059)	1.124 (0.062)	0.166 (0.012 to 0.341)	0.053
Stick	0.017 (0.010)	0.024 (0.010)	-0.007 (-0.033 to 0.024)	0.598
Zimmer frame	0.054 (0.018)	0.028 (0.010)	0.026 (-0.014 to 0.068)	0.205
Grab Rail	0.046 (0.020)	0 (0)	0.046 (0.013 to 0.090)	0.019

	Plaster Cast (N=266)	**Functional brace (N=274)**	**Mean difference (Bootstrapped 95% CI)**	**p-value[1]**
Dressing aids	0.008 (0.008)	0.008 (0.006)	0 (-0.016 to 0.024)	0.976
Long-handle shoe horn	0.004 (0.004)	0 (0)	0.004 (0 to 0.016)	0.309
Other	0.387 (0.045)	0.220 (0.043)	0.166 (0.040 to 0.277)	0.008
Personal social services	**No. of contacts (SE)**			
Frozen meals on wheels	0	0	-	-
Hot meals on wheels	0	0	-	-
Laundry services	0.029 (0.029)	0 (0)	0.029 (0 to 0.095)	0.309
Social worker contacts	0	0	-	-
Care worker/home help	0.668 (0.542)	0 (0)	0.668 (0 to 2.165)	0.210
Other	0	0	-	-
Productivity losses	**Mean days off work (SE)**			
Days off work	21.227 (1.682)	20.786 (1.637)	0.441 (-3.947 to 5.176)	0.851
Three-month follow-up				
Inpatient Care	**Mean length of stay in days (SE)**			
Hospital stay	0.009 (0.009)	0 (0)	0.009 (0 to 0.034)	0.298
Outpatient care	**Mean no. of visits (SE)**			
Orthopaedics	0.428 (0.055)	0.318 (0.045)	0.110 (-0.035 to 0.256)	0.121
Pathology	0.017 (0.011)	0.024 (0.014)	-0.007 (-0.044 to 0.026)	0.694

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
Radiology	0.057 (0.020)	0.045 (0.017)	0.012 (-0.038 to 0.062)	0.644
Physiotherapy NHS	0.978 (0.070)	0.959 (0.067)	0.019 (-0.175 to 0.180)	0.845
Physiotherapy Private	0.271 (0.073)	0.180 (0.045)	0.091 (-0.069 to 0.279)	0.283
Emergency Department (Injury –related)	0.061 (0.022)	0.033 (0.011)	0.028 (-0.013 to 0.085)	0.241
Emergency Department (other reasons)	0.009 (0.006)	0.004 (0.004)	0.005 (-0.008 to 0.023)	0.524
Other	0.057 (0.018)	0.050 (0.024)	0.007 (-0.057 to 0.062)	0.817
Community health care	**Mean no. of contacts (SE)**			
GP Visits (surgery)	0.088 (0.022)	0.107 (0.029)	-0.019 (-0.099 to 0.057)	0.610
GP (home visits)	0 (0)	(0)	-	-
GP (telephone contacts)	0.044 (0.017)	0.029 (0.013)	0.015 (-0.026 to 0.057)	0.487
Practice nurse contacts	0.004 (0.004)	0.008 (0.008)	-0.004 (-0.026 to 0.009)	0.689
District nurse contacts	0.004 (0.004)	0.004 (0.004)	0 (-0.011 to 0.013)	0.964
Community physiotherapy contacts	0.253 (0.065)	0.201 (0.044)	0.052 (-0.085 to 0.223)	0.500
Calls to NHS direct	0.004 (0.004)	0.004 (0.004)	0 (-0.009 to 0.013)	0.964
Calls for an ambulance or paramedic	0.013 (0.010)	0.004 (0.004)	0.009 (-0.008 to 0.036)	0.385
Occupational therapy contacts	0.022 (0.014)	0.049 (0.027)	-0.027 (-0.096 to 0.022)	0.382
Other	0.061 (0.032)	0.021 (0.012)	0.041 (-0.017 to 0.122)	0.226
Medicines	**Proportion of participants prescribed each class of drug (SE)**			
Analgesics	0.109 (0.021)	0.049 (0.014)	0.060 (0.014 to 0.111)	0.015
Anti-inflammatories	0.008 (0.006)	0.008 (0.006)	0.001 (-0.015 to 0.019)	0.949

	Plaster Cast (N=266)	**Functional brace (N=274)**	**Mean difference (Bootstrapped 95% CI)**	**p-value[1]**
Anti-coagulant	0.022 (0.010)	0.016 (0.008)	0.005 (-0.019 to 0.031)	0.665
Other	0.017 (0.009)	0 (0)	0.017 (0.004 to 0.039)	0.038
Aids and adaptations	**Mean count (SE)**			
Crutches	0.118 (0.030)	0.106 (0.029)	0.012 (-0.071 to 0.100)	0.778
Stick	0.070 (0.20)	0.033 (0.014)	0.037 (-0.009 to 0.086)	0.124
Zimmer frame	0 (0)	0.004 (0.004)	0.004 (-0.016 to 0)	0.335
Grab Rail	0.022 (0.013)	0 (0)	0.022 (0 to 0.055)	0.084
Dressing aids	0.031 (0.020)	0 (0)	0.031 (0.004 to 0.083)	0.112
Long-handle shoe horn	0.013 (0.008)	0 (0)	0.013 (0 to 0.032)	0.073
Other	0.227 (0.064)	0.155 (0.038)	0.072 (-0.056 to 0.244)	0.330
Personal social services (PSS)	**No. of contacts (SE)**			
Frozen meals on wheels	0 (0)	0 (0)	-	-
Hot meals on wheels	0 (0)	0 (0)	-	-
Laundry services	0 (0)	0.008 (0.008)	-0.008 (-0.033 to 0)	0.333
Social worker contacts	0 (0)	0 (0)	-	-
Care worker/home help	0 (0)	0 (0)	-	-
Other	0.009 (0.009)	0 (0)	0.009 (0 to 0.029)	0.301
Productivity losses	**No. of days off work**			
Days off work	4.511 (0.820)	5.44 (0.880)	-0.930 (-3.342 to 1.494)	0.441

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
Six-month follow-up				
Subsequent Inpatient Care	**Mean length of stay in days (SE)**			
Hospital stay	0 (0)	0 (0)	-	-
Outpatient care	**Mean no. of visits (SE)**			
Orthopaedics	0.224 (0.043)	0.289 (0.059)	-0.065 (-0.230 to 0.071)	0.379
Pathology	0.018 (0.011)	0.030 (0.015)	-0.012 (-0.048 to 0.024)	0.532
Radiology	0.044 (0.015)	0.033 (0.012)	0.011 (-0.027 to 0.050)	0.564
Physiotherapy NHS	1.946 (0.257)	1.915 (0.182)	0.031 (-0.550 to 0.674)	0.920
Physiotherapy Private	0.417 (0.103)	0.366 (0.091)	0.051 (-0.218 to 0.316)	0.710
Emergency Department (Injury –related)	0.013 (0.008)	0.026 (0.010)	-0.012 (-0.039 to 0.014)	0.353
Emergency Department (other reasons)	0.013 (0.008)	0.017 (0.008)	-0.004 (-0.026 to 0.018)	0.756
Other	0.093 (0.031)	0.067 (0.031)	0.026 (-0.065 to 0.103)	0.551
Community health care	**Mean no. of contacts (SE)**			
GP Visits (surgery)	0.094 (0.037)	0.060 (0.018)	0.035 (-0.034 to 0.122)	0.390
GP (home visits)	0 (0)	0.009 (0.009)	-0.009 (-0.028 to 0)	0.331
GP (telephone contacts)	0.018 (0.011)	0.021 (0.015)	-0.003 (-0.046 to 0.031)	0.861
Practice nurse contacts	0 (0)	0.004 (0.004)	-0.004 (-0.017 to 0)	0.331
District nurse contacts	0 (0)	0 (0)	-	-

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
Community physiotherapy contacts	0.605 (0.187)	0.557 (0.101)	0.048 (-0.311 to 0.547)	0.819
Calls to NHS direct	0 (0)	0 (0)	-	-
Calls for an ambulance or paramedic	0 (0)	0 (0)	-	-
Occupational therapy contacts	0.067 (0.033)	0.043 (0.023)	0.025 (-0.054 to 0.115)	0.537
Other	0.058 (0.043)	0.106 (0.077)	-0.048 (-0.264 to 0.085)	0.589
Medicines	**Proportion of participants prescribed each class of drug (SE)**			
Analgesics	0.103 (0.020)	0.064 (0.016)	0.040 (-0.008 to 0.090)	0.124
Anti-inflammatories	0.009 (0.006)	0.021 (0.009)	-0.012 (-0.036 to 0.009)	0.286
Anti-coagulant	0.004 (0.004)	0.013 (0.007)	-0.008 (-0.025 to 0.009)	0.343
Other	0.009 (0.006)	0.008 (0.006)	0 (-0.013 to 0.019)	0.955
Aids and adaptations	**Mean count (SE)**			
Crutches	0.054 (0.021)	0.051 (0.020)	0.003 (-0.051 to 0.066)	0.917
Stick	0.031 (0.012)	0.030 (0.015)	0.002 (-0.041 to 0.035)	0.929
Zimmer frame	0.009 (0.009)	0.013 (0.007)	-0.004 (-0.022)	0.742
Grab Rail	0.018 (0.011)	0.008 (0.008)	0.009 (-0.013 to 0.038)	0.495
Dressing aids	0 (0)	0 (0)	-	-
Long-handle shoe horn	0.018 (0.009)	0.008 (0.006)	0.009 (-0.009 to 0.032)	0.376
Other	0.144 (0.047)	0.091 (0.030)	0.054 (-0.031 to 0.188)	0.329
Personal social services	**No. of contacts (SE)**			

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
Frozen meals on wheels	0 (0)	0 (0)	-	-
Hot meals on wheels	0 (0)	0 (0)	-	-
Laundry services	0 (0)	0 (0)	-	-
Social worker contacts	0 (0)	0 (0)	-	-
Care worker/home help	0.036 (0.036)	0 (0)	0.036 (0 to 0.138)	
Other	0 (0)	0 (0)	-	-
Productivity losses	**No. of days off work**			
Days off work	1.894 (0.743)	4.301 (1.172)	-2.407 (-5.642 to -0.110)	0.085
Nine-month follow-up				
Subsequent Inpatient Care	**Mean length of stay in days (SE)**			
Hospital stay	0 (0)	0 (0)	-	-
Outpatient care	**Mean no. of visits (SE)**			
Orthopaedics	0.090 (0.024)	0.077 (0.030)	0.013 (-0.060 to 0.081)	0.736
Pathology	0.016 (0.008)	0.073 (0.027)	-0.057 (-0.120 to -0.012)	0.047
Radiology	0.029 (0.011)	0.012 (0.009)	0.017 (-0.005 to 0.047)	0.209
Physiotherapy NHS	0.709 (0.108)	0.857 (0.147)	-0.148 (-0.540 to 0.178)	0.423
Physiotherapy Private	0.234 (0.073)	0.174 (0.058)	0.060 (-0.103 to 0.260)	0.520

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
Emergency Department (injury –related)	0.004 (0.004)	0.008 (0.005)	-0.004 (-0.016 to 0.012)	0.599
Emergency Department (other reasons)	0.020 (0.011)	0.030 (0.014)	-0.010 (-0.051 to 0.019)	0.566
Other	0.140 (0.058)	0.089 (0.045)	0.051 (-0.090 to 0.206)	0.487
Community health care	**Mean no. of contacts (SE)**			
GP Visits (surgery)	0.058 (0.024)	0.046 (0.017)	0.011 (-0.046 to 0.072)	0.697
GP (home visits)	0 (0)	0 (0)	-	-
GP (telephone contacts)	0.008 (0.006)	0.004 (0.004)	0.004 (-0.007 to 0.021)	0.527
Practice nurse contacts	0 (0)	0.004 (0.004)	-0.004 (-0.016 to 0)	0.333
District nurse contacts	0 (0)	0 (0)	-	-
Community physiotherapy contacts	0.169 (0.052)	0.255 (0.066)	-0.085 (-0.258 to 0.071)	0.317
Calls to NHS direct	0 (0)	0 (0)	-	-
Calls for an ambulance or paramedic	0 (0)	0 (0)	-	-
Occupational therapy contacts	0.074 (0.038)	0.031 (0.017)	0.043 (-0.033 to 0.128)	0.291
Other	0.136 (0.070)	0.131 (0.100)	0.005 (-0.307 to 0.214)	0.967
Medicines	**Proportion of participants prescribed each class of drug (SE)**			
Analgesics	0.037 (0.012)	0.031 (0.011)	0.006 (-0.027 to 0.037)	0.703
Anti-inflammatories	0.012 (0.007)	0 (0)	0.012 (0 to 0.029)	0.073
Anti-coagulant	0.004 (0.004)	0 (0)	0.004 (0 to 0.016)	0.301
Other	0.004 (0.004)	0.004 (0.004)	0 (-0.008 to 0.016)	0.964

	Plaster Cast (N=266)	Functional brace (N=274)	Mean difference (Bootstrapped 95% CI)	p-value[1]
Aids and adaptations	**Mean count (SE)**			
Crutches	0 (0)	0.008 (0.008)	-0.008 (-0.029 to 0)	0.334
Stick	0.012 (0.009)	0.004 (0.004)	0.009 (-0.008 to 0.036)	0.383
Zimmer frame	0 (0)	0 (0)	-	-
Grab Rail	0.008 (0.008)	0 (0)	0.008 (0 to 0.031)	0.301
Dressing aids	0 (0)	0 (0)	-	-
Long-handle shoe horn	0.004 (0.004)	0 (0)	0.004 (0 to 0.017)	0.301
Other	0.062 (0.025)	0.093 (0.026)	-0.031 (-0.097 to 0.046)	0.397
Personal social services	**No. of contacts (SE)**			
Frozen meals on wheels	0.045 (0.045)	0 (0)	0.045 (0 to 0.182)	0.301
Hot meals on wheels	0 (0)	0 (0)	-	-
Laundry services	0.045 (0.045)	0 (0)	0.045 (0 to 0.182)	0.301
Social worker contacts	0 (0)	0 (0)	-	-
Care worker/home help	0.008 (0.008)	0 (0)	0.008 (0 to 0.037)	0.301
Other	0 (0)	0 (0)	-	-
Productivity losses	**No. of days off work**			
Days off work	0.340 (0.340)	1.952 (0.758)	-1.613 (-3.357 to 0.019)	0.055

[1]Comparisons of Plaster Cast vs Functional Brace groups carried out using Student t-tests for continuous variables and χ^2 test for categorical variables.

[B] GP: general practitioner