An Investigation into Accelerated Rehabilitation Strategies Following an Achilles Tendon Rupture

By

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Volume One of Two

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Acknowledgements

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Declaration

This thesis is my work, with the exception of a sample size calculation within Chapter 3 and the randomisation generation within Chapters 3 and 5, which were carried out by Nicholas Parsons (Statistician). This thesis has not been submitted for a degree at another university.

The following research papers have been published as a direct result of the work contained in this thesis. These were published prior to examination of, but during the study period of the thesis:

Kearney R, S Lamb, N Parsons, J Achten, M Costa, The Achilles tendon Total Rupture Score: A Study of Responsiveness, Internal Consistency and Convergent Validity on Patients with Acute Achilles tendon Ruptures, Health and Quality of Life Outcomes (*In Press*)

Kearney R, S Lamb, J Achten, C Plant and M Costa, A systematic review of patient reported outcome measures used to assess Achilles tendon rupture management: What's being used and should we be using it? *British Journal of Sports Medicine (In Press)*

Kearney R and M Costa, Current concepts in the rehabilitation of an acute rupture of the Achilles tendon, *Journal of Bone and Joint Surgery (Br)*, **94**, 2012, 21-28.

Kearney R, J Achten, K McGuiness and M Costa, A systematic review of early rehabilitation methods following a rupture of the Achilles tendon. *Physiotherapy,* **98**, 2012, 24-32.

Kearney R, S Lamb, J Achten, N Parsons and M Costa, In-Shoe plantar pressures within ankle foot orthoses: Implications for the management of Achilles tendon ruptures. *American Journal of Sports Medicine,* **39**, 2011, 2679-2685.

The following research has been presented at local and national conferences, as a direct result of the work contained in this thesis. These presentations occurred prior to the examination of, but during the study period of the thesis:

Jan 2011: Warwick Medical School Symposium: Poster Presentation: An investigation into accelerated rehabilitation strategies following an Achilles tendon rupture

Feb 2011: Society for Research in Rehabilitation: Poster Presentation: A systematic review of early rehabilitation methods following an Achilles tendon rupture

March 2011: Arthritis Research UK: Poster Presentation: An investigation into accelerated rehabilitation strategies following an Achilles tendon rupture

May 2011: British Trauma Society: Poster Presentation: The effect of maintained plantarflexion within an ankle foot orthoses on functional outcomes and gait parameters following an Achilles tendon rupture

May 2012: European Federation of National Associations of Orthopaedics and Traumatology: The Achilles tendon Total Rupture Score: A Study to Explore Further Aspects of Validity.

June 2012: International Society for Posture and Gait Research: Poster Presentation: The effect of orthotic design and the number of heel-wedges on in-shoe plantar pressures during walking: implications for Achilles tendon rupture rehabilitation.

Chapter 7 of this thesis contains some data previously published for a separate clinical trial, not part of this thesis. This data was collected by me in addition to my involvement with the implementation, analysis, final write-up and subsequent published article:

Kearney R, J Achten, N Parsons, M Costa, The comprehensive cohort model in a pilot trial in orthopaedic trauma. *BMC Medical Research Methodology,* 11, 2011, p.11-39.

Preface

This thesis firstly provides a narrative overview of the literature to date regarding the management of an Achilles tendon rupture, which leads to four specific aims. These four aims directly relate to the Medical Research Councils framework for developing complex interventions. They address the interrelated concepts of defining the intervention components, developing an appropriate theoretical framework to establish why and to what extent each of these components is important, piloting the interventions and assessing their effectiveness.

To achieve these aims a wide range of research methods have been implemented. These have included systematic reviews, experimental designs, pilot clinical trials and outcome validation research. To successfully implement these methods, completion of this thesis has required research management skills including costing the project, applying for funding, completing and gaining NHS ethics approval, research and development approval and presentation of progress reports.

The capacity to successfully complete the aims of this thesis using the described methods was achieved through appropriate supervision and a tailored programme of courses and conferences to develop these skills, outlined at the end of this thesis. Furthermore to demonstrate the original contribution of this work, selected chapters have been submitted and accepted for publication, in addition to being accepted for national and international conference presentations.

This thesis will lead the reader through the development of a complex intervention for Achilles tendon rupture management, whilst also highlighting of the strengths and limitations of each chapter. This reflects my on-going development to enable future independent research leadership in this area.

Thesis Abstract

Background
Rupture of the Achilles tendon occurs in over 11,000 people annually in the UK. Traditional management using cast immobilisation is being slowly replaced by immediate weight bearing rehabilitation, but currently there is no consensus regarding the exact protocol to be used.

The aim of this thesis was to develop an immediate weight bearing rehabilitation protocol for patients who have sustained an acute rupture of their Achilles tendon to inform a definitive evaluation of its effectiveness. To achieve this aim a framework (by the Medical Research Council) for defining and developing interventions with several components was used to underpin the structure of this thesis.

Pre-Clinical Development
The first two objectives of this thesis were focussed on the 'pre-clinical' development phase. Firstly, a systematic review of the evidence base identified the components that define immediate weight bearing rehabilitation. Two of these were evaluated in controlled gait analysis studies to inform and develop a rationale for the intervention to establish what changes are expected and why. The key findings showed that rigid orthoses designs with a large degree of plantarflexion, increased heel pressures, reduced forefoot pressures and decreased the amount of time spent in the terminal stance and pre-swing phase of the gait cycle.

Feasibility and Piloting
The first clinical phases (feasibility/piloting) followed, which included testing procedures, establishing likely recruitment and follow up. Alongside this, a further systematic review was undertaken to identify what outcome measures are used in research for this injury to determine effectiveness. The Achilles tendon Total Rupture score was the only disease specific patient reported measure identified with supporting validation research. Further evaluation of its measurement properties found the score to be internally consistent, responsive and with good construct validity.

Conclusions
This thesis defines the rehabilitation components, proposes a theoretical framework and tests this in practice. The results will ensure that rehabilitation after an acute Achilles tendon rupture is based on a systematically developed protocol rather than ad hoc practice. This will now be used to inform future definitive research in this area.

Abbreviations

AAOS	American Association of Orthopaedic Surgery
AFO	Ankle Foot Orthoses
AMED	The Allied and Complementary Medicine Database
ATRS	Achilles tendon Total Rupture Score
B1	Rigid rocker bottom ankle foot orthoses
B2	Ankle foot orthoses 'dynamic'
B3	Ankle foot orthoses 'ToeOff'
CE	Clause Eiermann
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CONSORT	Consolidated Standards of Reporting Trials
CP	Caroline Plant
CRF	Clinical Reporting Forms
DF	Dorsiflexion
DMC	Data Monitoring Committee
DRI	Disability Rating Index
EMBASE	The Excerpta Medica database
FU	Follow Up
GCP	Good Clinical Practice
HTA	Health Technology Assessment
IDEAL	Idea, Development, Evaluation, Assessment and Long term study
ISRCTN	International Standard Randomised Controlled Trial Number
IWB	Immediate Weight Bearing
KM	Katie McGuinness
KPa	Kilopascal
L	Left
MEDLINE	Database on biomedicine as they relate to health care
MRC	Medical Research Council
NWB	Non Weight Bearing
PFO	Pedro Foguet
PF	Plantarflexion
PROM	Patient Reported Outcome Measure

Abbreviations

R	Right
RCT	Randomised Controlled Trial
R&D	Research and Development
RK	Rebecca Kearney
ROM	Range of Movement
SAE	Serious Adverse Event
SD	Standard Deviation
TA	Tendo Achilles
TSC	Trial Steering Committee
VAS	Visual Analogue Scale
WB	Weight Bearing
W0	No heel inserts
W1	One heel insert
W2	Two heel inserts
W3	Three heel inserts

1 Introduction and Thesis Aims

Declarations

This work has been published:

Kearney, R and M Costa, Current concepts in the rehabilitation of an acute rupture of the Achilles tendon, *Journal of Bone and Joint Surgery (Br)* **94**, 2012, 21-28.

Funding Body

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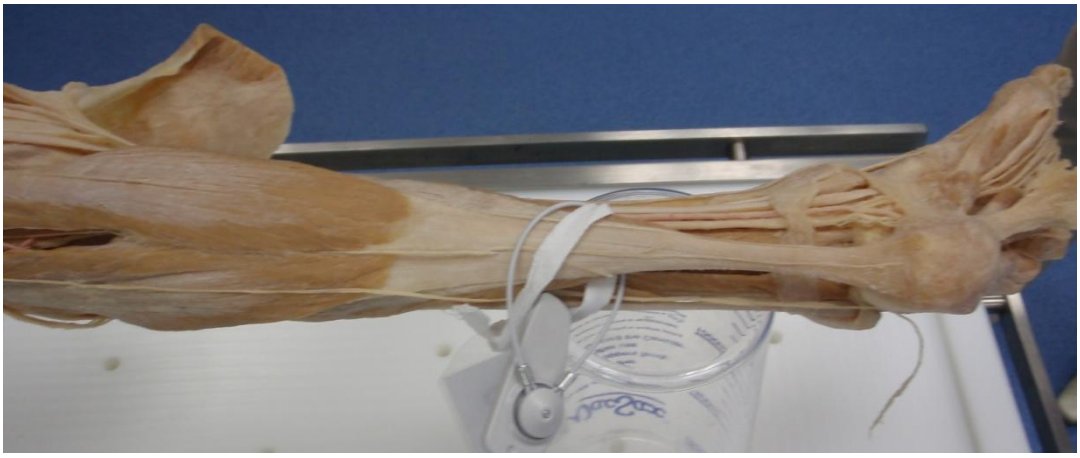
1.1 Achilles tendon: normal structure and function

Figure 1.1 depicts the overall muscular anatomy of the lower leg. The muscles of the lower leg are divided into three fascial compartments; the anterior, lateral and posterior. They are separated by the anterior and posterior intermuscular septa and the interosseous membrane. The anterior compartment muscles are predominantly responsible for dorsiflexion at the ankle. The lateral compartment muscles predominantly evert the foot, and weakly contribute to ankle plantarflexion. Finally, the largest of the three compartments comprises of the posterior compartment muscles, which are the strong plantarflexors of the ankle[1].



(a) Posterior aspect

(b) Medial aspect

Figure 1.1: Lower leg

The posterior calf muscles are subdivided into a superficial and deep layer. The superficial layer is formed by three muscles. These muscles are the gastrocnemius, soleus and plantaris. The deep layer is formed by popliteus, flexor digitoum longus, flexor hallucis longus and tibialis posterior. Both are innervated by the tibial nerve (arising from S1 and S2)[1].

The gastrocnemius starts from the condyles of the posterior surface of the distal femur to approximately the mid calf. The soleus runs deep to this, with plantaris crossing obliquely between the two[2], this is known as the triceps surae. As the muscles descend they enter a broad aponeurosis. Moving from the musculotendinous junction, distally, the tendon gradually becomes more rounded to 4cm above the calcaneus. The tendon then attaches distally to the middle one third of the posterior surface of the calcaneus. This tendon is the tendo Achilles (TA)[3]. The TA is the largest tendon in the human body, it enables the forces generated by the triceps surae to be transmitted. In doing this the TA facilitates joint motion[2].

The blood supply to the TA comes from three sources. These are the musculotendinous junction, the paratenon and at the tendon insertion to the bone. There is an area of hypovascularity located 3-6 cm above the calcaneal insertion. This is where the tendon fibres spiral laterally through 90^{o}, such that the anterior fibres become medial[4].

The macroscopic structure of the TA displays a hierarchical organisation demonstrated in Figure 1.2. The smallest sub-unit being a tropocollagen triple helix through to the largest macrostructure consisting of grouped fascicles within an epitenon envelope. This is surrounded by a fluid filled paratenon, which functions to minimise friction[2]. The collagen fibres are surrounded by a matrix ground substance,

of which the hydration is regulated by proteoglycons. This provides structural support and a medium for diffusion of nutrients and is biosynthesised by tenocytes.

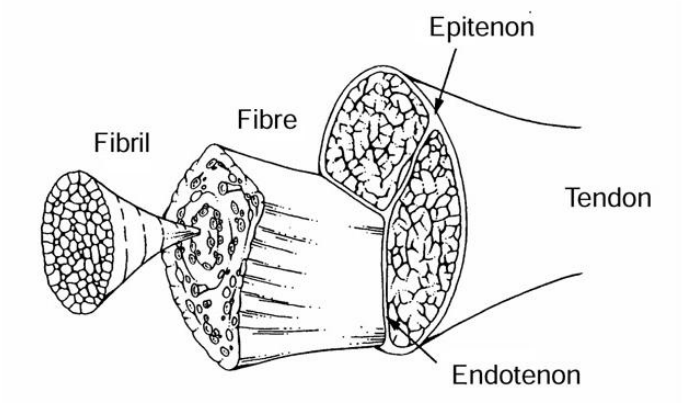


Figure 1.2: Tendon structure (Source: Fenwick *et al* [5])

The organisation of a tendon has important characteristics which contribute to the biomechanical properties of it. The first of these structural features are seen amongst the arrangement of microfibrils (formed by five grouped tropocollagens). Each microfibril overlaps each other by a quarter and these cross links contribute to the tensile strength of the tendon. Secondly, the fibres are arranged in a parallel arrangement, which at rest have a crimped configuration. This crimped configuration straightens when the tendon is loaded. When the load is removed the stored elastic energy is released and fibres re-crimp[2].

Ultimately these characteristics work together to resist high tensile forces with minimal loss of energy and deformation. These mechanical responses of the tendon to stress and strain have been defined by the stress-strain curve[6], shown in Figure 1.3. It contains four key regions; the first is the toe region whereby the crimped fibre arrangement straightens up to 2% of strain. Beyond this the fibres are straight and respond linearly to stress up to 4% strain. Under 4% strain the tendon can return to its resting state. Beyond 4% the tendon begins to undergo micro-failure, involving

the breakage of cross-links and irreversible plastic deformation. By 8% the tendon undergoes complete failure[6].

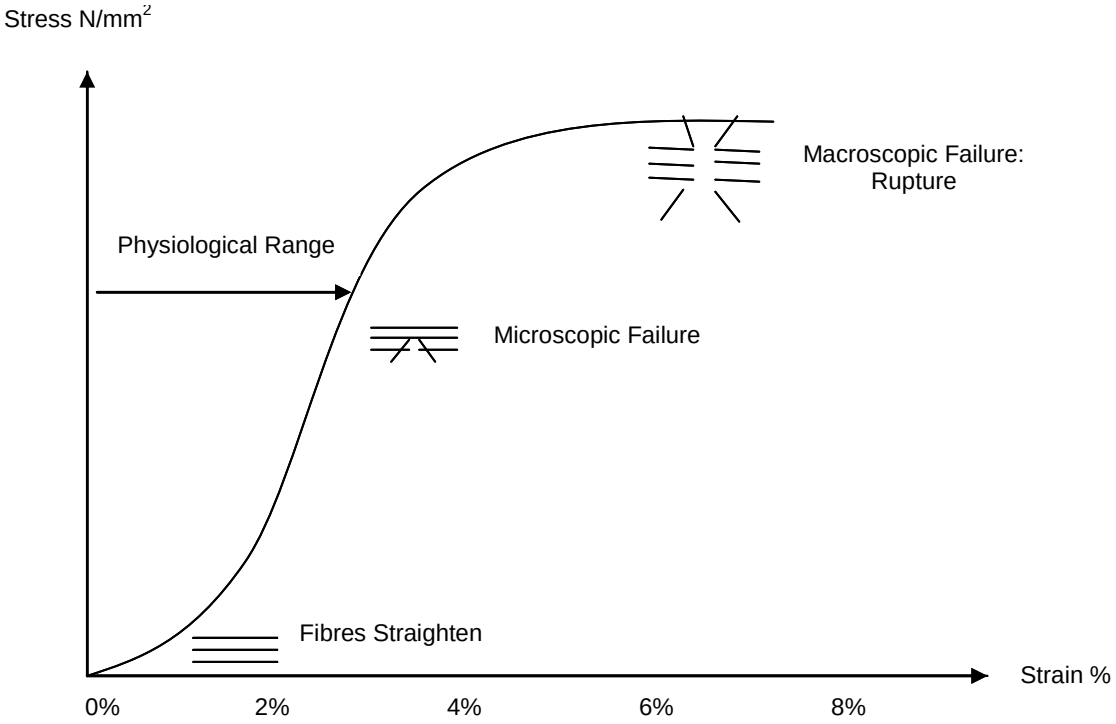


Figure 1.3: Stress-strain curve (Source: Evans and Stanish[2])

However, tendon characteristics are not dependent on these mechanisms alone. Tendons are also viscoelastic tissues (time and rate dependent). This property results in decreased stress with time under constant deformation (stress relaxation) and increased deformation with time under constant load (creep). Tendons also display mechanical hysteresis, which is the amount of elastic strain energy lost as heat during the stretch-recoil cycle[7]. The tension generated across the tendon is also dependent upon the type of muscle contraction. Eccentric loads producing the highest, followed by concentric and finally isometric muscle actions. These are all important features when considering the mechanisms of tendon injury and rehabilitation[2].

1.2 Achilles tendon rupture: epidemiology, etiology and diagnosis

The TA is the most commonly ruptured tendon in the human body[8]. European figures show that there is an incidence of approximately 18 per 100 000 people per year[9]. This common injury has a bi-modal distribution, the first peak being within males aged 30-40 years and the second amongst non-athletic women aged 60-80 years[10]. The first peak in incidence is often associated with sport participation, predominantly football and racquet sports, whereas the second peak often occurs during normal daily activities[10]. However both are the result of the same mechanisms.

The mechanism by which a rupture occurs has been broadly classified into two. The most common happens whilst pushing off with the foot and extending at the knee (e.g. sprint starts, jumping, lunging). The second occurs during forced and unexpected dorsiflexion of the ankle (e.g. fall, road traffic accident). In relation to the biomechanics of the Achilles tendon, outlined in Chapter 1.1, the first mechanism often occurs under 4% of strain, below the threshold for macro-failure, whereas the second mechanism occurs above the threshold for macro-failure[11].

The reasons proposed for spontaneous rupture of the TA, below the threshold for macro-failure, is multi-factorial[11]. The most widely accepted explanation is that spontaneous ruptures are the consequence of a previously abnormal tendon[12]. These abnormalities can result in a painful tendon condition termed ‘tendinopathy’. Yet, many tendons with degenerative features are asymptomatic. The degeneration of the tendon results in decreased cellularity, decreased matrix organisation, increased infiltration of blood vessels and increased type III collagen. It is considered to be the result of an imbalance between the protective/regenerative functions that metalloproteinase enzymes are thought to have a key role[13].

The cause of tendon abnormalities have been attributed to a number of external factors including topical corticosteroids[14], fluoroquinolone antibiotics[15] and mechanical abnormalities of the foot[16]. Intrinsic factors have also been associated with a predisposition to tendinopathy. Examples of these include autoimmune and neurological conditions[17]. However, degenerative changes within tendons are common amongst the population as a whole, regardless of the presence or absence of any of these factors.

When a patient sustains a TA rupture they typically present with sudden pain in the area of the TA. Often patients report a feeling of being 'kicked' in the back of the leg[11]. In December 2009 the American Academy of Orthopaedic Surgeons (AAOS) published the first guidelines on the topic of mid-substance TA ruptures. These guidelines included how to diagnose a TA rupture[18]. Following a systematic review of the literature the AAOS concluded there was strong evidence to support the diagnosis based on two, of four, physical findings. These physical findings were, a positive Thompson test (Simmonds squeeze test), decreased ankle plantarflexion strength, presence of a palpable gap or increased ankle dorsiflexion with gentle manipulation[19]. The AAOS were unable to recommend the use of routine magnetic resonance imaging, ultrasound or radiographs for the diagnosis of Achilles tendon ruptures. However, imaging has been suggested to be of use in the context of a selection tool for management and on-going assessment post rupture[20].

1.3 Achilles tendon rupture: healing, repair and common problems

Studies regarding tendon healing have pre-dominantly been undertaken in transected animal models. These methods have limitations to the application of human models that are associated with degenerative mechanisms. However, the

research has consistently shown that there are three overlapping phases regarding the healing response. These are inflammation, proliferation and remodelling[21].

When the tendon ruptures, the gap quickly fills with a blood clot. By 24 hours monocytes and macrophages predominate and phagocytosis of necrotic tissues occurs. Over the next few days angiogenesis is initiated and tenocyte proliferation, leading to the occurrence of type III collagen synthesis. After a few days the proliferative phase begins. This results in a peak of type III collagen synthesis and organisation. By approximately six weeks, remodelling occurs which is characterised by decreased cellularity, decreased collagen synthesis, an increase in type I collagen compared to type III and a gradual change to scar-like tendon tissue. This process continues up to 12 months[21-22].

Throughout the healing process there are a number of complications that can occur. These commonly include, adhesions, disturbed sensibility, re-rupture, tendon lengthening, delayed/poor healing response, superficial/deep wound infection, muscle atrophy, venous thromboembolism and gait abnormalities[9,23-24]. Furthermore the physiological effects of decreased mechanical loading and immobilisation of the tendon result in detrimental alterations in collagen fibre organisation and decreased tenocyte proliferation[21]. Subsequently research has been focused on decreasing the incidence of these common problems within clinical practice, in combination with optimising the healing and functional recovery of this debilitating injury.

1.4 Achilles tendon rupture: management options

Management of a TA rupture was first described in the literature in 1575 by Ambroise Pare. The author presented a method of non-operative management, using none weight bearing rehabilitation (NWB). This method remained the

management of choice until the 1920's. At this time an alternative approach, using an open operative method, to stitch the two tendon ends together, followed by NWB, was reported[25]. This method grew in popularity and by the 1970's there was a strong debate regarding which method of management was superior. This was summarised by an editorial within the Lancet in 1973, stating that it would be difficult to justify a surgical procedure if non-operative methods are capable of equivalent results[26].

In 1981 Nistor *et al*[27] published the first randomised controlled trial (RCT) to address this very question. They randomly allocated 105 patients to receive either operative or non-operative management, followed by six to nine weeks of NWB cast immobilisation. The results were based on strength measurements, calf circumference and complications.

The results of this first RCT showed two deep wound infections and two re-ruptures within the operative group. This was in comparison to five re-ruptures within the non-operative group. No differences were found between all other outcomes. Subsequently the authors concluded that due to the minimal differences between the groups operative management was unnecessary.

This article was very important for the development of TA rupture management. This is because of its RCT design, which was novel at that particular point in time. However the key limitation of this article was its inadequate method of randomisation, based upon which operating surgeon was working on the day the patient presented. Further limitations include inadequate reporting of inclusion and exclusion criteria, no defined follow-up outcome collection points and excluding trial protocol violations from the final analysis.

This land mark study was followed by the first review of the literature in 1986. This was reported by Wills *et al*[25]. They presented literature from the previous 25 years regarding operative versus non-operative management. They concluded the opposite to Nistor *et al*[27], reporting much higher rates of re-rupture with non-operatively managed patients compared to operatively managed patients (17.7% compared to 1.54%). This was in contrast to other complications which were reported to be higher within the operative group (20%) compared to non-operative management (10%).

This article was important in that it was the first article that summarised the literature to date, however, this was only a narrative review. It had no systematic, reproducible methodology to identify appropriate articles. Therefore it is unknown if key articles were included or not included by the authors, leading to potential selection bias. Furthermore the articles were not subject to a scoring system or critique to determine the reliability and validity of the results reported by the included articles.

Further randomised controlled trials were carried out comparing operative to non-operative management to address some of the limitations within the 1981 Nistor *et al*[27] study. These were carried out by Cetti *et al*[28] in 1993, Thermann *et al*[29], Majewski *et al*[30] and Moller *et al*[31] in 2001. Although the research question within each study was to compare operative to non-operative management, there was a common confounding factor within each one. This was the fact that within each RCT the operative and non-operatively managed groups received different rehabilitation programmes. Therefore it is not clear if the results are a reflection of a different rehabilitation approach or the operative/non-operative management. This is in

contrast to current practice involving the same rehabilitation programmes for operative and non-operatively managed patients[32].

The method of rehabilitation used post rupture has recently become a more pertinent research question within the literature associated with TA ruptures, rather than operative versus non-operative management. These RCT's have compared traditional NWB cast immobilisation to an earlier weight bearing cast or a NWB cast followed by a weight bearing ankle foot orthoses (AFO). These were carried out by Saleh *et al* 1992[33], Cetti *et al* 1994[34], Mortensen *et al* 1999[35], Kangas *et al* 2003[36] and Maffulli *et al* 2003[37]. All these studies concluded favourable results for early weight bearing compared to prolonged NWB.

The first meta-analysis, using randomised and quasi-randomised evidence, on the topic of TA rupture management was published in 2002 by Bhandari *et al*[38]. This was shortly followed by a Cochrane review on the same topic, including RCT's only, published in 2004[39]. Both meta-analyses concluded that the incidence of re-rupture amongst operatively managed patients was lower compared to non-operatively managed patients (3% compared to 12%). However this needed to be balanced against the increase in incidence of other complications compared to non-operative management (34% compared to 3%).

The key finding within the Cochrane review laid within their comparison of NWB cast immobilisation to weight bearing protocols. This demonstrated a reduction of re-rupture incidence from 12% to 2% within non-operatively managed patients (equivalent results seen in patients managed operatively). Therefore, with an already low incidence of other complications (3%) the authors discussed the need to investigate rehabilitation strategies further.

The Cochrane review group addressed all the previously discussed limitations of the earlier narrative reviews. They reported a systematic and reproducible methodology, with subsequent quality assessment of the articles, using a scoring system. The only limitation of this review was the use of re-rupture rate as the primary outcome. This is because although this is an important consideration, this outcome provides no indication of the functional results obtained with each treatment group. However, a meta-analysis in this topic area using functional outcomes as the primary outcome would not be possible secondary to the range that are currently used.

As a consequence of these meta-analysis findings, accelerated rehabilitation strategies were progressed further. In 2006 the first RCT's comparing NWB cast immobilisation to immediate weight bearing (IWB) within an AFO were published[40]. This article, by Costa *et al,* comprised of two separate RCT's within the same paper. The first compared these two rehabilitation strategies within patients managed operatively and the second compared them within patients managed non-operatively. The author's key findings were that IWB is safe in both groups and also offers the practical mobility advantages of IWB as opposed to NWB using crutches. However, no comparisons could be made between operatively and non-operatively managed patients because patients were not randomised to these interventions.

This resulted in a subsequent research question comparing operative to non-operative management using IWB rehabilitation methods. This was carried out by Metz *et al* in 2008[41], who found no statistically significant differences between the two groups regarding complications or return to sport and Willits *et al* in 2010[32], who concluded the same regarding re-rupture rates, as the primary outcome.

However a number of limitations exist within the design of these studies. Firstly within the study by Metz *et al*[41], although both groups used IWB rehabilitation, they followed different rehabilitation protocols. The reasons for these differences were not discussed by the authors and are a confounding factor within the study. Furthermore no valid patient reported outcome measure (PROM) was used by the authors, only a question asking patients to retrospectively re-call 'return to sports' at follow-up appointments. This is open to both re-call bias and interpretation of when a patient regards return to sport (i.e. first training session or first competition). This study also does not take into account the second peak within the bi-modal distribution of this injury (non-athletic women aged 60-80 years) for whom this outcome measure may be irrelevant.

Conversely within the study by Willits *et al*[32], the same rehabilitation method was used within both groups. However the key limitation of this paper is its external validity, secondary to the patient sample being recruited exclusively from two sports medicine clinics. Consequently the question regarding operative versus non-operative management using accelerated rehabilitation currently requires further investigation.

Alongside these two research areas, the method of operative management has also been debated. Due to high wound complication rates within open operative techniques, clinicians began to develop percutaneous approaches. This was first addressed by Schroeder *et al*[42] through an RCT reported in 1997, followed by two further RCT's in 2001 and 2008[43-44]. These articles have concluded favourable results, regarding complication rates, towards a percutaneous approach. However it has been discussed within the literature that there is a higher rate of sural nerve injury within percutaneous approaches. Consequently a range of surgical

approaches that sit between the open longitudinal and fully percutaneous approach have been developed. These predominantly involve three transverse skin incisions as shown in Figure 1.4. Consequently there is currently no standard procedure amongst surgeons.

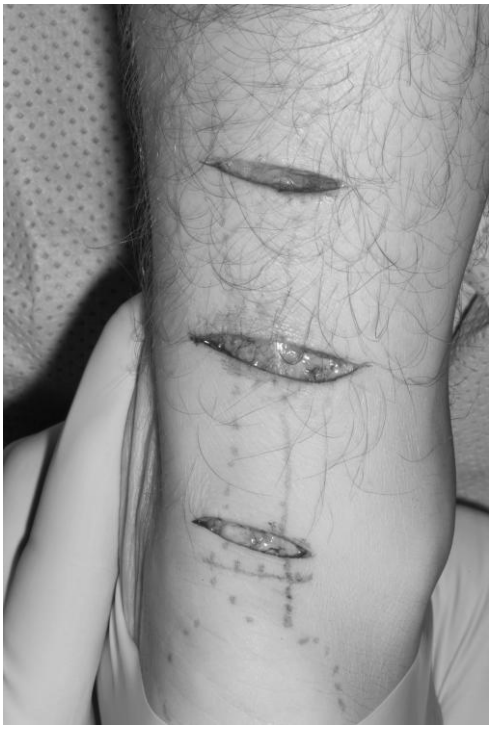


Figure 1.4: Example of a semi-percutaneous approach

In summary, the literature to date has focused on three areas. These have been, to operate or not, whether to use NWB cast immobilisation or IWB functional bracing and finally, methods of surgery. These have been the traditional areas of research for the management of a TA ruptures. However, new and emerging themes are developing as a result of advances in basic science and animal led research, which are increasingly being translated to clinical settings.

One such area is improving the biology which governs tendon healing. Published animal studies have investigated the use of various growth factors including bone

morphogenetic proteins, autologous conditioned serum, fibroblast growth factor, vascular endothelial growth factor, platelet derived growth factor and insulin-like growth factor-1[21,45-47]. There is currently a trial registered on the International Standard Randomised Controlled Trial database (ISRCTN) outlining a pilot RCT comparing the use of autologous platelet rich plasma to standard treatment within human participants (ISRCTN: 93608625). This demonstrates the links being made between basic science and clinical practice.

A second area of emerging research is focused upon the methods of rehabilitation. Animal experiments have consistently illustrated the detrimental effects of prolonged NWB and immobilisation. The findings of these studies have been translated to clinical practice with the introduction of IWB rehabilitation[48-49].

However, the introduction of IWB and early active range of movement is as far as research into rehabilitation has been taken within the context of human clinical trials. This is despite a range of basic science research, which demonstrates beneficial effects of tendon loading, tension and movement[21,50-54]. Yet the implication of applying these mechanisms to TA rupture injuries, in a clinical setting, remains largely unknown.

To summarise the literature to date, the next chapter of this thesis (Chapter 2) will aim to systematically search and review all currently published IWB functional bracing rehabilitation protocols used for the management of TA ruptures. This review, combined with the narrative overview of the literature to date, will form the basis of specific research questions this PhD thesis will address.

1.5 Achilles tendon rupture: outcome measures used in research

To ascertain superiority of one intervention over and above another, a primary outcome measure must be defined on which conclusions can be based. Traditionally, within trauma and orthopaedics, published studies have focused on the technical outcomes of procedures rather than measures of function and quality of life[55]. More recently this has been highlighted by the Department of Health, who have outlined that effectiveness from the patients perspective is essential for putting quality at the centre of NHS practice[56].

Within the published literature regarding TA rupture management, authors have traditionally based their conclusions on objective measures of complication rates, muscle strength, range of ankle movement, calf circumference, ultrasound assessment and gait analysis. Additionally, some authors have recorded patient reported return to sport, return to work, return to stair climbing and return to walking[27-28,31].

Gradually within the orthopaedic literature the emphasis has been placed on PROMs. These have broadly been split into two categories. The first has been termed ‘quality of life measures’ and are largely used as secondary outcome scores for cost analysis purposes. Examples include EQ-5D and SF-36. The second category has been termed ‘disease specific measures’. These measures are argued to have greater discriminatory validity than general quality of life scores because the questions within them are often focused on specific problems associated with a specific injury/disease area[56].

The change in type of reported outcomes in research has led to the development of a range of measures specific to orthopaedic foot and ankle pathologies/injuries.

Examples of outcome measures that have been developed for patients who have sustained a TA tendon rupture are wide ranging. They include the American Academy of Orthopaedic Surgeons (AAOS) lower limb outcomes assessment instrument[57], the ankle-hind-foot scale of the American Orthopaedic Foot and Ankle Society[58], the ankle rating scale of Kaikkonen[59] and the foot and ankle outcome score[60].

Yet many of these outcomes have not been evaluated against the different facets of validity. These facets include, but are not limited to, internal consistency, test-retest reliability, inter-observer reliability, responsiveness, construct validity, content validity and criterion validity. A key criticism of the above generic foot and ankle scores is that they lack discriminatory validity and often have not been evaluated within patients who have sustained a TA rupture. Instead they have been evaluated with a population of patients with a range of other foot and ankle conditions[61].

This issue of how to measure outcomes following a TA rupture has resulted in the development of TA specific outcomes. One such example is the Achilles rupture performance score (Leppilahti Score)[62]. However these scores were developed without any evaluation of validity or reliability. This limitation to the evaluation of interventions following a TA rupture has been recognised within the literature. Subsequently in 2007 Nilsson-Helander *et al* [61] published the first validity research into a disease specific PROMs for TA ruptures.

Within this article the author's addressed face validity, content validity, construct validity, convergent validity, test-retest reliability and responsiveness. However this is a single paper based upon a select population of patients aged 20 to 70 years, within a Swedish sample. This outcome has not yet been evaluated in the English

language, using a UK population amongst all patients who have sustained an acute TA rupture. These aspects of validity will be discussed in greater depth within chapter 7 of this thesis, which will evaluate further elements of validity of this new disease specific patient reported outcome score.

1.6 Thesis aims and objectives

The overall aim of this thesis is to develop an IWB intervention for patients who have sustained an acute rupture of their TA to inform a definitive evaluation of its effectiveness.

To determine the effectiveness of a health care intervention, it is universally accepted that an RCT is the most appropriate research design[63]. This is relatively straight forward within areas such as pharmacology, in which only one component is changed (drug 'A' vs. drug 'B'). This becomes less straight forward in other areas of health care, such as rehabilitation in which the ability to define, control and standardise the trial intervention becomes more problematic.

The acknowledgement and implications of this challenge has resulted in the development of the Medical Research Council (MRC) framework for developing and evaluating complex interventions[64]. They use the term 'complex intervention' to define any intervention that contains a number of interacting components. These can manifest at either the interventional level, through multiple interacting components, the number of targeted groups or organisational levels or the difficulty of behaviours required for delivery/receiving the intervention, the key elements of this process are shown in Figure 1.5.

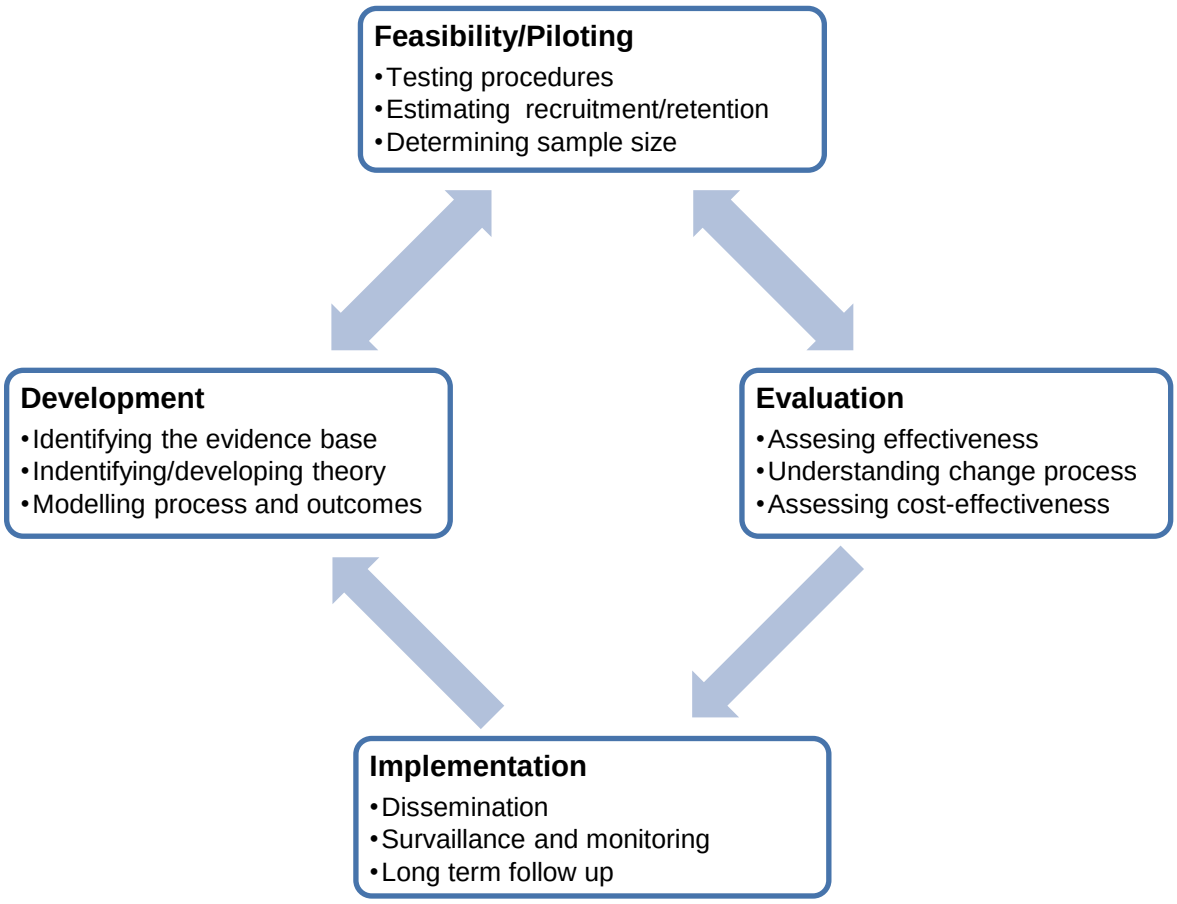


Figure 1.5: MRC framework for developing and evaluating complex interventions

Briefly, this consists of a 'pre-clinical' or 'development' phase in which the evidence base is identified (ideally by systematic review), alongside exploratory work to develop a rationale for the intervention to establish what changes are expected and why. This is followed by the first clinical phases (feasibility/piloting), which include testing procedures, establishing likely recruitment/follow-up and evaluating outcome measures and their variability. These two stages are then used to inform a definitive trial, which is the evaluation phase, followed by getting the evidence into practice through the implementation phase.

Consequently, to develop an IWB intervention for patients who have sustained an acute rupture of their TA, to inform a definitive evaluation of its effectiveness, the following objectives will be addressed, throughout this thesis:

1) Systematically identify and summarise, from clinical studies, the components that define IWB interventions currently documented for the treatment of acute TA ruptures.
2) Evaluate how these identified IWB components affect gait parameters within healthy participants, to provide a theoretical basis on which to develop interventions within a patient population.
3) Pilot the IWB interventions in a patient population to enable evaluation of patient recruitment rates, follow-up, PROM variability and CRF design.
4) Systematically identify and critically evaluate what PROMS are used within the published literature, and further evaluate elements of measurement properties of an appropriate disease specific PROM to be used as a primary outcome measure within the evaluation phase.

More specifically objectives one and two relate to the outlined ‘development’ phase and objectives three and four relate to feasibility/piloting. These objectives will then be summarised and discussed in the context of the subsequent phases of definitive evaluation and implementation within the conclusions of this thesis.

Declarations

This work has been presented at a national conference:

Feb 2011*: Society for Research in Rehabilitation:* A systematic review of early rehabilitation methods following an Achilles tendon rupture.

This work has also been published:

Kearney R, J. Achten, K McGuiness, M Costa, A Systematic Review of Early Rehabilitation Methods Following a rupture of the Achilles tendon. *Physiotherapy,* **98**, 2012, 24-32.

Funding Body

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Table of Contents

Abstract

Background
Rupture of the Achilles tendon is a debilitating injury. Advances in management have led to the development of immediate weight bearing rehabilitation protocols, of which a range exists. The first steps towards developing a complex intervention are to identify and define the components that define it. In doing this, research can then be focused on each interacting component to develop an optimum intervention.

Objectives
The aim of this systematic review was to identify and summarise, from clinical studies, the individual components that define immediate weight bearing rehabilitation protocols for the treatment of acute Achilles tendon ruptures.

Methods
The electronic databases MEDLINE, EMBASE, CINAHL, AMED and the register of current controlled trials were searched up to March 2010.

All study designs and languages were included. Using pre-defined inclusion and exclusion criteria, two independent reviewers identified all eligible articles. Eligible articles were summarised and critically reviewed regarding the reporting of their interventions using the extension of the CONSORT statement for non-pharmacological interventions.

Results
Two hundred and fifteen articles were screened for eligibility, nine were included. These included articles presenting the results of 236 operatively and 188 non-operatively managed patients.

There were a range of rehabilitation protocols that were defined by four identified components. These components consisted of the type of ankle foot orthoses worn, the degree of maintained plantarflexion, how long the ankle foot orthoses is worn for and whether daily range of movement exercises were permitted.

Conclusions
Within articles reporting of immediate weight bearing rehabilitation protocols, four components were identified. The efficacy of different immediate weight bearing rehabilitation protocols following an acute Achilles tendon rupture remains unclear. Consequently, further research is required to evaluate these identified components.

2.1 Protocol

Rupture of the TA is a debilitating injury, resulting in prolonged rehabilitation[65]. Throughout history, the preferred method of rehabilitation has changed several times. Traditionally it has involved immobilisation within a NWB plaster cast. However advances in research have led to a newer method of IWB bearing within an AFO[23,66].

The benefits of IWB rehabilitation compared to NWB have been consistently documented within the literature by RCT's and meta-analysis[23,39]. IWB rehabilitation has been further supported by animal studies that have evaluated the effects on tendon healing and muscle atrophy[48-50]. However, although the literature consistently agrees that IWB is superior to NWB immobilisation, it does not agree on the method of IWB rehabilitation clinicians should be implementing[39].

The concept of IWB rehabilitation has been translated from basic science to clinical practice. It is acknowledged that this new area of rehabilitation is a complex intervention that involves several interacting components, as defined by the MRC complex interventions framework[64]. However IWB rehabilitation strategies in this area have not yet been developed to optimise their potential benefits.

The development of a new concept to increase effectiveness to an optimum is the next stage in the process of a complex intervention. This development process has been described in the Lancet by McCulloch *et al*[67]. This is a topic that has also been raised by the British Medical Journal, recognising that health research should not just be evaluating what complex interventions work, but to further define the interacting components that make up the intervention and consequently evaluate which of these components works or fails in specific circumstances[68].

Subsequently the aim of this chapter is to systemically review and summarise the range of IWB rehabilitation protocols documented within the literature and the individual components that make them. In doing this, the known variations can be investigated further, to develop this new complex intervention.

This aim will be achieved by employing a search strategy across relevant databases. These databases will then be assessed against eligibility criteria for inclusion, before finally summarising the components of the interventions using the consort checklist extension for complex interventions. The protocols will then be discussed in relation to the wider literature.

2.1.1 Objectives

This systematic review will identify and summarise, from clinical studies, the range of IWB interventions within AFO's currently documented for the treatment of acute TA ruptures. This review will also summarise the individual components that define each complex intervention. This will answer the following research question:

'Following a TA rupture what IWB interventions within AFO's are currently documented in the literature?'

2.1.2 Criteria for including studies for this review

All study designs and languages were included and translated where necessary in this review. The review included all subjects over 18 years of age with an isolated, primary acute TA rupture. An acute rupture was defined as being less than 14 days old[69]. Articles reporting subjects presenting with delayed presentation (over 14 days), re-rupture or previous TA surgery were excluded.

All articles had to document an IWB (within one week), AFO protocol. This would be after either operative or non-operative management of a ruptured TA. The minimum information required to define a protocol consisted of which AFO was worn, how long it was worn for and what degree of PF was permitted. Any articles that did not contain these minimum criteria, but did mention an IWB protocol were contacted for further information. If the authors were unable to provide further information the articles were excluded.

2.1.3 Search strategy

The primary search employed the electronic databases of MEDLINE, AMED and EMBASE, searched via Ovid. CINHL was also searched via EBSCO Host using the search strategies in Table 2.1 to Table 2.3:

The secondary search assessed unpublished literature using the register of current controlled trials database for recently completed trials (http://controlled-trials.com/isrctn). A hand search was also undertaken using the reference lists of review papers that were evaluated to identify any additional relevant articles. Relevant experts in the field were also contacted where further clarification was required.

Table 2.1: Search strategy MEDLINE and AMED

	Searches
1	exp Achilles Tendon/
2	exp Rupture/
3	Achill$.m_titl.
4	Tendo Achill$.m_titl.
5	exp Weight Bearing/
6	Orthotic Devices/ or Athletic Tape/ or Braces/ or Walkers/
7	exp Rehabilitation/
8	Mobi$.m_titl.
9	Rupture$.m_titl.
10	1 or 3 or 4
11	2 or 9
12	10 and 11
13	5 or 6 or 7 or 8
14	12 and 13

Table 2.2: Search strategy CINAHL

	Search
1	MM. Achilles Tendon/
2	Ti. Achilles Tendon
3	1 OR 2
4	MM. Rupture/
5	Ti. Rupture
6	4 OR 5
7	3 AND 6
8	MM Rehabilitation
9	MM. Foot Orthosis
10	8 OR 9
11	7 AND 10

Table 2.3: Search strategy EMBASE

	Search
1	exp Achilles Tendon/
2	exp Rupture/
3	Achill$.m_titl.
4	Tendo Achill$.m_titl.
5	exp Weight-Bearing/
6	exp Rehabilitation/
7	Mobi$.m_titl.
8	Rupture$.m_titl.
9	1 or 3 or 4
10	2 or 8
11	9 and 10
12	orthotics/
13	5 or 6 or 7 or 12
14	11 and 13

2.1.4 Methods of review

Trials were independently assessed for inclusion by two reviewers (RK and KM). The second reviewer (KM) was employed by the University of Warwick as a research physiotherapist, within the same department and had four years experience of working in orthopaedic pragmatic research. The reviewers evaluated all identified titles and abstracts independently and excluded any clearly irrelevant articles at this point. The remaining articles were ordered in full and assessed against the eligibility criteria. Differences were resolved by discussion.

Data was extracted from all included articles. This was undertaken by a single reviewer (RK) and verified by the second reviewer (KM). An example of the pre-defined data extraction table is summarised in Table 2.4 and includes study design, sample size, population characteristics, description of the AFO intervention, follow-up (FU) period, outcomes assessed and the author's conclusions.

In addition to the data extraction table below, all studies were scored against the consort statement for reporting complex interventions. This score consists of three components. The first relates to whether or not the authors have reported a description of the different components of the intervention. The second details how the interventions were standardised and the third relates to how adherence of care providers with the protocol were assessed[70].

Table 2.4: Example of data extraction table

Paper	*Study design*	*Sample size*	*Population characteristics*	*Intervention*	*Follow-up, outcomes & conclusions*
				AFO type: Worn for: ROM: Other details:	

This research question was focused on the description of IWB interventions. Therefore it was anticipated that a range of study designs would be included whose primary research question was not focused on the evaluation of the rehabilitation protocols, but other aspects of TA rupture management. Such examples were expected to include operative versus non-operative or NWB versus IWB, in which the rehabilitation protocol is described but not evaluated. Consequently it was considered that a critical appraisal tool to assess the methodological quality of the overall study designs was inappropriate for this review, however it was considered appropriate to critically appraise the quality of intervention documentation, using the CONSORT statement extension for non-pharmacologic treatments[71].

2.2 Results

2.2.1 Search results

The individual search strategies, carried out on 28 March 2010, for each of the databases, are shown in Table 2.5 through to Table 2.8. Figure 2.1 shows the results of the search strategy. It illustrates that once duplicates were removed, 215 articles remained to be screened for eligibility. Of these 118 articles were excluded, based on title and abstract information.

Ninety-seven full text articles were subsequently ordered and further assessed against the eligibility criteria. Of the 97 articles ordered, one non-English article could not be obtained from the British library; therefore 96 full text articles were assessed. Of these 96 articles 15 were non-English and translated (CE and PFO), 10 articles were review articles of overall management for TA ruptures and excluded, however their reference lists were checked for potentially eligible articles. Sixty-three of the 96 articles were subsequently excluded for not using an IWB intervention. A further seven were excluded for including a sample who had not sustained an acute TA rupture and eight articles used IWB but within a below knee cast, these were also excluded as they do not allow the patient the capacity to carry out range of movement exercises. This resulted in eight included articles from the original 96, in addition to one article found within a reference list.

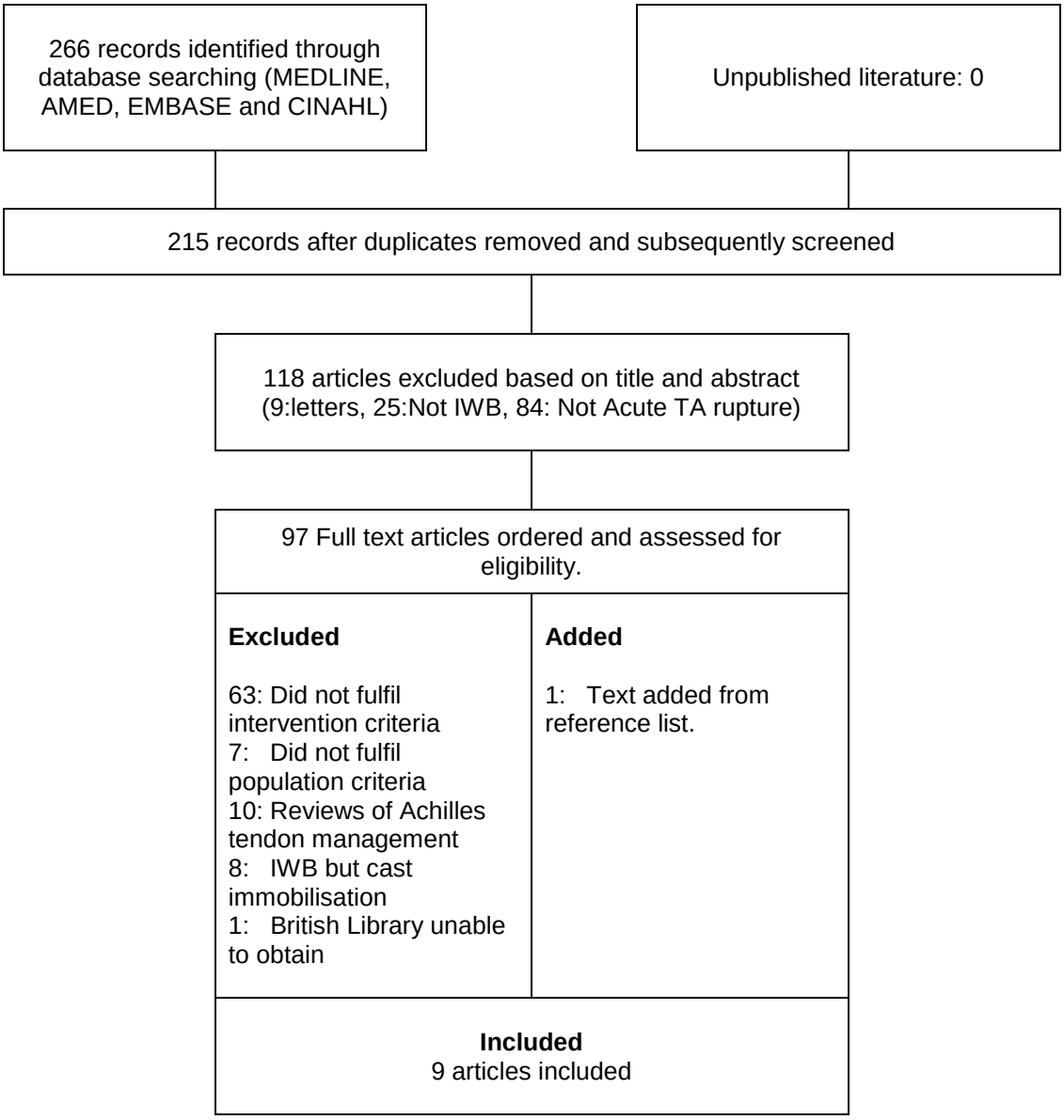

Figure 2.1: Search strategy

Table 2.5: Search strategy results: MEDLINE

	Searches	Results
1	exp Achilles Tendon/	4758
2	exp Rupture/	30299
3	Achill$.m_titl.	3372
4	Tendo Achill$.m_titl.	120
5	exp Weight Bearing/	11026
6	Orthotic Devices/ or Athletic Tape/ or Braces/ or Walkers/	8042
7	exp Rehabilitation/	116316
8	Mobi$.m_titl.	25945
9	Rupture$.m_titl.	31747
10	1 or 3 or 4	5391
11	2 or 9	48099
12	10 and 11	1484
13	5 or 6 or 7 or 8	158627
14	12 and 13	92

Table 2.6: Search strategy results: AMED

	Searches	Results
1	exp Achilles Tendon/	408
2	exp Rupture/	283
3	Achill$.m_titl.	458
4	Tendo Achill$.m_titl.	30
5	exp Weight-Bearing/	694
6	Orthotic Devices/ or Athletic Tape/ or Braces/ or Walkers/	1560
7	exp Rehabilitation/	31554
8	Mobi$.m_titl.	1224
9	Rupture$.m_titl.	349
10	1 or 3 or 4	491
11	2 or 9	411
12	10 and 11	155
13	5 or 6 or 7 or 8	34161
14	12 and 13	27

Table 2.7: Search strategy results: EMBASE

	Search	Results
1	exp Achilles Tendon/	2663
2	exp Rupture/	35057
3	Achill$.m_titl.	2523
4	Tendo Achill$.m_titl.	102
5	exp Weight-Bearing/	10727
6	exp Rehabilitation/	115936
7	Mobi$.m_titl.	20496
8	Rupture$.m_titl.	19760
9	1 or 3 or 4	4122
10	2 or 8	42495
11	9 and 10	1195
12	orthotics/	1035
13	5 or 6 or 7 or 12	146792
14	11 and 13	146

Table 2.8: Search strategy results: CINAHL

	Search	Results
1	MM. Achilles Tendon/	
2	Ti. Achilles Tendon	
3	1 OR 2	687
4	MM. Rupture/	
5	Ti. Rupture	
6	4 OR 5	1712
7	3 AND 6	192
8	MM Rehabilitation	
9	MM. Foot Orthosis	
10	8 OR 9	6189
11	7 AND 10	1

2.2.2 Description of studies

Table 2.9 summarises the nine included articles from the above search strategies and Table 2.10 summarises the quality assessment of intervention reporting.

The first report of an IWB rehabilitation intervention within an AFO was published by Speck *et al* in 1998[72]. This was a prospective case series of 20 patients. All patients had an open operative procedure. Following this procedure all patients wore a rigid rocker bottom AFO for six weeks, locked in neutral. This series of patients were followed up for 12 months. The authors reported one complication during this time frame, a deep vein thrombosis. The remaining patients were reported to have returned to normal activities by six months.

The conclusions of the above article had important implications because it was the first to describe an IWB AFO intervention. However due to its small sample size, research design, and lack of validated outcome measures, limited conclusions can be made regarding this intervention, based on this article alone. However it did demonstrate that IWB did not result in an increase in complications such as tendon lengthening or re-rupture.

In 2003 Costa *et al*[73] carried out a pilot RCT on patients operatively managed, to compare IWB to NWB cast immobilisation. The rehabilitation protocol differed from Speck *et al*[72]. Instead of using a rigid rocker bottom AFO with no heel raises, Costa *et al*[73] used a flexible carbon fibre AFO with three heel raises, which were reduced gradually over an eight week time period. The purpose of their pilot study was to determine safety of the rehabilitation protocol, which was then developed into a larger RCT published in 2006[40].

Table 2.9: Summary of included articles

Paper	Sample size	Study design/question	Population characteristics	IWB Intervention	Follow up (FU), outcomes and authors conclusions
Speck *et al* 1998[72]	20	Case Series	Operative (open) 15 men, 5 women 27-83 years Unilateral No previous rupture or surgery	**AFO Type**: Rigid rocker **Worn for:** 6 weeks **ROM:** Neutral **Other details:** WB Day 1, ankle exercises 4 times/day	**FU:** 6 weeks and 3,6 and 12 months **Outcomes:** Own scoring system, ultrasound, strength **Complications:** 1 DVT **Conclusion:** IWB is safe. All returned to normal 6 months.
Costa *et al* 2003[73]	14 per group	RCT (Brace Vs Cast)	Operative (any) 24 men, 4 women Over 18 (average 41 years) Unilateral No previous injury or surgery	**AFO Type**: Flexible carbon fibre **Worn for:** 8 weeks **ROM:** Three 1.5cm heel raises One raise removed every 2 weeks **Other details:** WB day 1	**FU:** 2,4,6,8 weeks and 3,6, and 12 months **Outcomes:** Calf muscle bulk, ultrasound, return to sport, strength **Complications:** 1 re-rupture, 1 sural nerve deficit, 1 delayed healing. **Conclusion:** IWB safe, return to sport 6 months (2 months sooner than cast group).

Paper	Sample size	Study design/question	Population characteristics	IWB intervention	Follow up (FU), outcomes and authors conclusions
Costa *et al* 2006[40]	23 IWB Op 25 Cast Op 22 IWB non-op 26 Cast non-op	2 RCT's 1) IWB Vs Cast Op 2) IWB Vs Cast Non-op	1) Operative (any) 28-69 years Unilateral No previous injury or surgery 2) Non-operative 21-79 years Unilateral No previous injury or surgery	**AFO Type**: Flexible carbon fibre for both **Worn for:** 8 weeks (Op) 12 weeks (Non-op) **ROM:** Three 1.5cm heel raises One raise removed every 2 weeks (Op) No change for first six weeks followed by above protocol (Non-op) **Other details:** Both groups WB day 1	**FU:** 3,6, and 12 months **Outcomes:** Return to sport, walking, work, stair climbing, EQ-5D and strength **Complications:** 2 re-ruptures (op group) 1 poor healing and 1 re-rupture(non-op) group **Conclusion:** IWB is safe and results in better functional outcomes within operatively managed patients compared to plaster cast. IWB is safe within non-operatively managed patients, but did not result in better functional outcome measures compared to a cast group.
Hufner *et al* 2006[74]	125	Case Series	Non-operative (10mm or less gap) 105 men, 20 women Over 18 (20-70 years) No previous injury or surgery	**AFO Type**: Flexible orthotic design **Worn for:** 8 weeks **ROM:** 3cm elevation of heel **Other details:** 3 days in cast, exercises out of boot at 4 weeks, 1cm heel rise within their shoe for 3 months.	**FU:** Not specified. **Outcomes:** Ultrasound, strength, return to sport **Complications:** 3 DVT's, 2 soft tissue discomfort, 8 re-ruptures, 21 lengthened tendons **Conclusion:** Poor compliance caused complications. Otherwise IWB is safe.

Paper	Sample size	Study design/question	Population characteristics	IWBiIntervention	Follow up (FU), outcomes and authors conclusions
Jacob *et al* 2007[75]	36	Case Series	Operative (open) Over 18 Unilateral No previous injury or surgery	**AFO Type**: Rigid rocker **Worn for:** 6-8 weeks **ROM:** Neutral **Other details:** WB day 1	**FU:** Minimum 2.5 years-6.5years **Outcomes:** Calf circumference, strength, pain, walking limp and satisfaction **Complications:** None **Conclusion:** IWB is safe and should be standard.
Majewski *et al* 2008[76]	14 matched pairs	Case controlled series (Cast Vs IWB)	Operative (percutaneous) 13 men and 1 women Over 18 (25-62 years) Unilateral No previous surgery or injury	**AFO Type**: Shoe, with anterior, medial and lateral support, high shaft. **Worn for:** 3 months **ROM:** 3cm heel wedge, removed gradually between weeks 4-7. Stabilisers removed 7 weeks. **Other details:** Day one: Splint to hold the foot in 20 degrees of plantar flexion then orthotic.	**FU:** 12 months **Outcomes:** Hannover Achilles tendon score, return to work, return to sport, strength, pain, ROM, calf circumference. **Complications:** 6 lengthened tendons in shoe group, 5 in cast group. **Conclusion:** Earlier return to work and sport within the shoe group. IWB is safe.

Paper	Sample size	Study Design/Question	Population characteristics	IWB intervention	Follow up (FU), outcomes and authors conclusions
Metz *et al* 2008[41]	41 Non-operative 42 Operative	RCT (Op Vs Non-op IWB)	Operative (open) and non-operative Over 18 (23-63 years) Unilateral No previous injury or surgery	**AFO Type**: Operative: Tape bandage Non-operative: Rigid rocker **Worn for:** Both 6 weeks **ROM:** Operative: 2cm heel rise Non-operative: 2 weeks 30^0, 2 weeks 15^0, 2 weeks neutral. **Other details:** Both had cast for one week Both not allowed to remove	**FU:** 1,3,5,7 weeks and 3 and 6 months **Outcomes:** Leppilahti score, ROM, strength. **Complications:** Non-operative: 5 re-ruptures, 1 sural nerve injury, 1 DVT, 13 skin complaints Operative: 3 re-ruptures, 3 sural nerve injury, 1 complex regional pain, 2 skin complaints, 3 scar adhesions. **Conclusion:** No functional differences between the two groups. Less risk of complications within the operative group.
Bhattacharyya *et al* 2009[77]	34 NWB 25 IWB	2 consecutive case series (IWB percutaneous Vs non WB open repair)	Operative 18-50 years Unilateral No previous injury or surgery	**AFO Type**: Rigid rocker **Worn for:** 8 weeks **ROM:** 3 heel rises, reduced every two weeks. **Other details:** Cast immobilisation for a couple of days first.	**FU:** 3,6, and 12 months **Outcomes:** Return to normal activities as reported by the patient, return to sport, work and walking. **Complications:** None in the IWB group **Conclusion:** IWB safe and resulted in faster return to normal activities when compared to the cast group.

Paper	Sample size	Study Design/Question	Population characteristics	IWB intervention	Follow up (FU), outcomes and authors conclusions
Doral *et al* 2009[78]	62	Case Series	Operative (percutaneous) Over 18 (27-38 years) No previous surgery or injury	**AFO Type**: Rigid Rocker **Worn for:** 3 weeks **ROM:** Neutral **Other details:** WB Day 1, daily exercises, resistance exercises from week 6, jogging week 10.	**FU:** 2, 6, 12, 24 weeks and 12 months **Outcomes:** Calf circumference, ROM, , return to sport and work, AOFAS, strength. **Complications:** None **Conclusion:** Calf atrophy is the biggest problem. Authors concluded this rehabilitation programme is safe.

Costa *et al*[40] published a report of two separate RCT's in 2006. One sample was within patients managed non-operatively (cast vs.IWB) and one was within a sample of patients managed operatively (cast vs. IWB). The authors concluded that IWB was safe in both groups and resulted in faster rehabilitation within patients managed operatively.

However, the primary outcome measure for these RCT's was the time taken to return to normal activities, as reported by the patient. This outcome measure is inherently flawed because firstly aspects pertaining to the validity and reliability of this single item question are lacking. Secondly, 'normal activities' will vary between individuals, for example those who are sedentary and work at a desk will inevitably return to normal activities sooner than a patient with a manual job who plays weekly football. Despite the problems with measuring functional outcomes, the reported complications within this article are of equal importance, because this was the first RCT to compare these two contrasting rehabilitation methods. However a difference may not have been found because the study was inadequately powered (type two error) to show such a difference in complications.

Three further case series have been published using IWB rehabilitation since this RCT. Two evaluated the rehabilitation within patients who had received operative management and one within a sample who had received non-operative management[74-75,78].

Both operative case series used a rigid rocker bottom orthotic, both with no heel raises, however there were differences in the amount of time each orthotic was worn. Jacob *et al*[75] reported 6-8 weeks within the AFO and Doral *et al* [78] reported a minimum of three weeks, but did not report the actual range of time patients wore

them for. In contrast the non-operative series by Hufner *et al*[74] used the same rehabilitation programme proposed by Costa *et al*[40] (carbon fibre AFO with three heel raises).

None of these three case series reported complications above those reported in relation to cast immobilisation. A range of outcome measures other than complications were also used by the three case series. These predominantly included objective measures such as strength, calf circumference and presence of a limp on walking. This is representative of the lack of validated PROMs for this specific disease area. However generic validated quality of life scores, such as SF-12 and EQ-5D could have been used to allow comparisons between studies.

The two further trials outlined in Table 2.9 make comparisons of the new IWB rehabilitation to cast immobilisation. Majewski *et al*[76] evaluated these contrasting interventions using a case controlled study design and Bhattacharyya *et al*[77] utilised two consecutive case series.

The first of these study designs is normally associated with epidemiology in order to ascertain whether exposure to any factor occurred more or less frequently in the cases than the controls. This choice of research method for a new intervention is open to selection bias, as the authors chose subjects in the new intervention group to match the cast group and in doing so may have neglected certain cases that would potentially change outcome. Furthermore, matching can only account for known confounding variables; unknown factors cannot be accounted for by this method. Consequently RCT's are the 'gold' standard for comparing two interventions, because the process of randomisation accounts for the known and unknown confounding variables.

The second study design, using two consecutive case series also does not take into consideration unknown confounding variables either. However the study by Bhattacharyya *et al* [77] does provide further evidence that IWB is safe within their small sample of 25 patients, reporting no adverse complications.

In relation to the rehabilitation protocols reported for these two studies, Bhattacharyya *et al*[77], used the same protocol first outlined by Costa *et al* in 2003[73]. Whereas Majewski *et al*[76] used what was described as a shoe with medial and lateral support and a high front shell, which were removed at four weeks and the whole shoe removed at seven weeks, with gradual reduction of three heel raises during this time.

The first, and only, RCT comparing operative to non-operative management using IWB rehabilitation was published in 2008 by Metz *et al*[41]. However, the authors chose to use different rehabilitation protocols for each treatment arm. The operative group were managed with tape bandage (bandage wrapped around the limb) and a 2cm heel raise and the non-operative group were managed with a rigid rocker bottom AFO set at 30^0 PF being gradually reduced over a six week period. Within this study neither group were allowed to remove their AFO for the duration it was worn. This resulted in 16 skin complications over the two groups. This frequency of incidence has not been reported by any other study.

The primary objective of this study was complications other than re-rupture, which is also unprecedented amongst previous literature, which has focused primarily on re-rupture rates, a key concern for clinicians. There was no justification given by the authors regarding the rationale for this outcome. Taking into account that 13/15 complications for the non-operative group were ‘skin complications’ ranging from a

blister to fungal infections, the clinical relevance of this measure is not only questionable, but the majority could have been prevented by allowing the patient to remove their AFO throughout the day, as other published articles have reported. The authors found no statistically significant differences between the two groups regarding complications other than re-rupture. However, the clinical relevance of this is limited and provides no information regarding what is most important, which is what the patient is functionally capable of achieving and how soon after the procedure this is achievable by.

Table 2.10 illustrates the quality of reporting for each of the nine included studies. From this table it is evident that none of the included articles described any aspects of standardising or adherence to the administration of the interventions. Such methodological examples include written instructions or a documented training programme, however all articles did fully describe the intervention components.

Table 2.10: Assessment of reporting quality

Paper:	Description of components (Yes/No)	Details standardisation (Yes/No)	Details of adherence (Yes/No)	Total score (max: 3 points)
Speck *et al* [72]	Yes	No	No	1
Costa *et al* [73]	Yes	No	No	1
Costa *et al* [40]	Yes	No	No	1
Hufner *et al* [74]	Yes	No	No	1
Jacob *et al* [75]	Yes	No	No	1
Majewski *et al* [76]	Yes	No	No	1
Metz *et al* [41]	Yes	No	No	1
Bhattacharyya *et al* [77]	Yes	No	No	1
Doral *et al* [78]	Yes	No	No	1

2.3 Discussion

The aim of this systematic review was to identify and summarise, from clinical studies, the range of IWB AFO interventions currently documented for the treatment of acute TA ruptures. This was to answer the research question: 'What IWB AFO, rehabilitation interventions are acknowledged in the literature for patients following an acute rupture of their Achilles tendon?'

This systematic review has outlined nine articles that have described an IWB AFO rehabilitation programme. These articles were published between 1998 and 2009 and consisted of four case series designs, ranging in sample size from 20 to 125 patients. These were predominantly concerned with the safety of this new intervention. Articles which were not case series designs were a combination of RCT's, case-controlled studies and parallel case series to answer research questions regarding IWB compared to cast immobilisation. The only study not posing this question was an RCT by Metz et al[41] which compared operative to non-operative management using IWB rehabilitation protocol's in both groups.

There were no articles that had compared different IWB rehabilitation protocols. This is despite the wide range of protocols published. This review has identified four variables which account for this range. The first is the type of AFO worn. There were two predominant designs within the literature, a flexible in-shoe AFO and a rigid rocker bottom style AFO. The second variable is the degree of fixed PF the patient's foot is maintained in within the AFO. This variable ranged from a 4.5cm heel raise to no fixed PF but restriction from DF only. The third variable consists of how long the AFO is worn for, all but one study used 6-8 weeks. One study recommended a minimum of three weeks, but gave no information regarding how long they were actually worn for. The final variable is whether or not the patient can remove the

AFO during the AFO wearing phase; this was allowed by all but one article. Within this article a high proportion of patients acquired skin complaints such as fungal infections and blisters, which were not evident amongst the other articles.

This systematic review has demonstrated the development of IWB rehabilitation from concept to clinical practice over an eleven year time frame. This process has been described by McCulloch *et al*[67] within the IDEAL recommendations. He proposed that for new complex interventions that are not governed by the strict standards used within the area of drug development, there should be a clear process of idea and development through to assessment and long term study.

The IDEAL recommendations proposed that the first stage involved in delivering a new intervention should be the description of the intervention, which occurs as a solution to a clinical problem. In this case the clinical problems have consistently been documented to include muscle atrophy, resulting in prolonged rehabilitation and functional deficits, in combination with the clinical complications mainly consisting of re-rupture, tendon lengthening, adhesions and infection[9].

The first report of functional IWB rehabilitation by Speck *et al* in 1998[72] was prompted by the possible solution to the clinical problem presented, within a range of animal studies. These studies were based predominantly upon rabbit, dog and rat models[79-82]. In all cases these studies were able to demonstrate the positive effects of load and movement on, tendon characteristics, healing orientation of collagen fibres and calf strength. Conversely they also demonstrated the detrimental effects of immobilisation on both tendon and muscle tissues. Consequently Speck *et al*[72] put theory into clinical practice with their case series. Publications since 1998 have all supported the safety of functional IWB rehabilitation.

The next stage involved in delivering a new complex intervention according to the IDEAL recommendation is development of the new intervention to ascertain what aspects of it are more effective. In doing so, the intervention evolves and should be reported in relation to validated PROMs. This systematic review has demonstrated that this next stage of complex intervention development has not yet been addressed. There have been no studies comparing different IWB rehabilitation protocols.

The IDEAL recommendations have been further supported by the MRC complex intervention framework and expansion of the CONSORT statement to improve reporting of non-pharmacologic interventions. More specifically, the need for health care research to be directed towards not only evaluating what works best, but to further investigate what specific components of the complex intervention work best and why. In doing this, interventions can be optimised. The MRC complex intervention framework has outlined that such interventions should be developed systematically with a series of pilot studies embedded within the biological plausibility of results found. In following this process research can be directed, leading to a definitive evaluation of a complex intervention.

Based on the review of the literature to date regarding TA rupture rehabilitation it can be concluded that ultimately IWB is safe. However the type of AFO that should be worn, the degree of PF the foot should be maintained in and amount of time it should be worn for, are all variables which have not been evaluated within the literature. The second conclusion from this review is that the uses of validated PROMs are not widely reported within this specific disease area, allowing comparisons to be problematic. Finally this review has also highlighted the poor

standards of published articles regarding the reporting of adherence and standardisation of the interventions.

Following the recommendations outlined in this chapter for developing a complex intervention the next stage from identifying the individual components is to evaluate these components and their interactions. In doing so a theoretical framework can be developed that will direct what complex interventions are trialled in clinical practice. Consequently the next chapter of this thesis will further investigate these identified components and their interactions, to develop a theoretical framework, upon which future clinical research in this area can be based.

Declarations

The sample size calculation and randomisation sequence were completed by Nicholas Parsons (Statistician). All other trial procedures were carried out by the candidate.

This study has been presented at an international conference:

March 2012: *International Society for Gait and Posture Research:* The effect of AFO design and the number of heel-wedges on in-shoe plantar pressures during walking: implications for Achilles tendon rupture rehabilitation.

This study has also been published:

Kearney R, S Lamb, J Achten, N Parsons, M Costa, In-Shoe plantar pressures within ankle foot orthoses: Implications for the management of Achilles tendon ruptures. *American Journal of Sports Medicine,* **39**, 2011, 2679-2685.

Sponsorship

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Ethics Committee Approval Date

1st September 2008

Funding Body

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Table of Contents

Abstract

Background
Advances in Achilles tendon rupture management have led to the development of immediate weight bearing protocols. These protocols vary regarding which ankle foot orthoses is used and the number of inserted heel wedges used within them.

Objectives
The primary purpose of this investigation was to evaluate plantar pressure measurements and temporal gait parameters, under different pre-defined conditions, within healthy participants. The secondary purpose was to draw inferences from these measurements to the application of Achilles tendon rupture rehabilitation.

Methods
Fifteen healthy subjects were evaluated using three different ankle foot orthoses designs, with four differing levels of inserted heel wedges. Subsequently, a total of 12 conditions were evaluated, in a sequence that was randomly allocated to each subject.

Pressure and temporal gait parameters were measured using an in shoe F scan pressure system, and range of movement was measured using an electrogoniometer.

Results
Ankle foot orthoses that were restrictive in design, combined with a higher number of inserted heel wedges, prevented production of forefoot pressures, increased heel pressures and decreased the amount of time spent in the terminal stance and pre-swing phase of the gait cycle ($p=0.029$, 0.002 and <0.001 respectively).

Conclusions
The choice of ankle foot orthoses design and number of inserted heel wedges has a significant impact on plantar pressure measurements and temporal gait parameters. The purpose of an ankle foot orthoses for this injury is to provide weight bearing within a protected range of movement. However, the findings of this study suggest that the balance between protected weight bearing and functional loading require further research within a clinical context.

3.1 Protocol

Rehabilitation following a TA rupture is often prolonged, with persistent functional deficits[9]. To address this clinical problem, research has focused on accelerated methods of rehabilitation. Chapter 2 illustrated that the first AFO IWB protocol was published in 1998[72], followed by the first RCT comparing IWB to NWB in 2003[73]. In 2009 the first guidelines[18] were published for TA rupture management, also advocating IWB management. It is clear that there is an overall clinical consensus regarding the use of IWB AFO protocols, supported by clinical evidence demonstrating lower re-rupture rates and reduced muscle atrophy[9,23,40].

Chapter 2 also demonstrated that there is currently a wide range of IWB AFO protocols used in practice. The guiding principles behind IWB AFO management have been to balance the proposed advantages against the risks of tendon re-rupture and lengthening. This has been achieved through restricting the degree of DF, and subsequently the contractile activity of the plantarflexors[83]. However, there is debate regarding the amount of restriction imposed and where this balance lies.

In addition to the degree of DF restriction inherent within the AFO design, a number of IWB protocols have also maintained the ankle in various degrees of PF, within the AFO's, using heel wedge inserts. This component may also have implications for subsequent recovery. For example, animal research has demonstrated that muscles immobilised in less than resting length atrophy at a faster rate than muscles fixed in stretched positions[84]. Furthermore, allowing a range of loaded movement has been shown to increase the biomechanical properties of the scar tissue, decrease excessive adhesion formation and subsequently enhance the gliding function of the tendon[48,85]. Consequently, the degree of permitted range of loaded movement requires further investigation.

Currently, there is no literature directly comparing different AFO designs within a range of fixed PF positions in clinical practice. Chapter 2 enabled the identification of the components which define an AFO IWB protocol. The next step outlined by the MRC[64] for systematically developing a complex intervention is to develop appropriate theory to guide what is piloted in a clinical context.

Consequently, to guide what could be developed and piloted in clinical practice the aim of this study was to investigate gait parameters under different pre-defined conditions, within participants with no previous lower limb injuries.

3.1.1 Objectives, research question and null hypotheses

The objectives of this study were:

1) To quantify plantar pressure measurements and temporal gait parameters from healthy participants IWB in three different AFO designs.
2) To quantify plantar pressure measurements and temporal gait parameters from healthy participants IWB within four different maintained ankle positions, using inserted heel lifts.
3) To quantify the interactions between the above two components (AFO design and ankle position).
4) To draw inferences from these findings to propose developments of IWB AFO protocols to be piloted in a clinical context.

These objectives would answer the following research question:

'How does changing the position of the ankle or the AFO design within healthy participants, change plantar pressure measurements at the heel and forefoot,

cadence and amount of time spent in the terminal stance and pre-swing phases of the gait cycle, and is there an interaction between these two components?'

Therefore, the null hypotheses were:

1) There are no differences of the three AFOs trialled (first factor) regarding plantar pressure measurements and temporal gait parameters within healthy participants.
2) There are no differences between the four different maintained ankle positions (second factor) regarding plantar pressure measurements and temporal gait parameters within healthy participants.
3) There is no interaction difference of the first and second factor regarding plantar pressure measurements and temporal gait parameters within healthy participants.

Further information regarding the justification and definition of the above outcomes are detailed later, within Chapter 3.1.5.

3.1.2 Trial summary and trial flow diagram

Participants were assessed, using in-shoe pressure analysis at one visit. They trialled three different AFOs, with the ankle set in four different levels of maintained PF. (Figure 3.1). For each analysis, an in-shoe pressure sensor was placed inside the AFO and the participant was asked to walk at normal walking pace down a flat corridor. Plantar pressures produced at the heel and forefoot, cadence, speed and amount of time spent in the terminal stance and pre-swing phases of the gait cycle were recorded. Range of movement permitted within the AFO throughout the gait cycle was also measured using an electro-goniometer.

Recruitment of participants and data collection was expected to take place over a period of three months. The final analysis and interpretation was expected to be complete within one month from the final data collection point.

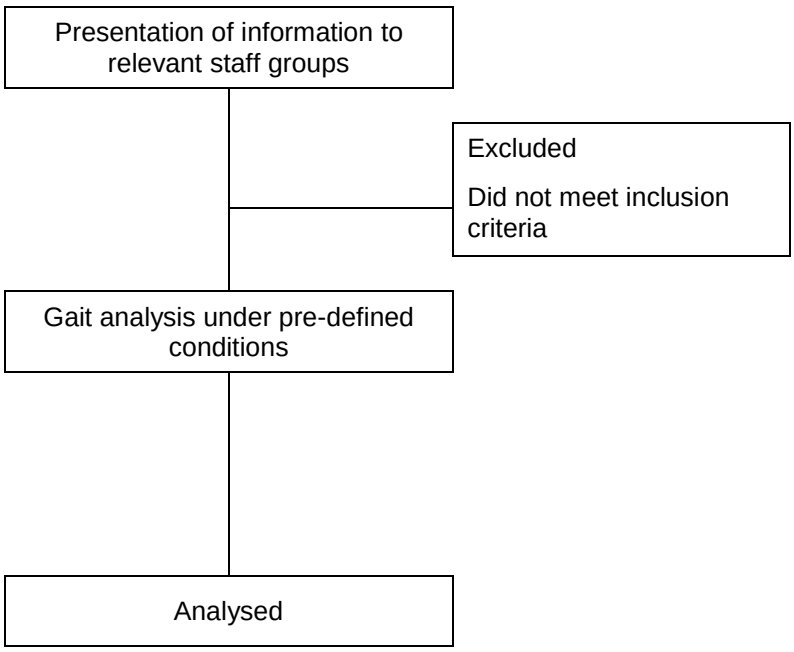


Figure 3.1: Trial flow diagram

3.1.3 Patient inclusion/exclusion criteria, recruitment and consent

This study had ethical approval from the Coventry Research Ethics Committee. All men and women over the age of 18 years working within the University Hospitals of Coventry and Warwickshire and the University of Warwick, with no history of lower limb pathologies or injuries, were invited to take part.

Participants with a history of lower limb pathology or injury were excluded because the effect of these past pathologies and/or injuries on the specified outcome measures is unknown and therefore a potential confounding variable. Participants under 18 years of age were excluded because this age group is not typical of the population who sustain a TA rupture[39].

The sample was limited to employees of the University Hospitals of Coventry and Warwickshire and the University of Warwick following discussions with the local ethics committee. During these discussions, it was decided that a sufficient number of eligible participants, representative of the population who sustain TA ruptures, was available within these departments to fulfil this convenience sample.

Recruitment of participants took place within the University Hospitals of Coventry and Warwickshire. I delivered presentations to the Trauma and Orthopaedic clinical teams and Research Department teams. This presentation outlined the background and purpose to the study, as documented within the participant information sheet (Appendix A) approved by the local ethics committee. Potential participants were then invited to register their interest.

Participants who had registered their interest were then screened using the predefined inclusion and exclusion criteria. Those who were both eligible and willing

were then provided with the approved participant information sheet (Appendix A). Once participants had read the participant information sheet, they then had the opportunity to ask any questions and have those questions answered to their satisfaction. If they were still willing, they then signed two consent forms. An example of the consent form can be found in Appendix B. The first copy was given to the participant for their information, and the second copy was stored as per the trial oversight and data management plan detailed in Chapter 3.1.9.

Eligible and willing participants were advised that they could withdraw from the study at any time without prejudice. Alternatively, participants were also advised that they could be withdrawn from the study at the discretion of the investigator and/or PhD supervisors due to concerns, such as health or environmental considerations.

3.1.4 Intervention

Following the consent of willing and eligible participants, plantar pressure measurements and temporal gait parameter data to be collected for the above objectives was gathered using the F-Scan system (Tekscan Incorporated, Boston, Massachusetts). The F-Scan system allows for evaluation of gait rather than isolated steps, which is the main advantage over force plate measurements[86]. Force plate measurements also have the additional disadvantage of ensuring correct 'targeting' of the foot strike, which has been reported to create unnatural gait patterns[87].

The F-Scan system uses a two layer ultra thin (0.18mm) flexible foot sensor. Each layer is made of a flexible polyester film and an electrically conductive ink is printed on the film and coated with a pressure sensitive resistive ink[88]. This is arranged in rows of electrodes that respond to an applied pressure resulting in an electrical

output. There are 960 individual pressure-sensing locations, at a sampling frequency of 50Hz (Figure 3.2).

Studies of the F-Scan in-shoe system have demonstrated reliability and validity of the equipment[88-90]. Previous research has quoted inter-class correlation coefficients of 0.83 for pairs of repeated measures[89] and coefficient variations of between one and eight percent for heel measurements when known forces were applied. Additionally, the discreet in-shoe sensors have been reported to be easier and more reliable to calibrate than larger force plates[86,91-92].

There was no internal testing of reliability and validity of the equipment used. However the manufacturers guidelines were followed during testing procedures in addition to following the international guidelines for plantar pressure measurements. These protocols in measurement and analysis procedures ensured the maximisation of intra reliability.

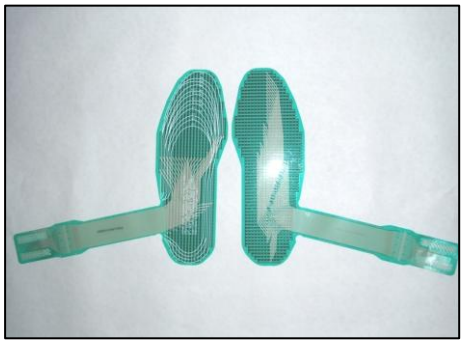


Figure 3.2: In-shoe foot sensors

Each participant had a new set of foot sensors individually prepared for them, as recommended by the manufacturers. This involved sizing the foot sensors to the participants own shoe size following the manufacturer's guidelines. This process consisted of trimming within the non-conductive rows and columns only (indicated by a darker colour within the sensor). This method ensured that no partial cells

existed within the sensor which is known to give inaccurate readings when loaded. Once the sensors had been sized accordingly, they were then placed inside the AFO. All participants wore socks as recommended by the international guidelines for plantar pressure measurements[93]. This is recommended because previous research has shown that warm, damp footwear can result in poor data[86]. The sensors were then connected to a 'cuff unit' and linked to the research software via a ten metre cable inserted from the cuff unit to a laptop containing the software.

Following the manufacturer's guidelines and the international protocol guidelines for plantar pressure measurements, the in-shoe pressure sensors were then conditioned by walking 20 steps on each sensor and then calibrated. Calibration is the method by which the raw digital output of the sensor is converted to actual pressure units; each sensor is calibrated individually. This process involved inputting the participants' weight into the gait analysis software and then asking them to stand on one leg for a period of one second.

Once each sensor had been conditioned and calibrated, each participant was asked to walk along a level, carpeted, pre-marked, six metre walkway at their normal walking speed. A six metre walkway was selected to allow some slack to remain within the cables. 'Normal' walking speed was implemented because enforcing the same absolute speed for each subject, via a treadmill or metronome, has been shown to result in altered gait patterns[86,94].

It is known that speed affects a variety of gait parameters and is therefore a confounding factor[95-96]. With increasing speeds, the literature consistently confirms that electromyography activity is altered, stance phase and double limb support time decrease and stride length increases[95,97-101]. Furthermore, increasing speed results

in higher ground reaction forces[97,102]. Speed is therefore an important factor and will be measured, but not controlled, for the reasons outlined above. Speed will be determined by timing the amount of time it takes each participant to walk the six metre walk way. It is also known that the type of flooring can alter the sensor outputs, with a relation between increased outputs with increased floor hardness, therefore this remained the same for each trial[88].

Each gait cycle was recorded for 500 frames (50 frames/second for 10 seconds). Based on an average cadence of 118 steps/minute for normal walking, this would allow approximately 19 steps to be recorded per cycle, which is sufficient for the analysis, and is explained and detailed further in the following section[103]. For each condition tested, five trials were recorded, as per international guidelines for plantar pressure measurements[93].

Two separate variables were assessed using the above method. The first variable was the AFO design.

It is current practice, within the University Hospital of Coventry and Warwickshire, for patients who have sustained a rupture of their TA, to be managed within a rigid rocker bottom style AFO (Donjoy, Guildford, UK, Figure 3.3). This AFO design is frequently documented for the IWB management of TA ruptures[75,104-105]. A carbon fibre dorsum AFO design has also been reported within the literature as an alternative to the rigid, rocker bottom AFO[73]. There are currently no studies comparing these different designs, as demonstrated by the systematic review outlined in Chapter 2.

Figure 3.3: Rigid rocker bottom AFO design

To achieve the first objective of this study, participants' gait patterns were assessed within a rigid rocker bottom AFO currently used within the hospital Trust (Figure 3.3) and with two alternative carbon fibre dorsum AFOs. The carbon fibre dorsum AFOs to be tested were chosen after discussions with the on-site hospital Trust appliances department regarding which companies currently supplied the hospital Trust. Those companies were then either invited to talk through their products or alternatively were seen at appropriate conferences.

Three companies were identified as supplying carbon fibre dorsum AFOs and all responded to the invitation. These companies were; Gilbert and Mellish, Ossur UK Ltd and Chaneco. Following demonstrations carried out by the company representatives, one company's design was regarded as being inappropriate because it was not designed to prevent DF. Preventing DF is important within the context of TA rupture management for preventing complications such as tendon lengthening[106].

Consequently, two carbon fibre dorsum AFO designs, from two separate companies were chosen to be tested within this convenience sample. The first, by Gillbert and Mellish, is named 'ToeOFF' (Figure 3.4) the second, by Ossur UK Ltd, is named 'AFO dynamic' (Figure 3.5). The AFOs are designed to wear within a participant's own footwear. However, for the purposes of standardisation, the AFOs in this study were worn within a standard shoe, but normal footwear was worn on the contralateral limb

Figure 3.4: 'ToeOFF'

Figure 3.5: 'AFO Dynamic'

The second variable to be assessed, outlined within the second objective, was the effect of four different levels of PF within the above three described AFOs.

NWB management of TA ruptures has traditionally involved serial casting, with the foot initially positioned in PF and gradually being reduced to neutral over a set period of time[40]. Since the introduction of IWB protocols, the same management principles of patients beginning their rehabilitation in PF and gradually reducing this

to neutral has remained the same[104]. Yet there is no known clinical indication why the TA needs to remain in a large degree of PF during the initial phases of rehabilitation. Furthermore, animal studies have shown that muscles which are immobilised in shortened positions undergo faster rates of muscle atrophy than muscles that are immobilised at resting lengths (neutral position)[104]. Therefore it is important to establish the effects of different degrees of PF, currently achieved with 1cm heel wedges, in clinical practice.

To establish the effects of different degrees of PF, participants' gait patterns were assessed within the above three described AFOs. They were assessed using three 1cm heel inserts, two 1cm heel inserts, one 1cm heel insert and no heel inserts. The effects which were measured are described in detail within the analysis plan. The uppermost range of three heel inserts was decided upon because this reflected current practice within the NHS Trust and the degree of PF achieved with three heel inserts has been shown to be sufficient enough to significantly reduce EMG activity of the triceps surae and decrease vertical ground reaction forces[107]. Therefore a higher number of inserted heel wedges would have no additional benefit.

There were, therefore, a total of four different ankle positions assessed within each of the three AFO designs, and one assessment with no AFO or heel wedge inserts, resulting in a total of 13 assessed conditions. The assessment of 'normal' gait without an AFO or heel wedge insert was taken first in all participants. Then, to account for known confounding factors such as learning effects and fatigue and all unknown confounding factors, the 12 intervention conditions were randomised using a row and column design[108] (Figure 3.6).

The row and column design, outlined in Figure 3.6, systematically randomises the order of AFO usage so that each is used first, second or third the same number of times (B1 = Rigid rocker bottom AFO, B2 = AFO dynamic, B3 = AFO ToeOff). Consequently, the sample size has to be a factor of three to achieve this. Additionally, along the side of each AFO condition are the terms W1, W2, W3 and W0. These relate to the randomised order and number and of inserted heel lifts within each trialled AFO (W1=one heel wedge, W2=two heel wedges etc).

In addition to the randomisation of AFOs and heel wedge inserts, a further randomisation sequence was used to allocate the participant to wear the AFO on either their left or right leg (R or L). Randomisation to the left or right leg was carried out because differences of between 9-16% in lower limb strength, within healthy participants, has been recorded within the literature[109] and is therefore a known confounding factor that needed to be taken into consideration.

The randomisation sequence below was generated by an independent researcher within the department and was accessed by telephone at the point of each participant arriving for data collection. Informed written consent for entry into the study was obtained prior to randomisation (Appendix B).

Researcher bias was reduced through including consecutive participants. This was in addition to randomisation of participants to trial conditions implementing a sequence which ensured that each AFO/heel wedge combination was used first or last the same number of times to account for any learning or fatigue effects. The randomisation sequence was concealed until the point of allocation.

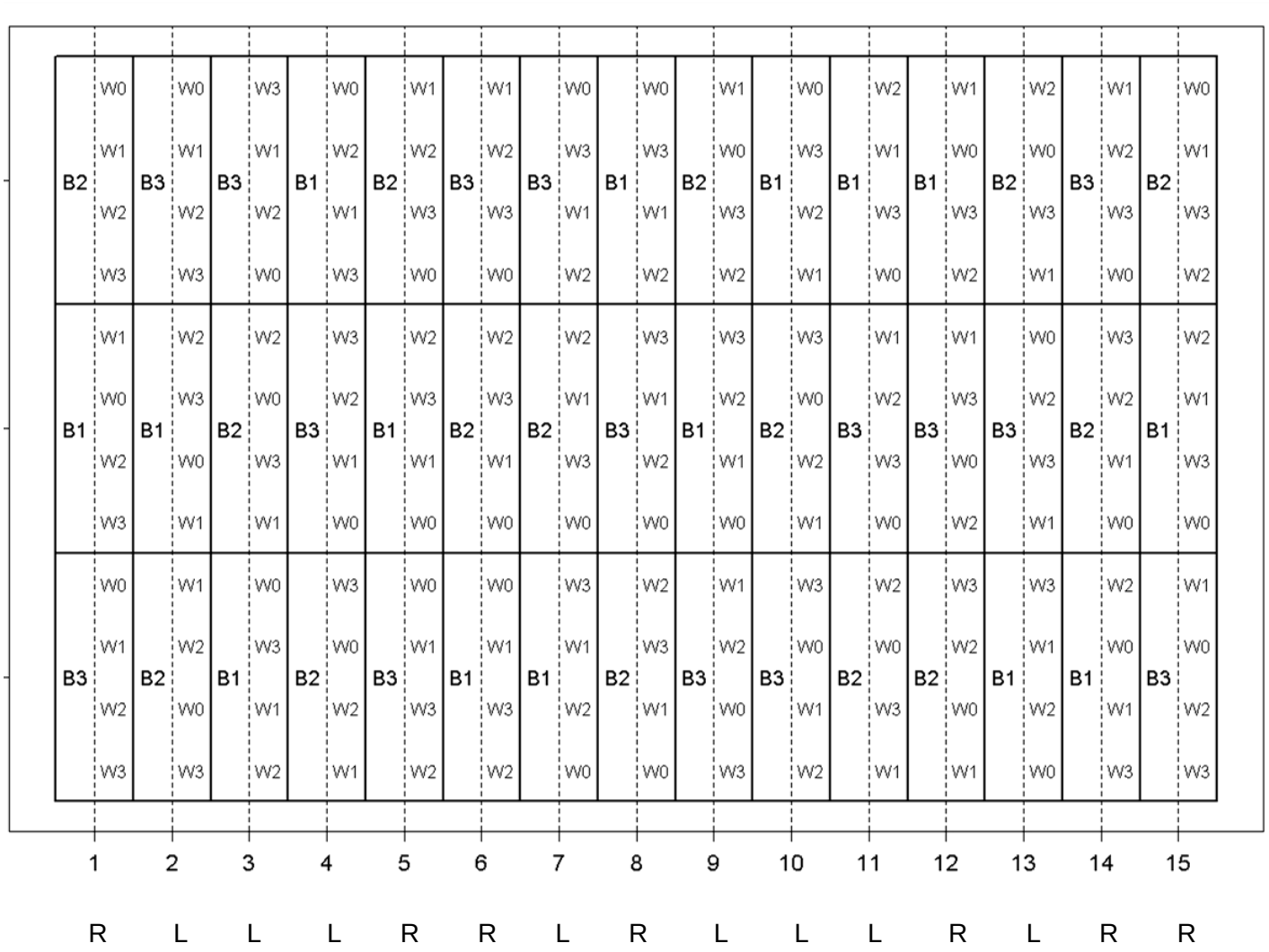


Figure 3.6: Randomisation sequence

In addition to the plantar pressure recordings, ROM permitted within the AFO was measured using an electrogoniometer system (Biometrics Ltd, Gwent). This measurement would allow comparisons to be made regarding the degree of DF and PF permitted across the different conditions. This is an important measure for the previously described clinical complication of tendon lengthening, which will manifest if there is no restriction of movement.

The electrogoniometer works via two end blocks connected by a spring and composite wire that has a series of strain gauges. As the angle between the end blocks changes, so does the strain along the wire, resulting in a measurement of angular displacement. Following the manufacturer's guidelines, double sided adhesive tape was used to attach the end blocks anterior to the ankle joint in line with the tibia and second metatarsal. With the knee at 90 degrees and the participant in a sitting position, the electrogoniometer reading was set to zero. This was carried out prior to placing the feet inside the specified footwear.

3.1.5 Analysis plan and outcome measures

For each condition, five cycles were recorded as per the international guidelines for plantar pressure measurements. The third recording was subsequently analysed. Within the third recording the second, third and fourth steps were analysed (Figure 3.7). This method has been advocated because current literature has demonstrated that there is no increase in reliability after the aggregation of three steps. The first and last steps were disregarded to account for the effects of acceleration and deceleration[90,93]. Recordings were rejected if they were considered under stridden, over stridden, hesitant or targeted, which has been accepted as a valid method by the foot pressure interest group[93].

All data was collected by the researcher. All data was recorded and saved for each test condition. The researcher analysed the data at the end of all testing procedures. As the researcher was both collecting and analysing the data, waiting to analyse the data at the end of testing procedures was one method of increasing reliability. However this method is limited because ideally the individual analysing the data would be blinded to the test conditions to further limit researcher bias.

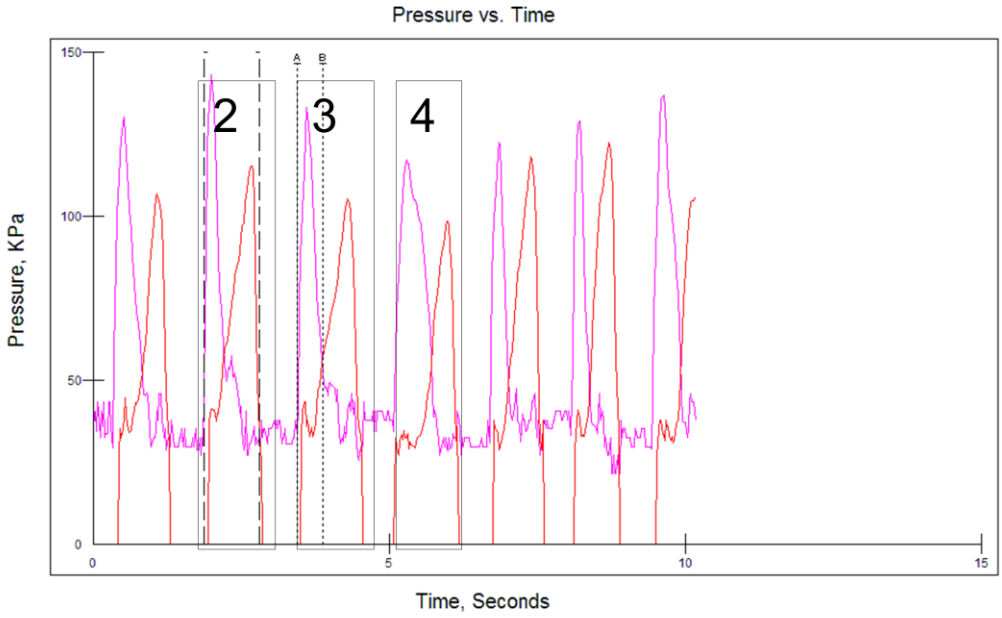


Figure 3.7: Example of the recorded data output

The TA connects the gastrocnemius and soleus muscles to the posterior aspect of the calcaneus to permit transmission of plantarflexion torque during the terminal stance and pre-swing phases of the gait cycle[110-111]. Therefore the first outcome to be assessed was the duration of the terminal stance and pre-swing phases as a proportion of the total stance component on the gait cycle. The beginning of terminal stance was defined as the point at which the patient's centre of gravity lay over the centre of the foot and the end of pre-swing was defined as the point at which the toes left contact with the floor.

The second outcome was quantification of plantar pressure measurements at the heel and forefoot. The forefoot and heel areas were defined as the distal 40% and proximal 30% respectively[93] (Figure 3.8). Each measurement was reported as a percentage of the value recorded for the contralateral limb because the absolute measurements vary between individuals based on height and weight parameters, enabling comparisons to be problematic. The analysis was therefore based upon the difference between the two lower limbs.

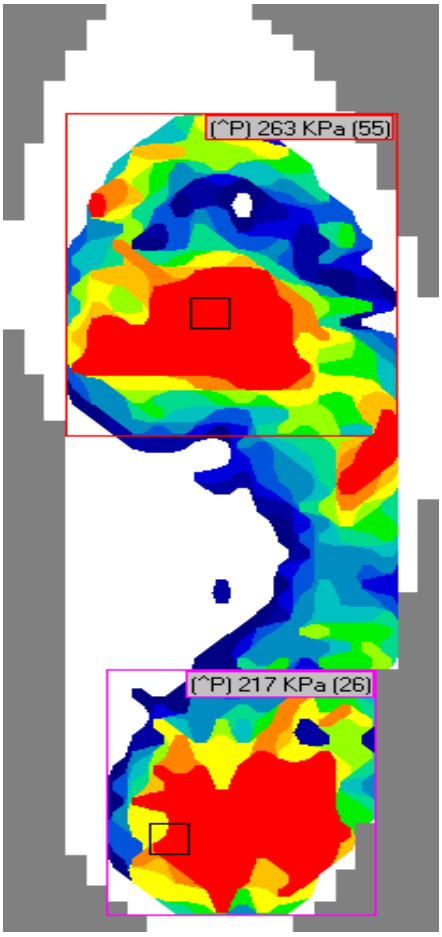


Figure 3.8: Example of a pressure recording

The third outcome to be assessed was cadence, defined as the number of steps within a set time. This was documented because previous research has suggested that the amount of PF within the AFO is important because it reduces cadence and consequently decreases vertical ground reaction forces. However, this previous

research did not compare different levels of PF, AFO designs or measure/control for speed[107]. Consequently, this outcome measure is being recorded to enable comparison with this previous study.

As previously stated, the second, third and fourth steps were analysed. The mean of these three separate recordings was then analysed as per previous recommendations[90]. The datasets were analysed using descriptive statistics including the mean, standard deviation and range of each condition. The descriptive dataset analysis was carried out using Microsoft Excel 2007. Inferential statistical analysis was performed using SPSS 17.0 to perform a two-way analysis of variance (ANOVA). This analysis determines firstly the effect of the number of heel wedge inserts regardless of the AFO design, secondly the effect of the AFO design regardless of the number of heel wedge inserts and thirdly the AFO and heel wedge number interaction.

Following the analysis of variance amongst the two factors (AFO design and number of heel wedge inserts) a post hoc analysis using 'Tukey' was used to differentiate where the exact differences lie. This test is designed to give only one type one error per 20 analyses when the null hypothesis is true, as opposed to doing a *t*-test for each pair of groups, which gives one error per 20 comparisons when the null hypotheses is true[112]. Final analysis included scatter plots and accompanying Pearson correlation coefficients to further explore relationships between the parameters.

To achieve the second part of this study's aims (to draw inferences from the above observations to the application of TA rupture management), the above analysis will be discussed in relation to previous literature within the field of TA rupture

rehabilitation. As previously outlined, there are many areas of TA rupture rehabilitation that remain unknown. To add to this complexity, it is beyond the scope of this study to conclude if these findings will translate to a clinical setting, within patients who have sustained this injury, secondary to using healthy participants. Further research will be required to determine if the findings within healthy participants translate to a clinical setting.

However, what is known in relation to the above recorded objective measures, is that the AFO needs to prevent pressures produced at the heel and forefoot beyond those recorded for normal walking[104]. In the case of forefoot pressures, this is because increased pressure relates to increased force production by the triceps surae. These forces are transmitted by the TA. The forces transmitted by the TA during the terminal stance and pre-swing phases of the gait cycle result are equivalent to 2.4 times an individual's body weight. One study found that approximately 553 Newton's (SD 182) are produced at the TA during normal walking[83]. Therefore, an AFO needs to prevent ankle DF or reduce the need for the posterior calf muscles to contract[107].

It is not known how much force is required to re-rupture a healing tendon or to separate the tendon ends, causing tendon lengthening. It is known that WB during the early phases of healing stimulates fibroblast activity and type III collagen synthesis[48]. Therefore, the purpose of the AFO is to provide 'protected' WB that represents normal gait parameters, within the limits of decreased permitted movement. In the case of heel pressures, clinically, it is observed that patients often report heel pain. It is thought that this is possibly related to the increased pressures reported in the heel area[113].

Furthermore, the AFO needs to reflect the normal proportions for the amount of time spent in terminal stance and pre-swing phases of the gait cycle as a percentage of the total stance phase. This is important because the triceps surae works eccentrically during this phase of the gait cycle, to prevent the tibia rotating forwards over the talus[111]. Therefore if this phase of the gait cycle is reduced it may lead to disuse atrophy of the triceps surae. Additionally, it is possible that patients may acquire a learned motor pattern during the time the AFO is worn[114], however this dimension is beyond the scope of this work.

If all the AFO designs fulfil these criteria, the AFO that most represents a normal gait cycle, within the limits of restricted movement, will be implemented within clinical practice to be compared to current practice.

3.1.6 Sample size

An appropriate sample size was obtained by Nicholas Parsons (Statistician) using R software, http://www.r-project.org/. This software demonstrated that a sample size of at least 14 participants was needed to achieve 90% power at the 5% significance level for this study design. This calculation used an effect size of 0.4 (medium to large). To allow flexibility, for potential outlying results, and to round to the nearest multiple of three, for reasons described previously, 15 participants were planned to be assessed. This assumed normally distributed data and that variability between groups was the same[115].

The R software calculated the sample size estimation for a two-way ANOVA, based on k groups, with n observations, effect size f and significance level α the power was calculated as follows:

$$\text{Power} = \mathbf{pf}\,(qf\,(\alpha, k\text{-}1, k\,(n\text{-}1)), k\text{-}1, k\,(n\text{-}1), \lambda); \qquad (1)$$

Where $pf\ (q,v_1,v_2,\phi)$ is the F distribution function, q is a quantile, v_1 and v_2 are degrees of freedom, ϕ is the non-centrality parameter and $qf\ (\alpha,v_1,v_2)$ is the F quantile function with significance level α. To determine sample sizes at set power levels (e.g. 90%), Equation (1) is solved to find values of n that give powers equal to 0.9 for known k, f and α. For 90% power, k=12, f=0.4 and α=0.05, then n≈13.5; which was rounded up to 15 for this study.

An effect size of 0.4 was chosen based on two separate unpublished case series of gait parameters following a TA rupture. (One from the University Hospital of Coventry and Warwickshire, that uses the rigid rocker bottom AFO as standard practice and a second within a separate hospital within the UK that uses the flexible carbon fibre dorsum AFO as standard practice.) Mean forefoot pressures two weeks following removal of the respective AFOs showed mean differences of 49% and 33% between the injured and uninjured limbs within the two samples. The standard deviation of both samples was 20%. Using this information, the mean of the first sample was subtracted from the mean of the second sample and divided by the standard deviation. This calculation indicated a possible effect size of 0.8 between the rigid rocker bottom and dorsum carbon fibre AFO designs. It was estimated that recruitment and data collection would take place over a three month time period.

3.1.7 Adverse event management

After the first and final visit, each participant was asked whether they had experienced any adverse events. Adverse events were defined as any untoward medical occurrence in a clinical trial subject, which does not necessarily have a causal relationship with the treatment. All reported adverse events would be listed on the appropriate case report form and reported centrally.

Serious adverse events were defined as any untoward and unexpected medical occurrence that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect or any other important medical condition, which although not included in the above, might require medical or surgical intervention to prevent one of the outcomes listed.

All serious adverse events will be entered onto the Serious Adverse Event reporting form. Once received by the Principal Investigator, causality and expectedness would be determined. Serious adverse events that were deemed to be unexpected and related to the trial would be notified to the main Research Ethics Committee within 15 days for a non life-threatening event and within seven days for a life-threatening event. All participants experiencing serious adverse events would be followed-up as per protocol until the end of the trial.

3.1.8 End of trial

The end of the trial was defined as the final visit of the last participant.

3.1.9 Trial organisation, oversight and data management

This was a small, healthy subject study so no formal TSC or DMC was necessary. All case report forms will be held in a secure, locked filing cabinet within the restricted area of the Clinical Sciences Research Laboratory. Participants will be identified by a code number only. All paper and electronic data will be retained for at least five years after completion of the study.

During the development of this study the PhD supervisors were responsible for critically reviewing and discussing key methodological considerations during

supervision meetings. Statistical and sample size advice was provided by Nicholas Parsons (statistician). All trial procedures (recruitment, consent, data collection, data recording, analysis and interpretation) were completed by myself and reviewed during PhD supervision meetings.

3.1.10 Resource use

To complete this study access was required to Microsoft office software, SPSS, F-Scan system, 15 pairs of Tekscan foot sensors and the electrogoniometer system.

3.2 Results

Fifteen participants consented to take part in this study. No participants were excluded or did not meet the inclusion criteria and 15 participants data were analysed.

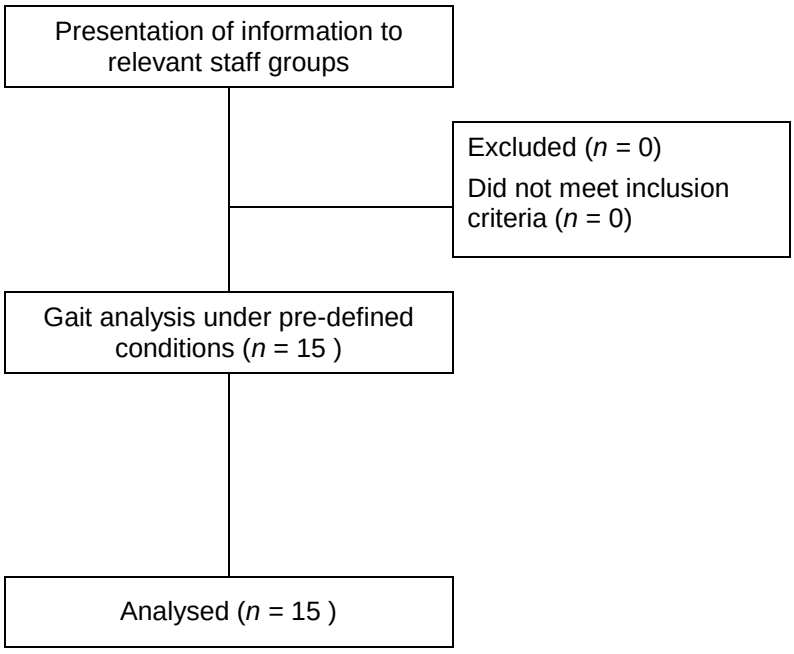


Figure 3.9: Flow chart of participant flow

3.2.1 Control group data

Table 3.1 illustrates the baseline demographics for the 15 included participants. The mean age of the sample was 31.3 years. Eight men and seven women took part; eight left and seven right lower limbs were randomised accordingly.

Table 3.1: Baseline demographics of control group

	Healthy participants (*n*=15)
Mean age in years (SD)	31.3 (4.7)
Male/Female	8/7
Left/Right	8/7
Mean height in cm (SD)	172.3 (8.7)
Mean weight in Kg (SD)	70.4 (14.5)

Figure 3.10 through to Figure 3.13 illustrate the speed, heel pressures, forefoot pressures, amount of time spent in terminal stance and pre-swing phase as a proportion of the stance phase and ROM during normal walking conditions. Each of these will be discussed in turn.

Each participant was asked to do five trials for each condition. Figure 3.10 shows the mean speeds and SD for each individual trial. To assess if participants' speed changed with increasing trial walks, a one-way analysis of variance was carried out. This result was non-significant (p=0.435), demonstrating that there were no differences between test walk speeds.

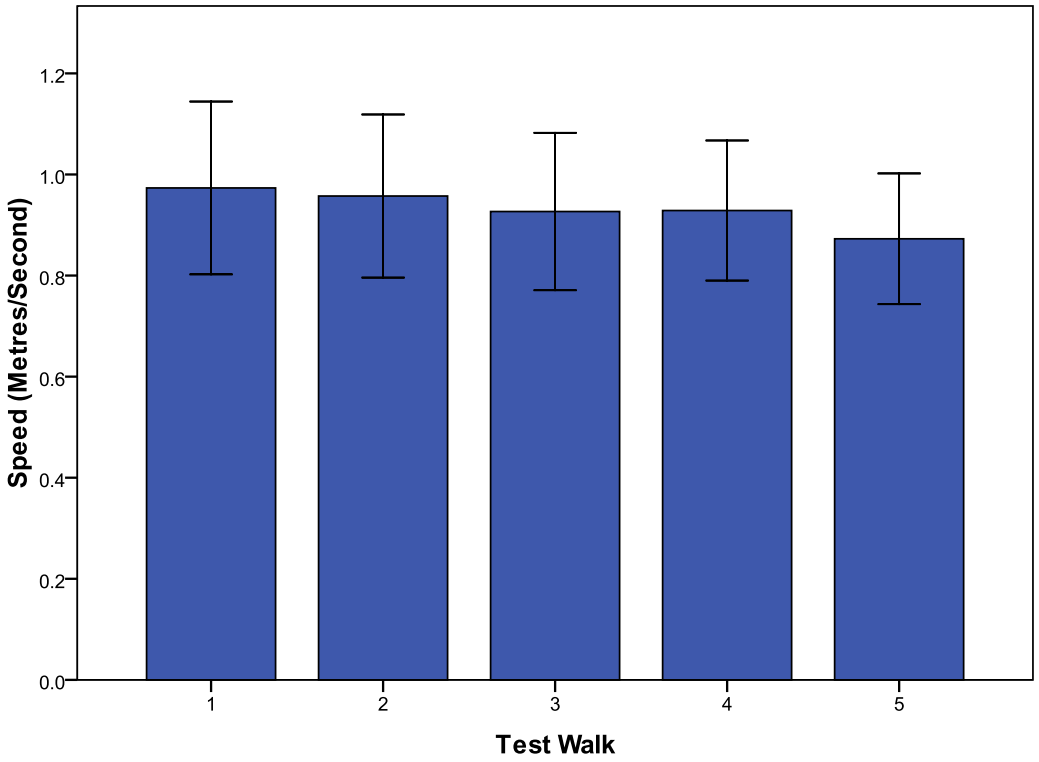


Figure 3.10: Mean and SD for each test walk speed (metres/second) control

Further analysis of the data showed that the average cadence for the control condition was 104 steps per minute (SD 11). The mean heel and forefoot pressures are shown in Figure 3.11 for each limb (± 2 SD). Mean heel pressures for each foot were 59 (KPa) and 64 (KPa) (~8% difference) and mean forefoot pressures were 65 (KPa) and 62 (KPa) (~ 5% difference). Figure 3.12 also shows the percentage of time spent in the terminal stance and pre-swing phases of the gait cycle as a proportion of the total stance phase. The figures are 48% and 49% for the control condition. The final parameter, ROM, is illustrated in Figure 3.13, showing that the average measure of DF in degrees at its peak was 7º and the average measure of PF at its peak was 12º.

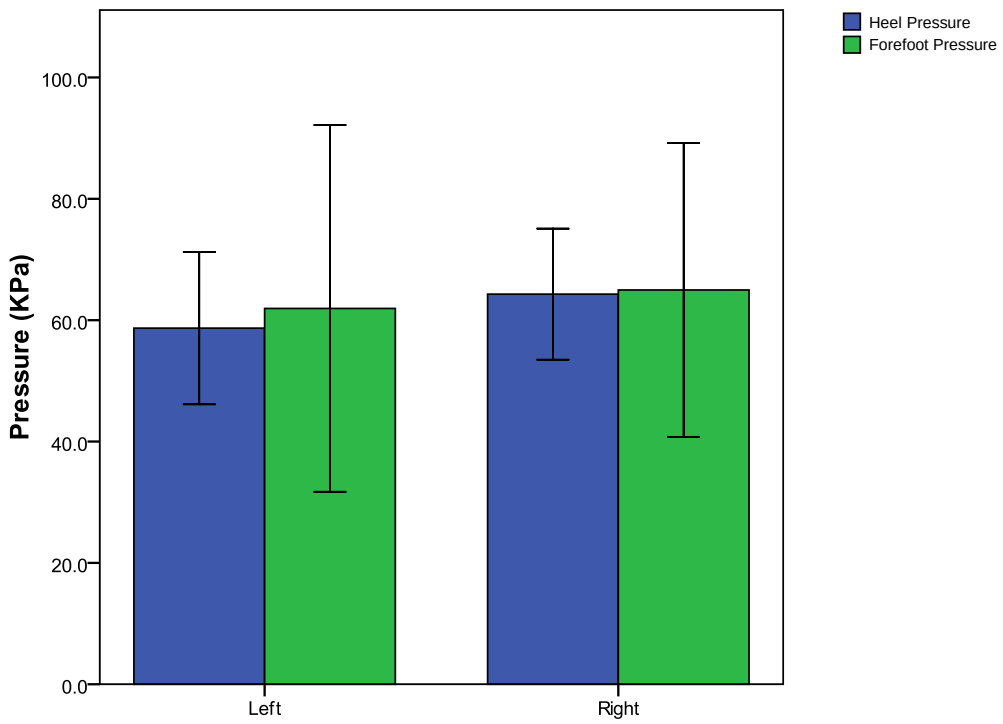


Figure 3.11: Mean and SD heel and forefoot pressures (KPa) control

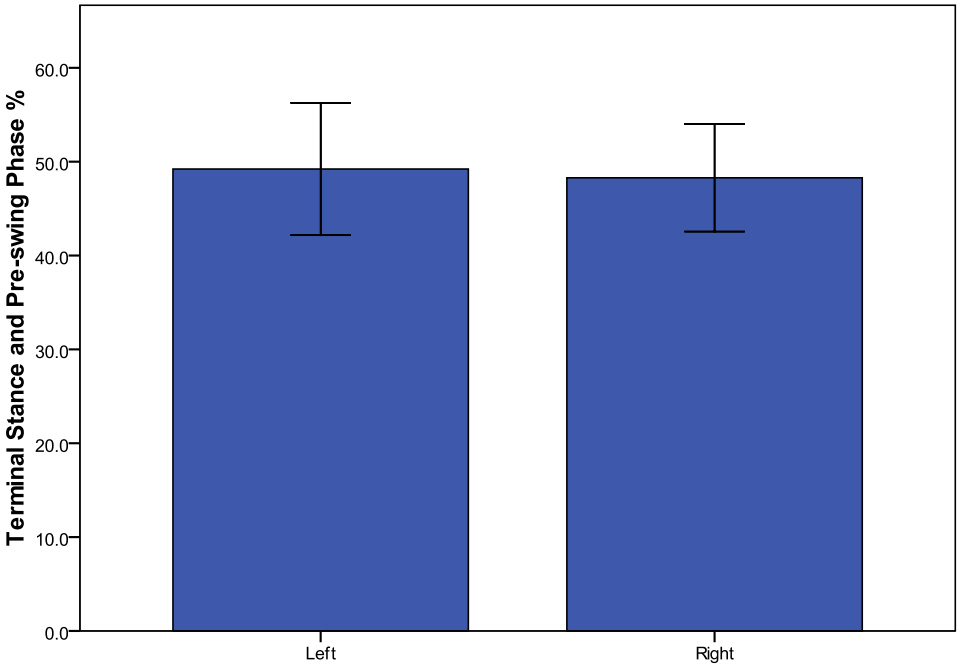


Figure 3.12: Mean and SD for % duration of terminal stance and pre-swing control

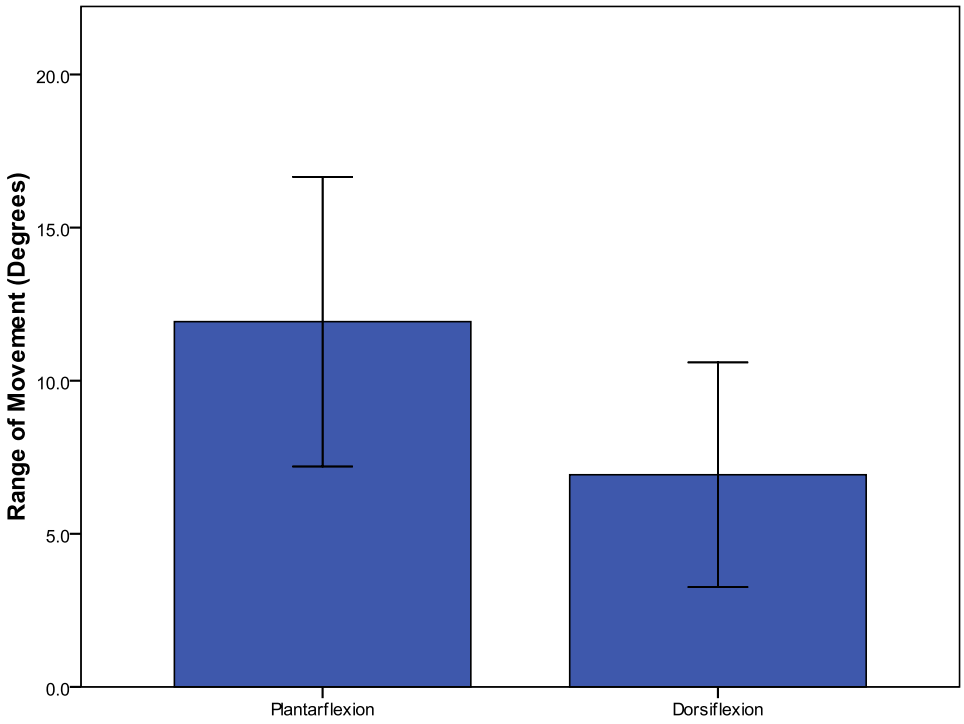


Figure 3.13: Mean and SD for ROM (degrees) control

In addition to the descriptive statistics carried out for the control condition, pair-wise correlations, with scatter plots, were produced to further investigate the relationships between these parameters within the control condition. Table 3.2 shows the Pearson Correlation Coefficients for each paired comparison, with significance values. Figure 3.14 through to Figure 3.19 illustrate the scatter plots for the following Pearson Correlation Coefficient analyses.

Speed was not significantly correlated to any assessed parameter except cadence ($p < 0.001$). Cadence was also significantly correlated with the amount of time spent within the terminal stance and pre-swing phase of the gait cycle as a proportion of the total stance phase ($p = 0.023$). As cadence increased so did the amount of time spent within the terminal stance and pre-swing phase of the gait cycle as a proportion of the stance phase.

Heel and forefoot pressures were not significantly correlated with speed or cadence. However they were correlated to each other (p=0.006). As heel pressures increased forefoot pressures decreased. Heel pressures were not significantly correlated to any other parameter. Conversely forefoot pressures were increased as the time spent within the terminal stance and pre-swing phase of the gait cycle increased (p< 0.001). (The p value in this analysis is in comparison to the assumption that the population correlation is zero, so if the p value is small you can conclude that the sample correlation is incompatible with zero correlation).

Table 3.2: Pearson correlation coefficients for pre-defined gait parameters control

Paired comparisons	Pearson correlation coefficient	Significance
Heel pressure & speed	0.05	0.794
Forefoot pressure & speed	0.07	0.697
Heel pressure & terminal stance and pre-swing %	-0.06	0.728
Forefoot pressure & terminal stance and pre-swing %	0.59	<0.001
Terminal stance and pre-swing % & speed	-0.25	0.170
Forefoot pressure & heel pressure	0.48	0.006
Speed & cadence	-0.71	<0.001
Terminal stance and pre-swing % & cadence	0.41	0.023
Heel pressure & cadence	0.08	0.669
Forefoot pressure & cadence	0.21	0.261

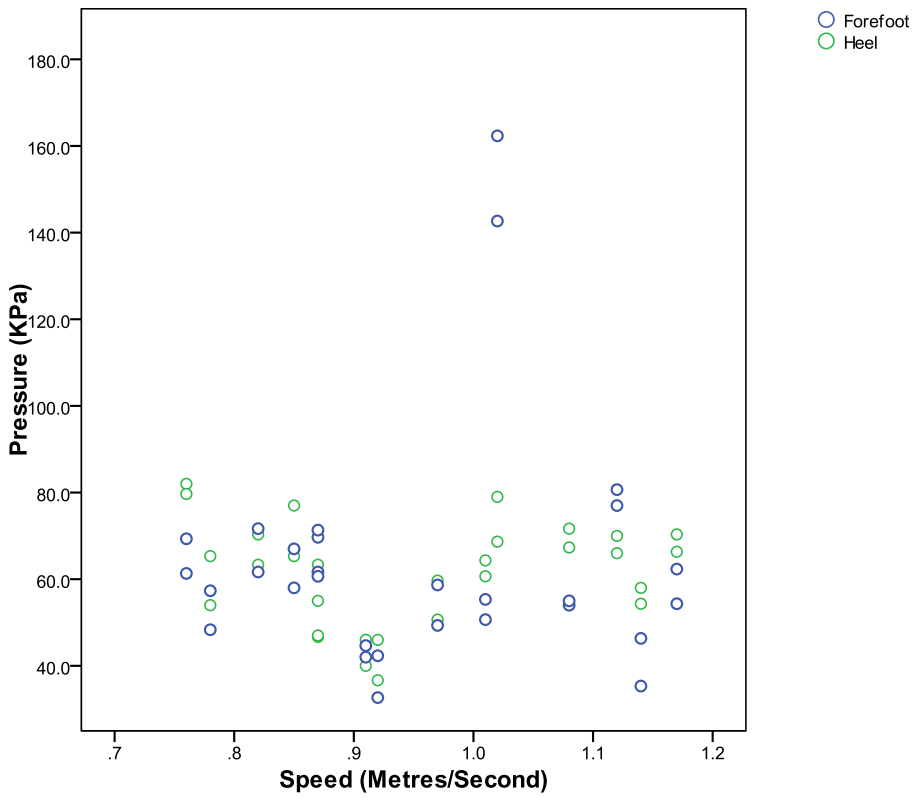


Figure 3.14: Scatter plot of pressure (KPa) and speed (metres/second) control

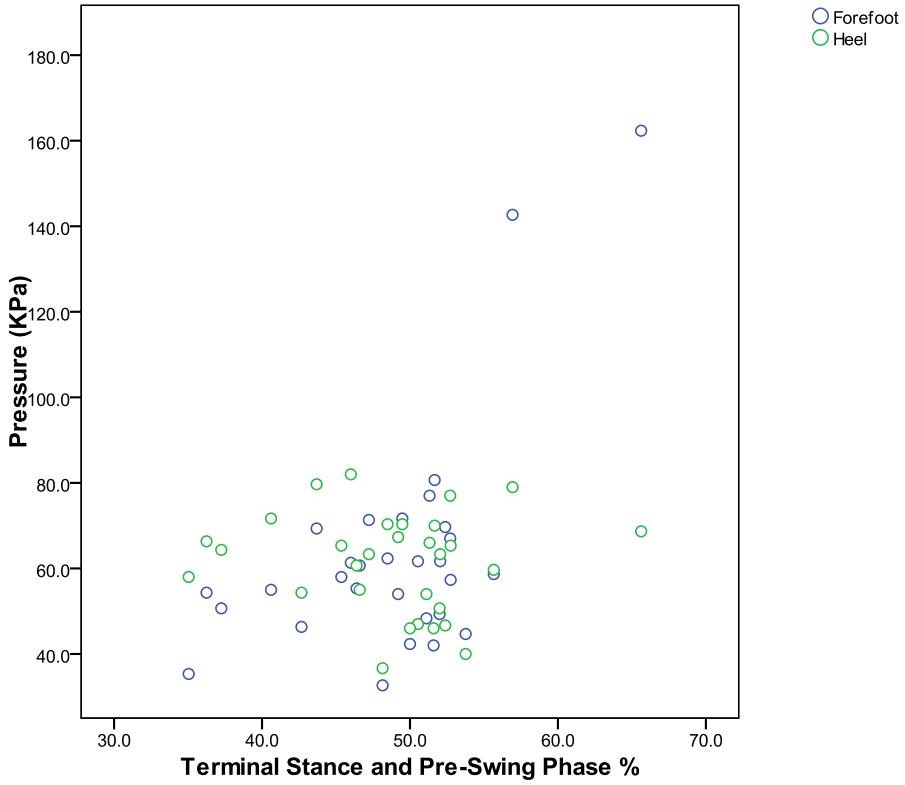


Figure 3.15: Scatter plot of pressure (KPa) and % duration of terminal stance and pre-swing phase control

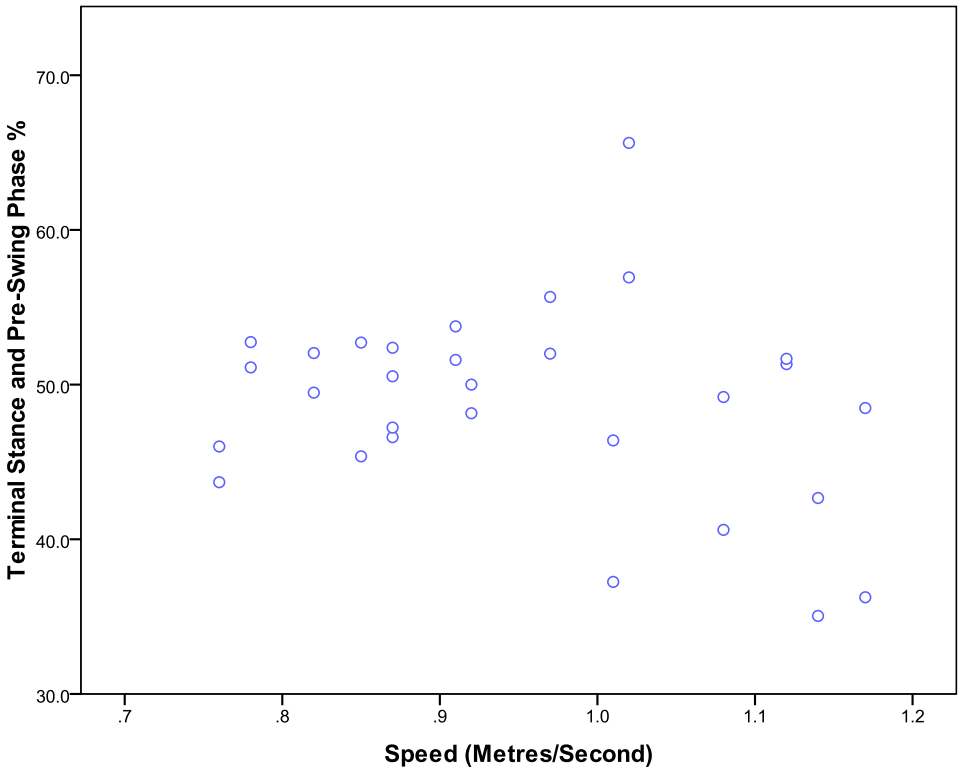


Figure 3.16: Scatter plot of terminal stance and pre-swing phase % and speed (metres/second) control

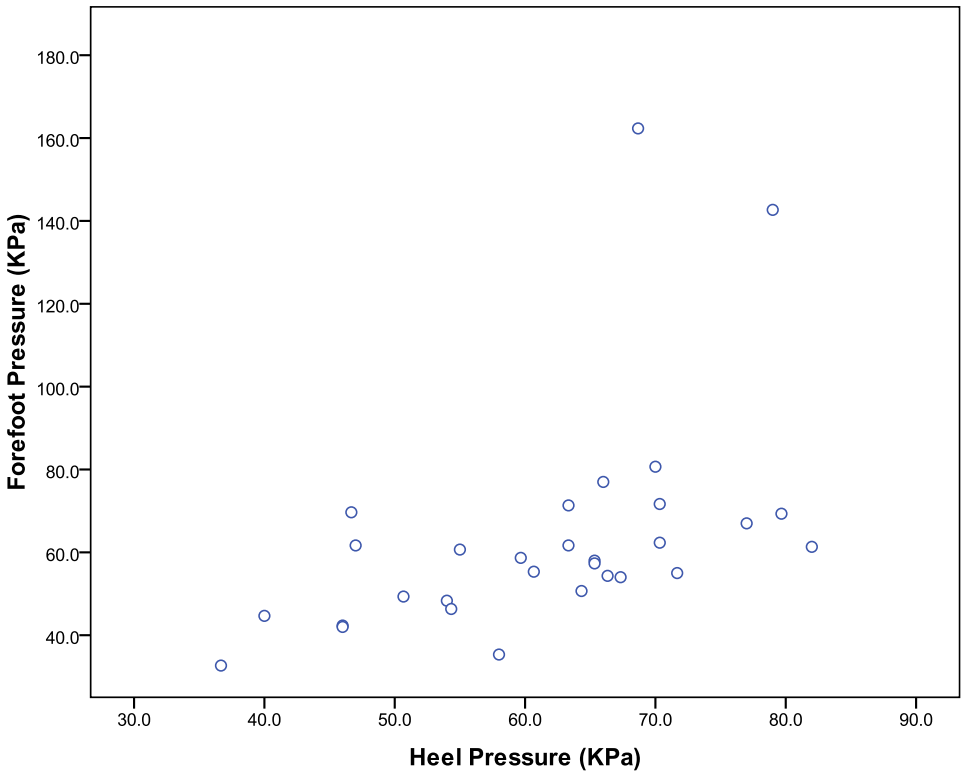


Figure 3.17: Scatter plot of forefoot pressure (KPa) and heel pressure (KPa) control

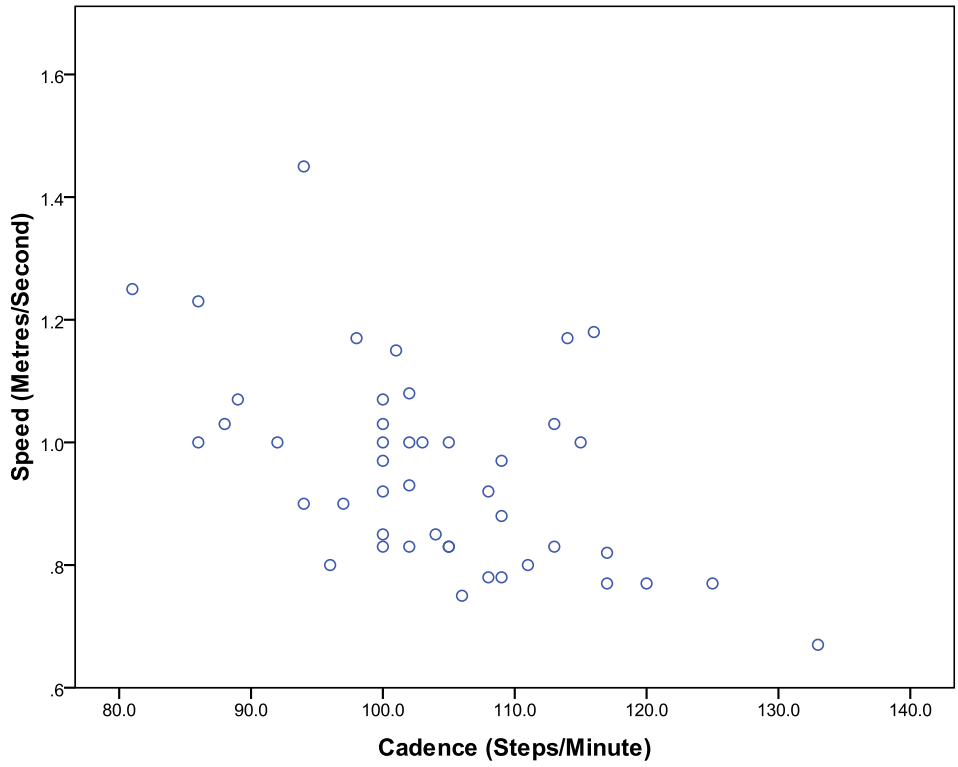


Figure 3.18: Scatter plot of speed (metres/second) and cadence (steps/minute) control

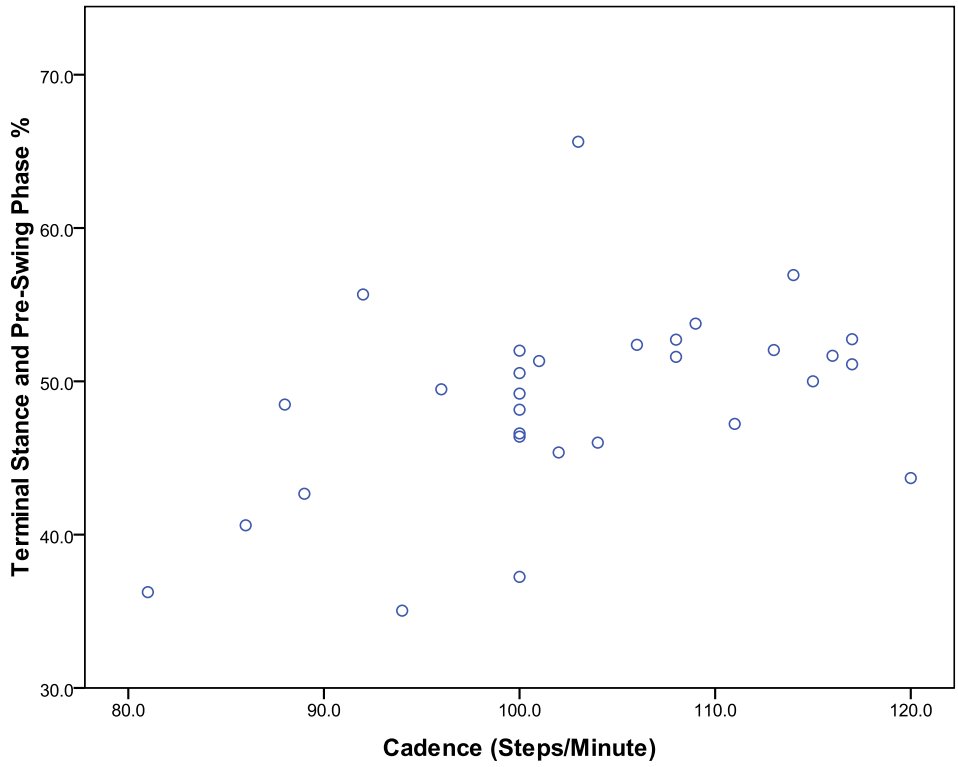


Figure 3.19: Scatter plot of terminal stance and pre-swing phase % and cadence (steps/minute) control

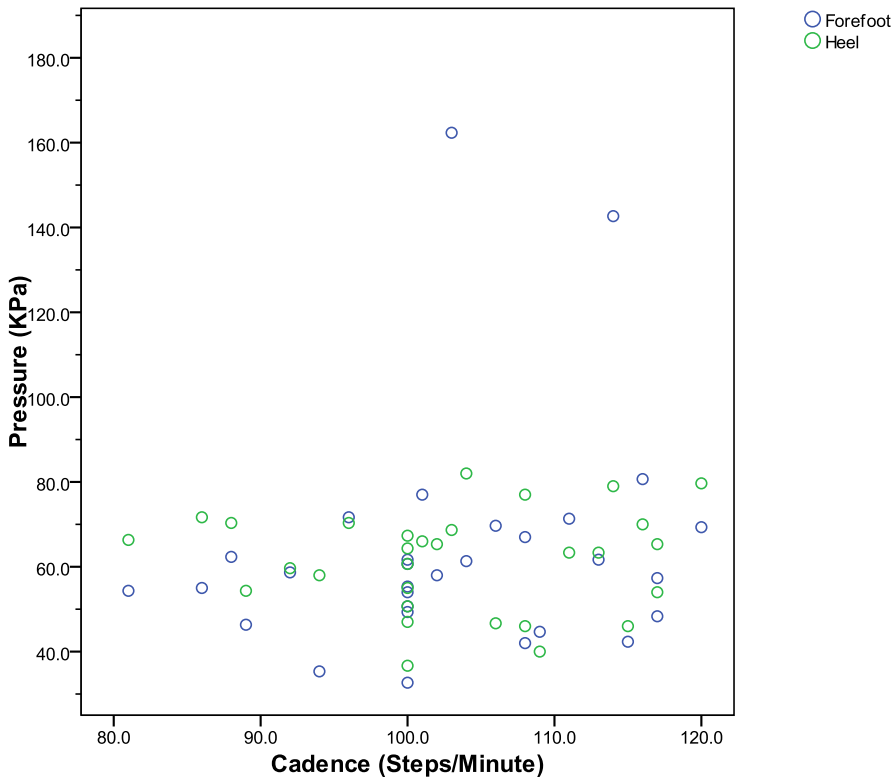


Figure 3.20: Scatter plot of pressure (KPa) and cadence (steps/minute) control

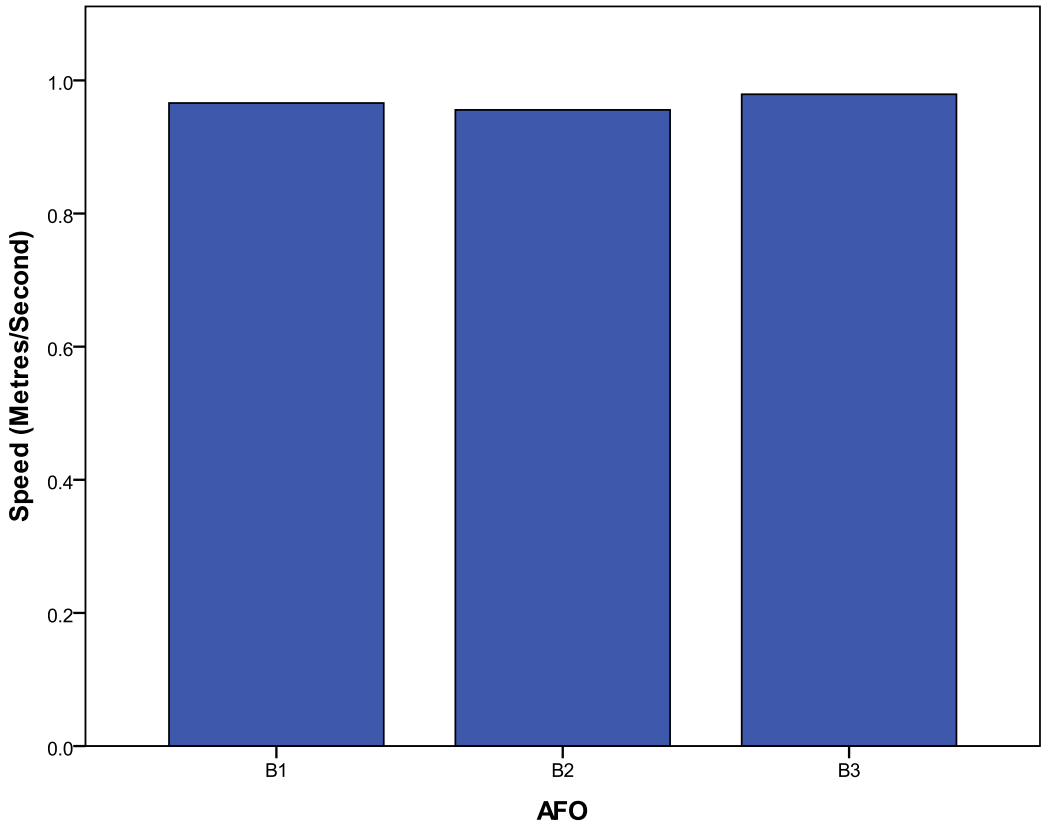
3.2.2 Trial conditions: speed, range of movement and cadence

Once the control walking trials had been completed, each participant then completed five walking trials under twelve different conditions, as previously described within the methods section. There were two key variables assessed; the first was the type of AFO design and the second was the number of heel wedge inserts within each AFO design.

There were three AFO designs assessed. These were a rigid rocker bottom AFO (Donjoy, Guildford, UK, Figure 3.3) and the two dorsum carbon fibre AFO designs (AFO Dynamic, Ossur, UK and ToeOFF, Gilbert and Mellish, Figure 3.4 and Figure 3.5). Throughout the analysis, these are referred to as B1, B2 and B3 respectively. Within each AFO design, participants walked with three, two, one and no heel wedge inserts within them. These are referred to as W3, W2, W1 and W0 respectively.

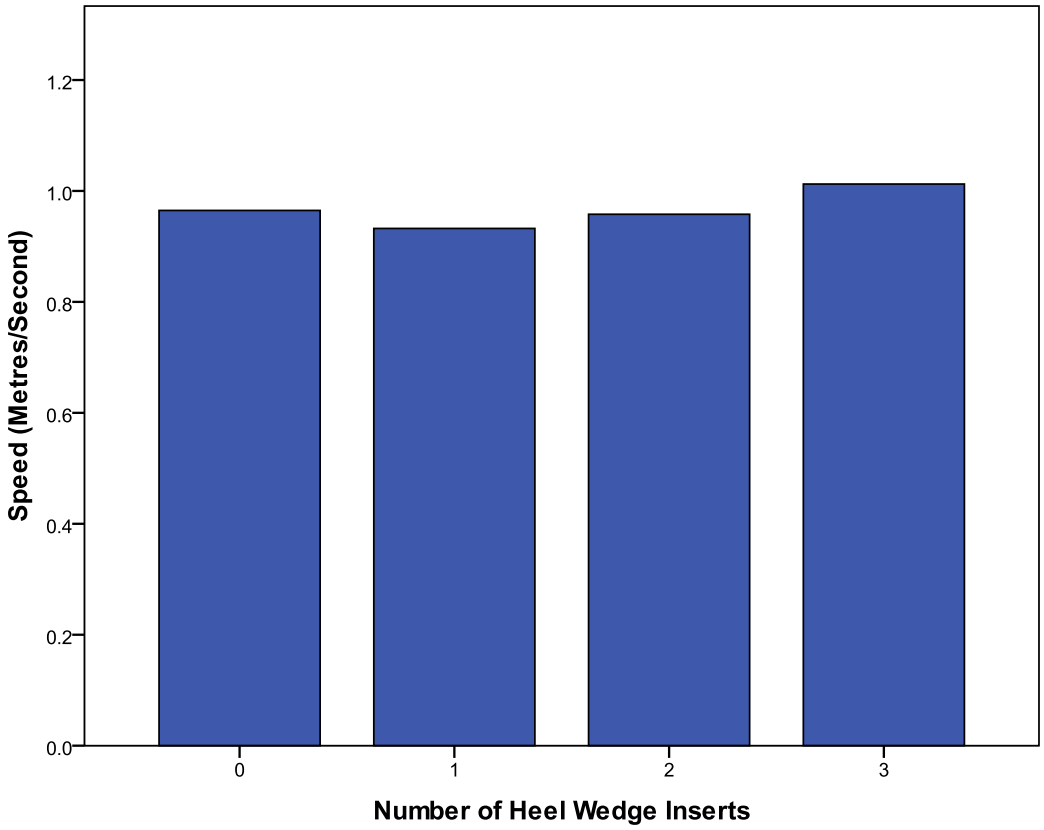
Figure 3.21 and Figure 3.22 illustrate the mean recorded speed and ANOVA F probability for the first variable (AFO design) regardless of the number of heel wedge inserts and conversely, for the second variable (number of heel wedge inserts) regardless of the AFO design.

The results show that there were no significant differences in recorded speed between AFO designs across all conditions (ANOVA: F Probability 0.368). However, there were significant differences between the number of heel wedge inserts used regardless of AFO design (ANOVA: F Probability < 0.001).



ANOVA: F Probability	0.368

Figure 3.21: Mean speed (metres/second) for B1, B2, B3, with ANOVA F probability



ANOVA: F Probability	<0.001

Figure 3.22: Mean speed (metres/second) for each heel wedge condition, with ANOVA F probability

Post-hoc analysis (using Tukey's Honestly Significant Difference[112]) showed that walking with three heel wedge inserts within an AFO is significantly different from walking with two, one and no heel wedge inserts. There were no differences between other pair wise comparisons as Table 3.3 demonstrates.

Table 3.3: Post hoc analysis for Figure 3.22 showing, mean difference, upper and lower limits and p-value for each comparison

Wedges	Difference	Lower	Upper	Significance
0 - 1	0.0	-0.1	0.0	0.103
0 - 2	0.0	0.0	0.0	0.946
0 - 3	0.0	0.0	0.1	0.006
1 - 2	0.0	0.0	0.1	0.301
1 - 3	0.1	0.0	0.1	<0.001
2 - 3	0.1	0.0	0.1	<0.001

Table 3.4 and Table 3.5 show the mean degrees of DF and PF permitted within each AFO design regardless of the number of heel wedge inserts and movement permitted across heel wedge inserts regardless of AFO design. The F Probability for DF and PF within the three AFOs regardless of the number of heel wedge inserts was statistically significant (0.002 and 0.026). Further post hoc analysis is shown in Table 3.4. This shows that there is a significant difference between B1 and B2 only for both DF and PF (Difference of 8º and -5º respectively).

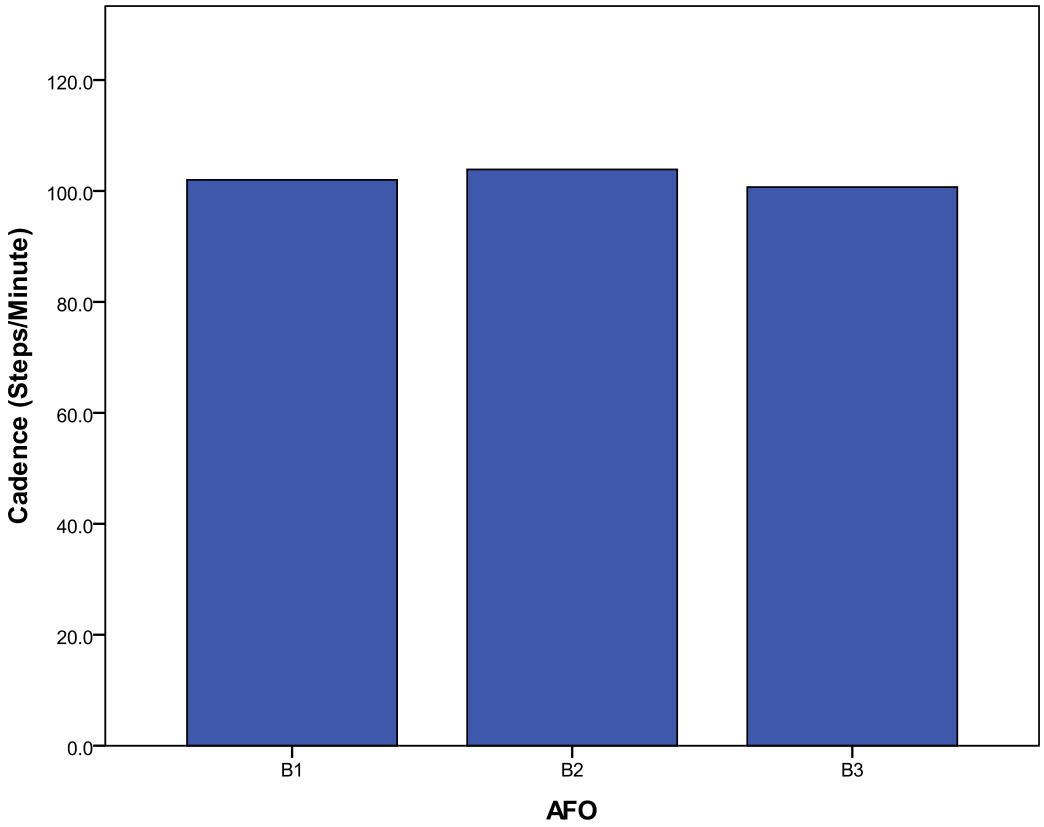
Table 3.4: Mean difference, upper and lower limits, and p-value for each comparison

	B1	B2	B3	
Mean DF (SD)	-3.4 (10.1)	5.1 (7.1)	1.1 (7.8)	
Mean PF (SD)	10.9 (9.7)	5.4 (7.4)	9.2 (7.9)	
DF	**Difference**	**Lower**	**Upper**	**Significance**
B1 - B2	8.5	3.2	13.7	<0.001
B1 - B3	4.4	-0.8	9.6	0.110
B2 - B3	-4.1	-9.3	1.2	0.150
PF				
B1 - B2	-5.5	-10.4	-0.7	0.022
B1 - B3	-1.8	-6.6	3.1	0.640
B2 - B3	3.8	-1.1	8.6	0.148

Range of permitted movement across the number of heel wedge inserts regardless of AFO design was also significant (F probability <0.001 and <0.001). Table 3.5 shows the results for the post hoc analysis, which were statistically significant for each comparison within measures of DF. At the extreme of no wedge inserts compared to three, there was a mean difference of seven degrees. The removal of each heel wedge insert was equivalent to approximately a two degree increase in DF. For PF, the mean difference between no heel wedge inserts and three was five degrees. With each heel wedge removed, the differences were small (between one to two degrees) and non-significant. However, the differences between none and two heel wedge inserts, one and three and none and three were larger (between three and five degrees) and were statistically significant.

Table 3.5: Mean difference, upper and lower limits and p-value for each comparison

	W0	W1	W2	W3
Mean DF (SD)	4.5 (8.3)	2.5 (8.0)	0.0 (9.2)	-3.2 (9.3)
Mean PF (SD)	5.9 (7.9)	7.5 (8.0)	9.2 (9.1)	11.4 (8.9)
DF	**Difference**	**Lower**	**Upper**	**Significance**
0 - 1	-2.0	-3.8	-0.2	0.025
0 - 2	-4.5	-6.3	-2.7	<0.001
0 - 3	-7.6	-9.4	-5.8	<0.001
1 - 2	-2.5	-4.3	-0.7	0.003
1 - 3	-5.6	-7.4	-3.8	<0.001
2 - 3	-3.1	-4.9	-1.3	<0.001
PF				
0 - 1	1.6	-0.5	3.7	0.215
0 - 2	3.3	1.2	5.5	0.001*
0 - 3	5.4	3.3	7.6	<0.001
1 - 2	1.7	-0.4	3.9	0.165
1 - 3	3.8	1.7	6.0	<0.001
2 - 3	2.1	0.0	4.3	0.051



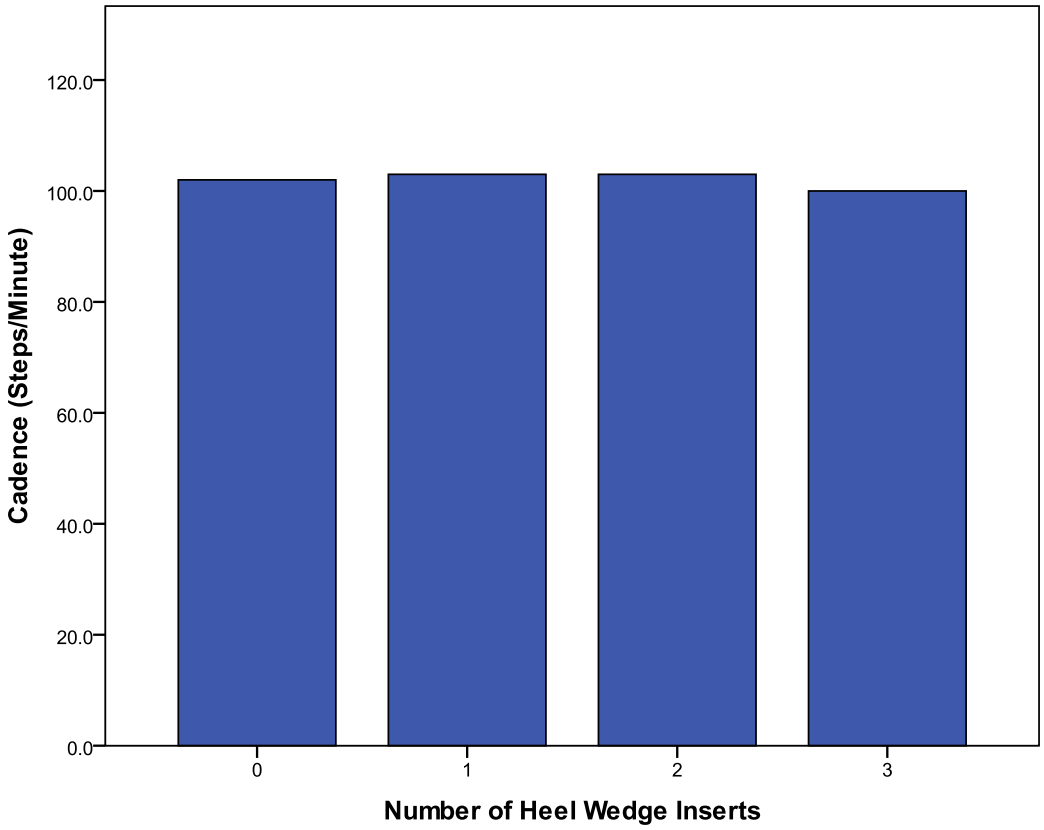
ANOVA: F Probability	0.042

Figure 3.23: Mean cadence (steps/minute) for B1, B2 and B3, with ANOVA F probability

Figure 3.23 demonstrates that there is a statistically significant difference between AFO designs. The post hoc analysis in Table 3.6 shows that the difference lies between AFOs B2 and B3 only, and there is a three steps per minute difference. Figure 3.24 shows no significant difference regarding cadence across heel wedge inserts.

Table 3.6: Post hoc analysis for Figure 3.23 showing the mean difference, upper and lower limits and p-value for each comparison

	Difference	Lower	Upper	Significance
B1 - B2	1.6	-1.3	4.5	0.382
B1 - B3	-1.6	-4.5	1.4	0.389
B2 - B3	-3.2	-6.1	-0.2	0.032



ANOVA: F Probability	0.063

Figure 3.24: Mean cadence (steps/minute), with ANOVA F probability for heel wedge inserts

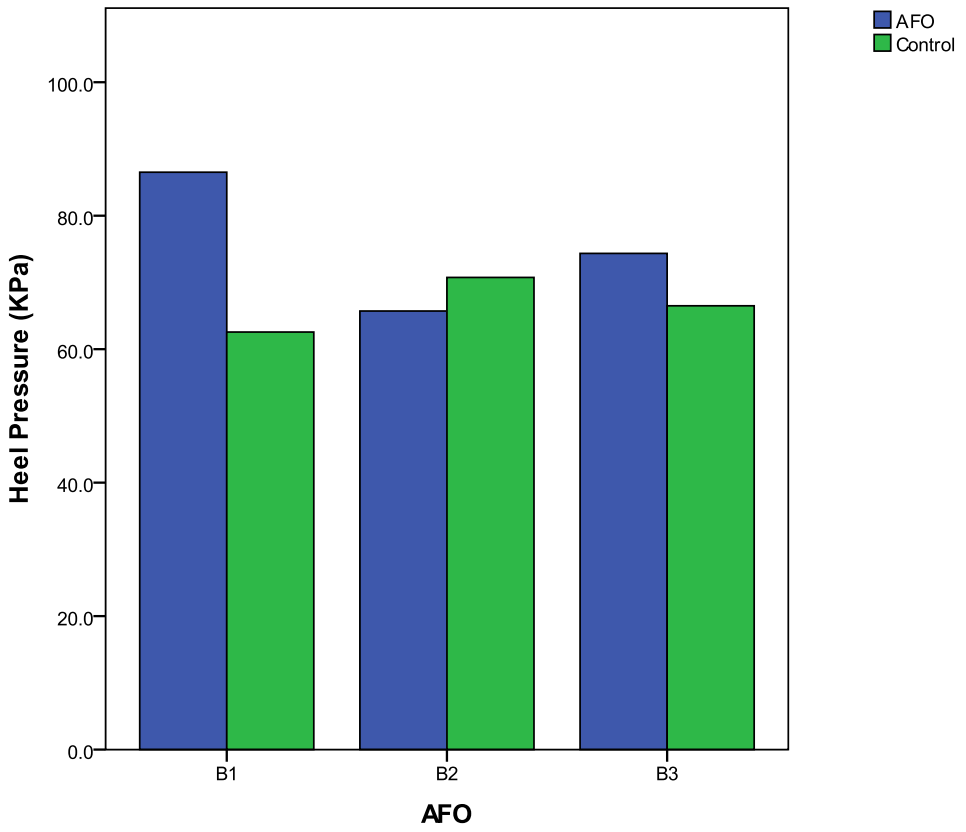
3.2.3 Trial conditions: control limb and AFO limb raw values

For each of the 12 conditions, participants wore the AFO and heel wedge combinations on either their left or right lower limb, as per the randomisation sequence. The side wearing the AFO shall be referred to as the 'AFO limb' and the side not wearing the AFO shall be referred to as the 'control limb'.

For this next section of analysis, raw values recorded for the control limb were compared across AFO designs and the number of heel wedge inserts to evaluate if the control limb varied across conditions. The AFO limb was also initially evaluated in the same way.

Figure 3.25 shows the differences between the control limb measurements across AFO designs and differences between the AFO limb across the AFO designs for heel pressures. Analysis of variance showed significant differences for both the control and AFO limb. The significance was greater for the AFO limb. Table 3.8 summarises the post hoc analysis for these separate lower limb heel pressures. The control limb had a statistically significant mean difference of 8 KPa between B1 and B2; no other differences were found. The AFO limb showed larger differences between both dorsum carbon fibre AFO designs (B2 and B3) compared to the rigid rocker bottom AFO orthotic design (B1) of 20 and 12 KPa less on average. There was also a difference between the two dorsum carbon fibre AFO designs, although this was a smaller 8KPa difference.

Across the number of inserted heel wedges, regardless of the AFO design, the heel pressure measurements recorded for the control limb were not significant. The difference across the AFO limb was significant and post hoc analysis showed significance across all comparisons except none compared to one inserted heel wedge and two compared to three. Overall, a difference in two heel wedge levels resulted in approximately 12 KPa difference in heel pressure.

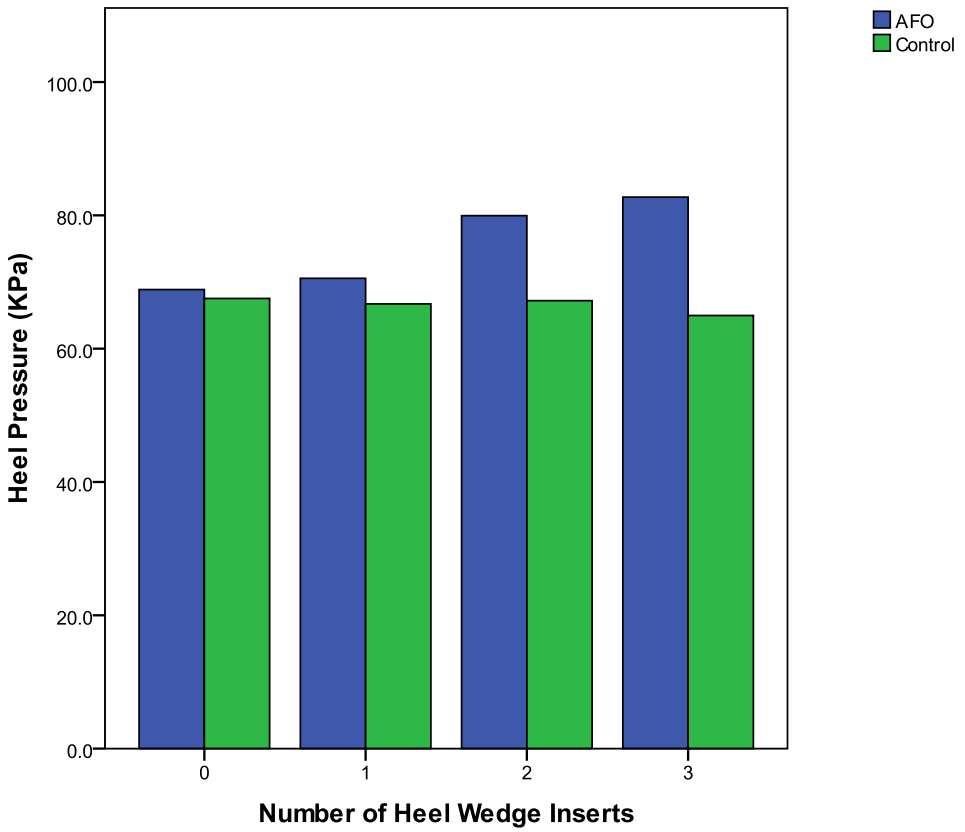


ANOVA: F Probability (Control)	0.004
ANOVA: F Probability (AFO)	<0.001

Figure 3.25: Mean heel pressures (KPa) across B1 B2 and B3 for control and AFO limb, with ANOVA F probability

Table 3.7: Post hoc analysis for Figure 3.25 showing the mean difference, upper and lower limits and p-value for each comparison

AFO Limb	Difference	Lower	Upper	Significance
B1 - B2	-20.8	-29.2	-12.4	<0.001
B1 - B3	-12.1	-20.5	-3.7	0.004
B2 - B3	8.6	0.2	17.0	0.044
Control Limb				
B1 - B2	8.2	2.8	13.6	0.002
B1 - B3	4.0	-1.4	9.4	0.179
B2 - B3	-4.2	9.6	1.2	0.151



ANOVA: F Probability (Control)	0.492
ANOVA: F Probability (AFO)	<0.001

Figure 3.26: Mean heel pressures (KPa) for control and AFO limb across heel wedge inserts, with ANOVA F probability

Table 3.8: Post hoc analysis for Figure 3.26 showing the mean difference, upper and lower limits and p-value for each comparison

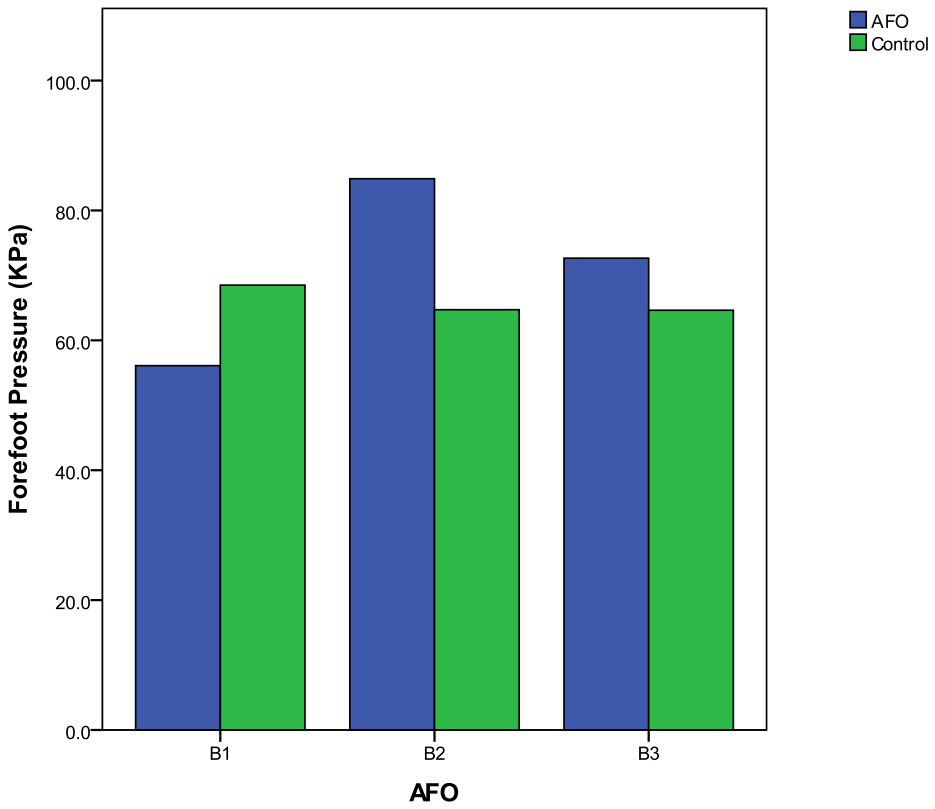
AFO Limb	Difference	Lower	Upper	Significance
0 - 1	1.8	-4.7	8.3	0.890
0 - 2	11.1	4.5	17.6	<0.001
0 - 3	13.9	7.3	20.4	<0.001
1 - 2	9.3	2.7	15.8	0.002
1 - 3	12.1	5.5	18.6	<0.001
2 - 3	2.8	-3.7	9.3	0.678

Forefoot pressures across AFO design for the control limb did not significantly differ. However, the forefoot pressure measurements across AFO designs for the AFO limb did differ significantly. These differences were again largest between the rigid rocker bottom AFO (B1) and two dorsum carbon fibre AFO designs (B2 and B3). There was a 28 KPa and 16 KPa deficit on average within B1 compared to B2 and B3 (Table 3.9). Again there are significant differences between the two dorsum carbon fibre AFO designs, but this was a smaller difference of 12 KPa, as shown in Figure 3.27 and Table 3.9.

Forefoot pressure measurements across heel wedge inserts for the control and AFO limb are significantly different as shown by Figure 3.28 and Table 3.10. For the control limb, forefoot pressures were increased when three heel wedges were inserted in the AFO limb. There were no differences between any other combinations. For the AFO limb, the differences were larger than the control and significantly different with no heel wedge inserts compared to one, two and three heel wedge inserts.

Figure 3.29 demonstrates that terminal stance and pre-swing percentage across AFO designs, regardless of the number of heel wedge inserts was significantly different for the control limb. However, post hoc analysis showed that this difference was only between B1 when compared to AFO's B2 and B3. Furthermore, the difference was small (2.7 to 3.6%) when compared to the differences across the AFO limb. Again the biggest difference here was found between the comparisons made between B1 and AFO's B2 and B3, the differences being 22.8 and 13.4% respectively. There were also significant differences found between B2 and B3; however this difference was smaller (4.2%).

Figure 3.30 demonstrates that the control limb was also significantly different across heel wedge conditions regardless of AFO design. Post hoc analysis shows that this difference was found between W0 and W2, W1 and W3 and W0 and W3 with a two heel wedge difference being equivalent to approximately a 3% difference. These differences were again much larger across the AFO limb with a two wedge difference being equivalent to approximately a 10% difference (p<0.001).

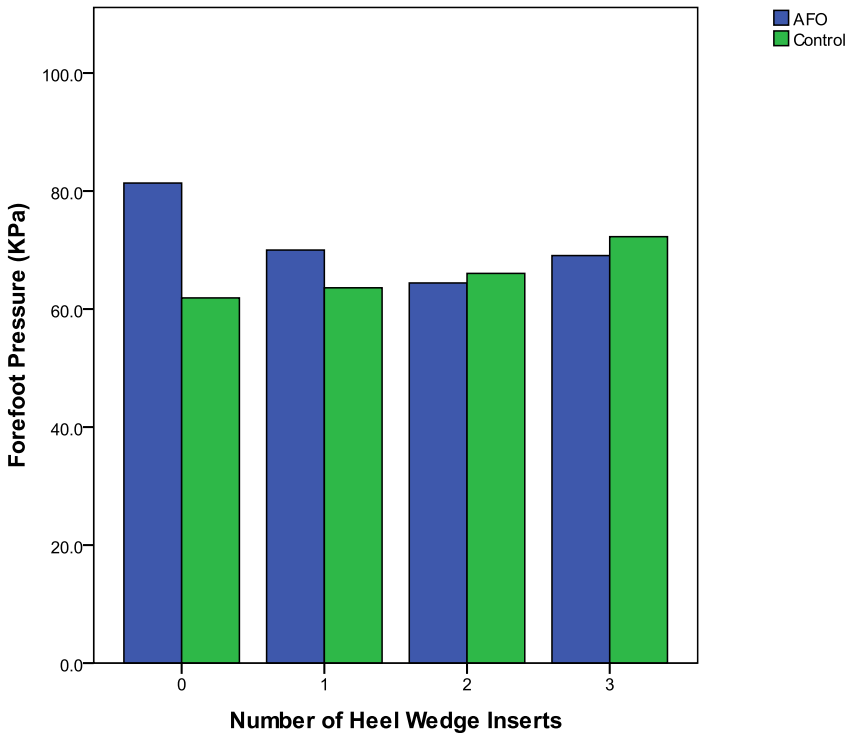


ANOVA: F Probability (Control)	0.167
ANOVA: F Probability (AFO)	<0.001

Figure 3.27: Mean forefoot pressures (KPa) for control and AFO limb across B1 B2 and B3, with ANOVA F probability

Table 3.9: Post hoc analysis for Figure 3.27 showing the mean difference, upper and lower limits and p-value for each comparison

AFO Limb	Difference	Lower	Upper	Significance
B1 - B2	28.7	21.7	35.8	<0.001
B1 - B3	16.5	9.5	23.6	<0.001
B2 - B3	-12.2	-19.2	-5.1	<0.001

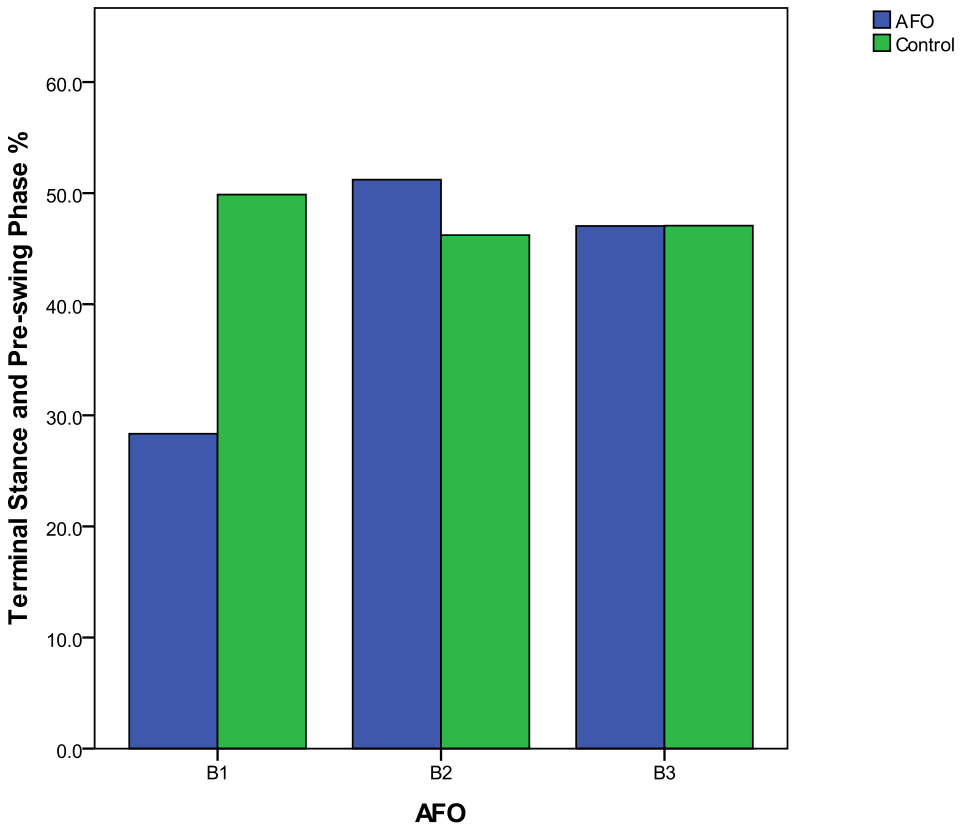


ANOVA: F Probability (Control)	<0.001
ANOVA: F Probability (AFO)	<0.001

Figure 3.28: Mean forefoot pressures (KPa) for control and AFO limb across heel wedge inserts, with ANOVA F probability

Table 3.10: Post hoc analysis for Figure 3.28 showing the mean difference, upper and lower limits and p-value for each comparison

AFO Limb	Difference	Lower	Upper	Significance
0 - 1	-11.4	-19.3	-3.5	<0.001
0 - 2	-17.0	-24.9	-9.1	<0.001
0 - 3	-12.3	-20.2	-4.4	<0.001
1 - 2	-5.6	-13.5	2.3	0.261
1 - 3	-0.9	-8.8	7.0	0.990
2 - 3	4.6	-3.3	12.5	0.423
Control Limb				
0 - 1	1.7	-3.7	7.2	0.844
0 - 2	4.1	-1.3	9.6	0.203
0 - 3	10.4	5.0	15.9	<0.001
1 - 2	2.4	-3.0	7.9	0.657
1 - 3	8.7	3.3	14.2	<0.001
2 - 3	6.3	0.9	11.8	0.016

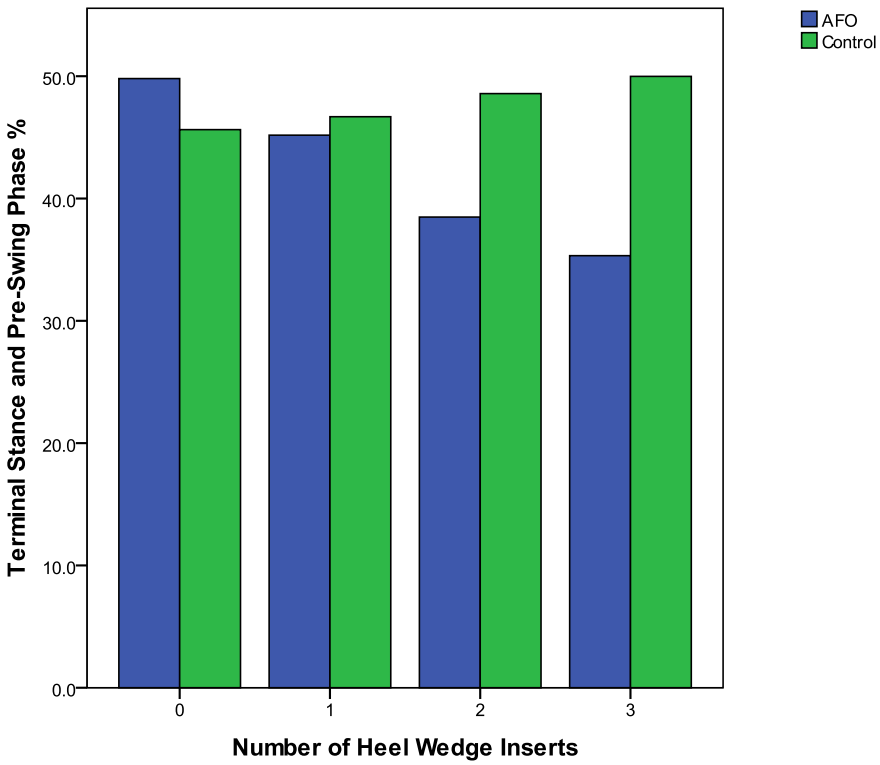


ANOVA: F Probability (Control)	0.002
ANOVA: F Probability (AFO)	<0.001

Figure 3.29: Mean terminal stance and pre-swing phase% for AFO and control limb across B1 B2 and B3, with ANOVA F probability

Table 3.11: Post hoc analysis for Figure 3.29 showing the mean difference, upper and lower limits and p-value for each comparison

AFO Limb	Difference	Lower	Upper	Significance
B1 - B2	22.9	17.5	28.2	<0.001
B1 - B3	13.4	13.4	24.0	<0.001
B2 - B3	-4.2	-9.5	1.2	0.147
Control Limb				
B1 - B2	-3.7	-6.1	-1.2	0.002
B1 - B3	-2.8	-5.2	-0.4	0.020
B2 - B3	0.9	-1.6	3.3	0.657



ANOVA: F Probability (Control)	<0.001
ANOVA: F Probability (AFO)	<0.001

Figure 3.30: Mean terminal stance and pre-swing phase% for control and AFO limb across number of heel wedge inserts, with ANOVA F probability

Table 3.12: Post hoc analysis for Figure 3.30 showing the mean difference, upper and lower limits and p-value for each comparison

AFO Limb	Difference	Lower	Upper	Significance
0 - 1	-4.6	-10.2	0.9	0.135
0 - 2	-11.3	-16.9	-5.8	<0.001
0 - 3	-14.5	-20.0	-9.0	<0.001
1 - 2	-6.7	-12.2	-1.2	0.011
1 - 3	-9.9	-15.4	-4.3	<0.001
2 - 3	-3.2	-8.7	2.4	0.447
Control Limb				
0 - 1	1.1	-1.2	3.3	0.616
0 - 2	2.9	0.7	5.2	0.005
0 - 3	4.4	2.1	6.6	<0.001
1 - 2	1.9	-0.4	4.1	0.136
1 - 3	3.3	1.0	5.6	<0.001
2 - 3	1.4	-0.8	3.7	0.366

3.2.4 Trial conditions: analysis of AFO limb as a proportion of the control limb

This section presents the analysis of raw values recorded for the control limb as a proportion of the AFO limb across AFO design, regardless of the number of heel wedge inserts and conversely, number of heel wedge inserts regardless of AFO design. This section will analyse the AFO limb heel pressure, forefoot pressures and amount of time spent in terminal stance and pre-swing phases as a proportion of the control limb.

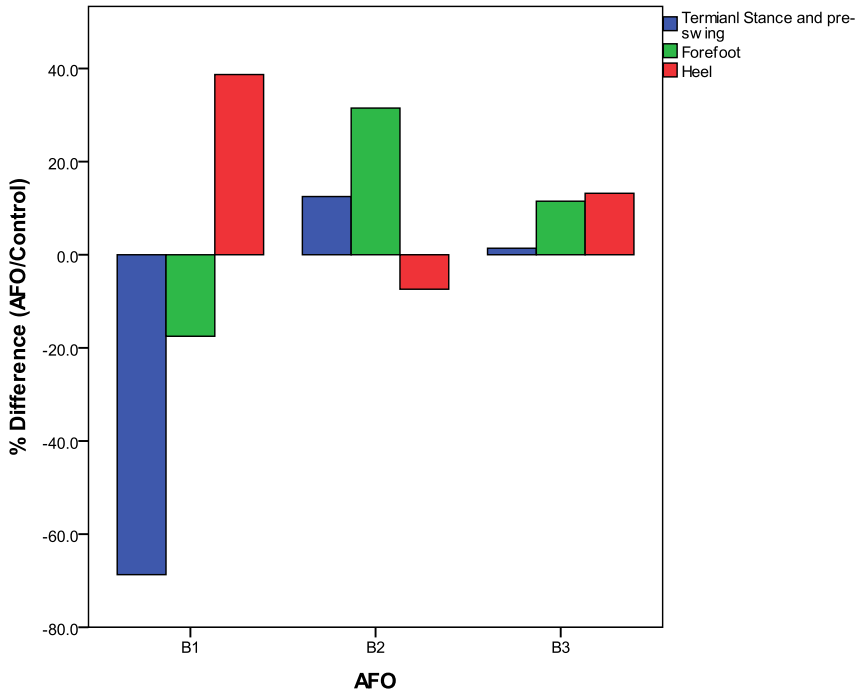
For the analysis to be valid, the data should follow a normal distribution and have some variance throughout the range. It is assumed that the relationships which are modelled are linear. However this is an assumption, therefore to ensure normal distribution of the ratio data, the data set was log transformed for analysis purposes. Once analysed the data was then back transformed to allow the actual figures to be presented in the following charts and tables to allow evaluation of clinical relevance of the statistical significance[112]. The equation used to back transform the analysed data was: 100 x EXP (Value).

Figure 3.31 shows the heel pressure (red bar) forefoot pressure (green bar) and terminal stance and pre-swing phase as proportion of the total stance phase (blue bar) for the AFO limb as a proportion of the control limb. Therefore 0% indicates no difference between the control limb and AFO limb. A positive percentage indicates a larger value within the AFO limb when compared to the control limb and a negative percentage indicates a larger value within the control limb.

Across AFO designs all measured parameters were statistically significant. Post hoc analysis showed that when assessing the terminal stance and pre-swing phases of the gait cycle the significant differences lay between the comparisons of the rigid

rocker bottom AFO (B1) when compared to the two dorsum carbon fibre AFOs. The same pattern occurs for forefoot pressures with larger differences between B1 when compared to B2 and B3 and a smaller (but still significant) difference between B2 and B3. Heel pressures were significantly higher in the AFO limb for B1 compared to B2 and B3. The largest difference was found between B1 and B2. B2 was the only AFO to produce heel pressures lower than the control limb.

Figure 3.32 shows the same proportional data across the number of heel wedge inserts. There is a clear trend that the amount of time spent in the terminal stance and pre-swing phases of the gait cycle increases, to match that of the control limb, as the number of heel wedge inserts decreases. Post hoc analysis also shows that these differences are statistically significant, with deficits of 56% with W3 when compared to the control limb. Figure 3.32 also shows that with decreasing heel wedge inserts, heel pressures decrease and forefoot pressures increase. These differences are statistically significant with forefoot deficits of 28% between W0 and W3 and heel pressures 24% greater than the control limb at W3 compared to W0 decreasing to 2% between W0 and W1.

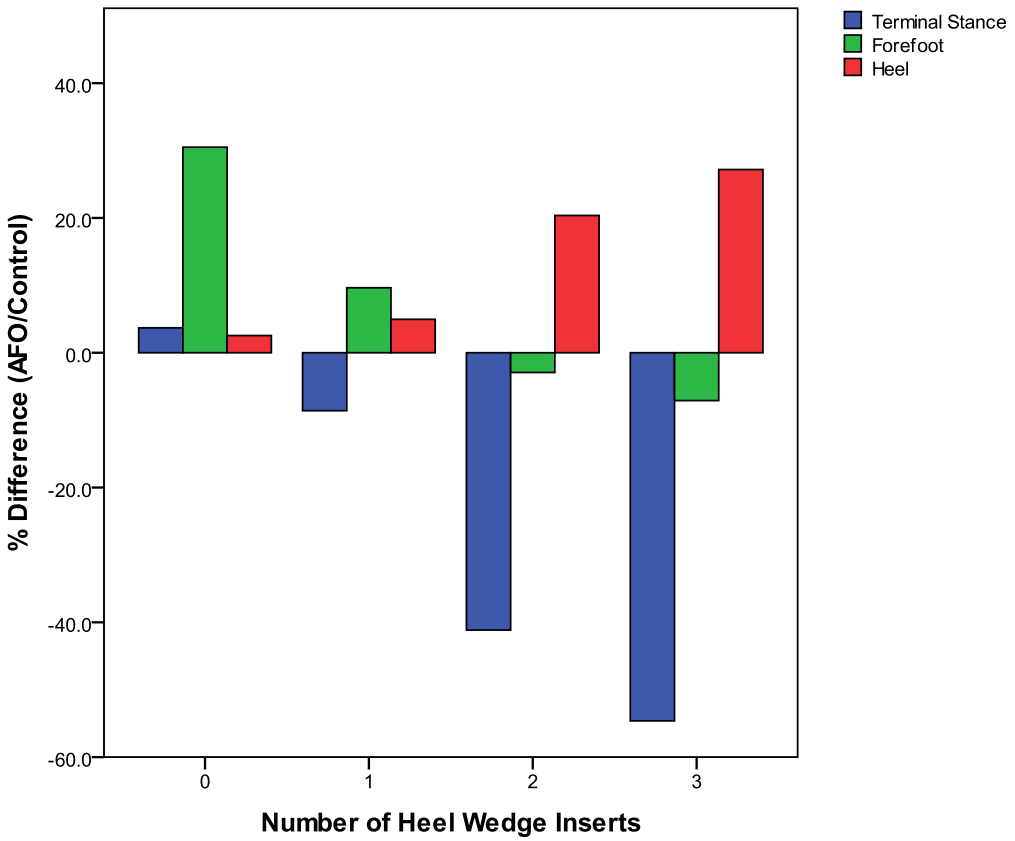


ANOVA: F Probability (Terminal Stance)	<0.001
ANOVA: F Probability (Forefoot)	<0.001
ANOVA: F Probability (Heel)	<0.001

Figure 3.31: Mean % difference between control and AFO limb across B1 B2 and B3, with ANOVA F probability

Table 3.13: Post hoc analysis for Figure 3.31 showing the mean difference, upper and lower limits and p-value for each comparison

Terminal Stance	% Difference	Lower	Upper	Significance
B1 - B2	72.2	58.1	81.6	<0.001
B1 - B3	69.2	53.5	79.6	<0.001
B2 - B3	-10.9	-67.3	26.5	0.807
Forefoot				
B1 - B2	59.3	43.6	76.8	<0.001
B1 - B3	35.1	21.7	50.0	<0.001
B2 - B3	-15.2	-23.6	-5.9	0.002
Heel				
B1 - B2	-33.2	-40.7	-24.8	0.000*
B1 - B3	-18.4	-27.5	-8.0	0.001*
B2 - B3	22.2	8.5	37.7	0.001*



ANOVA: F Probability (Terminal Stance)	<0.001
ANOVA: F Probability (Forefoot)	<0.001
ANOVA: F Probability (Heel)	<0.001

Figure 3.32: Mean % difference between control and AFO limb across number of heel wedge inserts, with ANOVA F probability

Table 3.14: Post hoc analysis for Figure 3.32 showing the mean difference, upper and lower limits and p-value for each comparison

Terminal Stance	% Difference	Lower	Upper	Significance
0 - 1	-12.0	-43.3	36.7	0.875
0 - 2	-43.3	-63.5	-11.9	0.006
0 - 3	-56.3	-71.8	-32.0	<0.001
1 - 2	-35.6	-58.5	0.1	0.051
1 - 3	-50.3	-68.0	-22.8	<0.001
2 - 3	-22.9	-50.4	19.8	0.419

Forefoot	% Difference	Lower	Upper	Significance
0 - 1	-16.0	-24.6	-6.3	<0.001
0 - 2	-25.6	-33.3	-17.1	<0.001
0 - 3	-28.8	-36.1	-20.7	<0.001
1 - 2	-11.5	-20.6	-1.3	0.021
1 - 3	-15.3	-24.0	-5.6	<0.001
2 - 3	-4.3	-14.1	6.7	0.718
Heel				
0 - 1	2.3	-9.1	15.2	0.957
0 - 2	17.4	4.2	32.2	0.003
0 - 3	24.0	10.1	39.6	<0.001
1 - 2	14.7	1.9	29.1	0.017
1 - 3	21.2	7.6	36.4	<0.001
2 - 3	5.7	-6.2	19.0	0.622

3.2.5 Trial conditions: analysis of AFO and heel wedge interaction

The first sub-chapter of this results section has assessed the control data only. The second part of the results section has evaluated the raw values of the AFO limb compared to the control limb and the third part has assessed these raw values as a proportion of each other. So far this has been carried out on the AFO design regardless of the number of heel wedge inserts and secondly on the number of heel wedge inserts regardless of the AFO design. This section will explore the 'interaction' between the individual AFO designs combined with W0, W1, W2 and W3. The next three figures demonstrate the AFO and heel wedge interaction for the pre-defined gait parameters for B1, B2 and B3 respectively.

Table 3.15: Analysis of variance results for the interaction between AFO design and heel wedge number

ANOVA: F Probability (Terminal Stance)	<0.001
ANOVA: F Probability (Forefoot)	0.029
ANOVA: F Probability (Heel)	0.002

Figure 3.33 clearly demonstrates that within B1, recorded heel pressures are highest with W3. This figure decreases with decreasing heel wedge inserts, to that of the control limb with no W0 (A statistically significant difference of 61% between W0 and W3). The reverse of this pattern is seen with forefoot pressures and the amount of time spent in terminal stance and pre-swing phases of the gait cycle. Deficits in forefoot pressures compared to the control limb are seen throughout W3 to W0 with statistical significance between two heel wedges (i.e. W0 and W2, W1 and W3). The pattern of increasing amount of time spent in terminal stance and pre-swing phase of the gait cycle with decreasing heel wedge inserts is also statistically significant across pair wise comparisons, except between W0 and W1 and W2 and W3. There were no differences in forefoot pressures and terminal stance phase duration between W0 and W1 indicating that the foot can be placed in a small amount of PF without detrimental reduction within these gait parameters.

From Figure 3.34 and Table 3.17, it is evident that within B2 the values for all three gait parameters change significantly between W3, W2 and W1. With no heel wedge inserts, forefoot pressures are significantly increased compared to W1, W2 and W3, however, this is the only statistically significant difference.

From Figure 3.35 and Table 3.18 it is evident that the values for heel pressures and terminal stance phase of the gait cycle do not significantly change between heel wedge conditions, however forefoot pressures do. They follow the same pattern as B1 regarding lower pressures being recorded in comparison to the control limb at W3 and gradually increasing towards W0.

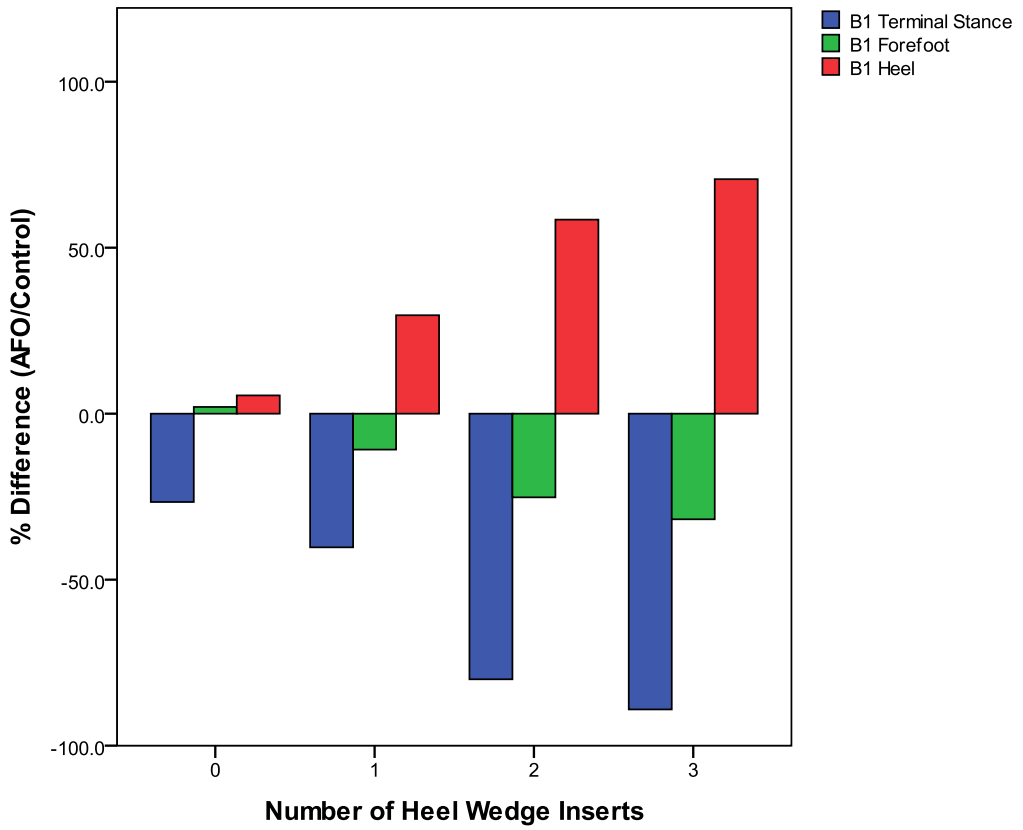


Figure 3.33: Mean % difference between control and AFO limb for gait parameters across B1 with all heel wedge conditions

Table 3.16: Post hoc analysis for Figure 3.33 showing the mean difference, upper and lower limits and p-value for each comparison

Terminal Stance B1	% Difference	Lower	Upper	Significance
0 - 1	-18.6	-62.1	74.5	0.896
0 - 2	-72.8	-87.3	-41.6	<0.001
0 - 3	-85.1	-93.1	-68.1	<0.001
1 - 2	-66.5	-84.4	-28.2	0.002
1 - 3	-81.7	-91.5	-60.8	<0.001
2 - 3	-45.4	-74.6	17.0	0.170
Forefoot B1				
0 - 1	-12.6	-27.6	5.5	0.250
0 - 2	-26.7	-39.3	-11.5	<0.001
0 - 3	-33.2	-44.6	-19.3	<0.001
1 - 2	-16.1	-30.5	1.2	0.076
1 - 3	-23.5	-36.7	-7.7	0.002
2 - 3	-8.8	-24.5	10.0	0.577

Heel B1	% Difference	Lower	Upper	Significance
0 - 1	22.9	0.1	50.9	0.049
0 - 2	50.2	22.3	84.4	<0.001
0 - 3	61.7	31.7	98.6	<0.001
1 - 2	22.2	-0.5	50.1	0.058
1 - 3	31.6	7.2	61.6	0.004
2 - 3	7.7	-12.3	32.3	0.784

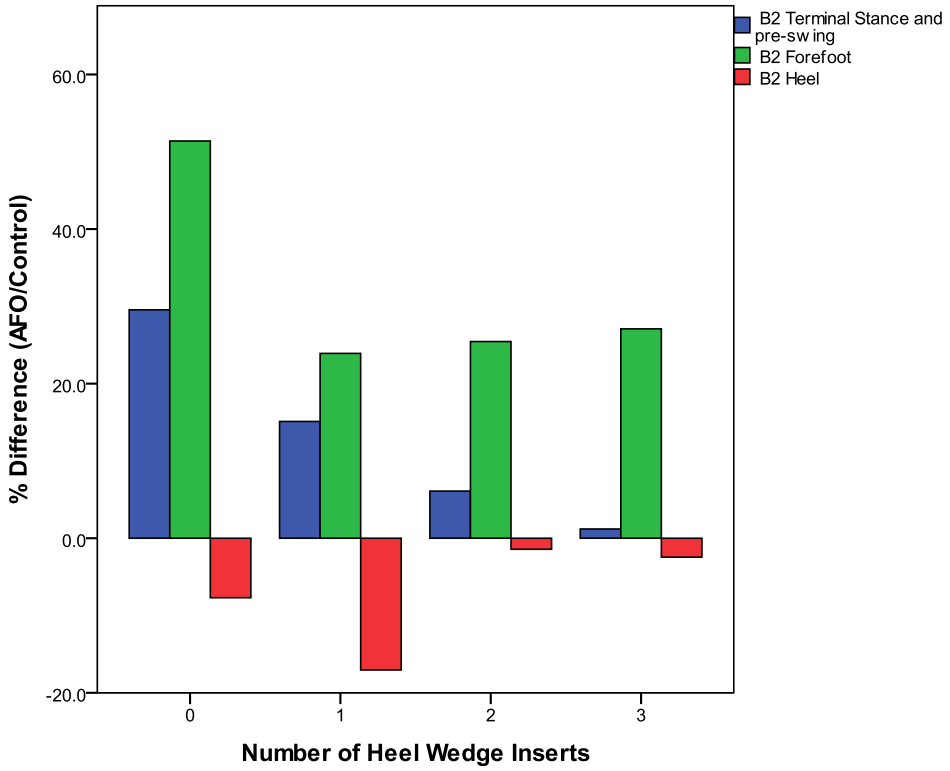


Figure 3.34: Mean % difference between control and AFO limb for gait parameters across B2 with all heel wedge conditions

Table 3.17: Post hoc analysis for Figure 3.34 showing the mean, upper and lower limits and p-value for each comparison

Terminal Stance B2	% Difference	Lower	Upper	Significance
0 - 1	-11.1	-58.6	90.5	0.978
0 - 2	-18.1	-61.8	75.6	0.904
0 - 3	-21.9	-63.6	67.5	0.834
1 - 2	-7.8	-57.0	97.7	0.992
1 - 3	-12.1	-59.0	88.5	0.972
2 - 3	-4.6	-55.5	104.6	0.999

Forefoot B2	% Difference	Lower	Upper	Significance
0 - 1	-18.2	-32.2	-1.2	0.032
0 - 2	-17.1	-31.4	0.0	0.050
0 - 3	-16.1	-30.5	1.3	0.078
1 - 2	1.2	-16.1	22.2	0.998
1 - 3	2.6	-15.0	23.8	0.985
2 - 3	1.3	-16.1	22.3	0.998
Heel B2	**% Difference**	**Lower**	**Upper**	**Significance**
0 - 1	-10.1	-26.8	10.4	0.531
0 - 2	6.8	-13.0	31.2	0.838
0 - 3	5.7	-13.9	29.8	0.897
1 - 2	18.8	-3.2	45.9	0.133
1 - 3	17.6	-4.3	44.4	0.174
2 - 3	-1.0	-19.4	21.5	0.999

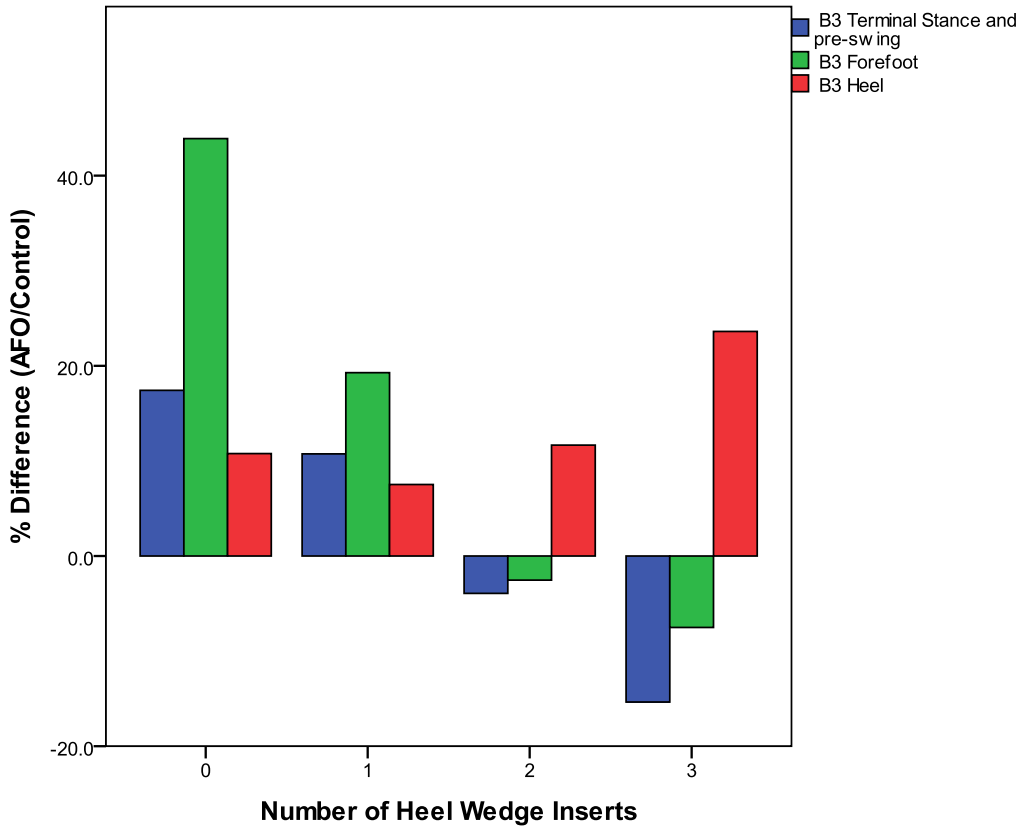


Figure 3.35: Mean % difference between control and AFO limb for gait parameters across B3 with all heel wedge conditions

Table 3.18: Post hoc analysis for Figure 3.35 showing the mean difference, upper and lower limits and p-value for each comparison

Terminal Stance B3	% Difference	Lower	Upper	Significance
0 - 1	-5.7	-56.0	102.3	0.997
0 - 2	-18.2	-61.8	75.5	0.903
0 - 3	-27.9	-66.4	54.6	0.680
1 - 2	-13.2	-59.5	86.1	0.962
1 - 3	-23.6	-64.4	63.9	0.796
2 - 3	-11.9	-58.9	88.9	0.973
Forefoot B3				
0 - 1	-17.1	-31.3	0.1	0.051
0 - 2	-32.3	-43.9	-18.2	<0.001
0 - 3	-35.7	-46.7	-22.4	<0.001
1 - 2	-18.3	-32.3	-1.4	0.030
1 - 3	-22.5	-35.8	-6.4	0.003
2 - 3	-5.1	-21.4	14.5	0.887
Heel B3				
0 - 1	-2.9	-21.0	19.2	0.982
0 - 2	0.8	-17.9	23.8	0.999
0 - 3	11.6	-9.1	37.0	0.508
1 - 2	3.9	-15.4	27.5	0.964
1 - 3	15.0	-6.4	41.2	0.294
2 - 3	10.7	-9.9	36.0	0.572

3.2.6 Trial intervention: correlation analysis

In addition to the two-way-analysis of variance and post hoc Tukey analysis, scatter plots for the measured gait parameters with Pearson Correlation Coefficients were evaluated to further explore potential relationships between the parameters. Table 3.19 illustrates the pair wise correlations with significance values.

Table 3.19: Pearson correlation coefficients

Paired Comparison	Pearson correlation coefficient	Significance
% Difference forefoot pressure & % difference heel pressure	-0.36	<0.001
% Difference forefoot pressure & % difference terminal stance phase	0.71	<0.001
% Difference forefoot pressure & plantar flexion	-0.39	<0.001
% Difference forefoot pressure & speed	-0.23	0.002
% Difference forefoot pressure & cadence	0.18	0.016
% Difference heel pressure & % difference terminal stance phase	-0.64	<0.001
% Difference heel pressure & plantar flexion	0.37	<0.001
% Difference heel pressure & speed	0.01	0.877
% Difference heel pressure & cadence	-0.40	0.598
% Difference terminal stance phase & speed	-0.13	0.810
% Difference terminal stance phase & plantar flexion	-0.36	<0.001
% Difference terminal stance phase & cadence	0.51	0.497
Plantarflexion & speed	0.01	0.866
Plantarflexion & cadence	-0.16	0.836
Speed & cadence	-0.72	<0.001
Speed & dorsiflexion	-0.03	0.672
Cadence & dorsiflexion	-0.02	0.781
% Difference heel pressure & dorsiflexion	-0.39	<0.001
% Difference terminal stance phase & dorsiflexion	0.45	<0.001
% Difference forefoot & dorsiflexion	0.45	<0.001

Figure 3.36 through to Figure 3.40 demonstrate the relationship between ROM, heel pressure, forefoot pressure, terminal stance phase, speed and cadence. The gait parameters were analysed as the percentage increase or decrease compared to the control limb. Figure 3.36 and Figure 3.38 show that as the amount of permitted DF increases, so does the amount of forefoot pressure and amount of time spent in the terminal stance phase within the AFO limb when compared to the control limb ($p < 0.001$). The scatter plots also show a reverse pattern for PF, regarding the two gait parameters. Therefore, as the foot is maintained in increased PF, forefoot pressures within the AFO limb decrease and the amount of time spent in terminal stance also decreases ($p < 0.001$).

Figure 3.37 further demonstrates the relationship between pressure and ROM showing that as the foot is maintained in PF, heel pressures increase and as the foot is allowed into DF, heel pressures reduce to those equal to the control limb ($p < 0.001$). There were, however, no significant correlations found between permitted ROM, speed and cadence as Figure 3.39, Figure 3.40 and Table 3.19 show.

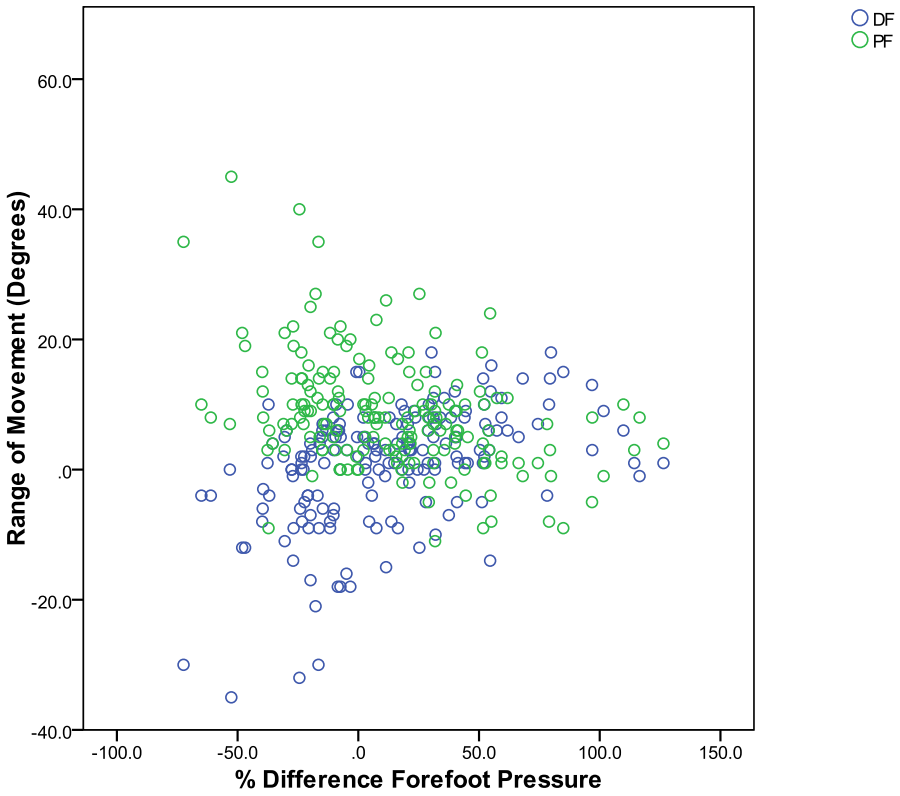


Figure 3.36: Scatter plot of % difference in forefoot pressure against ROM (degrees) within the AFO

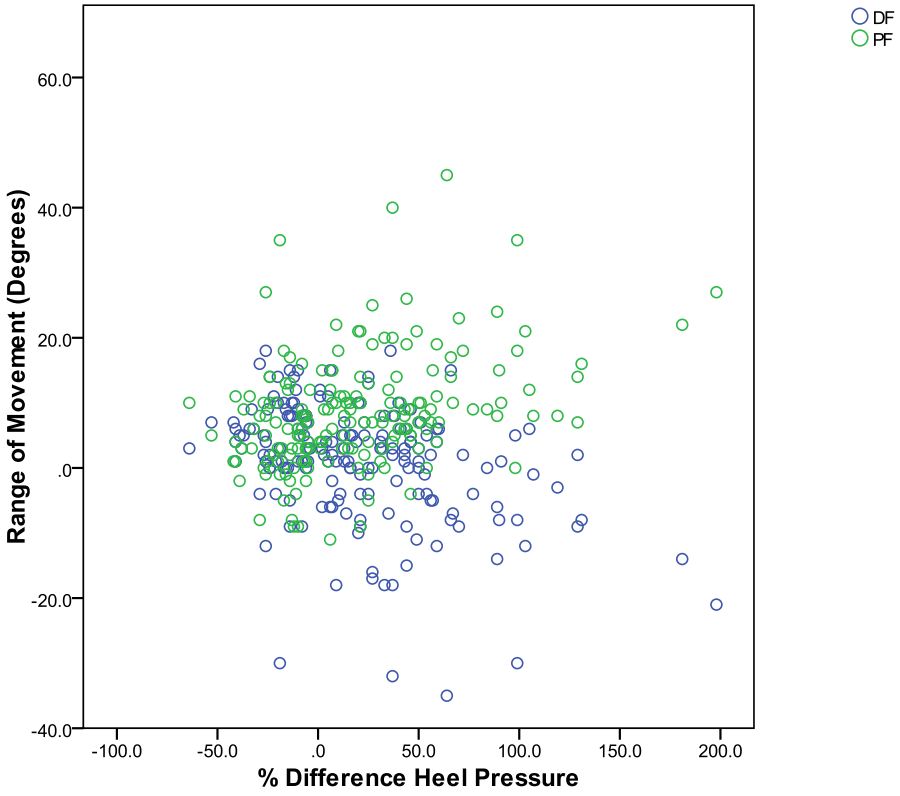


Figure 3.37: Scatter plot of % difference in heel pressure against ROM (degrees) within the AFO

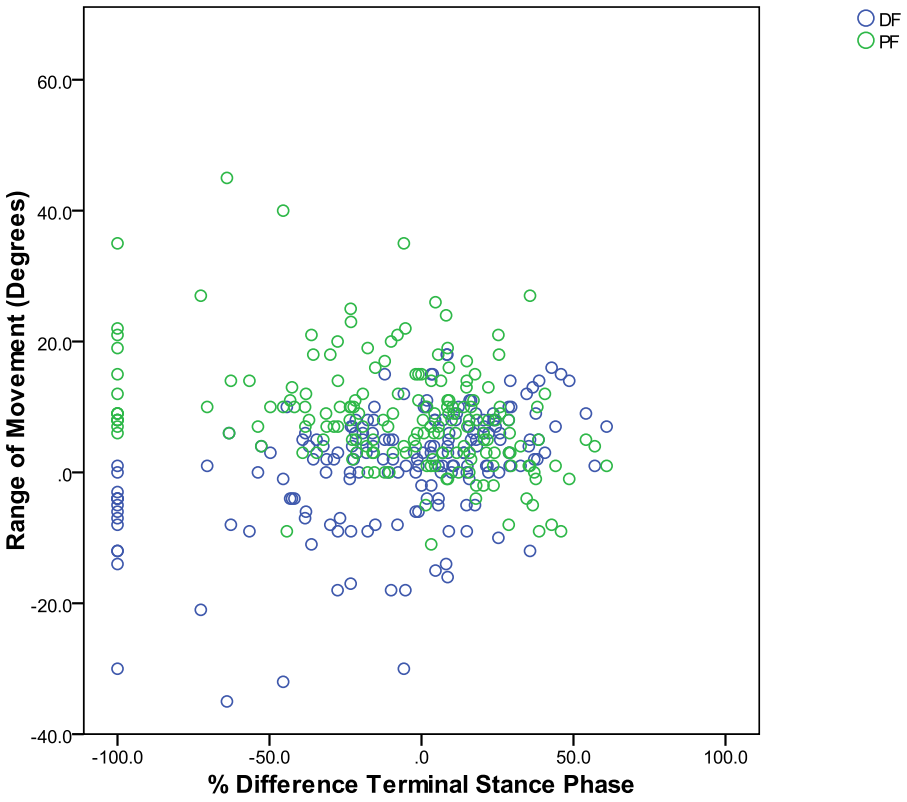


Figure 3.38: Scatter plot of % difference in terminal stance phase and ROM (degrees) within the AFO

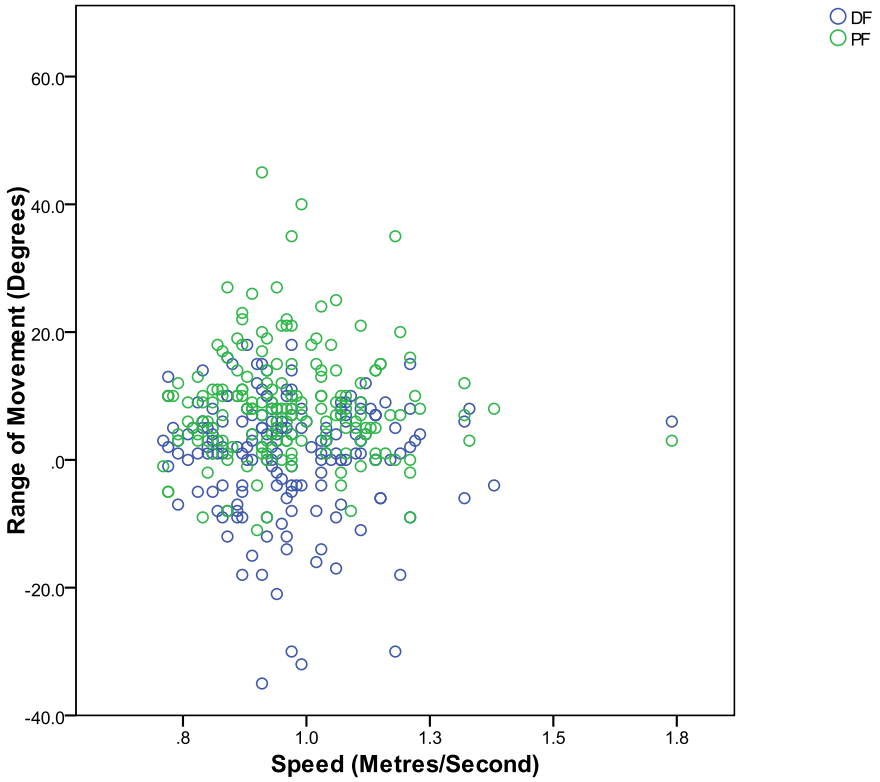


Figure 3.39: Scatter plot of speed (metres/second) and ROM (degrees) within the AFO

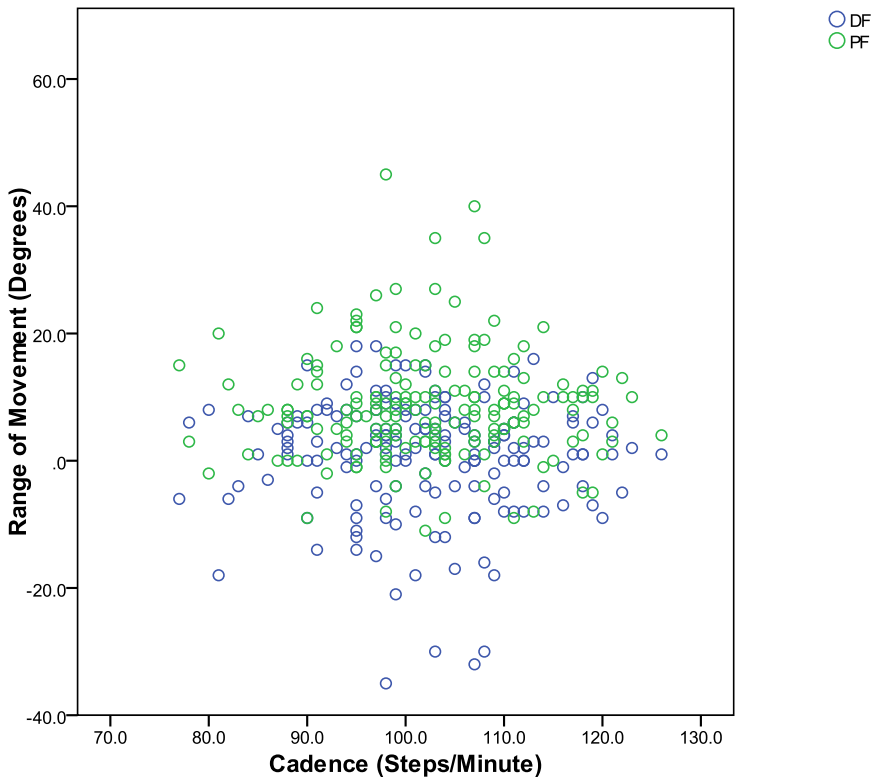


Figure 3.40: Scatter plot of cadence (steps/minute) and ROM (degrees) within the AFO

The next correlations from Figure 3.41 to Figure 3.43 demonstrate the correlation between heel pressure, forefoot pressure and terminal stance phase independent of permitted range of movement. As the first scatter plots have suggested, there is a significant correlation between these parameters. As heel pressures increase above those recorded for the control limb, forefoot pressures decrease in comparison and so does the amount of time spent in terminal stance and pre-swing phases of the gait cycle.

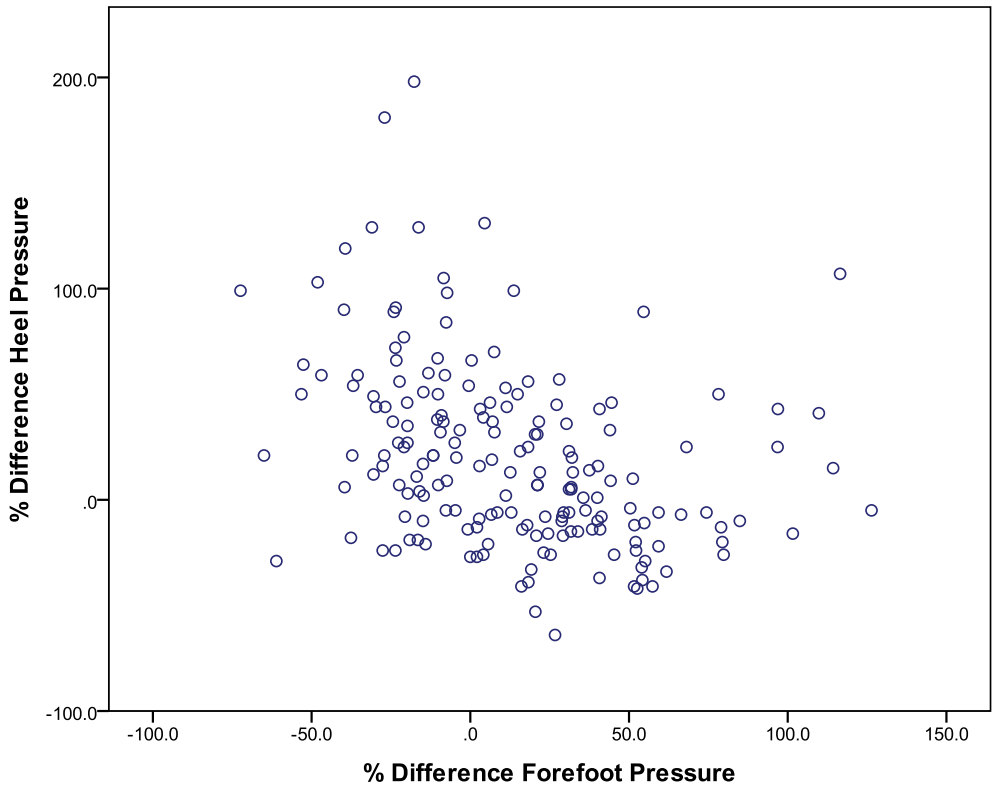


Figure 3.41: Scatter plot of % difference in heel pressure and forefoot pressure within the AFO

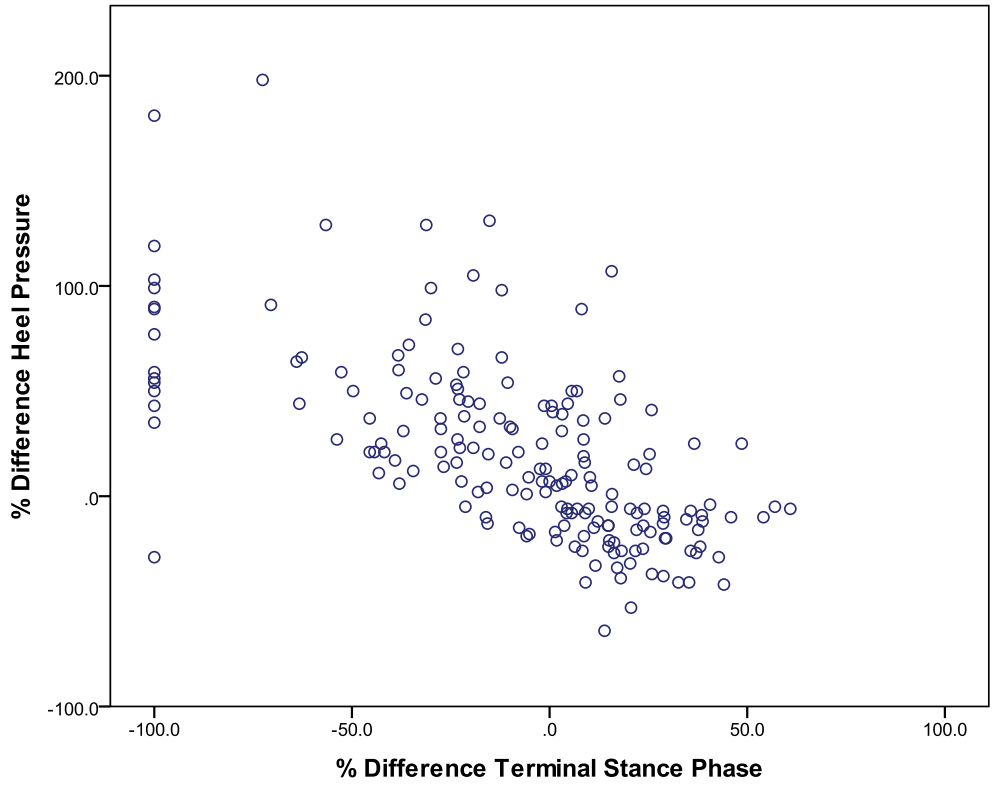


Figure 3.42: Scatter plot of % difference in heel pressure and terminal stance phase within the AFO

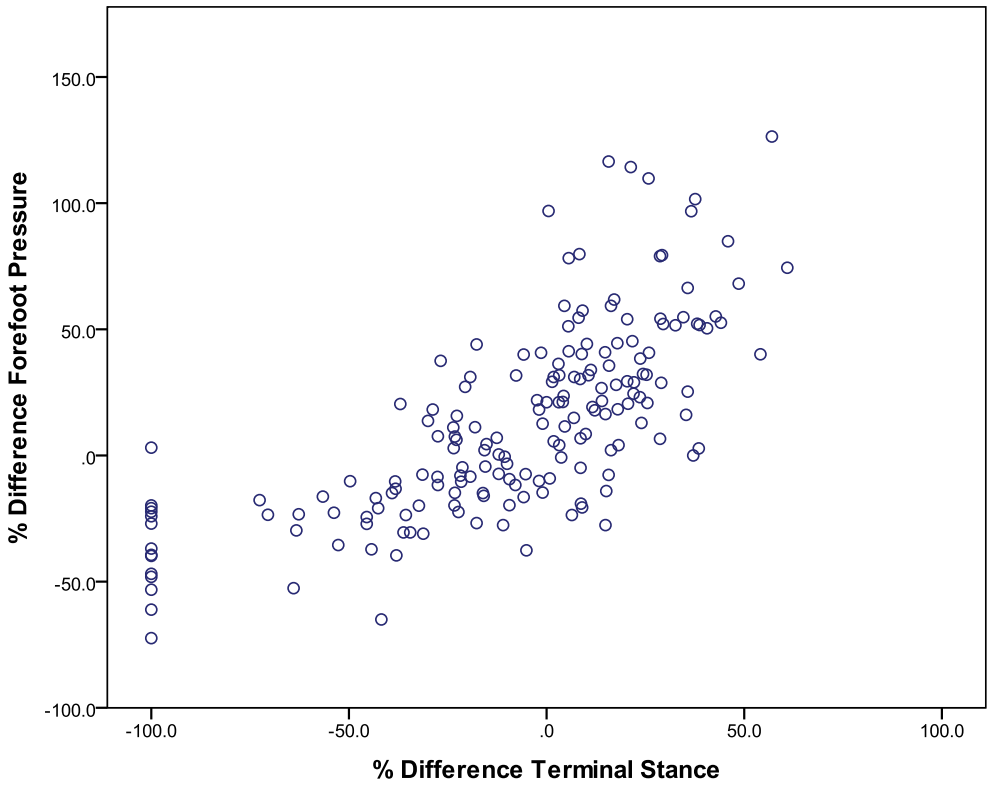


Figure 3.43: Scatter plot of % difference in forefoot pressure and terminal stance duration within the AFO

The correlations between speed, cadence and amount of time spent within the terminal stance phase of gait were then analysed. Figure 3.44 and Figure 3.45 illustrate no correlation between the parameters. There were also no significant correlations found between heel pressure, speed and cadence (Figure 3.49 and Figure 3.50). However, a significant correlation was found between forefoot pressures, speed and cadence (Figure 3.47 and Figure 3.48). As speed increased, forefoot pressure decreased and cadence decreased. There was also a significant correlation found between speed and cadence (Figure 3.46).

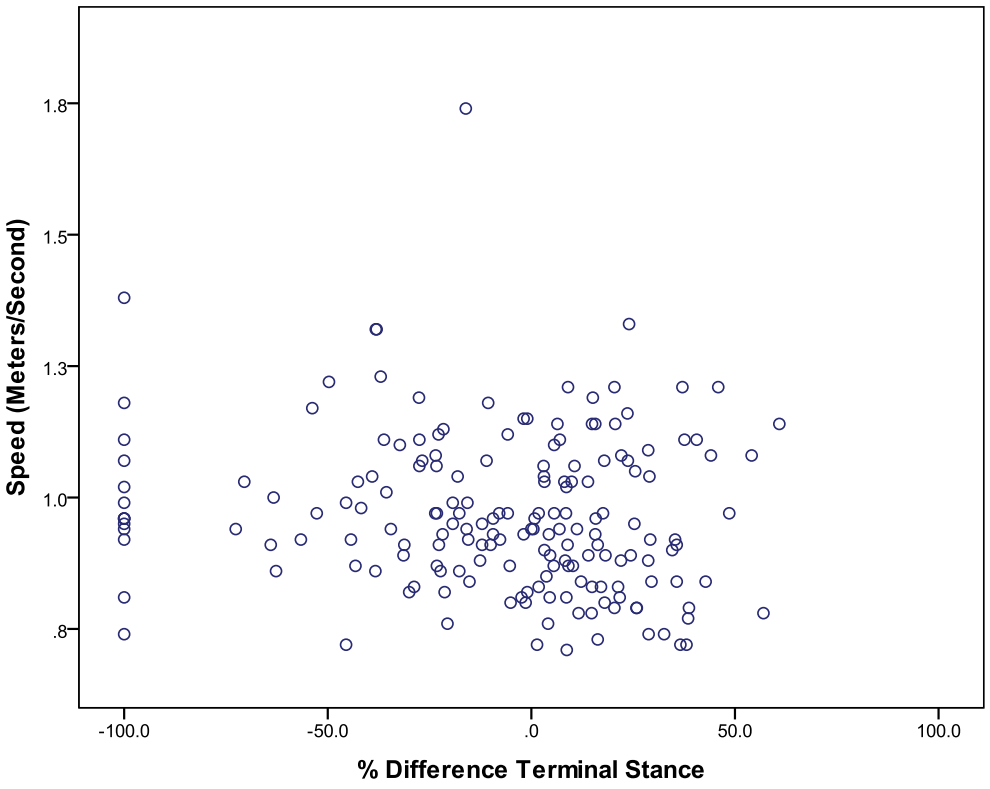


Figure 3.44: Scatter plot of speed (metres/second) and % difference in terminal stance within the AFO

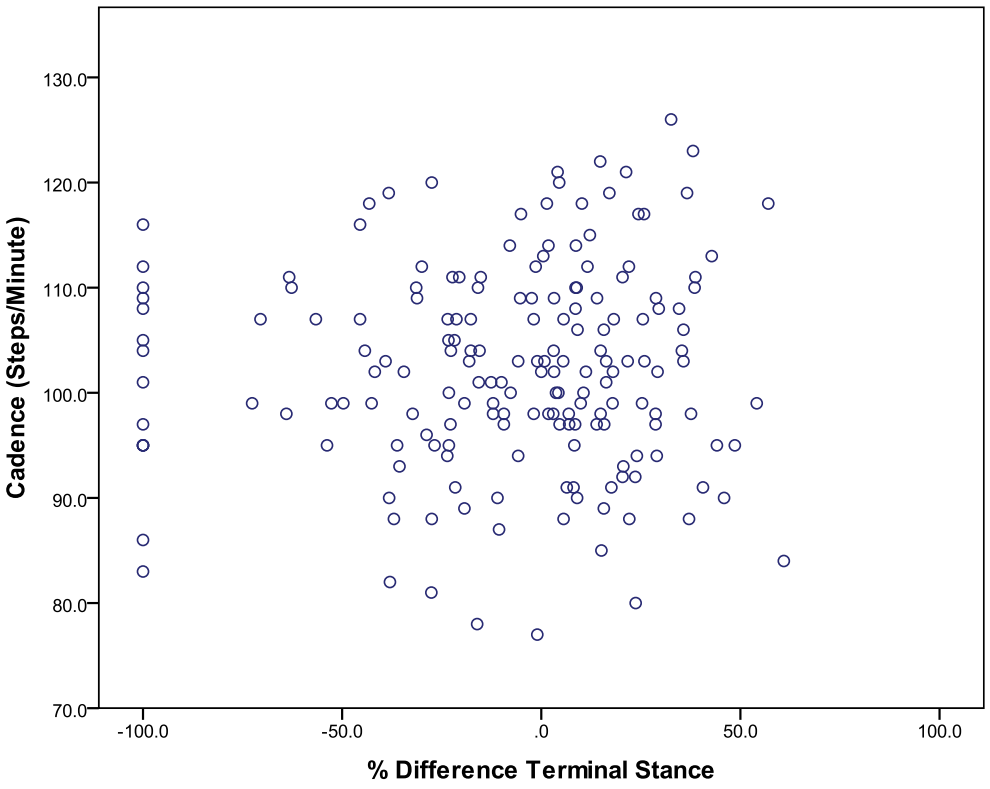


Figure 3.45: Scatter plot of cadence (steps/minute) and % difference in terminal stance phase within the AFO

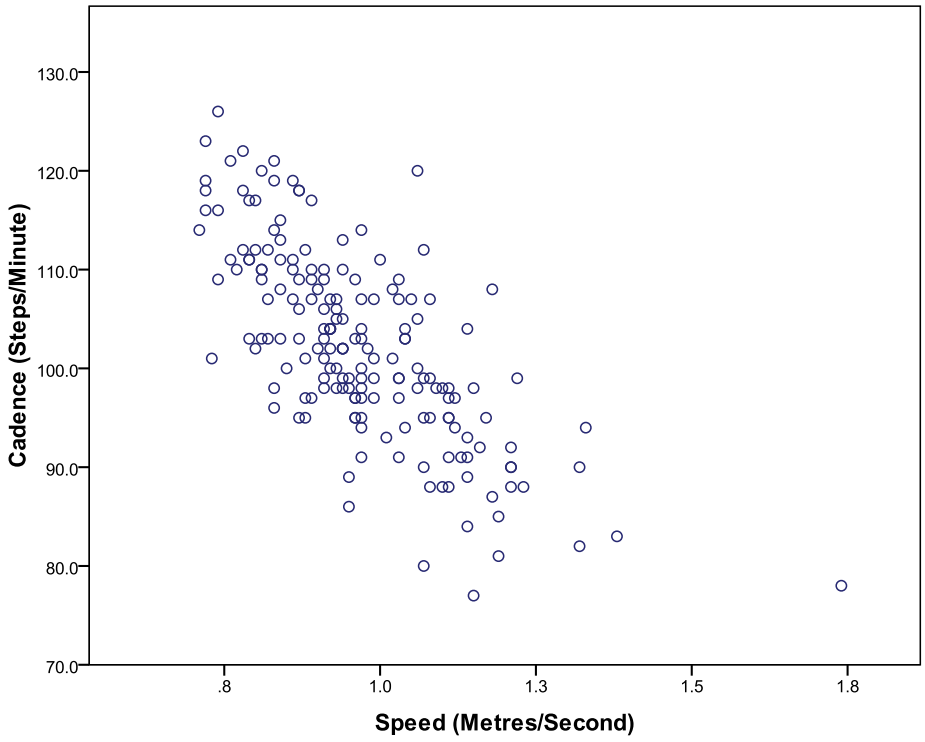


Figure 3.46: Scatter plot of cadence (steps/minute) and speed (metres/second) within the AFO

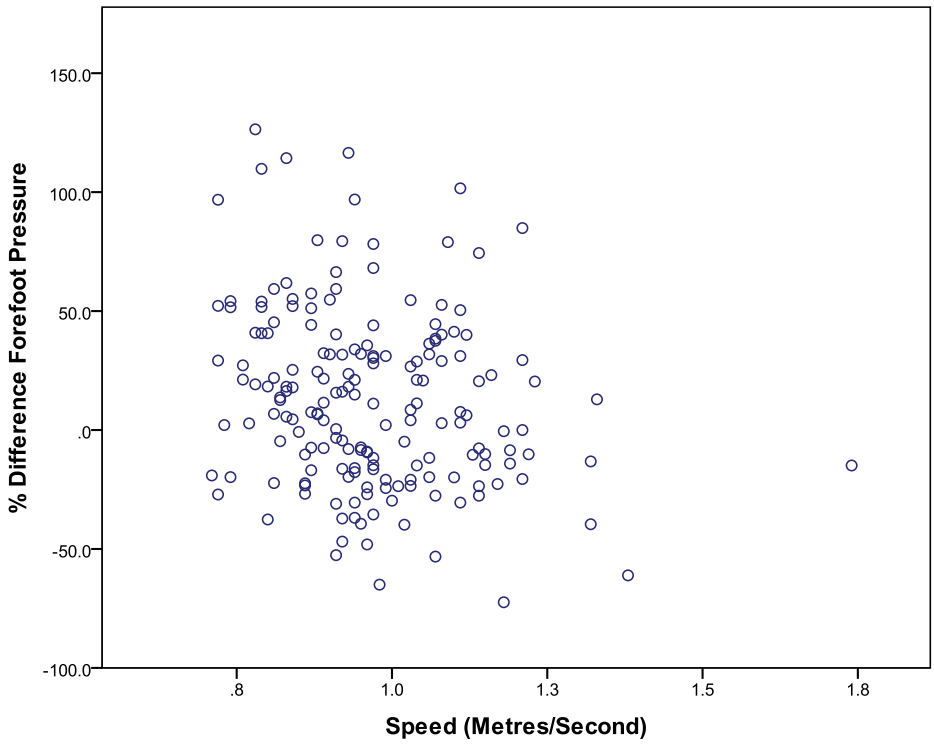


Figure 3.47: Scatter plot of speed (metres/second) and % difference in forefoot pressure within the AFO

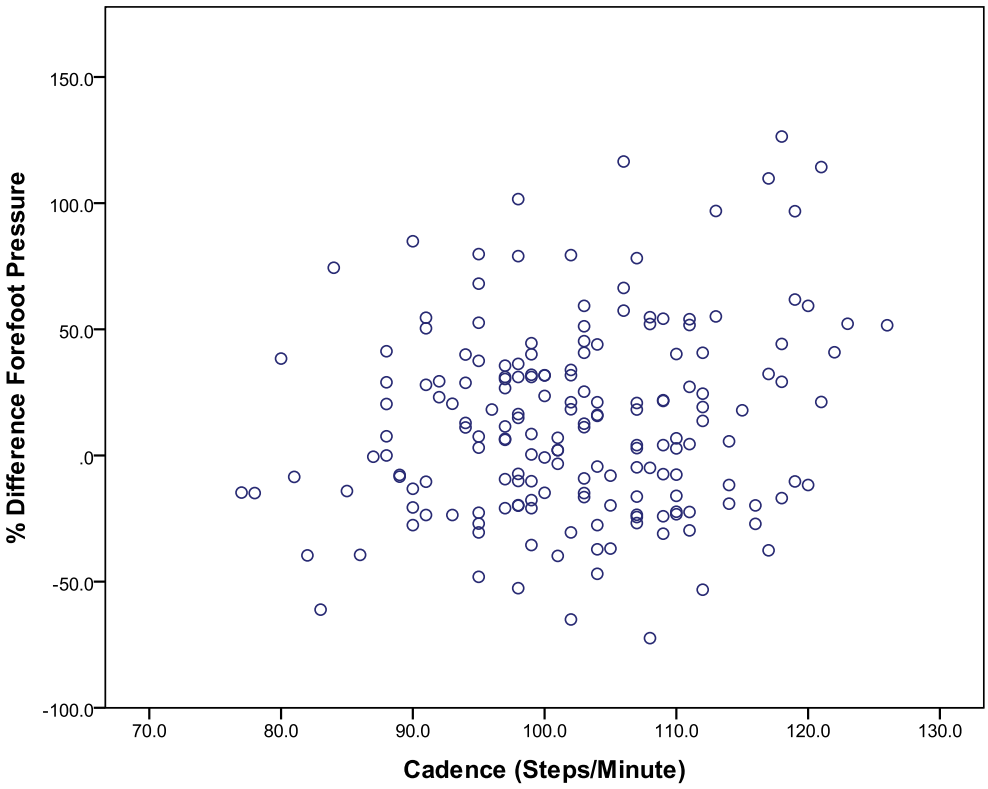


Figure 3.48: Scatter plot % difference in forefoot pressure and cadence (steps/minute) within the AFO

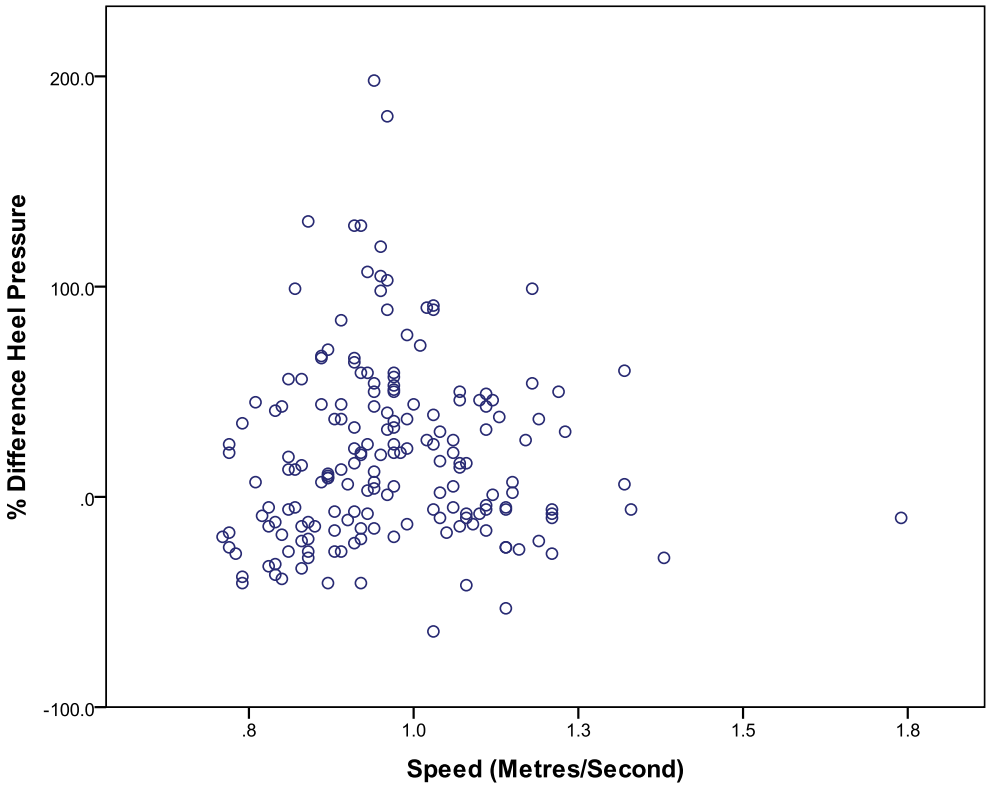


Figure 3.49: Scatter plot of speed (metres/second) and % difference in heel pressure within the AFO

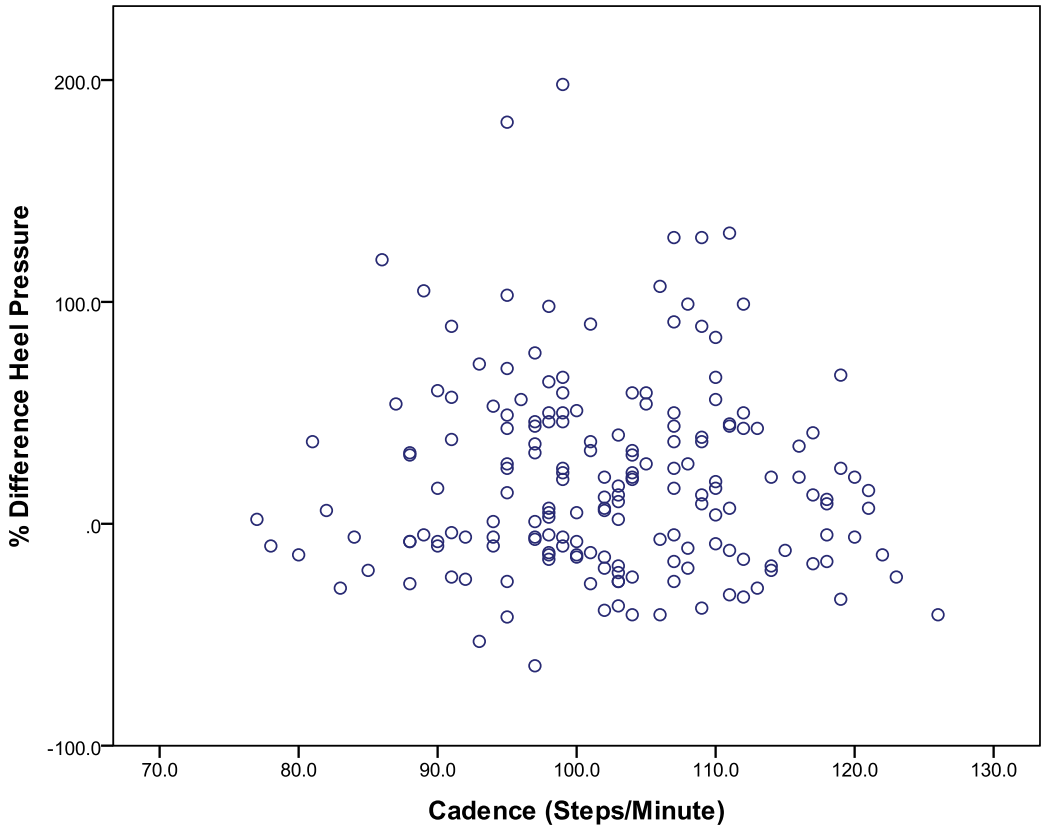


Figure 3.50: Scatter plot % difference in heel pressure and cadence (steps/minute) within the AFO

3.3 Discussion

The first aim of this study was to investigate plantar pressure distributions of the foot and temporal gait parameters under different pre-defined conditions within participants with no previous lower limb injuries. The second aim of this chapter was to draw inferences from these measurements to the application of TA rupture rehabilitation.

The discussion of this study will firstly focus on the null hypotheses in relation to the analysis and results. This will then be followed by an explanation of the possible mechanisms for these findings, within the context of previous literature. These concepts will then be discussed in relation to the application of TA rupture

rehabilitation and the clinical implications. Finally, the limitations of this study will be outlined alongside the methods which were used to minimise these.

3.3.1 Null hypothesis: there is no effect of the trialled AFOs on gait parameters

The first hypothesis was that the population means of the three AFOs (B1, B2 and B3) were equal regarding plantar pressure distributions and temporal gait parameters within healthy participants. This hypothesis was true for the measurement of speed only, which did not differ between AFO designs (p >0.05). Range of movement, cadence, heel pressures, forefoot pressures and the amount of time spent in terminal stance and pre-swing phase of the gait cycle were significantly different between AFO designs (p <0.05).

For the measurement of ankle ROM there was a mean difference of eight degrees of DF between B1 (rigid rocker bottom style AFO) and B2 (AFO dynamic) across all conditions evaluated. This shows that B1 is very restrictive regarding movement and B2 is the opposite, being within normal limits when compared to the 'normal' data. B3 (ToeOff AFO) was not significantly different from either B2 or B1 (mean difference of approximately four degrees less than B2 and four degrees more than B1).

This is an important observation because permitted movement was also found to be strongly correlated to the production of forefoot pressures within the AFOs. As DF was restricted, so was the capacity to load the forefoot. This correlation was inversely related to heel pressures, which were increased with decreased forefoot pressure production (Figure 3.36, Figure 3.37 and Figure 3.41). Range of movement was also correlated with the third gait parameter evaluated, amount of time spent in terminal stance and pre-swing phase as a proportion of the total

stance phase. As the amount of permitted DF was increased, so was the amount of time spent in this phase of the gait cycle, as a proportion of the stance phase. This finding also correlated inversely to heel pressure measurements (Figure 3.38, Figure 3.42 and Figure 3.43). Therefore these four parameters were significantly interlinked.

These trends were also reflected within the analysed raw values for the AFO limb and control limb (Chapter 3.2.3). The data clearly demonstrates that B1 (rigid rocker bottom AFO), which restricts DF the most, also has much higher heel pressures than the control limb, lower forefoot pressures and a decreased amount of time spent in terminal stance and pre-swing phase of the gait cycle as a proportion of the total stance phase.

Chapter 3.2.4 shows the analysis of the data of the AFO limb as a proportion of the control limb. Again the largest differences were found between B1 (rigid rocker bottom AFO) when compared to the two dorsum carbon fibre AFOs, B2 and B3. The B1 AFO design, across all conditions, had on average approximately 70% less time spent within the terminal stance and pre-swing phase of the gait cycle, 20% less forefoot pressures compared to the control limb and 40% greater heel pressures. This is in contrast to the dorsum carbon fibre AFO's (B2 and B3), of which B3 (ToeOff AFO) demonstrated values proportionally closer to the control limb, and this was a statistically significant difference from the B2 AFO.

3.3.2 Null hypothesis: there is no effect of different PF levels on gait parameters

The second hypothesis assessed was that the population means of four differing maintained PF levels were equal regarding plantar pressure distributions and

temporal gait parameters within healthy participants. This null hypothesis was rejected in relation to all pre-defined measured gait parameters.

Firstly, speed was found to be statistically significant when three heel wedge inserts were compared to two, one and none, respectively. However, the largest difference, between three and one heel wedge insert, was a difference of only 0.079 metres/second and this was not affected by AFO design.

Secondly, ROM was found to be statistically significant between each heel wedge condition, with the range of DF increasing with decreasing heel wedges used. As previously highlighted, this is significantly correlated with forefoot pressures, heel pressures and the amount of time spent in terminal stance and pre-swing phase of the gait cycle. Table 3.3 clearly demonstrates how DF increases with decreasing heel wedge inserts and PF decreases with a decreasing number of heel wedge inserts.

As with the data analysing AFO design regardless of the number of heel wedge inserts, the raw values analysing heel wedge inserts regardless of AFO design, follow the same patterns associated with ROM. Consequently, Figure 3.26 shows how heel pressure decreases with decreasing heel wedge number. Figure 3.28 and Figure 3.30 show how forefoot pressures and the amount of time spent in terminal stance and pre-swing phase increase with decreasing heel wedge number.

When this data was analysed as a proportion of the control limb (Figure 3.32) the same patterns presented consistently. Post hoc analysis showed that within heel pressures and forefoot pressures, these differences were not significant between three and two heel wedge inserts but were for all other comparisons, except one,

and no heel wedge inserts for heel pressures. Between individual wedges, the largest difference was observed when participant's heel wedges were changed from two to one (15% mean difference in heel pressures and 11% mean difference in forefoot pressures). This was also the largest difference between individual heel wedge conditions within the amount of time spent in terminal stance and pre-swing phase (35% difference).

3.3.3 Null hypothesis: there is interaction effect on gait parameters

The above data supports statistically significant differences between both AFO designs and the number of inserted heel wedges used. The final null hypothesis stated that there were no interactions between the above two factors (AFO design and inserted heel wedge number) regarding plantar pressure distributions and temporal gait parameters within healthy participants. This analysis is demonstrated graphically by Figure 3.33 through to Figure 3.35.

Within all three AFO designs the amount of time spent in terminal stance and pre-swing phase of the gait cycle was highest with no heel wedge inserts and lowest with three heel wedge inserts. However, across B1 (rigid rocker bottom AFO) this difference remained below the value of the control limb throughout, whereas for B3 (ToeOff AFO) this begins below the value for the control limb rises above it with one and no heel wedge inserts, whereas within B2 (AFO Dynamic) this value was never below that of the control limb.

Forefoot pressure differences between the number of inserted heel wedges follow the same trends for B1 (rigid rocker bottom AFO) and B3 (ToeOff AFO), reaching statistical significance. However, B2 (AFO Dynamic) did not follow this trend for forefoot pressures. Instead, there are minimal differences between changing from

three to two to one heel wedge insert, with only 1-2% difference between them, all higher than the control limb. This then rises by 18% when changed from one to no heel wedge inserts.

Finally, heel pressures again follow similar trends described previously for B1(rigid rocker bottom AFO) and B3(ToeOff AFO). However, for B3 the difference between heel wedges is only small and does not reach statistical significance. Whereas within the B1, AFO heel pressures are much higher than the control limb with three heel wedge inserts gradually reaching values equivalent to the control limb with no heel wedge inserts. These values are significant between a two wedge difference. For B2 (AFO Dynamic) heel pressures were consistently below those recorded for the control limb and were not significantly different from each other.

3.3.4 Theoretical concepts and previous literature in relation to study findings

The purpose of tendons is to transmit muscular force to bone and in doing so allow the limb to move[2]. More specifically, the TA connects the gastrocnemius and soleus muscles to the posterior aspect of the calcaneus to permit transmission of plantarflexion torque, during the terminal stance and pre-swing phases of the gait cycle[110-111]. During this phase of the gait cycle the triceps surae works eccentrically to prevent the tibia rotating forwards over the talus resulting in forces equivalent to 2.4 times of an individuals' body weight being applied through the TA[107,111]. The degree of loading is dependent on a combination of permitted ROM at the ankle and contractile activity of the triceps surae[83].

Within healthy participants, Akizuki *et al*[83] demonstrated these mechanisms in practice. They found that by increasing the amount of PF the ankle is positioned in (using heel wedge inserts), whilst restricting DF, plantarflexion torque was reduced.

However, the design of this study was not randomised and only two heel wedge conditions were tested within a single rigid AFO design.

In contrast, Frőberg *et al*[104] tested the same hypothesis, that restricting DF is associated with decreased triceps surae activity, but found the opposite to Akizuki *et al*[83]. The reason for the two opposite results is that the second study allowed IWB, but without heel wedge inserts. Instead participants were mobilising on the forefoot only, therefore although DF was restricted the full force required for walking was being transmitted though the forefoot. Whereas, the first study was achieving the opposite effect by using heel wedge inserts and subsequently preventing forefoot load.

A third study evaluating a more flexible AFO design with one heel wedge condition[107] found minimal differences between mean vertical ground reaction forces between normal walking and walking with a single heel wedge. However, the results of this study are questionable as they only used four healthy participants, the trials were not randomised and no details were provided regarding the analysis of gait data or methods of statistical analysis.

There have been no studies evaluating the effect of different AFO designs within healthy participants throughout a range of heel wedge conditions. Furthermore the small numbers of studies that have evaluated heel wedge conditions within a single AFO design have not been randomised, have used small samples, with no justification of this decision and evaluated a limited range of heel wedge conditions.

This study implemented an experimental design, using randomisation to account for known confounding factors such as learning effects and fatigue and unknown

confounding factors. The results of this study show that B1 (rigid rocker bottom AFO) imposed a greater degree of DF restriction when compared to the two dorsum carbon fibre AFO's (B2 and B3). This led to decreased forefoot pressures and subsequent increased heel pressures. These relationships are demonstrated within the scatter plots and accompanying Pearson correlation coefficients within the results section. They show that decreasing forefoot pressures and restricting DF lead to a statistically significant correlated decrease in the terminal stance phase of the gait cycle.

These findings are in keeping with the study by Akizuki et al [83] and the biomechanics of tendon loading outlined earlier. This is because if DF is restricted, the TA is unable to transfer forces from the heel to the forefoot, as the tibia is unable to rotate forwards. Subsequently, the terminal stance phase of the gait cycle is reduced because there is limited transmission of load to the forefoot.

Within the dorsum carbon fibre designs (B2 and B3) the same principles can be applied. B2 (AFO Dynamic) was the opposite of B1 (rigid rocker bottom AFO), in that it permitted a statistically significant greater degree of DF. Therefore, when the interaction between heel wedges and AFO design were analysed, there were no significant effects regardless of the number of heel wedge inserts because the AFO did not restrict movement. Whereas B3 (ToeOFF AFO) was found to be not significantly different from B1 or B2. This is apparent within the results demonstrating the heel wedge and AFO interaction which gradually allows increased production of forefoot pressures with decreasing number of heel wedge inserts. This is accompanied by a gradually increasing amount of time within the terminal stance phase of the gait cycle and decreasing amount of heel pressures.

The changes in heel wedge number did not produce equal differences. For both B1 (rigid rocker bottom) and B3 (ToeOff AFO), the change from three heel wedges to two heel wedges produced only minimal differences across all three gait parameters (forefoot pressure, heel pressure and amount of time spent in terminal stance phase). However, the change from two to one heel wedge inserts was much greater (double the effect of three to two heel wedges, across all gait parameters). A possible explanation for this can be hypothesised from Table 3.4. This shows that between three and two heel wedge inserts, DF is restricted to neutral, whereas between two and one heel wedge inserts some movement into DF is permitted, therefore allowing some forefoot loading and increasing the amount of time spent in terminal stance and pre-swing phases of the gait cycle.

3.3.5 Application of study findings to Achilles tendon rupture rehabilitation

Rehabilitation after a TA rupture is prolonged, with reports of plantar flexor strength deficits between limbs still evident two years post rupture, and only 50-60% of patients returning to previous sporting levels[110]. One of the key factors limiting recovery is an abnormality of gait, which is not surprising given the relevance of the triceps surae muscle function during the gait cycle[111,116]. Development of clinical gait analysis and assessment of kinetic and kinematics parameters are becoming more valuable in clinical decision making, partly due to advancements in technology, resulting in more accurate analysis[117].

If a ruptured TA is not clinically managed immediately following the injury (within 2 weeks) the two ends of the ruptured tendon retract and there is a fibrous tissue in-growth, which fills the previously palpable gap between the two tendon ends. Therefore, if unmanaged, a ruptured TA will heal[118]. However, this results in gross tendon lengthening, which has severe functional consequences[119]. Therefore the

first characteristic of an AFO to be used within clinical practice needs to restrict the amount of permitted DF, specifically within the immediate phase following the injury. This criteria was not met by the B2 AFO (AFO Dynamic).

In addition to preventing gross tendon lengthening, commonly seen within late presentations, controversy also exists regarding the development of 'gap formation' during the early healing phases. This is thought to be secondary to constant cyclic loading during weight bearing rehabilitation, subsequently pulling the two tendon ends apart[20,85].

The phases of tendon healing can be divided into inflammation (first week), proliferation (weeks 2-8) and remodelling (up to 12 months)[120]. Throughout these phases, the tendon's tensile strength gradually increases, but remains inferior to the uninjured tissue. This is because the properties of the newly formed scar tissue are biomechanically inferior, displaying increased stiffness and subsequently decreased visco-elastic properties[2]. Some authors therefore believe that limiting gap formation, and subsequently the amount of the inferior scar tissue is of the up-most importance[20,41].

The clinical implications of this study demonstrate that the B1 AFO (rigid rocker bottom) with three heel wedge inserts provides the greatest restriction to DF and keeps the foot in the up-most PF. Consequently, this AFO could offer a theoretical decrease in the risk of developing 'gap formation'. Some literature would suggest that the practice of using a rigid support in a high degree of PF is the safest and most effective form of rehabilitation. Indeed, this has been the preferred method within my own department, due to its close representation to 'traditional' casting.

This very rigid approach is not however without problematic consequences. Animal studies have consistently demonstrated that allowing early protected loaded movement increases the biomechanical properties of the scar tissue, decreases excessive adhesion formation and subsequently enhances the gliding function of the tendon[85]. Further literature has also demonstrated that exact end-to-end opposition of a ruptured tendon, achieved by surgery, is no different in its bio-mechanical properties at two weeks compared to tendon ends not in exact end-to-end opposition using non-operative functional bracing in a rat model[121]. Therefore, the relevance of a small degree of tendon gapping is questionable.

In addition to the considerations of the effects of rigid mobilisation on tendon healing, there is also the consideration of the effects on the gait cycle. This study showed that the B1 AFO (rigid rocker bottom) consistently demonstrated increased heel pressures, over 50% more than those recorded for the control limb, large forefoot pressure deficits and a decrease in time spent in the terminal stance and pre-swing phase of the gait cycle. The consequence of this is potential development of heel pad pain, secondary to the increase in heel pressures, disuse atrophy of the triceps surae, secondary to decreased forefoot loading and decreased time spent in the terminal stance phase of the gait cycle.

These same observations have also been seen in clinical practice following cast immobilisation or a combination of immobilisation and functional bracing, following a TA rupture[113,122-123]. Previous research has also reported decreased forefoot pressures, increased heel pressures and decreased push off time. These were recorded from two weeks post cast removal, up to 24 months. This highlights how the problem is not just during the AFO wearing phase, but persists into the midterm.

Therefore, the B1 AFO design (rigid rocker bottom) with three heel wedge inserts, although the most restrictive combination, may not be the most appropriate for the rehabilitation of TA ruptures. The B2 AFO (AFO Dynamic), with no heel wedge inserts, is at the other extreme. Although this AFO design demonstrates normal gait parameters, it does so without restriction of movement. The clinician is therefore ultimately faced with the dilemma of preventing disuse atrophy, within the limits of permitted ankle movement that will protect the tendon from gapping at the repair site whilst minimising adhesions.

A further consideration to the application of these results to clinical practice is the problem associated with tendon re-ruptures in combination with the previous factors[39]. It is known that WB during the early phases of healing stimulates fibroblast activity and type III collagen synthesis [48]. It is also known that full WB is clinically safe, not resulting in an increased re-rupture rate[23]. Furthermore, approximately 553 Newtons are produced at the TA during normal walking[83]. But it is not known how much force is required to re-rupture a TA during, or even after, the early stages of healing. Therefore, the results of this study cannot make any assumptions regarding this factor.

Consequently, the purpose of the AFO is to provide 'protected' WB that represents normal gait parameters, within the limits of decreased range of permitted movement. These criteria were not met by B1 (rigid rocker bottom AFO), which consistently produced forefoot pressure deficits compared to the control limb and increased heel pressures across three and two heel wedge insert conditions, but not one. The AFO design of B2 (AFO Dynamic) did not produce heel pressures over and above the control limb and forefoot pressures were consistently higher than the control limb, however this was achieved within minimal limits of movement. The B3

AFO design (ToeOff) began with high heel pressures and forefoot pressure deficits, but only in combination with three heel wedge inserts. These values then gradually returned to values equivalent to the control limb with two, one and no heel wedge inserts. Therefore the B3 AFO was capable of loading the forefoot within the restraints of DF, as it was not significantly different from B1.

3.3.6 Trial summary, limitations and recommendations for future research

In summary, this study is the largest and only randomised study to evaluate the effects of changing the heel wedge height and AFO design, for the rehabilitation of a TA rupture. However, as previous literature has demonstrated, there are many methods for evaluating gait parameters, of which plantar pressure measurements is only one. Furthermore, these results have limited external validity because they were assessed within healthy participants, rather than patients who have sustained the injury.

This study has demonstrated significant differences within gait parameters for different AFO designs and the number of incorporated heel wedges. However, it is beyond the scope of this study to conclude if these findings will translate to a clinical setting within patients who have sustained this injury. Additionally, there is a balance that needs further investigation regarding the potential benefits of increasing movement and forefoot loading, against the potential complications (discussed previously), before gaining clinical acceptability. Finally, the results of this study cannot determine if differences within gait parameters will lead to improved patient reported functional outcome measures, or to what extent these differences will be.

Further research is required within the context of patient reported functional outcome measures and the practicalities of these changes in practice. In line with the MRC framework and the development of an intervention, this theoretical basis would be taken forward. Having completed a systematic review to define the components of an accelerated rehabilitation programme (Chapter 2) and developed a theoretical basis on which to direct developments (Chapter 3), the next steps involve piloting and feasibility studies of these components in practice.

It is acknowledged that these next steps of piloting and feasibility will not answer the question regarding the 'best' rehabilitation method. This can only be achieved by an adequately powered randomised controlled trial comparing these different interventions. However, these next stages are imperative to test their acceptability in a clinical setting, estimating likely patient consent rates for future research, alongside expected loss to follow-up within this patient population and acquiring additional data on which to guide sample size calculations. Consequently, the next chapter of this thesis will focus on aspects of piloting and feasibility of these components within a clinical context.

Declarations

This study has been presented at a national conference:

May 2011: British Trauma Society: Poster Presentation: The effect of maintained plantarflexion within an ankle foot orthoses on functional outcomes and gait parameters following an Achilles tendon rupture

Sponsorship

This study is jointly sponsored by the University of Warwick and University Hospitals Coventry and Warwickshire NHS Trust

Ethics Committee Approval Date

1st September 2008

Funding Body

This study was funded by Arthritis Research UK

Table of Contents

Abstract

Background
Following an Achilles tendon rupture there is evidence to support immediate weight bearing management. This management consists of two key interacting components. The first is the type of ankle foot orthoses to be worn and the second is the range of movement to be used within it. To determine what should be used healthy subject studies have investigated gait parameters on which to develop a theoretical framework. However, clinical studies are required to determine if these results will translate into practice. To inform a clinical study, a pilot study is required.

Objectives
The primary objective was to quantitatively evaluate trial processes to determine aspects of feasibility of future research; including patient recruitment, follow up rates and variability within a proposed primary outcome measure.

The secondary objective was to trial the clinical processes of changing one component of an established rehabilitation programme.

Methods
Following local presentations, clinical teams consented to implementing a stepwise reduction in the number of heel wedge inserts, within the currently used rigid rocker bottom orthoses. Ethical approval was gained to evaluate three groups consisting of five consecutive patients with three initial heel wedge inserts, followed by a further five managed with two heel wedge inserts and a final five, managed with one heel wedge insert. All patients were reviewed every two weeks for twelve weeks and at six and nine months. At these time points the Disability Rating Index, Achilles tendon Total Rupture Score and EQ-5D questionnaires were collected, alongside in-shoe gait analysis and clinical complications.

Results
The results of this study demonstrated a consistent referral rate of 2.5 patients per month; with low refusal rate (16 patients were eligible, of which one refused). There were 11 men and 4 women, aged 21 to 65 years. One patient was lost to follow-up. All three groups gradually returned to pre-injury functional scores by nine months and the standard deviation at this primary outcome point was 15 points within the Achilles tendon Total Rupture Score. There were four adverse events, two within the second consecutive group and two within the third consecutive group (two and one heel wedge inserts).

Conclusions
This feasibility phase has provided invaluable information on expected referral rates, loss to follow up and variability in outcome measures. These are all essential elements required for designing a definitive clinical trial. The secondary outcome of changing one component of the rehabilitation protocol did not pose any implementation challenges.

4.1 Protocol

The functional impact of sustaining a TA rupture is prolonged, requiring extensive rehabilitation[10]. Chapter 2 highlighted that many facets of the rehabilitation of this injury still remain unknown. The key variations identified were the AFO design, the degree of permitted movement within the AFO and the amount of time the AFO is worn for.

Experimental models have shown that allowing early movement in combination with early loading prevents detrimental alterations in muscle characteristics and favourably influences maturation of collagen[48-49]. In addition to these experimental models, investigations using human healthy subjects (including the work published from Chapter 3 of this thesis) provide a further theoretical framework on which to direct the development of clinical interventions for this injury.

Identifying the evidence base and developing theory are important steps towards developing an intervention, as outlined by the MRC complex intervention framework[64]. However, at this point it is beyond the scope of this thesis to conclude if these findings will translate to a clinical setting within patients who have sustained this injury. This can only be achieved by an appropriately designed clinical study.

The highest level of clinical study design is universally accepted as an RCT[63]. However, appropriately designed RCTs in an orthopaedic setting are both time and cost intensive. Recent examples of such trials include the Ankle Injury Management trial (AIM) and the Distal Radius Acute Facture Fixation Trial (DRAFFT)[124]. These have planned study periods of 5 and 4 years respectively, costing £2,260,183 and £1,432,708. Secondary to these associated timescales and costs with definitive clinical studies in orthopaedics, it is imperative to pilot procedures to assess how

they work in practice and ensure that estimated recruitment rates, loss to follow up and variance within outcome measures are acceptable, achievable and appropriate.

4.1.1 Objectives and research questions

The primary objective was to quantify patient recruitment rates, follow up rates and variability within a proposed primary outcome measure. This will address the following research questions:

1. What is the throughput of eligible patients?
2. What proportion of patients will be lost to follow-up at the primary outcome point?
3. To inform a sample size, what is the standard deviation of the primary outcome measure at the primary outcome point?
4. What percentages of administered Clinical Reporting Forms are completed?

The secondary objective was to trial the clinical processes of changing one component of an established rehabilitation programme. This would address the following research questions:

1. Are the rehabilitation protocols feasible in clinical practice?
2. What proportion of patients complete the allocated rehabilitation protocols?

4.1.2 Trial summary and trial flow diagram

Following consultation with clinical teams there was a consensus that only one component of the established rehabilitation protocol should be evaluated using a stepwise approach. Consequently at this stage of piloting there was no change in AFO design or implementation of randomisation procedures.

Following this initial consultation period, all patients who presented with an acute TA rupture to the University Hospitals Coventry and Warwickshire NHS Trust fracture clinic, were potentially eligible to take part in this trial. The only eligibility criteria were that they had no other serious injuries to either lower limb or a previous history of tendon rupture. These broad eligibility criteria were used to ensure that the results of the study could be readily generalised to the wider population.

All patients, whether treated operatively or non-operatively were then placed in the currently used rigid rocker bottom AFO for eight weeks. During this period of time heel wedges were inserted into the AFO to maintain the foot in a PF position. Within this study, the first five consecutive patients initially had three heel wedge inserts, the second five consecutive patients had two heel wedge inserts and finally a third consecutive group of patients had one heel wedge insert.

Every two weeks, for twelve weeks, then at six and nine months, all participants returned to fracture clinic for routine clinical assessment. At these time points in-shoe pressure sensors were used to collect gait parameters (using the same methods outlined in Chapter 3). In addition to these outcome measures, at baseline, two weeks, six weeks, three months, six months and nine months three patient reported outcome scores and complications were recorded (Figure 4.1).

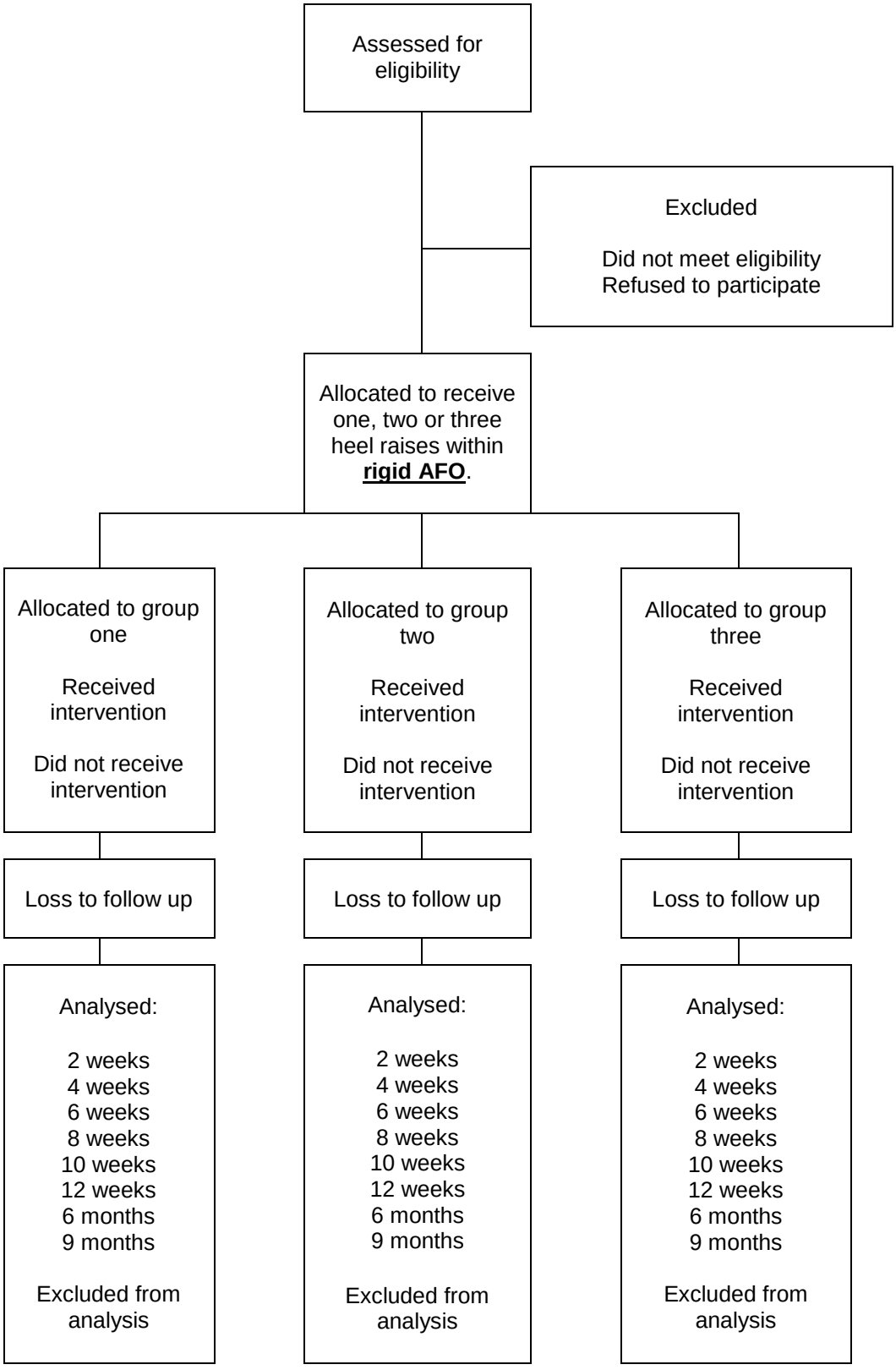


Figure 4.1: Expected flow of participants

4.1.3 Eligibility, recruitment, allocation and consent

This study had ethical approval from Coventry research ethics committee. All patients over 18 years presenting at the University Hospitals Coventry and Warwickshire NHS Trust fracture clinic, with a primary acute rupture of their TA, (within ten days of rupture) were eligible to take part.

Patients presenting after ten days from injury or with a history of previous TA rupture were excluded because these are considered a separate population, with different management requirements. These differences in management are secondary to the quality of the tendon tissue and retraction of the tendon ends[125]. Patients who had other serious injuries to either lower limb that would alter the intervention and subsequent rehabilitation were also excluded[116]. This was in addition to patients who were unable to give informed consent or adhere to trial procedures, with explicit reasons documented and reported.

If a patient taking part in the study sustained a contralateral rupture during the trial period the second rupture would not be included in the study because the result of this intervention would not be independent from the first intervention.

Recruitment of participants took place within the fracture clinic setting at University Hospitals Coventry and Warwickshire NHS Trust. Each patient was initially treated in an equinus plaster cast (for their comfort) and then referred to the next clinic run by the principal investigator. These clinics took place once each week. The investigator then assessed eligibility of potential participants.

A TA rupture was diagnosed by the researcher and then confirmed by the principal investigator by subjective history and physical examination, confirming a palpable

gap and a positive Thompson test[126]. Once clinical diagnosis and eligibility had been confirmed the patient was then presented with a patient information sheet (Appendix C) and was verbally informed of what the trial would involve. The patients were then given the opportunity to discuss any issues with the research team, their consultant, friends and family.

After allowing sufficient time for the patient to consider their decision and ask questions about the trial, eligible and willing participants signed a consent form, approved by Coventry ethics committee (Appendix D). Prior to this a list of information to be covered before consent was obtained was checked to ensure that all essential information had been provided to the potential participant. Any eligible and unwilling participants were recorded and presented within the final report. Once eligible patients had consented to take part in the study they attended routine clinical follow up every two weeks for twelve weeks and then at six and nine months.

Any new information during the trial that may have affected a participant's willingness to take part was reviewed by me and my allocated supervisors. As necessary this information was communicated to all participants, and a revised consent form then completed as required. Participants were also advised that they could withdraw from the trial treatment, and/or whole trial at any time without prejudice. If participants withdrew from the trial treatment, they were followed up wherever possible and data collected as per protocol until the end of the trial. The only exception to this was when the participant had also explicitly withdrawn consent for follow up.

To ensure minimal loss to follow up, contact addresses, telephone numbers and email addresses were collected from participants. In the event of a patient not attending clinic, a system of reminders was instituted. The system included an initial phone call to reschedule the appointment. If contact was not possible by telephone after one week an email was sent along with a letter outlining the rescheduled appointment. If there was no contact within two weeks a further phone call was made to an alternative point of contact given by the participant at their initial consent. If no contact was made with the alternative contact a letter was sent to them. If there was no response from the participant, or their alternative point of contact, within these time frames they were recorded as lost to follow up.

Following discussions with the clinical teams, allocation to the number of inserted heel wedges within the AFO was carried out in a consecutive manner, as opposed to randomisation. This allowed for a gradual reduction in heel wedge inserts across three consecutive groups. The implications from Chapter 3 being a greater degree of forefoot pressure production, a corresponding decrease in heel pressure production and an increase in the amount of time spent in the terminal stance and pre-swing phase of the gait cycle. As previously highlighted these changes in gait parameters need to be balanced against the potential clinical risks of re-rupture and tendon lengthening.

The sample size for this study was too small to determine the 'safety' of the intervention. It was discussed amongst the teams that this would not be feasible to assess, secondary to the low incidence of re-ruptures and tendon lengthening. Consequently using such outcomes would require a large sample size, beyond the scope of a pilot sample. This same topic of using uncommon complications as outcome measures has also been recently highlighted within a multi-centre RCT,

comparing operative to non-operative management for TA ruptures[32]. However, adverse events would be monitored throughout, as detailed in chapter 4.1.6.

Consequently the first stage of three consecutive groups would not evaluate the safety of the intervention or patient acceptability to be randomised to the different conditions. This first stage would allow evaluation of trial procedures, including the provision of data to later determine achievable recruitment rates, loss to follow up, sample size calculations and testing of clinical procedures.

4.1.4 Sample size and intervention

As discussed, ideally the participants' would have been randomised to the different treatment groups, and a corresponding sample size would be calculated to sufficiently power the study. However at this stage of interventional development randomisation was not undertaken, to gain acceptance from the clinical team. Secondly the primary research questions at this stage are focussed on trial feasibility/procedures and currently there is no method for determining sample sizes for feasibility studies. Therefore a sample size of five for each group was chosen based on discussions with experts in the field in the hospital, and what was achievable within the given time constraints.

Previous experience of providing a service for patients post TA rupture showed that two patients would be recruited per month. Therefore fifteen patients would require eight months to recruit. Within this population, with the above mechanisms in place for preventing loss to follow up it was expected that there would be less than 10% loss to follow up.

Once consent had been obtained from relevant participants the first consecutive group of five patients were placed within the rocker bottom AFO with three heel wedge inserts, which were reduced to two at two weeks, one at four weeks, none at six weeks and the AFO removed at eight weeks. Group two received two heel wedges, being reduced to one at four weeks, none at six weeks and the AFO removed at eight weeks. Group three received one heel wedge, being reduced to none at six weeks and the AFO removed at eight weeks.

During the AFO wearing phase all patients were advised not to IWB without wearing their AFO. Furthermore all patients were advised to remove their AFO daily to perform ankle ROM exercises, as tolerated. Elevation of the injured limb was recommended intermittently throughout the day, to control swelling. At eight weeks all patients were referred for routine physiotherapy offered within the hospital, for which there is a standard guideline. All participants then continued to attend clinic at standard follow up time points of ten weeks, three, six and nine months.

At baseline all pre-existing concomitant illnesses and medications were recorded in addition to specific questions regarding conditions and medications known to predispose to tendon rupture. These included specifically the presence of tendinosis (pain, swelling or thickening within the tendon), the use of fluroquinolone antibiotics, steroids, disease modifying anti-rheumatic drugs and diabetic medication[9]. Additionally patient demographics (age, height, weight, ethnic minority and gender) were recorded along with the date and mechanism of injury. This information was used to assess the baseline characteristics of the groups.

4.1.5 Outcome measures, method of assessment and analysis

As discussed earlier, using uncommon complications such as re-rupture rate or tendon lengthening within a definitive study has been recently highlighted by a multi-centre study as being 'unfeasible'. However, in addition to the considerations given to sample size calculations, there is also the consideration of whether or not complications are the most appropriate outcome.

The primary outcome of this piloting phase was a PROM. Such a measure would also be planned as the primary outcome within the design of a subsequent definitive RCT investigating an IWB intervention, following an acute TA rupture. This choice of primary outcome was chosen in contrast to clinical measures such as complication rates and quantification of gait parameters secondary to a combination of factors that have been outlined within the orthopaedic literature, and more recently the Department of Health's 2009/10 operating framework[56]. These documents outline that ultimately the most important outcome is from the patient's perspective.

The primary outcome measure would ideally need to be disease specific to allow for greater discriminatory validity. The Achilles tendon Total Rupture score (ATRS) is the only such validated measure available for use with patients post TA rupture[61], as discussed in more detail within Chapter 6. However, this outcome measure has only recently been published, and has only been validated within a Swedish population between the ages of 20-70 years. Therefore further data is required within a UK population across all age ranges before this may be appropriate to be used as a primary outcome measure. This score is therefore being collected as part of a wider validation study, outlined in Chapter 7, as part of this PhD thesis (Appendix E).

With no validated disease specific PROMs to choose from the next most appropriate currently validated PROM for this population is the Disability Rating

Index (DRI)[127], the reasons for this are discussed in greater detail within Chapter 6. Although not disease specific, it has been validated within an orthopaedic clinic setting for a range of orthopaedic presentations. It is a self-administered form with twelve questions regarding common physical activities, to which patients respond using a 100mm visual analogue scale. There are two anchor points 'without difficulty = 0' and 'not at all = 100'. The twelve questions are subdivided into three broad categories; common basic activities of daily life, more demanding daily physical activities and work-related or more vigorous activities (Appendix F). This was asked in conjunction with a more generic quality of life measure (EQ-5D questionnaire)[128].

The EQ-5D is a standard instrument for use as a measure of health outcome. It is self-completed and comprises of five domains, mobility, self-care, usual activities, pain/discomfort and anxiety/depression. These combined domains result in a single health index score; there are 243 possible health states, plus unconscious and death. The second part of the outcome is a visual analogue scale of 0-100 that asks participants to rate how good or bad their own health state is, no points being 'worst imaginable health state' and 100 being 'best imaginable health state'. This outcome measure has been validated within an orthopaedic context and in a range of populations and languages (Appendix G).

Within the study of healthy participants, outlined in Chapter 3, altering the number of heel wedge inserts had an effect on heel and forefoot pressures as well as the proportion of time spent in the terminal stance and pre-swing phase of the gait cycle as a proportion of the total stance phase. It was not known if these changes in planter pressure distribution would translate into clinical practice. Therefore measurement of in-shoe plantar pressures took place during each visit, using the same protocol outlined in Chapter 3 to provide important secondary observations.

As discussed in Chapter 3 the interventions being assessed will allow increased movement and potentially increased force production within the healing tendon. However, there is a balance between subjecting a healing tendon to enough stress/strain to promote the healing response (discussed in Chapter 1) and subjecting it to too much, resulting in complications. Expected serious adverse events commonly associated with TA rupture rehabilitation include re-rupture, tendon lengthening, adhesion, disturbed sensibility, keloid scarring and infection. These adverse events would be recorded and reported to the trial sponsor and ethics committee, in line with the trial protocol.

The time points at which to record these outcomes was based on knowledge surrounding healing time frames, as well as routine practice follow up appointments. Patients were reviewed every two weeks for the first twelve weeks predominantly to screen for the development of any complications. Two further clinic appointments were then made at six and nine months, to review progress with return to activities of daily living; complications were also evaluated at these time points. Patient reported outcomes were collected at 2,6,12, 24 and 36 weeks to allow evaluation of functional recovery during both the acute and mid-term phases. At nine months patients have normally returned to previous levels of activity, therefore outcomes were not recorded beyond this time point[129].

The datasets were analysed using descriptive statistics only. No inferential statistical analysis was planned because no conclusions would be drawn between these three consecutive groups of patients, this would not be appropriate to the objectives of this study.

4.1.6 Adverse event management

At each visit following initial consent procedures each patient was asked whether they had experienced any adverse events since their last visit. An adverse event was defined as any untoward medical occurrence in a clinical trial subject which does not necessarily have a causal relationship with the treatment. All adverse events were listed on the appropriate CRF for routine return to the central office (Appendix H).

A serious adverse event (SAE) was defined as any untoward and unexpected medical occurrence that resulted in death, was life-threatening, required hospitalisation or the prolonging of existing hospitalisation, resulted in persistent or significant disability or incapacity, was a congenital anomaly or birth defect, 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, as per the Universities standard operating procedures.

All SAEs events were entered onto the SAE reporting form. Once received by the principal investigator causality and expectedness was determined. Serious adverse events that were deemed to be unexpected and related to the trial were notified to the main Research Ethics Committee within 15 days for a non-life-threatening event and within seven days for a life-threatening event. All participants experiencing SAEs were followed up as per protocol until the end of the trial.

4.1.7 End of trial

The end of the trial was defined as the final visit to the clinic of the last participant.

4.1.8 Data management, statistical analysis and trial organisation

The CRFs were designed in conjunction with the principal investigator (PhD supervisor, Mr Matthew Costa) and guidance from the trial's statistician. All CRFs were also completed with the participant present and inputted and stored centrally. All CRFs can be found in Appendix H.

All electronic patient-identifiable information was held on a secure, password-protected database accessible only to essential personnel. Paper forms with patient-identifiable information were held in secure, locked filing cabinets within a restricted area of Warwick Medical School. Patients were identified by a code number only. Data was entered by the research physiotherapist onto the electronic database immediately following each research clinic.

Direct access to source data/documents was required for trial related monitoring and analysis only. All paper and electronic data will be retained for at least five years after completion of the trial. As part of my on-going PhD supervision, the supervisors had reviewed the protocol for this study and had received progress reports at their request. Accumulating data was monitored at frequent intervals to identify and facilitate the early remedial action of certain problems that may include recruitment, data collection and compliance. Yearly progress reports were also submitted to the funders of this project (Arthritis Research UK), as outlined in the terms and conditions of the awarded grant.

The day to day management of this project was overseen by the PhD supervisors. There was standard NHS cover for negligent harm in place. There was no cover for non-negligent harm. Insurance was in place until 31/07/10 and renewed accordingly. Ethical and research and development approvals were in place.

Additionally a contract was in place with the University of Warwick and an honorary contract for research services with the University Hospitals Coventry and Warwickshire NHS Trust.

The principal investigator was Mr Matthew Costa, who had undertaken relevant mandatory training in GCP and the University of Warwick 'Chief Investigators' course. Clinically Mr Costa is also an orthopaedic consultant and all trial participants were under his clinical care as per NHS practice. This role involved Mr Costa overseeing and being ultimately responsible for the trial conduct. However he had no role in the set up and implementation of the trial.

As a research physiotherapist, mandatory GCP training had been undertaken, in addition to non-mandatory training to facilitate this role including 'how to consent participants for clinical research' and an MSc in Trauma and Orthopaedic Surgery. Health Professions Council registration was also up to date. The principal investigator delegated duties as appropriate to the research team, and these were recorded on a delegation of authority log within the trial site file.

Financial support for this project had been awarded by Arthritis Research UK. Treatment costs associated with this study had been reviewed by the NHS research and development department and in line with trust policy they had agreed that there were no service support costs for this project and identified additional treatment costs would be paid via normal commissioning arrangements. The project timetable and milestones are outlined in Table 4.1.

Table 4.1: Project timetable

Number of months	0	4	8	12	16	20
Tasks to be completed	Jan 09	Apr 09	Aug 09	Dec 09	April 10	Aug 10
Ethics, R&D, sponsorship and insurance.						
Prepare and refine materials						
Recruitment						
Finish all data collection						
Analysis						
Write-up and report						

4.2 Results

The primary objective of this study was to evaluate patient recruitment rates, follow up and variability within the proposed primary outcome measure. The secondary objective was to trial the clinical processes of changing one component of an established rehabilitation programme and measure gait parameters.

Recruitment took place between January 2009 and June 2009 at a recruitment rate of 2.5 per month. Twenty-six patients were screened, ten were not eligible. Eight were secondary to being musculotendinous junction ruptures, one patient presented with a delayed presentation and one patient was unable to adhere to trial procedures secondary to chronic emphysema, preventing assessment of gait analysis.

Sixteen patients were eligible and 15 consented to take part. One patient refused to take part on the basis of not wanting to complete questionnaires, leaving 15 eligible

and consenting patients. One patient consented to take part and subsequently received private health care and therefore no longer wished to be followed up. There were no further losses to follow up as shown in Figure 4.2.

The baseline demographics for the three groups of five participants are shown in Table 4.2. This shows that the groups were comparable with regards to age, weight, height, foot involvement, ethnic background and smoking history. There were more males in the two and one heel wedge insert group compared to the three heel wedge insert group. Furthermore, within the three heel wedge insert group, three patients had pre-existing pathologies, which was higher than the groups with one and two heel wedge inserts; this was reflected within the baseline functional outcome scores. The mechanism of injury was predominantly sport related (9/15) and the mean number of days from injury to study consent was three (SD was two).

Within the single heel raise group there were two SAEs, which occurred at the three month time point. The first was a re-rupture, resulting in operative management and a further 12 weeks within an AFO. The second event was the result of a sprain to the tendon two months post rupture, resulting in wearing an AFO for an additional five weeks. There were two other SAEs, both within group two, one was a superficial wound infection managed with a short course of antibiotics and the second an unrelated episode of back pain which resolved within one month, with a course of pain medication. Neither of these events resulted in a deviation from the rehabilitation protocol.

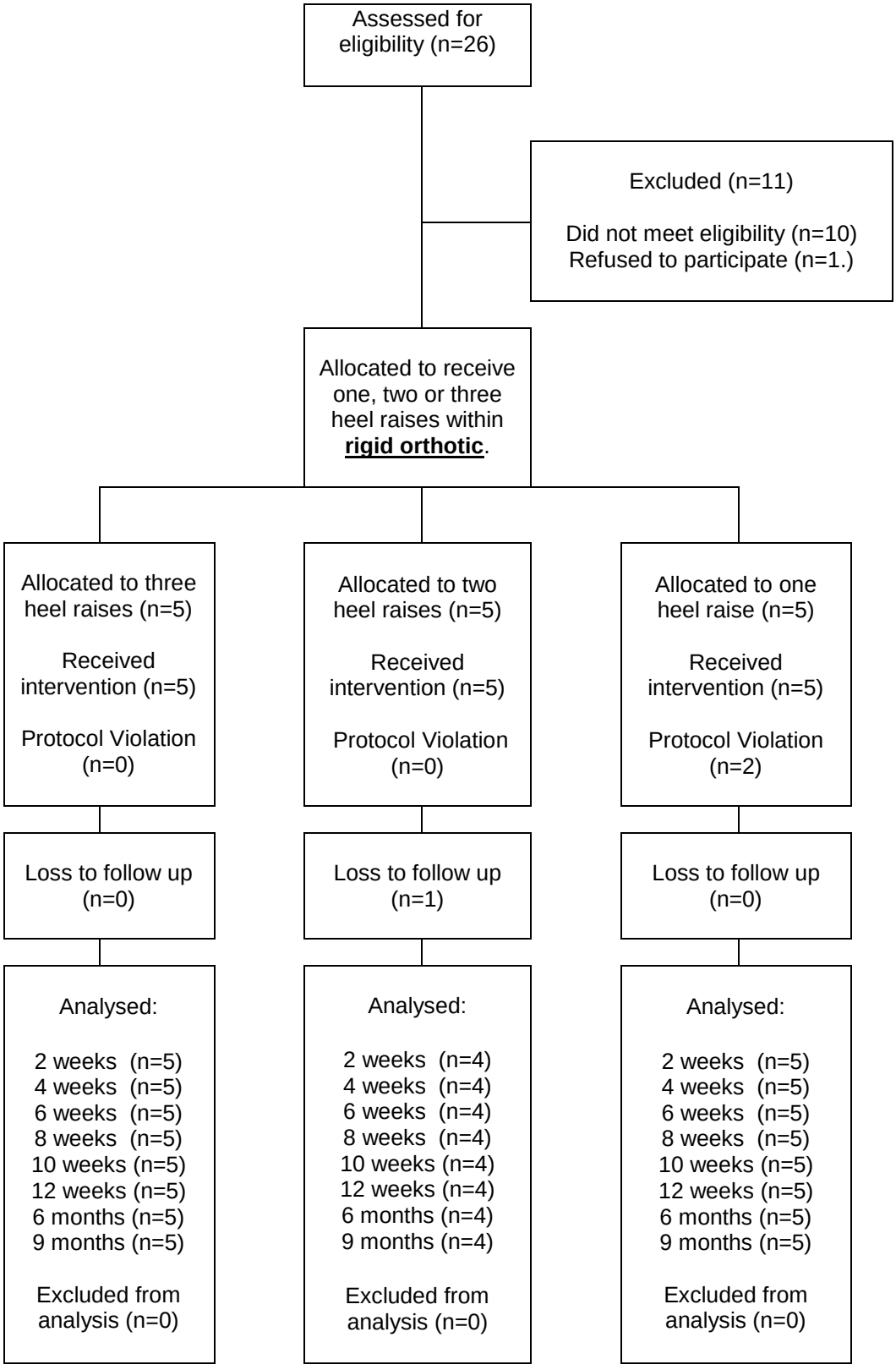


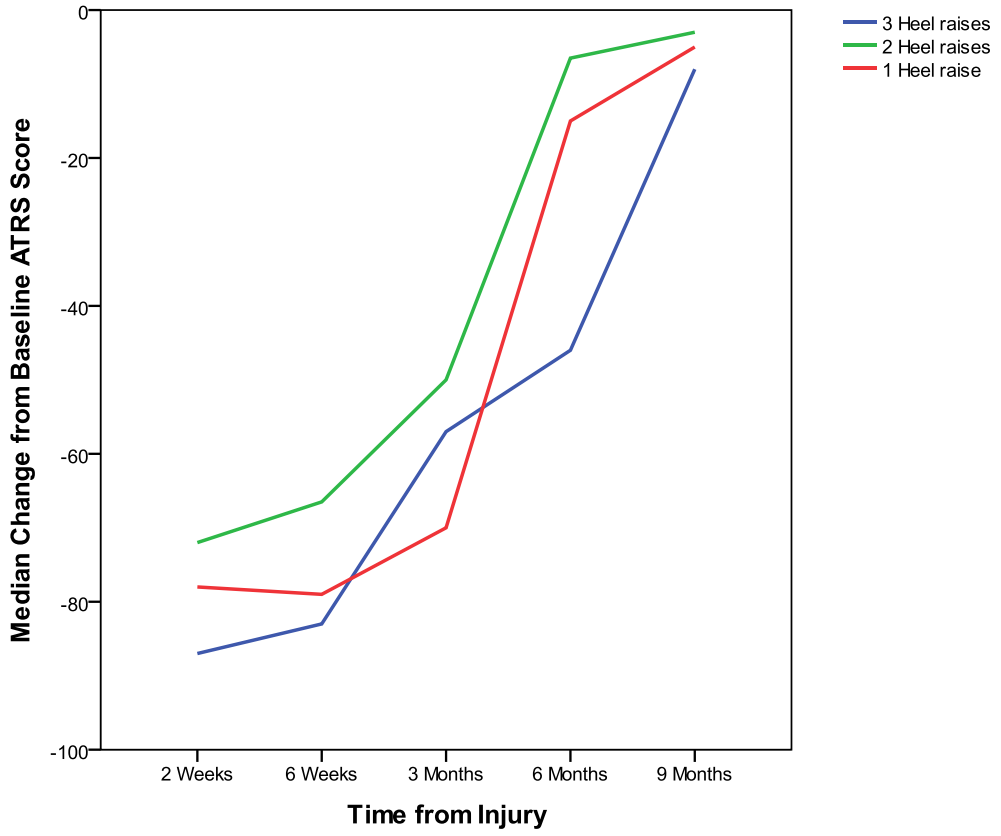
Figure 4.2: Flow chart of participants through the trial

Table 4.2: Baseline demographics for the three study groups

	Three heel raises	Two heel raises	One heel raise
Mean age in years (SD)	46 (9)	35 (9)	39 (7)
Male/Female	3/2	4/1	4/1
Left/Right	2/3	2/3	3/2
Mean height in cm (SD)	173 (13)	177 (6)	174 (10)
Mean weight in Kg (SD)	81 (7)	82 (13)	77 (14)
Smokes (Y/N)	0/5	0/5	1/4
Smoked in past (Y/N)	1/4	1/4	1/4
Ethnic background	White: 5	White: 4 Chinese: 1	White: 5
Current medication	5 patients: No medications	3 patients: No medications 2 patients: Steroid inhaler for asthma	4 patients: No medications 1 patient: B12 injections every 3 months for anaemia
Pre-existing ipsilateral problem	2 patients: No problems 1 patient: MTP arthritis 2 patients: Prior Achilles pain	4 patients: No problems 1 patient: Prior Achilles tendon pain and swelling	5 patients: No problems
Pre-existing contralateral problem	4 patients: No problems 1 patient: MTP arthritis	5 patients: No problems	5 patients: No problems
Any other new injuries	None	None	None
Mechanism of injury	Sport: 3 RTA: 1 Stairs: 1	Sport:5	Sport:1 Lifting: 2 Dancing:1 Unknown:1
Management (Op/Non-Op)	2/3	4/1	1/4

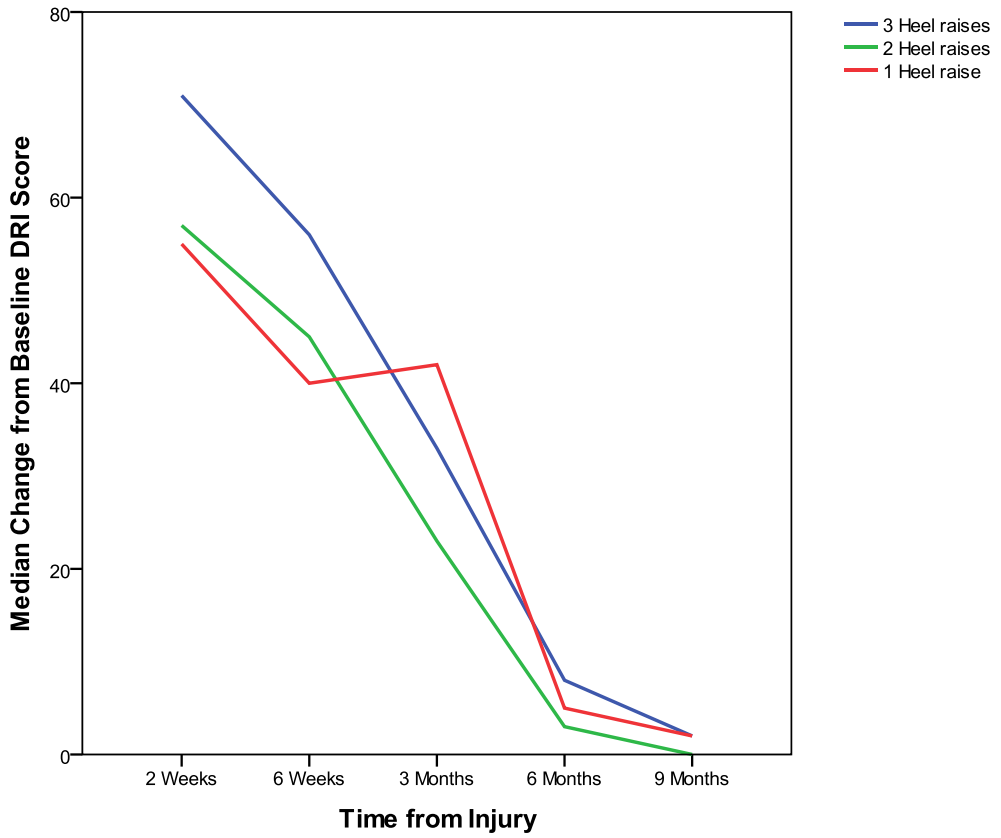
To provide further information on variability of the PROM's data, to inform a sample size calculation, Figure 4.3 through to Figure 4.5 provide graphical illustrations of the functional outcome scores for the three groups as a change from median baseline scores. The ranges of results around the median change from baseline are shown in a table underneath each figure. Furthermore, Figure 4.6 through to Figure 4.13 demonstrate the mean and standard deviation for each accumulating patient, as a collective of the three groups, at each time point within the DRI and ATRS scores.

Figure 4.6 illustrates the SD gradually increasing to approximately patient 9 and then stabilising through to the 15th patient for baseline, two and six week scores within the DRI. Figure 4.7 shows how this changes at the three, six and nine month time points. At these later time points the SD again gradually reduces with each additional patient, up until the 12th patient, from this point onwards the SD increases but remains constant through to the 15th patient. This is possibly secondary to the adverse events reported previously. The ATRS scores shown in Figure 4.8 and Figure 4.9 show the same patterns described for the DRI score.



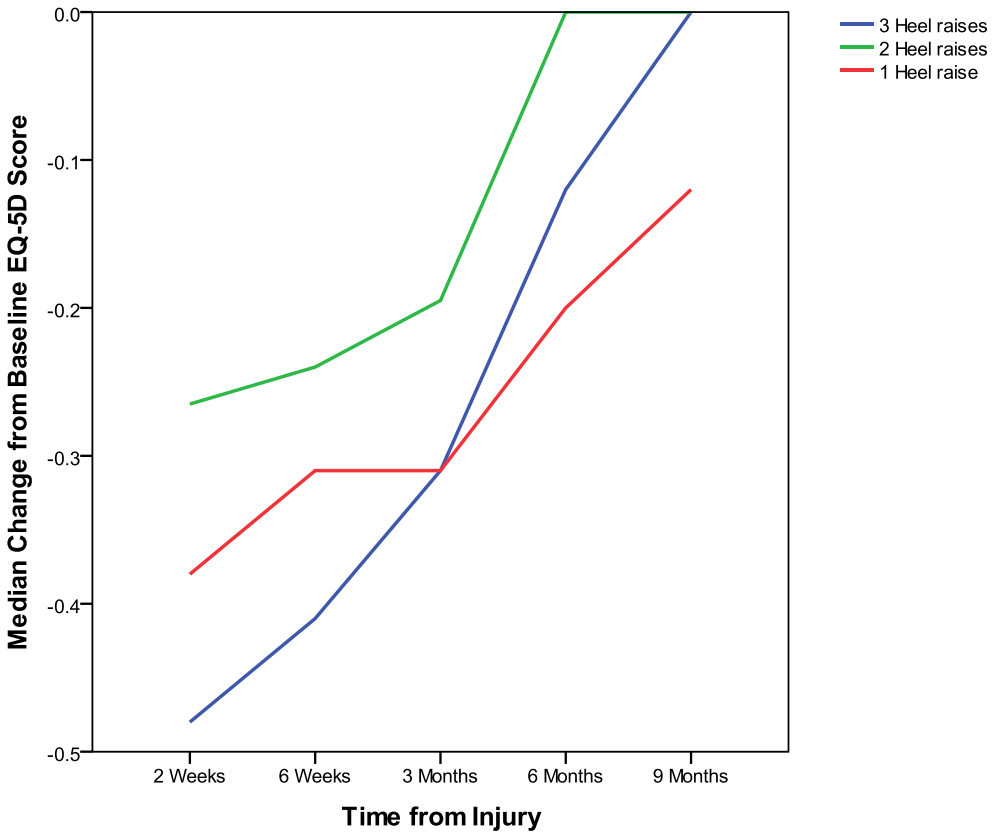
Range of results at each time point (As change from median baseline score)	Three heel raises	Two heel raises	One heel raise
Two weeks	-80 to -92	-59 to -84	-69 to -88
Six weeks	-41 to -92	-23 to -73	-46 to -81
Three months	-54 to -69	-29 to -78	-30 to -80
Six months	-18 to -66	2 to -25	-10 to -75
Nine months	-4 to -43	2 to -10	-2 to -39

Figure 4.3: Median change from baseline for ATRS scores with table demonstrating the range of values at each time point for the three groups



Range of results at each time point (As change from median baseline score)	Three heel raises	Two heel raises	One heel raise
Two weeks	47 to 76	25 to 70	49 to 73
Six weeks	22 to 58	28 to 65	26 to 54
Three months	19 to 39	10 to 34	4 to 48
Six months	4 to 14	0 to 11	3 to 49
Nine months	0 to 16	0 to 5	0 to 30

Figure 4.4: Median change from baseline for DRI scores with table demonstrating the range of values at each time point for the three groups



Range of results at each time point (As change from median baseline score)	Three heel raises	Two heel raises	One heel raise
Two weeks	-0.29 to -0.71	0 to -0.81	-0.31 to -0.81
Six weeks	-0.19 to -0.48	-0.12 to -0.88	-0.12 to -0.48
Three months	-0.19 to -0.38	0 to -0.38	-0.15 to -0.38
Six months	0 to -0.31	0 to -0.24	0 to -0.38
Nine months	0 to –0.2	0 to 0	0 to -0.27

Figure 4.5: Median change from baseline for EQ-ED scores with table demonstrating the range of values at each time point for the three groups

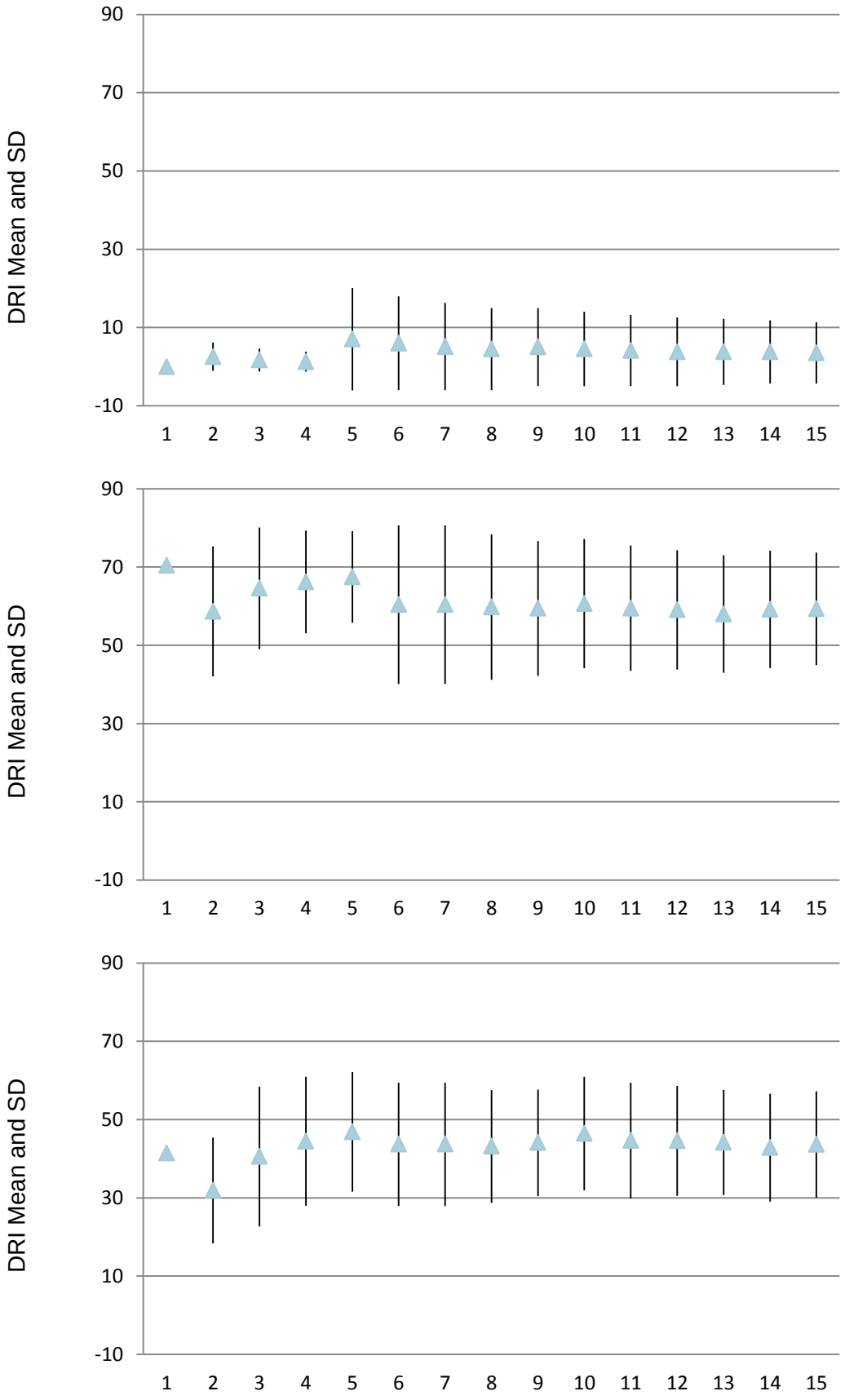


Figure 4.6: Mean and SD DRI scores for each accumulating participant, from top to bottom: baseline, 2 and 6 weeks follow up results

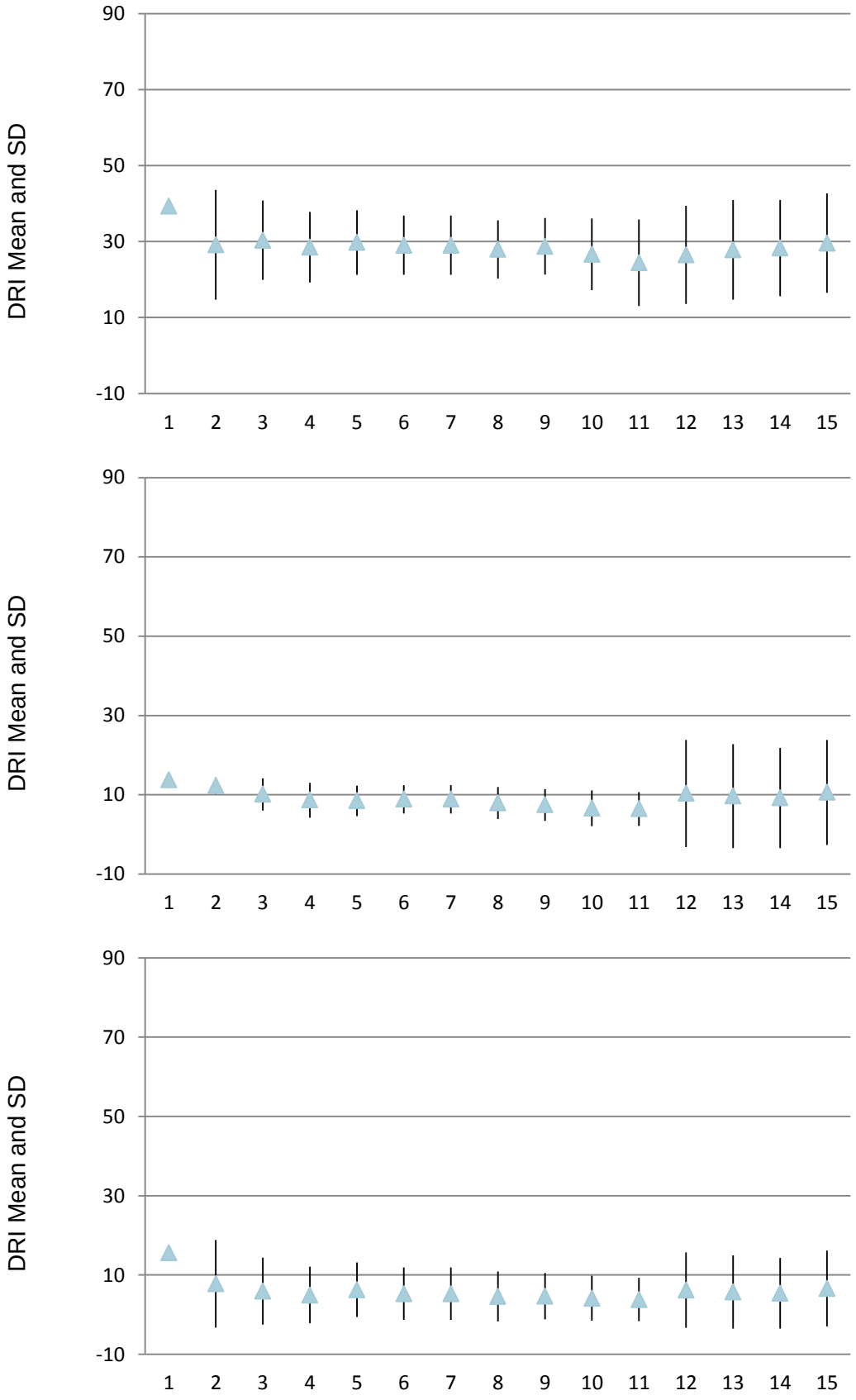


Figure 4.7: Mean and SD DRI scores for each accumulating participant, from top to bottom: 3, 6 and 9 month follow up results

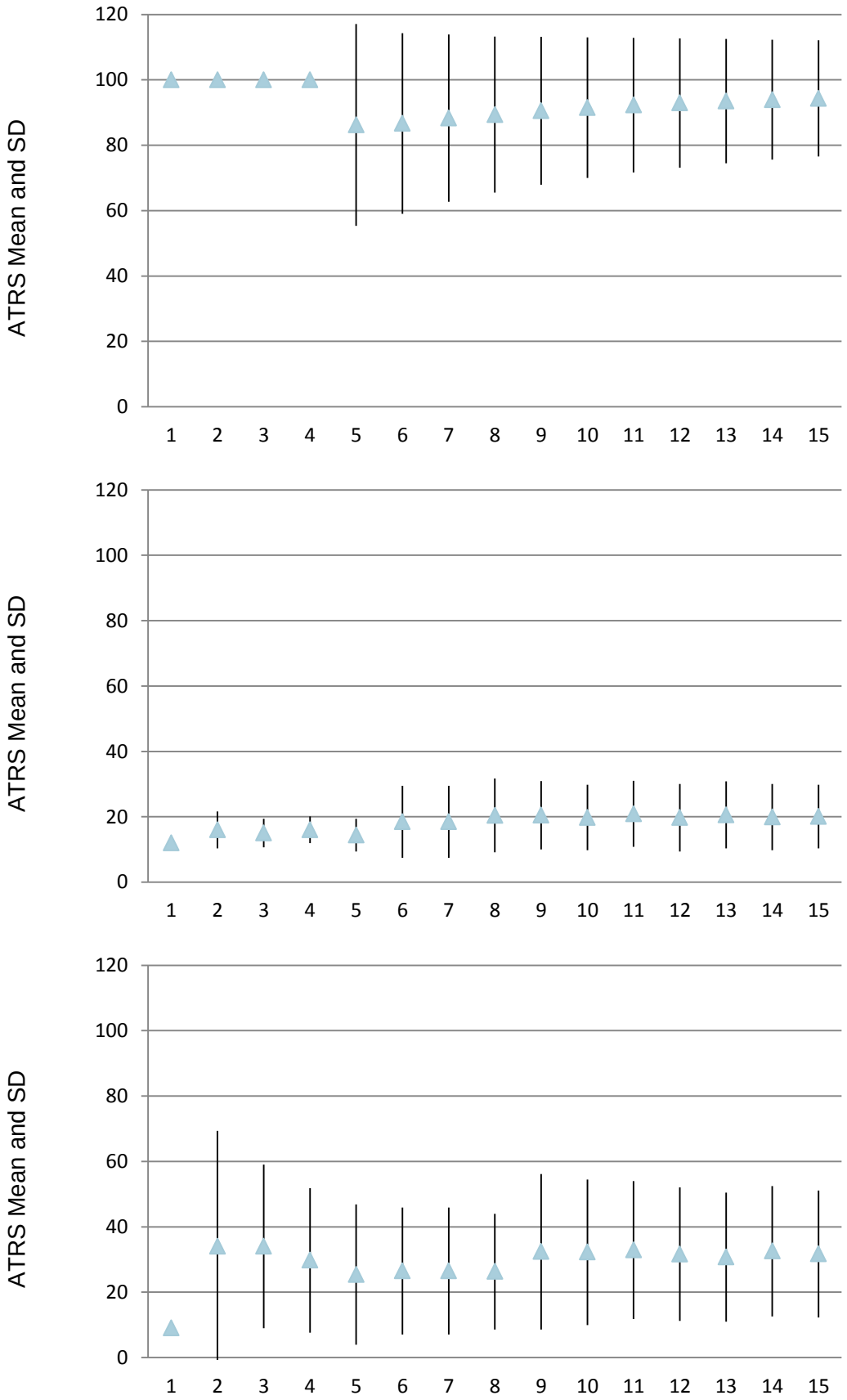


Figure 4.8: Mean and SD ATRS scores for each accumulating participant, from top to bottom: baseline, 2 and 6 week follow up results

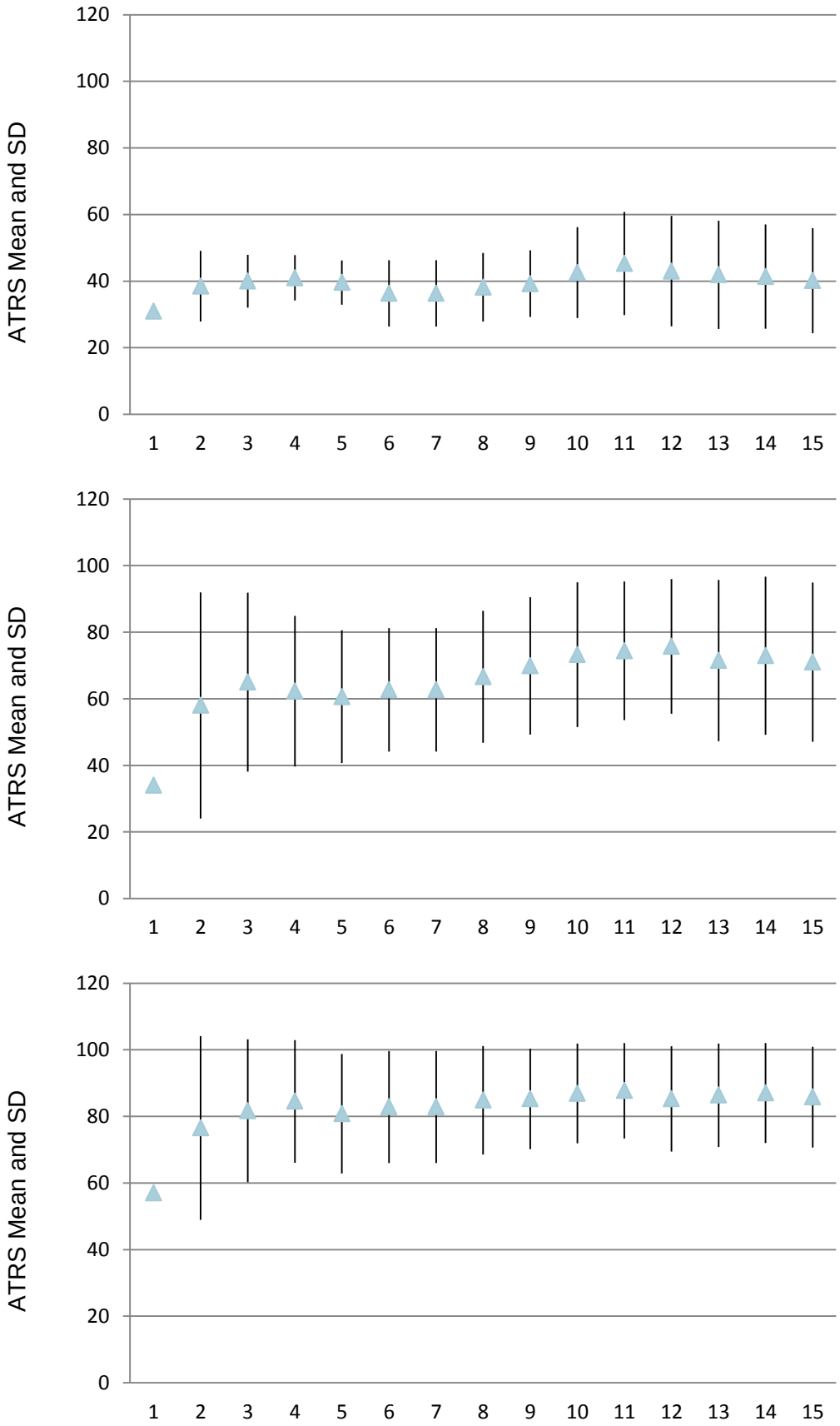


Figure 4.9: Mean and SD ATRS scores for each accumulating participant, from top to bottom: 3, 6 and 9 month follow up results

Alongside PROMs, gait parameters were also evaluated as a secondary objective. Figure 4.10 demonstrates the mean heel pressures (KPa) and standard deviations for the injured and uninjured limb at each time point for each group. It is clearly demonstrated that heel pressures are above those recorded for the uninjured limb within all three groups. These high recordings all return to within 10% of the contralateral limb, by the nine month time point. Heel pressures within the uninjured limb rise slightly across time, but remain largely unchanged.

Figure 4.11 demonstrates the mean forefoot pressures (KPa) for the three groups, with standard deviations. It is clear that the opposite pattern is apparent to that of heel pressures. The forefoot pressures for the injured limb are consistently below those recorded for the uninjured limb. Again there is a trend towards return to foot pressures equivalent to the contralateral limb by the nine month time point. It is also noticeable that forefoot pressures in the uninjured limb over time also increase. However it is not possible from this gait parameter alone to determine the mechanisms for this.

Figure 4.12 shows the percentage amount of time spent in terminal stance and pre-swing phase as a proportion of the total stance phase. These figures show the same patterns as those seen within the injured forefoot pressures. The injured limb is consistently below the value recorded for the uninjured limb, returning to within 10% of the contralateral limb by nine months. The uninjured limb remains unchanged across time for this parameter.

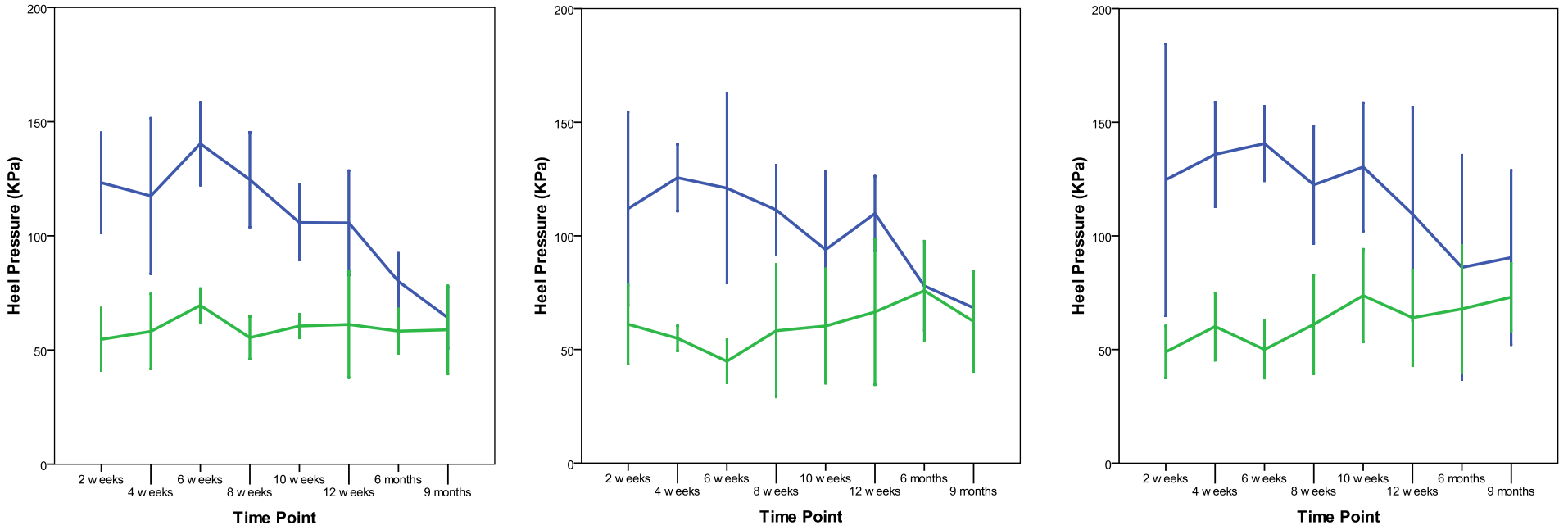


Figure 4.10: Mean and SD for heel pressure measurements (KPa) for injured (blue line) and uninjured (green line) limb at each time point. From left to right: Three heel raise group, two heel raise group and the one heel raise group

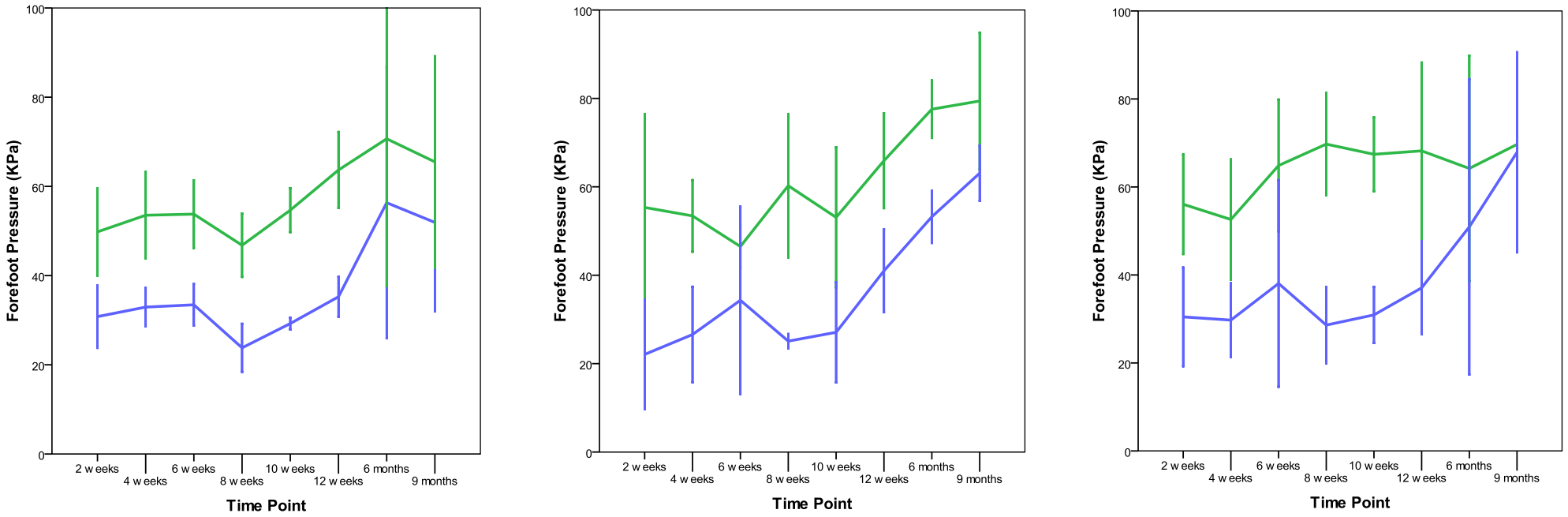


Figure 4.11: Mean and SD for forefoot pressure measurements (KPa) for injured (blue line) and uninjured (green line) limb at each time point. From left to right: Three heel raise group, two heel raise group and the one heel raise group

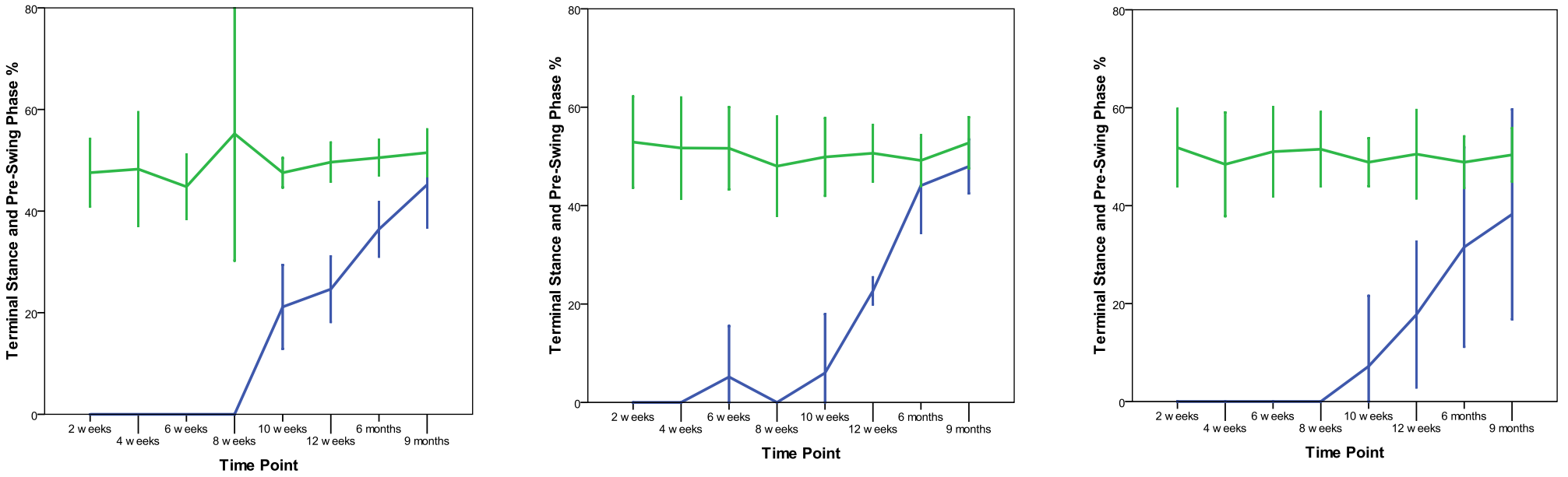


Figure 4.12: Mean and SD for terminal stance and pre-swing (%) for injured (blue line) and uninjured (green line) limb at each time point. From left to right: Three heel raise group, two heel raise group and the one heel raise group

Scatter plots for the above measured gait parameters along with Pearson Correlation Coefficients were evaluated to explore if the same relationships found within chapter 3, within healthy participants, also existed within participants who had sustained the injury. These are shown in Table 4.3 and Figure 4.13 to Figure 4.15, which clearly demonstrate the same relationships as those found in chapter 3 with significant correlations between the three parameters.

Table 4.3: Pearson correlation coefficients

Paired comparison	Pearson correlation coefficient	Significance
Heel pressure & forefoot pressure (KPa)	-0.42	<0.001
Forefoot pressure (KPa) & terminal stance and pre-swing %	0.69	<0.001
Heel pressure (KPa) & terminal stance and pre-swing %	-0.81	<0.001

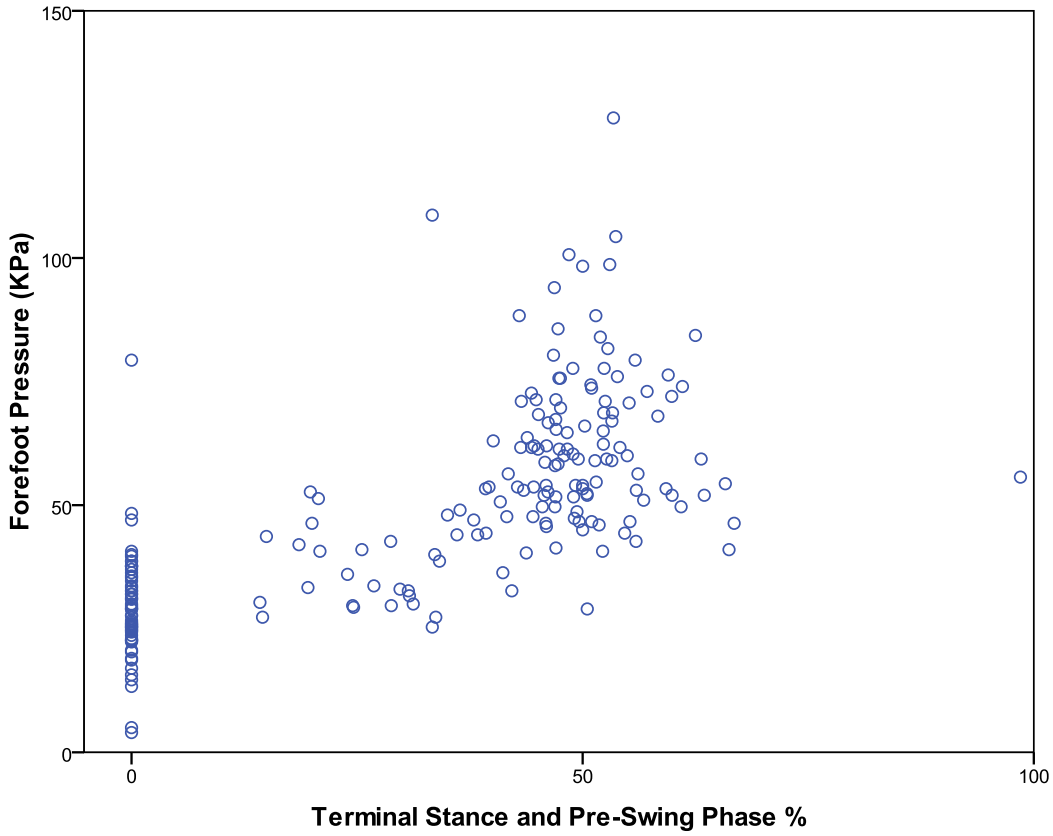


Figure 4.13: Scatter plot of forefoot pressure and amount of time spent in terminal stance and pre-swing phase %

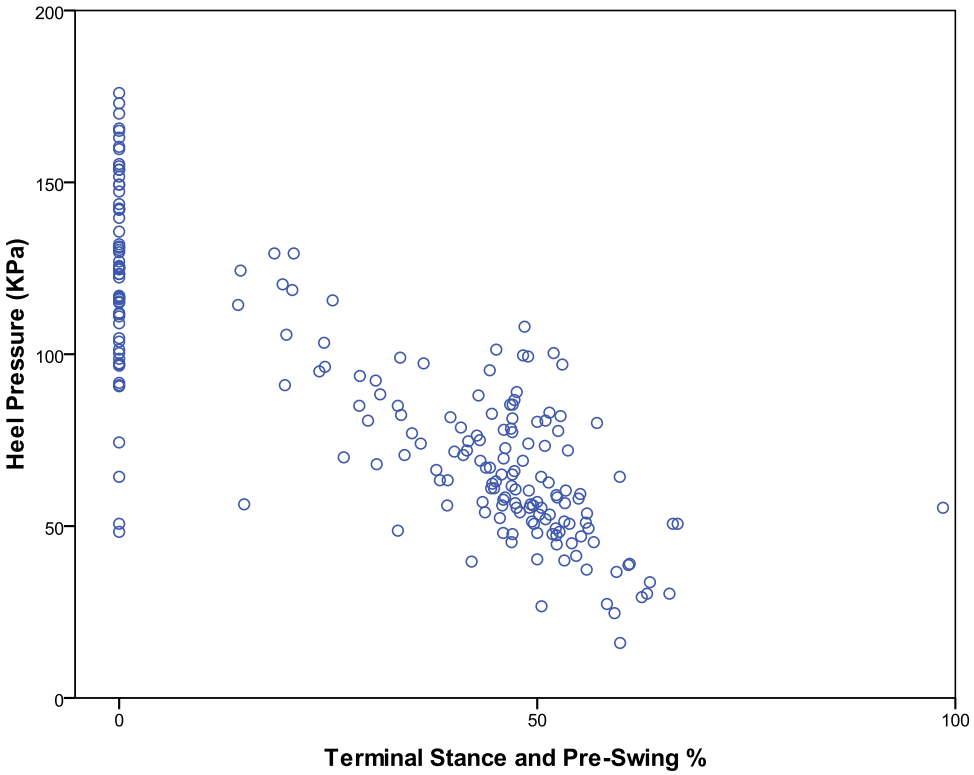


Figure 4.14: Scatter plot of heel pressure and terminal stance and pre-swing phase%

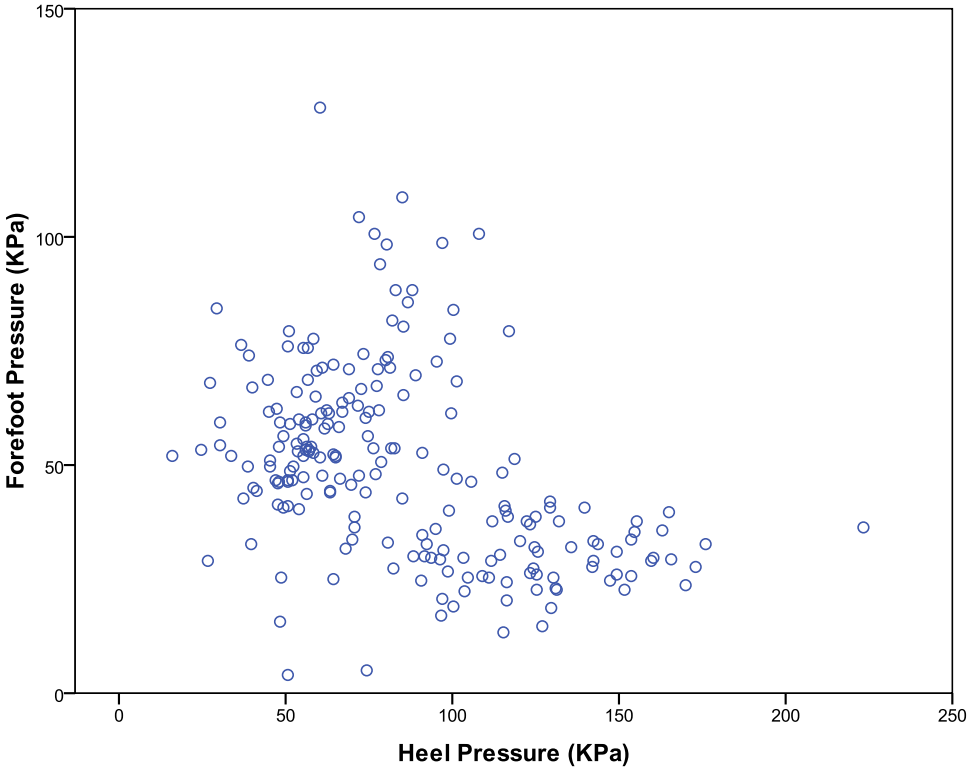


Figure 4.15: Scatter plot of heel pressure and forefoot pressure

4.3 Discussion

The primary objective of this study was to evaluate patient recruitment rates, follow up rates and variability within a proposed primary outcome measure. The secondary objective was to trial the clinical processes of changing one component of an established rehabilitation programme. These aspects of piloting are necessary for the appropriate development of future clinical studies.

With the outlined trial processes in place, patient recruitment was achieved at a rate of 2.5 per month and resulted in <10% loss to follow up. This was due in part to the CRF design which incorporated the collection of multiple contact points, including telephone number, email and postal address. Regarding collection of all other outlined data, including PROMs and SAEs, the CRF designs (Appendix H) enabled 100% collection of data from patients, illustrating their ease of use in practice. Only one patient refused to take part based on the need to complete the questionnaires.

Variability of PROM's data for the whole group within the disease specific ATRS score ranged from nine (at two weeks) to twenty three (at six months). If the ATRS were to be used as a primary outcome measure for an RCT the sample size would be based on a predefined minimally clinical important difference, SD, significance level and power at the primary outcome point between the intervention and control groups[115].

The SD at the primary outcome point (nine months in this study) was 15 points on the 100 point scale. The authors of the ATRS have suggested that a ten point difference is clinically relevant. Regarding the determination of sample size calculations the loss to follow up rate also needs to be considered. Loss to follow up in this patient group was <10%. There is also the consideration of the number of

treatment arms within the RCT design, the greater the number of comparative interventions, the greater the required sample size will be. Consequently the discussion regarding possible sample size requirements will be based on both the preliminary information collected as part of this study and the proposed design of future proposed research, based on the work to date. This will be outlined further within the conclusion section of this thesis (Chapter 8)

In addition to the PROMs data, on which sample sizes will be based, gait data was also collected as a secondary outcome. The collected gait parameters demonstrated increased heel pressures, decreased forefoot pressures and decreased amount of time spent in terminal stance and pre-swing phase as a proportion of the stance phase in relation to the uninjured limb, as seen within Chapter 3. These findings were present, not only within the AFO wearing phase of rehabilitation, but persisted through to a minimum of six months in all three groups. Although these patterns were demonstrated within healthy participants wearing the rocker bottom style AFO within Chapter 3, there is a further question to be addressed, regarding why these patterns persisted into the mid-term.

Costa *et al*[113] and Neumann *et al*[123] have demonstrated gait abnormalities in keeping with these results at two weeks, six months and one year following NWB rehabilitation. Further authors have evaluated gait parameters post rupture in the longer term between two and fourteen years, these studies have found no differences in comparison to the contralateral limb[105,116,122,130]. There are a number of possible mechanisms for these mid and long-term differences post AFO removal.

One possible explanation is the inability of the triceps surae to restrain forward rotation of the tibia on the talus during the stance phase of the gait cycle (eccentric

muscle action), resulting in increased knee flexion and consequently a longer heel contact time (decreased time spent in the terminal stance and pre-swing phase as a proportion of the total stance phase). This mechanism was proposed by Sutherland *et al,* who assessed gait parameters within healthy participants following a tibial nerve block to assess the role of plantarflexors[111]. A further explanation was put forward by Neumann *et al*[123] who proposed that in addition to muscle atrophy, muscle innervation patterns are equally important. Their research showed that compared to healthy controls, patients presenting one year post TA rupture had different innervation patterns. These changes were higher activity recordings during the landing and stance phase and lower activity recordings during the push-off phase, resulting in a time shift in innervation patterns, which remains at one year.

Due to the small sample size of five in each group this case series was not powered to detect any differences between the three groups, and unlike the healthy participant sample this was not a randomised sample and therefore does not account for confounding variables. Consequently it was not appropriate to perform any formal analysis to determine any differences between inserted heel raise conditions.

To summarise, these consecutive case series have provided data on recruitment rates, loss to follow up rates and outcome measure variability on which to base decisions for future research. Furthermore, secondary data on gait analysis has shown similar patterns in gait parameters to those observed within healthy participants wearing a rocker bottom AFO design. Further pilot research is required to evaluate using an alternative dorsum carbon fibre AFO in clinical practice and to explore the interaction between the AFO and heel wedge insert interaction, using appropriate methodology.

Bibliography

1. Dalley, A. and L. Moore. *Clinically Oriented Anatomy.* 4th ed. Maryland: Lippincott Williams and Wilkins, 1999

2. Evans, N.A. and W.D. Stanish, The basic science of tendon injuries. *Current Orthopaedics*, **14**, 2000, p.403-412.

3. Standring, S. *Gray's Anatomy.* 39th ed. London: Elseiver: Churchill Livingstone, 2005

4. Zantop, T., B. Tillmann and W. Petersen, Quantitative assessment of blood vessels of the human Achilles tendon: an immunohistochemical cadaver study. *Archives of Orthopaedic and Trauma Surgery*, **123**, 2003, p.501-504.

5. Fenwick, S.A., B.L. Hazleman and G.P. Riley, The vasculature and its role in the damaged and healing tendon. *Arthritis Research*, **4**, 2002, p.252-260.

6. Wang, J.H., M.I. Iosifidis and F.H. Fu, Biomechanical basis for tendinopathy. *Clinical Orthopaedics and Related Research*, **464**, 2006, p.320-332.

7. Maganaris, C.N., M.V. Narici and N. Maffulli, Biomechanics of the Achilles tendon. *Disability and Rehabilitation*, **30**, 2008, p.1542-1547.

8. Leppilahti, J., J. Puranen and S. Orava, Incidence of Achilles tendon rupture. *Acta Orthopadica Scandinavica*, **67**, 1996, p.277-279.

9. Khan, R.J., D. Fick, A. Keogh, J. Crawford, T. Brammar and M. Parker, Treatment of acute achilles tendon ruptures. A meta-analysis of randomized, controlled trials. *Journal of Bone and Joint Surgery (Am)*, **87**, 2005, p.2202-2210.

10. Maffulli, N., S.W. Waterston, J. Squair, J. Reaper and A.S. Douglas, Changing incidence of Achilles tendon rupture in Scotland: a 15-year study. *Clinical Journal of Sport Medicine*, **9**, 1999, p.157-160.

11. Maffulli, N., Rupture of the Achilles tendon. *Journal of Bone and Joint Surgery (Am)*, **81**, 1999, p.1019-1036.

12. Tallon, C., N. Maffulli and S.W. Ewen, Ruptured Achilles tendons are significantly more degenerated than tendinopathic tendons. *Medicine and Science in Sports and Exercise*, **33**, 2001, p.1983-1990.

13. Riley, G., Tendinopathy-from basic science to treatment. *Nature Clinical Practice Rheumatology*, **4**, 2008, p.82-89.

14. Newnham, D.M., J.G. Douglas, J.S. Legge and J.A. Friend, Achilles tendon rupture: an underrated complication of corticosteroid treatment. *Thorax*, **46**, 1991, p.853-854.

15. Royer, R.J., C. Pierfitte and P. Netter, Features of tendon disorders with fluoroquinolones. *Therapie*, **49**, 1994, p.75-76.

16. Clement, D.B., J.E. Taunton and G.W. Smart, Achilles tendinitis and peritendinitis: etiology and treatment. *American Journal of Sports Medicine*, **12**, 1984, p.179-84.

17. Maffulli, N. and D. Kader, Tendinopathy of tendo achillis. *Journal of Bone and Joint Surgery (Br)*, **84**, 2002, p.1-8.

18. AAOS, *The Diagnosis and Treatment of Acute Achilles Tendon Rupture: Guideline and Evidence Report [Online]. (http://www.aaos.org/research/guidelines/atrguideline.pdf)*. 2009.

19. Maffulli, N., The clinical diagnosis of subcutaneous tear of the Achilles tendon. A prospective study in 174 patients. *American Journal of Sports Medicine*, **26**, 1998, p.266-270.

20. Kotnis, R., S. David, R. Handley, K. Willett and S. Ostlere, Dynamic ultrasound as a selection tool for reducing achilles tendon reruptures. *American Journal of Sports Medicine*, **34**, 2006, p.1395-1400.

21. Sharma, P. and N. Maffulli, Tendon injury and tendinopathy: healing and repair. *Journal of Bone and Joint Surgery (Am)*, **87**, 2005, p.187-202.

22. Woo, S.L., K. Hildebrand, N. Watanabe, J.A. Fenwick, C.D. Papageorgiou and J.H. Wang, Tissue engineering of ligament and tendon healing. *Clinical Orthopaedics and Related Research*, **457**, 1999, p.S312-2S313.

23. Suchak, A.A., C. Spooner, D.C. Reid and N.M. Jomha, Postoperative rehabilitation protocols for Achilles tendon ruptures: a meta-analysis. *Clinical Orthopaedics and Related Research*, **464**, 2006, p.216-221.

24. Healy, B., R. Beasley and M. Weatherall, Venous thromboembolism following prolonged cast immobilisation for injury to the tendo Achillis. *Journal of Bone and Joint Surgery (Br)*, **92**, 2010, p.646-650.

25. Wills, C.A., S. Washburn, V. Caiozzo and C.A. Prietto, Achilles tendon rupture. A review of the literature comparing surgical versus nonsurgical treatment. *Clinical Orthopaedics and Related Research*, **453**, 1986, p.156-163.

26. Editorial, Achilles tendon rupture. *Lancet*, **1**, 1973, p.189-190.

27. Nistor, L., Surgical and non-surgical treatment of Achilles Tendon rupture. A prospective randomized study. *Journal of Bone and Joint Surgery (Am)*, **63**, 1981, p.394-399.

28. Cetti, R., S.E. Christensen, R. Ejsted, N.M. Jensen and U. Jorgensen, Operative versus nonoperative treatment of Achilles tendon rupture. A prospective randomized study and review of the literature. *American Journal of Sports Medicine*, **21**, 1993, p.791-799.

29. Thermann, H., O. Frerichs, A. Biewener, C. Krettek and P. Schandelmeier, Functional treatment of acute rupture of the Achilles tendon. An experimental biomechanical study. *Unfallchirurg*, **98**, 1995, p.507-513.

30. Majewski, M., M. Rickert and K. Steinbruck, Achilles tendon rupture. A prospective study assessing various treatment possibilities. *Orthopade*, **29**, 2000, p.670-676.

31. Moller, M., T. Movin, H. Granhed, K. Lind, E. Faxen and J. Karlsson, Acute rupture of tendon Achillis. A prospective randomised study of comparison between surgical and non-surgical treatment. *Journal of Bone and Joint Surgery (Br)*, **83**, 2001, p.843-848.

32. Willits, K., A. Amendola, D. Bryant, N.G. Mohtadi, J.R. Giffin, P. Fowler, C.O. Kean and A. Kirkley, Operative versus nonoperative treatment of acute Achilles tendon ruptures: a multicenter randomized trial using accelerated functional rehabilitation. *Journal of Bone and Joint Surgery (Am)*, **92**, 2010, p.2767-2775.

33. Saleh, M., P.D. Marshall, R. Senior and A. MacFarlane, The Sheffield splint for controlled early mobilisation after rupture of the calcaneal tendon. A prospective, randomised comparison with plaster treatment. *Journal of Bone and Joint Surgery (Br)*, **74**, 1992, p.206-209.

34. Cetti, R., L.O. Henriksen and K.S. Jacobsen, A new treatment of ruptured Achilles tendons. A prospective randomized study. *Clinical Orthopaedics and Related Research*, **452**, 1994, p.155-165.

35. Mortensen, H.M., O. Skov and P.E. Jensen, Early motion of the ankle after operative treatment of a rupture of the Achilles tendon. A prospective, randomized clinical and radiographic study. *Journal of Bone & Joint Surgery (Am)*, **81**, 1999, p.983-990.

36. Kangas, J., A. Pajala, P. Siira, M. Hamalainen and J. Leppilahti, Early functional treatment versus early immobilization in tension of the musculotendinous unit after Achilles rupture repair: a prospective, randomized, clinical study. *Journal of Trauma*, **54**, 2003, p.1171-1180.

37. Maffulli, N., C. Tallon, J. Wong, K.P. Lim and R. Bleakney, Early weightbearing and ankle mobilization after open repair of acute midsubstance tears of the achilles tendon. *American Journal of Sports Medicine*, **31**, 2003, p.692-700.

38. Bhandari, M., G.H. Guyatt, F. Siddiqui, F. Morrow, J. Busse, R.K. Leighton, S. Sprague and E.H. Schemitsch, Treatment of acute Achilles tendon ruptures: a systematic overview and meta-analysis. *Clinical Orthopaedics and Related Research*, **460**, 2002, p.190-200.

39. Khan, R.J., D. Fick, T.J. Brammar, J. Crawford and M.J. Parker, Interventions for treating acute Achilles tendon ruptures. *Cochrane Database of Systematic Reviews*, 2004, p.CD003674.

40. Costa, M.L., K. MacMillan, D. Halliday, R. Chester, L. Shepstone, A.H. Robinson and S.T. Donell, Randomised controlled trials of immediate weight-bearing mobilisation for rupture of the tendo Achillis. *Journal of Bone and Joint Surgery (Br)*, **88**, 2006, p.69-77.

41. Metz, R., E.-J.M.M. Verleisdonk, G.J.M.G. van der Heijden, G.-J. Clevers, E.R. Hammacher, M.H.J. Verhofstad and C. van der Werken, Acute Achilles tendon rupture: minimally invasive surgery versus nonoperative treatment with immediate full weightbearing--a randomized controlled trial. *American Journal of Sports Medicine*, **36**, 2008, p.1688-1694.

42. Schroeder, L., Steinbrueck, Treatment of acute achilles tendon ruptures: open vs. percutaneous repair vs. conservative treatment. *Orthopaedic Transactions*, **21**, 1997, p.1228.

43. Lim, J., R. Dalal and M. Waseem, Percutaneous vs. open repair of the ruptured Achilles tendon: a prospective randomized controlled study. *Foot and Ankle International*, **22**, 2001, p.559-568.

44. Gigante, A., A. Moschini, A. Verdenelli, M. Del Torto, S. Ulisse and L. de Palma, Open versus percutaneous repair in the treatment of acute Achilles tendon rupture: a randomized prospective study. *Knee Surgery, Sports Traumatology, Arthroscopy*, **16**, 2008, p.204-209.

45. Majewski, M., P.E. Ochsner, F. Liu, R. Fluckiger and C.H. Evans, Accelerated healing of the rat Achilles tendon in response to autologous conditioned serum. *American Journal of Sports Medicine*, **37**, 2009, p.2117-2125.

46. Bolt, P., A.N. Clerk, H.H. Luu, Q. Kang, J.L. Kummer, Z.L. Deng, K. Olson, F. Primus, A.G. Montag, T.C. He, R.C. Haydon, and B.C. Toolan, BMP-14 gene therapy increases tendon tensile strength in a rat model of Achilles tendon injury. *Journal of Bone and Joint Surgery (Am)*, **89**, 2007, p.1315-1320.

47. Chan, B.P., K.M. Chan, N. Maffulli, S. Webb and K.K. Lee, Effect of basic fibroblast growth factor. An in vitro study of tendon healing. *Clinical Orthopaedics and Related Research*, **455**, 1997, p.239-247.

48. Enwemeka, C.S., Functional loading augments the initial tensile strength and energy absorption capacity of regenerating rabbit Achilles tendons. *American Journal of Physical Medicine and Rehabilitation*, **71**, 1992, p.31-38.

49. Enwemeka, C.S., N.I. Spielholz and A.J. Nelson, The effect of early functional activities on experimentally tenotomized Achilles tendons in rats. *American Journal of Physical Medicine and Rehabilitation*, **67**, 1988, p.264-269.

50. Rantanen, J., T. Hurme and H. Kalimo, Calf muscle atrophy and Achilles tendon healing following experimental tendon division and surgery in rats. Comparison of postoperative immobilization of the muscle-tendon complex in relaxed and tensioned positions. *Scandinavian Journal of Medicine and Science in Sports*, **9**, 1999, p.57-61.

51. Palmes, D., H.U. Spiegel, T.O. Schneider, M. Langer, U. Stratmann, T. Budny and A. Probst, Achilles tendon healing: long-term biomechanical effects of postoperative mobilization and immobilization in a new mouse model. *Journal of Orthopaedic Research*, **20**, 2002, p.939-946.

52. Bring, D., C. Reno, P. Renstrom, P. Salo, D. Hart and P. Ackermann, Prolonged immobilization compromises up-regulation of repair genes after tendon rupture in a rat model. *Scandinavian Journal of Medicine and Science in Sports*, **19**, 2009, p.411-417.

53. Bring, D.K., C. Reno, P. Renstrom, P. Salo, D.A. Hart and P.W. Ackermann, Joint immobilization reduces the expression of sensory neuropeptide receptors and impairs healing after tendon rupture in a rat model. *Journal of Orthopaedic Research*, **27**, 2009, p.274-280.

54. Almekinders, L.C., A.J. Baynes and L.W. Bracey, An in vitro investigation into the effects of repetitive motion and nonsteroidal antiinflammatory medication on human tendon fibroblasts. *American Journal of Sports Medicine*, **23**, 1995, p.119-123.

55. Gartland, J.J., Orthopaedic clinical research. Deficiencies in experimental design and determinations of outcome. *Journal of Bone and Joint Surgery (Am)*, **70**, 1988, p.1357-1364.

56. DH, *Guidance on the routine collection of patient reported outcome measures (PROMs)*. 2008, COI.

57. Johanson, N.A., M.H. Liang, L. Daltroy, S. Rudicel and J. Richmond, American Academy of Orthopaedic Surgeons lower limb outcomes assessment instruments. Reliability, validity, and sensitivity to change. *Journal of Bone and Joint Surgery (Am)*, **86-A**, 2004, p.902-909.

58. SooHoo, N.F., M. Shuler and L.L. Fleming, Evaluation of the validity of the AOFAS Clinical Rating Systems by correlation to the SF-36. *Foot and Ankle International*, **24**, 2003, p.50-55.

59. Kaikkonen, A., P. Kannus and M. Jarvinen, A performance test protocol and scoring scale for the evaluation of ankle injuries. *American Journal of Sports Medicine*, **22**, 1994, p.462-469.

60. Roos, E.M., S. Brandsson and J. Karlsson, Validation of the foot and ankle outcome score for ankle ligament reconstruction. *Foot and Ankle International*, **22**, 2001, p.788-794.

61. Nilsson-Helander, K., R. Thomee, K. Gravare-Silbernagel, P. Thomee, E. Faxen, B.I. Eriksson and J. Karlsson, The Achilles tendon Total Rupture Score (ATRS): development and validation. *American Journal of Sports Medicine*, **35**, 2007, p.421-426.

62. Leppilahti, J., K. Forsman, J. Puranen and S. Orava, Outcome and prognostic factors of achilles rupture repair using a new scoring method. *Clinical Orthopaedics and Related Research*, **456**, 1998, p.152-161.

63. Blackwood, B., Methodological issues in evaluating complex healthcare interventions. *Journal of advanced nursing*, **54**, 2006, p.612-622.

64. MRC, *Developing and evaluating complex interventions: New guidance [Online].*

(http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004871). 2006.

65. Leppilahti, J. and S. Orava, Total Achilles tendon rupture. A review. *Sports Medicine*, **25**, 1998, p.79-100.

66. Kearney, R.S., J. Achten, N.R. Parsons and M.L. Costa, The comprehensive cohort model in a pilot trial in orthopaedic trauma. *BMC Medical Research Methodology*, **11**, 2011, p.39.

67. McCulloch, P., D.G. Altman, W.B. Campbell, D.R. Flum, P. Glasziou, J.C. Marshall, J. Nicholl, J.K. Aronson, J.S. Barkun, J.M. Blazeby, I.C. Boutron, P.A. Clavien, J.A. Cook, P.L. Ergina, L.S. Feldman, G.J. Maddern, B.C. Reeves, C.M. Seiler, S.M. Strasberg, J.L. Meakins, D. Ashby, N. Black, J. Bunker, M. Burton, M. Campbell, K. Chalkidou, I. Chalmers, M. de Leval, J. Deeks, A. Grant, M. Gray, R. Greenhalgh, M. Jenicek, S. Kehoe, R. Lilford, P. Littlejohns, Y. Loke, R. Madhock, K. McPherson, J. Meakins, P. Rothwell, B. Summerskill, D. Taggart, P. Tekkis, M. Thompson, T. Treasure, U. Trohler, and J. Vandenbroucke, No surgical innovation without evaluation: the IDEAL recommendations. *Lancet*, **374**, 2009, p.1105-1112.

68. Groves, T., Research methods and reporting. *British Medical Journal*, **337**, 2008, p.979-980.

69. Lansdaal, J.R., J.C. Goslings, M. Reichart, G.A. Govaert, K.M. van Scherpenzeel, R. Haverlag and K.J. Ponsen, The results of 163 Achilles tendon ruptures treated by a minimally invasive surgical technique and functional aftertreatment. *Injury*, **38**, 2007, p.839-844.

70. Boutron, I., D. Moher, D.G. Altman, K.F. Schulz and P. Ravaud, Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of Internal Medicine*, **148**, 2008, p.295-309.

71. Boutron, I., D. Moher, D.G. Altman, K.F. Schulz and P. Ravaud, Methods and processes of the CONSORT Group: example of an extension for trials assessing nonpharmacologic treatments. *Annals of Internal Medicine*, **148**, 2008, p.W60-66.

72. Speck, M. and K. Klaue, Early full weightbearing and functional treatment after surgical repair of acute achilles tendon rupture. *American Journal of Sports Medicine*, **26**, 1998, p.789-793.

73. Costa, M.L., L. Shepstone, C. Darrah, T. Marshall and S.T. Donell, Immediate full-weight-bearing mobilisation for repaired Achilles tendon ruptures: a pilot study. *Injury*, **34**, 2003, p.874-876.

74. Hufner, T.M., D.B. Brandes, H. Thermann, M. Richter, K. Knobloch and C. Krettek, Long-term results after functional nonoperative treatment of achilles tendon rupture. *Foot and Ankle International*, **27**, 2006, p.167-171.

75. Jacob, K.M. and R. Paterson, Surgical repair followed by functional rehabilitation for acute and chronic achilles tendon injuries: excellent

functional results, patient satisfaction and no reruptures. *ANZ Journal of Surgery*, **77**, 2007, p.287-291.

76. Majewski, M., S. Schaeren, U. Kohlhaas and P.E. Ochsner, Postoperative rehabilitation after percutaneous Achilles tendon repair: early functional therapy versus cast immobilization. *Disability and Rehabilitation*, **30**, 2008, p.1726-1732.

77. Bhattacharyya, M. and B. Gerber, Mini-invasive surgical repair of the Achilles tendon: does it reduce post-operative morbidity? *International Orthopaedics*, **33**, 2009, p.151-156.

78. Doral, M.N., M. Bozkurt, E. Turhan, M. Ayvaz, O.A. Atay, A. Uzumcugil, G. Leblebicioglu, D. Kaya and T. Aydog, Percutaneous suturing of the ruptured Achilles tendon with endoscopic control. *Archives of Orthopaedic Trauma Surgery*, **129**, 2009, p.1093-1101.

79. Gelberman, R.H., P.R. Manske, J.S. Vande Berg, P.A. Lesker and W.H. Akeson, Flexor tendon repair in vitro: a comparative histologic study of the rabbit, chicken, dog, and monkey. *Journal of Orthopaedic Research*, **2**, 1984, p.39-48.

80. Lehto, M., V.C. Duance and D. Restall, Collagen and fibronectin in a healing skeletal muscle injury. An immunohistological study of the effects of physical activity on the repair of injured gastrocnemius muscle in the rat. *Journal of Bone and Joint Surgery (Br)*, **67**, 1985, p.820-828.

81. Kjaer, M., Role of extracellular matrix in adaptation of tendon and skeletal muscle to mechanical loading. *Physiological Reviews*, **84**, 2004, p.649-698.

82. Kjaer, M., H. Langberg, B.F. Miller, R. Boushel, R. Crameri, S. Koskinen, K. Heinemeier, J.L. Olesen, S. Dossing, M. Hansen, S.G. Pedersen, M.J. Rennie, and P. Magnusson, Metabolic activity and collagen turnover in human tendon in response to physical activity. *Journal of Musculoskeletal and Neuronal Interactions*, **5**, 2005, p.41-52.

83. Akizuki, K.H., E.J. Gartman, B. Nisonson, S. Ben-Avi and M.P. McHugh, The relative stress on the Achilles tendon during ambulation in an ankle immobiliser: implications for rehabilitation after Achilles tendon repair. *British Journal of Sports Medicine*, **35**, 2001, p.329-333.

84. Booth, F.W., Effect of limb immobilization on skeletal muscle. *Journal of Applied Physiology*, **52**, 1982, p.1113-1118.

85. Lin, T.W., L. Cardenas and L.J. Soslowsky, Biomechanics of tendon injury and repair. *Journal of Biomechanics*, **37**, 2004, p.865-877.

86. Cavanagh, P., F. Hewitt and J. Perry, In-shoe plantar pressure measurement: a review. *The Foot*, **2**, 1992, p.185-194.

87. Harrison, A.J. and J.P. Folland, Investigation of gait protocols for plantar pressure measurement of non-pathological subjects using a dynamic pedobarograph. *Gait & Posture*, **6**, 1997, p.50-55.

88. Luo, Z.P., L.J. Berglund and K.N. An, Validation of F-Scan pressure sensor system: A technical note. *Journal of Rehabilitation Research and Development*, **35**, 1998, p.186-191.

89. Ahroni, J.H., E.J. Boyko and R. Forsberg, Reliability of F-Scan in-shoe measurements of plantar pressure. *Foot & Ankle International*, **19**, 1998, p.668-673.

90. Mueller, M.J. and M.J. Strube, Generalizability of in-shoe peak pressure measures using the F-scan system. *Clinical Biomechanics*, **11**, 1996, p.159-164.

91. Orlin, M.N. and T.G. McPoil, Plantar pressure assessment. *Physical Therapy*, **80**, 2000, p.399-409.

92. Woodburn, J. and P.S. Helliwell, Observations on the F-Scan in-shoe pressure measuring system. *Clinical Biomechanics*, **11**, 1996, p.301-304.

93. Barnett, S., International protocol guidelines for plantar pressure measurement. *The Diabetic Foot*, **1**, 1998, p.137-140.

94. Zhu, H.S., J.J. Wertsch, G.F. Harris and H.M. Alba, Walking cadence effect on plantar pressures. *Archives of Physical Medicine and Rehabilitation*, **76**, 1995, p.1000-1005.

95. Hanlon, M. and R. Anderson, Prediction methods to account for the effect of gait speed on lower limb angular kinematics. *Gait Posture*, **24**, 2006, p.280-287.

96. Moe-Nilssen, R. and J.L. Helbostad, Estimation of gait cycle characteristics by trunk accelerometry. *Journal of Biomechics*, **37**, 2004, p.121-126.

97. Chiu, M.C. and M.J. Wang, The effect of gait speed and gender on perceived exertion, muscle activity, joint motion of lower extremity, ground reaction force and heart rate during normal walking. *Gait Posture*, **25**, 2007, p.385-392.

98. Shiavi, R. and P. Griffin, Changes in electromyographic gait patterns of calf muscles with walking speed. *IEEE Transactions on Biomedical Engineering*, **30**, 1983, p.73-76.

99. Kirtley, C., M.W. Whittle and R.J. Jefferson, Influence of walking speed on gait parameters. *Journal of Biomedical Engineering*, **7**, 1985, p.282-288.

100. Mockel, G., C. Perka, K. Labs and G. Duda, The influence of walking speed on kinetic and kinematic parameters in patients with osteoarthritis of the hip using a force-instrumented treadmill and standardised gait speeds. *Archives of Orthopaedic and Trauma Surgery*, **123**, 2003, p.278-282.

101. Voloshin, A., The influence of walking speed on dynamic loading on the human musculoskeletal system. *Medicine and Science in Sports Exercise*, **32**, 2000, p.1156-1159.

102. Zeni, J.A., Jr. and J.S. Higginson, Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: a result of altered walking speed? *Clinical Biomechanics* **24**, 2009, p.372-378.

103. Whittle, M. *Gait Analysis and Introduction.*3rd ed. Great Britain: Reed Educational and Professional Publishing, 2002

104. Froberg, A., P. Komi, M. Ishikawa, T. Movin and A. Arndt, Force in the achilles tendon during walking with ankle foot orthosis. *American Journal of Sports Medicine*, **37**, 2009, p.1200-1207.

105. Saw, Y., V. Baltzopoulos, A. Lim, P.K. Rostron, B.G. Bolton-Maggs and R.F. Calver, Early mobilization after operative repair of ruptured Achilles tendon. *Injury*, **24**, 1993, p.479-484.

106. Costa, M.L., K. Logan, D. Heylings, S.T. Donell and K. Tucker, The effect of achilles tendon lengthening on ankle dorsiflexion: a cadaver study. *Foot and Ankle International*, **27**, 2006, p.414-417.

107. Hockings, M. and C. Nester, Use of dorsal ankle orthoses in the management of Achilles tendon rupture. *The Foot*, **10**, 2000, p.51-54.

108. Baily, R. *Design of Comparative Experiments.*1st ed. Cambridge: Cambridge University Press, 2008

109. Krishnan, C. and G.N. Williams, Evoked tetanic torque and activation level explain strength differences by side. *European Journal of Applied Physiology*, **106**, 2009, p.769-774.

110. Bressel, E. and P.J. McNair, Biomechanical behavior of the plantar flexor muscle-tendon unit after an Achilles tendon rupture. *American Journal of Sports Medicine*, **29**, 2001, p.321-326.

111. Sutherland, D.H., L. Cooper and D. Daniel, The role of the ankle plantar flexors in normal walking. *Journal of Bone and Joint Surgery (Am)*, **62**, 1980, p.354-363.

112. Bland, M. *Medical Statistics.*3rd ed. Great Britain: Oxford University Press, 2000

113. Costa, M.L., D. Kay and S.T. Donell, Gait abnormalities following rupture of the tendo Achillis: a pedobarographic assessment. *Journal of Bone and Joint Surgery (Br)*, **87**, 2005, p.1085-1088.

114. Trew, M. and T. Everett. *Human Movement An Introductory Text.*4th ed. China: Harcourt Publishers Limited, 2001

115. Cohen, J. *Statistical power analysis for the behaviour sciences.*Hillsdale: Routledge Academic, 1988

116. McComis, G.P., D.A. Nawoczenski and K.E. DeHaven, Functional bracing for rupture of the Achilles tendon. Clinical results and analysis of ground-

reaction forces and temporal data. *Journal of Bone and Joint Surgery (Am)*, **79**, 1997, p.1799-1808.

117. Orendurff, M.S., A.D. Segal, M.D. Aiona and R.D. Dorociak, Triceps surae force, length and velocity during walking. *Gait and Posture*, **21**, 2005, p.157-163.

118. Lee, D.K., Achilles tendon repair with acellular tissue graft augmentation in neglected ruptures. *Journal of Foot and Ankle Surgery*, **46**, 2007, p.451-455.

119. Hahn, F., C. Maiwald, T. Horstmann and P. Vienne, Changes in plantar pressure distribution after Achilles tendon augmentation with flexor hallucis longus transfer. *Clinical Biomechanics*, **23**, 2008, p.109-116.

120. Maffulli, N., H.D. Moller and C.H. Evans, Tendon healing: can it be optimised? *British Journal of Sports Medicine*, **36**, 2002, p.315-316.

121. Thermann, H., O. Frerichs, A. Biewener and C. Krettek, Healing of the Achilles tendon: an experimental study. *Foot and Ankle International*, **22**, 2001, p.478-483.

122. Don, R., A. Ranavolo, A. Cacchio, M. Serrao, F. Costabile, M. Iachelli, F. Camerota, M. Frascarelli and V. Santilli, Relationship between recovery of calf-muscle biomechanical properties and gait pattern following surgery for achilles tendon rupture. *Clinical Biomechanics*, **22**, 2007, p.211-220.

123. Neumann, D., L. Vogt, W. Banzer and U. Schreiber, Kinematic and neuromuscular changes of the gait pattern after Achilles tendon rupture. *Foot and Ankle International*, **18**, 1997, p.339-341.

124. Rangan, A. and N. Maffulli, Multicentre randomised clinical trials in trauma care. *The Journal of Bone and Joint Surgery (Br)*, **93**, 2011, p.720-721.

125. Jennings, A.G. and G.K. Sefton, Chronic rupture of tendo Achillis. Long-term results of operative management using polyester tape. *Journal of Bone & Joint Surgery (Br)*, **84**, 2002, p.361-363.

126. Thompson, T.C. and J.H. Doherty, Spontaneous rupture of tendon of Achilles: a new clinical diagnostic test. *Journal of Trauma*, **2**, 1962, p.126-129.

127. Salen, B.A., E.V. Spangfort, A.L. Nygren and R. Nordemar, The Disability Rating Index: an instrument for the assessment of disability in clinical settings. *Journal of Clinical Epidemiology*, **47**, 1994, p.1423-1435.

128. Brooks, R., EuroQol: the current state of play. *Health Policy*, **37**, 1996, p.53-72.

129. Myerson, M.S., Achilles tendon ruptures. *Instructional Course Lectures*, **48**, 1999, p.219-230.

130. Boyden, E.M., H.B. Kitaoka, T.D. Cahalan and K.N. An, Late versus early repair of Achilles tendon rupture. Clinical and biomechanical evaluation. *Clinical Orthopaedics and Related Research*, **453**, 1995, p.150-158.

131. Fitzpatrick, R., C. Davey, M.J. Buxton and D.R. Jones, Evaluating patient-based outcome measures for use in clinical trials. *Health Technology Assessment*, **2**, 1998, p.i-iv, 1-74.

132. Garratt, A., Patient reported outcome measures in trials. *British Medical Journal*, **338**, 2009, p.a2597.

133. Terwee, C.B., S.D. Bot, M.R. de Boer, D.A. van der Windt, D.L. Knol, J. Dekker, L.M. Bouter and H.C. de Vet, Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of Clinical Epidemiology*, **60**, 2007, p.34-42.

134. Naal, F.D., F.M. Impellizzeri and P.F. Rippstein, Which are the most frequently used outcome instruments in studies on total ankle arthroplasty? *Clinical Orthopaedics and Related Research*, **468**, 2010, p.815-826.

135. Malviya, A., N. Makwana and P. Laing, Correlation of the AOFAS scores with a generic health QUALY score in foot and ankle surgery. *Foot and Ankle International*, **28**, 2007, p.494-498.

136. Bland, J.M. and D.G. Altman, Cronbach's alpha. *British Medical Journal*, **314**, 1997, p.572.

137. Barr, S., N. Bellamy, W.W. Buchanan, A. Chalmers, P.M. Ford, W.F. Kean, G.R. Kraag, E. Gerecz-Simon and J. Campbell, A comparative study of signal versus aggregate methods of outcome measurement based on the WOMAC Osteoarthritis Index. Western Ontario and McMaster Universities Osteoarthritis Index. *Journal of Rheumatology*, **21**, 1994, p.2106-2112.

138. Kessler, R.C. and D.K. Mroczek, Measuring the effects of medical interventions. *Medical Care*, **33**, 1995, p.AS109-119.

139. Donovan, J.L., S.J. Frankel and J.D. Eyles, Assessing the need for health status measures. *Journal of Epidemiology and Community Health*, **47**, 1993, p.158-162.

140. Mokkink, L.B., C.B. Terwee, D.L. Knol, P.W. Stratford, J. Alonso, D.L. Patrick, L.M. Bouter and H.C. de Vet, The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: a clarification of its content. *BMC Medical Reseasech Methodology*, **10**, 2010, p.22-30.

141. Vavken, P., Rationale for and Methods of Superiority, Noninferiority, or Equivalence Designs in Orthopaedic, Controlled Trials. *Clinical Orthopaedics and Related Research*, **457**, 1999, p.1773-1776.

142. Byrne, M., M.E. Cupples, S.M. Smith, C. Leathem, M. Corrigan, M.C. Byrne and A.W. Murphy, Development of a complex intervention for secondary prevention of coronary heart disease in primary care using the UK Medical Research Council framework. *American Journal of Managed Care*, **12**, 2006, p.261-266.

143. Paul, G., S.M. Smith, D. Whitford, F. O'Kelly and T. O'Dowd, Development of a complex intervention to test the effectiveness of peer support in type 2 diabetes. *BMC Health Services Research*, **7**, 2007, p.136-146.

144. Bird, L., A. Arthur and K. Cox, "Did the trial kill the intervention?" experiences from the development, implementation and evaluation of a complex intervention. *BMC Medical Research Methodology*, **11**, 2011, p.24 - 31.

145. MacPherson, H. and S. Schroer, Acupuncture as a complex intervention for depression: a consensus method to develop a standardised treatment protocol for a randomised controlled trial. *Complementry Therapies in Medicine*, **15**, 2007, p.92-100.

146. Montgomery, A.A., T.J. Peters and P. Little, Design, analysis and presentation of factorial randomised controlled trials. *BMC Medical Research Methodology*, **3**, 2003, p.26-31.

147. McAlister, F.A., S.E. Straus, D.L. Sackett and D.G. Altman, Analysis and reporting of factorial trials: a systematic review. *Journal of the American Medical Association*, **289**, 2003, p.2545-2553.

148. Green, S., P.Y. Liu and J. O'Sullivan, Factorial design considerations. *Journal of Clinical Oncology*, **20**, 2002, p.3424-3430.

149. Creswell J and Plano-Clark V *Designing and conducting mixed methods research.*CA: Sage Thousand oaks, 2007.

An Investigation into Accelerated Rehabilitation Strategies Following an Achilles Tendon Rupture

By

Rebecca Samantha Kearney

Volume Two of Two

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Medical Sciences

University of Warwick, Faculty of Medicine

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Abbreviations

AAOS	American Association of Orthopaedic Surgery
AFO	Ankle Foot Orthoses
AMED	The Allied and Complementary Medicine Database
ATRS	Achilles tendon Total Rupture Score
B1	Rigid rocker bottom ankle foot orthoses
B2	Ankle foot orthoses ‘dynamic’
B3	Ankle foot orthoses ‘ToeOff’
CE	Clause Eiermann
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CONSORT	Consolidated Standards of Reporting Trials
CP	Caroline Plant
CRF	Clinical Reporting Forms
DF	Dorsiflexion
DMC	Data Monitoring Committee
DRI	Disability Rating Index
EMBASE	The Excerpta Medica database
FU	Follow Up
GCP	Good Clinical Practice
HTA	Health Technology Assessment
IDEAL	Idea, Development, Evaluation, Assessment and Long term study
ISRCTN	International Standard Randomised Controlled Trial Number
IWB	Immediate Weight Bearing
KM	Katie McGuinness
KPa	Kilopascal
L	Left
MEDLINE	Database on biomedicine as they relate to health care
MRC	Medical Research Council
NWB	Non Weight Bearing
PFO	Pedro Foguet
PF	Plantarflexion
PROM	Patient Reported Outcome Measure

Abbreviations

R	Right
RCT	Randomised Controlled Trial
R&D	Research and Development
RK	Rebecca Kearney
ROM	Range of Movement
SAE	Serious Adverse Event
SD	Standard Deviation
TA	Tendo Achilles
TSC	Trial Steering Committee
VAS	Visual Analogue Scale
WB	Weight Bearing
W0	No heel inserts
W1	One heel insert
W2	Two heel inserts
W3	Three heel inserts

Declarations

The randomisation sequence was completed by Nicholas Parsons (Statistician).

Sponsorship

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Funding Body

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Abstract

Background
Systematically developing complex interventions, combined with appropriate theory and evidence are the guiding principles within the Medical Research Council's complex intervention framework. These principles form the foundations of the previous chapters within this thesis. The next steps require further piloting of the orthoses/heel wedge interactions to inform the development of future clinical studies.

Objectives
To measure patient reported outcomes between the interaction of three different orthoses and heel wedge insert combinations.

To trial the clinical processes of using the different orthoses/heel wedge combinations; measure the level of patient acceptance of randomisation to these interventions, and measure pre-defined gait parameters.

Methods
Following an acute Achilles tendon rupture, fifteen patients were randomly allocated to receive three, two or one heel wedge insert within an alternative carbon fibre orthoses. Post randomisation, all patients were reviewed every two weeks for twelve weeks and at six and nine months. At these time points the Disability Rating Index, Achilles tendon Total Rupture Score and EQ-5D questionnaires were collected, alongside in-shoe gait analysis and clinical complications.

Results
Twenty-six patients were screened to take part in this trial, of which fifteen were eligible and consented to take part. Six were male and nine were female, ages ranged from 30 to 75 years. All patients who were approached to take part in the study consented to be randomised; one patient declined the intervention post randomisation. The one heel raise group consistently achieved higher scores on collected PROMs than the two and three heel raise group.

Conclusions
This pilot study has provided invaluable information on the potential interaction of heel wedge insert/AFO interaction on PROMs data. This pilot study has also highlighted that the intervention is feasible in clinical practice. However, issues surrounding acceptability and attitudes to changing rehabilitation practice require further research from a qualitative perspective.

5.1 Protocol

Chapter 2 highlighted that although IWB is a widely documented rehabilitation protocol following a rupture of the TA, the individual components which constitute this treatment modality vary within the literature. The key variations identified were the design of the AFO, the degree of permitted movement and the amount of time for which the AFO is worn.

Chapter 3 evaluated the effect of two of these variables on gait parameters within healthy participants. The first variable evaluated was the effect of AFO design and the second was the effect of inserted heel wedge number within the AFOs. The research found statistically significant differences within both variables. However it was beyond the scope of that research to conclude if the gait analysis findings would translate into patient benefit within a clinical setting. Secondly, the results could not determine if the differences found between the identified variables would lead to subsequent improved PROMs, or to what extent these differences would be.

Chapter 4 was the first step towards addressing the limitations of Chapter 3. Within this chapter the common obstacles associated with clinical trials were discussed, and the subsequent need to evaluate parameters such as patient recruitment rates, follow-up rates and variability within the proposed primary outcome measures to develop future clinical trials. The results of Chapter 4 illustrated a recruitment rate of 2.5 patients per month with a <10% loss to follow up rate, using the outlined trial processes. The SD of the proposed primary outcome measure (ATRS) was found to range from nine to twenty three points, on the 100 point scale, across a nine month time period.

However, in line with the MRC recommendations, a further stage of piloting is necessary, prior to planning definitive clinical trials in this complex clinical area. The aims of further piloting work would be to evaluate the interaction of the AFO and heel wedge insert number through an appropriate interventional study design.

5.1.1 Objectives

The primary objective was to measure patient reported outcomes between the interaction of three different AFO and heel wedge insert combinations.

The secondary objectives were to trial the clinical processes of using these AFO/heel wedge combinations; measure the level of patient acceptance of randomisation to these interventions, and measure pre-defined gait parameters.

5.1.2 Trial summary and trial flow diagram

Following ethical committee approval all patients who presented with an acute rupture of their TA to the University Hospitals Coventry and Warwickshire NHS Trust fracture clinic were potentially eligible to take part in this trial. The only eligibility criteria were that they had no other serious injuries to either lower limb or a previous history of tendon rupture. These broad eligibility criteria were used to ensure that the results of the study could be readily generalised to the wider population.

All patients, whether treated operatively or non-operatively were placed in a carbon fibre AFO (Toe OFF, Gilbert and Mellish) for eight weeks. All included patients were then randomly allocated to receive either three, two or one inserted heel wedge to wear inside the AFO. Five patients were randomly allocated to each group.

Every two weeks, for twelve weeks, then at six and nine months, all participants returned to fracture clinic for routine clinical assessment. At these time points in-shoe pressure sensors were used to collect gait parameters (using the same methods outlined in Chapter 3). In addition to these outcome measures, at baseline, two weeks, six weeks, three months, six months and nine months, three patient reported outcome scores were collected alongside complications (Figure 5.1).

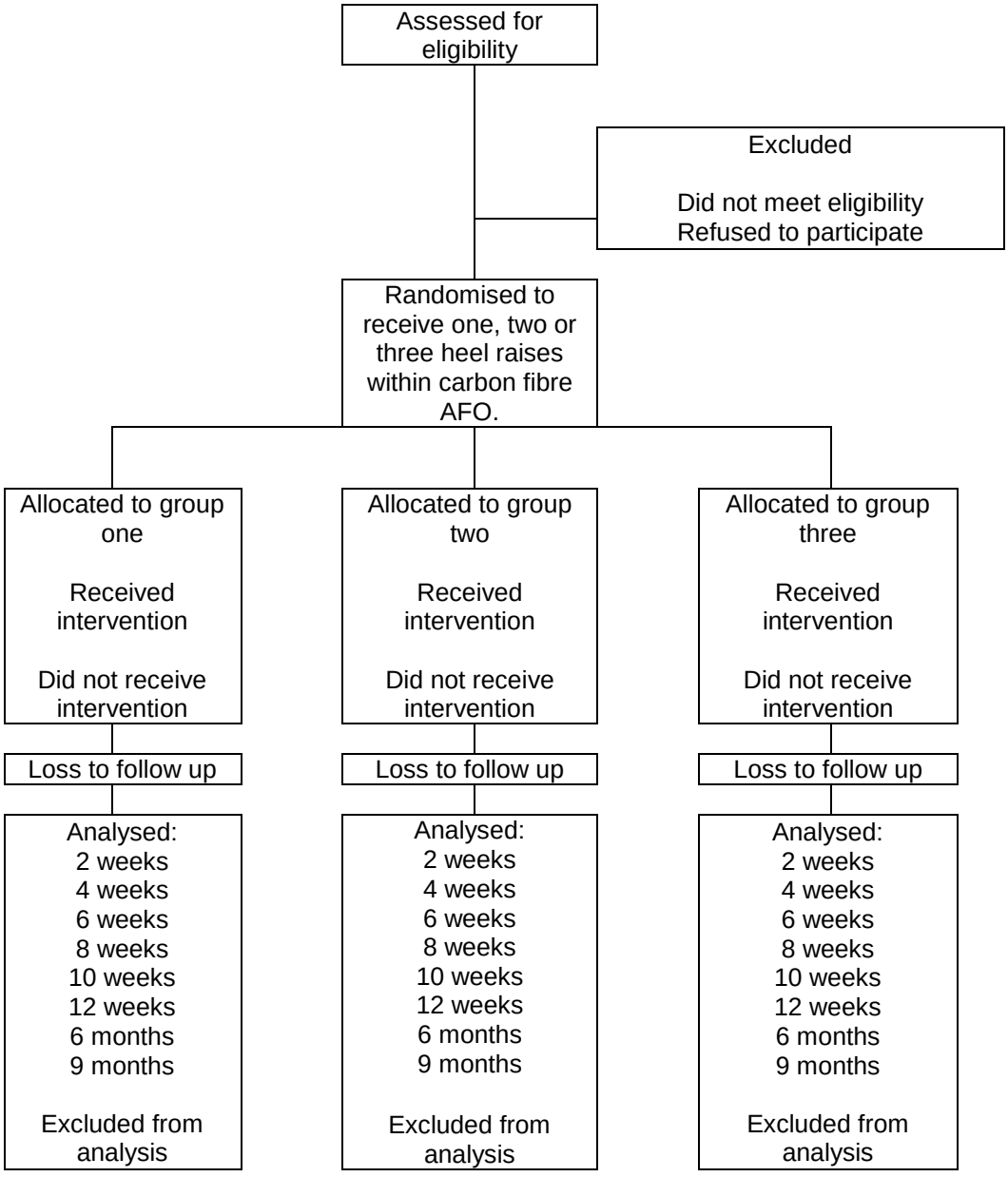


Figure 5.1: Expected flow of participants

5.1.3 Eligibility, recruitment, allocation and consent

This study had ethical approval from the Coventry research ethics committee. All patients over 18 years presenting at the University Hospitals Coventry and Warwickshire NHS Trust fracture clinic, with a primary acute rupture of their TA (less than ten days) were eligible to take part.

Patients presenting after ten days from injury or with a history of previous tendon rupture were excluded because these are a separate population, with different management requirements. These differences in management are secondary to the quality of the tendon tissue and retraction of the tendon ends[125]. Patients who had other serious injuries to either lower limb that would alter the intervention and subsequent rehabilitation were also excluded[116]. This was in addition to patients who were unable to give informed consent or adhere to trial procedures, with explicit reasons documented and reported.

If a patient taking part in the study sustained a contralateral rupture during the trial period, the second rupture would not be included in the study because the result of this intervention would not be independent from the first intervention.

Ethical approval was obtained by Coventry Research Ethics Committee prior to the start of this study. Recruitment of participants took place within the fracture clinic setting at University Hospitals Coventry and Warwickshire NHS Trust. This was achieved by the researcher checking the new patient fracture clinic list daily. On identifying potentially eligible patients, they were then approached in clinic to determine eligibility. If eligible, patients were then provided with a patient information sheet and provided with the opportunity to ask questions with family, friends, consultant or research team. If willing, patients were then asked to sign a consent

form prior to any trial procedures. *Each participant was provided with time in the clinic to read the consent information and was informed that they could make the decision the following day after taking time to discuss with family or friends as they required*

A TA rupture was diagnosed by the researcher in the first instance and then verified by the principal investigator by subjective history and physical examination, confirming a palpable gap and a positive Thompson test[41,126].

Once clinical diagnosis and eligibility had been confirmed the patient was then presented with a patient information sheet by the researcher. This was the same as that outlined in Appendix C with the additional sentence inserted under the heading 'research practice'. This additional sentence required a notice of substantial amendment to the ethics committee, which was approved 3rd August 2010. The additional sentence was as follows:

'*Within the orthotic differing numbers of heel wedges are normally inserted, but at present we do not know what the optimum number is. If you take part in the trial the number of inserted heel wedges inside the orthotic will be randomly allocated to you'*

In addition to the written patient information sheet, a lay summary was also verbally provided to patients. The patients were given the opportunity to discuss any issues with the research team, their consultant as well as members of their family and friends. Additionally a list of information to be covered before consent was obtained was checked to ensure that all essential information had been provided to the potential participant. Any eligible and unwilling participants were recorded at this point.

After allowing sufficient time for the patient to consider their decision and ask questions about the trial, eligible and willing participants signed a consent form. This form was approved by the Coventry ethics committee, and reflected the new version number of the amended patient information sheet being used. Once eligible patients had consented to take part in the study they attended routine clinical follow up every two weeks for twelve weeks and finally at six and nine months.

Any new information during the trial that may have affected a participant's willingness to take part was reviewed by the research team. As necessary, this information was communicated to all research participants, and a revised consent form then completed. Participants were also advised that they may withdraw from the trial treatment, and/or whole trial at any time without prejudice. If participants withdrew from the trial treatment, they were followed up wherever possible and data collected as per protocol until the end of the trial. The only exception to this was when the participant also explicitly withdrew consent for follow up.

To ensure minimal loss to follow up, contact addresses, telephone numbers and email addresses were collected by the researcher. In the event of a patient not attending clinic, a system of reminders was instituted. The system included an initial phone call to reschedule the appointment. If contact was not possible by telephone, after one week, an email was sent along with a letter outlining the rescheduled appointment. If there was no contact within two weeks, a further phone call was made to an alternative point of contact given by the participant at their initial consent. If no contact was made with the alternative contact, a letter was sent to them. If there was no response from the participant or their alternative point of contact within these time frames they were recorded as lost to follow up.

Patients were then placed in a carbon fibre AFO; the allocation of inserted heel wedges was randomised. The randomisation sequence was generated on a 1:1:1 basis by an independent trial statistician. The randomisation sequence was allocated via telephone following consent of each individual participant and administered by the researcher. This randomised trial design was chosen to account for all known and unknown confounding factors. It was not possible to blind the participant to the trial intervention.

Based on previous research using this population, the baseline demographics were expected to be similar across the three groups but were recorded at baseline to assess this.

5.1.4 Sample size and intervention

A formal sample size calculation was not carried out because this was a pilot study, and therefore not appropriate at this stage. As there are no methods for determining sample sizes for pilot studies, a sample size of five for each group was chosen based on discussions with experts in the field. Our previous experience was that two patients can be recruited per month. Therefore fifteen patients would require eight months to recruit. With the above mechanisms in place for preventing loss to follow up, it was expected that there would be <10% loss to follow up. Indeed within chapter 4 there was only one patient lost to follow up, of the fifteen included participants (7%).

Once consent had been obtained participants were placed within the carbon fibre AFO (Toe OFF, Gilbert and Meillish) and randomly allocated to receive three, two or one heel wedge insert. If allocated to three heel wedges, they were reduced to two at two weeks, one at four weeks, none at six weeks and the AFO removed at eight

weeks. If allocated to two heel wedges, they were reduced to one at four weeks, none at six weeks and the AFO removed at eight weeks. Finally if allocated to one heel wedge, they were reduced to none at six weeks and the AFO removed at eight weeks.

During the AFO wearing phase all patients were advised not to IWB without wearing their AFO. Furthermore all patients were advised to remove their AFO daily to perform ankle ROM exercises, as tolerated. Elevation of the injured limb was recommended intermittently throughout the day, to control swelling. At eight weeks all patients were referred for routine physiotherapy offered within the hospital, for which there is a standard guideline. All participants then continued to attend clinic at standard follow up time points of ten weeks, three, six and nine months.

At baseline all pre-existing concomitant illnesses and medications were recorded in addition to specific questions regarding conditions and medications known to predispose to tendon rupture. These included specifically the presence of tendinosis (pain, swelling, thickening within the tendon), the use of fluroquinolone antibiotics, steroids, disease modifying anti-rheumatic drugs and diabetic medication[9]. Additionally patient demographics (age, height, weight, ethnic minority and gender) were recorded along with the date and mechanism of injury. This information was used to assess the baseline characteristics of the groups.

5.1.5 Outcome measures, method of assessment and analysis

The primary outcome of this pilot RCT phase was a PROM. Such a measure would also be planned as the primary outcome within the design of a subsequent definitive RCT investigating an IWB intervention, following an acute TA rupture. This choice of primary outcome has been chosen in contrast to clinical measures such as

complication rates and quantification of gait parameters secondary to a combination of factors that have been outlined within the orthopaedic literature, and more recently the Department of Health's 2009/10 operating framework[56]. These outline that ultimately the most important outcome is from the patient's perspective.

The primary patient reported outcome measure to be used would ideally need to be disease specific to allow for greater discriminatory validity. The ATRS is the only such validated measure available for this population[61], as discussed in more detail in Chapter 6. This outcome measure has only recently been published and has only been validated within a Swedish population between the ages of 20-70 years. Therefore further data is required within a UK population across all age ranges before this may be appropriate to be used as a primary outcome measure. This score is therefore being collected as part of a wider validation study, outlined in Chapter 7, as part of this PhD thesis (Appendix E).

With no validated disease specific PROMs to choose from, the next most appropriate currently validated patient reported measure for this population is the disability rating index[127]; again the reasons for this are discussed in greater detail within Chapter 6. Although not disease specific, it has been validated within an orthopaedic clinic setting for a range of orthopaedic presentations. It is a self-administered form with twelve questions regarding common physical activities, to which patients respond using a 100mm visual analogue scale. There are two anchor points 'without difficulty = 0' and 'not at all = 100'. The twelve questions are subdivided into three broad categories; common basic activities of daily life, more demanding daily physical activities and work-related or more vigorous activities (Appendix F). This was taken in conjunction with a more generic quality of life measure (EQ-5D questionnaire)[128].

The EQ-5D is a standard instrument for use as a measure of health outcome. It is self-completed and comprises of five domains; mobility, self-care, usual activities, pain/discomfort and anxiety/depression. These combined domains result in a single health index score; there are 243 possible health states, plus unconscious and death. The second part of the outcome is a visual analogue scale of 0-100 that asks participants to rate how good or bad their own health state is, no points being 'worst imaginable health state' and 100 being 'best imaginable health state'. This outcome measure has been validated within an orthopaedic context and in a range of populations and languages (Appendix G).

Within the study of healthy participants, outlined in Chapter 3, altering the number of heel wedge inserts had an effect on heel and forefoot pressures as well as the proportion of time spent within the terminal stance and pre-swing phase of the gait cycle as a proportion of the total stance phase. It was not known if these changes in planter pressure distribution would translate into clinical practice. Therefore measurement of in-shoe plantar pressures during each visit, using the same protocol outlined in Chapter 3 will provide important secondary observations.

As discussed in Chapter 3, the interventions being assessed will allow increased movement and potentially increased force production within the healing tendon. Consequently there is a balance between subjecting a healing tendon to enough stress/strain to promote the healing response (discussed in Chapter 1) and subjecting it to too much, resulting in complications. Expected serious adverse events associated with TA rupture rehabilitation include re-rupture, tendon lengthening, adhesion, disturbed sensibility, keloid scarring and infection. These adverse events will be recorded and reported to the trial sponsor and ethics committee, in line with the trial protocol.

The time points at which to record these outcomes was based on knowledge surrounding healing time frames, as well as routine practice follow up appointments. Patients were reviewed every two weeks for the first twelve weeks predominantly to screen for the development of any complications. Two further clinic appointments were then made at six and nine months to review progress with return to activities of daily living. Therefore, complications were evaluated at each time point. Patient reported outcome scores were collected at 2,6,12, 24 and 36 weeks to allow evaluation of functional recovery during both the acute and mid-term phases.

The datasets were analysed using descriptive statistics only, secondary to the small sample sizes between these three groups of patients.

5.1.6 Adverse event management

At each visit following initial consent procedures, each participant was asked whether they had experienced any adverse events since their last visit. An adverse event was defined as any untoward medical occurrence in a clinical trial subject, which does not necessarily have a causal relationship with the treatment. All adverse events were listed on the appropriate CRF for routine return to the central office.

Serious adverse events were defined as any untoward and unexpected medical occurrence that resulted in death, was life-threatening, required hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability or incapacity, was a congenital anomaly or birth defect, 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 SAEs were entered onto the SAE reporting form. Once received by the Principal Investigator, causality and expectedness was determined. Serious adverse events that were deemed to be unexpected and related to the trial were notified to the main Research Ethics Committee within 15 days for non-life-threatening event and within seven days for a life-threatening event. All participants experiencing serious adverse events were followed-up as per protocol until the end of the trial.

5.1.7 End of trial

The end of the trial is defined as the final visit to the clinic of the last participant.

5.1.8 Data management, statistical analysis and trial organisation

The CRFs were designed by the researcher and reviewed by the Principal Investigator (PhD supervisor Mr Matthew Costa) and guidance from the trial's statistician. All CRFs were completed by the research team, with the participant present, and managed centrally. All CRFs can be found in Appendix H.

All electronic patient-identifiable information was held on a secure, password-protected database accessible only to essential personnel. Paper forms with patient-identifiable information were held in secure, locked filing cabinets in a restricted area of Warwick Medical School. Patients were identified by a code number only. Data was entered onto an electronic database immediately following each research clinic.

Direct access to source data/documents was required for trial related monitoring. All paper and electronic data would be retained for at least five years after completion of the trial. As part of my on-going PhD supervision the supervisors had reviewed the protocol for this study and had received progress reports at their request.

Accumulating data was monitored at frequent intervals to identify and facilitate the early remedial action of certain problems such as recruitment, data collection and compliance. Yearly progress reports were also submitted to the funders of this project (Arthritis Research UK), as outlined within the terms and conditions of the awarded grant.

The day to day management of the project was overseen by the PhD supervisors. There was standard NHS cover for negligent harm in place. There was no cover for non-negligent harm. Insurance was in place until July 2011 and renewed accordingly. Ethical and research and development approvals were also in place. Additionally, all research staff involved held a contract with the University of Warwick and an honorary contract for research services with the University Hospitals Coventry and Warwickshire.

The Principal Investigator was Mr Matthew Costa, who had undertaken relevant mandatory training in GCP and the University of Warwick 'Chief Investigators' course. Clinically, Mr Costa is also an orthopaedic consultant and all trial participants were under his clinical care as per NHS practice.

As a research physiotherapist, mandatory GCP training had been undertaken in addition to non-mandatory training to facilitate this role, including 'how to consent participants for clinical research' and an MSc in Trauma and Orthopaedic Surgery. Health Professions Council registration was also up to date. The principal investigator delegated duties as appropriate to the research team, and these were recorded on a delegation of authority log within the trial site file.

Financial support for this project had been awarded by Arthritis Research UK. Treatment costs associated with this study had been reviewed by the NHS research and development department, and they had agreed that there were no service support costs for this project and that the identified additional treatment costs would be paid via their normal commissioning arrangements as agreed with the local primary care trust. The project timetable and milestones are outlined in Table 5.1.

Table 5.1: Project timetable

Number of months	0	4	8	12	16
Tasks to be completed	Sept 10	Dec 10	Apr 11	Aug 11	Dec 11
Ethics, R&D, sponsorship and insurance.					
Prepare and refine materials					
Recruitment					
Finish all data collection					
Analysis					
Write-up and report					

5.2 Results

The primary objective of this study was to measure patient reported outcomes between the interactions of the three different AFO/heel wedge insert combinations. The secondary objectives were to trial the clinical processes of using this AFO/heel wedge combination, measure the level of patient acceptance of randomisation to these interventions, and measure pre-defined gait parameters.

Recruitment took place between September 2010 and April 2011, a recruitment rate of 2.1 per month. Twenty six patients were screened and eleven were not eligible; five were secondary to being ruptures at the musculotendinous junction, three were delayed presentations and three were unable to adhere to trial procedures as they were not remaining in the UK for follow up clinics. Fifteen patients were eligible and subsequently consented to take part in the study. There was no loss to follow-up as shown in Figure 5.2.

The baseline demographics for the three randomised groups of five participants are shown in Table 5.2. This table demonstrates that the one heel raise group was an older age group compared to the other two and, unlike the other two groups, was all female. However, all other baseline demographics were comparable, including height, weight and pre-existing pathologies. Sport was the most prevalent mechanism of injury (10/15).

Within the three heel raise group one patient was consented and randomised to the intervention, but subsequently refused the intervention. This patient was still managed with three heel raises but within a rigid rocker bottom AFO rather than the carbon fibre AFO. There were two further protocol violations within this group; the first was a re-rupture at the six week time point, resulting in an additional four week period wearing the AFO. The second occurred five months post rupture, and was a re-rupture secondary to being involved in a physical attack, resulting in a further eight weeks in an AFO.

There were no SAEs or protocol violations within the two heel raise group. Within the one heel raise group one patient sustained a re-rupture at the ten week time point. This was subsequently managed in an AFO for a further nine weeks. At the ten week time point the same patient sustained a further re-rupture which was managed with a further period of non-operative management within an AFO for a longer period of time (16 weeks).

Figure 5.3 to Figure 5.5 demonstrate the functional outcome scores for the three AFO/heel wedge combination groups as a change from median baseline scores. The ranges of results around the median change from baseline are shown in the table underneath each figure.

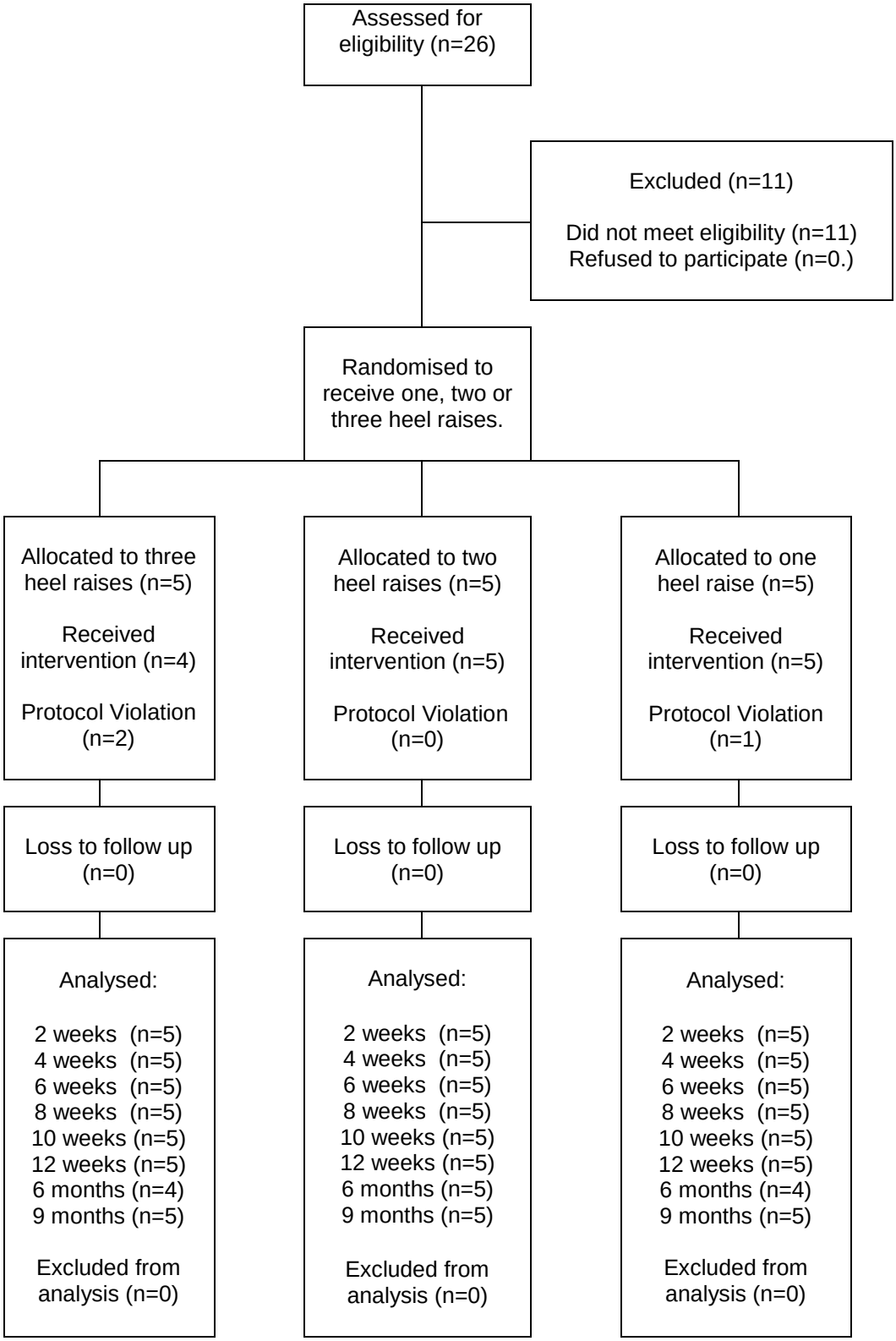
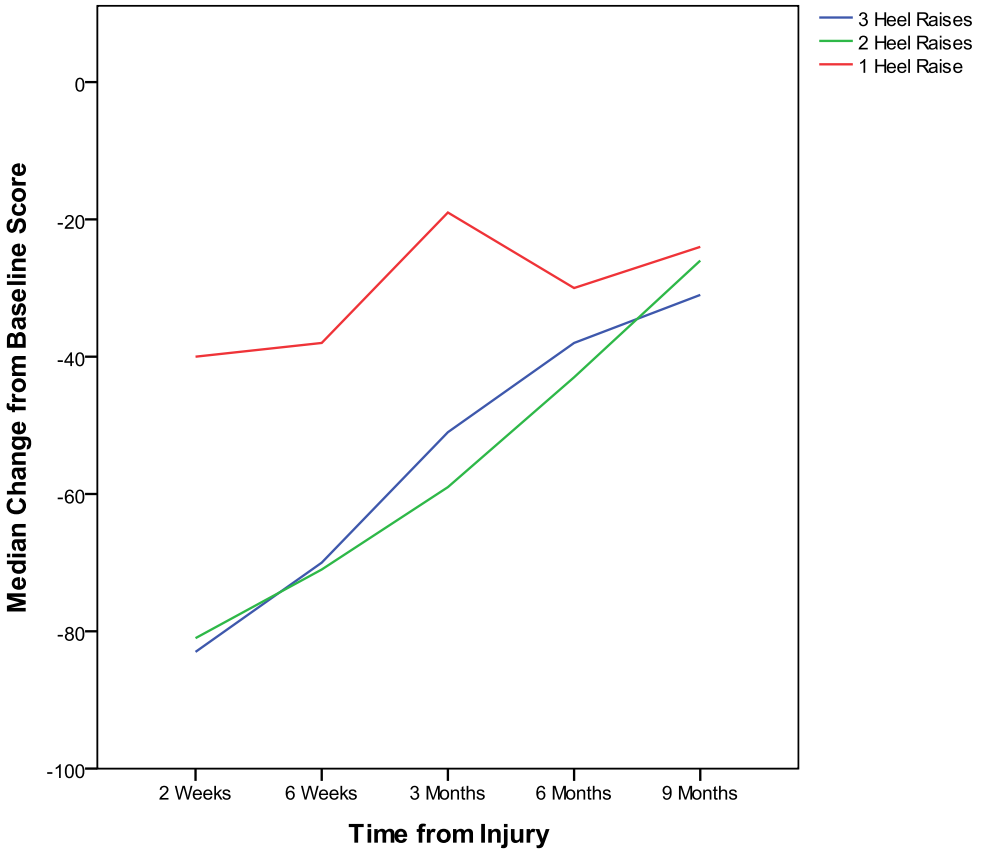


Figure 5.2: Flow chart of participants through the trial

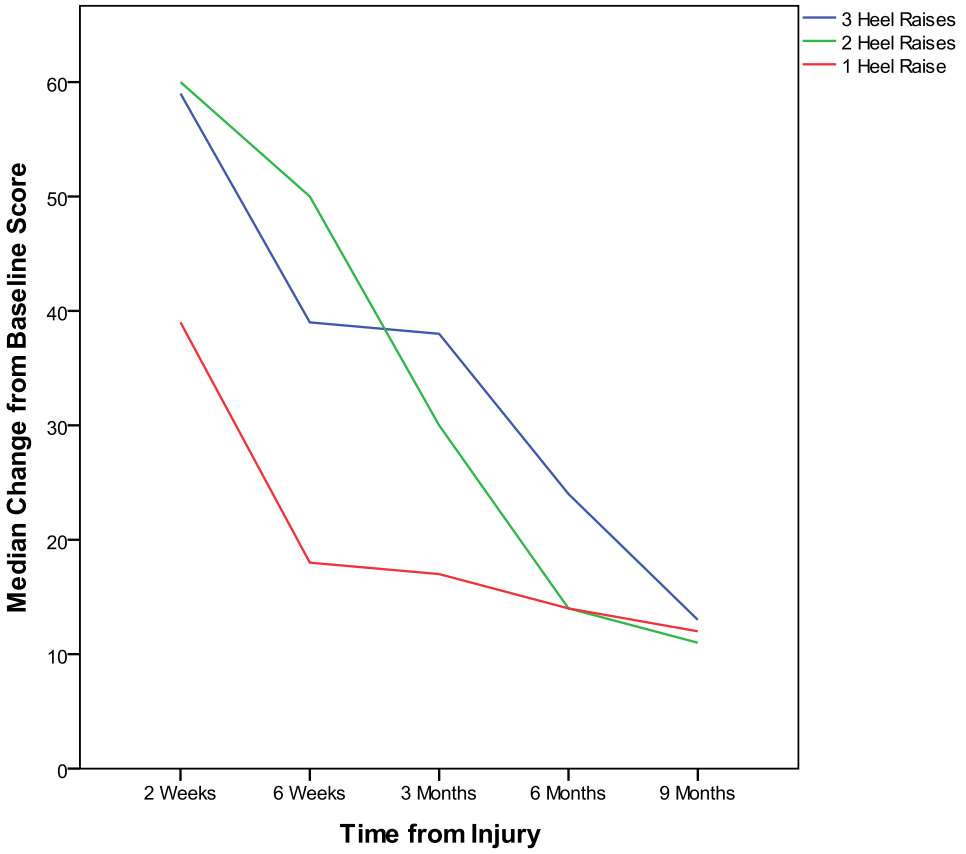
Table 5.2: Baseline demographics for the three study groups

	Three heel raises	Two heel raises	One heel raise
Mean age in years (SD)	38.6 (7.3)	42.2 (13.8)	56.8 (12.0)
Male/Female	2/3	4/1	0/5
Left/Right	4/1	4/1	3/2
Mean height in cm (SD)	170.0 (7.5)	171.8 (11.0)	170.8 (7.8)
Mean weight in Kg (SD)	76.6 (12.1)	85.0 (37.7)	72.4 (6.8)
Smokes (Y/N)	1/4	0/5	1/4
Smoked in past (Y/N)	0/5	1/4	5/0
Ethnic background	White: 4 Indian: 1	White: 2 Indian: 2 Black Caribbean: 1	White: 5
Current medication	2 patients: No medications 1 patient: anti-depressant 1 patient: beta blocker 1 patient: simvastatin	4 patients: No medications 1 patients: inhaler for asthma	4 patients: No medications 1 patient: Prozac
Pre-existing ipsilateral problem	3 patients: No problems 1 patient: patella tendinopathy 1 patient: TA tendinopathy	3 patients: No problems 1 patient: Hip arthroscopy (2010) 1 patient: Knee cartilage removal (1976)	4 patients: No problems 1 patient: TA tendinopathy
Pre-existing contralateral problem	4 patients: No problems 1 patient: TA tendinopathy	5 patients: No problems	3 patients: No problems 1 patient: Hip resurfacing 1 patient: Ankle fracture (15 years ago) 1 patient: Knee arthroscopy (10 years ago)
Any other new injuries	None	None	None
Mechanism of injury	Sport: 4 Dancing: 1	Sport:4 Pushing Car: 1	Sport:2 Walking: 2 Dancing:1 Stairs:1
Management (Op/Non-Op)	0/5	1/4	1/4



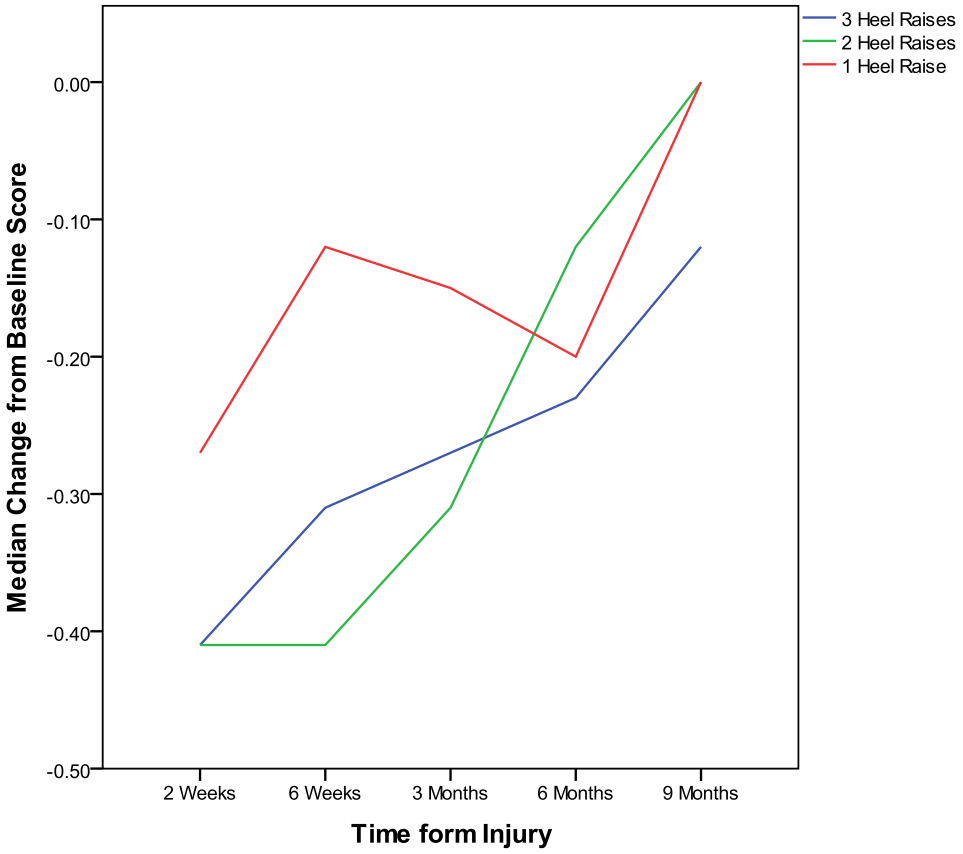
Range of results at each time point (As change from median baseline score)	Three heel raises	Two heel raises	One heel raise
Two weeks	-72 to -96	-47 to -93	-33 to -88
Six weeks	-40 to -86	-62 to -79	-27 to -60
Three months	-41 to -76	-52 to -73	-13 to -67
Six months	-28 to -71	-31 to -43	-32 to -41
Nine months	-3 to -37	-11 to -45	0 to -44

Figure 5.3: Median change from baseline for ATRS scores with table demonstrating the range of values at each time point for the three groups



Range of results at each time point (As change from median baseline score)	Three heel raises	Two heel raises	One heel raise
Two weeks	39 to 78	7 to 84	16 to 50
Six weeks	30 to 70	42 to 72	4 to 34
Three months	22 to 46	21 to 68	7 to 40
Six months	10 to 36	10 to 72	0 to 40
Nine months	16 to 0	69 to 4	34 to 0

Figure 5.4: Median change from baseline for DRI scores with table demonstrating the range of values at each time point for the three groups



Range of results at each time point (As change from median baseline score)	Three heel raises	Two heel raises	One heel raise
Two weeks	-0.19 to -0.48	-0.19 to -0.64	0 to -0.31
Six weeks	0 to -0.64	-0.31 to -0.48	0 to -0.31
Three months	-0.12 to -0.31	-0.12 to -0.41	0 to -0.31
Six months	0 to -0.31	0 to -0.27	0 to -0.38
Nine months	0 to -0.15	0 to -0.41	0 to -0.31

Figure 5.5: Median change from baseline for EQ-ED scores with table demonstrating the range of values at each time point for the three groups

Alongside PROMs, gait parameters were also evaluated as a secondary objective. Figure 5.6 and Figure 5.7 demonstrate the mean heel and forefoot pressures (KPa) and standard deviations for the injured and uninjured limb at each time point for each group up to three months. Figure 5.8 illustrates the percentage amount of time spent in terminal stance and pre-swing phase as a proportion of the total stance phase at each time point, also up to three months. Data collection at the six and nine month time points was planned, however due to technical failures the gait analysis system was not available.

The graphs clearly demonstrate the same patterns seen within the previous Chapter. These patterns include the injured limb displaying increased heel pressures, decreased forefoot pressures and a decrease in the amount of time spent in the terminal stance and pre-swing phase of the gait cycle, gradually returning to values of the uninjured limb over time.

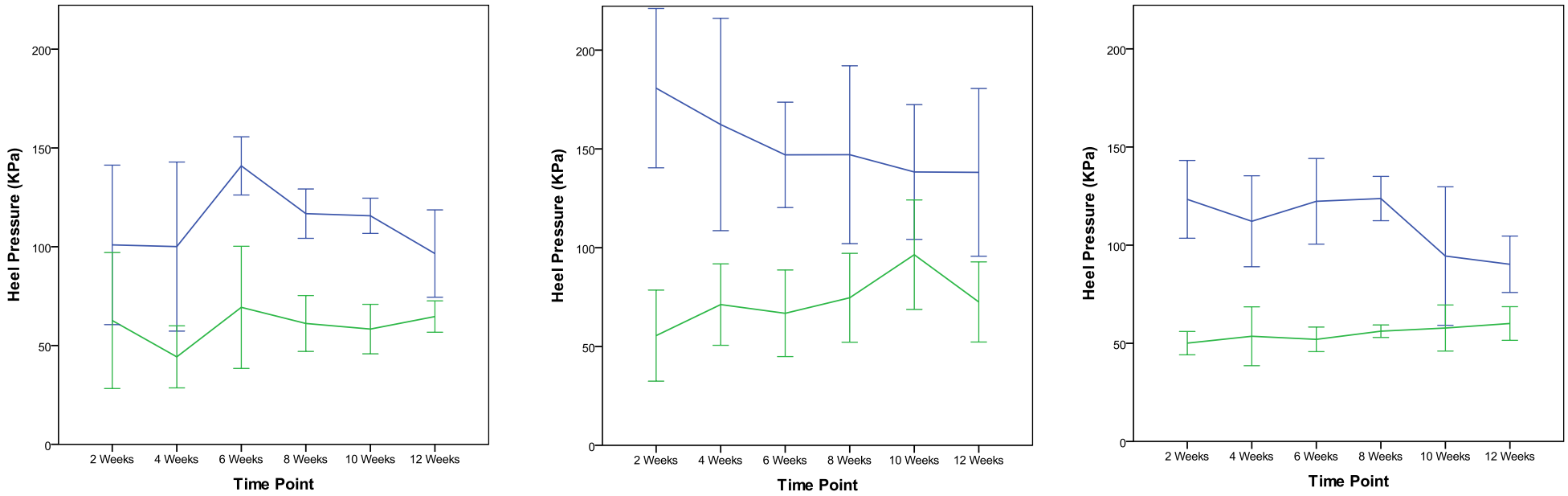


Figure 5.6: Mean and SD for heel pressure measurements (KPa) for injured (blue line) and uninjured (green line) limb at each time point. From left to right: Three heel raise group, two heel raise group and the one heel raise group

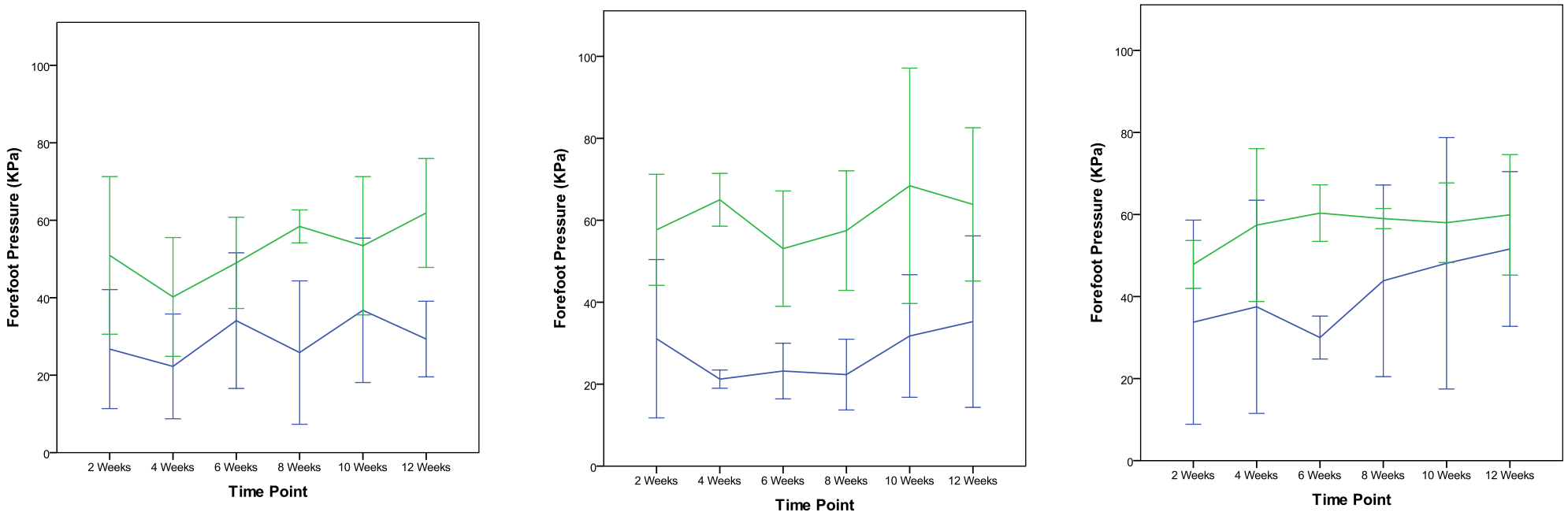


Figure 5.7: Mean and SD for forefoot pressure measurements (KPa) for injured (blue line) and uninjured (green line) limb at each time point. From left to right: Three heel raise group, two heel raise group and the one heel raise group

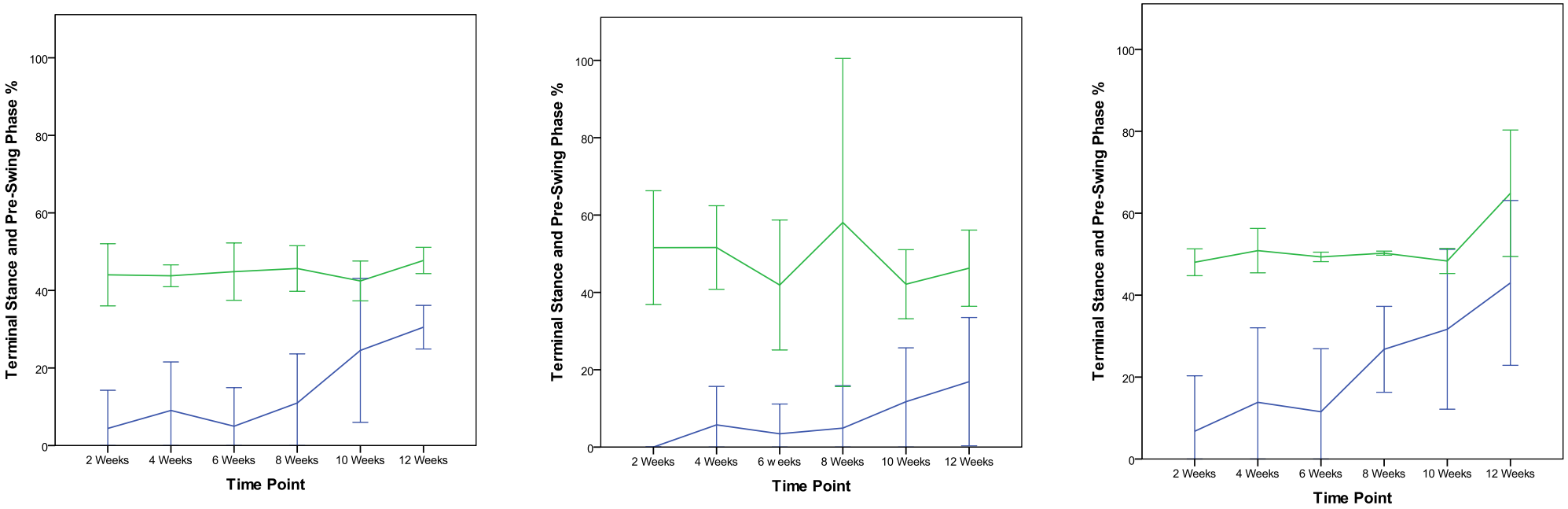


Figure 5.8: Mean and SD for terminal stance and pre-swing (%) for injured (blue line) and uninjured (green line) limb at each time point. From left to right: Three heel raise group, two heel raise group and the one heel raise group

5.3 Discussion

The primary objective of this study was to measure patient reported outcomes between the interactions of the three different AFO/heel wedge insert combinations. The secondary objectives were to trial the clinical processes of using this AFO/heel wedge combination, measure the level of patient acceptance of randomisation to these interventions and measure pre-defined gait parameters.

Across the three reported PROMs, all three patient groups gradually returned to pre-injury scores over the nine month time period. There were also a wide range of scores within the groups at each time point, as would be expected with a small sample of five in each group. It was also clear to see that there was a trend in the one heel raise group to consistently achieve higher PROM's outcomes when compared to the two and three heel raise groups, throughout the earlier time points. However by six months a convergence of the results occurs across the three groups. These trends between the groups were not observed within the secondary outcome gait data; however this was also limited by the missing data at the final two time points, secondary to irreconcilable technical faults with the gait analysis system.

This could imply that the theoretical advantages of using one heel raise, as opposed to two or three, proposed in Chapter 3 may result in improved PROMs data only during, and immediately after the AFO wearing phase. However this is only pilot data and consequently does not provide definitive evidence, but can be used to inform the estimate of potential effect sizes and consequently the possibility of future clinical trials. Therefore, in relation to the first objective of this study, there is an indication that there is an interaction between the AFO and heel wedge insert

combination. How this information will be used to guide future research will be discussed in the final chapter.

The secondary objectives of this study were to investigate the clinical processes and patient acceptance of randomisation to the interventions. All patients who were approached to take part in the study did so. However one patient decided not to proceed with the intervention once they had been fitted with the AFO and heel wedge insert combination. In this particular case the patient felt that the AFO design did not look robust and requested an alternative design. This raises important questions in relation to the importance of not just the quantitative aspects of what interventions work and why, but also the qualitative aspects of intervention development.

These questions from a qualitative paradigm are as equally as important as the quantitative aspects, which the scenario described above exemplifies. However these qualitative issues surrounding attitudes and acceptability to proposed changes to treatment interventions to be researched in the future go beyond the patient.

To investigate attitudes, acceptance and experiences of the proposed developments in TA rupture rehabilitation; future research would need to include a vast range of stakeholders. These would include not only patients, but also the health care professionals who would be responsible for delivering the interventions (consultants and allied health professionals), members of the public who may be involved with helping patients and also more broadly, charities that represent these patient groups and ethics committee members who would be responsible for

approving future research. Exactly how and when these issues could be further explored will be discussed in detail within the final chapter.

Alongside the integration of qualitative research in future developments, there is also the outstanding question regarding the correct quantitative outcomes being measured. Throughout this and previous chapters it has been discussed that the authors of the ATRS PROM have advocated it as the only disease specific validated PROM for use with this patient population. Consequently the final key focus of this PhD will be on identifying what PROMs have been used by researchers previously, and further investigating the validity and reliability of the properties of these commonly used measurement tools.

Declarations

This work has been published:

Kearney R, S Lamb, J Achten, C Plant and M Costa, A systematic review of patient reported outcome measures used to assess Achilles tendon rupture management: What's being used and should we be using it? *British Journal of Sports Medicine* (*In Press)*

Funding Body

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Table of Contents

Abstract

Background
Currently there is no consensus regarding the optimal management for patients following an Achilles tendon rupture. To allow comparisons across research a universally accepted outcome measure is required. However, there are currently a range of these reported within the literature.

Purpose
The first aim of this research was to identify the most frequently used patient reported outcomes for patients following a rupture of their Achilles tendon. The secondary aim was to then analyse the evidence to support their use.

Methods
The electronic databases MEDLINE, EMBASE and AMED were searched up to September 2010. Predefined inclusion and exclusion criteria were then applied to identify what outcome measures are reported in the literature. Aspects of validity were then defined and a checklist used to determine which aspects have been evaluated.

Results
Twenty one outcome measures in fifty research papers were identified. The most commonly used was the American Orthopaedic Foot and Ankle Society hind-foot score. Of these twenty one outcome measures only four cited independent validation data. Of these four, only the 'Achilles tendon Total Rupture Score' reported evidence to support multiple facets of validity, as defined by a predetermined criteria checklist.

Conclusions
The Achilles tendon Total Rupture Score is the only outcome measure which has demonstrated multiple facets of validity for use in this group of patients. However, even this tool has limitations. Researchers should be aware of the limitations of the available outcome measurement tools and evaluate their validity before they use them in clinical research.

6.1 Protocol

The MRC complex intervention framework outlines a process of developing theory, piloting procedures and assessing effectiveness. However to assess effectiveness the researcher requires a valid, reliable and responsive tool to achieve this. Within trauma and orthopaedics, the traditional method for determining the benefits of a new intervention have been focused on clinical objective measures. Such measures for TA rupture research have included muscle strength, calf circumference and ROM[55].

More recently, the Department of Health have outlined that technical and clinical measures should come secondary to treatment effectiveness from the patient's perspective. This is seen as an essential component for putting quality at the centre of NHS practice[56]. Consequently, there is a growing trend, across health care specialities, to use PROMs as primary outcome measures within clinical research[131].

Two broad types of PROMs have been developed[132]. The first is categorised as 'disease specific' and the second as 'quality of life'[131]. Both are multi item questionnaires, predominantly completed by the patient. They include questions that ask the patient about various constructs. Such construct examples include physical activities, pain and social functioning. These are then quantitatively scored, using a predefined scoring or indexing system.

The key difference between these two broad categories is that disease specific measures have been developed within the construct of a specific pathology or anatomical region. Consequently they ask questions specifically directed to those conditions/areas. In contrast, quality of life measures are more generic in their

questioning and applied across disease areas and anatomical regions. Currently there is a range of multi-item PROMs used within the context of TA rupture management, as outlined in chapter 1.

The purpose of this chapter is to systematically review which multi-item outcome measures are most frequently used within the research pertaining to acute TA rupture management. The secondary objective is to evaluate aspects of validity of these commonly used measures. It is intended that this review will provide structured evidence to guide the selection of an outcome measure to be used within a research context.

6.1.1 Research questions

To achieve these objectives the following research questions will be addressed:

1. What are the most frequently used multi-item outcome instruments in studies reporting acute TA rupture management?
2. Does the literature provide evidence to support the identified disease specific outcomes in terms of aspects of validity, reliability and responsiveness as defined by a quality criteria score?

6.1.2 Criteria for including studies: Identifying what outcomes are currently used

To address the first research question all interventional study designs and languages were included and translated where necessary. The review included all subjects over 18 years old with an isolated, primary acute TA rupture. An acute TA rupture was defined as being less than 14 days old[69]. Articles reporting subjects presenting with delayed presentation (over 14 days), re-rupture or previous TA surgery were excluded.

All articles had to document the use of a multi-item health outcome measure. Articles reporting single item outcomes such as strength, re-rupture or patient satisfaction were excluded. Additionally, multi-item scoring systems containing no patient reported items were also excluded.

6.1.3 Criteria for including studies: Supporting validation evidence

To address the second research question, all identified disease specific outcome measures identified from the first research question were included in this second stage of the review. Any outcome measure used within an article without independent validation data cited was excluded.

All study designs and languages were included and translated where necessary in this review. All studies reporting the development and construct of the identified outcomes were also included. Any subsequent studies reporting validity, reliability or responsiveness of the specified outcome measures within a population who had sustained an acute TA rupture were also included. Articles not reporting aspects of development, validity, reliability or responsiveness were excluded. Articles reporting aspects of subsequent, validity, reliability or responsiveness within populations other than those who have sustained an acute TA rupture were also excluded.

6.1.4 Search strategy: Identifying what outcomes are currently used

This search employed the electronic databases of MEDLINE, AMED and EMBASE using the Ovid search engine. The following search strategies in Table 6.1 were used within these databases to identify which outcome instruments are used in practice to address the first research question. Within the MEDLINE search an additional MeSH heading '*outcome assessment*' was used which is not available

within AMED and EMBASE. The remainder of the search terms are exact for all three databases.

Table 6.1: Search strategies used to identify what outcome measures are used

MEDLINE

	Search terms
1	exp. Achilles Tendon/
2	exp. Rupture/
3	Achill$.m_titl
4	TendoAchill$.m_titl
5	Rupture$.m_title
6	1 OR 3 OR 4
7	2 OR 5
8	6 AND 7
9	exp Treatment Outcome/
10	exp. Questionnaires/
11	exp 'Quality of Life'/or exp 'Outcome Assessment (Health Care)'/or exp Health Status
12	9 OR 10 OR 11
13	8 AND 12

AMED and EMBASE

	Search terms
1	exp. Achilles Tendon/
2	exp. Rupture/
3	Achill$.m_titl
4	TendoAchill$.m_titl
5	Rupture$.m_title
6	1 OR 3 OR 4
7	2 OR 5
8	6 AND 7
9	exp Treatment Outcome/
10	exp. Questionnaires/
11	exp 'Quality of Life'/or exp Health Status/
12	9 OR 10 OR 11
13	8 AND 12

6.1.5 Search strategy: Supporting validation evidence

To address the second research question, the reference lists of the included articles were checked for references pertaining to the development of the identified outcome measures. In addition to this a second search strategy was employed using MEDLINE, AMED and EMBASE, searched via Ovid. The search strategy used is outlined in Table 6.2. The individual search terms were based on the quality criteria proposed for measurement properties of health status questionnaires by Terwee *et al*[133].

Table 6.2: Search strategy used to identify studies to support the validity, reliability and responsiveness of the identified outcome measures

	Search terms
1	*Specified Outcome Measure.mp*
2	Content validity.mp
3	Internal Consistency.mo
4	Criterion Validity.mp
5	Construct Validity.mp
6	Reproducibility Agreement.mp
7	Reproducibility Reliability.mp
8	Responsiveness.mp
9	Floor and Ceiling Effects.mp
10	Interpretability.mp
11	2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10
12	1 AND 11

6.1.6 Methods of review: Identifying what outcomes are currently used

Articles produced from the search strategies were independently assessed for inclusion by two reviewers (RK and CP). The reviewers evaluated all identified titles and abstracts independently and excluded any clearly irrelevant articles at this point. The remaining articles were ordered in full and assessed against the eligibility criteria, differences were resolved by discussion.

Data was extracted from all included articles by a single reviewer (RK) and verified by a second reviewer (CP). An example of the predefined data extraction table is summarised in Table 6.3. It includes information regarding the title of the outcome measure, how many have cited it, a description of the number of items it contains, item content, response scale and score range.

Table 6.3: Example of data extraction table for the identified outcome measures

Name of outcome	*Total citations*	*Outcome type*	*Total Items*	*Item content*	*Response scale*	*Score range*	*Subjective or subjective and objective*

6.1.7 Methods of review: Supporting validation evidence

Articles produced from the search strategies were independently assessed for inclusion by two reviewers (RK and CP). The reviewers evaluated all identified titles and abstracts independently and excluded any clearly irrelevant articles at this point. The remaining articles were ordered in full and assessed against the eligibility criteria, differences were resolved by discussion.

To investigate the evidence pertaining to the validity, reliability and responsiveness of the identified outcomes measures reported within the literature a checklist was applied. The checklist outlines nine quality criteria for questionnaires of health status. These quality criteria include content validity, internal consistency, criterion validity, construct validity, reproducibility (agreement and reliability), reliability, responsiveness, floor/ceiling effects and interpretability. Each quality criteria is then

assigned one of three outcomes, a positive rating, intermediate rating or negative rating as outlined by Terwee *et al*[133] (Appendix I).

An example of the data extraction table can be found below (Table 6.4). The data was extracted from the included articles, from the secondary search, by a single reviewer (RK) and verified by a second reviewer (CP).

Table 6.4: Example of data extraction table

Name of outcome	***Content validity***	***Internal consistency***	***Criterion validity***	***Construct validity***	***Reproducibility agreement***	***Reproducibility reliability***	***Responsiveness***	***Floor/ceiling fffect***	***Interpretability***

6.2 Results

6.2.1 Search results: Identifying what outcomes are currently used

The search was carried out 29/09/10. The individual search strategies for each database are shown in Table 6.5 through to Table 6.7; Figure 6.1 shows the overall results of the combined databases. Once duplicates were removed from the combined results, 414 records were screened for eligibility. Of these 327 were excluded, based on the title and abstract information. Eighty seven full text articles were ordered, to be assessed against the eligibility criteria.

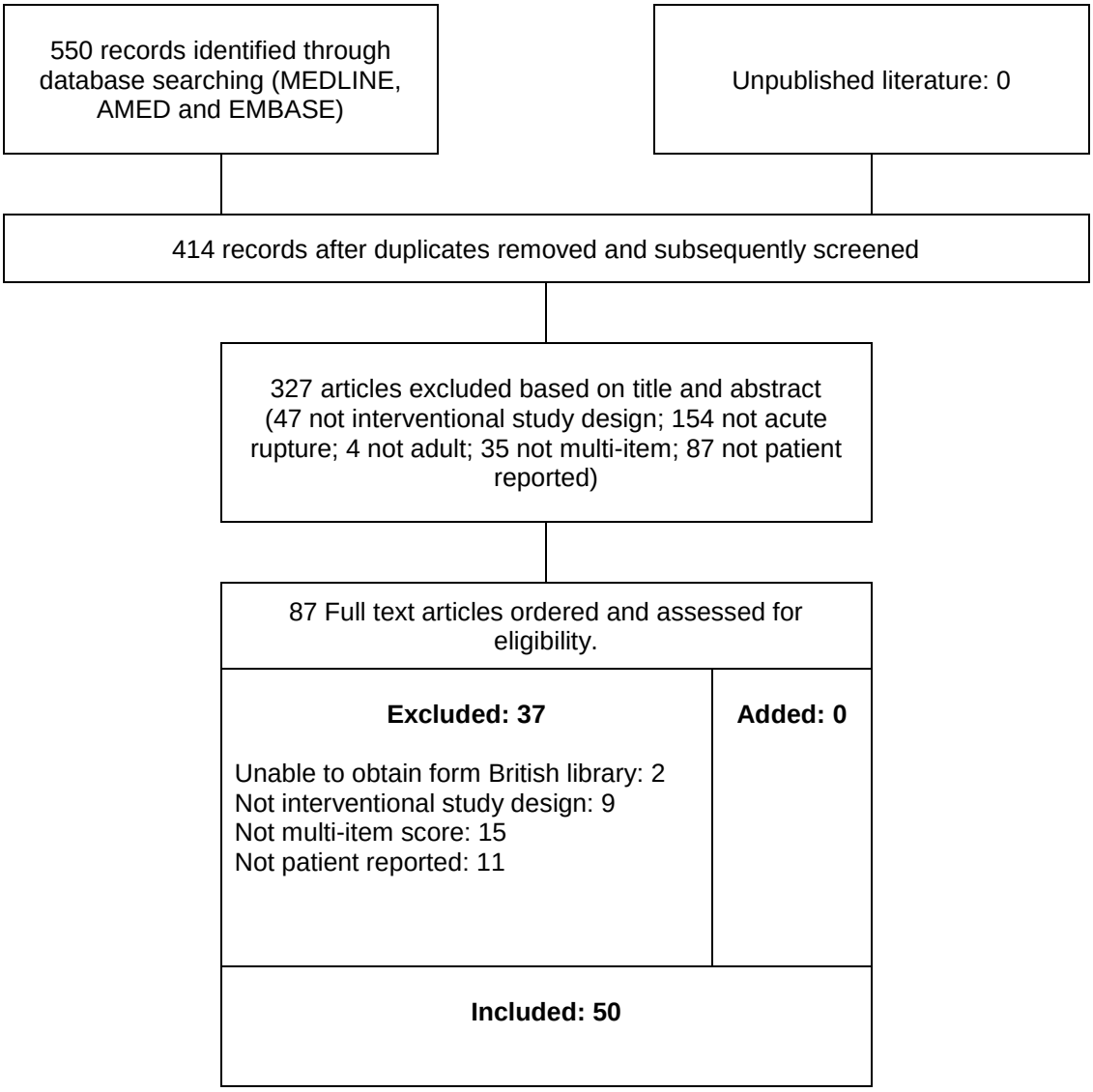

Figure 6.1: Search strategy results to identify what outcomes are used

Table 6.5: Search strategy results: MEDLINE

	Search terms	Results
1	exp. Achilles Tendon/	4942
2	exp. Rupture/	30983
3	Achill$.m_titl	3514
4	TendoAchill$.m_titl	124
5	Rupture$.m_title	32396
6	1 OR 3 OR 4	5606
7	2 OR 5	49158
8	6 AND 7	1532
9	exp Treatment Outcome/	458841
10	exp. Questionnaires/	223377
11	exp 'Quality of Life'/or exp 'Outcome Assessment (Health Care)'/or exp Health Status	624370
12	9 OR 10 OR 11	807821
13	8 AND 12	208

Table 6.6: Search strategy results: AMED

	Search terms	Results
1	exp. Achilles Tendon/	421
2	exp. Rupture/	290
3	Achill$.m_titl	472
4	TendoAchill$.m_titl	32
5	Rupture$.m_title	259
6	1 OR 3 OR 4	505
7	2 OR 5	383
8	6 AND 7	148
9	exp Treatment Outcome/	12877
10	exp. Questionnaires/ or ' Quality of Life'	7602
11	exp Health Status/	2175
12	9 OR 10 OR 11	21184
13	8 AND 12	30

Table 6.7: Search strategy results: EMBASE

	Search terms	Results
1	exp. Achilles Tendon/	4789
2	exp. Rupture/	58696
3	Achill$.m_titl	4160
4	TendoAchill$.m_titl	146
5	Rupture$.m_title	26143
6	1 OR 3 OR 4	6699
7	2 OR 5	67401
8	6 AND 7	1835
9	exp Treatment Outcome/	699633
10	exp. Questionnaires/	256675
11	exp 'Quality of Life'/or exp Health Status/	249850
12	9 OR 10 OR 11	1097462
13	8 AND 12	312

The outcome measures identified from the included articles are summarised within the predefined data extraction table in Table 6.8. In total 21 multi-item patient reported outcomes were identified. Of these four were generic quality of life outcome measures; two were region specific and 15 were disease specific outcome measures. The AOFAS was the most frequently used score (19 articles).

Total items for the questionnaires ranged from 5 to 36 covering a range of content areas. The responses to the questions involved responding to a number of set categories in all 21 outcomes, these were then either summed to achieve a score or applied to an index which then translated to a single score. Of the 21 outcome measures 13 contained an objective component in addition to the subjective patient reported component and the remaining eight were patient reported only.

Table 6.8: Summary of outcome measures used in published research

Name of outcome	*Total citations*	*Outcome type*	*Total items*	*Item content*	*Response scale*	*Score range*	*Subjective (A) or subjective and objective (B)*
Generic Quality of Life Outcome Measures							
EQ-5D	1	Global	5	Mobility, self-care, usual activities, pain, anxiety/depression	Categories: Three responses. Combined responses result in one of 245 combinations, which each is allocated a score	Range: -1 to +1	A
SF-12	1	Global	12	Physical and mental components	Categories: Five responses Scored using an algorithm	Responses applied to an algorithm range from 0 to 100 Profile measure that yields two summary scores (physical and mental health)	A
SF-36	1	Global	36	Eight domains of health: physical function, physical role, bodily pain, general health, vitality, social functioning, emotional role and mental health	Categories: Five responses Scored using an algorithm	Responses applied to an algorithm range from 0 to 100 Profile measure that yields two summary scores (physical and mental health)	A
Rand 36	1	Global	36	Eight domains of health: physical function, physical role, bodily pain, general health, vitality, social functioning, emotional role and mental health	Categories: Five responses Scored using an algorithm	Responses applied to an algorithm range from 0 to 100 Profile measure that yields two summary scores (physical and mental health)	A

Name of outcome	*Total citations*	*Outcome type*	*Total items*	*Item content*	*Response scale*	*Score range*	*Subjective (A) or subjective and objective (B)*
Region Specific Outcome Measures							
AOFAS	19	Region Specific: Ankle-Hindfoot,	9	Pain, function, walking distance, walking surface, ROM, foot alignment, gait	Categories: Between 2 and 4 responses Assigned points per response between 0 and 40	Range: 0 to100	B
Olerud Molander Ankle Score	1	Region Specific: Ankle	9	Pain, stiffness, swelling, stair climbing, running, jumping, squatting, supports, work activities.	Categories: Between 2 and 5 responses Assigned points per response between 0 and 2	Range: 0 to100 Excellent: 91-100 Good: 61-90 Fair: 60-31 Poor: 0-30	A
Achilles Tendon Specific Outcome Measures							
Holz Score	4	Disease Specific (TA)	5	ROM, gait, strength, pain, return to sports	Categories: Three responses assigned 1,2 or 3 points	Range: 5 to 5 Good: 12-15 Fair: 8-11 Poor: <7	B
Hannover Achilles Score	1	Disease Specific (TA)	11	ROM, calf circumference, Thompson test, strength, pain, return to sport, weather related problems, satisfaction.	Categories: Between 2 and 4 response. Assigned points per response between 0 to 10	Range: 0 to100 Excellent: 9-1000 Very good: 8-890 Good: 70-79 Sufficient: 6-690 Poor: <60	B
Thermann Score	8	Disease Specific: (TA)	11	ROM. Calf circumference, strength, pain, return to sport, sensitivity to weather, patient satisfaction, Thompson test	Categories: Between 2 and 4 responses Assigned points per response between 0 and 10	Range: 0 to100 Excellent: 90-100 Good: 80-89 Fair: 70-79 Poor: 60-69	B

Name of outcome	*Total citations*	*Outcome type*	*Total items*	*Item content*	*Response scale*	*Score range*	*Subjective (A) or subjective and objective (B)*
Modified Thermann Score	2	Disease Specific (TA)	11	ROM, calf circumference, strength, pain, return to sports, sensitivity to weather, patient satisfaction	Categories: Between 2 and 5 responses Assigned points per response between 0 and 10	Range: 0 to 100 Very good: 100-90 Good: 89-80 Moderate: 79-70 Fair: 69-60 Poor: <60	B
Modified Thermann Score	1	Disease Specific (TA)	10	ROM, calf circumference, return to sports, patient satisfaction	Categories: Between 3 and 4 responses Assigned points per response between 0 and 10 points	Range: 0 to 100	B
Modified Thermann Score	1	Disease Specific (TA)	8	ROM, strength, pain, return to sport, patient satisfaction	Categories: Four responses Assigned points per response between 0 and 10	Range: 0 to 80 Very Good: 70-80 Good: 60-69 Fair: 50-59 Poor: <50	B
Leppilahti Score	5	Disease Specific (TA)	7	Pain, stiffness, subjective strength, ROM, footwear restrictions, isokinetic muscle strength, satisfaction	Categories: Between 3 and 4 responses Assigned points per response between 0 and 15	Range: 0 to100 Excellent: 90-100 Good: 75-85 Fair: 60-70 Poor: <55	B
Modified Leppilahti Score	2	Disease Specific (TA)	5	Pain, Stiffness, subjective strength, footwear restrictions, patient satisfaction	Categories: Between 3 and 4 responses Assigned points per response between 0 and 15.	Range: 0 to70	A

Name of outcome	*Total citations*	*Outcome type*	*Total items*	*Item content*	*Response scale*	*Score range*	*Subjective (A) or subjective and objective (B)*
Rupp Achilles tendon score	1	Disease Specific (TA)	13	Strength, ROM, calf circumference, activities of daily living, pain, patient satisfaction	Categories: Between 4 and 5 responses Assigned points per response, between -5 and +5	Range: -53 to 58 Excellent: 40-60 Good: 20-39 Satisfactory: 0-19 Poor: <0	B
Modified Rupp Score	1	Disease Specific (TA)	7	Pain, patient satisfaction, function, return to work and sport.	Categories: Between two and four responses Assigned points per response between -5 and 5	Range: -24 to 28 Excellent: Over 30 Good: 15-30 Fair: 5-15 Poor: <5	A
ATRS	3	Disease Specific (TA)	10	Patient reported strength, fatigue, stiffness, pain, activities of daily living, walking on even surfaces, walking uphill, running, jumping physical labour	Categories: Eleven responses Assigned points per response between 0 and 10	Range: 0 to 100	A
Modified Mandelbaum and Pavanini Scale	1	Disease Specific	5	ROM, patient satisfaction, strength, pain, return to sports	Categories: Between 2 and 3 responses Assigned points per response between 0 and 10	Range: 5 to 50	B
Objective and Subjective Outcome Score	1	Disease Specific	8	ROM, calf circumference, strength, pain, complications, satisfaction	Categories: Between 3 and 4 responses Assigned points per response between 0 and 15	Range: 0 to 100	B
Achilles Tendon Evaluation Score	1	Disease Specific (TA)	11	Gait, strength, Thompson test, patient satisfaction	Categories: Three responses Assigned points per response between 0 and 10	Range: 0 to 100 Excellent: 90-100 Good: 80-89 Fair: 70-79 Poor: <70	B

Name of outcome	*Total citations*	*Outcome type*	*Total items*	*Item content*	*Response scale*	*Score range*	*Subjective (A) or subjective and objective (B)*
Post-operative Rating Scale	1	Disease Specific (TA)	7	Pain, ROM, jumping capacity, calf atrophy, VAS, wound healing, gait	Categories: Between 3 and 4 responses Assigned points per response between 0 and 15	Range:0 to 100 Excellent: 90-100 Good: 90-80 Fair: 80-70 Poor: <70	B

6.2.2 Search results: Supporting validation evidence

Twenty one multi-item outcome measures were reported within the literature pertaining to acute TA rupture management. Of these 21 articles, four were excluded from this second stage of the review because they were not disease specific and a further 13 were excluded for not citing independent validation data within the article. This resulted in four included outcome measures in this second stage of the review. These outcomes were the AOFAS, Olerud Molander Ankle Score, Leppilahti Score and ATRS.

The second literature search was carried out on 30/11/10 for the above outcome measures. The individual search results for each database can be found in Table 6.9 through to Table 6.11. The combined results for each outcome measure are demonstrated in Figure 6.2 through to Figure 6.5.

The first literature search was in regard to the AOFAS. A total of three articles were identified from the search, of which three were excluded because they did not report either the development of the outcome measure or any independent validation data that included patients who had sustained a TA rupture. On searching the reference lists of articles that had cited the AOFAS, all referred to one article from 1994 outlining the development of the score, which was included.

Figure 6.2: Search strategy results for AOFAS

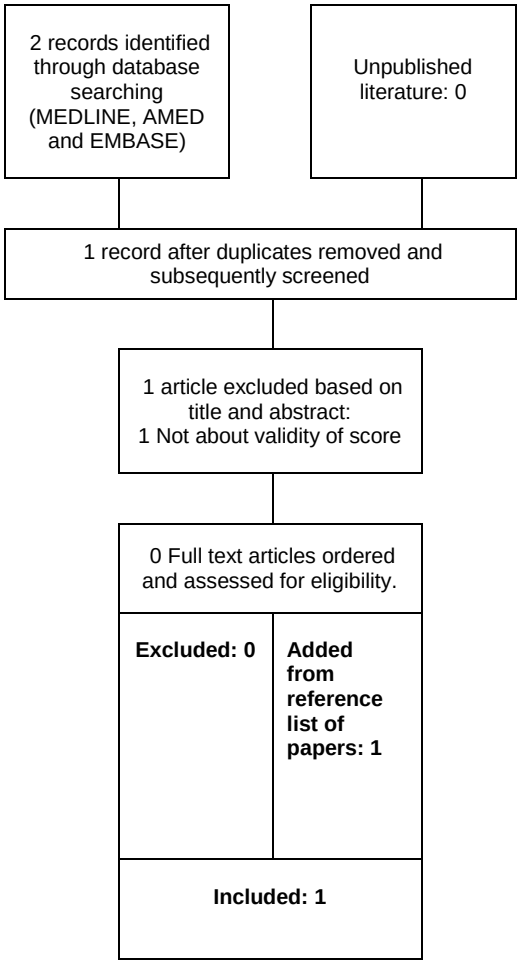

Figure 6.3: Search strategy results for Olerud and Molander ankle score

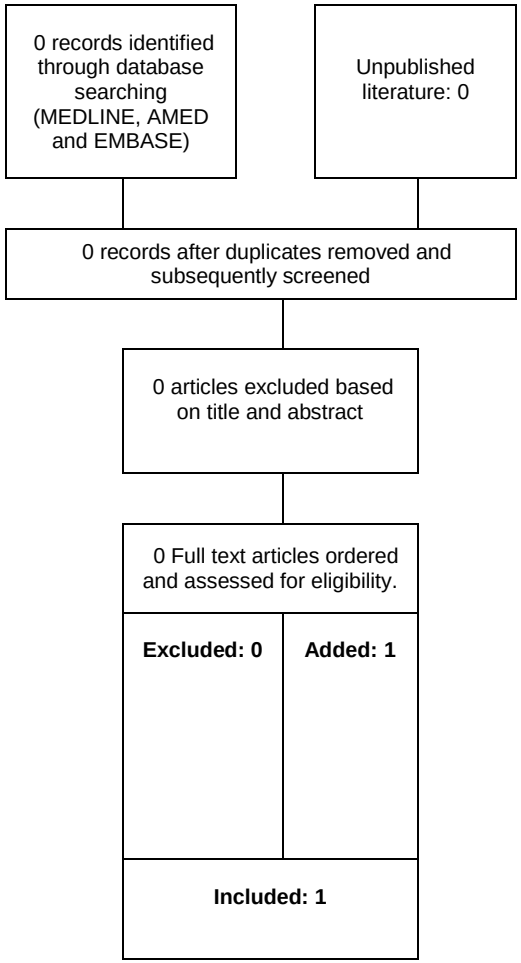

Figure 6.4: Search strategy results for Leppilahti Score

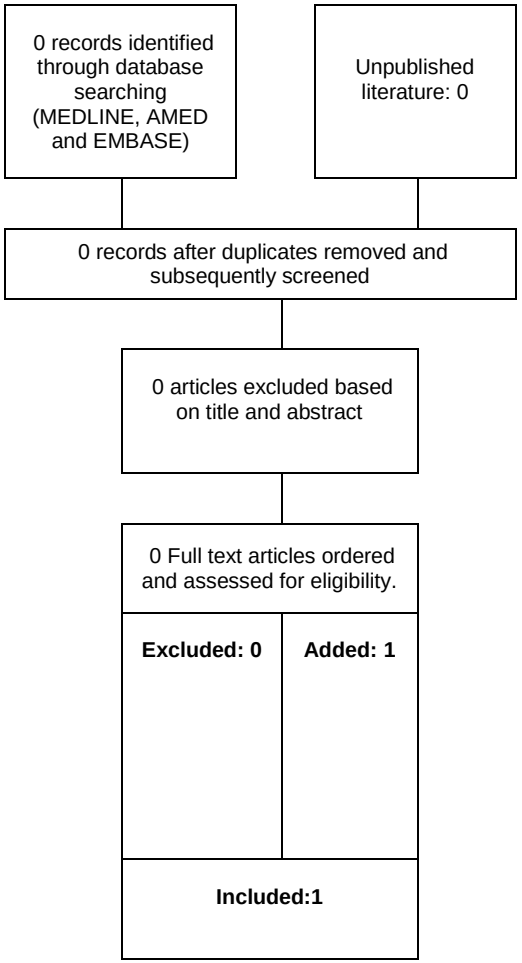

Figure 6.5: Search strategy results for ATRS

Table 6.9: Search strategy results: MEDLINE

	Search terms	Results
1	American Orthopaedic Foot and Ankle Society Hindfoot Score.mp	30
2	Leppilahti score.mp	2
3	Achilles tendon total rupture score.mp	2
4	Olerud and molander ankle score.mp	18
5	Content validity.mp	2092
6	Internal Consistency.mp	10302
7	Criterion Validity.mp	1254
8	Construct Validity.mp	7052
9	Reproducibility Agreement.mp	16
10	Reproducibility Reliability.mp	42
11	Responsiveness.mp	69424
12	Floor and Ceiling Effects.mp	365
13	Interpretability.mp	676
14	5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13	85889
15	1 AND 14	3
16	2 AND 14	0
17	3 AND 14	0
18	4 AND 14	1

Table 6.10: Search strategy results: AMED

	Search terms	Results
1	American Orthopaedic Foot and Ankle Society Hindfoot Score.mp	24
2	Leppilahti score.mp	0
3	Achilles tendon total rupture score.mp	1
4	Olerud and molander ankle score.mp	4
5	Content validity.mp	239
6	Internal Consistency.mp	976
7	Criterion Validity.mp	146
8	Construct Validity.mp	818
9	Reproducibility Agreement.mp	1
10	Reproducibility Reliability.mp	7
11	Responsiveness.mp	884
12	Floor and Ceiling Effects.mp	69
13	Interpretability.mp	29
14	5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13	2430
15	1 AND 14	0
16	2 AND 14	0
17	3 AND 14	0
18	4 AND 14	0

Table 6.11: Search strategy results: EMBASE

	Search terms	Results
1	American Orthopaedic Foot and Ankle Society Hindfoot Score.mp	29
2	Leppilahti score.mp	4
3	Achilles tendon total rupture score.mp	6
4	Olerud and molander ankle score.mp	22
5	Content validity.mp	2998
6	Internal Consistency.mp	12731
7	Criterion Validity.mp	1484
8	Construct Validity.mp	8866
9	Reproducibility Agreement.mp	21
10	Reproducibility Reliability.mp	51
11	Responsiveness.mp	80497
12	Floor and Ceiling Effects.mp	416
13	Interpretability.mp	862
14	5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13	101260
15	1 AND 14	3
16	2 AND 14	0
17	3 AND 14	0
18	4 AND 14	1

The second search was focused on the Olerud and Molander ankle fracture scoring system. A total of one article was identified from the search, this article was excluded because it did not report either the development of the outcome measure or any independent validation data that included patients who had sustained a TA rupture. On searching the reference lists of articles that had cited the Olerud and Molander ankle fracture scoring system, all referred to one article from 1984 outlining the development of the score, which was included.

The final two searches, encompassing the Leppilahti score and ATRS score identified no articles from the searches. One article reporting the development of the outcome measures was identified from the reference lists of citing articles for each outcome measure.

Consequently each outcome measure identified did not have any published independent validation data, within a population of patients who had sustained an acute Achilles tendon rupture, outside of the original development article. Each of these articles were subsequently assessed against the checklist proposed for measurement properties of health status questionnaires by Terwee *et al*[133]. The criteria definitions for this checklist can be found in Appendix I.

Table 6.12 summarises the results obtained from applying the checklist to the four articles outlining the development of the individual outcome measures. For the Leppilahti score and AOFAS no information was available beyond a description of the target population. The Olerud and Molander ankle score provided some additional information regarding criterion validity and interpretability; however this was not within the context of patients who had sustained a TA rupture.

In contrast to the other scores, the ATRS score did fulfil a higher proportion of the quality criteria. The ATRS scored six positive ratings across content validity, criterion validity, construct validity, reproducibility (agreement and reliability) and responsiveness; with two further scores of an intermediate rating within internal consistency and interpretability. There was no information regarding floor and ceiling effects.

Table 6.12: Quality criteria checklist

Name of outcome	*Content validity*		*Internal consistency*		*Criterion validity*		*Construct Validity*		*Reproducibility (agreement)*		*Reproducibility (reliability)*		*Responsiveness*		*Floor/ceiling effect*		*Interpretability*	
ATRS	+	Clear description of measurement aim, both target population and experts were involved in item selection and development	+	Factor analysis and Chronbach's alpha calculated	?	Correlation analysis demonstrated with another outcome measure. Doubt regarding appropriate 'gold standard'	+	Presented hypothesis and results for the extent to which the new outcome was consistent with another outcome	+	Data presented and discussed regarding measurement error and minimally important change	+	Evaluated the extent to which patients could be distinguished from each other	+	Effect sizes were presented	0	No Information available	?	Mean and standard deviation of scores presented, but not for different sub-groups
Leppilahti Score	-	Item selection developed by experts only	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available
AOFAS	-	Item selection developed by experts only	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available
Olerud Molander Ankle Score	-	Target population, ankle fractures, items developed by experts only	0	No Information available	?	Insufficient information regarding method of correlation analysis presented and 'gold standard'	0	No Information available	0	No Information available	0	No Information available	0	No Information available	0	No Information available	+	Different patient sub-groups presented

+ = Positive rating **? = Intermediate rating** **- = Negative rating** **0 = No information available**

6.3 Discussion

A universal choice of outcome measure used within clinical and research practice is imperative to allow comparisons across different treatment modalities to determine optimum management strategies. Therefore this chapter aimed to address two questions. Firstly, what is currently used, as defined by what is reported within the literature, and secondly are these outcome measures appropriate, as defined by the quality criteria outlined by Terwee *et al*[133].

Twenty one different multi-item outcome measures were identified from the first search strategies. This large range highlights the lack of agreement amongst researchers and clinicians regarding what should be reported. Furthermore this also makes comparisons across studies problematic. However, the most reported outcome was the AOFAS hind-foot score, being cited by 38% of all included articles.

Of the 21 identified outcome measures, only four cited independent validation data. Of these four outcome measures two contained both subjective and objective components (AOFAS and Leppilahti score). This split has been criticised because the clinical component could introduce bias due to differences between clinical examiners and secondly does not provide any additional information regarding treatment benefit from the patient's perspective[134].

Three of the four outcome measures also lacked methodology regarding their development, consisting of expert discussion only. This is in contrast to the development of the ATRS which utilised a systematic method of item generation, test construction and item reduction, using a range of health care professionals and comments from patients. Furthermore the ATRS was the only score to present validation data across a range of quality criteria.

Consequently although the AOFAS is the most widely cited outcome measure within the literature regarding TA rupture management, it has no independent validation data to support its use. There have been further validation papers published within different patient populations to provide aspects of validity for the AOFAS. These have included investigating correlations with the SF-36 and other generic measures such as EQ-5D. However these have shown only weak correlations and have raised concern regarding the use of AOFAS in these other patient populations that are included in this region specific outcome measure[58,135].

In contrast, the ATRS was only cited in 6% of the included articles, which may be a reflection of its recent development (first published 2007). However the development article presents data on many important aspects of validity, including content, internal consistency, criterion validity, construct validity, reliability, responsiveness and interpretability. This is the only disease specific PROM with accompanying exploration of aspects of validity presented in this review.

It is important for the development of clinical research that both a practical and appropriate PROM is universally accepted. This will allow comparisons and meta-analysis of high quality RCTs possible into this increasingly common injury. At present the best available evidence suggests that the ATRS could be the most appropriate outcome measure for evaluating the management of acute TA ruptures.

However, the ATRS is a new patient reported outcome measure that has been evaluated within a single sample, three months post injury. Consequently further studies evaluating the validity, reliability and responsiveness of this outcome measure are required outside the developing research group. This is needed across a range of patients, at differing points in their rehabilitation.

7 Validation: The Achilles tendon Total Rupture Score (ATRS)

Declarations

This study contains data previously published for a separate clinical trial, not part of this thesis. This data was collected by me in addition to my involvement with the implementation, analysis, final write-up and subsequent published article:

Kearney R, J Achten, N Parsons, M Costa, The comprehensive cohort model in a pilot trial in orthopaedic trauma. *BMC Medical Research Methodology,* 11, 2011, p.11-39.

This study has been published:

Kearney R, S Lamb, N Parsons, J Achten, M Costa, The Achilles tendon Total Rupture Score: A Study of Responsiveness, Internal Consistency and Convergent Validity on Patients with Acute Achilles tendon Ruptures, Health and Quality of Life Outcomes (*In Press*)

This study has been presented at a national conference for presentation:

May 2012*: European Federation of National Associations of Orthopaedics and Traumatology:* The Achilles tendon Total Rupture Score: A Study to Explore Further Aspects of Validity.

Sponsorship

This study is jointly sponsored by the University of Warwick and University Hospitals Of Coventry and Warwickshire NHS Trust

Ethics Committee Approval Date

23rd August 2007

Funding Body

This study was funded by Arthritis Research UK

Table of Contents

Abstract

Background
The Achilles tendon Total Rupture Score was first developed in 2007 in response to the need for a disease specific patient reported outcome measure for this population. Beyond this original development paper, no further validation studies have been published.

Objectives
The purpose of this study was to evaluate internal consistency, criterion validity, construct validity and responsiveness of the Achilles tendon Total Rupture Score within a UK population.

Methods
Between August 2007 and June 2009, 70 consecutive patients were screened and 64 eligible patients with an acute rupture of their Achilles tendon completed the Achilles tendon Total Rupture Score alongside two further patient reported outcome measures, the Disability Rating Index and EQ-5D. These were completed at baseline, six weeks, three months, six months and nine months post injury.

The Achilles tendon Total Rupture Score was evaluated for internal consistency using Cronbach's alpha, in addition to criterion and construct validity through correlation analysis. Finally responsiveness of the score was evaluated by analysing floor and ceiling effects and calculating its relative efficiency in comparison to the Disability Rating Index and EQ-5D scores at defined time points.

Results
At each time point the Achilles tendon Total Rupture Score demonstrated high internal consistency (Cronbachs alpha > 0.8) and correlated significantly ($p<0.001$) with the Disability Rating Index. Furthermore, the ability of the new score to detect clinically important changes over time (responsiveness) was shown to be greater than both the Disability Rating Index and EQ-5D.

Conclusions
The Achilles tendon Total Rupture Score has been advocated as the only validated PROM available for use with patients following an Achilles tendon rupture. However beyond the original development paper, no further validation studies have been published.

This is the first study to evaluate aspects of validity of this newly developed outcome measure, outside of the developing centre. This research supports further aspects of validity of the newly developed patient reported outcome measure for patients who have sustained a rupture of their Achilles tendon.

7.1 Protocol

Chapter 6 outlined that there are a range of region specific and disease specific outcome measures used to evaluate TA rupture management[57-60]. The region specific outcomes have been criticised for lacking discriminatory validity, and being validated against a sample of patients with a range of foot and ankle pathologies that do not specifically include patients with TA ruptures[61]. Of the identified disease specific outcome measures, only the newly developed ATRS presented validation data across a range of quality criteria as defined by Terwee *et al*[61].

The ATRS contains 10 items, for which patients are asked to respond using an 11 point Likert scale. The authors of the ATRS detailed the methods used to generate the final measure, through a panel of wide ranging experts and patients. This process addressed the content and face validity of the new outcome score. Following the agreed content of the final measure, further facets of validity were evaluated including test-re-test reliability, internal consistency and responsiveness. Finally, elements of construct validity between the overall ATRS score and subscales of the FAOS and VISA-A measures were evaluated, alongside factor analysis to determine how many dimensions the new ATRS measured.

However, a newly developed PROM cannot be deemed 'valid' based on a single sample, within a single country alone. The processes involved in developing a PROM have been widely discussed and have resulted in published quality criteria checklists, to quantify the extent to which the developed measures have been investigated. The checklist published by Terwee *et al*[133] is one such example. The checklist comprises of quality criteria including content validity, internal consistency, criterion validity, reproducibility (agreement and reliability), responsiveness, floor/ceiling effects and interpretability. These elements of outcome measure

construction are also consistent with those reported by the HTA, within their document entitled *'Evaluating patient-based outcome measures for use in clinical tri*als'[131].

Chapter 6 highlighted which of these quality criteria had been investigated within the original ATRS development paper. The aim of this study was to evaluate further components of validity within a UK sample across all age ranges at immediate, as well as longer term outcome points. This will address the following specific aspects of validity:

1. Internal consistency
2. Criterion (concurrent) validity
3. Construct (divergent and convergent)validity
4. Responsiveness at six weeks, three, six and nine months post injury.

7.1.1 Objectives and null Hypotheses

The primary objectives of this chapter are to evaluate further aspects of validity of the ATRS to address the following null hypotheses:

1. *Internal Consistency*: There are no inter-correlations between individual items of the ATRS, as defined by a Cronbach alpha of less than 0.7.
2. *Criterion Validity:* There is no correlation between the overall score of the ATRS and the DRI questionnaire as defined by a correlation coefficient of less than 0.7.
3. *Construct Validity*: There is no correlation between the overall ATRS score when compared to measures of similar constructs of symptoms and physical activity as defined by a correlation coefficient of less than 0.7.

4. *Responsiveness*: There are no floor or ceiling effects, as defined by <15% of respondents achieving the highest/lowest scores and the relative efficiency will be less than one when compared to the DRI and EQ-5D measures.

7.1.2 Trial summary and trial flow diagram

All patients who presented to the University Hospitals Coventry and Warwickshire NHS Trust fracture clinic with an acute rupture of their TA were screened. The only eligibility criteria were that they had no other serious injuries to either lower limb, previous history of tendon rupture, or inability to read English. These broad eligibility criteria were used to ensure that the results of the study could be readily generalised to the wider population, whom this outcome measure would be used for.

Following ethical approval, a consecutive series of 64 patients, whether treated operatively or non-operatively, were placed in an IWB AFO for eight weeks and attended clinic for routine clinical follow up every two weeks, for twelve weeks, then at six and nine months. Initially patients were asked to complete three questionnaires (ATRS, DRI and EQ-5D) based on pre-injury status. This was then followed by the same questionnaires at the defined follow up time points (Figure 7.1).

Following recruitment and follow up of the consecutive series of patient's, descriptive and inferential statistical methods were carried out using SPSS v.17 and Microsoft Excel 2007. Internal consistency was evaluated using Cronbachs alpha. Criterion validity was assessed by correlation coefficients between the overall DRI and ATRS scores. Construct validity was evaluated by correlation coefficients between the overall ATRS score and subscales of DRI (1: common basic activities, 2: more demanding physical activities, 3: work related or more vigorous activities)

and EQ-5D scores. Finally, responsiveness was evaluated by evaluating floor and ceiling effects alongside the relative efficiency of the ATRS in comparison to the DRI and EQ-5D.

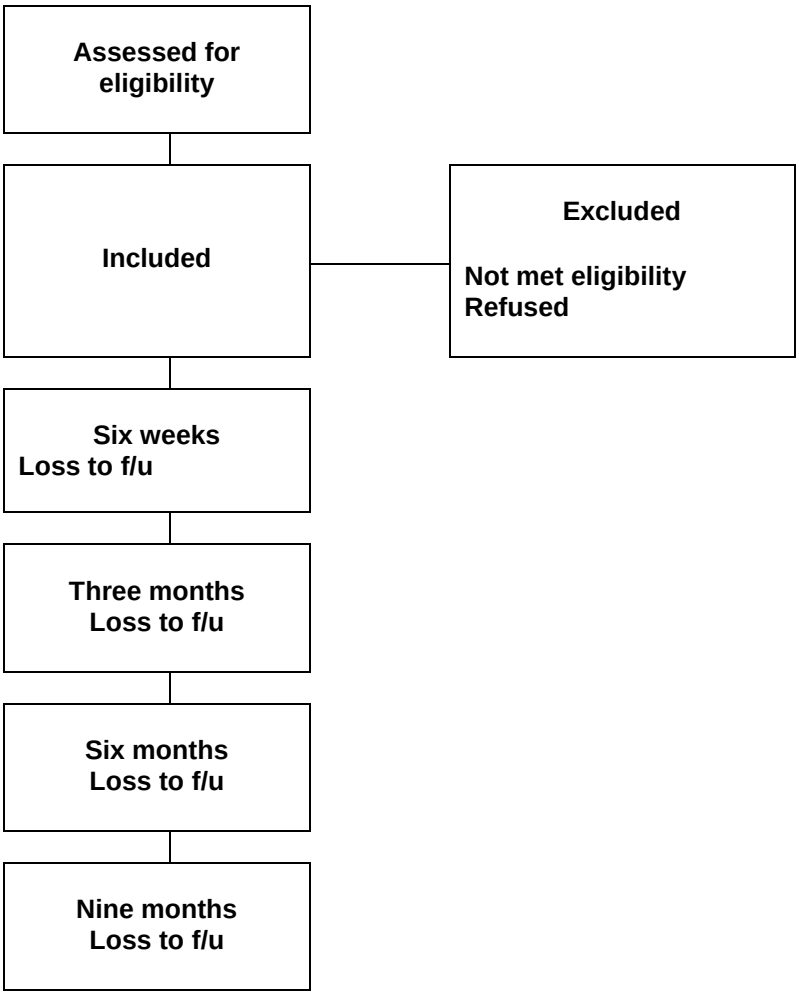

Figure 7.1: Expected flow of participants through the trial

7.1.3 Eligibility and recruitment

All patients over 18 years presenting at the University Hospitals of Coventry and Warwickshire fracture clinic with a primary acute rupture of their TA (less than ten days) were eligible. A TA rupture was diagnosed by the consultant within the fracture clinic by subjective history and physical examination confirming a palpable gap and a positive Thompson test[126].

Patients presenting after ten days from injury, or with a history of previous tendon rupture, were excluded. Patients who had other serious injuries to either lower limb at the time of rupture that would alter the intervention and subsequent rehabilitation were also excluded. In addition to these, patients who were unable to read English and were therefore unable to complete the questionnaires were excluded also.

Once eligible patients had consented to complete the questionnaires, they attended routine clinical follow up every two weeks for twelve weeks and finally six and nine months. At these routine clinics they were reviewed by the orthopaedic consultant, as necessary. In the event of a patient not attending fracture clinic a letter outlining a rescheduled appointment was sent, as per routine practice. If there was no contact within four weeks from the participant they were discharged and recorded as lost to follow up.

7.1.4 Sample size

The department's statistician was consulted regarding appropriate sample sizes for the five null hypotheses, in addition to the review of appropriate literature. There was a consensus amongst the literature that there are no standards for determining sample sizes for validation research of patient reported outcome measures[133]. This is secondary to the descriptive nature of the interpretation. However a sample size

of over 50 patients has been advocated as the minimum requirement[134]. The sample was subsequently collected as part of a previously published comprehensive cohort study[66].

7.1.5 Evaluation and analysis

As outlined in the introduction to this chapter, there is some consensus regarding terminology used in reference to aspects of validity. However, these can vary between publications. Therefore, for the purposes of this study the definitions of each term evaluated are outlined below. These definitions are consistent with an article published in 1998 entitled *'Evaluating patient-based outcome measures for use in clinical trials'*[131] and the quality criteria for measurement properties by Terwee *et al*[133].

Internal Consistency: The ATRS evaluates a single construct of symptoms and physical activity measured through a patient's response to ten individual questions. The reason for multiple items that assess the same construct is based on the principle that multiple measurements of the same construct will provide a more reliable measure than if one question were asked[136]. Consequently, we assume that items on a scale are positively correlated with each other because they are all evaluating the same construct. Internal consistency was evaluated using Cronbach's alpha at each time point within SPSS (v.17.0). Values between 0.7 and 0.9 were regarded as satisfactory[136].

Criterion Validity: Criterion validity can be split into predictive and concurrent validity. This study evaluated concurrent validity. This is defined as how a new measure correlates with a current 'gold standard'. This was evaluated using

Spearman's rank correlation coefficients for non-parametric data and Pearson's correlation coefficient for parametric data at each time point.

As there are no previous PROMs specific to acute TA ruptures, the 'gold standard' used within our practice was the DRI[127]. Although not disease specific, it has been validated within an orthopaedic clinic setting for a range of orthopaedic presentations. The DRI is a self-administered form with twelve questions regarding common physical activities, to which patients respond using a 100mm visual analogue scale. There are two anchor points 'without difficulty = 0' and 'not at all = 100'. The twelve questions are subdivided into three broad categories; common basic activities of daily life, more demanding daily physical activities and work related or more vigorous activities (Appendix F). The expected size of the correlation when a measure is correlated against a 'gold standard' has been defined as being of at least 0.7[133].

Construct Validity: The ATRS has been shown to measure one construct defined as 'symptoms and physical activity', as determined by factor analysis. To further evaluate construct validity, the overall ATRS scores will be evaluated to determine how strongly it correlates with measures of the same construct and measures evaluating different constructs. This will be achieved by firstly evaluating correlation coefficients between the overall ATRS score and subscales of the DRI, which measure three constructs of differing levels of physical activity. Secondly correlation coefficients will also be analysed between the ATRS and EQ-5D, which is a generic quality of life measure (Appendix G). This was achieved using Spearman's rank correlation coefficient for non-parametric data and Pearson's correlation coefficient for parametric data within SPSS (v 17.0) at each time point. The expected size of the correlation was again defined as being of at least 0.7[133].

Responsiveness: This is defined as the ability of the measurement to detect change across time. There are many methods associated with measuring this facet, as outlined by the HTA report[131]. For the ATRS to be responsive it needs to demonstrate a lack of floor and ceiling effects, subsequently demonstrating a distribution of scores around the middle score. Therefore to evaluate responsiveness of the ATRS, the floor and ceiling effects were firstly evaluated and defined as being present if more than 15% of respondents achieved the lowest or highest possible scores[133]. This was followed by a relative efficiency calculation to analyse responsiveness of the ATRS versus the EQ-5D and DRI, according to Barr *et al*[137]*.* Using this method a score of greater than one would indicate the ATRS was more responsive than the EQ-5D and DRI, conversely a score less than one would indicate the ATRS to be less responsive than the EQ-5D and DRI.

7.1.6 End of study

The end of the study was defined as the final visit to the clinic of the last participant.

7.1.7 Data management

The questionnaires were compiled by the researcher in conjunction with the lead PhD Supervisor (Mr Matthew Costa) who is also the clinical lead for this service.

All electronic patient-identifiable information was held on a secure, password-protected database accessible only to essential personnel, as per standard operating procedures for Warwick University. Patients were identified by a code number only. Data was entered by the research physiotherapist onto the electronic database immediately following each research clinic.

Direct access to source data/documents was required for clinical governance and by the research team for data entry and analysis only. All paper and electronic data would to be retained for at least five years after completion of the study. Additionally, as part of ongoing PhD supervision, the supervisors had reviewed this protocol for this study and have received progress reports at their request.

Accumulating data was monitored at frequent intervals to identify and facilitate the early remedial action of certain problems that may include data collection and compliance. Yearly progress reports were also submitted to the funders of this project (Arthritis Research UK), as outlined within the terms and conditions of the awarded grant.

The day to day management of the project was carried out by the researcher and overseen by the PhD supervisors. Financial support for this project had been awarded by Arthritis Research UK. Treatment costs associated with this study had been reviewed by the NHS research and development department. The project timetable and milestones are outlined in Table 7.1.

Table 7.1: Project timetable

Number of Months	0	6	12	18	24	30	36	42
Tasks to be completed	Aug 07	Feb 08	Aug 08	Feb 09	Aug 09	Feb 10	Aug 10	Feb 11
Prepare and refine materials								
Recruitment								
Finish all data collection								
Analysis								
Write-up and report								

7.2 Results

Recruitment took place between August 2007 and June 2009. During this time 70 midsubstance TA ruptures presented to the fracture clinic. Of these 70 patients, three did not meet the eligibility criteria because they were unable to complete the questionnaires. A further three patients were eligible and refused to complete the questionnaires.

The remaining 64 patients completed the ATRS, DRI and EQ-5D questionnaires at six weeks, three months, six months and nine months. At the six week time point one patient was lost to follow up, therefore 63 (98%) patients were followed up, followed by 60 (94%) patients at three months, 58 (91%) at six months and 56 (88%) at nine months.

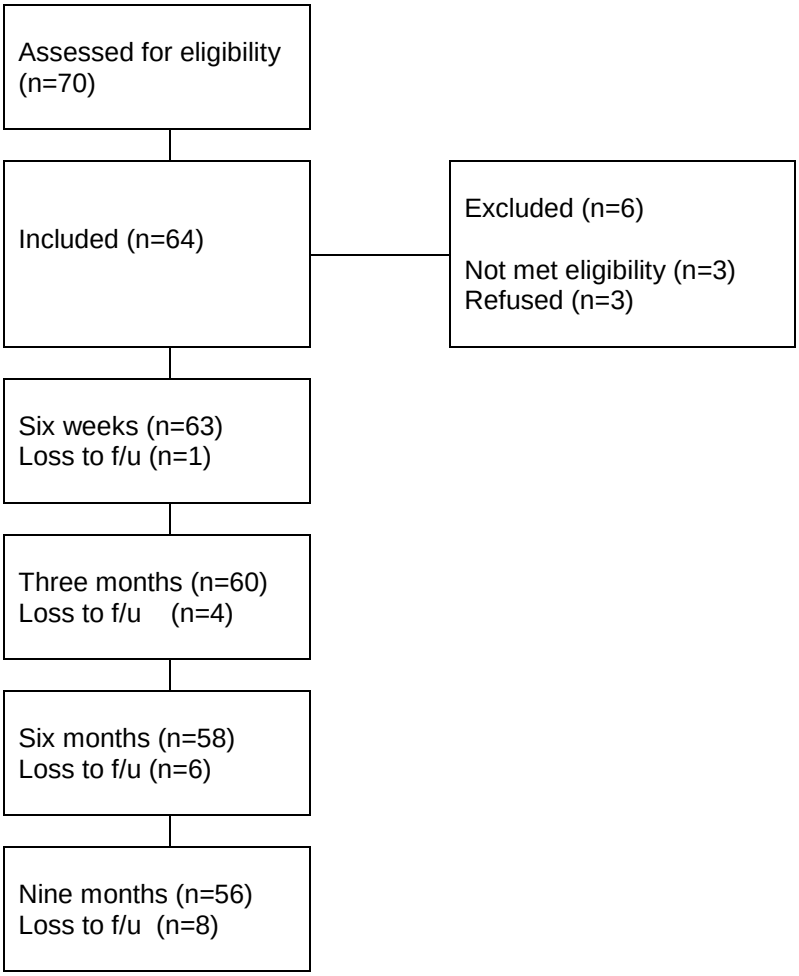

Figure 7.2: Flow of participants throughout the trial period

The baseline demographics of the included patients are presented in Table 7.2. These demographics illustrate that this sample is consistent with the current literature, identifying the male, 30-40 year age group the most likely to sustain this injury. There was an even distribution of left and right feet affected and the majority received non-operative management.

Table 7.2: Patient demographics

	Baseline demographics
Mean age in years (SD)	44 years (12)
Male/Female	48/16
Left/Right	34/30
Mean height in cm (SD)	172cm (10)
Mean weight in Kg (SD)	80Kg (17)
Management (Op/Non-Op)	19/45

7.2.1 Analysis: Descriptive

Table 7.3 through to Table 7.7 illustrate the minimum, maximum, mean, standard deviation, median and inter-quartile ranges for the overall scores of the ATRS, DRI and EQ-5D, and for the individual items within each questionnaire that together form the overall score.

The tables illustrate how the three overall outcome measures demonstrate a gradual return to pre-injury scores over the nine month time period. Over this nine month period overall scores from the ATRS ranged from 2 to 100, DRI ranged from 0 to 81 and EQ-5D ranged from 0.12 to 1. The standard deviations across all time points of the overall ATRS scores ranged from 16 to 23, DRI ranged from 12 to 17 and EQ-5D from 0.09 to 0.19. The standard deviation amongst the individual items that formed each score ranged from 1 to 4 within the ATRS and DRI, which are both measured on a ten point scale. The items with the larger standard deviations were those asked at the six and nine month time points within the items regarding heavier/higher impact activities such as heavy work, return to sports, jumping and running.

Table 7.3: Descriptive statistics for ATRS, DRI and EQ-5D pre-injury scores

Q.	Item	n =	Min	Max	Mean	SD	Med	IQR
	Overall ATRS Score	**64**	**7**	**100**	**91**	**21**	**100**	**5**
1	Are you limited because of decreased strength in the calf/Achilles tendon/foot?	64	1	10	9	2	10	0
2	Are you limited because of fatigue in the calf/Achilles tendon/foot?	64	1	10	9	2	10	0
3	Are you limited due to stiffness in the calf/Achilles tendon/foot?	64	1	10	9	2	10	0
4	Are you limited because of pain in the calf/Achilles tendon/foot?	64	1	10	9	2	10	0
5	Are you limited during activities of daily living?	64	1	10	9	2	10	0
6	Are you limited when walking on uneven surfaces?	64	1	10	9	2	10	0
7	Are you limited when walking quickly upstairs or uphill?	64	1	10	9	2	10	0
8	Are you limited during activities that include running?	64	0	10	9	3	10	1
9	Are you limited during activities that include jumping	64	0	10	9	3	10	1
10	Are you limited in performing hard physical labour	64	0	10	9	3	10	0
	Overall DRI Score	**64**	**0**	**65**	**6**	**13**	**1**	**5**
1	Dressing (without help)	64	0	5	0	1	0	0
2	Out-door walks	64	0	8	0	1	0	0
3	Climbing Stairs	64	0	7	0	1	0	0
4	Sitting longer time	64	0	5	0	1	0	0
5	Standing bent over a sink	64	0	9	1	2	0	0
6	Carrying a bag	64	0	6	0	1	0	0
7	Making a bed	64	0	6	0	1	0	0
8	Running	64	0	10	1	3	0	1
9	Light work	64	0	6	0	1	0	0
10	Heavy work	64	0	10	1	2	0	0
11	Lifting heavy objects	64	0	10	1	3	0	0
12	Participating in exercise/sports	64	0	10	1	2	0	0
	Overall EQ-5D	**64**	**0.64**	**1**	**0.96**	**0.09**	**1.00**	**0.00**
1	Mobility	64	1	2	1	0	1	0
2	Self-care	64	1	2	1	0	1	0
3	Usual activities	64	1	2	1	0	1	0
4	Pain and Discomfort	64	1	2	1	0	1	0
5	Anxiety and Depression	64	1	2	1	0	1	0

Table 7.4: Descriptive statistics for ATRS, DRI and EQ-5D recorded at six weeks

Q.	Item	n =	Min	Max	Mean	SD	Med	IQR
	Overall ATRS Score	**63**	**5**	**88**	**35**	**19**	**35**	**25**
1	Are you limited because of decreased strength in the calf/Achilles tendon/foot?	63	0	10	4	3	3	5
2	Are you limited because of fatigue in the calf/Achilles tendon/foot?	63	0	10	4	3	5	5
3	Are you limited due to stiffness in the calf/Achilles tendon/foot?	63	0	10	5	3	4	5
4	Are you limited because of pain in the calf/Achilles tendon/foot?	63	0	10	6	3	7	5
5	Are you limited during activities of daily living?	63	1	10	5	3	5	5
6	Are you limited when walking on uneven surfaces?	63	0	10	4	3	3	4
7	Are you limited when walking quickly upstairs or uphill?	63	0	10	3	3	3	4
8	Are you limited during activities that include running?	63	0	10	1	2	0	1
9	Are you limited during activities that include jumping	63	0	10	1	2	0	1
10	Are you limited in performing hard physical labour	63	0	10	2	2	1	2
	Overall DRI Score	**63**	**0**	**81**	**41**	**17**	**39**	**23**
1	Dressing (without help)	63	0	7	1	1	1	1
2	Out-door walks	63	0	10	4	3	4	4
3	Climbing Stairs	63	0	9	3	2	2	4
4	Sitting longer time	63	0	8	1	2	0	3
5	Standing bent over a sink	63	0	9	2	2	1	3
6	Carrying a bag	63	0	10	2	3	1	4
7	Making a bed	63	0	9	2	2	1	3
8	Running	63	0	10	9	2	10	0
9	Light work	63	0	10	3	3	2	5
10	Heavy work	63	0	10	7	3	8	5
11	Lifting heavy objects	63	0	10	7	4	9	7
12	Participating in exercise/sports	63	0	10	9	3	10	1
	Overall EQ-5D	**63**	**0.12**	**1.00**	**0.70**	**0.19**	**0.69**	**0.23**
1	Mobility	63	1	2	2	0	2	1
2	Self-care	63	1	2	1	0	1	1
3	Usual activities	63	1	3	2	1	2	0
4	Pain and Discomfort	63	1	3	2	1	1	1
5	Anxiety and Depression	63	1	2	1	0	1	0

Table 7.5: Descriptive statistics for ATRS, DRI and EQ-5D recorded at three months

Q.	Item	n =	Min	Max	Mean	SD	Med	IQR
	Overall ATRS Score	**60**	**2**	**71**	**40**	**16**	**38**	**24**
1	Are you limited because of decreased strength in the calf/Achilles tendon/foot?	60	1	9	4	2	5	4
2	Are you limited because of fatigue in the calf/Achilles tendon/foot?	60	0	10	5	3	5	4
3	Are you limited due to stiffness in the calf/Achilles tendon/foot?	60	0	10	5	2	5	4
4	Are you limited because of pain in the calf/Achilles tendon/foot?	60	0	10	6	3	7	4
5	Are you limited during activities of daily living?	60	0	10	6	2	6	4
6	Are you limited when walking on uneven surfaces?	60	0	10	5	3	5	4
7	Are you limited when walking quickly upstairs or uphill?	60	0	10	4	2	4	4
8	Are you limited during activities that include running?	60	0	5	1	1	0	1
9	Are you limited during activities that include jumping	60	0	4	0	1	0	1
10	Are you limited in performing hard physical labour	60	0	7	2	2	2	2
	Overall DRI Score	**60**	**0**	**79**	**33**	**15**	**33**	**20**
1	Dressing (without help)	60	0	5	0	1	0	0
2	Out-door walks	60	0	10	3	2	2	5
3	Climbing Stairs	60	0	8	2	2	2	4
4	Sitting longer time	60	0	8	1	2	0	0
5	Standing bent over a sink	60	0	8	1	2	0	1
6	Carrying a bag	60	0	8	1	2	0	1
7	Making a bed	60	0	8	1	2	0	2
8	Running	60	0	10	9	2	10	0
9	Light work	60	0	8	2	2	1	3
10	Heavy work	60	0	10	6	3	6	6
11	Lifting heavy objects	60	0	10	6	3	5	6
12	Participating in exercise/sports	60	0	10	8	3	10	4
	Overall EQ-5D	**60**	**0.52**	**1.00**	**0.76**	**0.11**	**0.69**	**0.12**
1	Mobility	60	1	2	2	0	2	1
2	Self-care	60	1	2	1	0	1	0
3	Usual activities	60	1	3	2	1	2	0
4	Pain and Discomfort	60	1	2	2	1	2	1
5	Anxiety and Depression	60	1	2	1	0	1	0

Table 7.6: Descriptive statistics for ATRS, DRI and EQ-5D recorded at six months

Q.	Item	n =	Min	Max	Mean	SD	Med	IQR
	Overall ATRS Score	58	15	100	66	23	**72**	**41**
1	Are you limited because of decreased strength in the calf/Achilles tendon/foot?	58	1	10	7	2	7	4
2	Are you limited because of fatigue in the calf/Achilles tendon/foot?	58	2	10	7	3	8	4
3	Are you limited due to stiffness in the calf/Achilles tendon/foot?	58	1	10	7	2	8	3
4	Are you limited because of pain in the calf/Achilles tendon/foot?	58	1	10	8	3	9	4
5	Are you limited during activities of daily living?	58	1	10	8	2	9	3
6	Are you limited when walking on uneven surfaces?	58	1	10	8	3	9	4
7	Are you limited when walking quickly upstairs or uphill?	58	1	10	7	3	8	5
8	Are you limited during activities that include running?	58	0	10	4	4	5	7
9	Are you limited during activities that include jumping	58	0	10	4	3	4	6
10	Are you limited in performing hard physical labour	58	0	10	6	3	7	5
	Overall DRI Score	58	0	72	16	14	**15**	**17**
1	Dressing (without help)	58	0	1	0	0	0	0
2	Out-door walks	58	0	7	1	2	0	1
3	Climbing Stairs	58	0	7	1	1	0	1
4	Sitting longer time	58	0	9	0	2	0	0
5	Standing bent over a sink	58	0	5	0	1	0	0
6	Carrying a bag	58	0	7	1	1	0	0
7	Making a bed	58	0	10	1	2	0	0
8	Running	58	0	10	5	4	5	8
9	Light work	58	0	7	1	1	0	0
10	Heavy work	58	0	10	2	3	1	5
11	Lifting heavy objects	58	0	10	2	3	1	3
12	Participating in exercise/sports	58	0	10	4	4	4	7
	Overall EQ-5D	58	0.43	1.00	0.87	0.14	**0.88**	**0.25**
1	Mobility	58	1	2	1	0	1	1
2	Self-care	58	1	1	1	0	1	0
3	Usual activities	58	1	3	1	1	1	1
4	Pain and Discomfort	58	1	2	1	1	1	1
5	Anxiety and Depression	58	1	2	1	0	1	0

Table 7.7: Descriptive statistics for ATRS, DRI and EQ-5D recorded at nine months

Q.	Item	n =	Min	Max	Mean	SD	Med	IQR
	Overall ATRS Score	**56**	**25**	**100**	**79**	**20**	**86**	**32**
1	Are you limited because of decreased strength in the calf/Achilles tendon/foot?	56	2	10	8	2	8	2
2	Are you limited because of fatigue in the calf/Achilles tendon/foot?	56	2	10	8	2	9	3
3	Are you limited due to stiffness in the calf/Achilles tendon/foot?	56	2	10	8	2	9	3
4	Are you limited because of pain in the calf/Achilles tendon/foot?	56	0	10	9	2	9	2
5	Are you limited during activities of daily living?	56	1	10	9	2	10	1
6	Are you limited when walking on uneven surfaces?	56	0	10	9	2	9	2
7	Are you limited when walking quickly upstairs or uphill?	56	0	10	8	2	9	2
8	Are you limited during activities that include running?	56	0	10	6	4	8	6
9	Are you limited during activities that include jumping	56	0	10	6	4	7	7
10	Are you limited in performing hard physical labour	56	0	10	8	3	9	3
	Overall DRI Score	**56**	**0**	**64**	**10**	**12**	**7**	**15**
1	Dressing (without help)	56	0	3	0	0	0	0
2	Out-door walks	56	0	4	1	1	0	0
3	Climbing Stairs	56	0	6	0	1	0	0
4	Sitting longer time	56	0	8	0	1	0	0
5	Standing bent over a sink	56	0	5	0	1	0	0
6	Carrying a bag	56	0	4	0	1	0	0
7	Making a bed	56	0	5	0	1	0	0
8	Running	56	0	10	4	4	2	8
9	Light work	56	0	5	0	1	0	0
10	Heavy work	56	0	9	1	2	0	2
11	Lifting heavy objects	56	0	10	2	3	0	1
12	Participating in exercise/sports	56	0	10	3	4	2	6
	Overall EQ-5D	**56**	**0.69**	**1.00**	**0.93**	**0.11**	**1.00**	**0.20**
1	Mobility	56	1	2	1	0	1	0
2	Self-care	56	1	1	1	0	1	0
3	Usual activities	56	1	2	1	0	1	0
4	Pain and Discomfort	56	1	2	1	0	1	0
5	Anxiety and Depression	56	1	2	1	0	1	0

7.2.2 Analysis: Internal consistency

The ATRS comprises of ten items that measure a single construct, 'symptoms and physical activity'. Consequently, we assume that all the items on a scale are positively correlated with each other because they are all evaluating the same construct. This concept can be evaluated using Cronbach's alpha at each time point, within SPSS (v.17.0). This is a reliability coefficient based on the average inter-item correlations. It is calculated using the following equation:

$$Cronbach's\ alpha = \frac{Nr}{1 + r\ (N - 1)}$$

Where N equals the number of items within the questionnaire and r is equal to the mean inter-item correlation. Based on this equation it is clear to see that the Cronbach's alpha will increase if either the number of items within the score is increased or the inter-item correlation increases.

The Cronbach's alpha results for the ATRS at each time point are shown in Table 7.8. It demonstrates that the ATRS outcome measure displays an acceptable level of internal consistency, as defined as a value above 0.7[136].

Table 7.9 through to Table 7.13 show the inter-item correlation matrix's for each time point. They illustrate how each item correlates with each other. For example, item one compared to item one has a correlation coefficient of one, as expected. These tables also show how the Cronbach's alpha would alter if a single item were deleted from the ATRS measurement tool.

Table 7.8: Cronbach's alpha for ATRS at each time point

Time point	Cronbach's alpha
Pre-injury	0.98
Six weeks	0.89
Three months	0.89
Six months	0.95
Nine months	0.94

The results of these tables consistently show, across all time points, that deletion of any single item only changes the internal consistency by a maximum of 0.03. Evaluating the inter-item correlation matrix's it is clear that items eight, nine and ten at the six week and three month time points correlate less with items one to seven. This would be expected at these time points, because these items measure jumping, running and hard physical labour that patients would not be expected to be doing at these time points. The inter-item correlations of items eight, nine and ten are more highly correlated with the remaining ten items at the six and nine month time points. At these time points the assessed patients would be expected to be performing these activities.

Table 7.9: Pre-injury inter-item correlation matrix and example of Cronbach's alpha result if a single item were deleted

	1	2	3	4	5	6	7	8	9	10	If deleted
1	1.00	0.96	0.89	0.93	0.90	0.94	0.95	0.80	0.81	0.87	0.98
2	0.96	1.00	0.92	0.93	0.90	0.95	0.94	0.79	0.75	0.80	0.98
3	0.89	0.92	1.00	0.92	0.85	0.91	0.85	0.70	0.68	0.79	0.98
4	0.93	0.93	0.92	1.00	0.81	0.89	0.86	0.70	0.70	0.75	0.98
5	0.90	0.90	0.85	0.81	1.00	0.91	0.95	0.82	0.79	0.88	0.98
6	0.94	0.95	0.91	0.89	0.91	1.00	0.95	0.81	0.81	0.85	0.98
7	0.95	0.94	0.85	0.86	0.95	0.95	1.00	0.86	0.85	0.89	0.98
8	0.80	0.79	0.70	0.70	0.82	0.81	0.86	1.00	0.94	0.83	0.98
9	0.81	0.75	0.68	0.70	0.79	0.81	0.85	0.94	1.00	0.88	0.98
10	0.87	0.80	0.79	0.75	0.88	0.85	0.89	0.83	0.88	1.00	0.98

Table 7.10: Six week inter-item correlation matrix and example of Cronbach's alpha result if a single item were deleted

	1	2	3	4	5	6	7	8	9	10	If deleted
1	1.00	0.80	0.61	0.47	0.59	0.57	0.60	0.27	0.24	0.24	0.87
2	0.80	1.00	0.84	0.62	0.58	0.58	0.57	0.30	0.25	0.23	0.87
3	0.61	0.84	1.00	0.63	0.48	0.49	0.39	0.21	0.14	0.10	0.88
4	0.47	0.62	0.63	1.00	0.65	0.49	0.43	0.20	0.13	0.31	0.88
5	0.59	0.58	0.48	0.65	1.00	0.47	0.60	0.07	0.06	0.40	0.88
6	0.57	0.58	0.49	0.49	0.47	1.00	0.81	0.25	0.26	0.37	0.87
7	0.60	0.57	0.39	0.43	0.60	0.81	1.00	0.44	0.45	0.55	0.87
8	0.27	0.30	0.21	0.20	0.07	0.25	0.44	1.00	0.84	0.63	0.89
9	0.24	0.25	0.14	0.13	0.06	0.26	0.45	0.84	1.00	0.68	0.89
10	0.24	0.23	0.10	0.31	0.40	0.37	0.55	0.63	0.68	1.00	0.89

Table 7.11: Three month inter-item correlation matrix and example of Cronbach's alpha result if a single item were deleted

	1	2	3	4	5	6	7	8	9	10	If deleted
1	1.00	0.79	0.64	0.33	0.50	0.58	0.55	0.30	0.30	0.30	0.87
2	0.79	1.00	0.73	0.55	0.53	0.63	0.58	0.13	0.15	0.31	0.86
3	0.64	0.73	1.00	0.49	0.54	0.65	0.65	0.18	0.13	0.24	0.87
4	0.33	0.55	0.49	1.00	0.66	0.58	0.47	0.02	0.03	0.39	0.88
5	0.50	0.53	0.54	0.66	1.00	0.70	0.48	0.10	0.10	0.39	0.87
6	0.58	0.63	0.65	0.58	0.70	1.00	0.80	0.15	0.12	0.49	0.86
7	0.55	0.58	0.65	0.47	0.48	0.80	1.00	0.32	0.29	0.54	0.86
8	0.30	0.13	0.18	0.02	0.10	0.15	0.32	1.00	0.92	0.31	0.89
9	0.30	0.15	0.13	0.03	0.10	0.12	0.29	0.92	1.00	0.34	0.89
10	0.30	0.31	0.24	0.39	0.39	0.49	0.54	0.31	0.34	1.00	0.88

Table 7.12: Six month inter-item correlation matrix and example of Cronbach's alpha result if a single item were deleted

	1	2	3	4	5	6	7	8	9	10	If deleted
1	1.00	0.79	0.73	0.61	0.63	0.56	0.65	0.66	0.66	0.65	0.94
2	0.79	1.00	0.79	0.69	0.67	0.57	0.69	0.60	0.57	0.81	0.94
3	0.73	0.79	1.00	0.72	0.79	0.62	0.69	0.49	0.42	0.65	0.94
4	0.61	0.69	0.72	1.00	0.82	0.73	0.73	0.49	0.40	0.72	0.94
5	0.63	0.67	0.79	0.82	1.00	0.82	0.86	0.56	0.46	0.72	0.94
6	0.56	0.57	0.62	0.73	0.82	1.00	0.85	0.58	0.47	0.74	0.94
7	0.65	0.69	0.69	0.73	0.86	0.85	1.00	0.68	0.57	0.74	0.94
8	0.66	0.60	0.49	0.49	0.56	0.58	0.68	1.00	0.93	0.65	0.94
9	0.66	0.57	0.42	0.40	0.46	0.47	0.57	0.93	1.00	0.59	0.95
10	0.65	0.81	0.65	0.72	0.72	0.74	0.74	0.65	0.59	1.00	0.94

Table 7.13: Nine month inter-item correlation matrix and example of Cronbach's alpha result if a single item were deleted

	1	2	3	4	5	6	7	8	9	10	If deleted
1	1.00	0.86	0.81	0.57	0.69	0.69	0.73	0.71	0.70	0.73	0.92
2	0.86	1.00	0.92	0.65	0.69	0.68	0.73	0.60	0.56	0.79	0.92
3	0.81	0.92	1.00	0.60	0.71	0.64	0.74	0.61	0.54	0.74	0.92
4	0.57	0.65	0.60	1.00	0.70	0.44	0.57	0.28	0.32	0.50	0.94
5	0.69	0.69	0.71	0.70	1.00	0.70	0.82	0.34	0.32	0.57	0.93
6	0.69	0.68	0.64	0.44	0.70	1.00	0.79	0.52	0.51	0.69	0.93
7	0.73	0.73	0.74	0.57	0.82	0.79	1.00	0.53	0.51	0.65	0.93
8	0.71	0.60	0.61	0.28	0.34	0.52	0.53	1.00	0.94	0.71	0.94
9	0.70	0.56	0.54	0.32	0.32	0.51	0.51	0.94	1.00	0.63	0.93
10	0.73	0.79	0.74	0.50	0.57	0.69	0.65	0.71	0.63	1.00	0.92

7.2.3 Analysis: Criterion (concurrent) validity

As outlined within the protocol, concurrent validity was to be evaluated through assessing correlation coefficients alongside scatter plots of the data for overall DRI scores compared with overall ATRS scores. Before the appropriate statistical evaluation could be undertaken (Pearson correlation coefficient for parametric data and Spearman's rank correlation coefficient for non-parametric data) exploratory data analysis was carried out.

Probability plots were used to assess whether or not the data sets for ATRS scores at each time point were normally distributed. The probability plots are graphs with

observed cumulative percentage on X axis and expected cumulative percentage on Y axis. If the selected variable matches the test distribution, the points cluster around a straight line. These were evaluated alongside histograms, plotting ATRS scores against frequency, with imposed distribution curves. These are shown in Figure 7.3 through to Figure 7.7.

Graphically it can be seen that the ATRS data at pre-injury, six months and nine months are not normally distributed. The data at six weeks and three months are normally distributed. To further analyse these data sets a shapiro-wilk analysis was carried out. This analysis is based upon the null hypothesis that the samples are taken from a normal distribution. This null hypothesis was shown to be true for the six week and three month data sets ($p=0.102$ and 0.449). However it was rejected for baseline ($p<0.001$), six month ($p=0.016$) and nine month ($p<0.001$) data points. Therefore Spearman's rank correlation coefficient, which can be used in both parametric and non-parametric situations, was used to evaluate concurrent validity of the ATRS when compared to the DRI at each time point.

As Table 7.14 demonstrates the ATRS scores are significantly correlated with the overall DRI scores at each time point. The correlations are stronger at the six and nine month time points (-0.7 and -0.9) when compared to pre-injury, six weeks and three months (-0.6, -0.5 and -0.5). Accompanying scatter plots are illustrated in Figure 7.8 to Figure 7.12, graphically representing these statistically significant correlations ($p<0.001$).

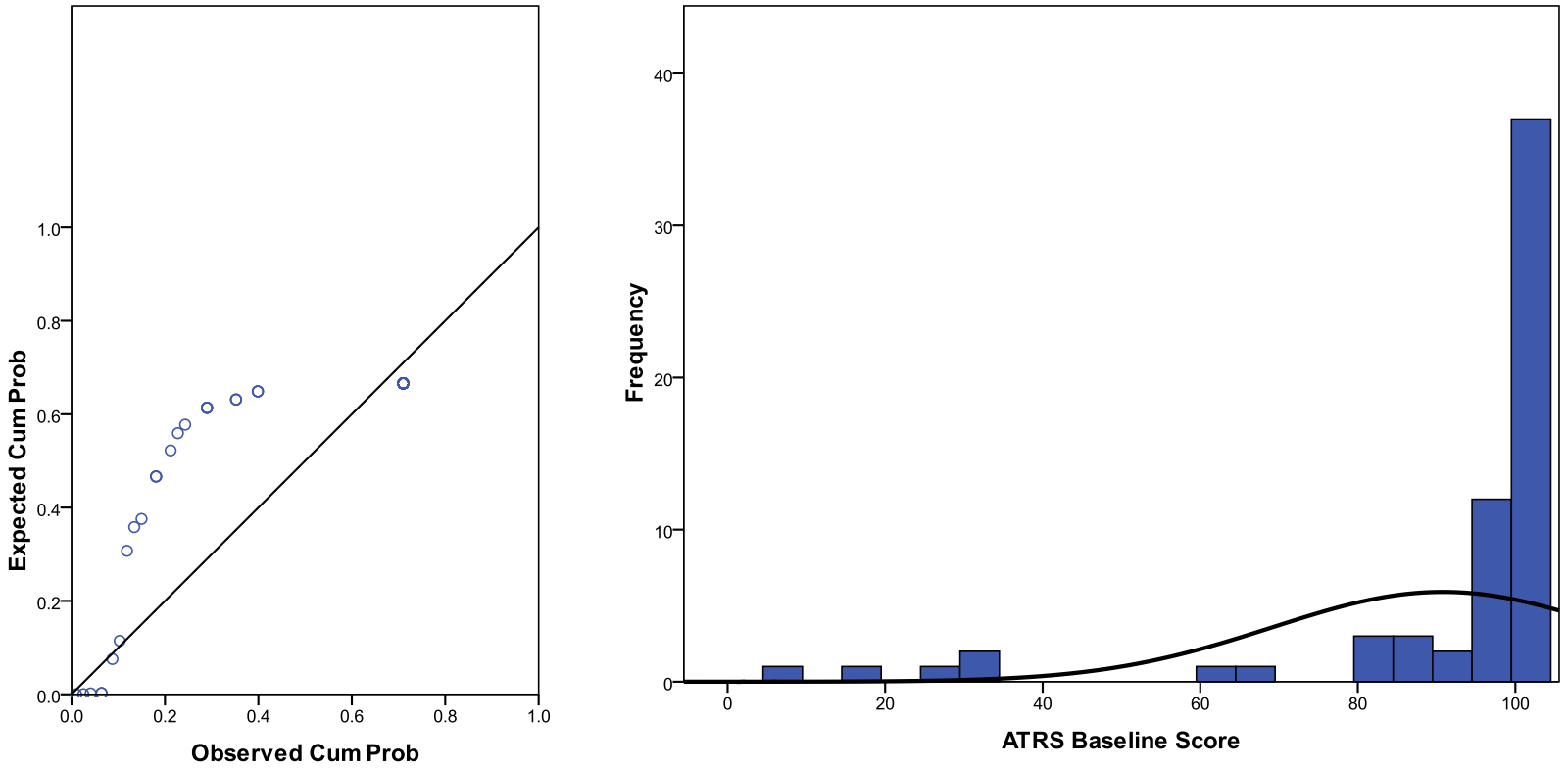

Figure 7.3: P-P plot and histogram with distribution curve for baseline ATRS scores

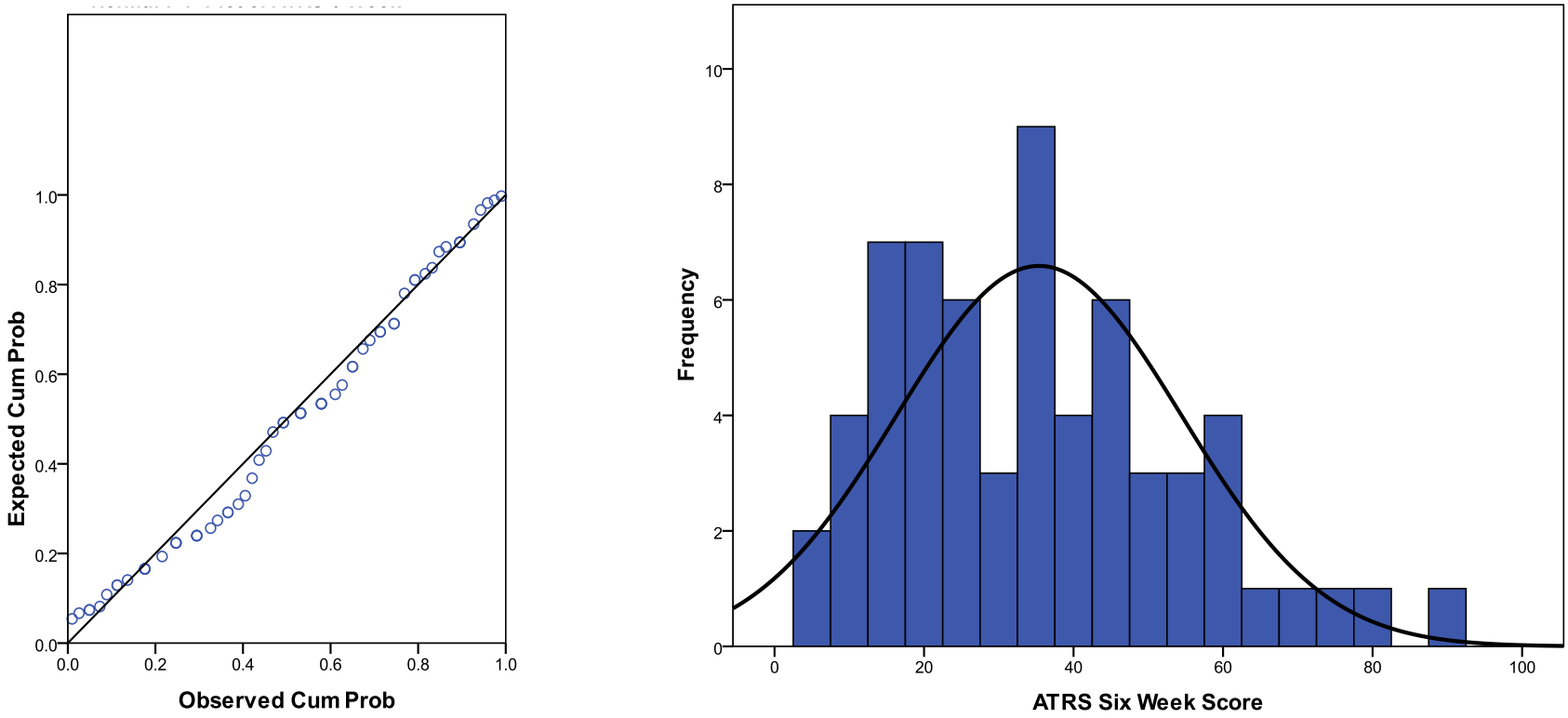

Figure 7.4: P-P plot and histogram with distribution curve for six week ATRS scores

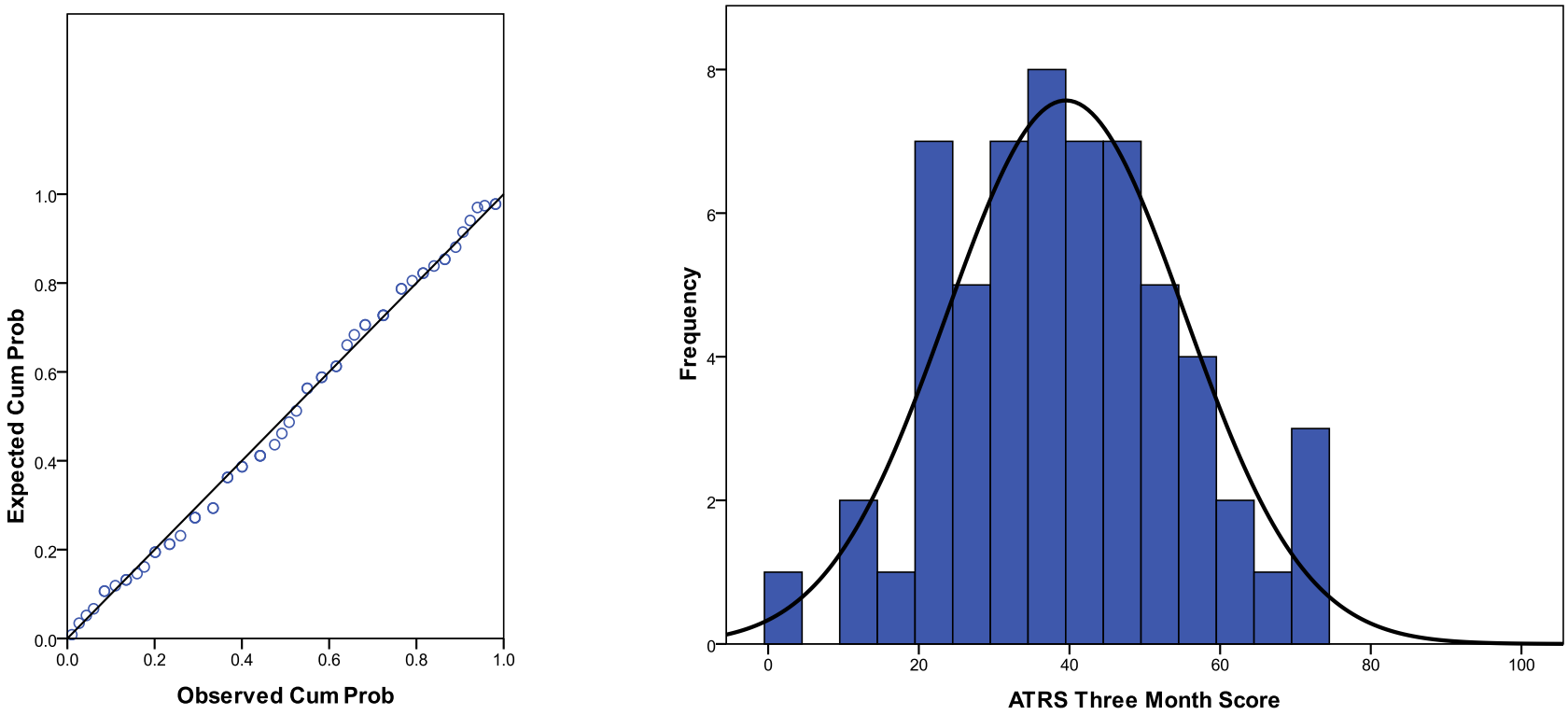

Figure 7.5: P-P plot and histogram with distribution curve for three month ATRS scores

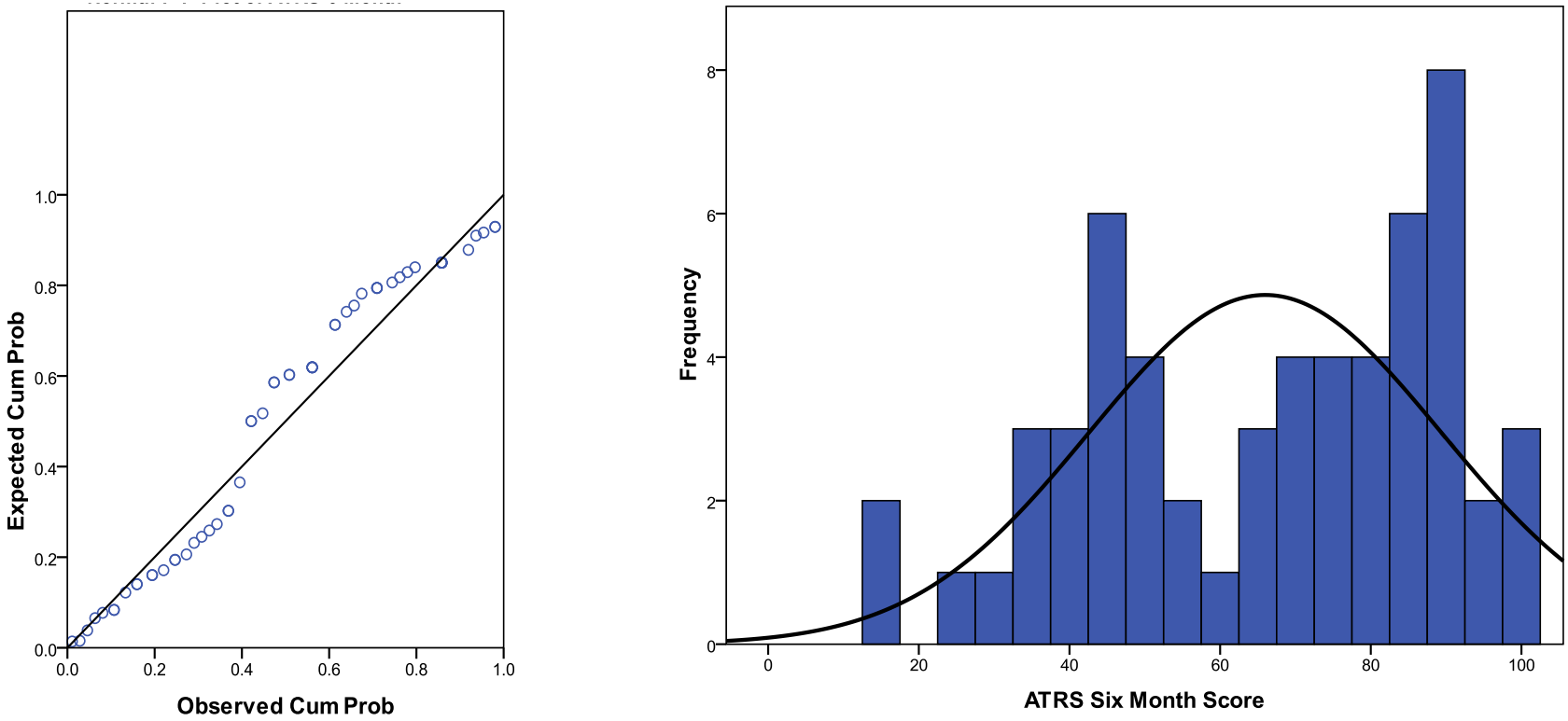

Figure 7.6: P-P plot and histogram with distribution curve for six month ATRS scores

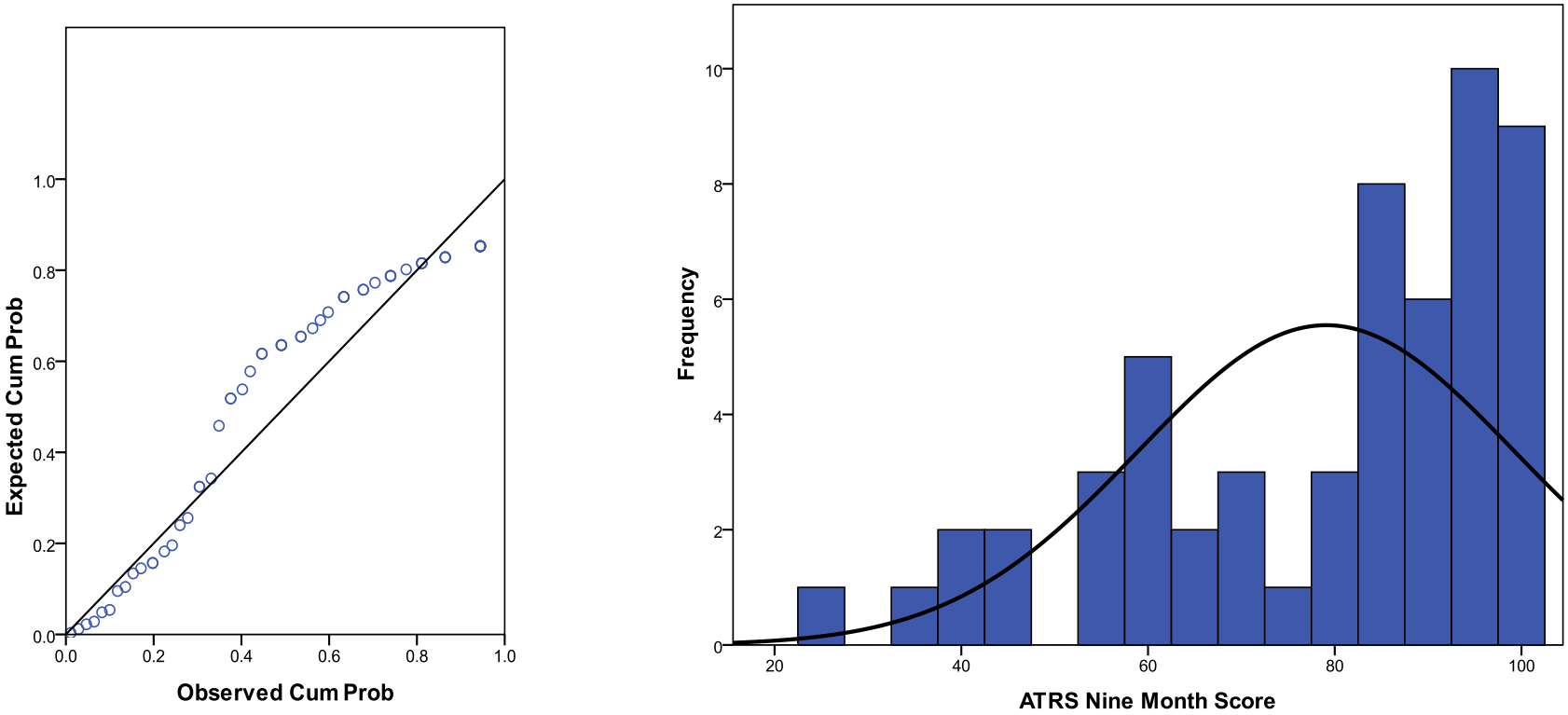

Figure 7.7: P-P plot and histogram with distribution curve for nine month ATRS scores

Table 7.14: Correlation coefficients (95% confidence intervals) for ATRS and DRI

	Correlation coefficient	Significance
Pre-injury	-0.6 (-0.78 to -0.30)	<0.001
6 Weeks	-0.5 (-0.68 to -0.28)	<0.001
3 Months	-0.5 (-0.76 to -0.37)	<0.001
6 Months	-0.7 (-0.80 to -0.36)	<0.001
9 Months	-0.9 (-0.94 to -0.83)	<0.001

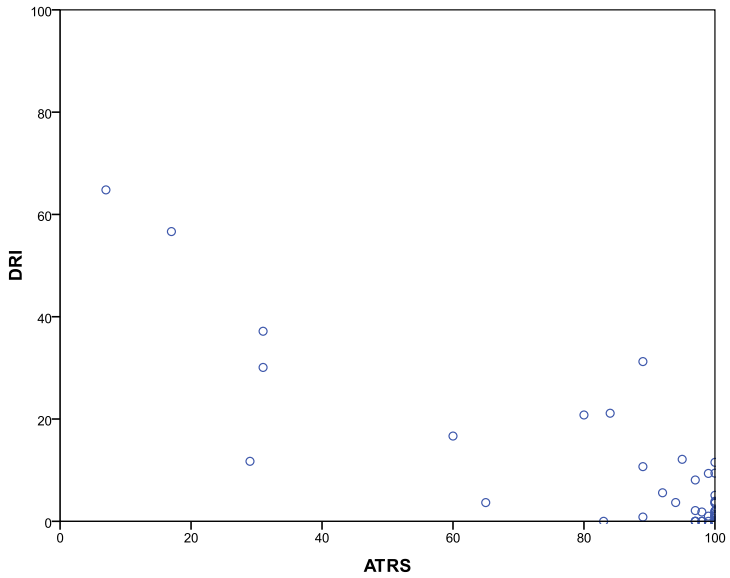

Figure 7.8: Scatter plot of ATRS and DRI baseline scores

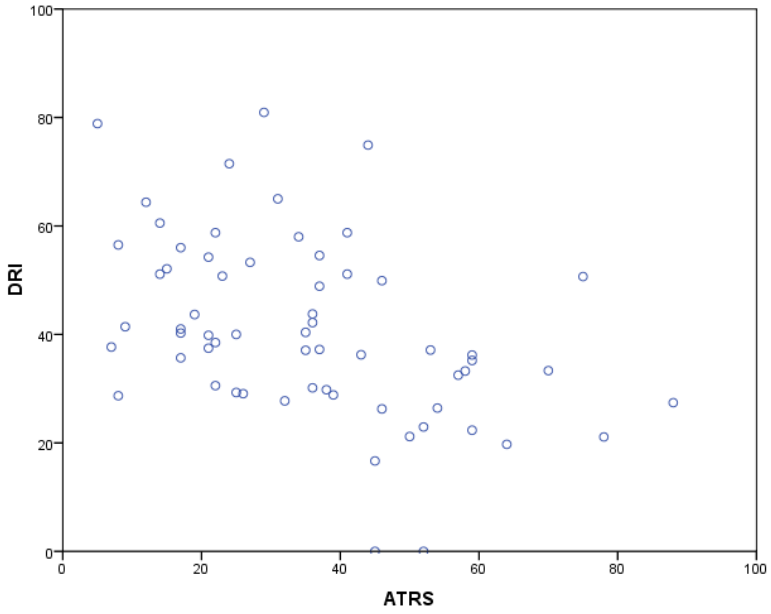

Figure 7.9: Scatter plot of ATRS and DRI six week scores

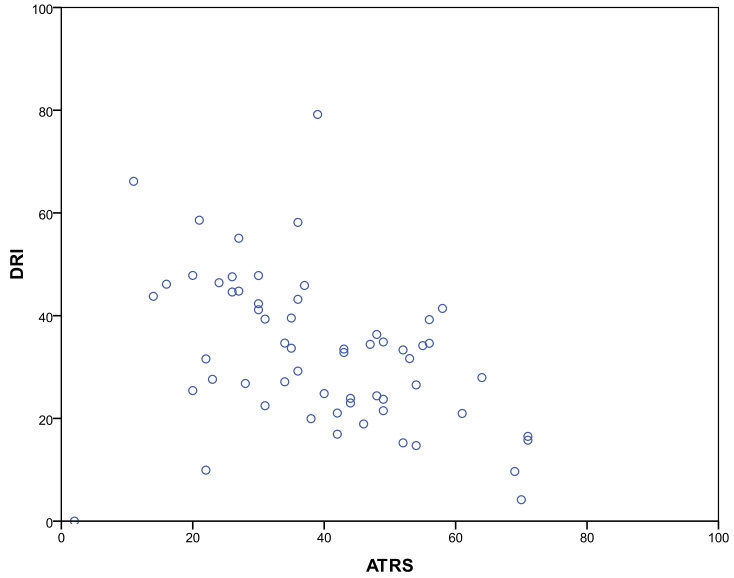

Figure 7.10: Scatter plot of ATRS and DRI three month scores

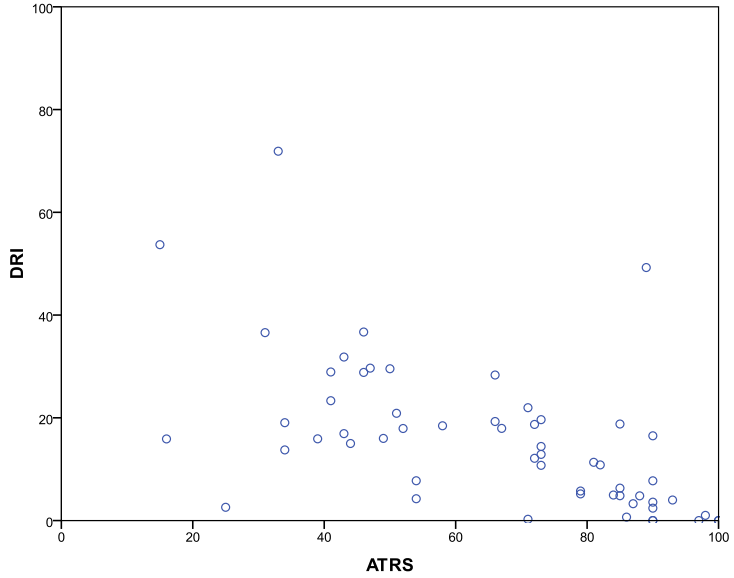

Figure 7.11: Scatter plot of ATRS and DRI six month scores

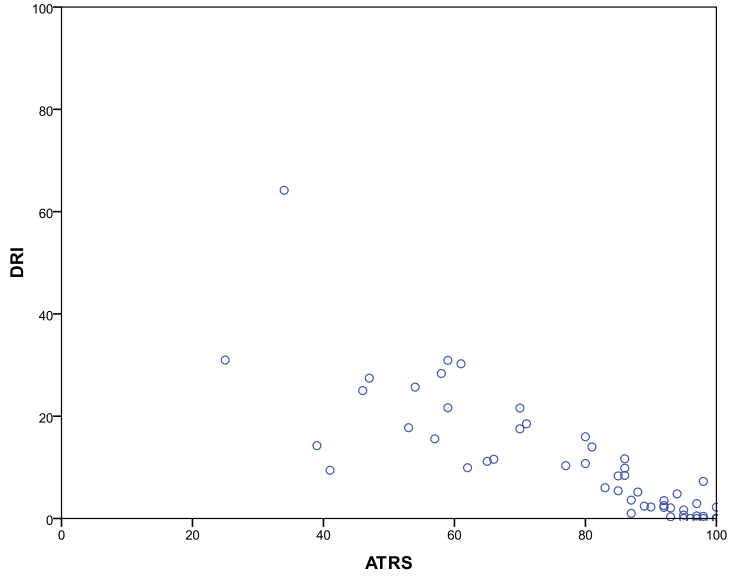

Figure 7.12: Scatter plot of ATRS and DRI nine month scores

7.2.4 Analysis: Construct validity

To evaluate construct validity the overall ATRS scores were compared to the three subscales of the DRI. ATRS scores were also compared to overall EQ-5D scores, which is a quality of life measure. This was achieved through Spearman's rank correlation coefficient analysis, with accompanying scatter plots at each time point.

The correlation coefficient results for the overall ATRS compared to EQ-5D and the sub-scales of DRI at each time point can be found in Table 7.15. In relation to the overall EQ-5D score the expected size of the correlations did not reach the 0.7 value. Regarding the three DRI sub-divisions, this was also not met by the first sub-division of 'common basic activities of daily life'. This criteria was only met within the last time point of the second and third sub-divisions.

Table 7.15: Correlation coefficients (95% confidence intervals) for overall ATRS scores when compared to the three sub-scales of the DRI and EQ-5D scores.

Time point		EQ-5D	DRI (1)	DRI (2)	DRI (3)
Pre-injury	Correlation coefficient	0.4 (0.65 to 0.20)	-0.5 (-0.74 to -0.25)	-0.5 (-0.71 to -0.21)	-0.6 (-0.80 to -0.40)
	Significance	<0.001	<0.001	<0.001	<0.001
6 Week	Correlation coefficient	0.5 (0.69 to 0.33)	-0.5 (-0.68 to -0.33)	-0.3 (-0.50 to -0.04)	-0.3 (-0.59 to -0.13)
	Significance	<0.001	<0.001	0.009	0.007
3 Month	Correlation coefficient	0.6 (0.75 to 0.32)	-0.5 (-0.74 to -0.28)	-0.5 (-0.72 to -0.24)	-0.3 (-0.55 to 0.20)
	Significance	<0.001	<0.001	<0.001	0.020
6 Month	Correlation coefficient	0.5 (0.70 to 0.21)	-0.5 (-0.73 to -0.24)	-0.7 (-0.85 to -0.45)	-0.6 (-0.78 to -0.41)
	Significance	<0.001	<0.001	<0.001	<0.001
9 Month	Correlation coefficient	0.3 (0.51 to 0.01)	-0.4 (-0.64 to -0.40)	-0.9 (-0.92 to -0.80)	-0.8 (-0.90 to -0.68)
	Significance	0.020	0.0010	<0.001	<0.001

Scatter plots graphically presenting the relationships between the overall ATRS and EQ-5D scores at each time point can be found in Figure 7.13 through to Figure 7.17.

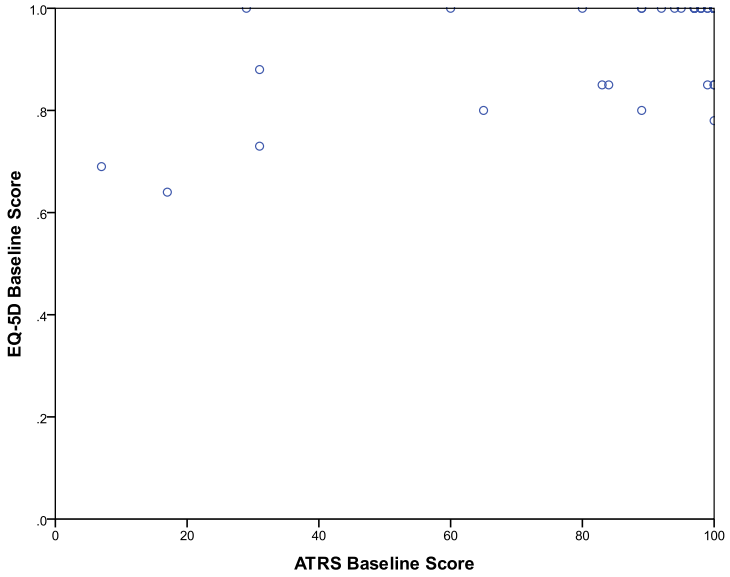

Figure 7.13:Scatter plot of pre-injury ATRS scores and EQ-5D scores

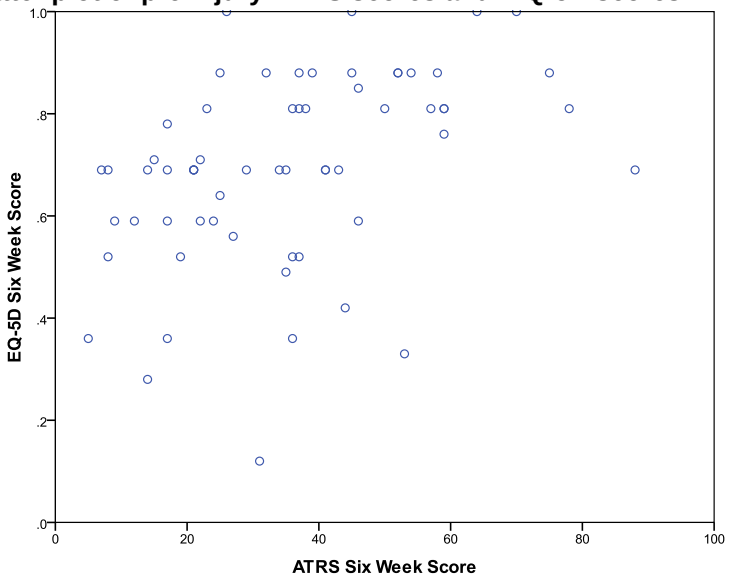

Figure 7.14: Scatter plot of six week ATRS scores and six week EQ-5D scores

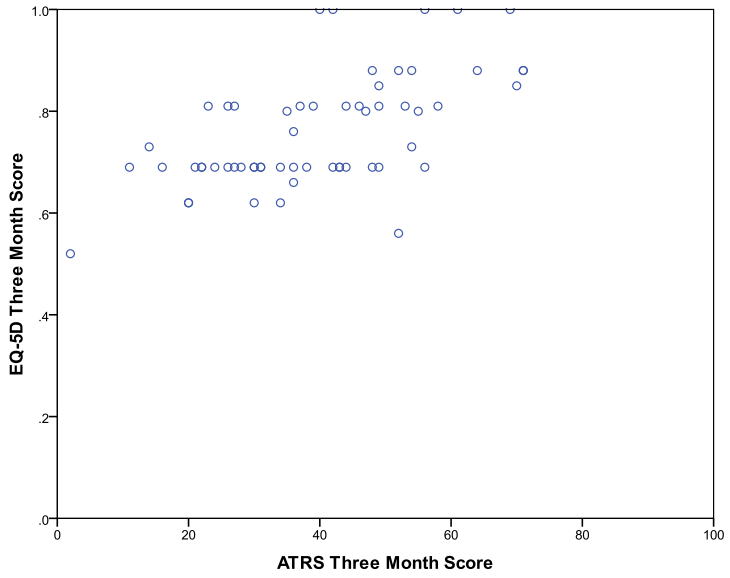

Figure 7.15: Scatter plot of three month ATRS scores and three month EQ-5D scores

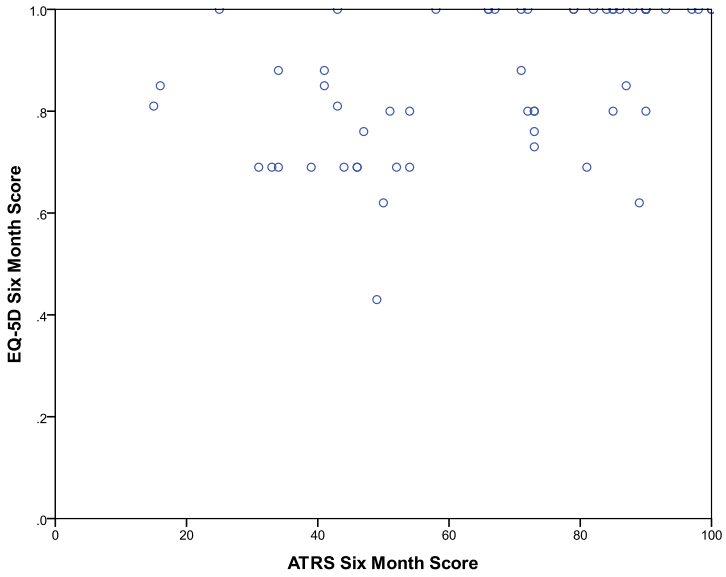

Figure 7.16: Scatter plot of six month ATRS scores and six month EQ-5D scores

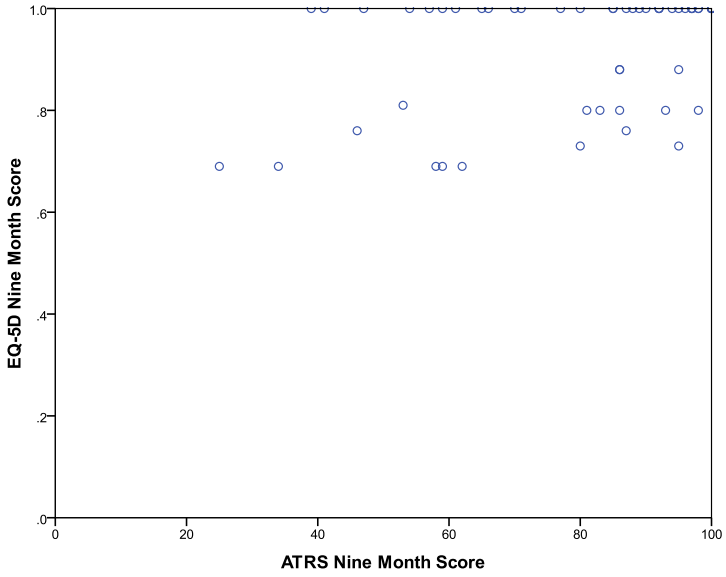

Figure 7.17: Scatter plot of nine month ATRS scores and nine month EQ-5D scores

Figure 7.18 through to Figure 7.25 graphically represent the relationship between the overall ATRS scores compared to the three sub-scales of the DRI at each time point.

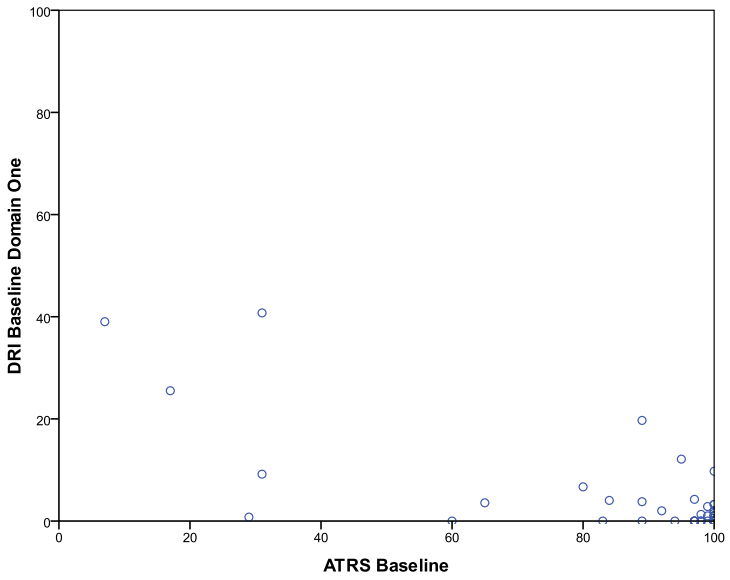

Figure 7.18: Scatter plot of pre-injury ATRS and DRI scores for domain one

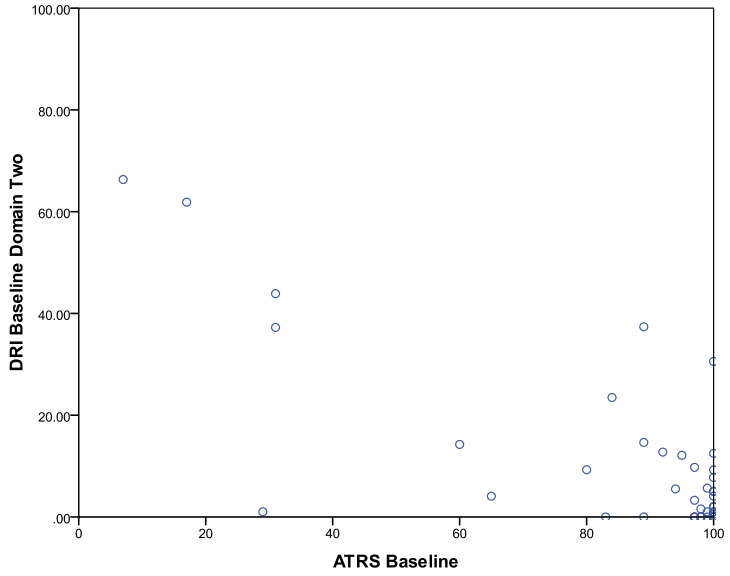

Figure 7.19: Scatter plot of pre-injury ATRS and DRI scores for domain two

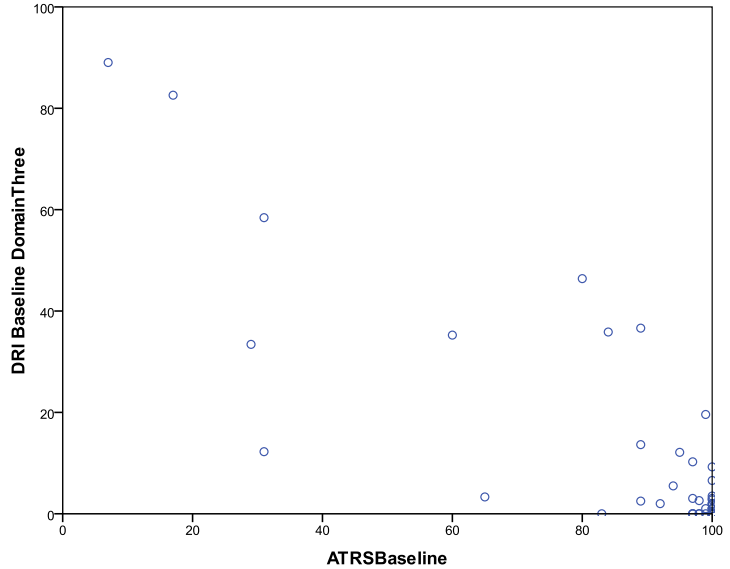

Figure 7.20: Scatter plot of pre-injury ATRS and DRI scores for domain three

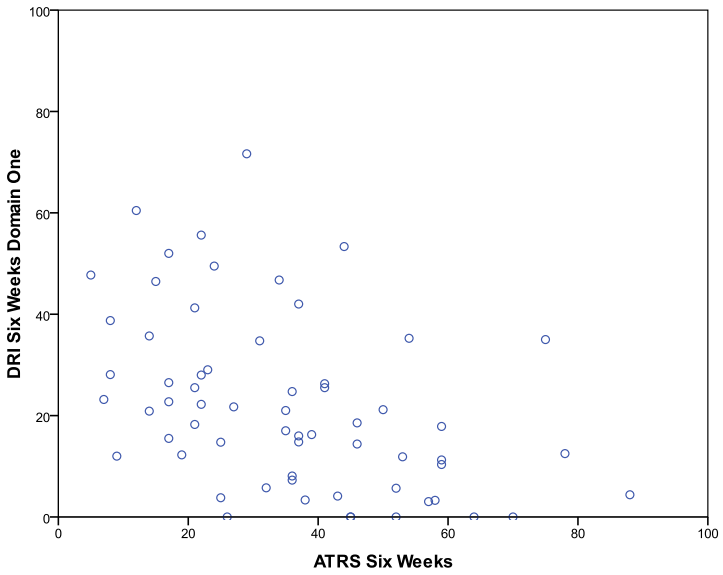

Figure 7.21: Scatter plot of six week ATRS and DRI six week scores for domain one

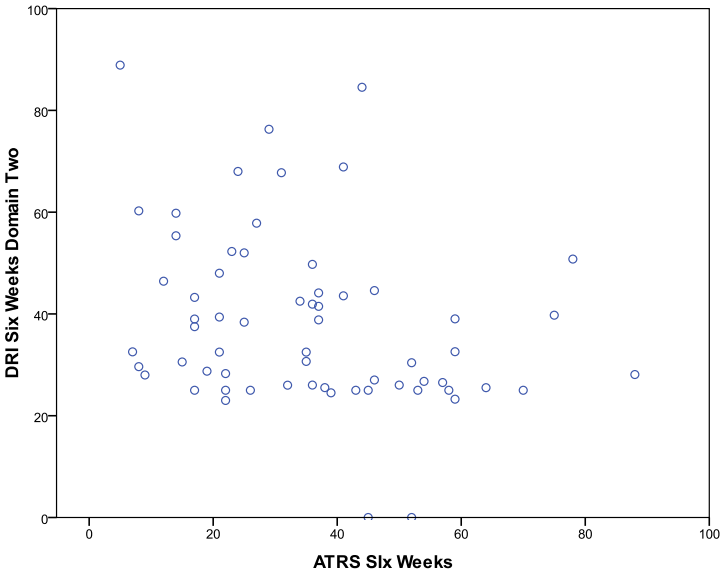

Figure 7.22: Scatter plot of six week ATRS and DRI six week scores for domain two

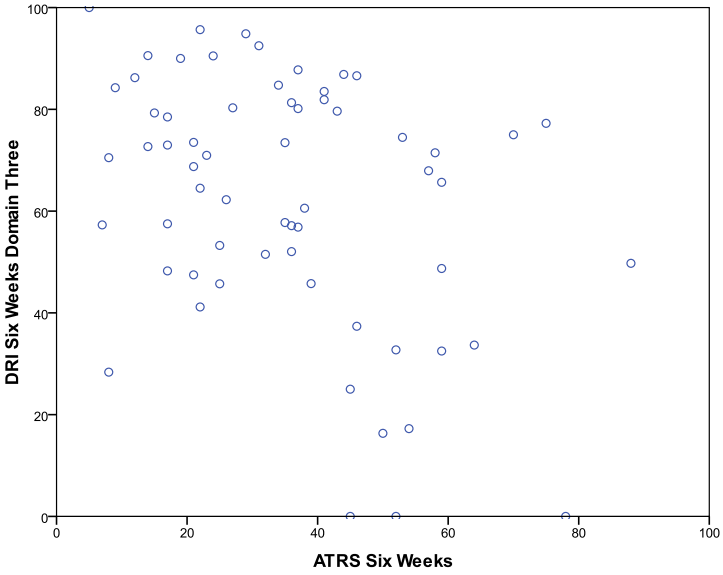

Figure 7.23: Scatter plot of six week ATRS and DRI six week scores for domain three

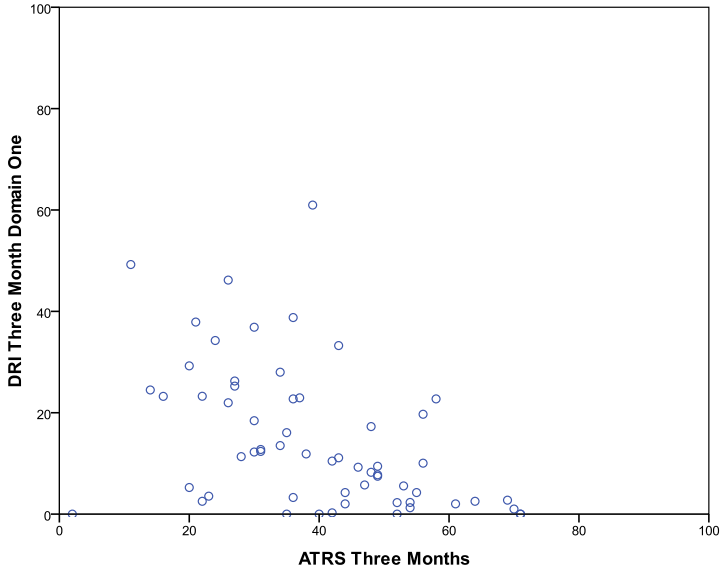

Figure 7.24: Scatter plot of three month ATRS and DRI three month scores for domain one

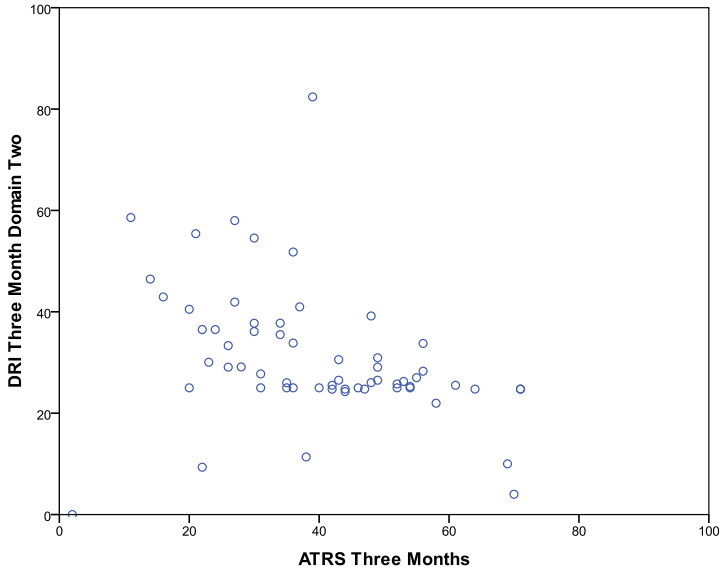

Figure 7.25: Scatter plot of three month ATRS and DRI three month scores for domain two

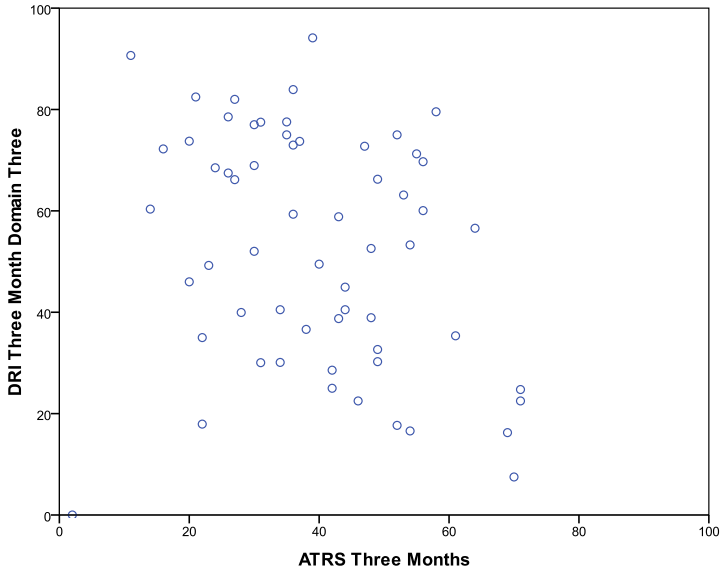

Figure 7.26: Scatter plot of three month ATRS and DRI three month scores for domain three

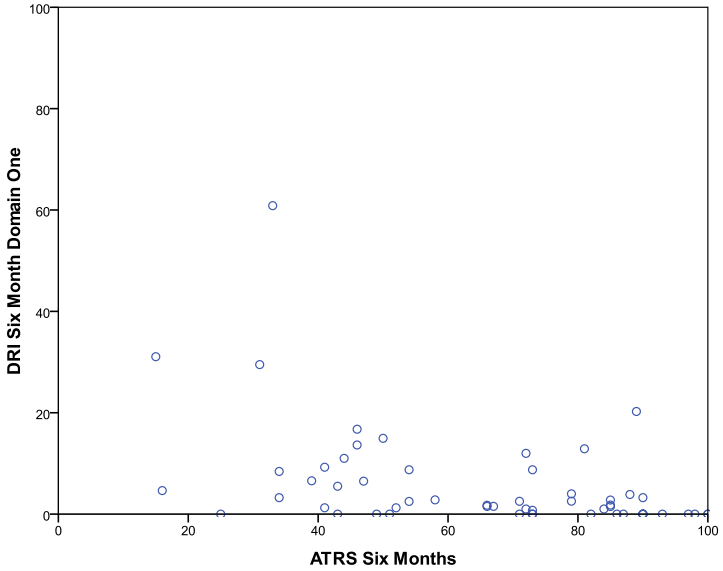

Figure 7.27: Scatter plot of six month ATRS and DRI six month scores for domain one

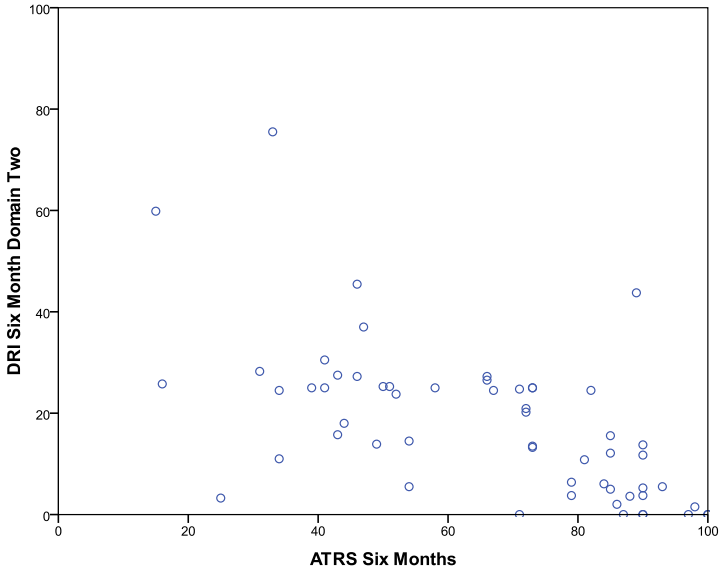

Figure 7.28: Scatter plot of six month ATRS and DRI six month scores for domain two

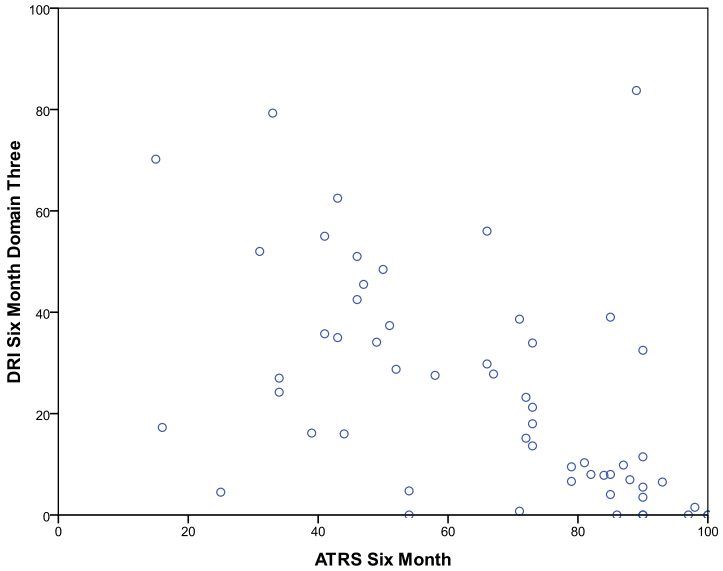

Figure 7.29: Scatter plot of six month ATRS and DRI six month scores for domain three

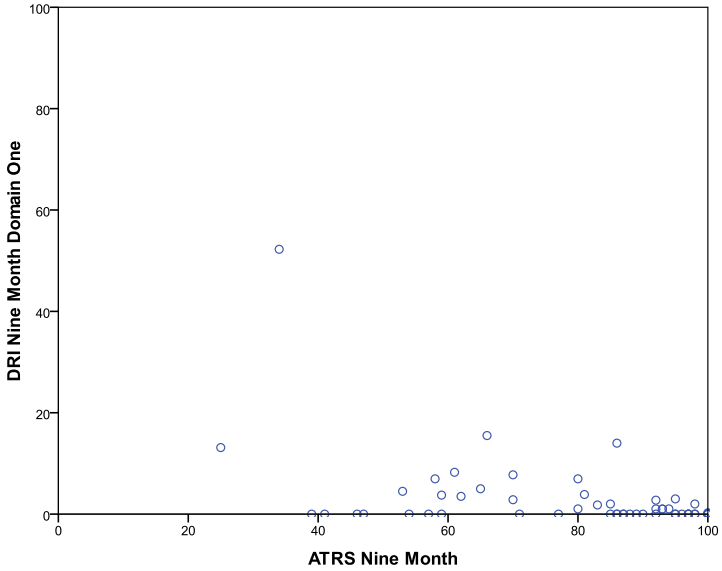

Figure 7.30: Scatter plot of nine month ATRS and DRI nine moth scores for domain one

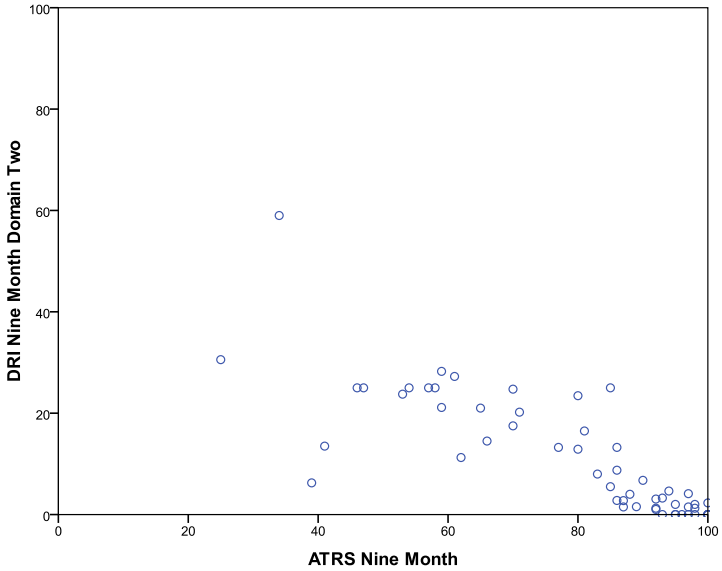

Figure 7.31: Scatter plot of nine month ATRS and DRI nine month scores for domain two

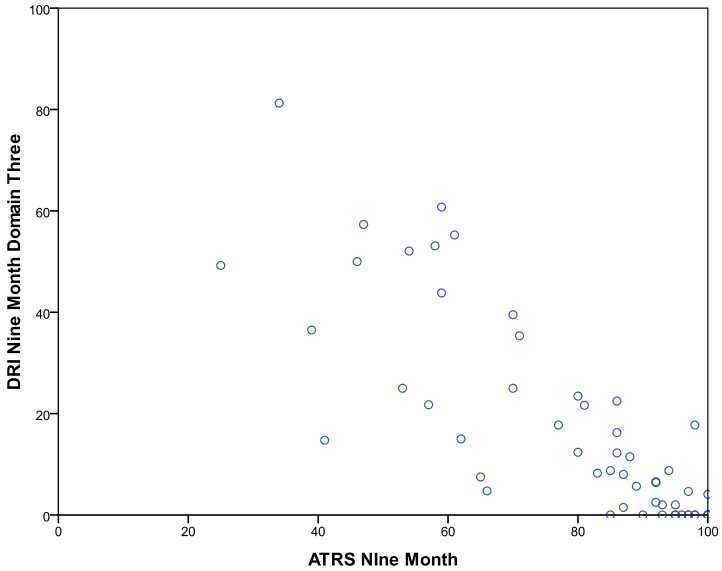

Figure 7.32: Scatter plot of nine month ATRS and DRI nine month scores for domain three

7.2.5 Analysis: Responsiveness

Floor and ceiling effects were the first aspect of responsiveness evaluated. Floor and ceiling effects were defined as being present if more than 15% of respondents achieved the highest or lowest scores. Table 7.16 illustrates the percentage of reported responses at the top (ceiling) of the total possible scores for the ATRS, DRI and EQ-5D and the percentage of reported responses at the bottom (floor) of the possible score for the ATRS, DRI and EQ-5D.

Table 7.16: Percentage of ATRS, EQ-5D and DRI respondents at either the floor or ceiling of the score.

Time point	% Ceiling			% Floor		
	ATRS	EQ-5D	DRI	ATRS	EQ-5D	DRI
Pre-injury	58%	81%	47%	0%	0%	0%
6 Weeks	0%	6%	3%	0%	0%	0%
3 Months	0%	8%	0%	0%	0%	0%
6 Months	4%	58%	9%	0%	0%	0%
9 Months	11%	66%	14%	0%	0%	0%

All three scores demonstrate a ceiling effect (defined as >15% respondents) for reported pre-injury scores, which was highest for the more generic quality of life measure, EQ-5D. The ATRS and DRI scores did not demonstrate a ceiling effect at any other time point. This was in contrast to the EQ-5D, which demonstrated further ceiling effects at the six and nine moth time points. None of the three outcome measures demonstrated any floor effects.

Table 7.17 shows the relative efficiency of the ATRS in relation to the EQ-5D and DRI at each time point. This method of evaluating responsiveness was chosen because it does not require parametric assumptions. The non-parametric relative efficiency is calculated using the *z* statistic derived from the Wicoxon sign rank test and the following equation:

$$Relative\ efficiency\ \ ATRS\ versus\ Alternative\ PROM\ = \frac{Z_{ATRS}}{Z_{Alternative\ PROM}}\ 2$$

Table 7.17: Relative efficiency of the ATRS across all time points

Time point	ATRS: Z statistic	EQ-5D: Z statistic	DRI Z statistic	Relative efficiency ATRS versus EQ-5D	Relative efficiency ATRS versus DRI
Pre-injury/6week	-6.8	-6.5	-6.7	$(-6.8/-6.5)^2 = 1.1$	$(-6.8/-6.7)^2 = 1.0$
Pre-injury/3 month	-6.7	-6.3	-6.2	$(-6.7/-6.3)^2 = 1.1$	$(-6.7/-6.2)^2 = 1.2$
Pre-injury/6 month	-5.5	-4.3	-4.8	$(-5.5/-4.3)^2 = 2.1$	$(-5.5/-4.8)^2 = 1.3$
Pre-injury/9 month	-4.6	-2.3	-2.8	$(-4.6/-2.3)^2 = 4$	$(-4.6/-2.8)^2 = 2.7$

On all occasions the ATRS demonstrated greater responsiveness when compared to the DRI and EQ-5D. At the six month time point the ATRS was 2.1 times more responsive than the EQ-5D, and at nine months it was four times more responsive. The same trends were evident when compared to the DRI, but to a lesser extent, with the ATRS being 1.3 times more responsive at six months and 2.7 times more responsive at nine months.

7.3 Discussion

The ATRS was published in 2007, and advocated by the authors as the only validated PROM available to evaluate patients following a TA rupture[61]. However, there has been no subsequent validation studies published. Therefore the objective of this chapter was to investigate aspects of validity of this newly developed PROM.

The original development of the ATRS was in Swedish, using a sample of patients aged 20-70 years, with acute TA ruptures. The questionnaires were administered at one time point to 115 patients, a minimum of three months post injury to a maximum of 3 years. Subsequently, it was considered important to further investigate data to support the English translation of this outcome measure. Secondly, it was considered that the original paper was not representative of the bi-modal distribution of this injury (affecting patients post 70 years of age) and therefore should also be evaluated in a sample with no upper age limit[10]. Finally the original paper did not evaluate the outcome measure, both, in the acute phases of this injury (pre-3 months) and across time within the same patient.

Within the context of the above, the specific aspects of validity addressed by this chapter were internal consistency, criterion validity, construct validity and responsiveness. The results demonstrated at each time point that the ATRS had high internal consistency (Cronbach's alpha between 0.89 and 0.95). However a result above 0.90 has been debated within the literature as being an indication that the outcome is too homogeneous[138-139], the implication of this is that further item reduction may be appropriate[131]. This finding is consistent with the original development article, which also reported a high internal consistency, with a Cronbachs alpha of 0.96, however no suggestion for item reduction was made by the authors in light of this result.

Criterion validity of the score was not evaluated within the original article. The authors stated that there was no gold standard with which to compare to. Within this study the DRI score was used as a 'gold standard' to evaluate criterion validity. It is acknowledged that this is not a disease specific outcome measure, but has validation studies to support its use in an orthopaedic outpatient setting. On this

basis the DRI score was used as a gold standard, however the limitations of this are acknowledged.

Spearman's rank correlation coefficients between the DRI and ATRS demonstrated stronger correlations at the six and nine month time points (-0.67 and -0.91) when compared to baseline, six weeks and three months (-0.59, -0.52 and -0.46).These correlation coefficients indicate a moderate correlation, this may be expected as opposed to an exact/strong correlation on the basis that the DRI is not a disease specific measure. Also of note is that the confidence intervals around the correlation coefficients were wide. These wide confidence intervals may be an indication that a larger sample size was required for this study.

Referring to the scatter plots for these correlations it is evident that the lower correlation coefficients at baseline, six weeks and three months are likely to be the result of higher scores being attained on the DRI compared to the ATRS. This could be secondary to none disease specific questions within the DRI pertaining to problems with sitting, washing-up and standing, which patients with Achilles tendon ruptures would not have any problems with at any stage of their recovery. This is also reflected within the descriptive data tables, which demonstrate the mean values for each score item at each time point.

Construct validity and responsiveness were also addressed within this chapter. As would be expected, the ATRS correlated more strongly towards the third subscale of the DRI, which evaluates more demanding physical activities. This is in contrast to the first two subscales which address normal and light activities and the EQ-5D which evaluates a quality of life construct. Again the key limitation of these correlations is that the scores are measuring only similar constructs as opposed to

exact constructs. Again there were also large confidence intervals reported, indicating a larger sample may have been required.

The more specific ATRS outcome measure demonstrated greater responsiveness than the more generic DRI and EQ-5D scores at each time point. These results were in keeping with the original development article. The level of responsiveness was only marginal in comparison to the DRI and EQ-5D up until the three month time point, with greater levels of responsiveness evident at the six month and nine month time points. This may by representative of the greater ceiling effects seen within the EQ-5D and DRI scores. There are many methods available to determine responsiveness[140]. This method was used as opposed to more routinely reported effect sizes because it does not require parametric assumptions.

Investigating aspects of validity within the area of 'PROM's' has been recognised as being a 'grey' area, where there is no consensus on the exact methodology to be used[140]. However there is agreement that validating a newly developed outcome measure is an ongoing process. This process involves the outcome measure being investigated in different countries, in different languages, across varying patient sub-groups, within a range of clinical contexts. In relation to the TA, this would involve further research including patients with a delayed presentation or following tendon shortening/reconstruction procedures as an example.

This chapter does not answer the question pertaining to whether or not the ATRS is a valid measure, but it does contribute further to the ongoing process of validating a newly developed outcome. Furthermore, despite the highlighted limitations, this is the only disease specific PROM available with any validation data to support its use, as discussed in the previous chapter. So whilst there is scope to further explore

aspects of validity of this new score, with larger samples, this study is a positive step towards the use of a universal measure of outcome for patients with a rupture of the Achilles tendon.

Declarations

None

Funding Body

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8.1 Review of thesis aims

Within trauma and orthopaedics there has been an ever increasing trend towards the implementation of controlled trials to determine the clinical and cost effectiveness of interventions[141]. However, prior to the planning and implementation of such cost and time intensive endeavours, it is imperative that the researcher has fully investigated the components of the interventions to be trialled[64].

Clearly defining the components and the importance of underpinning them with relevant theory and context is pivotal to ensuring that the interventions to be later trialled are appropriate in design[67]. It is acknowledged that this in itself is not a simple task, and is reflected in the range of methodologies used to achieve these goals within different clinical contexts[142-143]. However in each case it is imperative to outline the literature to date, leading to the specific questions to be addressed. The first chapters of this thesis served this purpose.

The introduction to this thesis summarised the clinical development of TA rupture management from the first documented report on the topic in 1575[25], through to the first RCT of operative versus non-operative repair in 1981[27]. Numerous RCTs on the same topic followed, which were meta-analysed by the Cochrane group in 2004[39].

This review group concluded that higher re-rupture rates were present amongst non-operatively managed patients. However, the key finding within this review lay within their comparison of NWB cast immobilisation to WB protocols. These comparisons demonstrated a reduction in re-rupture incidence from 12% to 2% within non-operatively managed patients which is equivalent to results seen in patients managed operatively. Therefore, with an already low incidence of other complications (3%), the authors discussed the need to investigate rehabilitation

strategies further, acknowledging that currently a wide range of protocols exists. Subsequently, before further research comparing rehabilitation protocols could proceed, this issue of the variation amongst protocols needed to be addressed.

Weight bearing protocols contain a number of interacting components, and as such are defined as complex interventions. The problems and challenges associated with developing and defining complex interventions have been outlined by the MRC in a framework for researchers. Subsequently this framework has informed the basis for the overall aim of this thesis, which was to develop IWB interventions for patients who have sustained an acute rupture of their TA to inform a definitive evaluation of their effectiveness. To achieve this overall aim, four specific objectives were set, as follows:

1) Systematically identify and summarise, from clinical studies, the components that define IWB interventions currently documented for the treatment of acute TA ruptures.
2) Evaluate how these identified IWB components affect gait parameters within healthy participants, to provide a theoretical basis on which to develop interventions within a patient population.
3) Pilot the IWB interventions in a patient population to enable evaluation of patient recruitment rates, follow up, PROM variability and CRF design.
4) Systematically identify and critically evaluate the PROMS used within the published literature, and further evaluate elements of measurement properties of an appropriate disease specific PROM, to be used as a primary outcome measure within the evaluation phase.

In relation to the MRC framework, objectives one and two relate to the development phase and objectives three and four relate to feasibility and piloting. These phases subsequently inform the evaluation and implementation phases of the MRC framework. Consequently, the remaining sections of this thesis will firstly summarise the findings of the four objectives and then discuss the implications of these findings in relation to the subsequent phases of the MRC complex intervention framework.

8.2 Limitations

In relation to the methods used in this thesis, a number of important limitations need to be considered when drawing on the final conclusions. Firstly within the two chapters systematically reviewing data, the key limitations were related to the heterogeneity of the included studies. This had the subsequent implication that it was not appropriate to combine the outcome data sets. Furthermore, steps could have been taken by the researcher to pre-publish search strategies to increase the reliability of the findings.

Within the experimental chapter (Gait analysis of healthy participant's) the key limitation was the use of healthy participant's. Consequently the results of this research could not be applied directly to a clinical context (limited external validity). Furthermore, this study had only evaluated a limited number of gait parameters. It is acknowledged that a variety of methods exist to evaluate gait parameters, of which pressure measurements and range of movement form only part. In relation to the specific conduct of the study, the main issues of reliability centred around the lack of independent intra tester data and lack of blinding of test conditions/analysis, which could introduce researcher bias.

In the later clinical studies, the sample size was the main concern and area for discussion. There are no formal methods for determining sample size calculations for pilot data, limiting the definitive conclusions that can be drawn from the data. However, this data was important for testing the interventions in practice and gaining data to inform future clinical studies in this area. These piloting phases also highlighted the potential confounding of including both operatively and non-operatively managed patient's, which is a further limitation of these studies.

Within the exploration of PROM validity the main limitations of this research were centred on the lack of a defined 'gold standard' on which to base criterion validity and a lack of validated foot and ankle scores in related areas to compare aspects of construct validity. There was also the same issue of determining a sample size for this research, as again there are no established methods in this research context.

Each study design was based around the MRC framework. However, this framework has also been subject to criticisms for not providing sufficient guidance to researchers regarding exactly how to achieve the aims of each phase. For example, although each of these chapters is based on the framework, other methodologies could have been implemented such as qualitative interviews with patients and staff, either prior to the piloting phase and/or after this phase. Such methods have been implemented by other authors to establish the implementation of the intervention from the staff and patient perspectives. However, it has also been discussed by previous authors that these processes prior to the evaluation stage are both cost and time intensive. Subsequently, with the lack of specific guidance provided by the framework, researchers have to judge the appropriate methods to be used, taking into account what is achievable within a specified time and budget, to ensure that the evaluation phase is not unduly delayed.

Consequently it can be clearly seen how although methodological issues were considered at each stage to ensure reliability and validity of the research findings, each chapter of this thesis could have been approached differently to further improve the methodological quality of the studies. These have been important learning points for the researcher throughout the thesis.

8.3 Summary of study findings

Following the introduction and aim of this thesis, Chapters 2 and 3 addressed the development phase of the MRC framework. More specifically, they aimed to systematically identify the evidence base and develop a theoretical framework on which to base future piloting and feasibility research.

The systematic review, outlined in Chapter 2, identified nine articles presenting the results of 236 operatively, and 188 non-operatively managed patients using IWB rehabilitation protocols. As previously described by the Cochrane group, a wide variation was obviously evident. However, the results from this review enabled the identification of four components, which defined the interventions. These components consisted of; the type of AFO worn, the degree of restricted movement, the length of time for which the AFO is worn and the use of ROM exercises. However, it was not possible from this review to determine how these components or their interactions may affect treatment outcomes. Consequently, Chapter 3 aimed to provide further research to evaluate these identified components.

The subsequent experimental design outlined in Chapter 3, trialled three AFOs with four heel wedge insert conditions to evaluate three hypotheses. These hypotheses were firstly, the effect of the AFO design regardless of the number of heel wedge

inserts, secondly, the effect of the heel wedge inserts regardless of the AFO design and thirdly, the interaction of the two conditions.

The results demonstrated that AFOs that were restrictive in design, combined with a higher number of inserted heel wedges, prevented production of forefoot pressures, increased heel pressures and decreased the amount of time spent in the terminal stance and pre-swing phase of the gait cycle. Consequently, the choice of AFO design and the number of inserted heel wedges were shown to have a significant impact on planter pressure measurements and temporal gait parameters. These findings provided a theoretical framework on which to base feasibility and piloting procedures in a clinical setting.

Chapters 4 and 5 relate specifically to the feasibility/piloting phase of the MRC framework. These chapters aimed to address a number of issues including the practicalities of implementing the interventions, compliance, estimating recruitment rates, follow up rates and parameters for determining sample size calculations. However, before this data can be used to move onto the next phase of evaluation and assessing effectiveness, the question regarding which outcome measure would be used and why required further investigation.

Chapters 6 and 7 were designed to investigate this issue of outcome measures further. This was achieved by performing a systematic review to establish the PROMs reported in research articles and the evidence to support their use. From this review of the literature, the most appropriate PROM was chosen and aspects of its validity were developed further.

The results from these Chapters found that 21 PROMs had been reported in the literature pertaining to acute TA rupture management. However, only one disease specific outcome measure was found to have further evidence to support multiple facets of its validity. This outcome measure was the ATRS, which was investigated further within this thesis. The results of these further investigations supported the initial findings of the authors who developed the ATRS, and provided further evidence in relation to internal consistency, responsiveness, construct validity and criterion validity.

In summary, the aim of this thesis was to develop an immediate weight bearing rehabilitation protocol, for patients who have sustained an acute rupture of their Achilles tendon, to inform a definitive evaluation of its effectiveness. To achieve this aim the MRC framework, for defining and developing interventions with several components, was used to underpin the structure of this thesis. This included the implementation of a range of study designs including systematic reviews, experimental designs, pilot clinical trials and outcome validation research. To achieve this, completion of this thesis has required demonstration of both research and personal development, overseen by expert supervisors.

Using the MRC framework, the first chapters were focussed on the 'pre-clinical' development phase. A systematic review of the evidence identified four components that defined immediate weight bearing rehabilitation. The first two were how long the AFO is worn and whether or not to include ROM exercises. Previous animal based research and an RCT have investigated tendon healing and the effects of early movement. This research has demonstrated that the proliferative phase of tendon healing lasts until approximately six weeks, at which point the healing tendon then enters a remodelling phase. Throughout these first weeks ROM

has been shown to have a preferential effect on these phases. The clinician can therefore justify wearing an AFO for at least six weeks whilst the patient simultaneously carries out ROM exercises from PF to neutral.

This thesis therefore investigated the final two components, the type of AFO worn and the ankle position within it. These components were firstly evaluated in controlled gait analysis studies. The key findings showed that rigid orthoses designs with a large degree of plantarflexion, increased heel pressures, reduced forefoot pressures and decreased the amount of time spent in the terminal stance and pre-swing phase of the gait cycle. However this research was conducted in healthy participants, not patients.

The feasibility and piloting phases of these different combinations of AFO types and maintained ankle positions followed. These studies highlighted the balance that is needed between allowing sufficient flexibility and loaded movement against the clinical risk of tendon re-rupture. This was highlighted by the occurrence of three re-ruptures in 15 patients during the second clinical phase using the more flexible AFO's, which is higher than that reported in the literature. Furthermore this second clinical phase also included a greater proportion of non-operatively managed patient. This may also be a factor that influenced the observed higher re-rupture rate. However, previous RCT's have shown immediate weight bearing in non-operatively managed patients to be safe and a Cochrane review has shown lower re-rupture rates when compared to cast immobilisation. Therefore although the results in this research show higher than reported re-rupture rates, this is only a small sample and in the context of the wider literature it is established that immediate weight bearing interventions are safe and offer advantages over and above immobilisation, such as decreasing the risks of DVT's.

This thesis defines the rehabilitation components, proposes a theoretical framework and tests this in practice. The results will ensure that rehabilitation after an acute Achilles tendon rupture is based on a systematically developed protocol rather than ad hoc practice. This will research will be used to inform future definitive research in this area.

Consequently, it can be seen how each Chapter of this thesis has contributed to the overall aim of intervention development through to the next phase of evaluation. There are numerous advantages to the methods that have been used to achieve this progression. For example, these approaches have taken a step beyond the traditional approach of simply performing a systematic review prior to designing a full evaluation study[64]. They also adopt a pragmatic approach to evaluation that will lead to interventions that can work in practice and lead to a greater likelihood of success, secondary to focussing the intervention on the relevant components.

However, these approaches have been based on the MRC framework, which has been subject to criticisms for not providing sufficient guidance to researchers regarding exactly how to achieve the aims of each phase[144-145]. For example, although each of these chapters is based on the framework, other methodologies could have been implemented such as qualitative interviews with patients and staff, either prior to the piloting phase and/or after this phase. Such methods have been implemented by other authors to establish the implementation of the intervention from the staff and patient perspectives[144-145,149]. However, it has also been discussed by previous authors that these processes prior to the evaluation stage are both cost and time intensive. Subsequently, with the lack of specific guidance provided by the framework, researchers have to judge the appropriate methods to

be used, taking into account what is achievable within a specified time and budget, to ensure that the evaluation phase is not unduly delayed[142].

8.4 Implications for future research

The contribution to knowledge that this thesis has made is evidenced through a combination of activities. These include peer reviewed publications across orthopaedic, physiotherapy and sports medicine journals in addition to national and international presentations in the same field. These have translated into clinical pathways locally and a debate surrounding the need for guidelines nationally. These knowledge contributions include the first steps towards systematically defining the intervention, proposing how to evaluate it (through validated PROM's) and piloting the interventions in clinical practice.

The work contained in this thesis has identified that IWB rehabilitation protocols vary within the literature, and has proposed a theoretical basis on which to develop rehabilitation interventions in practice. These interventions have been trialled in a clinical setting in a pilot/feasibility context, alongside further research investigating PROMs validity, to ensure that appropriate measures are used in the next evaluation phase. Therefore, the final logical conclusions of this thesis will be directed towards proposals for the next phase of evaluation.

The first consideration needs to be directed towards defining the interventions to be trialled and why. This is because the greater the number of interventions to be evaluated, the greater the number of participants needed to reject the null hypotheses, which has a subsequent effect on resource allocation, recruitment time frames and ultimately the feasibility of conducting a definitive evaluative study. Inevitably, there are a number of methods to approaching this.

Firstly, interpreting the data collected and analysed across the healthy subject experimental study in Chapter 3, and the clinical pilot phases in Chapters 4 and 5, it is clear that three heel wedge inserts within either of the AFO designs results in both significantly altered gait parameters and decreased scores within the PROM's data sets. Consequently, there is both theoretical context and preliminary clinical data on which to base the rejection of the three heel wedge insert condition.

Rejecting this intervention then leaves four further options. These are the carbon fibre AFO with one or two heel wedge inserts or the rigid rocker bottom AFO with one or two heel wedge inserts. When these conditions were trialled within the experimental study design of healthy participants, there was a statistically significant affect with changing both the heel wedge insert condition and AFO design. Further evidence of this is seen within the randomised pilot work in Chapter 5, which demonstrates with PROMs data that scores improve with reduction in heel wedge inserts. However, it must be noted that this is only pilot work, and is therefore not sufficiently powered to accept or reject specific null hypotheses. Consequently, it would appear justified to evaluate these four options within a definitive evaluative study. Therefore at this stage it could be proposed that a four arm RCT could be designed to answer the following research question:

'Is there a difference in ATRS scores at nine months between four different IWB interventions for patients with an acute TA rupture?'

As discussed earlier in this thesis, the widely accepted 'gold standard' within trials of clinical effectiveness is the standard RCT. The aim of an RCT is to accept or reject the predefined null hypothesis. However, there is another possibility regarding trial design.

Instead of considering the interventions as one treatment block, they could be considered as an intervention consisting of two independent factors (AFO and heel wedge insert number) which have two levels within them (Flexible AFO/Rigid AFO and 1 heel wedge/2heel wedges). Consequently, using a factorial design would be another method in which the AFO design, heel wedge insert number and the interaction of these two factors could be investigated in one trial[146]. Furthermore, this trial design would enable definitive evaluation of which individual factor is most pertinent to the early rehabilitative phase.

The advantages of factorial designs have been documented to include the need for smaller sample sizes than would be required to answer the questions individually. Consequently, this results in a more efficient use of time and resources[147-148]. The disadvantages have been discussed by authors as requiring a more detailed analysis plan, and consequently the possibility of overcomplicating subsequent reporting of the results. This in turn may then lead to losing clinically important messages. Therefore, to plan this next stage would require careful consideration of the analysis and reporting to ensure successful implementation was possible.

For analysis purposes, the two heel wedge insert condition and rigid rocker bottom AFO would be considered the ‘standard treatment’. To explain the analysis plan further, the number of heel wedge inserts will be referred to as treatment A and the AFO design will be referred to as treatment B. By defining a standard treatment, the analysis can then be performed by what is termed an ‘at the margins’ approach (Table 8.1). This allows the efficacy of the treatment with two heel wedge inserts to be evaluated by comparing the outcomes of all the patients managed with two heel wedge inserts against all those not managed with one heel wedge insert and all

those managed with a rigid rocker bottom AFO against those not managed with the rigid rocker bottom AFO. This is widely accepted as the most powerful analysis for this trial design[147]. The analysis would then be performed using a two way analysis of variance.

Table 8.1: Outline of factorial trial design and analysis

		Treatment B		
		Rigid (B2)	**Flexible (B1)**	**Margin**
Treatment A	**Two Wedges (A2)**	A2 and B2	A2 and B1	All A2 cells
	One Wedge (A1)	A1 and B2	A1 and B1	All non A2 cells
	Margin	All B2 cells	All non B2 cells	

Montgomery *et al*[146] published an article on the design considerations of factorial trial designs. Most importantly, the authors highlighted that traditionally factorial designs have only evaluated interactions as a secondary analysis (the primary analysis being that of treatments A and B). However, if an interaction is considered of primary importance then it is acceptable to include interactions as a primary analysis if the study has been sufficiently powered to perform this analysis. They discuss that to evaluate interactions, the sample size needs to increase fourfold to detect the same differences in effect size, for the reasons illustrated in the above table (only half as many patients can be included in the analysis compared to analysing the main factors alone).

Consequently, the decision to include the analysis of interactions as a primary question requires careful consideration. Within this thesis an interaction between the numbers of heel wedge inserts and the AFO type has been demonstrated.

As an example, assuming approximate normality of the primary outcome measure (ATRS) and also assuming that analysis will be based on a standard ANOVA ('at the margins analysis'), and assuming significance is set to 5%, the total number of participants for a minimum clinically important difference of 10 points is shown in Table 8.2 for 80% and 90% power for a range of standard deviations from 16 (the figure recorded at three months within Chapter 7) going up in units of two through to 26 (demonstrating effect sizes of between 0.4 to 0.6). These would be divided equally amongst the 4 treatments groups (AFOs x wedges) and are adequately powered to detect an interaction twice as large as the main effects.

Table 8.2: Sample size calculations for 80 and 90% power

S.D	Power	
	80%	**90%**
16	84	112
18	104	140
20	128	172
22	156	208
24	184	244
26	216	288

So, for example, at 80% power and SD=20, 128 participants would be required (32 in each of the four combinations of AFOs and wedges). This design assumes that interactions are not of primary interest, or if interactions were likely to be very large, very unlikely. If we thought interactions were important (the effect of wedges was likely to be different within each AFO) then we would want to multiply this by four times, to give 512 participants in total (128 in each group).

So far, the options explored include developing a four armed RCT or implementing a 2X2 factorial design. However, an alternative method could be undertaken to further develop the proposed IWB interventions which was briefly discussed in Chapter 5, prior to further definitive research. This was the proposal to introduce a stream of qualitative research across all involved stakeholders (patients, health care professionals, charities and ethics committee members) to further qualitatively explore treatment priorities and attitudes towards the proposed trial interventions. This further research could also include a stream of survey research to ascertain if what has been documented within the literature regarding clinical practice is reflective of what actually occurs in UK practice. In doing this, both the quantitative and qualitative research could be integrated at the point of interpretation to determine the interventions that need to be trialled in a further definitive RCTs.

This mixed methods approach to developing trial interventions is not uncommon, and ensures a pragmatic response to such complex health care questions[142-143]. Mixed methods research designs in this context use both quantitative and qualitative methods to either sequentially inform each subsequent stage of the interventional development or can be used in parallel and integrated at the point of interpretation. Based on my pilot clinical research there is a need to incorporate such work prior to undertaking any further definitive studies.

It is clear that this next stage of research would require not only the skills demonstrated throughout this PhD, but also many that require further development in new qualitative research areas and training to enable successful management, leadership and research impact. This initial outline will now form the basis for a post-doctoral fellowship application, to learn and develop these required skills under expert mentorship arrangements, using the outlined future research as a platform for achieving this.

This series of studies has demonstrated the successful planning, implementation and dissemination of a broad range of research methods, within the context of the MRC complex interventions framework. These have included systematic reviews, experimental designs, pilot clinical trials and outcome validation research. The overall aim of which, was to facilitate the development of an evaluative study. To achieve this, completion of this thesis has required demonstration of both research and personal development, overseen by expert supervisors.

The conclusions that can be drawn from this combined series of studies are firstly that rehabilitation of this injury is a complex intervention. The systematic review in the second chapter of this thesis demonstrated it is an intervention that consists of four components. These are the type of AFO worn, the degree of PF within it, how long it is worn for and whether or not to include ROM exercises.

In relation to how long the AFO is worn for and whether or not to include ROM exercises, previous animal based research and an RCT have investigated tendon healing and the effects of early movement. This research demonstrated that the proliferative phase of tendon healing lasts until approximately six weeks, at which point the healing tendon then enters a remodelling phase. Throughout these first

weeks, ROM has been shown to have a preferential effect on these phases. The clinician can therefore justify wearing an AFO for at least six weeks whilst the patient simultaneously carries out ROM exercises from PF to neutral.

In relation to which AFO should be worn and the degree maintained PF within it, the third chapter of this thesis demonstrated that the flexibility of the AFO and amount of maintained PF significantly correlated with the amount of forefoot and heel pressures produced. The results showed that the greater the restriction and the higher the degree of maintained PF, the greater the heel pressure production and lower the forefoot pressure production. However this research was conducted in healthy participants, not patients.

Subsequent clinical research piloting these different combinations of AFO types and maintained PF highlighted the balance that is needed between allowing sufficient flexibility and loaded movement against the risk of tendon re-rupture. This was evident through the occurrence of three re-ruptures in 15 patients during the second clinical phase, which is higher than that reported in the literature. However this clinical research was only piloting/feasibility work and subsequently issues of safety could not be definitively concluded without a larger sample. Furthermore it contained a sample of both operatively and non-operatively managed patients, which is a confounding factor and further limitation of the study.

However the combination of defining these components, providing a theoretical framework for what could work in clinical practice and then piloting these interventions are the first and only steps that have been taken to systematically develop this intervention. Therefore although further research is clearly required, currently this is the best available published evidence and patients require

management today. Consequently this research has led to the development of a clinical pathway locally and opened up discussions with clinical interest groups directed at developing guidelines nationally and research priorities in this important area.

The next steps personally, have resulted in planning of a subsequent fellowship application to facilitate future research leadership in this area, addressing the outstanding questions posed in this thesis (surrounding current UK practice and patient/clinician acceptability), alongside other important areas of rehabilitation in the field of trauma and orthopaedics. However there is clearly a wider need for healthcare researchers, who deliver complex interventions, to recognise the importance of defining the intervention components, identifying which of these components are important and why, ensuring acceptability of the intervention in practice to both patients and clinicians. These aims cannot be achieved with the traditional RCT, but instead require a mixed methods approach.'

Declarations

None

Funding Body

This was funded by Arthritis Research UK

Table of Contents

9.1 Research school skills training

Date	Course
13/11/09	Elements of writing structure
20/11/09	Elements of paragraph construction
11/12/09	Developing a critical argument
20/01/10	Grammatical accuracy
10/02/10	Engaging the reader
25/01/10	IT SPSS
19/02/10	Upgrading process to PhD
30/04/10	Presenting academic writing to specific audiences
14/05/10	How NOT to write
19/05/10	Presenting to an academic audience
11/06/10	Getting published successfully
24/06/10	Writing for publication
09/11/10	Early career planning
10/11/10	Project management - Processes
16/11/10	How to network
25/01/11	Making an impact in job applications
08/02/11	Making successful grant applications
23/02/11	Interview success
23/03/11	Project management - Communication

9.2 Warwick medical school training

Date	Course
2009-2011	Post graduate certificate: Medical education
18/11/09	GCP Update.
02/12/09	Chief investigator course
09/12/09	Supervision training workshop for dissertations
01/04/10	Design analysis and interpretation of epidemiological research
29/09/10	Human tissue act training
15/03/11	GCP Update

9.3 Conferences and other courses attended

Date	Conference/Course
16/10/09	Conference: Chartered Society of Physiotherapy
04/11/09	Conference: British Orthopaedic Foot and Ankle Society
30/01/10	Course: Tendon biology and healing
10/03/10	Fellows meeting: Arthritis Research UK
29/03/10	Fellows meeting: NICE
20/05/10	Conference: British Trauma Society
03/06/10	Workshop: NICE methodology
12/09/10	Conference: British Orthopaedic Association
05/11/10	Fellows meeting: NICE
03/11/10	Conference: British Orthopaedic Foot and Ankle Society
22/02/11	Conference: Society for Research in Rehabilitation
09/03/11	Fellows meeting: Arthritis Research UK
05/05/11	Conference: British Trauma Society
10/05/11	Conference: NICE
13/06/11	Course: Sports foot and ankle
04/11/11	Conference: Clinical trials methodology
23/06/12	International Society Conference for Posture and Gait Research

9.4 Research grants obtained

Sept 2009: Arthritis Research UK: AHP Training Fellowship: £124,580.
March 2011: Roberts Fund: Travel Award: £950

9.5 Postgraduate awards and prizes

March 2010: NICE Scholarship
May 2010: Awarded best podium presentation at the British Trauma Society

9.6 National conference presentations

May 2010: British Trauma Society: Podium Presentation: Pilot RCT: Operative Vs Non-operative management of Achilles tendon ruptures

Jan 2011: WMS Symposium: Poster Presentation: An investigations into accelerated rehabilitation strategies following an Achilles tendon rupture

Feb 2011: Society for Research in Rehabilitation: Poster Presentation: A systematic review of early rehabilitation methods following an Achilles tendon rupture

March 2011: Arthritis Research UK: Poster Presentation: An investigation into accelerated rehabilitation strategies following an Achilles tendon rupture

May 2011: British Trauma Society: Poster Presentation: The effect of maintained plantarflexion within an ankle foot orthoses on functional outcomes and gait parameters following an Achilles tendon rupture

9.7 International conference presentations

May 2012: European Federation of National Associations of Orthopaedics and Traumatology: The Achilles tendon Total Rupture Score: A Study to Explore Further Aspects of Validity.

June 2012: International Society for Posture and Gait Research: Poster Presentation: The effect of orthotic design and the number of heel-wedges on in-shoe plantar pressures during walking: implications for Achilles tendon rupture rehabilitation.

9.8 Publications

Kearney R, S Lamb, N Parsons, J Achten, M Costa, The Achilles tendon Total Rupture Score: A Study of Responsiveness, Internal Consistency and Convergent Validity on Patients with Acute Achilles tendon Ruptures, Health and Quality of Life Outcomes (*In Press*)

Kearney R, S Lamb, J Achten, C Plant and M Costa, A systematic review of patient reported outcome measures used to assess Achilles tendon rupture management: What's being used and should we be using it? *British Journal of Sports Medicine (In Press)*

Kearney, R, J. Achten, K M^{c}Guinness, M. Costa, A Systematic Review of Early Rehabilitation Methods Following a rupture of the Achilles tendon. *Physiotherapy,* **98**, 2012, 24-32

Kearney R and M Costa, Current concepts in the rehabilitation of an acute rupture of the Achilles tendon, *Journal of Bone and Joint Surgery (Br)*, **94**, 2012, 21-28

Kearney, R, J. Achten, N. Parsons, M. Costa, The comprehensive cohort model in a pilot trial in orthopaedic trauma. *BMC Medical Research Methodology,* 11, 2011, p.11-39.

Kearney, R, S Lamb, J Achten, N Parsons and M Costa, In-Shoe plantar pressures within ankle foot orthoses: Implications for the management of Achilles tendon ruptures. *American Journal of Sports Medicine,* **39**, 2011, 2679-2685

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10 Appendices

Appendix A Participant Information Sheet

University Hospitals Coventry and Warwickshire NHS Trust

THE UNIVERSITY OF WARWICK

Participant Information Sheet

Chief Investigator: Mr Matt Costa

Background information

Rupture of the Achilles tendon is a serious and disabling injury. The condition typically affects young active adults and is associated with prolonged periods off work and much longer abstinence from sporting activity. Prolonged hospital stay and delayed rehabilitation have significant financial and health implications for both the NHS and society as a whole. Therefore, it is important to find the best way to treat patients with this injury in order to get them back to their normal activity as quickly as possible.

What is the purpose of this study?

We are assessing foot pressure measurements taken inside an orthotic to determine the best treatment for acute Achilles tendon ruptures. This foot pressure data is important to inform and lead advancements in rehabilitation protocols.

Why have I been chosen?

Healthy subjects with no history of lower limb pathology working within the University Hospitals of Coventry and Warwickshire and Warwick University will be invited to take part in this trial. A total of 15 participants will be recruited.

What will happen after I have been entered in the trial?

You will be given an appointment to attend one research clinic. During this clinic a research physiotherapist will fit you with a walking boot containing three heel raises. Inside the boot thin plastic insoles will be used to measure foot pressure distributions. The range of movement you have at your ankle will also be assessed. You will then be asked to walk ten metres down a flat corridor wearing the walking boot. This procedure will be repeated using different numbers of heel raises inside the boot.

Do I have to take part?

It is up to you whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

What are the possible disadvantages and risks of taking part?

There are no known disadvantages to taking part in this trial.

What are the possible benefits of taking part?

There is no specific advantage to you for taking part in the study. However, the information we get from this study may help us to treat future patients with Achilles tendon Ruptures.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your research physiotherapist will tell you about it and discuss with you whether you want to continue in the study. If you decide to continue in the study you will be asked sign an updated consent form.
Also, on receiving new information your research physiotherapist might consider it to be in your best interest to withdraw you from the study. If this happens He/she will explain the reasons.

What happens if something goes wrong?

In the unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you. Alternatively you can contact Mrs Ceri Jones at Research & Development Services, University Hospital Coventry and Warwickshire NHS trust, Clifford Bridge Road, Coventry, CV2 2DX. Direct telephone number 024 7696 6196.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

What will happen to the results of the research study?

This study is expected to last 2 years. At the end of the study we will publish the findings in medical journals and at medical conferences. You will not be identified in any reports or publications resulting from the study. If you would like to obtain a copy of the published results, please ask your doctor.

What will happen if I decide not to participate in the research study?

There will be no action.

Who has reviewed this study?

This study has been reviewed by Coventry Research Ethics Committee.

Contacts for further information

If you would like further information please contact Mr Matt Costa who is leading the project by telephoning 02476 968618 or Dr Juul Achten who is responsible for the overall management of the study (02476 968614, J.Achten@warwick.ac.uk).

Appendix B Consent Form

University Hospitals Coventry and Warwickshire NHS Trust

THE UNIVERSITY OF WARWICK

Consent Form

Trial Centre ID:		Date (dd/mm/yy):	
Name of Patient:		D.O.B (dd/mm/yy):	

Chief Investigator Mr Matt Costa

Please initial box

1. I confirm that I have read and understand the information sheet dated 31st of July 2008 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

_____ _____ _____

Name of Patient Date Signature

_____ _____ _____

Name of Person taking consent Date Signature

_____

Role of Person taking consent

Appendix C Participant Information Sheet

University Hospitals Coventry and Warwickshire NHS Trust

THE UNIVERSITY OF WARWICK

Participant Information Sheet

Plantar pressures in Achilles tendon rupture

Chief Investigator: Mr Matt Costa

Background information

Rupture of the Achilles tendon is a serious and disabling injury. The condition typically affects young active adults and is associated with prolonged periods off work and much longer abstinence from sporting activity. Prolonged hospital stay and delayed rehabilitation have significant financial and health implications for both the NHS and society as a whole. Therefore, it is important to find the best way to treat patients with this injury in order to get them back to their normal activity as quickly as possible.

What is the purpose of this study?

We are assessing foot pressure measurements taken inside an orthotic to determine the best treatment for acute Achilles tendon ruptures. This foot pressure data is important to inform and lead advancements in rehabilitation protocols.

Why have I been chosen?

All patients attending this hospital who present with an acute Achilles tendon rupture will be invited to take part in this trial. A total of 15 patients will be recruited.

What will happen after I have been entered in the trial?

Standard Practice: You will have the option to have your Achilles tendon operatively or non-operatively managed. Regardless of the treatment option chosen, your injured leg will be placed in a walking boot to start the recovery process. You will need to attend a clinic every two weeks for twelve weeks and then two further appointments at six and nine months after your injury, this is normal clinical practice.

Research Practice: If you take part in the trial, within the orthotic differing numbers of heel wedges are normally inserted, but at present we do not know what the optimum number is. If you take part in the trial the number of inserted heel wedges inside the orthotic will be allocated to you. At each of these visits a research physiotherapist will measure the range of movement you have at your ankle and foot pressure distributions inside your walking boot will be measured using thin plastic insoles. For this measurement, you will be asked to walk up and down a corridor five times. In addition, at each visit you will be asked to fill out 3 questionnaires to assess how disabled you feel due to your injury, your current health status and your activity level.

Do I have to take part?

It is up to you whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part will not affect the standard of care you receive; you will receive the same normal care as someone not invited to take part in the experiment.

What are the possible disadvantages and risks of taking part?

There are no known disadvantaged to taking part in this trial because your treatment will not change.

What are the possible benefits of taking part?

There is no specific advantage to you for taking part in the study. However, the information we get from this study may help us to treat future patients with Achilles tendon Ruptures.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your research physiotherapist will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw your research physiotherapist will make arrangements for your care to continue. If you decide to continue in the study you will be asked sign an updated consent form.

Also, on receiving new information your research physiotherapist might consider it to be in your best interest to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

What happens when the research study ends?

You will be in the study for 9 months. If you are still having problems after this time, we will arrange for you to have an appointment with an appropriate specialist to continue your care.

What happens if something goes wrong?

In the unlikely event of you being harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you. Alternatively you can contact Mrs Ceri Jones at Research & Development Services, University Hospital Coventry and Warwickshire NHS trust, Clifford Bridge Road, Coventry, CV2 2DX. Direct telephone number 024 7696 6196.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

What will happen to the results of the research study?

This study is expected to last 3 years. At the end of the study we will publish the findings in medical journals and at medical conferences. You will not be identified in any reports or publications resulting from the study. If you would like to obtain a copy of the published results, please ask your doctor.

What will happen if I decide not to participate in the research study?

There will be no change to your treatment.

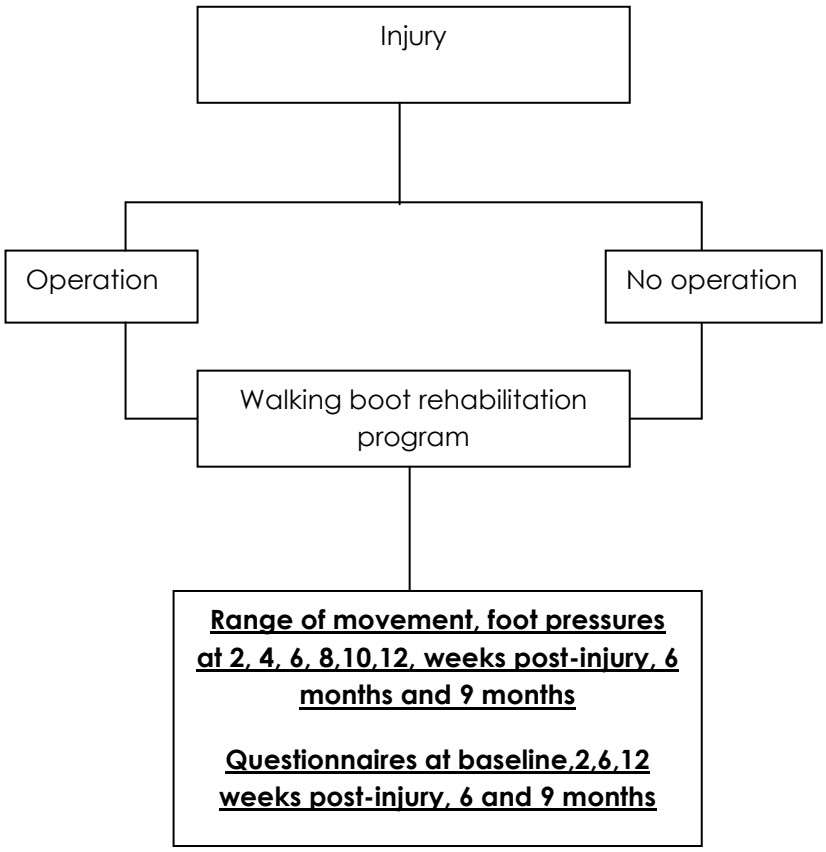
Who has reviewed this study?

This study has been reviewed by Coventry Research Ethics Committee.

Contacts for further information

If you would like further information please contact Mr Matt Costa who is leading the project by telephoning 02476 968618 or Dr Juul Achten who is responsible for the overall management of the study (02476 968614, J.Achten@warwick.ac.uk).

Flow chart of the study



Appendix D Consent Form

University Hospitals Coventry and Warwickshire NHS Trust

THE UNIVERSITY OF WARWICK

Consent Form

Trial Centre ID:		Date (dd/mm/yy):	
Name of Patient:		D.O.B (dd/mm/yy):	

Chief Investigator Mr Matt Costa

Please initial box

1. I confirm that I have read and understand the information sheet dated 31st July 2008 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

_____	_____	_____
Name of patient	Date	Signature
_____	_____	_____
Name of person taking consent	Date	Signature

_____

Role of person taking consent

Appendix E Achilles tendon Total Rupture Score

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

1. Are you limited due to decreased strength in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

2. Are you limited due to fatigue in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **0 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

3. Are you limited due to stiffness in the calf/Achilles tendon/foot

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

4. Are you limited due to pain in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

5. Are you limited during activities of daily living?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

6. Are you limited when walking on uneven surfaces?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

7. Are you limited when walking quickly up the stairs or up a hill?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

8. Are you limited during activities that include running?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

9. Are you limited during activities that include jumping?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

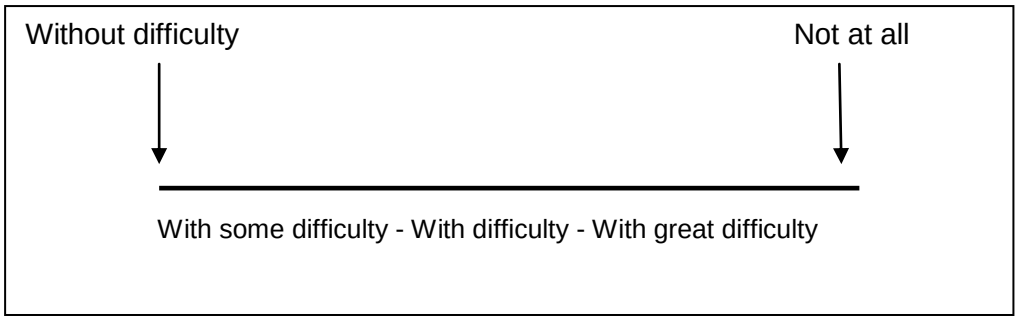
0	1	2	3	4	5	6	7	8	9	10

10 . Are you limited in performing hard physical labour?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

Appendix F Disability Rating Index



How do you manage the following activities?

After each question, please mark ONE POINT on the line

Please answer ALL questions

	Without difficulty — Not at all
Dressing (without help)	
Out-door walks	
Climbing stairs	
Sitting longer time	
Standing bent over a sink	
Carrying a bag	
Making a bed	
Running	
Light work	
Heavy work	
Lifting heavy objects	
Participating in exercise/sports	

Appendix G EQ-5D

These questions refer to your health before your injury. Please answer this questionnaire based on how you were **before** your injury. By placing a cross in one box in each group below, please indicate which statement best describes your own health state today.

Please put a cross in **one** box for each question

Q1. Mobility:

I have no problems in walking about	☐ 1
I have some problems in walking about	☐ 2
I am confined to bed	☐ 3

Q2. Self-Care:

I have no problems with self-care	☐ 1
I have some problems washing or dressing myself	☐ 2
I am unable to wash or dress myself	☐ 3

Q3. Usual Activities (e.g. work, study, housework, family or leisure activities)**:**

I have no problems with performing my usual activities	☐ 1
I have some problems with performing my usual activities	☐ 2
I am unable to perform my usual activities	☐ 3

Q4. Pain / Discomfort:

I have no pain or discomfort	☐ 1
I have moderate pain or discomfort	☐ 2
I have extreme pain or discomfort	☐ 3

Q5. Anxiety / Depression:

I am not anxious or depressed	☐ 1
I am moderately anxious or depressed	☐ 2
I am extremely anxious or depressed	☐ 3

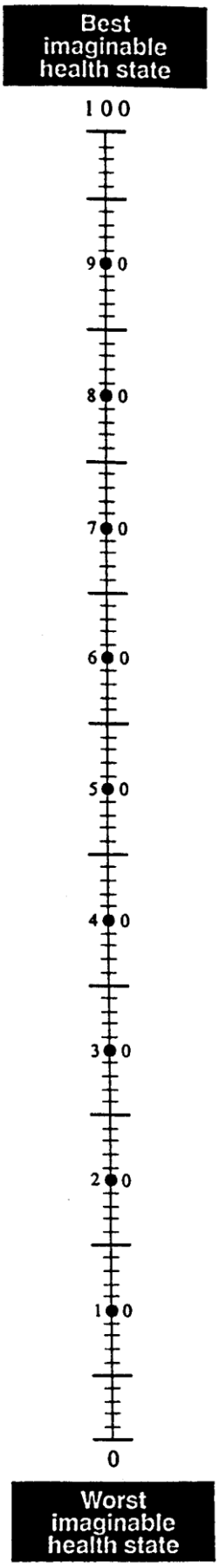
Your own health state before your injury

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale **how good or bad <u>your own health was before your injury</u>, in your opinion.**

Please do this by <u>drawing a line from the box below</u>, to whichever <u>point on the scale indicates how good or bad your current health state was before your injury</u>.

Your own health state before your injury



Appendix H Clinical Reporting Forms

Patient Screening Form

Trial Centre ID:		Date (dd/mm/yy):	
Name of Patient:		D.O.B (dd/mm/yy):	
R.A. Name:			

Eligibility check list:

Section 1: ***The answer must be "yes" to all the following questions for the patient to be eligible for the trial:***

Aged 18 years or over?	Yes ☐ 1	No ☐ 2
Acute TA Rupture (< 10 days after injury)	Yes ☐ 1	No ☐ 2
Able to give informed consent?	Yes ☐ 1	No ☐ 2

Section 2: ***The answer must be "no" to all the following questions for the patient to be eligible for the trial:***

Is this a re-rupture?	Yes ☐ 1	No ☐ 2
Any other serious injuries to either lower limb that would interfere with rehabilitation of the TA rupture?	Yes ☐ 1	No ☐ 2
Evidence that the patient would be unable to adhere to trial procedures, or complete questionnaires, such as dementia or IV drug abuse?	Yes ☐ 1	No ☐ 2

If yes, please give details……

Is the patient willing to participate in the trial? **Yes** ☐ 1 **No** ☐ 2

If "no", please ask the patient to identify reason:

I feel being part of the trial will interfere too much with my work or daily routine	☐ 1
I am not happy about being part of a research project	☐ 2
I do not want to fill in the questionnaire	☐ 3
Other – please state:……	☐ 4

PATIENT ID:

Background Information

Trial Centre ID:		Date (dd/mm/yy):	
Name of Patient:		D.O.B (dd/mm/yy):	
R.A. Name:			

Section 1: *Patient details*

Patient's Name: .....

Patient's Address: .....

.....

Post Code: .....

Telephone:

Home .....

Work .....

Mobile .....

E – Mail Address: .....

Preferred Method and Time of Contact: .....

Is the participant able to answer questions in English?

Yes ☐ 1

No ☐ 2

If no, which language would they choose to use?.....

Section 2: *Medical History*

Patient's height……..(cms) and weight……..(kgs)

Current medication:

Fluroquinolone Antibiotics Yes ☐ 1 No ☐ 2

Steroids Yes ☐ 1 No ☐ 2

DMARD's Yes ☐ 1 No ☐ 2

Diabetic Mediation Yes ☐ 1 No ☐ 2

Other Please State:

……

Pre-existing:

History of congenital or acquired condition leading to a gait abnormality? Yes ☐ 1 No ☐ 2

Other……

Lower Limb Pathology in either leg (For example hip/knee OA) Yes ☐ 1 No ☐ 2

Give Details

……..

Ipsilateral leg (pre-injury)

Achilles Symptoms - Pain Yes ☐ 1 No ☐ 2

Achilles Symptoms - Swelling Yes ☐ 1 No ☐ 2

Fusiform Swelling / Thickening Yes ☐ 1 No ☐ 2

Use of Orthotics: Yes ☐ 1 No ☐ 2

Contralateral leg (pre-injury)

Achilles Symptoms - Pain Yes ☐ 1 No ☐ 2

Achilles Symptoms - Swelling Yes ☐ 1 No ☐ 2

Fusiform Swelling / Thickening Yes ☐ 1 No ☐ 2

Section 3: *Current Injury*

Date of this injury: -- / -- / -- -- -- -- (dd/mm/yyyy)

Side of Injury: Left / Right

Management: Operative / Non-Operative

Orthotic:.....

Mechanism of injury:

Fall From Height	Yes ☐ 1	No ☐ 2		
Sports	Yes ☐ 1	No ☐ 2		
Walking / Stairs	Yes ☐ 1	No ☐ 2		
Other				

Any new injury to:

Ipsilateral Leg	Yes ☐ 1	No ☐ 2		
Give Details				
Contra- lateral Leg	Yes ☐ 1	No ☐ 2		
Give Details				
Any Other New Injury,	Yes ☐ 1	No ☐ 2		
Give Details				

PATIENT ID:

Baseline Information

Trial Centre ID:		Date (dd/mm/yy):	
Patient ID:		R.A. Name:	

1. Do you smoke?

Yes ☐ 1

No ☐ 2

If yes, how many cigarettes do you smoke per day___and how many years have you smoked___?

If no, have you smoked regularly in the past?

Yes ☐ 1

No ☐ 2

2. How many units of alcohol do you drink in a normal week? (One unit of alcohol is equivalent to ½ pint of ordinary beer, lager or cider; one small glass of wine, or one single pub measure of spirits).

0-7 units ☐ 1

8-14 units ☐ 2

15-21 units ☐ 3

>21 units ☐ 4

3. Please place a cross in the box that most closely describes your ethnic background:

White ☐ 1 *Black Caribbean* ☐ 2 *Black African* ☐ 3 *Black other* ☐ 4

Indian ☐ 5 *Pakistani* ☐ 6 *Bangladeshi* ☐ 7 *Chinese* ☐ 8

Other ☐ 9 *(Please specify)* .....

Section 1:

These questions refer to your health before your injury. Please answer this questionnaire based on how you were **before** your injury. By placing a cross in one box in each group below, please indicate which statement best describes your own health state today.

Please put a cross in **one** box for each question

Q1. Mobility:

I have no problems in walking about	☐ 1
I have some problems in walking about	☐ 2
I am confined to bed	☐ 3

Q2. Self-Care:

I have no problems with self-care	☐ 1
I have some problems washing or dressing myself	☐ 2
I am unable to wash or dress myself	☐ 3

Q3. Usual Activities (e.g. work, study, housework, family or leisure activities)**:**

I have no problems with performing my usual activities	☐ 1
I have some problems with performing my usual activities	☐ 2
I am unable to perform my usual activities	☐ 3

Q4. Pain / Discomfort:

I have no pain or discomfort	☐ 1
I have moderate pain or discomfort	☐ 2
I have extreme pain or discomfort	☐ 3

Q5. Anxiety / Depression:

I am not anxious or depressed	☐ 1
I am moderately anxious or depressed	☐ 2
I am extremely anxious or depressed	☐ 3

PATIENT ID:

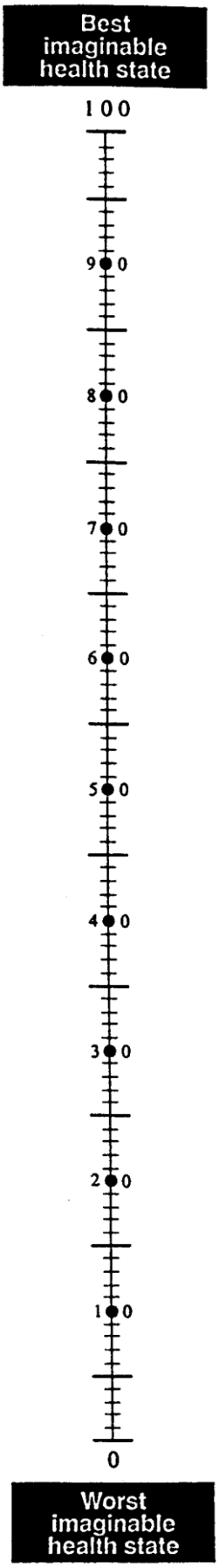
Your own health state before your injury

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale **how good or bad <u>your own health was before your injury</u>, in your opinion.**

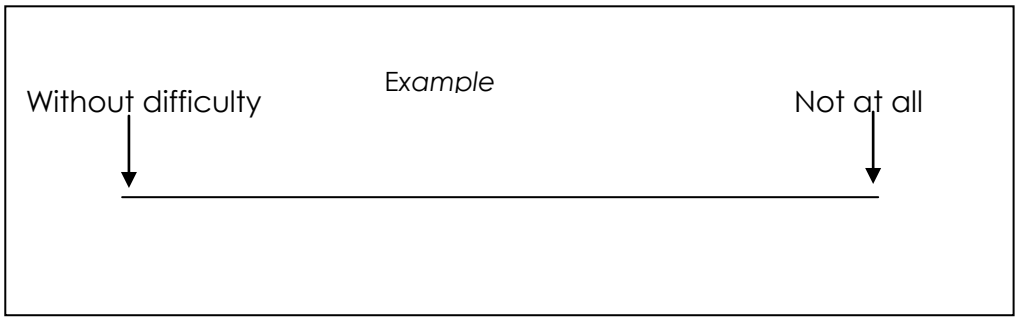
Please do this by <u>drawing a line from the box below</u>, to whichever <u>point on the scale indicates how good or bad your current health state was before your injury</u>.

Your own health state before your injury



PATIENT ID:

Section 2:



How do you manage the following activities?
After each question, please mark ONE POINT on the line

Please answer ALL questions

	Without difficulty — Not at all
Dressing (without help)	
Out-door walks	
Climbing stairs	
Sitting longer time	
Standing bent over a sink	
Carrying a bag	
Making a bed	
Running	
Light work	
Heavy work	
Lifting heavy objects	
Participating in exercise/sports	

PATIENT ID:

Section 3:

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

1. Are you limited due to decreased strength in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

2. Are you limited due to fatigue in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

3. Are you limited due to stiffness in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

4. Are you limited due to pain in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

5. Are you limited during activities of daily living?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

PATIENT ID:

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

6. Are you limited when walking on uneven surfaces?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

7. Are you limited when walking quickly up the stairs or up a hill?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

8. Are you limited during activities that include running?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

9. Are you limited during activities that include jumping?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

10 . Are you limited in performing hard physical labour?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

PATIENT ID:

Follow Up Questionnaires

Trial Centre ID:		Date (dd/mm/yy):	
Patient ID:		R.A. Name:	

1. Which treatment did the patient receive?

   Operative ☐ 1

   Non-operative ☐ 2

2. Which orthotic and rehabilitation plan has the patient received and gait analysis details:

Male/Female:	
Weight:	
Height:	
Left / Right TA rupture	
Orthotic type and rehab plan	

3. Wound Complications: *answer "no" for those in the non-operative arm as appropriate*".

   a. Were the following complications present? *Tick all that apply*

		Yes		No	
1	Erythema	☐	1	☐	2
2	Persistent serous drainage longer than 14 days	☐	1	☐	2
3	Purulent drainage	☐	1	☐	2
4	Microbiological confirmation of infection	☐	1	☐	2
5.	Re-rupture	☐	1	☐	2

PATIENT ID:

Was patient treated with:

		Yes	No
1	Antibiotics	☐ 1	☐ 2
2	Surgical management	☐ 1	☐ 2
3	Conservative management	☐ 1	☐ 2

b. If complications were treated surgically, give date and place of surgery and details:

i. Date……..

ii. Details……

4. Has the patient had a neurological injury? *if patient had non-operative treatment, tick no*

Yes ☐ 1

No ☐ 2

5. If Yes was this neurological injury:

Sural Nerve ☐ 1

Other ☐ 2

6. Has the patient had a vascular injury? *If patient had non-operative treatment, tick no*

Yes ☐ 1

No ☐ 2

7. Has the patient had a diagnosis of DVT or PE since discharge from hospital?

Yes ☐ 1

No ☐ 2

If yes, give details of date -- / -- / -- -- -- -- (dd/mm/yyyy)

Investigations……

Treatment given……..

PATIENT ID:

8. Have there been any other complications or adverse events since last attendance at hospital?

Yes ☐ 1

No ☐ 2

If yes, give details of date -- / -- / -- -- -- -- (dd/mm/yyyy)

Investigations……

Treatment given……..

9. Do documented complications qualify as a serious adverse event (SAE):

a. Life-threatening

b. Required hospitalisation or prolongation of existing hospitalisation

c. Resulted in persistent or significant disability or incapacity

d. Required medical intervention to prevent one of the above

e. Otherwise considered medically significant by the investigator?

Yes ☐ 1

No ☐ 2

If **yes**, complete the SAE report form. This form is to be sent to the central office Please ensure that this is done **within 24 hours** of the patient attending the follow-up clinic.

For central office use only:

a) Serious / not serious
b) Mild / moderate / severe
c) Probably related / possibly related / unlikely to be related / unrelated to treatment
d) Expected / unexpected

Signed (CI): Reported to LREC: Yes / No / NA
Date:

10. Have any of the participant's contact details changed, or are there likely to be any changes in the next 3 months?

Yes ☐ 1

If so, please give the new details……

……

No ☐ 2

PATIENT ID:

Section 1:

These questions refer to your health before your injury. Please answer this questionnaire based on how you were **before** your injury. By placing a cross in one box in each group below, please indicate which statement best describes your own health state today.

Please put a cross in **one** box for each question

Q1. Mobility:

I have no problems in walking about	☐ 1
I have some problems in walking about	☐ 2
I am confined to bed	☐ 3

Q2. Self-Care:

I have no problems with self-care	☐ 1
I have some problems washing or dressing myself	☐ 2
I am unable to wash or dress myself	☐ 3

Q3. Usual Activities (e.g. work, study, housework, family or leisure activities)**:**

I have no problems with performing my usual activities	☐ 1
I have some problems with performing my usual activities	☐ 2
I am unable to perform my usual activities	☐ 3

Q4. Pain / Discomfort:

I have no pain or discomfort	☐ 1
I have moderate pain or discomfort	☐ 2
I have extreme pain or discomfort	☐ 3

Q5. Anxiety / Depression:

I am not anxious or depressed	☐ 1
I am moderately anxious or depressed	☐ 2
I am extremely anxious or depressed	☐ 3

PATIENT ID:

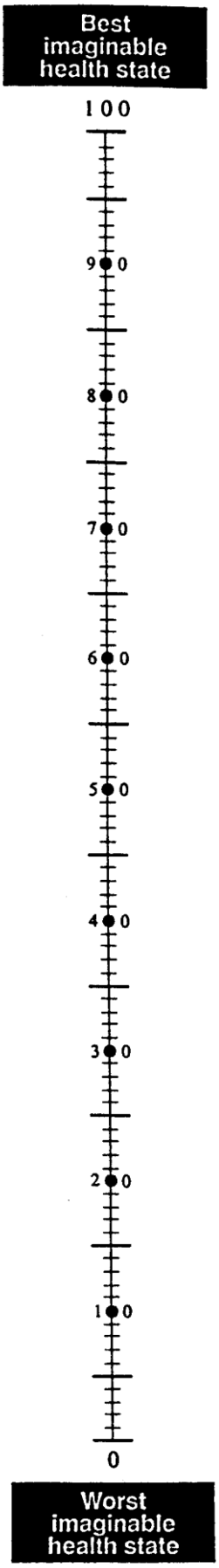
Your own health state before your injury

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale **how good or bad <u>your own health was before your injury</u>, in your opinion.**

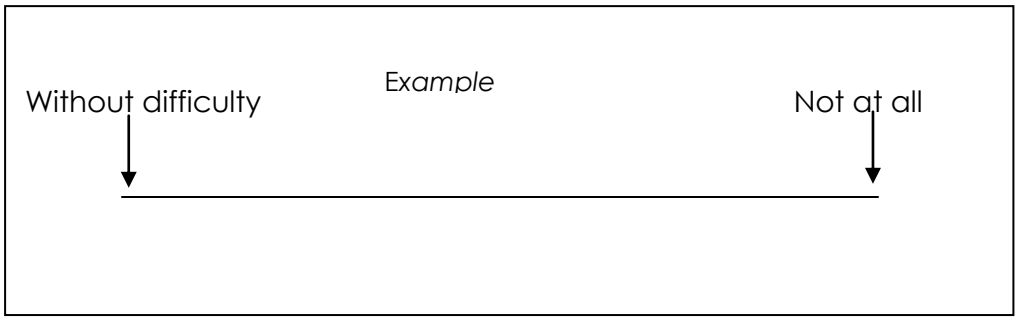
Please do this by <u>drawing a line from the box below</u>, to whichever <u>point on the scale indicates how good or bad your current health state was before your injury</u>.

Your own health state before your injury



PATIENT ID:

Section 2:



How do you manage the following activities?
After each question, please mark ONE POINT on the line

Please answer ALL questions

	Without difficulty — Not at all
Dressing (without help)	
Out-door walks	
Climbing stairs	
Sitting longer time	
Standing bent over a sink	
Carrying a bag	
Making a bed	
Running	
Light work	
Heavy work	
Lifting heavy objects	
Participating in exercise/sports	

PATIENT ID:

Section 3:

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

10. Are you limited due to decreased strength in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

11. Are you limited due to fatigue in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

12. Are you limited due to stiffness in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

13. Are you limited due to pain in the calf/Achilles tendon/foot?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

14. Are you limited during activities of daily living?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

All questions refer to your limitations/difficulties related to your injured Achilles tendon.

Mark with an X in the box which matches your level of limitation!

15. Are you limited when walking on uneven surfaces?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

16. Are you limited when walking quickly up the stairs or up a hill?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

17. Are you limited during activities that include running?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

18. Are you limited during activities that include jumping?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

11 . Are you limited in performing hard physical labour?

0 = Major limitations/symptoms **10 = No limitations/symptoms**

0	1	2	3	4	5	6	7	8	9	10

PATIENT ID:

Serious Adverse Event Reporting Form

Trial Centre ID:		Date (dd/mm/yy):	
Patient ID:		R.A. Name:	

1. Date of event -- / -- / -- -- *(dd/mm/yy)*

2. Nature of event: (please give as much information as possible, and if necessary attach a detailed report). Information must include incident, investigations and treatment given and outcome of the event (ongoing, resolved, resolved with sequelae *tick boxes*)

   ……..

   ……..

   Outcome: Ongoing ☐ 1

   Resolved ☐ 2

   Resolved with sequelae ☐ 3

3. Was the event something that: (tick as appropriate)

   a. Resulted in death ☐ 1

   b. Is life-threatening ☐ 2

   c. Required hospitalisation or prolongation of existing hospitalisation ☐ 3

   d. Resulted in persistent or significant disability or incapacity ☐ 4

   e. Required medical intervention to prevent one of the above ☐ 5

   f. Is otherwise considered medically significant by the investigator? ☐ 6

If the answer to any of Question 3 (parts a-f) is yes, this is a serious adverse event and must be reported to the Trial central office within 24 hours of the local investigator becoming aware of it.

In the opinion of the Principal Investigator:
Is this event related to the trial treatment

Yes ☐ 1

No ☐ 2

Is it an expected ☐ 1 or unexpected ☐ 2 event?

Date event reported to Principal Investigator……

Research associate name……

Research associate signature……

Principal Investigator name……..

Principal Investigator signature……

Date of signature……

Date and time received by Trial central office……..

Outcome……..

Requirement for onward reporting?.....

Date?.....

Appendix I Quality Criteria Checklist

Property	Definition	Quality criteria[a,b]
1. Content validity	The extent to which the domain of interest is comprehensively sampled by the items in the questionnaire	+A clear description is provided of the measurement aim, the target population, the concepts that are being measured, and the item selection AND target population and (investigators OR experts) were involved in item selection; ?A clear description of above-mentioned aspects is lacking OR only target population involved OR doubtful design or method; −No target population involvement; 0No information found on target population involvement.
2. Internal consistency	The extent to which items in a (sub)scale are intercorrelated, thus measuring the same construct	+Factor analyses performed on adequate sample size (7 * # items and ⩾100) AND Cronbach's alpha(s) calculated per dimension AND Cronbach's alpha(s) between 0.70 and 0.95; ?No factor analysis OR doubtful design or method; −Cronbach's alpha(s) <0.70 or >0.95, despite adequate design and method; 0No information found on internal consistency.
3. Criterion validity	The extent to which scores on a particular questionnaire relate to a gold standard	+Convincing arguments that gold standard is "gold" AND correlation with gold standard ⩾0.70; ?No convincing arguments that gold standard is "gold" OR doubtful design or method; −Correlation with gold standard <0.70, despite adequate design and method; 0No information found on criterion validity.
4. Construct validity	The extent to which scores on a particular questionnaire relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts that are being measured	+Specific hypotheses were formulated AND at least 75% of the results are in accordance with these hypotheses; ?Doubtful design or method (e.g., no hypotheses); −Less than 75% of hypotheses were confirmed, despite adequate design and methods; 0No information found on construct validity.
5. Reproducibility		
5.1. Agreement	The extent to which the scores on repeated measures are close to each other (absolute measurement error)	+MIC < SDC OR MIC outside the LOA OR convincing arguments that agreement is acceptable; ?Doubtful design or method OR (MIC not defined AND no convincing arguments that agreement is acceptable); −MIC ⩾ SDC OR MIC equals or inside LOA, despite adequate design and method; 0No information found on agreement.
5.2. Reliability	The extent to which patients can be distinguished from each other, despite measurement errors (relative measurement error)	+ICC or weighted Kappa ⩾ 0.70; ?Doubtful design or method (e.g., time interval not mentioned); −ICC or weighted Kappa < 0.70, despite adequate design and method; 0No information found on reliability.
6. Responsiveness	The ability of a questionnaire to detect clinically important changes over time	+SDC or SDC < MIC OR MIC outside the LOA OR RR > 1.96 OR AUC ⩾ 0.70; ?Doubtful design or method; −SDC or SDC ⩾ MIC OR MIC equals or inside LOA OR RR ⩽ 1.96 OR AUC < 0.70, despite adequate design and methods; 0No information found on responsiveness.
7. Floor and ceiling effects	The number of respondents who achieved the lowest or highest possible score	+⩽15% of the respondents achieved the highest or lowest possible scores; ?Doubtful design or method; −>15% of the respondents achieved the highest or lowest possible scores, despite adequate design and methods; 0No information found on interpretation.
8. Interpretatability	The degree to which one can assign qualitative meaning to quantitative scores	+Mean and SD scores presented of at least four relevant subgroups of patients and MIC defined; ?Doubtful design or method OR less than four subgroups OR no MIC defined; 0No information found on interpretation.

MIC = minimal important change; SDC = smallest detectable change; LOA = limits of agreement; ICC = Intraclass correlation; SD, standard deviation.

[a] + = positive rating; ? = indeterminate rating; − = negative rating; 0 = no information available.

[b] Doubtful design or method = lacking of a clear description of the design or methods of the study, sample size smaller than 50 subjects (should be at least 50 in every (subgroup) analysis), or any important methodological weakness in the design or execution of the study.

(Reproduced from Terwee *et al*[133])

Bibliography

1. Dalley, A. and L. Moore. *Clinically Oriented Anatomy.* 4th ed. Maryland: Lippincott Williams and Wilkins, 1999

2. Evans, N.A. and W.D. Stanish, The basic science of tendon injuries. *Current Orthopaedics*, **14**, 2000, p.403-412.

3. Standring, S. *Gray's Anatomy.* 39th ed. London: Elseiver: Churchill Livingstone, 2005

4. Zantop, T., B. Tillmann and W. Petersen, Quantitative assessment of blood vessels of the human Achilles tendon: an immunohistochemical cadaver study. *Archives of Orthopaedic and Trauma Surgery*, **123**, 2003, p.501-504.

5. Fenwick, S.A., B.L. Hazleman and G.P. Riley, The vasculature and its role in the damaged and healing tendon. *Arthritis Research*, **4**, 2002, p.252-260.

6. Wang, J.H., M.I. Iosifidis and F.H. Fu, Biomechanical basis for tendinopathy. *Clinical Orthopaedics and Related Research*, **464**, 2006, p.320-332.

7. Maganaris, C.N., M.V. Narici and N. Maffulli, Biomechanics of the Achilles tendon. *Disability and Rehabilitation*, **30**, 2008, p.1542-1547.

8. Leppilahti, J., J. Puranen and S. Orava, Incidence of Achilles tendon rupture. *Acta Orthopadica Scandinavica*, **67**, 1996, p.277-279.

9. Khan, R.J., D. Fick, A. Keogh, J. Crawford, T. Brammar and M. Parker, Treatment of acute achilles tendon ruptures. A meta-analysis of randomized, controlled trials. *Journal of Bone and Joint Surgery (Am)*, **87**, 2005, p.2202-2210.

10. Maffulli, N., S.W. Waterston, J. Squair, J. Reaper and A.S. Douglas, Changing incidence of Achilles tendon rupture in Scotland: a 15-year study. *Clinical Journal of Sport Medicine*, **9**, 1999, p.157-160.

11. Maffulli, N., Rupture of the Achilles tendon. *Journal of Bone and Joint Surgery (Am)*, **81**, 1999, p.1019-1036.

12. Tallon, C., N. Maffulli and S.W. Ewen, Ruptured Achilles tendons are significantly more degenerated than tendinopathic tendons. *Medicine and Science in Sports and Exercise*, **33**, 2001, p.1983-1990.

13. Riley, G., Tendinopathy-from basic science to treatment. *Nature Clinical Practice Rheumatology*, **4**, 2008, p.82-89.

14. Newnham, D.M., J.G. Douglas, J.S. Legge and J.A. Friend, Achilles tendon rupture: an underrated complication of corticosteroid treatment. *Thorax*, **46**, 1991, p.853-854.

15. Royer, R.J., C. Pierfitte and P. Netter, Features of tendon disorders with fluoroquinolones. *Therapie*, **49**, 1994, p.75-76.

16. Clement, D.B., J.E. Taunton and G.W. Smart, Achilles tendinitis and peritendinitis: etiology and treatment. *American Journal of Sports Medicine*, **12**, 1984, p.179-84.

17. Maffulli, N. and D. Kader, Tendinopathy of tendo achillis. *Journal of Bone and Joint Surgery (Br)*, **84**, 2002, p.1-8.

18. AAOS, *The Diagnosis and Treatment of Acute Achilles Tendon Rupture: Guideline and Evidence Report [Online]. (http://www.aaos.org/research/guidelines/atrguideline.pdf)*. 2009.

19. Maffulli, N., The clinical diagnosis of subcutaneous tear of the Achilles tendon. A prospective study in 174 patients. *American Journal of Sports Medicine*, **26**, 1998, p.266-270.

20. Kotnis, R., S. David, R. Handley, K. Willett and S. Ostlere, Dynamic ultrasound as a selection tool for reducing achilles tendon reruptures. *American Journal of Sports Medicine*, **34**, 2006, p.1395-1400.

21. Sharma, P. and N. Maffulli, Tendon injury and tendinopathy: healing and repair. *Journal of Bone and Joint Surgery (Am)*, **87**, 2005, p.187-202.

22. Woo, S.L., K. Hildebrand, N. Watanabe, J.A. Fenwick, C.D. Papageorgiou and J.H. Wang, Tissue engineering of ligament and tendon healing. *Clinical Orthopaedics and Related Research*, **457**, 1999, p.S312-2S313.

23. Suchak, A.A., C. Spooner, D.C. Reid and N.M. Jomha, Postoperative rehabilitation protocols for Achilles tendon ruptures: a meta-analysis. *Clinical Orthopaedics and Related Research*, **464**, 2006, p.216-221.

24. Healy, B., R. Beasley and M. Weatherall, Venous thromboembolism following prolonged cast immobilisation for injury to the tendo Achillis. *Journal of Bone and Joint Surgery (Br)*, **92**, 2010, p.646-650.

25. Wills, C.A., S. Washburn, V. Caiozzo and C.A. Prietto, Achilles tendon rupture. A review of the literature comparing surgical versus nonsurgical treatment. *Clinical Orthopaedics and Related Research*, **453**, 1986, p.156-163.

26. Editorial, Achilles tendon rupture. *Lancet*, **1**, 1973, p.189-190.

27. Nistor, L., Surgical and non-surgical treatment of Achilles Tendon rupture. A prospective randomized study. *Journal of Bone and Joint Surgery (Am)*, **63**, 1981, p.394-399.

28. Cetti, R., S.E. Christensen, R. Ejsted, N.M. Jensen and U. Jorgensen, Operative versus nonoperative treatment of Achilles tendon rupture. A prospective randomized study and review of the literature. *American Journal of Sports Medicine*, **21**, 1993, p.791-799.

29. Thermann, H., O. Frerichs, A. Biewener, C. Krettek and P. Schandelmeier, Functional treatment of acute rupture of the Achilles tendon. An experimental biomechanical study. *Unfallchirurg*, **98**, 1995, p.507-513.

30. Majewski, M., M. Rickert and K. Steinbruck, Achilles tendon rupture. A prospective study assessing various treatment possibilities. *Orthopade*, **29**, 2000, p.670-676.

31. Moller, M., T. Movin, H. Granhed, K. Lind, E. Faxen and J. Karlsson, Acute rupture of tendon Achillis. A prospective randomised study of comparison between surgical and non-surgical treatment. *Journal of Bone and Joint Surgery (Br)*, **83**, 2001, p.843-848.

32. Willits, K., A. Amendola, D. Bryant, N.G. Mohtadi, J.R. Giffin, P. Fowler, C.O. Kean and A. Kirkley, Operative versus nonoperative treatment of acute Achilles tendon ruptures: a multicenter randomized trial using accelerated functional rehabilitation. *Journal of Bone and Joint Surgery (Am)*, **92**, 2010, p.2767-2775.

33. Saleh, M., P.D. Marshall, R. Senior and A. MacFarlane, The Sheffield splint for controlled early mobilisation after rupture of the calcaneal tendon. A prospective, randomised comparison with plaster treatment. *Journal of Bone and Joint Surgery (Br)*, **74**, 1992, p.206-209.

34. Cetti, R., L.O. Henriksen and K.S. Jacobsen, A new treatment of ruptured Achilles tendons. A prospective randomized study. *Clinical Orthopaedics and Related Research*, **452**, 1994, p.155-165.

35. Mortensen, H.M., O. Skov and P.E. Jensen, Early motion of the ankle after operative treatment of a rupture of the Achilles tendon. A prospective, randomized clinical and radiographic study. *Journal of Bone & Joint Surgery (Am)*, **81**, 1999, p.983-990.

36. Kangas, J., A. Pajala, P. Siira, M. Hamalainen and J. Leppilahti, Early functional treatment versus early immobilization in tension of the musculotendinous unit after Achilles rupture repair: a prospective, randomized, clinical study. *Journal of Trauma*, **54**, 2003, p.1171-1180.

37. Maffulli, N., C. Tallon, J. Wong, K.P. Lim and R. Bleakney, Early weightbearing and ankle mobilization after open repair of acute midsubstance tears of the achilles tendon. *American Journal of Sports Medicine*, **31**, 2003, p.692-700.

38. Bhandari, M., G.H. Guyatt, F. Siddiqui, F. Morrow, J. Busse, R.K. Leighton, S. Sprague and E.H. Schemitsch, Treatment of acute Achilles tendon ruptures: a systematic overview and meta-analysis. *Clinical Orthopaedics and Related Research*, **460**, 2002, p.190-200.

39. Khan, R.J., D. Fick, T.J. Brammar, J. Crawford and M.J. Parker, Interventions for treating acute Achilles tendon ruptures. *Cochrane Database of Systematic Reviews*, 2004, p.CD003674.

40. Costa, M.L., K. MacMillan, D. Halliday, R. Chester, L. Shepstone, A.H. Robinson and S.T. Donell, Randomised controlled trials of immediate weight-bearing mobilisation for rupture of the tendo Achillis. *Journal of Bone and Joint Surgery (Br)*, **88**, 2006, p.69-77.

41. Metz, R., E.-J.M.M. Verleisdonk, G.J.M.G. van der Heijden, G.-J. Clevers, E.R. Hammacher, M.H.J. Verhofstad and C. van der Werken, Acute Achilles tendon rupture: minimally invasive surgery versus nonoperative treatment

with immediate full weightbearing--a randomized controlled trial. *American Journal of Sports Medicine*, **36**, 2008, p.1688-1694.

42. Schroeder, L., Steinbrueck, Treatment of acute achilles tendon ruptures: open vs. percutaneous repair vs. conservative treatment. *Orthopaedic Transactions*, **21**, 1997, p.1228.

43. Lim, J., R. Dalal and M. Waseem, Percutaneous vs. open repair of the ruptured Achilles tendon: a prospective randomized controlled study. *Foot and Ankle International*, **22**, 2001, p.559-568.

44. Gigante, A., A. Moschini, A. Verdenelli, M. Del Torto, S. Ulisse and L. de Palma, Open versus percutaneous repair in the treatment of acute Achilles tendon rupture: a randomized prospective study. *Knee Surgery, Sports Traumatology, Arthroscopy*, **16**, 2008, p.204-209.

45. Majewski, M., P.E. Ochsner, F. Liu, R. Fluckiger and C.H. Evans, Accelerated healing of the rat Achilles tendon in response to autologous conditioned serum. *American Journal of Sports Medicine*, **37**, 2009, p.2117-2125.

46. Bolt, P., A.N. Clerk, H.H. Luu, Q. Kang, J.L. Kummer, Z.L. Deng, K. Olson, F. Primus, A.G. Montag, T.C. He, R.C. Haydon, and B.C. Toolan, BMP-14 gene therapy increases tendon tensile strength in a rat model of Achilles tendon injury. *Journal of Bone and Joint Surgery (Am)*, **89**, 2007, p.1315-1320.

47. Chan, B.P., K.M. Chan, N. Maffulli, S. Webb and K.K. Lee, Effect of basic fibroblast growth factor. An in vitro study of tendon healing. *Clinical Orthopaedics and Related Research*, **455**, 1997, p.239-247.

48. Enwemeka, C.S., Functional loading augments the initial tensile strength and energy absorption capacity of regenerating rabbit Achilles tendons. *American Journal of Physical Medicine and Rehabilitation*, **71**, 1992, p.31-38.

49. Enwemeka, C.S., N.I. Spielholz and A.J. Nelson, The effect of early functional activities on experimentally tenotomized Achilles tendons in rats. *American Journal of Physical Medicine and Rehabilitation*, **67**, 1988, p.264-269.

50. Rantanen, J., T. Hurme and H. Kalimo, Calf muscle atrophy and Achilles tendon healing following experimental tendon division and surgery in rats. Comparison of postoperative immobilization of the muscle-tendon complex in relaxed and tensioned positions. *Scandinavian Journal of Medicine and Science in Sports*, **9**, 1999, p.57-61.

51. Palmes, D., H.U. Spiegel, T.O. Schneider, M. Langer, U. Stratmann, T. Budny and A. Probst, Achilles tendon healing: long-term biomechanical effects of postoperative mobilization and immobilization in a new mouse model. *Journal of Orthopaedic Research*, **20**, 2002, p.939-946.

52. Bring, D., C. Reno, P. Renstrom, P. Salo, D. Hart and P. Ackermann, Prolonged immobilization compromises up-regulation of repair genes after tendon rupture in a rat model. *Scandinavian Journal of Medicine and Science in Sports*, **19**, 2009, p.411-417.

53. Bring, D.K., C. Reno, P. Renstrom, P. Salo, D.A. Hart and P.W. Ackermann, Joint immobilization reduces the expression of sensory neuropeptide receptors and impairs healing after tendon rupture in a rat model. *Journal of Orthopaedic Research*, **27**, 2009, p.274-280.

54. Almekinders, L.C., A.J. Baynes and L.W. Bracey, An in vitro investigation into the effects of repetitive motion and nonsteroidal antiinflammatory medication on human tendon fibroblasts. *American Journal of Sports Medicine*, **23**, 1995, p.119-123.

55. Gartland, J.J., Orthopaedic clinical research. Deficiencies in experimental design and determinations of outcome. *Journal of Bone and Joint Surgery (Am)*, **70**, 1988, p.1357-1364.

56. DH, *Guidance on the routine collection of patient reported outcome measures (PROMs)*. 2008, COI.

57. Johanson, N.A., M.H. Liang, L. Daltroy, S. Rudicel and J. Richmond, American Academy of Orthopaedic Surgeons lower limb outcomes assessment instruments. Reliability, validity, and sensitivity to change. *Journal of Bone and Joint Surgery (Am)*, **86-A**, 2004, p.902-909.

58. SooHoo, N.F., M. Shuler and L.L. Fleming, Evaluation of the validity of the AOFAS Clinical Rating Systems by correlation to the SF-36. *Foot and Ankle International*, **24**, 2003, p.50-55.

59. Kaikkonen, A., P. Kannus and M. Jarvinen, A performance test protocol and scoring scale for the evaluation of ankle injuries. *American Journal of Sports Medicine*, **22**, 1994, p.462-469.

60. Roos, E.M., S. Brandsson and J. Karlsson, Validation of the foot and ankle outcome score for ankle ligament reconstruction. *Foot and Ankle International*, **22**, 2001, p.788-794.

61. Nilsson-Helander, K., R. Thomee, K. Gravare-Silbernagel, P. Thomee, E. Faxen, B.I. Eriksson and J. Karlsson, The Achilles tendon Total Rupture Score (ATRS): development and validation. *American Journal of Sports Medicine*, **35**, 2007, p.421-426.

62. Leppilahti, J., K. Forsman, J. Puranen and S. Orava, Outcome and prognostic factors of achilles rupture repair using a new scoring method. *Clinical Orthopaedics and Related Research*, **456**, 1998, p.152-161.

63. Blackwood, B., Methodological issues in evaluating complex healthcare interventions. *Journal of advanced nursing*, **54**, 2006, p.612-622.

64. MRC, *Developing and evaluating complex interventions: New guidance [Online]. (http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004871)*. 2006.

65. Leppilahti, J. and S. Orava, Total Achilles tendon rupture. A review. *Sports Medicine*, **25**, 1998, p.79-100.

66. Kearney, R.S., J. Achten, N.R. Parsons and M.L. Costa, The comprehensive cohort model in a pilot trial in orthopaedic trauma. *BMC Medical Research Methodology*, **11**, 2011, p.39.

67. McCulloch, P., D.G. Altman, W.B. Campbell, D.R. Flum, P. Glasziou, J.C. Marshall, J. Nicholl, J.K. Aronson, J.S. Barkun, J.M. Blazeby, I.C. Boutron, P.A. Clavien, J.A. Cook, P.L. Ergina, L.S. Feldman, G.J. Maddern, B.C. Reeves, C.M. Seiler, S.M. Strasberg, J.L. Meakins, D. Ashby, N. Black, J. Bunker, M. Burton, M. Campbell, K. Chalkidou, I. Chalmers, M. de Leval, J. Deeks, A. Grant, M. Gray, R. Greenhalgh, M. Jenicek, S. Kehoe, R. Lilford, P. Littlejohns, Y. Loke, R. Madhock, K. McPherson, J. Meakins, P. Rothwell, B. Summerskill, D. Taggart, P. Tekkis, M. Thompson, T. Treasure, U. Trohler, and J. Vandenbroucke, No surgical innovation without evaluation: the IDEAL recommendations. *Lancet*, **374**, 2009, p.1105-1112.

68. Groves, T., Research methods and reporting. *British Medical Journal*, **337**, 2008, p.979-980.

69. Lansdaal, J.R., J.C. Goslings, M. Reichart, G.A. Govaert, K.M. van Scherpenzeel, R. Haverlag and K.J. Ponsen, The results of 163 Achilles tendon ruptures treated by a minimally invasive surgical technique and functional aftertreatment. *Injury*, **38**, 2007, p.839-844.

70. Boutron, I., D. Moher, D.G. Altman, K.F. Schulz and P. Ravaud, Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of Internal Medicine*, **148**, 2008, p.295-309.

71. Boutron, I., D. Moher, D.G. Altman, K.F. Schulz and P. Ravaud, Methods and processes of the CONSORT Group: example of an extension for trials assessing nonpharmacologic treatments. *Annals of Internal Medicine*, **148**, 2008, p.W60-66.

72. Speck, M. and K. Klaue, Early full weightbearing and functional treatment after surgical repair of acute achilles tendon rupture. *American Journal of Sports Medicine*, **26**, 1998, p.789-793.

73. Costa, M.L., L. Shepstone, C. Darrah, T. Marshall and S.T. Donell, Immediate full-weight-bearing mobilisation for repaired Achilles tendon ruptures: a pilot study. *Injury*, **34**, 2003, p.874-876.

74. Hufner, T.M., D.B. Brandes, H. Thermann, M. Richter, K. Knobloch and C. Krettek, Long-term results after functional nonoperative treatment of achilles tendon rupture. *Foot and Ankle International*, **27**, 2006, p.167-171.

75. Jacob, K.M. and R. Paterson, Surgical repair followed by functional rehabilitation for acute and chronic achilles tendon injuries: excellent functional results, patient satisfaction and no reruptures. *ANZ Journal of Surgery*, **77**, 2007, p.287-291.

76. Majewski, M., S. Schaeren, U. Kohlhaas and P.E. Ochsner, Postoperative rehabilitation after percutaneous Achilles tendon repair: early functional therapy versus cast immobilization. *Disability and Rehabilitation*, **30**, 2008, p.1726-1732.

77. Bhattacharyya, M. and B. Gerber, Mini-invasive surgical repair of the Achilles tendon: does it reduce post-operative morbidity? *International Orthopaedics*, **33**, 2009, p.151-156.

78. Doral, M.N., M. Bozkurt, E. Turhan, M. Ayvaz, O.A. Atay, A. Uzumcugil, G. Leblebicioglu, D. Kaya and T. Aydog, Percutaneous suturing of the ruptured Achilles tendon with endoscopic control. *Archives of Orthopaedic Trauma Surgery*, **129**, 2009, p.1093-1101.

79. Gelberman, R.H., P.R. Manske, J.S. Vande Berg, P.A. Lesker and W.H. Akeson, Flexor tendon repair in vitro: a comparative histologic study of the rabbit, chicken, dog, and monkey. *Journal of Orthopaedic Research*, **2**, 1984, p.39-48.

80. Lehto, M., V.C. Duance and D. Restall, Collagen and fibronectin in a healing skeletal muscle injury. An immunohistological study of the effects of physical activity on the repair of injured gastrocnemius muscle in the rat. *Journal of Bone and Joint Surgery (Br)*, **67**, 1985, p.820-828.

81. Kjaer, M., Role of extracellular matrix in adaptation of tendon and skeletal muscle to mechanical loading. *Physiological Reviews*, **84**, 2004, p.649-698.

82. Kjaer, M., H. Langberg, B.F. Miller, R. Boushel, R. Crameri, S. Koskinen, K. Heinemeier, J.L. Olesen, S. Dossing, M. Hansen, S.G. Pedersen, M.J. Rennie, and P. Magnusson, Metabolic activity and collagen turnover in human tendon in response to physical activity. *Journal of Musculoskeletal and Neuronal Interactions*, **5**, 2005, p.41-52.

83. Akizuki, K.H., E.J. Gartman, B. Nisonson, S. Ben-Avi and M.P. McHugh, The relative stress on the Achilles tendon during ambulation in an ankle immobiliser: implications for rehabilitation after Achilles tendon repair. *British Journal of Sports Medicine*, **35**, 2001, p.329-333.

84. Booth, F.W., Effect of limb immobilization on skeletal muscle. *Journal of Applied Physiology*, **52**, 1982, p.1113-1118.

85. Lin, T.W., L. Cardenas and L.J. Soslowsky, Biomechanics of tendon injury and repair. *Journal of Biomechanics*, **37**, 2004, p.865-877.

86. Cavanagh, P., F. Hewitt and J. Perry, In-shoe plantar pressure measurement: a review. *The Foot*, **2**, 1992, p.185-194.

87. Harrison, A.J. and J.P. Folland, Investigation of gait protocols for plantar pressure measurement of non-pathological subjects using a dynamic pedobarograph. *Gait & Posture*, **6**, 1997, p.50-55.

88. Luo, Z.P., L.J. Berglund and K.N. An, Validation of F-Scan pressure sensor system: A technical note. *Journal of Rehabilitation Research and Development*, **35**, 1998, p.186-191.

89. Ahroni, J.H., E.J. Boyko and R. Forsberg, Reliability of F-Scan in-shoe measurements of plantar pressure. *Foot & Ankle International*, **19**, 1998, p.668-673.

90. Mueller, M.J. and M.J. Strube, Generalizability of in-shoe peak pressure measures using the F-scan system. *Clinical Biomechanics*, **11**, 1996, p.159-164.

91. Orlin, M.N. and T.G. McPoil, Plantar pressure assessment. *Physical Therapy*, **80**, 2000, p.399-409.

92. Woodburn, J. and P.S. Helliwell, Observations on the F-Scan in-shoe pressure measuring system. *Clinical Biomechanics*, **11**, 1996, p.301-304.

93. Barnett, S., International protocol guidelines for plantar pressure measurement. *The Diabetic Foot*, **1**, 1998, p.137-140.

94. Zhu, H.S., J.J. Wertsch, G.F. Harris and H.M. Alba, Walking cadence effect on plantar pressures. *Archives of Physical Medicine and Rehabilitation*, **76**, 1995, p.1000-1005.

95. Hanlon, M. and R. Anderson, Prediction methods to account for the effect of gait speed on lower limb angular kinematics. *Gait Posture*, **24**, 2006, p.280-287.

96. Moe-Nilssen, R. and J.L. Helbostad, Estimation of gait cycle characteristics by trunk accelerometry. *Journal of Biomechics*, **37**, 2004, p.121-126.

97. Chiu, M.C. and M.J. Wang, The effect of gait speed and gender on perceived exertion, muscle activity, joint motion of lower extremity, ground reaction force and heart rate during normal walking. *Gait Posture*, **25**, 2007, p.385-392.

98. Shiavi, R. and P. Griffin, Changes in electromyographic gait patterns of calf muscles with walking speed. *IEEE Transactions on Biomedical Engineering*, **30**, 1983, p.73-76.

99. Kirtley, C., M.W. Whittle and R.J. Jefferson, Influence of walking speed on gait parameters. *Journal of Biomedical Engineering*, **7**, 1985, p.282-288.

100. Mockel, G., C. Perka, K. Labs and G. Duda, The influence of walking speed on kinetic and kinematic parameters in patients with osteoarthritis of the hip using a force-instrumented treadmill and standardised gait speeds. *Archives of Orthopaedic and Trauma Surgery*, **123**, 2003, p.278-282.

101. Voloshin, A., The influence of walking speed on dynamic loading on the human musculoskeletal system. *Medicine and Science in Sports Exercise*, **32**, 2000, p.1156-1159.

102. Zeni, J.A., Jr. and J.S. Higginson, Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: a result of altered walking speed? *Clinical Biomechanics* **24**, 2009, p.372-378.

103. Whittle, M. *Gait Analysis and Introduction.*3rd ed. Great Britain: Reed Educational and Professional Publishing, 2002

104. Froberg, A., P. Komi, M. Ishikawa, T. Movin and A. Arndt, Force in the achilles tendon during walking with ankle foot orthosis. *American Journal of Sports Medicine*, **37**, 2009, p.1200-1207.

105. Saw, Y., V. Baltzopoulos, A. Lim, P.K. Rostron, B.G. Bolton-Maggs and R.F. Calver, Early mobilization after operative repair of ruptured Achilles tendon. *Injury*, **24**, 1993, p.479-484.

106. Costa, M.L., K. Logan, D. Heylings, S.T. Donell and K. Tucker, The effect of achilles tendon lengthening on ankle dorsiflexion: a cadaver study. *Foot and Ankle International*, **27**, 2006, p.414-417.

107. Hockings, M. and C. Nester, Use of dorsal ankle orthoses in the management of Achilles tendon rupture. *The Foot*, **10**, 2000, p.51-54.

108. Baily, R. *Design of Comparative Experiments.*1st ed. Cambridge: Cambridge University Press, 2008

109. Krishnan, C. and G.N. Williams, Evoked tetanic torque and activation level explain strength differences by side. *European Journal of Applied Physiology*, **106**, 2009, p.769-774.

110. Bressel, E. and P.J. McNair, Biomechanical behavior of the plantar flexor muscle-tendon unit after an Achilles tendon rupture. *American Journal of Sports Medicine*, **29**, 2001, p.321-326.

111. Sutherland, D.H., L. Cooper and D. Daniel, The role of the ankle plantar flexors in normal walking. *Journal of Bone and Joint Surgery (Am)*, **62**, 1980, p.354-363.

112. Bland, M. *Medical Statistics.*3rd ed. Great Britain: Oxford University Press, 2000

113. Costa, M.L., D. Kay and S.T. Donell, Gait abnormalities following rupture of the tendo Achillis: a pedobarographic assessment. *Journal of Bone and Joint Surgery (Br)*, **87**, 2005, p.1085-1088.

114. Trew, M. and T. Everett. *Human Movement An Introductory Text.*4th ed. China: Harcourt Publishers Limited, 2001

115. Cohen, J. *Statistical power analysis for the behaviour sciences.*Hillsdale: Routledge Academic, 1988

116. McComis, G.P., D.A. Nawoczenski and K.E. DeHaven, Functional bracing for rupture of the Achilles tendon. Clinical results and analysis of ground-reaction forces and temporal data. *Journal of Bone and Joint Surgery (Am)*, **79**, 1997, p.1799-1808.

117. Orendurff, M.S., A.D. Segal, M.D. Aiona and R.D. Dorociak, Triceps surae force, length and velocity during walking. *Gait and Posture*, **21**, 2005, p.157-163.

118. Lee, D.K., Achilles tendon repair with acellular tissue graft augmentation in neglected ruptures. *Journal of Foot and Ankle Surgery*, **46**, 2007, p.451-455.

119. Hahn, F., C. Maiwald, T. Horstmann and P. Vienne, Changes in plantar pressure distribution after Achilles tendon augmentation with flexor hallucis longus transfer. *Clinical Biomechanics*, **23**, 2008, p.109-116.

120. Maffulli, N., H.D. Moller and C.H. Evans, Tendon healing: can it be optimised? *British Journal of Sports Medicine*, **36**, 2002, p.315-316.

121. Thermann, H., O. Frerichs, A. Biewener and C. Krettek, Healing of the Achilles tendon: an experimental study. *Foot and Ankle International*, **22**, 2001, p.478-483.

122. Don, R., A. Ranavolo, A. Cacchio, M. Serrao, F. Costabile, M. Iachelli, F. Camerota, M. Frascarelli and V. Santilli, Relationship between recovery of calf-muscle biomechanical properties and gait pattern following surgery for achilles tendon rupture. *Clinical Biomechanics*, **22**, 2007, p.211-220.

123. Neumann, D., L. Vogt, W. Banzer and U. Schreiber, Kinematic and neuromuscular changes of the gait pattern after Achilles tendon rupture. *Foot and Ankle International*, **18**, 1997, p.339-341.

124. Rangan, A. and N. Maffulli, Multicentre randomised clinical trials in trauma care. *The Journal of Bone and Joint Surgery (Br)*, **93**, 2011, p.720-721.

125. Jennings, A.G. and G.K. Sefton, Chronic rupture of tendo Achillis. Long-term results of operative management using polyester tape. *Journal of Bone & Joint Surgery (Br)*, **84**, 2002, p.361-363.

126. Thompson, T.C. and J.H. Doherty, Spontaneous rupture of tendon of Achilles: a new clinical diagnostic test. *Journal of Trauma*, **2**, 1962, p.126-129.

127. Salen, B.A., E.V. Spangfort, A.L. Nygren and R. Nordemar, The Disability Rating Index: an instrument for the assessment of disability in clinical settings. *Journal of Clinical Epidemiology*, **47**, 1994, p.1423-1435.

128. Brooks, R., EuroQol: the current state of play. *Health Policy*, **37**, 1996, p.53-72.

129. Myerson, M.S., Achilles tendon ruptures. *Instructional Course Lectures*, **48**, 1999, p.219-230.

130. Boyden, E.M., H.B. Kitaoka, T.D. Cahalan and K.N. An, Late versus early repair of Achilles tendon rupture. Clinical and biomechanical evaluation. *Clinical Orthopaedics and Related Research*, **453**, 1995, p.150-158.

131. Fitzpatrick, R., C. Davey, M.J. Buxton and D.R. Jones, Evaluating patient-based outcome measures for use in clinical trials. *Health Technology Assessment*, **2**, 1998, p.i-iv, 1-74.

132. Garratt, A., Patient reported outcome measures in trials. *British Medical Journal*, **338**, 2009, p.a2597.

133. Terwee, C.B., S.D. Bot, M.R. de Boer, D.A. van der Windt, D.L. Knol, J. Dekker, L.M. Bouter and H.C. de Vet, Quality criteria were proposed for measurement properties of health status questionnaires. *Journal of Clinical Epidemiology*, **60**, 2007, p.34-42.

134. Naal, F.D., F.M. Impellizzeri and P.F. Rippstein, Which are the most frequently used outcome instruments in studies on total ankle arthroplasty? *Clinical Orthopaedics and Related Research*, **468**, 2010, p.815-826.

135. Malviya, A., N. Makwana and P. Laing, Correlation of the AOFAS scores with a generic health QUALY score in foot and ankle surgery. *Foot and Ankle International*, **28**, 2007, p.494-498.

136. Bland, J.M. and D.G. Altman, Cronbach's alpha. *British Medical Journal*, **314**, 1997, p.572.

137. Barr, S., N. Bellamy, W.W. Buchanan, A. Chalmers, P.M. Ford, W.F. Kean, G.R. Kraag, E. Gerecz-Simon and J. Campbell, A comparative study of signal versus aggregate methods of outcome measurement based on the WOMAC Osteoarthritis Index. Western Ontario and McMaster Universities Osteoarthritis Index. *Journal of Rheumatology*, **21**, 1994, p.2106-2112.

138. Kessler, R.C. and D.K. Mroczek, Measuring the effects of medical interventions. *Medical Care*, **33**, 1995, p.AS109-119.

139. Donovan, J.L., S.J. Frankel and J.D. Eyles, Assessing the need for health status measures. *Journal of Epidemiology and Community Health*, **47**, 1993, p.158-162.

140. Mokkink, L.B., C.B. Terwee, D.L. Knol, P.W. Stratford, J. Alonso, D.L. Patrick, L.M. Bouter and H.C. de Vet, The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: a clarification of its content. *BMC Medical Reseasech Methodology*, **10**, 2010, p.22-30.

141. Vavken, P., Rationale for and Methods of Superiority, Noninferiority, or Equivalence Designs in Orthopaedic, Controlled Trials. *Clinical Orthopaedics and Related Research*, **457**, 1999, p.1773-1776.

142. Byrne, M., M.E. Cupples, S.M. Smith, C. Leathem, M. Corrigan, M.C. Byrne and A.W. Murphy, Development of a complex intervention for secondary prevention of coronary heart disease in primary care using the UK Medical Research Council framework. *American Journal of Managed Care*, **12**, 2006, p.261-266.

143. Paul, G., S.M. Smith, D. Whitford, F. O'Kelly and T. O'Dowd, Development of a complex intervention to test the effectiveness of peer support in type 2 diabetes. *BMC Health Services Research*, **7**, 2007, p.136-146.

144. Bird, L., A. Arthur and K. Cox, "Did the trial kill the intervention?" experiences from the development, implementation and evaluation of a complex intervention. *BMC Medical Research Methodology*, **11**, 2011, p.24 - 31.

145. MacPherson, H. and S. Schroer, Acupuncture as a complex intervention for depression: a consensus method to develop a standardised treatment protocol for a randomised controlled trial. *Complementry Therapies in Medicine*, **15**, 2007, p.92-100.

146. Montgomery, A.A., T.J. Peters and P. Little, Design, analysis and presentation of factorial randomised controlled trials. *BMC Medical Research Methodology*, **3**, 2003, p.26-31.

147. McAlister, F.A., S.E. Straus, D.L. Sackett and D.G. Altman, Analysis and reporting of factorial trials: a systematic review. *Journal of the American Medical Association*, **289**, 2003, p.2545-2553.

148. Green, S., P.Y. Liu and J. O'Sullivan, Factorial design considerations. *Journal of Clinical Oncology*, **20**, 2002, p.3424-3430.

149. Creswell J and Plano-Clark V *Designing and conducting mixed methods research.*CA: Sage Thousand oaks, 2007.