# UNIVERSITY OF SOUTHAMPTON

FACULTY OF HEALTH SCIENCES


# The diagnosis of symptomatic forefoot neuroma from a clinical diagnostic protocol for podiatric assessment


By

Charlotte Dando


Thesis for the degree of doctor of philosophy

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Doctor of Philosophy

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## Abstract


There is limited evidence reporting the epidemiology of forefoot neuroma (FFN) in the general population of the United Kingdom (UK). Consequently, estimated incidence or prevalence are not known although the condition is considered common in the National Health Service (NHS) and private health care sectors. Therefore, there is a need to determine the extent of this condition to inform appropriate healthcare provision. Furthermore, it is thought that an accurate and timely diagnosis would improve the patient experience and use of pathways through the NHS. A specific set of symptoms, associated with FFN, has been consistently documented in the literature. Despite this, the optimal method for FFN diagnosis is challenging and anecdotally highly variable between clinicians; currently no reliable or valid clinical diagnostic protocol exists for the diagnosis of symptomatic FFN in podiatric practice. Therefore, there is a need to develop a clinical diagnostic protocol and to determine its reliability and validity. It was anticipated that accurate diagnosis will inform more targeted service planning and promote effective clinical decision making on the management options available to address participant reported symptoms.

Three sequential studies were designed and delivered within a local NHS podiatry service line. In study one, the clinical pathways were reviewed and the numerical values of individuals accessing the local podiatry service for a forefoot assessment were defined. Study two developed a clinical assessment protocol (FNCAP) with agreed expert consensus for the diagnosis of FFN. Through study three, the content validity and reliability of FNCAP for the diagnosis of FFN was established.

The findings of this thesis validate the estimated regional incidence and prevalence rates of symptomatic persons registered to the podiatry service line. However, records provided little insight into the diagnostic methods used to identify FFN from other forefoot pathology. This led to the development of a clinical diagnostic protocol from expert consensus for FFN. Through the Delphi study, six themes related to the clinical diagnosis of FFN: location of pain, non weight-bearing sensation, weight-bearing sensation, observations, clinical tests and imaging were identified. The themes were integrated such that 21 recommendations were identified and refined to form a clinical diagnostic protocol for FFN. The diagnostic test study indicated that there is content validity for the items that form FNCAP. The intra-rater reliability tests for the FNCAP revealed a ‘moderate’ threshold of agreement value. The sensitivity (100%) and specificity (95.6%) scores for FNCAP were high and indicated the FNCAP could be useful for diagnosing FFN in most cases. Feasibility testing of the FNCAP has indicated some usefulness in diagnosing FFN but further investigations are required to determine the FNCAP applicability in clinical practice.

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**Academic Thesis: Declaration Of Authorship**

I, Charlotte Dando declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

The diagnosis of symptomatic FFN from a valid and reliable clinical diagnostic protocol

I confirm that:

1. This work was done wholly while in candidature for a research degree at this University;
2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
3. Where I have consulted the published work of others, this is always clearly attributed;
4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
5. I have acknowledged all main sources of help;
6. Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
7. Parts of this work have been published and are referenced below.

Signed: Charlotte Dando

Date: 30th July 2018

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This thesis is in loving memory of my grandfather who sadly passed away before he knew I was going to be a clinical academic podiatrist. He always told me to ‘go and have an adventure!’. An adventure I have definitely had!

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# Awards, Presentations, Publications and Training

The awards, presentations, publications and training are listed below, were as a result of the work involved in the Doctorate of Philosophy:

**Awards:**

**CLAHRC Clinical Academic Doctoral Research Fellowship** to fund PhD Studentship (2012- 2017)

**The College of Podiatry Conference Bursary Scheme: Year 2015** to fund expenses to the Annual College of Podiatry Conference (2015)

**3 minute thesis presentation winner** for the Faculty of Health Sciences, University of Southampton (2016)

**'Innovations in Science'**. Poster Award. The College of Podiatry (2016)

**CLAHRC Wessex Transitional Post Doctorate Award** (£15,000) (2018)

**Invited Speaker/Poster (Peer Reviewed):**

Dando C, Bowen CJ, Cherry L (2015) **Clinical Diagnosis of symptomatic Forefoot Neuroma in the general population: Delphi Based Recommendations.** The College of Podiatry Annual Conference

Dando C, Bailey J, Jones S, Ferguson R, Cherry L, Bowen C (2016) **Introduction of Diagnostic ultrasound into MSK podiatry services** The College of Podiatry Annual Conference

Dando C, Bailey J, Jones S, Ferguson R, Cherry L, Bowen C (2016) **The integration of musculoskeletal ultrasound into clinical practice** The College of Podiatry Annual Conference

Dando C, Bailey, J, Jones, L, Cherry, L and Bowen, C (2017) **The content validity and reliability of an expert derived clinical assessment protocol for the identification of forefoot neuroma** Solent NHS Conference

Dando c., Cherry L. and Bowen, C (2017) Forefoot Neuroma: a pain between the toes. Research Network, Annual College of Podiatry Conference

**Invited Speaker/Poster:**

Dando C, Bowen CJ, Cherry L (2013) **New Graduate: Insight into being a Clinical Academic Fellow.** The Society of Chiropodists and Podiatrists Annual Conference

Dando C, Bowen CJ, Cherry L (2013) **What is the optimal clinical diagnosis for Forefoot Neuroma?** Clinical Academic Programme Event, Solent NHS Trust

Dando C, Bowen CJ, Cherry L (2014) **The Tangle of Tendons.** Hampshire Branch Meeting

Dando C, Cherry L and Bowen CJ (2014) **What is the best way to clinically diagnose forefoot neuroma in the general population?** Solent NHS Research Conference

**Publications:**

Adams, J, Woods - Townsend, K, Grace, Warner M, Bowen C, McQueen P, Dando C, Stokes M. (2015) **Raising Teenagers awareness of musculoskeletal health through LIFELAB: a collaboration between school students, teachers and clinical academic researchers** Rheumatology 54(S1):i37

Bowen CJ, Paton J, Alcacer-Pitarch B, Dando C, Westwood G. **How clinical academic podiatrists are transforming participant care** Podiatry Now 2014.17(9): 17-19.

I have recently had my manuscript titled: **The clinical diagnosis of symptomatic forefoot neuroma in the general population: a Delphi consensus study** accepted for publication by the Journal of Foot and Ankle Research.

**Training:**

Podiatry: Musculoskeletal Ultrasound Short Course at the Centre for Ultrasound Studies, AECC. CASE Accredited. (2016)

Introduction to Good Clinical Practice. (2013). NIHR Southampton General Hospital

Epidemiology for Clinicians (2014) MRC Lifecourse Epidemiology Unit, University of Cambridge

**Lecturing:**

Dando C, Bowen CJ, Cherry L (2014 and 2015) **Forefoot Neuroma: History and Clinical Assessment** University of Southampton, Health Sciences, Podiatry

Dando C, Bowen CJ, Cherry L (2014 and 2015) **Forefoot Neuroma: Ultrasound technique and imaging features** University of Southampton (Ultrasound training in Malta)

**Mentoring/ Job Role:**

MRes Student (to completion)

# Abbreviations

AUKUH – Association of UK University Hospitals

CASE – Consortium for the Accreditation of Sonographic Education

CB – Catherine Bowen (Supervisor)

CCG's – Clinical Commissioning Group

CD – Charlotte Dando

CLAHRC – Collaboration for Leadership in Applied Health Research and Care

CNS – Central Nervous System

COPD - Chronic obstructive pulmonary disease

CPG – Clinical Practice Guidelines

CPRD – Clinical Practice Research Datalink

CRF – Case Report Form

CT – computerised Tomography

CVR – Content Validity Ratio

DM – Diabetes Mellitus

DNA - Deoxyribonucleic Acid

DOH – Department of Health

ERGO – Ethics and Research Governance Online

FFN – Forefoot Neuroma

FG – Focus Group

FNCAP – Forefoot Neuroma Clinical Assessment Protocol

GCP Training – Good Clinical Practice Training

GP – General Practitioner

HRA – Health Research Authority

IM – Inter metatarsal

IRAS – Integrated Research Application System

JB – Jonathan Bailey (Podiatrist/Sonographer)

LA – Local Anaesthetic

LC – Lindsey Cherry (Supervisor)

LR – Likelihood Ratio

MRI – Magnetic Resonance Imaging

MSK – Musculoskeletal

MTPJ – Metatarsal Phalangeal Joint

MUS – Musculoskeletal ultrasound

NGF – Nerve Growth Factor

NGT – Nominal Group Technique

NHS - National Health Service

NICE – National Institute for Health and Care Excellence

NPV – Negative Predictive Value

NSAID's – Non Steroidal Anti-Inflammatory Drugs

OA – Osteoarthritis

PhD - A Doctor of Philosophy

PIS – Participant Information Sheet

PNS – Peripheral Nervous System

PPV – Positive Predictive Value

RA – Rheumatoid Arthritis

RCT – Randomised Control Trial

REC – Research Ethics Committee

SOLLAR – Southampton and Oxford Lower Limb Arthritis Research

SPSS – Statistical Packages for Social Sciences

SSI/SI – Semi Structured and Structured Interviews

UK - United Kingdom

WHO – World Health Organization

# 1.0 Chapter One

## Introduction

### 1.1 Musculoskeletal Podiatry

Podiatry is a branch of medicine devoted to the study, diagnosis, medical treatment and/or management of disorders affecting the foot, ankle and lower limb (Woodburn and Turner, 2010). Podiatrists are those individuals who have trained and gained a qualification in this branch of medicine (Woodburn and Turner, 2010). Often podiatrists will specialise in a specific topic field such as diabetes, rheumatology, podiatric surgery or even musculoskeletal (MSK) health. In MSK health, a podiatrist has expertise in managing foot and ankle MSK conditions. Broadly speaking, 'MSK conditions' refers to the assessment and management of bones, joints, muscles, and the spine, as well as rarer autoimmune conditions such as lupus. It has been thought that musculoskeletal conditions interfere with people's ability to carry out their normal daily activities (Arthritis Research UK, 2017). One of these conditions is Forefoot Neuroma (FFN). Existing literature has reported that FFN can be a challenge to identify from a clinical assessment (Mahadevan et al., 2015) and Mann and Reynolds (1983) further support this observation as they suggested that there are a 'handful of clinical treatment options although they produce mixed effect to relieve symptoms, which suggests that clinical diagnosis of FFN is difficult'. Therefore the idea of standardising clinical assessment to gain a precise diagnosis could promote early identification of FFN. In turn, this would allow podiatrists in clinical practice to make informed clinical decisions about their patients treatment options, as well as the appropriate use of resources. For patients, a timely diagnosis would lead to a targeted intervention where expectations could be established, with the ultimate aim of supporting people to stay mobile and active for longer.

Anecdotally in a NHS podiatry service it was observed that podiatrists use a range of forefoot assessments. The combination of forefoot assessment methods used varied between podiatrists. Podiatrists reported that assessments were chosen based on participant reported medical history and previous clinical experience although the success rate on accurately diagnosing forefoot pathology was unclear. The podiatry team identified FFN as a difficult condition to accurately diagnose. Even with the clinical use of guidelines, policies and protocols, participants were still receiving inconsistent clinical assessments. In turn, participants had to attend multiple appointments and participant feedback reported limited response to interventions set by the podiatrist. From this, the

idea to develop and test a set of clinical items to diagnose FFN in the general population was devised.

## 1.2 The Research Topic

### 1.2.1 Definition

The National Institute for Health and Care Excellence (NICE) (2017) has defined FFN as a ‘benign fibrotic thickening of the plantar inter digital nerve that is a response to irritation’. The lesion can be very painful and may affect walking (NHS.uk, 2017).

Alternative names for this condition are; Morton's Metatarsalgia, Morton’s Neuroma, Morton's Syndrome, Inter Digital Neuroma, Inter-Metatarsal Neuroma, Plantar Inter Digital Neuritis, and Plantar Inter- Metatarsal Neuroma (Cohen et al., 2016, Childs, 2002 and Mann and Reynolds, 1983). Throughout this document, FFN will be used as the key terminology for this condition.

As there are currently no reported adaptations or changed within the anatomical structures of the foot and ankle the descriptions and locations of bone and soft tissue pathology have predominantly been adapted from Saladin (2014)

### 1.2.2 The nervous system

The central nervous system (CNS) compromises of the brain, spinal cord and nerves. In total, there are four types of nerve: cranial, central, peripheral and autonomic. The peripheral nervous system (PNS) operates the nerves and nerve pathways throughout the body. The cranium and the vertebrae bones form the spinal column and protect the CNS. Within the hollow openings of the vertebrae, a combination of nerve cell bodies, dendrites, axon terminals, synapses (grey matter) and axons (white matter) are situated for processing, responding, and sending stimulus received by the PNS. The peripheral nerves enter and exit through openings in each of the vertebrae.

Nerves are made up of cells called neurons. Neurons can gather and transmit electrochemical signals over long or short distances throughout the body. A neuron has 3 main parts:

1. Cell body; contains the cell components to survive such a DNA, endoplasmic reticulum and ribosomes to help build proteins as well as mitochondria to help produce energy for function.
2. Axons; are long, thin cable like projections of the cell that are responsible for carrying the electrochemical signal (nerve pulses through action potential). In the

PNS the axons are covered in myelin which helps speed up the transmission of electrochemical signals. Neurons are bundled together with blood vessels travelling through the nerve tissue to provide oxygen and remove waste products.

3. Dendrites; are small branch like projections which make connections with other cells.

As a side note, when nerves regenerate they secrete a substance called nerve growth factor (NGF). NGF attracts other nerves to develop and regenerate nearby however the scientific reasoning for this phenomenon is not clearly understood. This is a process that is known to happen in podiatric and/or orthopedic surgery whereby symptoms return after excision of the nerve. This is commonly called a stump neuroma.

### 1.2.3 Nerves of the Lower Limb

From the hip to the foot there are complex networks of nerves; in particular the nerve network associated with FFN is the tibial nerve from a branch of the sciatic nerve which arises at the apex of the popliteal fossa. The tibial nerve branches to the muscles (plantaris, soleus and gastrocnemius) in the superficial posterior compartment of the leg as well as branching to the sural nerve that innervates at the posterolateral aspect of the leg. The tibial nerve travels down the leg position posterior to the tibia and supports the deep muscles (popliteus, flexor hallucis longus, flexor digitorum longus and tibialis posterior) of the posterior leg.

At the foot, the tibial nerve passes posteriorly and inferiorly to the medial malleolous through the tarsal tunnel that is covered superiorly by the flexor retinaculum. Within the tarsal tunnel, the tibial nerve branches to supply the cutaneous innervation of the heel. Distal to the tarsal tunnel the tibial nerve terminates by dividing into sensory branches which innervate the sole of the foot with three nerve branches. The medial calcaneal nerve arises within the tarsal tunnel and innervates the skin over the heel. The plantar nerve innervates the plantar surface of the medial three and half digits with the sole area. The lateral plantar nerve innervates the plantar surface of the lateral one and a half digits with the sole area.

### 1.2.4 Anatomy of the Forefoot

At the level of the metatarsal heads there is the superficial transverse metatarsal ligament. Proximal to the metatarsal heads the plantar aponeurosis forms a sagittal septa that compartmentalises the tendons and neurovascular bundle to each digit. In some texts the nerves, arteries and veins are commonly referred to as the ‘neurovascular bundle’ (Saladin, 2014).

From the level of the metatarsal heads (Figure 1), the deep fascia is attached to the skin by vertical fibres. The vertical fibres and the deep transverse metatarsal ligament form a hollow passage that the plantar neurovascular bundle passes through. The neurovascular bundle is protected inferiorly by fat bodies (adipose tissue) that extend throughout the weight bearing areas of the forefoot.

The aim of the fat bodies is to act as a cushion so that the plantar vessels and nerves are not compressed when the forefoot is weight bear. The deep fascia of the digits is continuous with the deep fascia of the foot. Specifically, the deep fascia of each digit forms sheaths dorsal to the metatarsal phalangeal joint and is know as the extensor expansion. The deep fascia covers the tendons and holds them against the phalanges. Similarly, the deep fascia forms sheaths to hold the flexor tendons against the phalanges on the plantar aspect of the foot. The sheaths prevent ‘bow stringing’ of the long and short tendons. At the point of which tendons attach to bone, synovial tendon sheaths allow the tendons to move freely due to its lubricating properties. The annualar ligaments surround the phalangeal joints while thin ligaments help to hold the tendons against the shaft of the phalanges. The deep fascia attaches directly to the medial and lateral side of the phalanges.

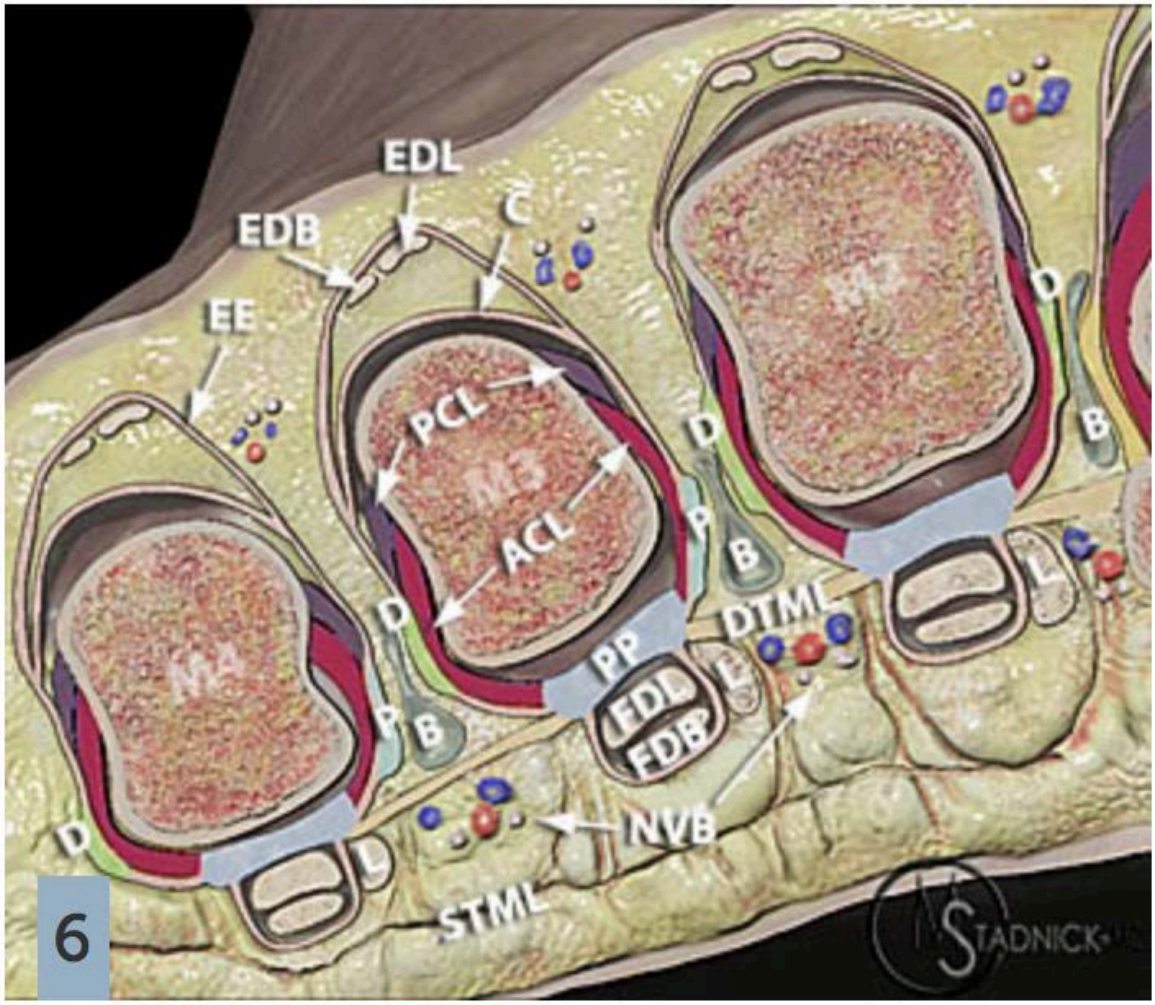



Figure 1: Transverse 3D representation of the anatomical structures at the level of the 2nd, 3rd and 4th metatarsal heads (Pinterest, 2017).

**Figure 1 Key:** extensor expansion (EE), extensor digitorum brevis (EDB), extensor digitorum longus (EDL), fibrous caspsule (C), proper collateral ligament (PCL), accessory collateral ligament (ACL), dorsal interosseous tendon (D), plantar interosseous tendon (P), inter metatarsal bursa (B), plantar plate (PP), deep transverse metatarsal ligament (DTML), lumbrical tendon (L), neurovascular bundle (NVB), flexor digitorum longus (FDL), flexor digitorum brevis (FDB) and superficial transverse metatarsal ligament (STML).

### 1.2.5 Histology

Based upon histological findings, the microscopic appearance of FFN is described as a fusiform configuration of yellow/white tissue that is relatively soft in consistency (Williams and Robinson, 2007).

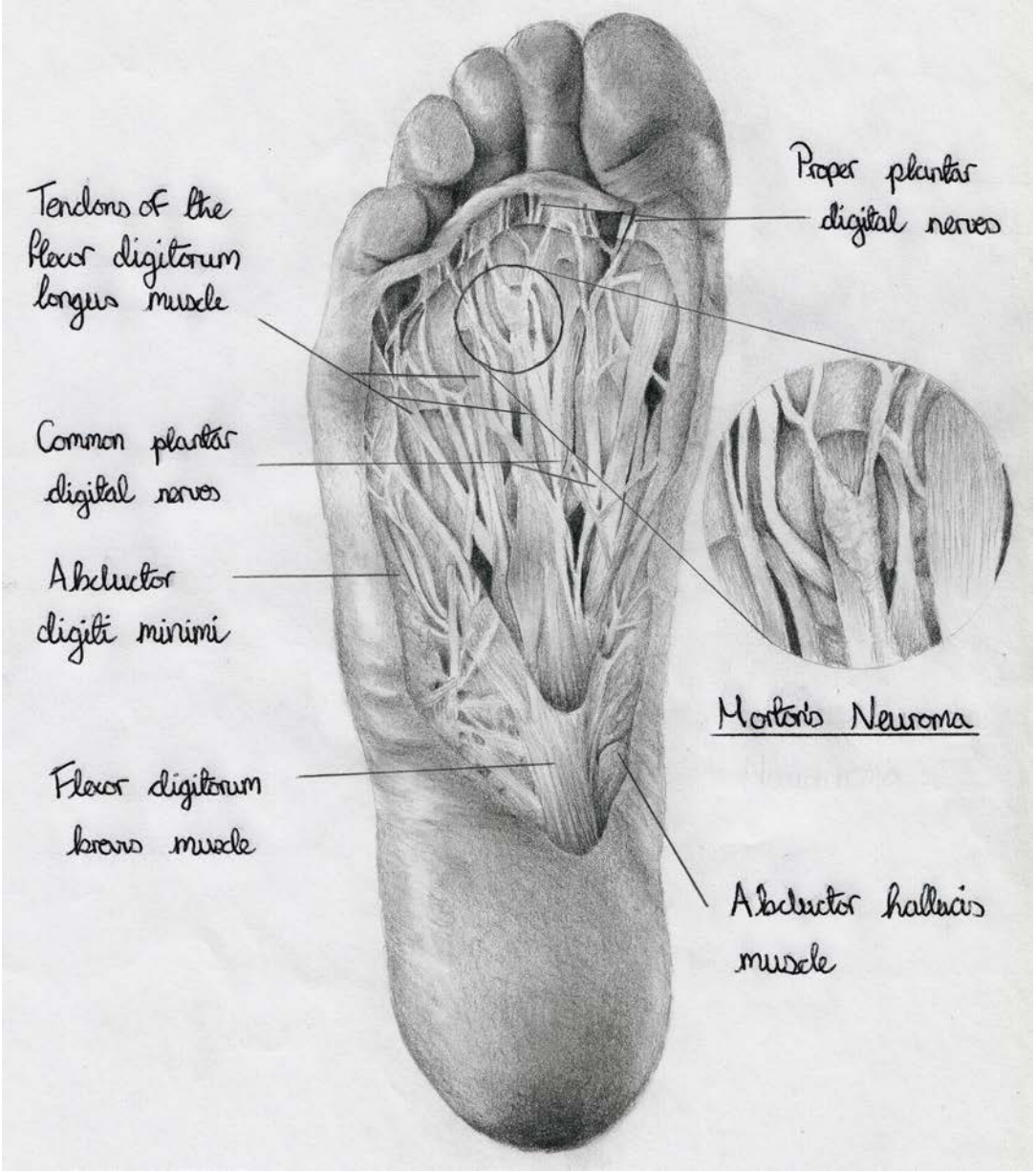



Figure 2: Anatomical drawing of FFN in the 2nd inter metatarsal space (IM space) (Authors own image, 2018)

Published work, using histopathological techniques, have documented several cellular changes which appear to be consistent with the over production of connective tissue. This might explain why this condition is sometimes referred to as a tumour (Morscher, Ulrich and Dick, 2000). In most cases these are non malignant (Morscher, Ulrich and Dick, 2000) (Figure 2).

Further histopathological investigation has demonstrated that the fusiform enlargement of

the plantar nerve is the result of deposited cellular material caused by oedema. The continual presence of edema in combination with the reparative fibrosis process of the epineurium (the outer layer of connective tissue surrounding a peripheral nerve) and perineurium (a sheath of connective tissue surrounding a bundle (fascicle) of nerve fibres) causes tissue scarring and thickening of these structures (Bencardino et al., 2000) (Figure 4). Under the microscope, this is shown via a series of multiple concentric shaped layers surrounding the nerve tissue (Figure 3).

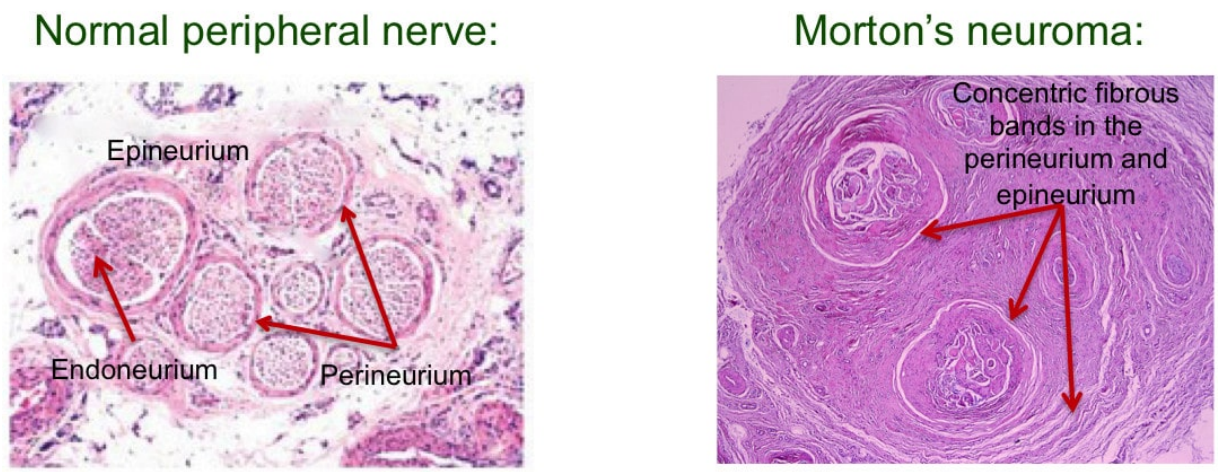



Figure 3: Normal and abnormal peripheral nerve under a microscope. The tissue has been stained to show structures (Morton's Neuroma, 2017).

The dense fibrosis thickening causes damage and a reduction in the endoneural space, which in turn reduces the number of functioning myelinated nerve fibres (Figure 3). This reduces the conductivity of the nerve fibre to accurately send and receive electrical stimulus (O'Connor et al., 2015).

In addition, hyalinization and endarteritis of the blood vessel walls starts to degenerate the tissues further (O'Connor et al., 2015). Moreover, mucoid degeneration in the fibro adipose tissue causes further separation and this can extend to the synovial lining of bursa or other tissue structures located in the inter metatarsal space hence the irregular nerve shape (Figure 3) (Oliver and Beggs, 1998).

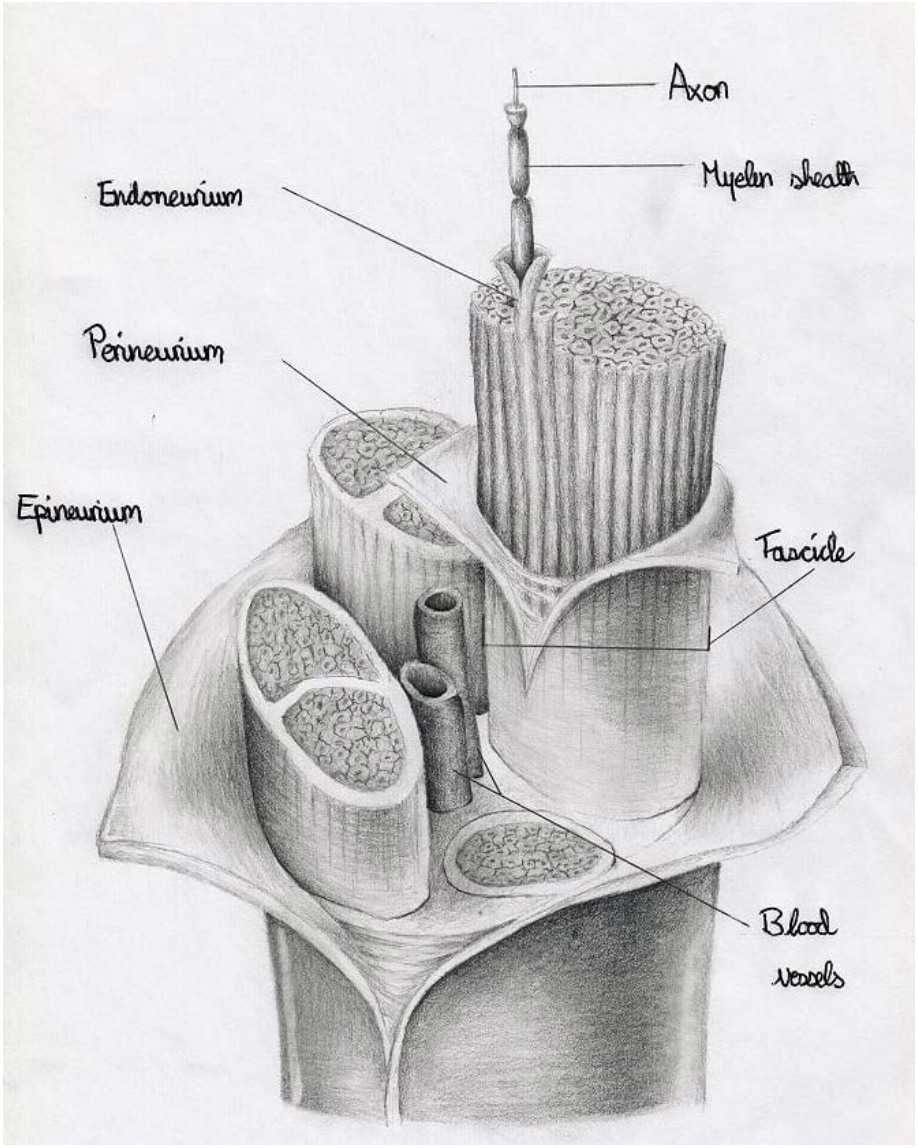



Figure 4: The structures of a nerve (Authors own image, 2018)

### 1.2.6 Anatomy in relation to the clinical problem

On review of the anatomical texts, there is agreement with regards to the perceived normal anatomical layout and structures that form the forefoot. However, there is an appreciation that variation exists within these anatomical structures which in turn has the potential to reduce the accuracy of directly locating pathology to provide a precise diagnosis. As discussed later in Chapter 2, patient reported symptoms and a comprehensive clinical assessment are fundamental in determining FFN from other forefoot pathology but with unreliable assessment techniques there is doubt as to a health professionals ability to accurately locate and interrogate the anatomical structures, to derive the cause of patient reported pain. To the author's knowledge, no clinical

assessment takes into consideration; the potential variation in anatomy located in the forefoot and how anatomical structures may vary over time through trauma, stress, injury, and adaptation.

More specifically, the complex anatomical layout of the nervous system and the structure as well as function of the nerves have demonstrated potentially why patient reported pain and recall can be difficult to locate on the foot. Furthermore, knowing that regeneration and repair of damage nerves can occur, although the mechanisms behind this are poorly understood, could indicate why interventions for FFN provide mixed outcomes for patients and in some cases symptoms increase. There is potential that soft tissue adaptions are influencing the stimuli that nerves feedback to the CNS and thus make clinical assessment difficult as health professionals are blinded to underlying tissue changes hence why its common practice for health professionals to provide a differential diagnosis and request further assessments such as imaging to justify their clinical decision making. As a result, resources become in demand, costs increase and waiting times are extended consequently having an impact on the patient experience if delays occur.

Another point to highlight is that patients who undergo invasive procedures such as surgery and/or steroid injection to resolve the pain symptoms can create further complications. There are multiple risks involved when having the procedures so may not be viable for all but due to the location of the FFN, health professionals have to cut, disrupt, or change soft tissue structures in the forefoot. Subsequently, once damage has occurred and healing has taken place known evidence supports the theory that tissues change. Currently, limited published evidence exists on describing the long-term anatomical risks of removing or modifying anatomy in the forefoot.

Taking this one step further, in the podiatric profession, podiatrists use orthotic therapy as a way to treat and manage skeletal foot and ankle complaints however limited understanding is known on what the implications and changes are on the soft tissue structures within the foot and ankle. It is thought by the author that by understanding the changes, adaptations and pressures that tissues under go through non weight bearing, weight bearing and activity it is hoped that better strategies can be devised and implemented in practice to reduce soft tissue damage and in some cases patient reported pain. This could be achieved through rehabilitation of soft tissues (exercise prescriptions), orthotic therapies, treatment interventions, and patient education/guidance. By accurately identifying pathology and soft tissues structures it is hoped that standardised clinical assessments can be used to ensure consistency and precise diagnoses are being determined by health professionals which in turn will improve clinical decision-making and patient care.

### 1.3 The PhD Aim

The overall PhD aim was to develop a novel expert-derived clinical assessment protocol to reliably diagnose FFN.

The objectives are therefore:

1. To determine the incidence rate of FFN in a single NHS service.
2. To develop a set of diagnostic criteria that has agreed expert consensus for the clinical diagnosis of FFN.
3. To determine the content validity and reliability of a novel expert derived clinical assessment protocol for the clinical diagnosis of FFN.

### 1.4 The Hypothesis

The PhD research hypothesis is therefore:

H1: ‘It is possible to develop an expert derived clinical assessment protocol for the diagnosis of FFN’

H0: ‘It is not possible to develop an expert derived clinical assessment protocol for the diagnosis of FFN’

### 1.5 The PhD Question

In order to achieve the research aim the following research question was proposed:

*‘What is the optimal clinical assessment protocol for the diagnosis of FFN?’*

### 1.6 The Structure of the Thesis

The thesis has been structured as follows:

Chapter 2: ‘Background & literature review’. This chapter details the background literature informing the research topic. An overview of foot specific complications reported in participants with symptomatic FFN, is given and differentiation between other pathologies present in the forefoot. In particular, the epidemiology, characterisation, diagnosis, treatment, and clinical importance of FFN are discussed.

This chapter also presents and justifies the overall philosophical approach and methodological design employed in this thesis. An overview of the aim and objectives for each interlinking study chapter is given. The ethical considerations related to this body of work are presented and discussed. A summary of the studied populations, outcome measures and analysis techniques used throughout the body of work are also presented

and justified.

Chapter 3: ‘The epidemiology and resource use of FFN in the general population accessing a NHS podiatry service’. This chapter draws upon retrospective data from electronic participant records to determine the presence of the participant population as well as illustrating the service pathways used to gain diagnosis and intervention.

Chapter 4: ‘The development of diagnostic criteria for FFN’. This chapter further explores individual’s beliefs, knowledge and behaviours on clinician diagnosed FFN. The naturalistic paradigm enabled the researcher to gain an informed insight into the reasons for and techniques that govern, clinical decision making for this condition. The findings of this study aid the development of diagnostic criteria to be compared against a reference standard. The need for a reliable, user dependent method of identifying FFN is proposed.

Chapter 5: ‘The content validity and reliability of an expert derived clinical assessment protocol for the identification of FFN’. This chapter reviews how the diagnostic criteria, developed in chapter 5, which can precisely and reliably diagnose FFN from other forefoot pathology. The findings from this cross sectional study will further refine the diagnostic criteria and determine its feasibility for use in clinical practice.

Chapter 6: ‘Discussion, conclusions & future research’. This chapter draws together the current findings from chapters 4, 5 and 6 and discusses the findings in the context of an integrated programme of research. The advancement in knowledge and contribution towards clinical practice made by this research programme is considered throughout both sequential research projects. Limitations within the reported studies are acknowledged and potential future work is discussed.

Chapter 7: ‘The Clinical Academic Role’. This chapter reflects upon the author’s journey throughout the PhD thesis programme. Specific reflection on the clinical teams development, the author’s leadership development, and the development of clinical academic career pathway locally.

### 1.7 Scope of the Thesis

The three studies that form this thesis were conducted over a 61 month period from October 2012 to December 2017. All data collection was completed at the University of Southampton or a clinical site within Solent NHS Trust Podiatry Services.

# 2.0 Chapter Two

## Background and Literature Review

### 2.1 Introduction

A narrative literature review was conducted to summarise and critique texts in the field of FFN. Using the PICO model, (Table 1) the related search terms were established to collect publications and additional texts.

Table 1: PICO model for FFN

| PICO | Term | Search Terms |
|---|---|---|
| **Population** | FFN | Forefoot Pain/ FFN/ Mortons Neuroma/ Digital Neuritis/ Plantar Neuritis/ Neuritis/ Inter Digital Neuritis/ Metatarsalgia/ Inter Digital Neuroma/ Mortons Metatarsalgia/ Mortons Toe/ Mortons Nerve |
| **Intervention** | Clinical Diagnosis | Diagnosis / Identification/ Examination/ Clinical Examination/ Clinical Assessment/ Screening/ Clinical Screening/ Assessment/ Tests/ Screening Tools/ Observations/ Observation Tools/ Clinical Tools |
| **Comparison** | Imaging/ Histology | Diagnostic Musculoskeletal Ultrasound/ Ultrasound Imaging/ Ultrasound Examination/ Ultrasonographer/ Sonography / Magnetic Resonance Imaging/ X-ray/ Radiograph/ Histology/ Histopathology |
| **Outcome** | Presence/absence of FFN | Tests/ Observations/ Questions/ Symptoms |

The inclusion criteria were as follows:

- Papers published in English
- Peer reviewed and non peer reviewed publications
- Publications conducted in any population or sample group

The exclusion criteria were as follows:

- Participants under the age of 18
- Neuromas not found within the foot and ankle

The search terms stated above were used on database systems that generated a list of publications. Screening the publications with the inclusion and exclusion criteria, the numbers of publications were reduced. Additional searches were carried out which specifically targeted opinion pieces, textbooks, historical texts and newspapers (Figure 5).

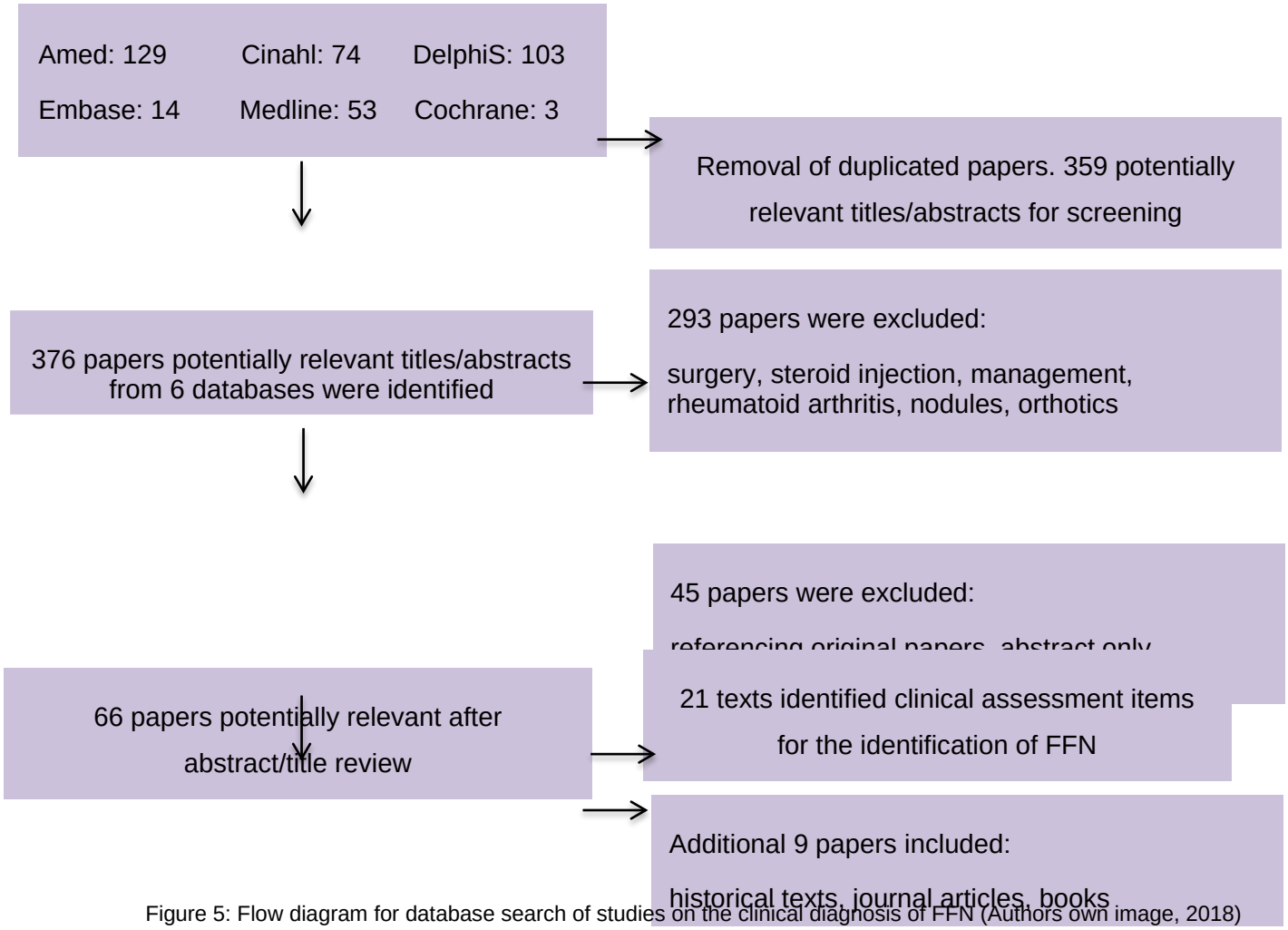



Figure 5: Flow diagram for database search of studies on the clinical diagnosis of FFN (Authors own image, 2018)

Overall, from the search, 21 texts were highlighted that identified items or methods used by health professionals and researchers to identify FFN in practice. These texts form Chapter Two's literature review on the historical background of FFN, the epidemiology, the diagnostic methods and the clinical guidance supporting health professionals to identify FFN.

## 2.2 The diagnosis of FFN – (1845 to present)

A neuroma is a benign tumour of the nerve tissue that can develop in various parts of the body however, in the foot, it is most commonly associated with the inter metatarsal (IM) spaces of the forefoot. In 1845 Lewis Durlacher, a dentist and chiropodist, first described the anatomical location and participant reported symptoms of this suspected condition (Pastides, El-Sallakh and Charalambides, 2012). In 1876, similar findings to those of Durlacher were also published by an American Orthopeadic Surgeon named Thomas George Morton. Morton (1876) had trialed a new surgical technique when conservative methods such as footwear modifications failed. This involved removing the patient's 4th metatarsal phalangeal joint (MTPJ) and surrounding soft tissue structures, which in some cases resolved participant reported symptoms. This in turn led Morton to assume that the cause of pain was a consequence of footwear style and shape that pinched on the IM structures of one or both feet. Unfortunately, Morton was unable to understand why conservative and surgical management did not work for everyone; one potential error was Morton's focus on the bone pathology rather than the soft tissue structures. This publication is still highly documented in the current literature, which might be one reason why FFN is often still referred to as "Morton's Neuroma" even though a range of evidence has been published on this topic area (Zanetti and Weishaupt, 2005).
Consequently, other orthopaedic surgeons such as Jones (1897 and 1898), Betts (1940) and McElvenny (1943) published their clinical opinions, observations and criticisms concerning surgical techniques within this field. Similarly to Durlacher and Morton, descriptive case studies were used with a small sample of less than 20 feet. These first publications do not identify the figures associated with prevalence or incidence for this condition but do highlight a pattern of symptomatic foot pain within English, Australian and American participant groups (Betts, 1940; Morton, 1876 and Pastides, El-Sallakh and Charalambides, 2012). These documents appear to highlight the early stages of identifying a clinical problem for research. Alternatively, some might argue that these combined publications are a form of expert opinion or consensus of agreement on how to provide a surgical intervention.

It was not until 1946 that Nissen, an English Orthopaedic Surgeon, described in detail the physical examination techniques used to identify FFN. Nissan (1946) also reviewed specimens and histological findings from the nerve lesions excised from surgery, concluding a change in physiology of the neurological, vascular and fibro-fatty tissues. Therefore, he hypothesised that foot biomechanics and foot shape could potentially contribute to the anatomical changes. Nissan (1946) also highlighted the importance of

histology in surgery to confirm lesions consistent with those described as FFN as a way of documenting technique success and identification. This way of measuring outcome success is still present in today's surgical outcome measures.

Following this, a podiatric surgeon known as Jacob Mulder (1951) developed a physical examination technique to identify the presence of FFN for clinical practice. This is most commonly known as Mulder's sign. Mulder (1951) also discussed the potential for pathology to co exist due to the complex anatomy of the foot. This hypothesis was built upon by two colleagues (a pathologist and orthopaedic surgeon) known as Bossley and Cairney who, in 1980, published a paper on their investigation dissecting cadavers, radiographic imaging techniques and injection therapy for participants with IM foot pain. Their study explored the possibility of IM bursa compressing on the inter-digital nerves as a potential cause of developing neurological symptoms. It was noted that loading and pressure created a physiological change in the forefoot tissues which led to tissue changes, consistent with inflammation. However, small participant samples were used although the methodology was clearly described and the results were arguably explored and justified with academic rigor.

Overall, these 8 key papers progressed the evidence-based practice surrounding symptomatic FFN but defining the cause of FFN is still highly debated (Figure 6). This would suggest that the pathophysiological evidence of FFN is poor and thus not beneficial to health professionals when linking FFN pathology to symptom presentation. Alternatively it could be argued that there is a need for studies to look into the mechanisms that govern FFN pathology and what roles this could play in linking soft tissue changes to participant report symptoms. However knowing if the pathophysiological appearance should be explored prior to developing a way to diagnose FFN is unclear, as this has not been discussed in the literature. The researcher has hypothesised that the development of a clinical assessment protocol for the diagnosis of FFN would establish how to identify people with the condition so that further studies into pathophysiology, epidemiology, and management interventions could subsequently be investigated in the future. Most of the clinical assessment techniques are still used in current clinical practice but how health professionals collectively use these methods to support clinical decision-making is unknown. This thesis considers the optimal methods needed to develop a clinical assessment protocol for clinical practice.

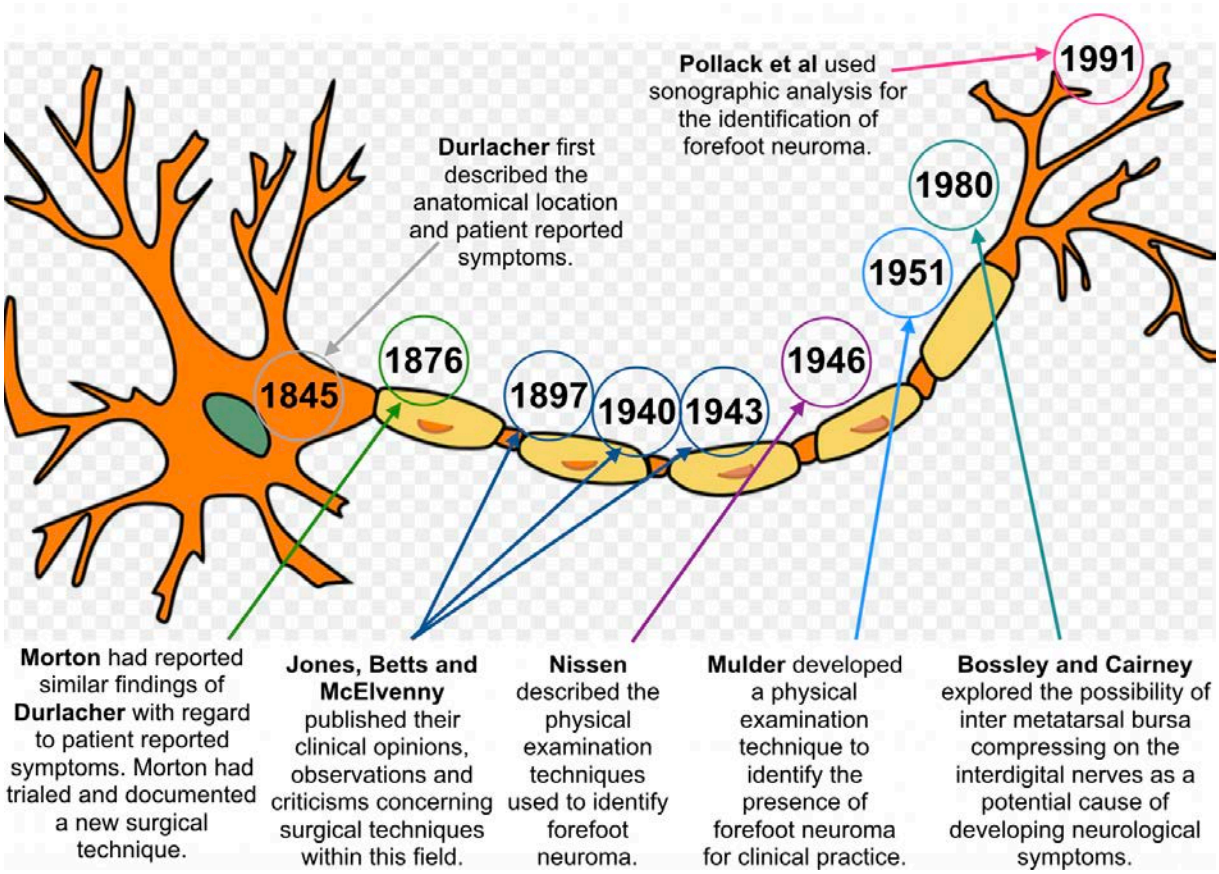



Figure 6: Timeline of key papers for developing FFN evidence base (Authors own image, 2018)

## 2.3 Epidemiology

### 2.3.1 Demographics

There is general researcher consensus that women, between 45 to 65 years of age, are more likely to be diagnosed with FFN than men (Kankanala and Jain, 2007, Nery et al., 2012, Yap and McNally, 2012 and Williams and Robinson, 2007). However, the cause and long term complications associated with the development of FFN is highly debated between published researchers (Soo, Perera and Payne, 2012, Owens et al., 2011; Pace, Scammell and Dhar, 2009 and Rout et al., 2009). The majority of researchers have selected participant reported symptoms as a way to differentiate from asymptomatic feet or other forefoot pathology (Nery et al., 2012; Owens et al., 2011 and Williams and Robinson, 2007). This still does not accurately demonstrate that clinicians can reliably identify this condition from the general population with metatarsalgia.

### 2.3.2 Incidence and Prevalence

The National Institute for Health and Clinical Excellence (NICE) in 2013 reported that FFN was a common condition in primary care services although no figures were available to further support this idea. It has been suggested that FFN is primarily a clinical diagnosis that is reached after examination and diagnostic testing have ruled out all other possible etiologies of symptoms. It is, however, evident that appropriate clinical assessment techniques for FFN have yet to be identified (Thomas et al., 2009 and Thomson et al., 2011).

Lee et al (2007) interpreted previous study estimations on prevalence for FFN to be about 30-33% but how this was calculated is not clearly outlined in the publication. Authors in the United Kingdom (UK) working on a systematic review for 'the management of FFN' suggested a calculation or estimate of incidence or prevalence is not available as a result of poorly written methodological and statistical publications (Thomson et al., 2011 and Thomas et al., 2009). One study by Latinovic (2006), reviewed the incident rate of common compressive neuropathies in primary care. Interestingly, FFN was classed within the metatarsalgia CPRD (Clinical Practice Research Datalink) codes. The GP surgery codes in 2000 identified new cases of metatarsalgia in the UK as 866/100,000 for women and 488/100,000 for men. Unfortunately, these figures cannot be further refined to separate out the percentage of suspected FFN. This could suggest that clinical identification of FFN is a challenge or that record systems at present are not sophisticated enough to accurately document this specific condition. On the other hand, the study design and data collection process may have skewed findings, thus encouraging error in the way clinicians or systems store and retrieve electronic information. Thomas et al (2009) suggested that no individual or team has been able to provide a prevalence or incidence figure locally, nationally or internationally that specifically captures the existence of FFN within a given population. This could potentially indicate the complexity of identifying potential participants within a large population.

Similarly, a data set collected from participants living in a rural community in North Carolina suggested that 9.5% (160/1691 people) of the population had been given a diagnosis of FFN. Further insight may be required to understand the methods used to identify this condition, as this was not made clear in the publication (Naraghi et al., 2016). It is hoped that, with accurate documentation, a standardised method can be developed.

### 2.4 Diagnostic Imaging Overview of Musculoskeletal Pain in the Forefoot

To assess the soft tissue and bony structures within the forefoot a number of imaging modalities can be used. Firstly, x-ray imaging is commonly used to detect bone fractures, osteomyelitis, abnormal masses, foreign objects, calcification, and osteoarthritic (OA) changes in the body. In most cases, an x-ray is requested from a health professional to examine the area of pain/discomfort, to monitor progression of a diagnosed disease or to review how an intervention might be working (Christman, 2015 and The Radiological Society of North America, 2018). However, x-rays produce ionizing radiation, which has the potential to do harm to living tissue. This risk is increased with the number of exposures an individual has over their life span. Therefore, if there are alternatives instead of x-ray to look at anatomy then these should be considered as well. With regards to the forefoot x-rays are usually requested to confirm diagnosis or in preparation for surgical planning. Conditions whereby forefoot x-rays maybe of benefit are: metatarsal and phalangeal fractures, Ligament instability and dislocations (lisfranc injury), joint space narrowing (OA changes), additional bone formations (accessory ossicles and exostosis on the toes), sesamoids (fracture) and hallux valgus deformity (bunions) (Christman, 2015).

Similarly, computed tomography (CT) or more commonly known as a CT scan which processes are traditional to an x-ray however the CT scan provides multiple cross sectional images that can show bone, tissue and positioning of organs from all angles. This machine is particularly useful in imaging the chest, abdomen and pelvis for tumours and/or blot clots (Cancer Research UK, 2015). For extremities such as the foot there is limited use compared to other imaging modalities such as musculoskeletal ultrasound (MUS) or magnetic resonance imaging (MRI) however, CT scans are useful for determining the level of bone mineral density throughout the body to determine if an individual has osteoporosis. For podiatrists who manage individuals with osteoporosis in the lower limbs, the overall aim is to support individuals to remain mobile and to reduce their risk of fractures thus promoting positive quality of life standards.

Alternatively, diagnostic MUS is a non-ionising, non-invasive imaging method which utilizes high frequency sound waves that are then interpreted by a computer to build a visual representation of tissues such as; muscle, ligaments, tendon and even fluid collections in and between anatomical structures (Smith and Finnoff, 2009). In real time, tissues can be examined, vascularity determined and structures monitored. With no known health risks, MUS is portable, has no side effects/contraindications and is painless do on an individual although it can sometimes be uncomfortable for the individual to sit in the right positions. It is user dependent and image quality depends on machine controls and functions (Smith and Finnoff, 2009). MUS can also be time consuming if the area of

interest consists of multiple joints or structures plus, deep structures can sometimes be difficult to visualise unlike MRI that has the ability to overcome this (Stokes et al, 1997).

MRI is also a non-invasive imaging technology that produces detailed anatomical images without dangerous ionizing radiation. MRI uses magnets to produce a strong magnetic field that forces protons in the body to align differently. When the magnetic field (radio frequency) is turned off, the MRI sensors are able to detect the energy released as the protons realign back to their original position. The time taken for realignment and the energy used to do this is detected by the MRI machine and thus can create a series of images that depict the different tissues in the body (The Radiological Society of North America, 2014). Although detail of soft tissue structures can be identified there are some potential disadvantages for instance, individuals with loose metal or electrical devices (theoretically jewellery/piercings too) can be at risk of further injury as the metal could be pulled in the direction of the magnetic field. Moreover, Individuals are asked to lie still for long periods of time and this can sometimes be uncomfortable or painful for certain conditions. This is also not tolerated well with people who are claustrophobic, anxious, or confused (The Radiological Society of North America, 2014). In comparison to MUS, MRI is expensive to run and can take time to set up and prepare the individual to scan. In relation to the forefoot, MRI can review a large anatomical area in detail with multiple tissue characteristics such as the bones, tendons and ligaments within a single examination period unlike other imaging modalities that focus on a small area of interest or on a particular tissue type (Rull, 2013).

Due to technological choice and access, there are multiple methods that can be used to determine to presence or absence of pathology in the foot and ankle however having expertise in choosing the right method is key to accessing imagery that is of benefit to supporting clinical decision-making. Published work by Halstead et al (2017) in foot Osteoarthritis and Siddle et al (2010) in Plantar Plate tears in patients with Rheumatoid Arthritis have started to demonstrate the benefits of using imaging techniques such as MRI and MUS to identify and monitor tissue changes in the foot and ankle.
For this scenario, FFN, MUS was the most appropriate choice compared to MRI due to its accessibility, low running costs and already trained health professionals utilising this as part of their hands on clinical assessment to manage foot and ankle pathology. This informed decision to use MUS over MRI was also highlighted by other published authors who have compared MUS and MRI results in participants to identify pathology, more specifically FFN and have found these to be comparable and similar in detection.

### 2.4.1 Use of diagnostic imaging for FFN

As a result of recent technological advancement in diagnostic musculoskeletal imaging, there has been an increase in publications identifying FFN even when presented atypically or where detection is hard to distinguish from other forefoot pathologies (Claassen et al., 2014 and Quinn et al., 2000). This has led to a collection of publications defining and documenting imaging protocols to obtain the appropriate images for diagnosis of FFN. Bowen et al (2013) explored clinical assessment in comparison to MUS in rheumatoid arthritis (RA) patients, with suspected forefoot pathology and demonstrated a high prevalence of soft tissue pathology that was detected by ultrasound but was often under diagnosed following clinical assessment alone. This could potentially highlight the importance of imaging to re-enforce clinical assessment findings. Alternatively, Claassen et al (2014) presented results implying that clinical assessment had a better diagnostic accuracy (by producing a sensitivity rate of 0.94 out of 1) compared to magnetic resonance imaging (MRI) (sensitivity rate of 0.84 out of 1) but both clinical assessment and MRI were able to determine the percentage of healthy individuals who were correctly identified as not having FFN. The specificity rate of 0.33 out of 1 was the same, hence the authors concluded that MRI, under routine clinical conditions, has a good detection rate for the evaluation of FFN but clinical assessment would have better accuracy on identification of this condition. However, it was acknowledged that within current clinical practice regular use of MRI might not be practical or feasible.

Torres-Claramunt et al (2012) have concluded that FFN is primarily based on clinical findings with MRI and MUS classed as complementary techniques. Their population was derived from participants who underwent surgical treatment due to symptoms consistent with neuroma such as; Mulder's Sign, numbness, radiation of neuritic pain, metatarsal pain. The investigators retrospectively reviewed 43 inter metatarsal spaces (37 patients) by clinical diagnosis (sensitivity 100%), MRI (sensitivity 82.9%), MUS scans (sensitivity 56.5%) and histopathology (100%). However these findings were derived from a population who were originally accessing the surgical pathway for intervention of their foot pain. This could have caused some participant selection bias which may have provided cases of neuroma which are considered chronic or long standing and therefore symptoms are well defined by the participants recall.

Moreover, Fazel, Khan and Thomas (2012) concluded that MUS has a higher sensitivity recording of 96% in contrast to MRI's sensitivity of 88% in detection of FFN. The authors further stated that 3 of the MRI scans had MUS to confirm the presence of neuroma where lesions were less than 5mm (Fazal, Khan and Thomas, 2012). Similarly, Xu et al (2015) concluded that MUS with a specificity rate of 88% and sensitivity rate of 90%

provides better overall accuracy for the diagnosis of FFN compared to MRI with a combined specificity rate of 68% and sensitivity rate of 93%. These figures were determined by 12 studies which met the inclusion criteria for the review. In total 217 participants received an MRI and 241 participants received an MUS (Xu et al., 2015). Some authors agree that MUS reported sensitivity for the diagnosis of FFN collectively as approximately 95% to 98% (Quinn et al., 2000 and Soo, Perera and Payne, 2010), further providing stronger evidence that MUS is more likely to identify FFN, but little evidence is apparent in being able to conclude if clinical assessment is comparable by sensitivity or specificity to imaging. MUS, can however, be reasonably used as a standard reference modality to inform clinical assessment comparisons of pathology within the forefoot.

**2.5 Clinical diagnosis**

On review of the literature, there is minimal clinical guidance available which specifically describes the process for diagnosing FFN. The “Diagnosis and Treatment of Forefoot Disorders. Section 3. Morton’s Intermetatarsal Neuroma” was published in 2009 by the Clinical Practice Guideline (GCP) Forefoot. The Disorders Panel of the American College of Foot and Ankle Surgeons (Thomas et al., 2009) paper was based upon consensus of current clinical practice and review of published literature. The paper identifies key themes for the diagnosis of forefoot pathology. The paper descriptively informs the reader to review participant reported symptoms as well as assessing the medical history of the patient. Thereafter clinical tests, clinical observations, and imaging requests should follow. By deduction of the reader to rule in or rule out forefoot conditions, a diagnosis should be determined. There are no statistics to inform the reader of how reliable this process is. Moreover, the paper does not state the potential risks to the reader if they incorrectly diagnose a condition. Plus it is unclear if diagnosis can be made via a number of positive tests/results or if the whole process has to be conducted.

Nonetheless, the National Institute for Health and Care Excellence (NICE), in 2010 provided primary health professionals with guidance on managing FFN. As part of this, the paper highlights the importance of reliable diagnosis (Thomas et al., 2009). Thomson et al (2011) acknowledges the inconsistencies in forefoot conditions, epidemiology, diagnostic techniques, and treatment outcomes by stating “We discovered a distinct lack of quality research for this common and troublesome condition.” The authors further conclude that an improved diagnostic strategy could improve the recording, the review, and monitoring of treatment interventions.

As a result of not having a standardised method or clinical protocol for the diagnosis of FFN, it is proposed that the ability of services like the National Health Service (NHS) to accurately plan to manage resources is unclear (Thomson et al., 2011). There is,

however, understanding that ‘no one clinical diagnostic feature is sensitive or specific enough to accurately diagnose this condition but a combination of features such as participant reported history, clinical observations and participant reported symptoms, should make a clinician suspect the presence of neuroma’ (Thomas et al., 2009). Of note, a refined combination of clinical diagnostic criteria could direct clinical decision-making and evaluate the use of services on offer for participants with FFN (Summers, 2010).

Within the NHS, local documentation is unspecific on how to clinically diagnose and differentiate FFN from other pathologies which demonstrate similar symptom characteristics (Figure five) (NHS.uk, 2017). In practice, most clinicians provide a working diagnosis or differential diagnosis to guide their treatment choices yet when intervention fails; correct identification is then sought via the use of expensive imaging modalities (Thomson et al., 2011).

The majority of investigators discuss pain affecting the 3rd IM web space, although FFN can occur within the other IM spaces (Koulouris and Morrison, 2005). There are many constructs discussed in relation to the potential aetiology of this condition but with little understanding as to why in particular, the 3rd IM space is recorded as predominantly the most common location for FFN to develop. For example, repetitive trauma, anatomical variations, mechanical loading and entrapment neuropathies have all been discussed with plausible evidence from mixed research studies (Bencardino et al, 2000; Koulouis and Morrison, 2005; Pace et al, 2010 and Rout et al, 2009). However, the majority of investigators agree that further research is required to investigate the most likely cause of FFN that in turn will aid the development of clinical diagnostic techniques (Sharp et al, 2003).

Multiple authors have stated that FFN is predominantly diagnosed from patient derived symptoms (Hassouna and Singh, 2005). The most commonly reported symptoms are localised pins and needles which manifest as a perceived burning sensation or paresthesia. In addition, partients may often complain of an onset of pain whilst walking or running and that this pain becomes so intense that mobility decreases (Hassouna and Singh, 2005; Pastides, El-Sallakh and Charalambides., 2012; Summers, 2010 and Vito and Talarico, 2003; Williams and Robinson, 2007). It is thought that patients seek intervention when daily activities are disrupted (Thomas et al., 2009). There is little evidence to support the idea whether individuals with systemic conditions or specific risk factors are more or less likely to develop FFN over time. Although, authors have discussed and commented on other factors that could potentially be related to neuroma such as lesser digit deformities, a hypermobile first ray as well as splaying of digits (Sullivan sign) and changes in alignment of toes around the localised area of pain

(Kankanala and Jain, 2007). In clinical settings, some authors have observed that little or no active inflammation or swelling exists within and around the IM space of a suspected neuroma, which seems counter intuitive since Bossley and Cairney (1980) had suggested soft tissue changes (Thomas et al., 2009). Moreover, these documented foot changes have been observations rather than tested and so application to use them as part of a diagnostic assessment is questionable. Likewise, Owens et al (2011) supports the idea that there are no specific clinical signs or characteristics for FFN but there are clinical tests closely associated with diagnosis of FFN in the current literature.

The most commonly used test for detecting the presence of neuroma is “Mulder’s Click or Mulder’s Sign”, first described by J.D Mulder in 1951. The simplest definition is a “click” in the painful region that is produced by medio-lateral compression of the metatarsal heads (Pace, Scammell and Dhar, 2009). The reliability of the Mulder’s sign test is highly contested between authors with the diagnostic accuracy (sensitivity and specificity) and repeatability challenged. Furthermore, it has been suggested that the “click” may be attributed to movement of a tendon, bursal sac or simply compression of the metatarsal heads against one another (Soo, Perera and Payne, 2010 and Vito and Talarico, 2003). In addition, the reproduction of IM pain being recognised in several IM spaces at once by some patients, can be misleading in identifying the exact location of the pain (Soo, Perera and Payne, 2010). As a result, some researchers have chosen to discount this clinical test because of its wide range of outcomes in signifying if neuroma are present in the forefoot; sensitivity range from 40% to 85% (Owens et al., 2011).

Alternatively, Owens at al (2011) described 4 potential clinical diagnostic tests for the identification of FFN. In total, 76 feet were assessed to which the treatment group scored significantly higher than those in the control group as web space tenderness was positive in 95%, foot squeeze in 88%, plantar percussion in 61%, and toe tip sensation deficit in 67%. All participants had an MRI which identified neuroma in 97% of the cases and the histological examination confirmed neuroma excision in 99% of the cases. Yet the study team appreciated that their work was unable to demonstrate whether or not diagnosis was missed in other participants as those on the study were seeking surgical intervention. Consequently, to conduct surgery on participants who potentially do not have the condition can be considered unethical and so sensitivity and specificity of each clinical test was not determined. Overall, Owens et al (2011) concluded that no pathognomonic diagnostic clinical test exists for FFN and expressed some hesitation over whether to promote imaging as a requirement for diagnosis. Similarly, Williams and Robinson (2007) concluded there were no single clinical features that could definitively predict presence of a neuroma.

Mahadevan et al (2015) assessed the diagnostic accuracy of 7 clinical tests for FFN in comparison to diagnostic musculoskeletal ultrasound (MUS) as reported sensitivity values are varied between papers, thus a consistent clinical test has yet to be reported. The 7 tests were as follows: thumb index finger squeeze test, Mulder's sign, lateral foot squeeze, plantar and dorsal percussion, light touch, pin prick test. From the study of 54 feet, the highest clinical test score was the thumb index finger squeeze test which had a confirmed sensitivity of 96% and specificity of 100% via MUS, irrespective of lesion size. Second was, Mulder's Sign (62% sensitivity and 100% specificity) and third lateral foot squeeze (41% sensitivity and 0% specificity) which also had MUS confirmation. Therefore, the authors concluded that clinical assessment is highly reliable for the detection of symptomatic FFN, with the thumb index finger squeeze test recorded as the most sensitive and specific clinical test. In addition, they felt they showed that clinical assessment was comparable with musculoskeletal ultrasound MUS for the diagnosis of FFN. Yet participants with forefoot pain, who were eligible for the study, had to have one or more positive symptom responses to the 7 clinical tests before a MUS image was reported. It was not made clear as to how the scores for multiple positive test results were evaluated as more than one positive test could influence the clinician in deciding whether FFN was present or absent compared to one clinical test. Potentially this could have introduced clinician bias. Thomas et al (2009), provided clinical consensus on using the Gauthier's Test, Digital Nerve Stress Test and Mulder's Sign to produce positive FFN symptoms. It was also agreed that FFN may demonstrate Tinel's Sign and Valleix Phenomenon due to the anatomical structures of the foot and ankle, therefore this is something to consider as part of the differential diagnosis. Nonetheless, data or figures concerning sensitivity and/or specificity for these clinical tests were documented, so a comparison of these methods in clinical practice is limiting. Hence, the comparison of literature is challenging which could potentially explain why identifying a specific clinical method for the diagnosis of FFN is difficult.

### 2.6. Clinical Guidance on FFN Assessment

On reflection of the literature, there is minimal clinical guidance available which specifically describes the diagnostic and intervention processes of managing FFN. The "Diagnosis and Treatment of Forefoot Disorders. Section 3. Morton's Intermetatarsal Neuroma" was published in 2009 by the Clinical Practice Guideline (GCP) Forefoot. The Disorders Panel of the American College of Foot and Ankle Surgeons (Thomas et al., 2009) paper was based upon consensus of current clinical practice and review of published literature. One limitation of this document is that it does not clearly state the potential risk, if any, for possible significant findings found by a health professional. It is unclear as to whether individuals should have all these significant findings to warrant

further investigation or if a specified number would suffice. In addition, the document provides little guidance on the approximate period of time that individuals should stay on one particular management option before moving onto the next.

Nonetheless, the National Institute for Health and Care Excellence (NICE), in 2010 provided primary health professionals with guidance on managing FFN. Likewise, similar evidence is used to derive the same intervention options as Thomas et al (2009) but highlighted a possible timeframe for participants to access primary and secondary care. NICE (2010) indicated a time frame of 3 months in conservative management before surgical interventions should be considered. Thomson et al (2011) tried to critique and assess the effectiveness of surgical and non surgical interventions for FFN to which they concluded that insufficient evidence exists but well designed trials are required to begin to establish an evidence base. Also, this document briefly describes the inconsistencies found within the conditions, epidemiology, diagnostic techniques and treatment outcomes by stating “We discovered a distinct lack of quality research for this common and troublesome condition” (Thomson et al., 2011) thus implying that an improved diagnosis strategy could potentially improve recording, reviewing and monitoring of treatment interventions.

As a result of having no standardised method or clinical protocol for the diagnosis of FFN, it is proposed that the ability of services like the National Health Service (NHS) to accurately plan to manage resources is unclear (Thomson et al., 2011). There is, however, an understanding that ‘no one clinical diagnostic feature is sensitive or specific enough to accurately diagnose this condition but a combination of features such as participant reported history, clinical observations and participant reported symptoms, should make a clinician suspect the presence of neuroma’ (Thomas et al., 2009). Of note, a refined combination of clinical diagnostic criteria could direct clinical decision-making and evaluate the use of services on offer for individuals with FFN (Summers, 2010).

Within the NHS, limited documentation exists on how to clinically diagnose and differentiate FFN from other pathologies which demonstrate similar symptom characteristics (Figure 7). In practice, most clinicians provide a working diagnosis or differential diagnosis to guide their treatment choices yet when intervention fails, correct identification is then sought (Thomson et al., 2011). Nonetheless, this is difficult to do when little evidence is published in this area. Recently, Edwards et al, 2017 conducted a systematic review of long-term conditions and highlighted the low level of evidence available in the area interest of musculoskeletal health. Publications were largely focused on retro case analysis or cross sectional data that was not always considered representative of the general population. Most cross sectional data reviewed used

populations that were considered the ‘worst cases’ for example populations who were undergoing foot surgery as conservative interventions failed. Furthermore, randomised control trials (RCT’s) investigating foot and ankle interventions do not exist and longitudinal studies that review the natural history of conditions affecting the foot and ankle are scarce. This data is needed and will be important for health professionals and organisations to understand the epidemiology, prognostic indicators, risk factors, and service provision and planning for people with these conditions in the future. Without this information, it is difficult for a health professionals or organisations to demonstrate their decision-making and rationale is in alignment with the evidence based medicine theory. This could suggest that a reason why patient outcome varies is due to the experience and clinical reflection. This can be costly, time consuming and places the individual who is of concern at risk of further complications.

### 2.7 The Treatment and Management of FFN

There are a number of interventions that are discussed within the published texts on how best to manage and treat FFN although a ‘gold standard’ method has not been identified. The conservative care surrounding FFN firstly consists of educating the individual on accommodative and supportive footwear in the aim to not squeeze or constrict the forefoot which could in turn pinch or irritate the nerve/neuroma. In addition to this, some health professionals including podiatrists may introduce holistic therapies such as the use manual therapy, soft tissue mobilisation or even soft tissue manipulation to improve tissue stiffness and manage pain in the body (Cashley and Cochrane, 2015). Alternatives methods include taping, padding and strapping to restrict movement and to offload forces around the metatarsal web space (Spina et al, 2002). Through case series analysis, there is some evidence to suggest a reduction in patient reported pain using these methods although there is an appreciation that to truly measure the impact of these methods further studies are required to look longitudinally at its affects on FFN. Similarly, with the same intention, some health professionals will use insoles with additional padding placed proximal to the metatarsal head in order to disperse the pressure during weight bearing activity; this is thought to be successful in 50% of cases (Menz at al, 2012). Again limited evidence is published which demonstrates the effective of insoles in managing this condition however in a clinical care setting is still used as anecdotally this method appears to allow patients to remain active and reduce symptoms for a period of time before invasive management options are considered.

If non-invasive methods do not reduce patient reported symptoms then a steroid injection is often selected. Admittedly, conclusive evidence regarding the clinical effectiveness of the injection is lacking whether this be undertaken with guided ultrasound or unguided

(Markovic et al, 2008). A number of studies have reviewed the effect of injecting corticosteroid, hyaluronic acid and alcohol into the metatarsal web space in order to manage this condition. Overall, it would appear that injection therapies for FFN neuroma provide appropriate short-term benefits to reduce pain and discomfort. It is also thought that those injections conducted via guided MUS may have a better clinical outcome then those injections that are conducted blind (Morgan et al, 2014). Nevertheless, evidence in this field could be misleading as study samples have been small and methodological rigor could be challenged hence why long term predictions are hard to justify or make.

Leading on, there are a number of surgical techniques that have been documented as effective in resolving pain symptoms associated with FFN. Over the years, surgical techniques have been adapted or modified as technology and knowledge has progressed in this field (Womack et., 2008). There are a number of possible surgical procedures such as: surgical excision, intermuscular transposition, Neurectomy and ligament release. The two most common surgical techniques performed to date for FFN are the excision (removing the neuroma) and neurectomy (to cut or partially cut the nerve and relocate to a site away from the irritation, usually nearby muscle). Like any surgical intervention there are risks associated with the procedures, for FFN the specific documented risks are: restriction of daily activities, scar tenderness, sensory loss in toes/ webspace(s), complex regional pain syndrome, unstable metatarsal phalangeal joints (usually requires further surgery) and stump neuroma (20% chance of occurring after excisional surgery) (Coughlin and Pinsonneault, 2001). Again, limited statistics are available for determining the perceived risks due to the low methodological rigor of studies. This further supports the need for comprehensive, longitudinal data on how interventions perform in terms of clinical effectiveness and patient outcomes to understand what interventions should be selected for individuals with FFN. This has the potential to infer the frequency of interventions, when the intervention should be implemented, who by and how best to do it so that individuals with FFN receive targeted care.

As the pathway for the management and treatment of FFN is not clear, other interventions such as cyrotherapy (nitrous oxide), use of collagen conduits, nerve allografts and radiofrequency thermoneurolysis have started to be introduced as potential treatments (Chuter et al., 2013, Gould et al., 2013, Lee et al., 2018, Moore et al., 2012 and Sauza et al, 2016). As these techniques are in their infancy, limited research is available to determine their effectiveness to treat FFN. Currently, academic and clinical institutions around the world are embedding these into the practice to review and determine the reliability and validly of clinical application and use.

A number of methods are available to manage FFN although it is not clear what order and for how long these methods should be used. It appears that a mixture of these methods

have some affect on the overall pain and mobility of individuals with FFN. Moreover, if an accurate diagnosis and definition of FFN was agreed then further investigations to test interventions using robust methodology such as RCT's could inform guidance and subsequently remodel treatment pathways for FFN following evidence based practice. This in turn could ensure pathways are appropriately funded, effective use of resources and individual's expectations of living with FFN could be managed.

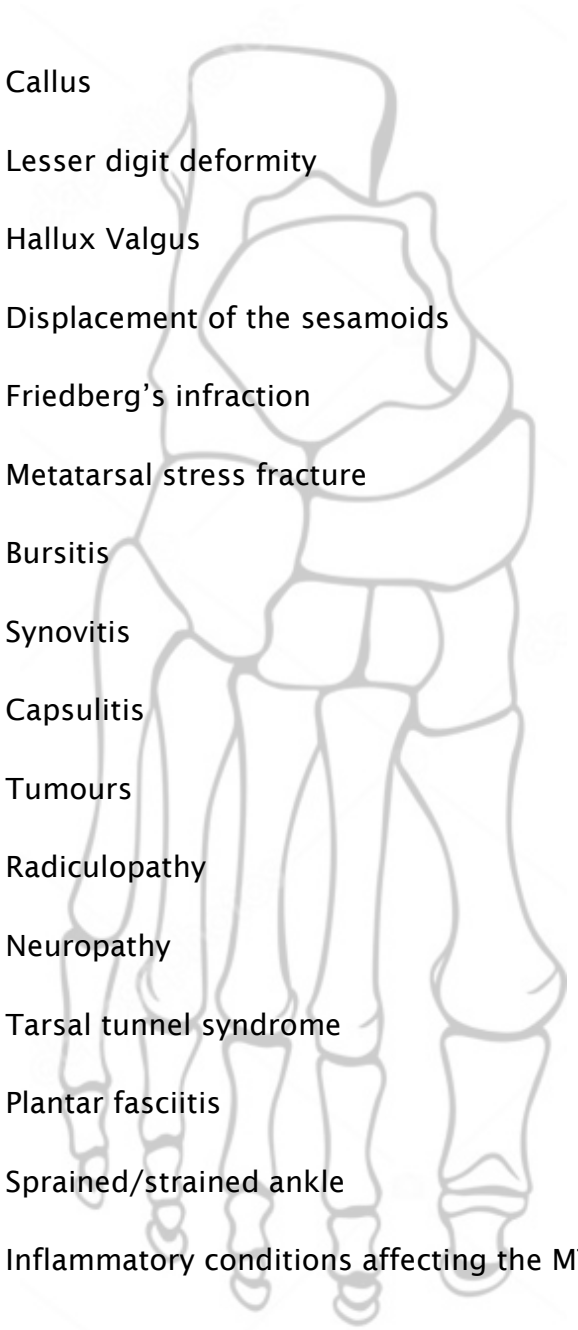



Figure 7: Adapted from Thomas et al (2009) and Childs (2002); Differential diagnoses which are similar to FFN.

## 2.8 Summary of Evidence

There is known variance between clinical methods and the reliability of health professionals to clinically diagnose FFN in clinical practice. With the development of imaging techniques and technology, this in turn has informed clinical decision making and intervention planning by health professionals. Although the evidence has suggested that the use of MUS and MRI is helpful in diagnosing FFN, the practicality of it being available to all health professionals in a clinical setting, who all have the appropriate training and the appropriate services to be able to afford to run the machines, means this not available for all. Therefore, there is a need to establish a set of clinical methods which inform clinical decision making for the diagnosis of FFN, as well as demonstrating appropriate validity and reliability thresholds. In order to achieve this, several sequential studies are required to build up the knowledge base surrounding the clinical diagnosis of FFN. Firstly, there is a need to establish what is currently happening within a service (Chapter Four), secondly what methods should be used to clinically diagnose FFN (Chapter Five) and thirdly to test these methods in a clinical setting (Chapter Six).

## 2.9 PhD Research Aim and Hypothesis

The PhD research hypothesis is therefore:

H1: ‘It is possible to develop an expert derived clinical assessment protocol for the diagnosis of FFN’

H0: ‘It is not possible to develop an expert derived clinical assessment protocol for the diagnosis of FFN’

## 2.10 Study Specific Research Question, Aim and Objectives

*Study One*

Research question: What is the annual incident rate of, and referral pathway use associated with, FFN in a single podiatry service population?

Aim: To determine the incidence rate of FFN in a single NHS service

Objectives:

- To retrospectively determine the number of participants with a diagnosis of FFN who have accessed podiatry services from Jan 2013 to Jan 2014
- To describe the potential seasonal variation of clinician diagnosed FFN in

participants accessing foot health services

- To determine the service use (number, type and location of appointments, clinician type and grade, and treatment type) associated with participants diagnosed with FFN

*Study Two*

Research question: What is the best way to clinically diagnose FFN in the symptomatic population?

Aim: To develop a set of diagnostic criteria that has agreed expert consensus for the clinical diagnosis of FFN

Objectives:

- To complete a literature review to identify the range of clinical practice methods used to diagnose FFN
- To complete a Delphi method to identify the range of clinical practice methods used to diagnose FFN
- To determine expert panel recommendations to inform development of a clinical protocol

*Study Three*

Research question: What is the content validity and reliability of an expert derived clinical assessment protocol for the identification of FFN?

Aim: To determine the content validity and reliability of the expert derived clinical assessment protocol (FNCAP) for the identification of FFN

Objectives:

- To determine the content validity of each item in FNCAP for the identification of FFN
- To determine the mean content validity of FNCAP for the identification of FFN
- To determine the repeatability of FNCAP for the identification of FFN
- To determine the sensitivity of FNCAP for the identification of FFN
- To determine the specificity of FNCAP for the identification of FFN
- To determine the likelihood ratios of each item in the FNCAP for the identification of FFN
- To determine the items which are most likely to differentiate FFN from other forefoot pathology

Conflicting evidence exists with regards to the optimal method for clinically diagnosing FFN. Histological confirmation remains the gold standard method of neuroma diagnosis, although this is invasive and therefore is not always an appropriate option that patients may wish to choose, as this requires tissue samples. Within current routine podiatry, MUS is not available. Thus, despite publications demonstrating MUS as an effective application in terms of diagnosis, it is acknowledged that there is still a need for clinical assessment approaches. Therefore, there is a need to develop an alternative, non invasive method, which can be used in clinical practice to diagnose FFN.

### 2.11 Outline of Method Designs for Thesis

In summary, three sequential studies were devised in order to answer the research question stated in Chapter 1, section 1.5, page 8. Firstly, Study One used a quantitative, observational study design to establish the base line data of the clinical problem. In this case, to count the number of individuals in a local NHS podiatry service and to identify the potential resource burden on diagnosing and managing FFN. Secondly, Study Two used a mixed qualitative and quantitative Delphi study technique to develop a clinical diagnostic protocol that has expert agreed consensus. The final study, Study Three used a quantitative, diagnostic study method to demonstrate the content validity and reliability of the developed expert derived clinical assessment protocol, in Study Two, in clinical practice.

### 2.12 The Research Paradigms

The term paradigm is used to represent a belief system or theory that guides the way researchers action or formally establish a set of practices (adapted from Cohen, Manion and Morrison, 2000). The post positivist paradigm seeks to understand the world through observation and measurement in order to seek the ‘truth’ (Trochim, 2017). The idea of understanding the ‘truth’ and how the ‘truth’ operates might allow researchers to predict and/or control outcomes in the future (Ryan, 2017). To do this, researchers use reasoning and theory to develop hypotheses to test (Trochim, 2017). A person with a post-positivist belief system understands that the ‘truth’ can be understood by following specific procedures to observe consistency, change and accuracy (Ryan, 2017. Aspects of this paradigm are demonstrated in chapter six where quantitative methodology is used to observe validity and reliability in a cross sectional sample of participants with forefoot pain who receive a novel clinical assessment, following a specific protocol, in order to diagnose FFN.

There are, however, elements of critical realism that have shaped some of the methodologies selected to address the thesis aims. The Delphi technique is one

methodology that utilises participant's opinions and beliefs to gain consensus. A critical realist believes that in order to understand the reality uncovered by science and social science, there is a need to look at the subject from all angles, with an openness about the way in which data is collected and analysed. Like the post positivist paradigm, a critical realist, seeks to understand the 'truth' but also appreciates there may be bias and/or error in achieving this (Archer et al., 2017). Therefore, methods that require multiple measurements and/or observations are more likely to cause different error variations. By using techniques such as triangulation, the data variations and errors could be anaylsed and provide further understanding on the subject under investigation. This view on the subject could highlight the errors and bias before the researcher makes judgments and statements about the subject (Archer et al., 2017). In some situations, this could encourage further objectivity. Using both these belief systems a post positivist, critical realist approach has informed the methodologies selected to answer the thesis aims.

The research paradigms ontology, epistemology, theory and methodology also inform the development of the thesis. Ontology is the concept of existence (Patel, 2017). Whereas, epistemology is the theory of understanding human knowledge and justification of choosing methods to further develop theory. Epistemology also considers the distinction between justified belief and opinion (Patel, 2017). Ontology and epistemology inform the development of new knowledge. This thesis programme proposes the development of a novel expert derived clinical assessment protocol for the identification of FFN. The development and application of this knowledge to a problem is sometimes referred to as a theory. A theory is a system of ideas intended to explain a problem or subject. In some cases, a theoretical framework is used to introduce, describe and support a theory of research study that explains why the research problem exists. From the development of the research problem, appropriate methodology can be applied to explore or determine the research problem.

A theoretical framework has been used in this thesis to answer a specific clinical problem. In the first instance, the approaches to diagnosing FFN in clinical practice are explored. This information formed the basis of a semi structured literature review that critiqued clinical diagnostic methods specific to the diagnosis of FFN (chapter two). It was then of interest to review the current practice in a single podiatry service (chapter four). Understanding the limitations and potential barriers of the current evidence provided recommendations for further study. One of these recommendations highlighted the need for accurate clinical diagnosis. Using a qualitative approach, an expert derived clinical assessment protocol was developed (chapter five). This informed the quantitative approach to assess the feasibility of this novel protocol (chapter six). Overall, the thesis programme has incorporated the development of different methodological designs to best

answer the thesis question in relation to the researchers philosophical questioning, reasoning, and logic surrounding the diagnosis of FFN. Figure 8 summarises the sequential theory process.

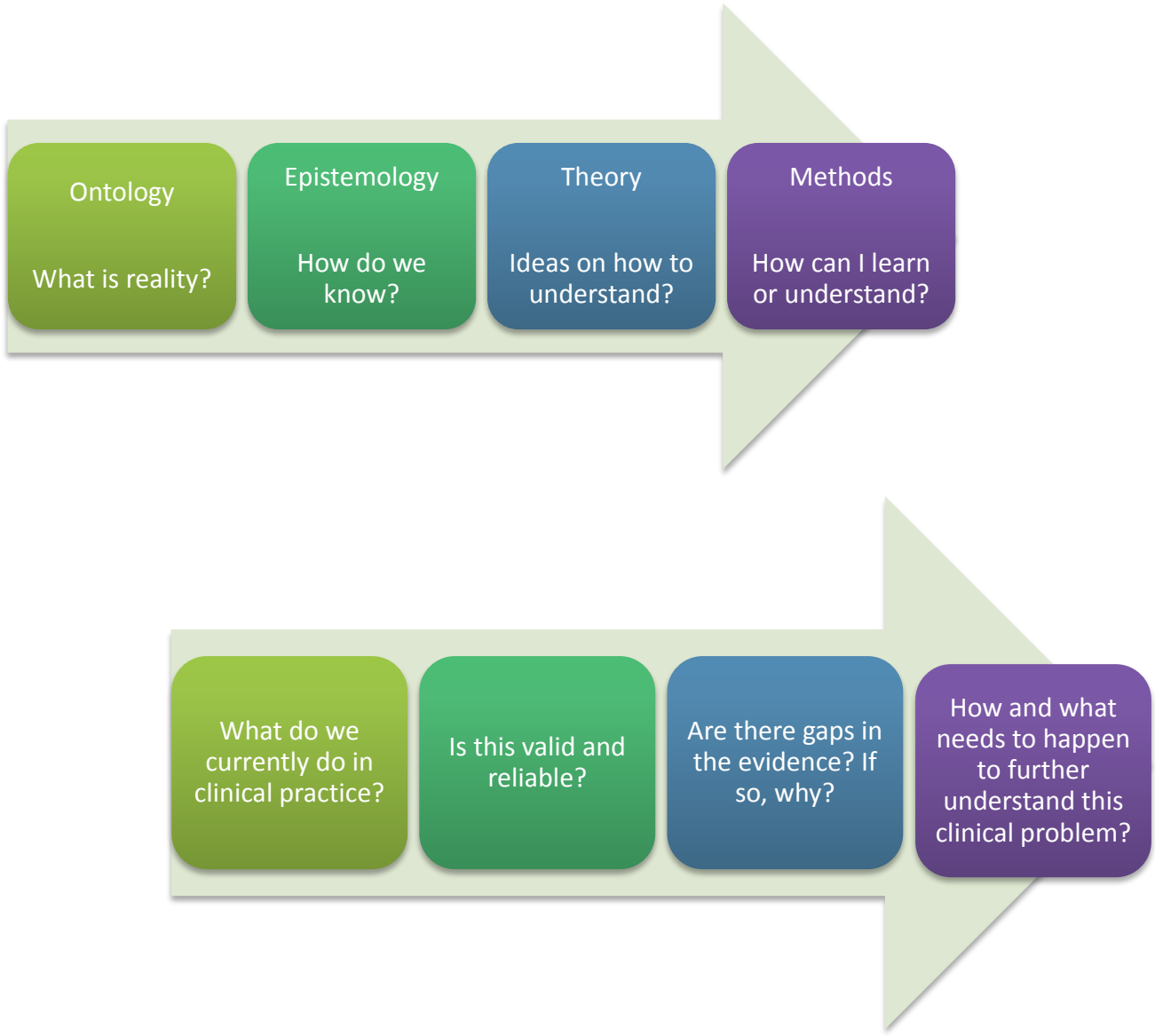
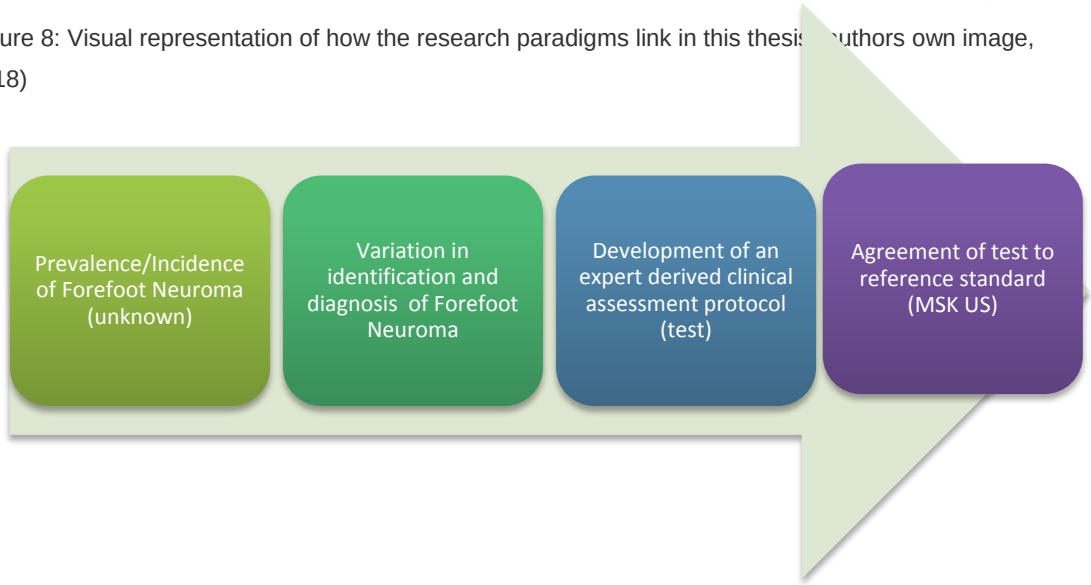



Figure 8: Visual representation of how the research paradigms link in this thesis (authors own image, 2018)




## 2.13 Ethical Approval and Research Governance

Solent NHS Trust approved the service evaluation request for Study One in March 2014.

A reference number (SE-095) was obtained for “FFNta in the Solent Podiatry Service population (annual incident rate & resource use)”. In February 2015, a completed service evaluation report was signed off by management staff within the Podiatry Service and was submitted to Solent NHS, Clinical Audit and Evaluation Team.

The University of Southampton agreed sponsorship of Study Two entitled “Clinical Diagnosis of Symptomatic FFN in the General Population: Delphi Based Recommendations” and ethical approval was granted in October 2014 by the University of Southampton, Faculty of Health Sciences ethics committee. Insurance for the study was granted by the University of Southampton research governance office in October 2014. In March 2015 an amendment was accepted by the University of Southampton, Faculty of Health Sciences ethics committee for an additional questionnaire. Online approval was documented by the University of Southampton research.

The University of Southampton agreed and approved insurance for study three: ‘Identification of Forefoot Pain using a Novel Expert Derived Protocol’ in May 2016. The Health Research Authority (HRA) gave approval for the study in September 2016 and Solent NHS Trust gave site approval in October 2016 (Appendix A).

### 2.14 Ethical Considerations

The following points were identified and acknowledged as potential ethical issues relevant to both experimental studies included in this thesis:

#### 2.14.1 Initial Approach

Information about the studies has be given prior to the potential participant attending their podiatry appointment or completing the study documentation. The information was sent via email or handed to the potential participant at their first clinical podiatry appointment. This gave the potential participants enough time to read the information, come to an informed decision and reply via instructions accompanying the documents. There were contact details specific to each study for the potential participant to contact if they felt they wished to ask any questions before replying.

#### 2.14.2 Informed Consent

Informed consent for Study Two, was obtained by the potential panel member completing a word document form and attaching this back to the researcher (Miss Charlotte Dando) via an email using the email address stated on the invitation letter. For Study Three, written consent was obtained on the day of the research appointment. Participants had previously been given the participant information sheet and replied to the invitation letter

via a reply slip. Participants could ask questions at the appointment and refuse to give consent and be withdrawn from the study if they wished to do so.

#### 2.14.3 Safe Guarding Clinical Decision-Making

Panel members were able to withdraw from the study at any time, without needing to give a reason for doing so. A decision to withdraw from the study did not affect their on-going clinical relationship with the researcher, University or NHS Trust in any way. Potential panel members for Study Two could withdraw from the study by informing the researcher (Miss Charlotte Dando) or by not replying to the emails. It was assumed that replying to the emails with the completed Delphi round questionnaires indicated continual participation throughout the Delphi process.

For Study Three, participants could withdraw from the study by informing the researcher (Miss Charlotte Dando) or by not replying to the emails or calls.

#### 2.14.4 Potentially Vulnerable Groups

Those panel members or participants requiring interpretation or further explanation would not be excluded from the study on this basis. Provision of an independent interpreter would be made via the use of the hospital's register or specialist translators or appropriate staff member not involved within the research team. For those clinicians unable to sign a declaration of informed consent, verbal consent would be obtained and observed by an independent witness and documented accordingly.

#### 2.14.5 Confidentiality

No personal information would be collected and survey responses would be collated anonymously. All responses received from the study would be strictly confidential, and the identity of panel members and participants were not divulged. Direct quotes to free-text answers would be used as part of the study report or later Delphi iterations, but these would be not be traceable back to any panel members.

For Study Three, images had no non-participant identifiable information on them. All data collection sheets were coded and anonymised.

### 2.15 Consent

Consent was attained in the following ways:

Study One: Direct consent was not required to access participant notes as specific participant data was not required. Consent and permission was attained from Solent NHS Research Department and the Podiatry Management Team to access coded group level data.

Study Two: Consent was obtained via a consent form with either an electronic or written signature which was enclosed as part of the initial study pack email with the invitation letter and participant information sheet. Consenting participants could withdraw by informing the researcher (Miss Charlotte Dando) or by not replying to the emails. It was assumed that replying to the emails with the completed round questionnaires indicated continual participation throughout the Delphi process.

Study Three: Consent was obtained via a consent form with a written signature that was completed on the day of the study assessment. Consenting participants could withdraw by informing the researcher (Miss Charlotte Dando).

**2.16 Data Coding, Handling and Storage**

In all the studies all data coding, handling and storage was documented and saved electronically. However, hard copies of anonymised, group data were printed and placed in a study folder, located and locked onsite at Adelaide Health Centre, Solent NHS Trust in case electronic storage failed, for example, deletion of email accounts or computer desktop/hard drive update.

Study One: The group level data was formed into a report on the participant electronic system and transferred to an excel spreadsheet. The excel spreadsheet was saved and password protected on the NHS hard drive.

Study Two: The original data from the individual panel members were grouped by the researcher to keep individual identities unknown. The results fed back to the panel members between each round were be collated and anonymised. Data related to individuals were handled carefully and in accordance with the Data Protection Act (2003). For any publication of work derived from the Delphi consensus group, all the individuals would be cited contributors. Copies for the research panel would be made available.

Study Three: The original data from the individual participant were anonymised and coded (e.g. FN01, FN02, FN03) by the researcher to keep individual identities unknown. All images and written reports were electronically scanned onto the participant records and ‘non-participant identifiable’ hard copies were printed and stored appropriately. Data related to individuals were handled carefully and in accordance with the Data Protection Act (2003).

Data would be stored in compliance with the Data Protection Act (2003) and in accordance with the University of Southampton Research Governance Office policy. Any electronically entered data would be stored on a password secure encrypted device. Paper copies would be contained within a lockable filing cabinet on University premises. Data processed will be kept for ten years and thereafter destroyed. The research protocol conforms to the highest principles of ethical professional practice.

### 2.17 Conflict of Interests

The PhD candidature completed in conjunction with this thesis are supported by a clinical academic doctoral research fellowship award from the National Institute for Health Research Collaboration for leadership in Applied Health Research and Care (NIHR CLAHRC) Wessex organisation. No personal benefits of any form were or will be received from any commercial party as a consequence of direct or indirect association with this research.

### 2.18 The Research Question

The research question for this programme of work asks:

*'What is the optimal clinical diagnosis protocol for the diagnosis of FFN?'*

# 3.0 Chapter Three

## Service Evaluation

## What is the annual incidence of clinician diagnosed FFN in the Solent Podiatry Service population?

### 3.1 Introduction

Having argued in the previous chapters that the epidemiological data surrounding metatarsalgia and more specifically FFN is clouded, it was of importance to establish an incidence and prevalence estimate for FFN and provide further understanding on how individuals with FFN pain symptoms were potentially diagnosed in clinical practice. In this chapter, a service evaluation design was adopted to retrospectively review episodes of care from individuals who were diagnosed with FFN in order to determine the incidence, the prevalence and resource use within service line pathways.

### 3.2 Chapter Abstract

**Background:** Limited evidence exists regarding the epidemiology, aetiology, risk factors, treatment and clinical impact associated with FFN. At present, it is unclear what proportion of participants accessing foot health services present with FFN. Therefore the number of participants identified with FFN in a single NHS service is unknown. As such, the service is unable to determine the potential demand for musculoskeletal foot health care related to FFN, or to forecast the potential costs of care provision (including appointment administration, clinician time, or costs of interventions e.g. insoles/injection therapy).

**Aim:** The main aim of the service evaluation was to establish the incidence and prevalence of FFN in a single NHS service. The second aim was to determine the seasonal variation (spring, summer, autumn and winter) of clinician diagnosed FFN in participants accessing foot health services. The third aim was to review the pathways used by participants who accessed foot health services associated with the diagnosis and management of FFN (number, type and location of appointments, clinician type and grade, and treatment type).

**Methods:** A podiatrist from a single Trust retrieved all clinical records between the 1st January 2013 and 1st January 2014 with the electronic code for neuroma. Participant records with the code for neuroma were reviewed for episodes of care related to this diagnosis until treatment was logged as complete or until the study end date.

**Results:** There were 38 new cases identified with the neuroma code thus an estimated incidence rate of 2.5 per 1000 symptomatic persons was calculated. The estimated regional period prevalence rate was 3.4 per 1000 symptomatic persons. A ratio of 4:1 for gender was found, with women more likely to be diagnosed with FFN than men. An increasing trend was identified in the incidence of FFN during the study period. The majority of referrals entering the podiatry service were from primary care services. Clinical diagnosis of FFN was made by podiatrists at NHS band 6 and band 7 in specialist musculoskeletal clinics.

**Conclusion:** Overall, it was possible to identify the number of new cases within a 12 month period, with the majority of diagnoses identified in November and December (2013). The service evaluation described the care pathways used by the participants who were identified with FFN.

## 3.3 Study Introduction

### 3.3.1 Study Aims and Objectives

The main aim of the service evaluation was to establish the incidence rate and prevalence of FFN in a single NHS service. The second aim was to review the seasonal variation of clinician diagnosed FFN in participants accessing foot health services. The third aim was to review the pathways used by participants who accessed foot health services associated with the diagnosis and management of FFN (number, type and location of appointments, clinician type and grade, and treatment type). To achieve these aims, several objectives were set:

- To retrospectively determine the number of participants with a diagnosis of FFN who have accessed podiatry services from the 1st January 2013 to 1st January 2014.

- To describe potential seasonal variation (spring, summer, autumn and winter) of clinician diagnosed FFN in participants accessing foot health services.

- To determine the service use (number, type and location of appointments, clinician type and grade, and treatment type) associated with the diagnosis and management of FFN.

### 3.3.2 Research questions

For the service evaluation, the questions were as follows;

- What is the prevalence rate of FFN in the podiatry service population?
- What is the incidence rate of FFN in the podiatry population?
- What is the seasonal variation of reporting ‘neuroma’ between 1st January 2013 and 1st January 2014?
- How many women were diagnosed with FFN between 1st January 2013 and 1st January 2014?
- How many men were diagnosed with FFN between 1st January 2013 and 1st January 2014?

## 3.4 Methods

A service evaluation method was adopted to gain quantitative date to be able to describe the care currently being received by patients with a diagnosis of FFN. The Health Research Authority (HRA) (2013) define the use of a service evaluation as “a method to define the current care measures that a service currently utilises without reference to a standard”. A clinical audit could not have been used as the information gathered needs to be assessed against a set of explicit criteria. This was not possible to achieve for patients with FFN, as there are no guidelines currently available that describe the standards for the diagnosis of FFN in practice.

### 3.4.1 Study Method

This study used a systematic methodological process to identify and collect data at group level. Several statistical formulas were calculated in order to derive numerical figures about the specified population. Consequently, the service evaluation focused on objectively measuring specific outcomes such as; number of patients, gender, age, the referral pathways and number of appointments. Some authors consider the data generated by a service evaluation to be a quick way to assess potential measures before further investigations are devised (Twycross and Shorten, 2014).

As a result of the service evaluation, the numerical data identified incidence and prevalence figures although no figures within the literature have been documented and

are thus incomparable. However there is consensus of agreement for FFN being a common condition in primary care (Thomson et al, 2011). It was hypothesised that one potential reason for the poor record keeping of participants presenting with FFN was a result of poor diagnosis. This seemed plausible as published evidence identified the varied reliability of clinical diagnosis methods specific for the identification of FFN.

### 3.4.2 Procedure and Recruitment

The local NHS Trust electronic record system (SystmOne) was used to identify cases for the service evaluation. Specifically, those cases who had a clinical diagnosis of FFN and had accessed the podiatry services for an assessment for ongoing treatment or review of their forefoot condition. Data records were retrospectively examined from 1st January 2013 to 1st January 2014 to which participant records were filtered using the following case selection steps:

1. NHS Trust record held
2. Podiatry service use shown
3. “Neuroma” diagnostic code recorded

Using the electronic participant record system, a “clinical diagnosis” of FFN was identified using the code Xa99W. The case records of identified participants were retrospectively reviewed for episodes of care related to this diagnosis until treatment was logged as complete or until the end of the study period.

### 3.4.3 Study Population and Size

The population sample (participant records) were identified through Solent NHS Podiatry Service System One codes for neuroma in a one year period from 1st January 2013 to 1st January 2014.

The time period was chosen due to several factors:

- The information technology service (IT service) provider changed contracts within podiatry from Rio to System One in 2010/2011 and therefore the data from that period and the following year may be subject to user error.
- 2013 accounted for the time required for clinicians to use and learn about System One.

The inclusion and exclusion criteria were as follows:

Table 2: Inclusion and Exclusion Criteria for Study One

| | |
|---|---|
| **Inclusion Criteria** | The FFN code had been selected within the electronic record. |
| | The electronic record identifies at least one episode of podiatry care. |
| **Exclusion Criteria** | The electronic code for FFN was attached to the wrong referral date for example; ‘ankle pain’ reported in 2013 and ‘neuroma’ reported in 2002. |

### 3.4.4 Data Collection

Data was collected via a standard operating procedure used to filter participant records. Through a series of settings the participant records which fit the case selection criteria were gathered (Figure 9).

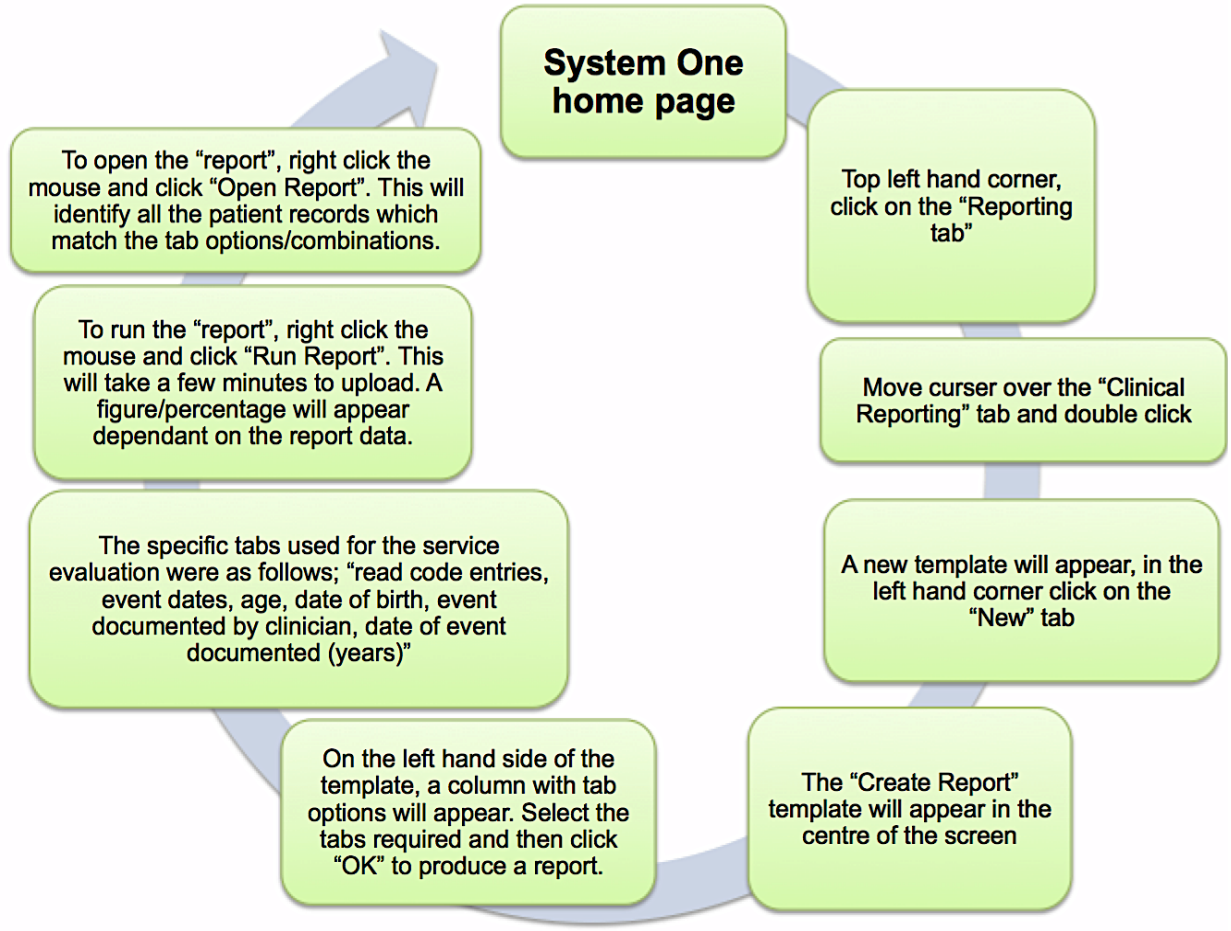



Figure 9: The standard operating procedure steps to identify participant records (authors own image, 2018)

### 3.4.5. Analysis

Statistical analysis was undertaken using IBM Statistical Packages for the Social Sciences (SPSS) Version 19.0 for Windows (SPSS Inc, Armonk, NY, USA). Presented data remains at group level and no case specific references were included. Raw data was checked by two fellow research podiatrists. This was achieved by following the algorithm and re running the SPSS calculations in order to demonstrate consistency and to pick up any potential calculation errors.

#### 3.4.5.1 Outcome measures

The following data was captured to describe the care pathway services for participants with a diagnosis of FFN (Table 3).

Table 3: Outcome Measures for Study One

| Outcome Measure | Purpose | Data Type |
|---|---|---|
| **Number of cases with FFN** | To define the NHS population compared to current literature findings on populations with a diagnosis of FFN | Ratio data<br><br>Mode, median, mean and range |
| **Age and Gender** | To compare a NHS podiatry population against the current literature findings on populations with a diagnosis of FFN | Nominal data (female, male or unknown)<br><br>Results can also be expressed as a ratio<br><br>Mode, median, mean and range |
| **Diagnostic** | To describe the consensus of current diagnostic tests used to diagnose FFN | Nominal data (Foot Posture Index (FPI), Hubschers Test, 'too many toes' Sign and |

| | | |
|---|---|---|
| **Tests** | in a NHS podiatry service | record of lesser digit deformities) |
| **Appointments** | To describe the number of appointments attended, missed or cancelled by participants with a diagnosis of FFN | Ratio date (number of appointments and percentages) |
| **Referral Pathway** | To describe the pathways used by participants to access a podiatry service appointment for the clinical diagnosis of FFN | Nominal data (lower limb pathway, community clinic, biomechanics/musculoskeletal clinic) |
| **Clinician Banding** | To determine the clinical banding of those who clinically diagnose FFN in the podiatry service | Nominal or Ordinal data (band 5, band 6, band 7 or band 8) |
| **Referral Date and Assessment** | To determine the seasonal variation/pattern in participants accessing the podiatry service | Ratio data (number of appointments and percentages) |

3.4.5.2 Calculations

Incidence is defined as the number of new cases in a population within a specified time period (Silman and Macfarlane, 2002). In the podiatry service, a symptomatic population of 15,310 was identified with 38 new cases identified in the specified 12 months.

Incidence rate was:

38 cases divided by 15,310 = 0.00248204

0.00248204 x 1000 = 2.48203788

= 2.5 per 1000 symptomatic persons

Prevalence is defined as the number of individuals within a population with the condition (Silman and Macfarlane, 2002). In the podiatry service, a symptomatic population of

15,310 was identified with 52 cases of FFN within the specified 12 months.

Period prevalence is defined as the number of cases in a given time period divided by the number of people in the population during this time period.

52 divided by 15,310 = 0.00339647

0.00339647 x 1000 = 3.39647289

= 3.4 per 1000 symptomatic persons

### 3.5 Results

From 1st January 2013 to 1st January 2014, the total number of participant records that were seen by the podiatry team were 15,310. From this, 302 participant records had the neuroma code reported in their file (1.97% of the electronic Solent Podiatry Service records). However the neuroma code included acoustic neuromas (tumor formation in the brain known as Vestibular Schwannoma) as well as FFN and this code is therefore subject to error of overestimation. Consequently, following case by case reviews, an incidence of 38 cases of FFN were identified. The 38 cases were recorded from 31 participant records as duplication of the code appeared with participants who had FFN diagnosed bilaterally. Out of the 31 participant records, 3 records had incomplete data about their care pathways. An estimated period prevalence of 3.4 per 1000 symptomatic persons was calculated.

31 participant records identified in the service evaluation demonstrated a gradual trend in diagnosis with March to October reporting 2 to 4 participant records a month, as shown in figure 10. Yet in November, 8 reports were documented and 11 in December. This trend could be linked to the idea that footwear style affects FFN symptoms, although this could be contested, as the author introduced the research study in October 2013, which could have influenced clinicians to change data recording habits. Alternatively, changes to the referral pathways, administration and clinical staff sickness or service contracts could have slowed down participant referrals thus creating a delay in issuing an appointment.

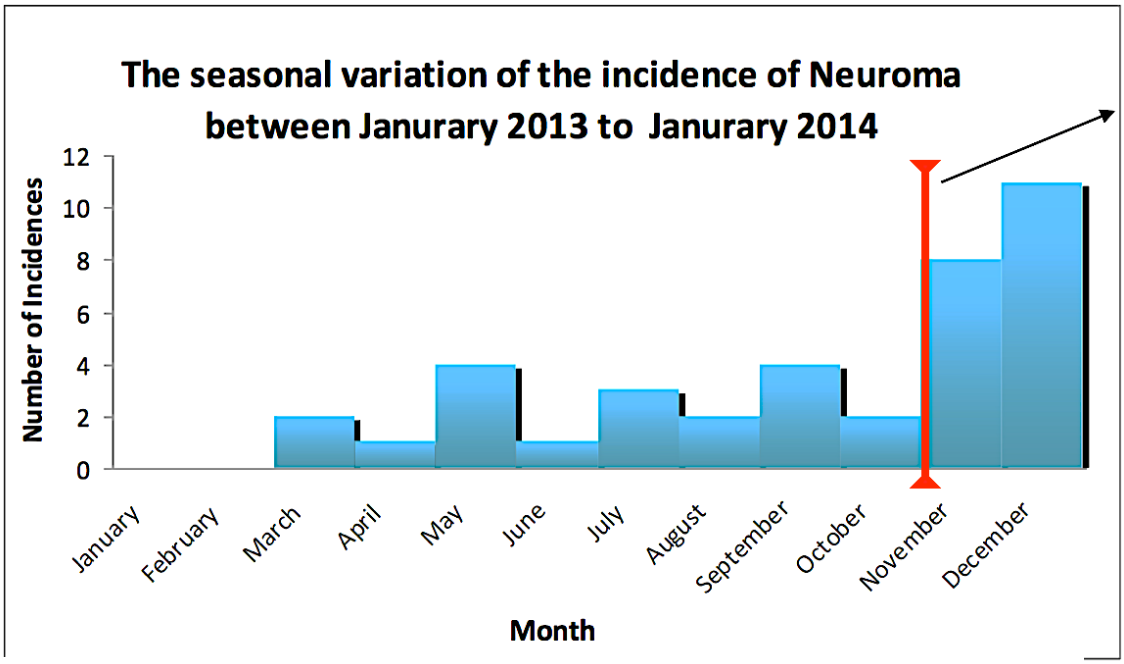



Figure 10: A gradual trend in clinician diagnosed FFN over a 12 month period.

### 3.5.1 Number of Appointments

In 2013, a total of 136 appointment slots were booked for the 31 participants with the clinical diagnosis of FFN. The mean appointment slots per participant was 5. Within the 31 participant records, the majority were still receiving intervention from podiatrists via the musculoskeletal pathway for footwear modification and insole intervention. In 5 case records their care had “ended” and participants had been referred on for intervention of a steroid injection or an assessment for surgery.

### 3.5.2 Number Who Did Not Attend (DNA) Appointments

In 2013, 7 out of 136 appointments were classed as DNA’s.

### 3.5.3 Number of Cancellations

In 2013, 0 out of the 136 appointments were cancelled

### 3.5.4 Type of Appointment(s)

Participants with FFN accessed the podiatry service via a range of referral pathways as shown in figure 11.

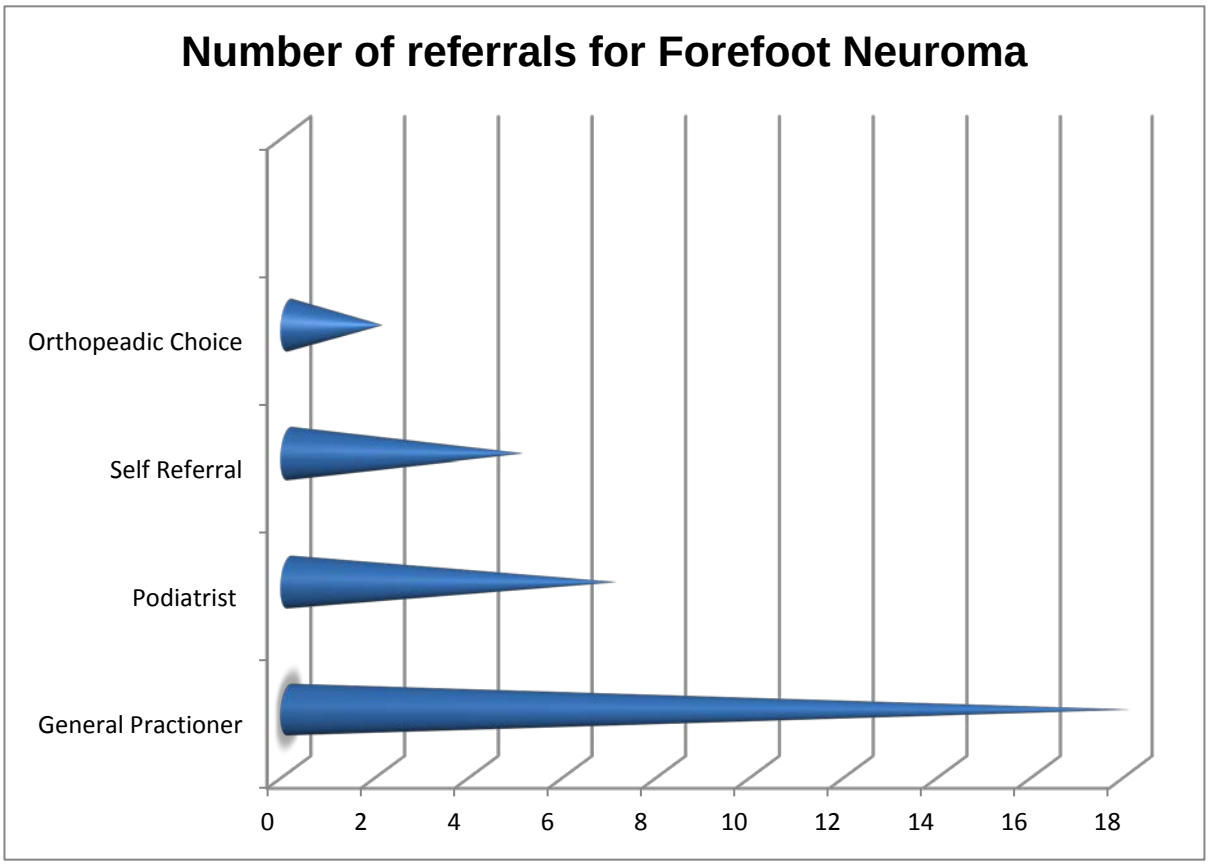



Figure 11: The referral pathway code attached to case records with the neuroma code.

From these referrals, 3 care pathways were used (Table 4):

Table 4: Number of participants using the 3 care pathways

| Clinical Pathway | Number of case records with the podiatry pathway code |
|---|---|
| **Community Clinical Pathway** | 3 |
| **Musculoskeletal Clinical Pathway** | 20 |

| | |
|---|---|
| **Lower Limb Pathway** | 5 |
| **Total**<br><br>**(3 incomplete records missing)** | 28 |

3.5.5 Clinician Type and Grade

The clinicians assessing the participants included community based podiatrists in either routine care or musculoskeletal (MSK) clinics, or MSK specialist podiatrists (Table 5).

Table 5: Clinician band grading for diagnosing FFN

| NHS Clinician Grade | Number of case records |
|---|---|
| Band 6 | 8 |
| Band 7 | 20 |
| Total<br><br>(3 missing due to incomplete records) | 28 |

3.5.6 Demographic Data

A ratio of 4:1 women to men were clinically diagnosed with FFN. Women are four times more likely to be diagnosed with FFN than men. From the 31 participant records the mean age was 56 (range 35 to 84 years), of those who were diagnosed with FFN.

**3.6 Discussion**

3.6.1 Introduction

The clinical diagnosis of FFN has been frequently reported as a challenge by multiple authors. This study has confirmed the presence of FFN in a podiatry service as well as gaining an insight into how participants are gaining a diagnosis and by whom. These findings have not been previously identified in the service. The findings from this study have thus generated a set of questions for understanding the methods used to clinically diagnose FFN. The study has fulfilled the aims and objectives set in Chapter One.

3.6.2 Sample Size

There was no defined sample size for the service evaluation. From a-priori discussions with 5 musculoskeletal podiatrists within Solent NHS Trust, it was estimated that within a year they would see over 100 cases of neuroma each, therefore a figure of around 500 was expected.

### 3.6.3 Incidence and Prevalence Figures

Results from this study indicate an estimated annual incidence rate of FFN as 38 new cases identified within a 12 month period i.e. 2.5 per 1000 symptomatic persons. The estimated period prevalence rate was 3.4 per 1000 persons. Within the literature review no reported incidence or prevalence figures were identified from any other investigators although in GP consensus records, 50.2 men per 100,000 and 87.5 per 100,000 women were reportedly diagnosed with Morton's Metatarsalgia (Latinovic, 2006 and Symeonidis et al., 2012). Morton's metatarsalgia is an alternative term used to describe FFN. The service evaluation results provide a useful baseline to estimate the burden of this condition within a single region.

### 3.6.4 Participant Demographic Data

Within Solent Podiatry participant population, women were four times more likely to be diagnosed with FFN than men. This is in agreement with other authors, suggesting that although lower, the observed regional sample is potentially generalisable in terms of gender (Quinn et al., 2000; Kankanala and Jain 2007, Brubaker, 2008, Summers, 2010 and Nery et al., 2012). On the other hand, the age range of our sample was wider (24 to 87 years) than reported by other authors but the mean age of 57 years (median 59 years) was comparable to that reported by others (Williams and Robinson, 2007).

### 3.6.5 Seasonal Variation Data

To our knowledge, no data trends have been previously reported on seasonal variation of clinician diagnosed FNN. Investigators have hypothesised that in the summer months, the condition will have less of an impact on participants than in the winter months due to footwear styes (Vito and Talarico, 2003). The idea of tight, closed-in or poor fitting footwear is agreed by many authors to be a contributory factor to developing FFN (Vito and Talarico, 2003). The pattern observed in the service evaluation cases demonstrated a gradual increase in diagnoses from January 2013 to December 2013. One potential contributing factor to the higher incidence rate recorded in November and December, could possibly be investigator bias (halo effect). The over arching PhD project was explained to the podiatrists in Solent in October 2013. This could have potentially influenced the podiatry clinicians by increasing their awareness of recording data leading

to more FFN cases being reported as the study progressed. In addition, the initiation of the service evaluation may have triggered an increase in either identification or change in record keeping behaviours of the podiatry clinicians as a notable increase in FFN was observed after that time point. We cannot make any claims for seasonal variation in the pathological presentation due to potential bias introduced by a change in clinician behaviour.

### 3.6.6 Clinician and Service Pathway Data

The service evaluation also gave some insight into the clinician NHS banding and service pathway use of those participants diagnosed with FFN. Each participant identified with FFN received 5 appointments (mean) although out of the 31 participant records, appointment allocation for clinical assessment, diagnosis and intervention of FFN ranged from 2 to 9 appointments. The reason for this variation is not clearly understood. One possible suggestion for participants receiving fewer appointments (2 to 3) could be a result of improved clinical access to other services such as radiology for ultrasound guided injection(s) or podiatric surgery. Alternatively, service pressures and reduced appointment availability may have led to participants sitting on clinical waiting lists. If those participants on the waiting list require an appointment, the process of receiving an appointment is quicker than waiting for a re referral from the GP and then waiting 18 weeks for an assessment. In some cases, participants might seek private podiatry services in order to receive a shorter appointment wait. Therefore, the higher number of appointments allocated (7 to 9) could be a result of participants reviewing their clinical care plan although symptoms may not have changed. It is possible that the clinician has inaccurately given a diagnosis but the intervention given has been recorded as effective. A number of forefoot conditions such as synovitis, capsulitis, bursitis and FFN symptoms can be reduced with footwear modifications and offloading devices such as insoles or toe props (Summers, 2011).

Of note, clinicians may document participant symptoms differently in relation to similar clinical diagnoses. For example, when reviewing current research, a number of authors stated that part of the clinical assessment and diagnostic criteria for FFN is determined by participant described symptoms (Thomas et al., 2009). Clinicians in this service evaluation omitted participant reported symptoms but did clearly outline the clinical assessment tests performed such as Foot Posture Index (FPI), Hubschers test and “too many” toes sign as well as any physical deformities/abnormalities, which then led to diagnoses of FFN.

The majority of referrals entering the podiatry service were from primary care services. From the collected data, 58% of the referrals were from GPs compared to 3% from Orthopaedic Choice. Orthopaedic Choice is an assessment and treatment pathway which

seeks to support, as well as aid, participants in resolving symptoms from conditions which affect a persons ability to move. This usually involves conditions associated with bone, muscle, tendon, ligament or cartilage damage/change. This is consistent with a Cochrane review that also reported that the majority of neuroma diagnoses are in primary care services (Thomas et al, 2009). This pattern of referring from the GPs confirms the access point for participants to seek help. Interestingly, 16% of the participant records reported a self-referral back into the service. Investigation of these specific cases indicated that participants had previously been given foot health advice or an intervention. In some cases, this had occurred months and even years previously indicating that self-management of their FFN was no longer effective.

Due to the nature of the podiatry service, there is an expectation that diagnosis of neuroma would be made by the clinicians working in a generalist community setting, for example, NHS grade band 5 and 6 podiatrists in routine or triage clinics where participants were more then likely to receive first clinician contact for assessment. Surprisingly, the majority of diagnoses were documented by NHS grade band 6 and 7 in specialist musculoskeletal clinics and the 3 cases managed in the community clinic setting were treated by a musculoskeletal specialist podiatrist. A potential explanation is the challenge of developing and using a multi -stage referral pathway in a large service where appointments, location of services and access are consistently changing. Although, as sophistication of data collecting improves, it should become easier to investigate multiple pathologies and resource burden.

### 3.7 Strengths and Limitations

This study had a number of strengths and possible limitations. Firstly, the service evaluation was able to identify participant records with the neuroma code. However, the accuracy of identifying all potential cases with clinician diagnosed FFN in the single Trust is questionable. To reduce bias in the reliability of identifying the participant cases, the review of the participant records were conducted by a second reviewer.

Due to the IT service provider changing contracts within podiatry, the data period was 12 months, in order to exclude data that may be subject to user error. It would have been helpful to access the service evaluation over a three year period to retrospectively describe the diagnosis of FFN, although the service evaluation did provide a cross sectional view of the service assessing and diagnosing FFN in a single NHS podiatry service.

The service evaluation provided little data on how clinicians undertake a diagnosis of FFN in a clinical setting. It did, however, suggest the NHS grade banding of those individuals

who make a diagnosis as well as the services they access and utilise to support participants in managing their foot pain. Therefore, this may have identified those clinicians locally who have expertise in diagnosing FFN.

### 3.8 Recommendations and Impact for Clinical Practice

The service evaluation explored current clinical practice within a single NHS podiatry service for the identification and assessment of FFN to which all objectives set were met. Consequently, the following recommendations were devised by the author and agreed by the podiatry service management team:

- To ensure that the clinical team are aware of the current literature informing clinical assessment of FFN.
- To ensure that the clinical team are able to use the electronic record system to record specific conditions.
- To ensure that the clinical team are aware of the clinical pathways and associated importance of accurate coding within the electronic record system used, in this case System One (TPP).
- To have an understanding of the clinical governance issues surrounding the use of participant data and to provide training to ensure staff are safe and competent.

Subsequently the following outcomes have been established to address the recommendations described above, these are;

By 1st December 2014, all clinicians who are diagnosing FFN will have had education about the importance of accurate participant history taking and symptom notation. This was achieved via an oral presentation delivered to the podiatry team by the author.

By 1st December 2014, all clinicians assessing/diagnosing FFN will be aware of the “neuroma code” box to identify participants on TPP with this condition for future audit/service evaluation. This was achieved via the author highlighting the data record button via verbal/written instructions and an online TPP demonstration.

By 1st December 2014, the podiatry team should have discussed and agreed the preferred use of outcome codes (DI, PR, RV) and length of time (e.g 12 weeks, 8 weeks,

18 weeks) on the waiting list before onward referral or discharge of the participant is required. This was achieved via an oral presentation delivered to the podiatry team by the author.

Clinically, this has led to staff training and support within the podiatry service to produce a number of service evaluation and clinical audit reviews across the disciplines of the podiatry service for example wound healing, musculoskeletal and participant satisfaction surveys. This has informed clinical practice by highlighting the appropriate documentation for guidance and procedures but also highlighted areas of improvement in access, clinician knowledge/skill set or development of a service. Finally, this specific service evaluation has given insight into the potential research questions required to further explore this topic area.

### 3.9 Conclusions and summary

Overall, this service evaluation has indicated the potential difficulties in using the electronic data system to collect data. The prevalence and incidence figures of this condition provide preliminary evidence that further epidemiological study is warranted as well as further exploration of diagnostic methods in order to accurately identify FFN. Furthermore, the evaluation has provided insight into how the referral pathways are being utilised and the potential barriers and facilitators to streamlining best participant care in the future.

# 4.0 Chapter Four

## Delphi Study

## The clinical diagnosis of symptomatic FFN in the general population: Delphi based recommendations

### 4.1 Introduction

The previous chapters have discussed a number of possible diagnostic methods for the identification of FFN. It is not clear how reliable or accurate these methods are to specifically determine FFN from other possible pathology. To the researchers knowledge, there are no standardised assessment protocols for the clinical diagnosis of FFN. Therefore this chapter identifies the current diagnostic methods that are used by clinicians to identify FFN in their clinical practice. In order to achieve this, a structured consensus study design was undertaken to develop a clinical assessment protocol that has agreed expert consensus for the clinical diagnosis of FFN.

### 4.2 Chapter abstract

**Background:** There are minimal publications available which describe a standardised approach for the diagnosis of FFN. Current methods of diagnosis include participant reported symptoms, observations and clinical tests although there is limited understanding of what specific method or methods should be used to influence clinical decision making. The aim of this study was to develop a clinical assessment protocol that has agreed expert consensus for the clinical diagnosis of FFN.

**Methods:** A four-round Delphi consensus study was completed with 16 expert health professionals from either a clinical or academic background, following completion of a structured literature review. Consensus was sought on the optimal methods to achieve the clinical diagnosis of FFN. Round 1 sought individual input with an open ended question: 'What are your current methods of diagnosing FFN?" This developed a list of recommendations. Round 2 and 3 asked the participants to accept or reject each of the recommendations in the list in relation to the question: "What is the best way to clinically diagnose neuroma in the forefoot?" Votes that were equal to or greater than 60% were accepted into the next round; participant's votes equal to or less than 20% were excluded. The remaining participants' votes between 20 to 60% were accepted and placed into the

following round for voting. Round 4 asked the participants to rank the list of recommendations according to the strength of recommendation they would give in relation to the question: “What is the best way to clinically diagnose neuroma in the forefoot?” The recruitment and Delphi rounds were conducted through email.

**Results:** 16 expert health professionals based in the United Kingdom participated in the Delphi exercise: Chiropractor (1), Radiologist (1), Orthopaedic Surgeon (1), Rheumatologist (2), Podiatric Surgeon (2) and Podiatrist (9). Clinical experience ranged from 5 to 34 years (mean: 19.5 years). In round 1, the 16 participants identified 68 recommendations for the clinical diagnosis of FFN. In round 2, 27 recommendations were accepted, 11 recommendations were rejected and 30 recommendations were assigned to be re-voted on. In round 3, 36 recommendations were accepted, 22 recommendations were rejected and 11 recommendations were assigned to be re-voted on. In round 4, 21 recommendations were selected by the participants to form the expert derived clinical assessment protocol for the clinical diagnosis of FFN. From these 21 recommendations, a set of themes were established: location of pain, non weight bearing sensation, weight bearing sensation, observations, tests and imaging.

**Conclusion:** Following the identification of 21 method recommendations, a core set of clinical diagnostic methods has been prepared as a clinical assessment protocol for the diagnosis of FFN. Based on expert opinion, the core set will assist clinicians in forming a clearer diagnosis of FFN.

### 4.3 Study Introduction

Williams and Robinson (2007) concluded that there was no single clinical feature that could definitively predict the presence of a FFN. Likewise, Owens et al (2011) indicated that there are no pathognomonic diagnostic clinical tests for FFN and so clinicians use clinical tests associated with forefoot pathology. As these are non-specific, a clinical diagnosis is predominantly achieved through a clinical history and an examination of the foot (Jones, 1987). Authors have started to report the sensitivity and specificity of specific clinical tests however the statistical data is not easily comparable. One reason for this is the limited numbers of published data sets as well as the selection of clinical tests; the authors selected these. This in turn makes it difficult to generalise the findings. This could potentially be supported through the perceived success of treatment interventions for this condition.  Jain and Mannan (2016) reported a breadth of potential treatment options available although they appreciated that the options could produce mixed outcomes for the relief of symptoms. This would suggest that outcomes success is multifactorial such as: clinician experience, clinical history recall, and possibly the accuracy of participant reported symptoms. The aim of this study was to develop a clinical protocol that had

agreed expert consensus for the clinical diagnosis of FFN.

In order to achieve the aim a classical Delphi design approach was adopted. A Delphi can be described as ‘a method for structuring a groups communication process’ (Vernon, 2009). The classical Delphi design seeks to obtain agreement of opinions from expert participants in a specific topic area. Firstly, participants are asked to establish a list of recommendations (methods) and from this list a series of voting rounds with anonymised feedback are disseminated to each participant until a level of agreement is procured (Hasson and Keeney, 2011). The use of a numerical scoring system was required to refine the final list of recommendations to achieve the set aims and objectives.

### 4.3.1 Study Aim and Objectives

The main aim of the study was to develop diagnostic criteria that had agreed expert consensus for the clinical diagnosis of FFN. To achieve this aim, several objectives were defined:

- To complete a literature review to identify the range of clinical practice methods used to diagnose FFN.
- To complete a Delphi method to identify the range of clinical practice methods used to diagnose FFN.
- To complete a Delphi method to determine consensus of recommendations regarding the optimal methods required to clinically diagnose FN.
- To determine expert panel recommendations to inform development of a clinical protocol.

### 4.3.2 Research Study Question

The research question was as follows:

What is the best way to clinically diagnose FFN in the general population?

### 4.4 Method

A number of potential study methods were available to identify the methods required to specifically diagnose FFN such as the Delphi method, nominal group technique (NGT), focus groups (FG), brainstorming or semi-structured/ structured interviews (SSI/SI). Similarly, each method utilised by a researcher, aims to ask individuals about their perceptions, beliefs, opinions or judgments towards a concept, issue or topic. However, for this study a Delphi method was used to develop an agreed set of items that were used for the clinical diagnosis of FFN. It was anticipated that health professionals would incorporate modified methods into the discussion so that the protocol design was reflective of practice. There are three types of Delphi methodology that are consistently reported in the literature, these are: conventional, real time and priority (Hasson et al, 2000). It is reported that the conventional Delphi method is characterised by five key features. These are: anonymity, iteration, controlled feedback, statistical group responses, and stability of responses amongst those with an expertise on the issue (Hanafin, 2004). In summary, the method consists of a questionnaire sent out to a group of panel members (experts), with a second questionnaire based on the results of the first. Subsequent questionnaires refine and define the facts or items, gauging their accuracy or support from the panel members (De Villiers, De Villers and Kent, 2005).

One of the primary strengths of using the Delphi method is the panel member's anonymity that encourages individuals to openly put forward their opinions without fear of judgement from others as the method is conducted through mediums such as email, telephone or postal services. Whereas NGT, FG, mindmapping and interviews require data to be collected from "face to face" interaction which can sometimes be subject to false agreement and conformity as a result of a pressured environment from other panel members (Van Zollingen and Klaassen, 2003). Similarly, those individual panel members who are vocal or highly opinionated could potentially refocus the discussion topic thus data collection is inaccurate or irrelevant. This is often witnessed in NGT and FG designs but Sackman (1975) reported that the Delphi method can encourage a sense of being non-accountable for controversial opinions which again could lead to inaccurate or inappropriate suggestions (Dalkey, 1972 and Van Zollingen and Klaassen, 2003). Hanafin (2004) suggested that some authors believe that NGT, FG, brainstorming and interviews are inappropriate methods to develop a set of indicators/recommendations for use in a health care setting but further clarification on why has yet to be identified. This would suggest that careful consideration of how the panel members will interact is vital in promoting teamwork and focus to minimise selection bias.

Another advantage is the use of electronic communication devices and/or programming to collect, store, organise and retrieve information throughout a study period. In particular, published evidence has acknowledged that the Delphi method could potentially save study costs in terms of resources, time and security compared to methods such as SSI/SI, FG or NGT where additional costs are often required to support the write-up of transcripts or to pay for individuals to use recording equipment and edit the data collected (Fink et al., 1984; Sackman, 1975 and Snyder-Halpern et al ., 2003). Moreover, the Delphi method has the ability to access potential panel members who either geographically, or due to clinical pressures, would not be able to attend frequent “face to face” meetings which could increase the chances of low recruitment numbers and additionally affect continued participation if organised/volunteered time is minimal (De Villiers, De Villiers and Kent, 2005). Further still, the Delphi provides an opportunity for panel members to reflect and contemplate the questionnaires in their own time and this is thought to provide a “truer” answer which is free from mis-representation (Goodman, 1987 and Linstone and Turoff, 1975). Consequently, the ability to incorporate electronic communication and information technology into the Delphi method could support the processes of data collection as well as providing potential cost and time saving advantages, which with a clear methodological process, could make data collection more efficient.

Although uncertainty does exist with determining the optimal sample size for the Delphi method (Hanafin, 2004), a range of figures have been quoted in the literature from 6 to 57 panel members (Cabral et al., 2005, Graham, Regiehr and Wright, 2003 and Zhang et al., 2007). Some authors have agreed that more than 30 panel members rarely produce improved results (De Villiers, De Villers and Kent, 2005; Fink et al, 1984; Murry and Hammons, 1995 and Clayton, 1997). On the other hand, many authors are in agreement that the number of panel members can vary depending on the study purpose, complexity of design, time and resources (Akins, 2005 and De Villiers, De Villiers and Kent, 2005). Some authors have stated that no consensus of agreement has been drawn upon to determine the sample size, nor recommended a definition of “small” or “large”(Akins, 2005 and Boulkedid et al., 2011). Hence, it would be reasonable to consider that no optimal sample size currently exists and that sample sizes should be realistic and manageable for the research study and this can be dependant on multiple factors.

Moreover, there has been discussion on how best to define a “panel expert”, Fink et al (1984) and Goodman (1987) are often quoted in the literature as defining a suitable expert as “someone who possesses the relevant knowledge and experience and whose opinions are respected by fellow workers in their field”.

Ideally, authors have suggested the inclusion of a wide range of professions, from a range of clinical backgrounds and from a wide geographical diversity who will develop the panel to be a representative group (Graham, Regiehr and Wright, 2003 and Cabral et al., 2005). Likewise, Boulkedid et al (2011) suggested that a heterogeneous group, with a range of stakeholders, encourages different outlooks and decision making which in turn enriches the data, leading to better outcomes of credibility and acceptability. In addition, credibility and acceptability are often debated in the process of achieving consensus and it is thought that a total of three rounds should suffice as anything more would lead to data saturation (Skulmoski, Hartman and Krahn, 2007). Bellamy et al (1991) proposed that the first and second rounds often achieve the largest alterations.

Overall there is author support in the continued use of the Delphi methodology for it's wide variety of applications in healthcare to gather real-time and real-world knowledge (Hsu and Sandford, 2007). Many authors believe that the Delphi methodology could sit in either the post-positivism or constructivist paradigm as qualitative and quantitative design methods could be used to inform data collection (Linstone and Turoff, 1975, Critcher and Gladstone, 1998). In this instance, a quantitative approach was used to determine the strength of consensus via the expert panel members. The quantitative approach best fits this Delphi study design as the items selected by the panel were statistically scored. Although some might argue that the qualitative approach best fits this Delphi method design as opinions, phrases and beliefs were collected and refined to produce a list of methods however these were not fully explored in great depth or detail. Therefore a mixed method or qualitative approach would not have been appropriate to achieve the research question or aim. The results from Study Two led to the methodological development of Study Three which focused on the agreement between the expert derived clinical assessment protocol (test) and the reference standard, in this case musculoskeletal ultrasound.

### 4.4.1 Design technique

This Delphi study design aimed to gather data via a group communication process to achieve a convergence of opinion on a specific topic area for the purpose of addressing what could and what should be done (Hsu and Sandford, 2007 and Miller, 2006). Approaches to Delphi study designs can be qualitative or quantitative to collect data (Miller, 2006). This design used a mixed qualitative and quantitative approach to data collection and to analyse the findings. In this Delphi study, there was a need to determine what current diagnostic methods were used within clinical practice to diagnose FFN.

The Delphi study design asked participants in the first round to firstly list their current methods of diagnosis. This included the participant's knowledge, perceptions, behaviours and reasoning behind a diagnosis of FFN. Following this, participants were asked to complete two rounds of voting either by rejecting or accepting methods formulated by the participants using electronic questionnaires via email. An additional fourth round encouraged the participants to rank the strength of the criteria recommendations. Health professionals were identified a-priori as routinely providing clinical assessment and/or diagnosis in a clinical setting. Health professionals were invited to participate in the study via email. This participation process allowed access to health professionals globally, which may have not been achievable with a focus group design. A nominal group technique was discounted as the method involved the panel members contributing to a list with little or no feedback.

The research team (CD, LC and CB) made an informed decision to conduct the Delphi method through email. From a practical point of view, it allowed the researcher (CD) to converse with participants in a timely manner with minimal interference to the participant's normal routine. This method of communication allowed a mutual rapport to build and thus increase the likelihood of the participants' on going commitment to complete the study process (Hasson, Keeney and McKenna, 2000). An additional benefit included the ability to trace the emails to confirm the participants had received the study information. Most importantly, the participants were anonymised to each other and thus were able to have a voice and share their thoughts on the clinical question without judgement (Hasson, Keeney and McKenna 2000).

### 4.4.2 Expert Identification and Sample Size

The Delphi technique is one example of gaining group consensus in a topic area where evidence is limited or contradictory (Vernon, 2009). Participants who took part in the study were considered experts in the identification of FFN. Vernon (2009) defined expertise as a 'variable notion which is determined by the topic for example clinicians as experts compared to the general population. It is up to the researcher to state and justify the criteria of an expert for their study'. For this study, the criteria was defined as follows (Table 6):

Table 6: Inclusion and Exclusion for Study Two

| | |
|---|---|
| **Inclusion Criteria** | Experience of diagnosing, assessing or managing at least 35 cases of neuroma in the forefoot in the last year |
| | Knowledge of pathology of FFN |
| | Individual post graduate |
| **Exclusion Criteria** | Undergraduate student |
| | Has never assessed, diagnosed or managed neuroma of the forefoot |

The Delphi sample size was informed by previous sample size studies that ranged from 6 to 57 participants (Cabral et al., 2005). Further evidence states there is no agreement on panel size, nor recommendation or unequivocal definition of “small” or “large” (Akin, Tolson and Cole, 2005 and Boulkedid et al., 2011) but does suggest that studies with panel groups over 30 rarely produced improved results (De Villiers, Devilliers and Kent, 2005). Many authors are in agreement that the number of panel members can vary depending on study purpose, complexity of design, time and resources (Akin, Tolson and Cole, 2005 and De Villiers, De Villiers and Kent, 2005). This study size was manageable for the researcher to produce sufficient responses to accommodate for uncompleted rounds or withdrawal from the study.

### 4.4.3 Recruitment

Initially, 10 participants were identified and invited by the researcher (CD) to participate in the study. Identification was determined via a literature review and professional networks. The researcher (CD) invited participants from a number of health professions. Inclusion of a wide range of professions from a range of clinical backgrounds with a geographical diversity is suggested as good practice as it develops the participants to be a representative group (Graham, Reiehr and Wright, 2003 and Cabral et al., 2005). A heterogenous group, with a range of stakeholders, encourages different outlooks and decision-making, which in turn enriches the data leading to better outcomes of credibility and acceptability (Boulkedid et al., 2011).

The initial 10 participants were then asked to identify and pass on the research information to a further 3 colleagues each who may wish to participate in the study. This sampling technique is known as ‘snowball sampling’ and is particularly effective at

identifying individuals in a population who are difficult to contact or have minimal members (Summer, 2001). This chain referral process continued until a sufficient sample size was reached. In total, 20 participants consented onto the study and 16 completed all 4 rounds.

#### 4.4.4 Ethical Approval

Approval for this study was obtained from the University of Southampton, Faculty of Health Sciences, Ethics and Research Governance Online (ERGO) (ID reference: 14364). All panel members provided electronic or written consent.

#### 4.4.5 Delphi Process

The Delphi study design was adopted in order to gain a group consensus of opinion via a structured communication process. An invitation email introducing the topic area, with an attached document on the synopsis of present literature/guidance in clinically assessing and diagnosing FFN, was provided for the participant to read. In addition to this, Round 1 instructions, the Delphi questionnaire and the participant demographic sheet were also attached in the email for the participant to complete. Participants were given a 3 week deadline to complete the questionnaire. At 2 weeks a reminder email was sent to the participant if they had not returned their questionnaire. After the deadline, the questionnaires were collated and duplicated answers were removed and terminology made consistent by the researcher (CD). The participants received the whole list and feedback from the first round 2 weeks after the deadline. This process was repeated for rounds 2 and 3. All participants completed the Delphi through email. In round 4, participants were asked to rank the strength of recommendation they would give (where 1 was the lowest rank or lowest strength of recommendation). The top 50% of the responses provided the recommendations for the expert derived clinical assessment protocol. This was determined by the researcher (CD) as an acceptable marker to capture the most valued recommendations for the clinical diagnosis of FFN.

### 4.5 Data Analysis

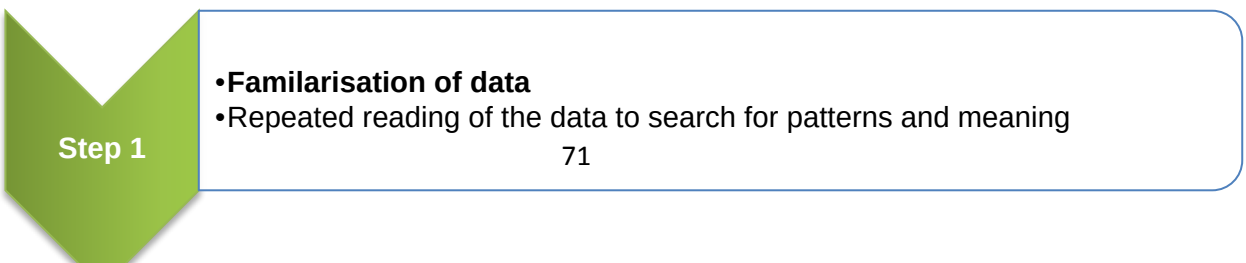
#### 4.5.1 Descriptive Statistics

Nominal demographic data for participants was collected for background information. The data was cleaned and analysed using IBM Statistical Packages for the Social Sciences (SPSS) Version 19.0 for Windows (SPSS Inc, Armonk, NY, USA) to determine: number of cases, median, mean, range and standard deviation.

### 4.5.2 Qualitative Data

A textual data set was used to capture complex implicit and explicit ideas and phrasing formulated by the Delphi question. This body of text was then analysed using thematic analysis to identify and describe the derived themes. This formed the recommendations for the development of the expert derived clinical assessment protocol. The thematic analysis process was conducted via six steps (Figure 12).

Figure 12: The thematic analysis process (authors own image, 2018)



### 4.5.3 Content Validity

Content validity refers to the extent at which a measure represents all features of a given idea. For instance whether or not the FNCAP contains the appropriate content to diagnose FFN. To determine the content validity of each item within FNCAP the following formula was used:

$CVR=(n_e-N/2)/(N/2)$

Key:

CVR = Content Validity Ratio

Ne = Number of panel members identifying the item as essential

N = Total Number of panel members

The formula produced values that ranged from +1 to -1. A positive value indicates at least 50% of the panel members rated this item as essential. The mean content validity ratio was used as an indicator of overall content validity thereby informing objectives 1 and 2 of the study (section 6.3.1, page 73).

### 4.5.4 Response Rate

The overall sample size was 16 panel members. Throughout the Delphi process there was an expectation that the response rate would decrease throughout the number of rounds as this was documented within existing literature (De Villiers, De Villiers and Kent, 2005). Interestingly, all 16 participants who started and completed round one continued to complete the following rounds. Furthermore, there was little guidance on the quantity of data which would be gathered from this design due to the nature of the specific topic area. In healthcare a body of work assessing diagnostic tools using the Delphi design indicated a figure of 20 to 40 recommendations, similarly the Delphi study has produced 21 recommendations (Graham, Regiehr and Wright, 2003) (Figure 13).

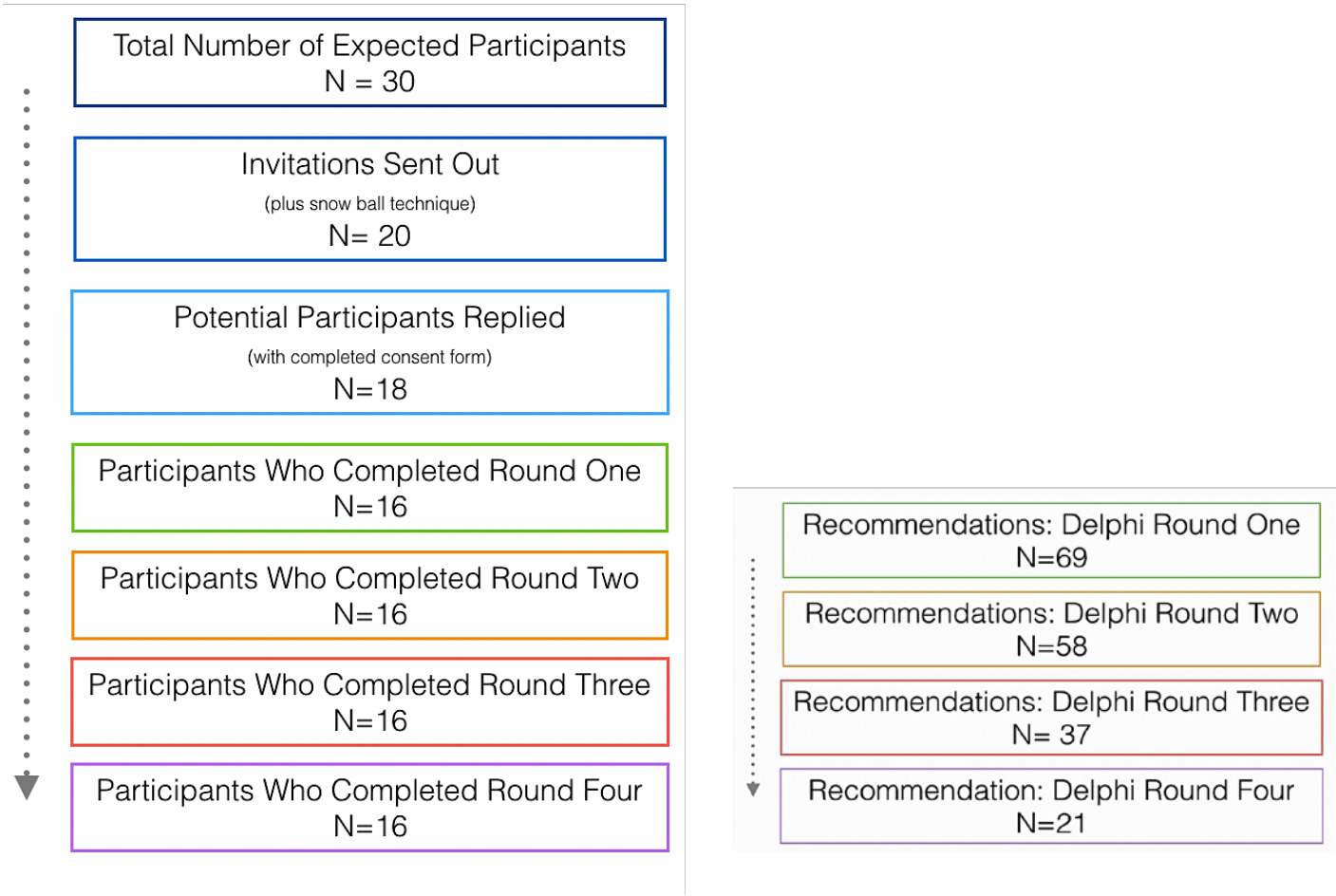



Figure 13: Delphi rounds and response rate

## 4.6 Results

### 4.6.1 Delphi Panellist

All 16 participants were based in the United Kingdom. The participant health professional groups were: Podiatrists (N=9), Radiologist (N=1), Rheumatologists (N=2), Orthopeadic surgeons (N=1), Chiropractor (N=1) and Podiatric surgeons (N=2). Clinical experience ranged from 5 years to 34 years (mean 19.5 years) in clinical practice.

### 4.6.2 The Recommendations

In round 1, the 16 participants identified 68 recommendations for the clinical diagnosis of FFN. In round 2, 27 recommendations were accepted, 11 recommendations were rejected and 30 recommendations were assigned to be re-voted on (Appendix B). In round 3, 36 recommendations were accepted, 22 recommendations were rejected and 10 recommendations were assigned to be re-voted on (Appendix C). After round 3, the participants still had 47 recommendations for the clinical diagnosis of FFN. The researcher (CD) reviewed round 1, 2 and 3 feedback and noted that theoretical data

saturation had occurred. Morse (1995) describes theoretical data saturation as ‘data adequacy’ whereby there is no additional data being added and the existing data has been explored.

Therefore the 4th round asked the participants to rank the 47 recommendations based on their perceived strength of importance to clinically diagnose FFN. The top 50% of responses form the derived clinical assessment protocol for the clinical diagnosis of FFN. In total 21 recommendations were finalised. From these 21 recommendations, a set of themes were established: location of pain, non weight bearing sensation, weight bearing sensation, observations, tests and imaging (Table 7).

Table 7: The expert derived clinical assessment protocol for the diagnosis of FFN

| Theme | Delphi Recommendation |
|---|---|
| **Location of Pain** | Pain located in the 2nd or 3rd inter metatarsal space |
| | Forefoot pain reported by patient |
| **Non Weight Bearing Sensation** | Paraesthesia radiating distally in the toes. |
| | Pins and needles reported by the patient |
| | Shooting pain reported by the patient |
| | Burning sensations reported by the patient |
| | Clicking reported by the patient |
| **Weight Bearing Sensation** | Walking on pebbles/lump/stone reported by the patient |
| | Separating the metatarsal heads e.g. met dome, padding, off the shelf insoles ease symptoms |
| | Shoe style: tight fitting/narrow aggravate pain symptoms reported by the patient |
| **Observations** | On palpation of joint margins no pain reported by the patient |
| | Diastasis of toes |
| | No pain on movement of joints |
| | No swelling |
| **Tests** | Diagnostic LA (plus/minus steroid injection) |
| | Tenderness/pain reported by participant on palpation of inter metatarsal space (usually 2nd/3rd) |
| | Mulders Click |
| | Pain reported by participant on lateral compression of the forefoot |
| | Pain on squeezing metatarsal heads (lateral and direct compression) |
| **Imaging** | Ultrasound |
| | X-ray (rule out other pathology or surgical planning) |

### 4.6.3 Content Validity Results

The FNCAP had a total of 21 items (Table 8). The overall mean CVR value was calculated as follows:

Total agreement scores of items (n=21) = 3.72 divided by 21 = 0.18

The mean CVR value was: 0.18

However, some of these items within the FNCAP could have been considered as imaging or surgical procedures. It is possible that some podiatry service lines would not have access to these. Therefore, to ensure the FNCAP was usable in a community podiatry setting the imaging and surgical items were removed from FNCAP. The overall CVR mean value with 18 items was calculated as follows:

Total agreement scores of items for the clinical assessment protocol (n=18) = 2.46 divided by 18 = 0.14

The mean CVR value was: 0.14

This indicates that the FNCAP as a whole had over 50% agreement that items within the protocol were essential for the identification of FFN. Whereas, the remaining 50% was considered not useful for the diagnosis of FFN. Repeating the formula for each item within the FNCAP produced the following results:

Table 8: CVR values for each item in FNCAP

| Items | CVR Value |
|---|---|
| **Ultrasound** | **1** |
| Participant reported burning sensation | 0.87 |
| Mulders click | 0.87 |
| Paraesthesia radiating distally in toes | 0.73 |
| Participant reported pins and needles | 0.5 |
| Participant reports shooting pain | 0.5 |
| Tenderness/pain on palpation of the inter-metatarsal space (usually 2nd/3$^{rd}$) | 0.46 |
| Pain on lateral compression | 0.33 |
| Pain on squeezing met heads | 0.33 |
| **X-ray** | **0.33** |
| Shoe style; tight/narrow fitting footwear aggravates symptoms | 0.2 |
| Pain located in 2$^{nd}$/3$^{rd}$ inter-metatarsal space | 0.07 |
| Walking on pebbles/stone/lump in shoe reported by patient | 0.07 |
| **Diagnostic Local Anesthetic** | **-0.07** |
| Participant reported forefoot pain | -0.2 |
| Separating metatarsal heads; met domes, insoles, padding eases symptoms | -0.2 |
| Joint margins palpated: no reported pain | -0.33 |
| No pain on movement of joint | -0.33 |
| Clicking reported by patient | -0.47 |
| Diastasis of toes | -0.47 |
| No swelling | -0.47 |

The results from the table 8 highlighted the highest to lowest ranked items based on clinician's beliefs and values of being 'essential' for the identification of FFN. With a unanimous agreement all panellists (n=16) identified 'diagnostic musculoskeletal ultrasound' as the most essential and 'no swelling' as the least essential (4/16 panellists). 11 out of 18 items were considered essential. Those items highlighted in black did not form part of the final FNCAP for clinical use in practice.

**4.7 Discussion**

This study has developed a single clinical protocol, which incorporates 21 recommendations, for the clinical diagnosis of FFN. The participants strongly agreed that participant reported symptoms were routinely used to provide a clinical diagnosis. The participants consistently accepted localised forefoot pain and pain specifically reported at the 2nd and 3rd inter metatarsal (IM) spaces to be valuable in aiding the diagnosis of FFN. Investigators have extensively discussed the potential aetiology of FFN in the 2nd and 3rd IM spaces but little clarity has been found within the literature to determine how valuable "localised forefoot pain" is as an indicator for the diagnosis of FFN (Koulouis and Morrison, 2005 and Hassouna and Singh, 2005). Investigators have also reported other participant reported symptoms specifically to the IM spaces such as; paraestheisa, pins and needles, shooting pains and burning sensations (Jones, 1987).

The use of diagnostic musculoskeletal ultrasound (MUS) imaging was the consistently highest scoring recommendation for the clinical diagnosis of FFN. Diagnostic MUS imaging has emerged over the past decade as a useful modality for identification and diagnosis of FFN (Koulouis and Morrison, 2005 and Pastides, EL-Sallakh and Charalambides, 2012), with a number of authors documenting sensitivity and specificity scores of approximately 80 to 95% (Quinn et al., 2000; Soo, Perera and Payne, 2010, Fazel, Khan and Thomas, 2012 and Claassen et al., 2014). Thus there appears to be good agreement between authors on the use of diagnostic US imaging as a reasonable method to be used to differentiate FFN from other forefoot pathology. However, the sonographic characteristics for determining the presence of FFN were not evaluated as part of this study. Participants just acknowledged that US was an important recommendation for diagnosing FFN.

One of the most highly scored tests by the participants was the Mulder's sign, even though there is evidence showing inconsistency in accuracy of identifying FFN through this method (Owens et al., 2011). One potential reason for this is a 'Mulder's click' which can be produced with a Mulder's sign test; it is thought that manipulation of the soft tissue structures or mechanical loading could cause anatomical tissue to bulge or slide over one another creating a false result (Bossley and Cairney,1980). Alternatively, Mahadevan et al

(2015) demonstrated that “squeezing the IM space” produced a tenderness/pain, which had a sensitivity of 96% and a specificity of 100% in 54 feet compared to US findings. Likewise, Owens et al (2011) found 95% of 76 feet had IM space tenderness with the presence of neuroma confirmed by US. Although different terminology is used, both the tests described in the papers by Mahadevan et al [11] and Owens et al [9] are identical ‘the symptomatic IM space is squeezed between the tips of the index finger and thumb’. Both investigators also acknowledged the potential use for reproducing pain via lateral compression of the metatarsal heads. Mahadevan et al (2015) demonstrated a 41% sensitivity and 0% specificity in their sample population (n=45 feet) whereas Owen et al (2011), found lateral compression of the metatarsal heads produced a positive response in 88% of their population (n=76 feet). Again, little evidence was present in describing pain on compression of the metatarsal heads and what implications this finding has on clinical decision-making.

Most surprisingly, the use of local anaesthesia (LA) (plus or minus a steroid injection) to determine whether the nerves locally in the foot are producing the symptoms, was also highly indicated. Those participants with the skill set strongly recommended the use of this method, even those who did not have the skill themselves but work in multi-disciplinary team(s) also ranked this highly. Evidence indicates this technique is used to confirm suspicions, if imaging is negative, or for surgical planning (Williams and Robinson, 2007). It is appropriate to suggest that this method could potentially be of benefit to those working in surgical teams who have the resources and training to ensure safe, competent practice is achieved.

The participants also commented on the use of X-ray when reported symptoms were poorly defined by the participant and negative clinical tests were documented. Interestingly the use of x-ray was considered an alternative way to exclude other potential pathology and/or for surgical planning (Hassouna and Singh, 2005). Koulouis and Morrison (2005) reported the use of Sullivan’s sign; disproportionate separation of the metatarsal heads in loading (weight bearing) using an antero-posterior radiographic view of the foot. No data is available on the sensitivity and specificity of this method for diagnosing FFN, as such it can only be considered as expert opinion at best.

With less certainty, the participants agreed that no swelling, no pain on movement of the metatarsal phalangeal joints (MTPJ’s) and no pain reported on palpation of the joint margins were important to document. These observations are documented in guidelines for assessing joint quality and pathology in participants with MTPJ pain (Palmer and Epler, 1998). This suggests that these recommendations were used to rule out other pathologies.

Participants also agreed that participant recall of symptoms in the forefoot was relevant, for example the expression of ‘I’m walking on pebbles, lump or stone’ to describe the sensations in their foot/feet. In some instances, these terms have been used to describe FFN (NHS Choices, 2015). The participants also agreed that the reporting of ‘separating the metatarsal heads’ with either padding or insoles to ease the symptoms was important to understand, although some may argue that this is a treatment recommendation rather then a diagnostic method (Thomas et al., 2009). Likewise, the participants thought it was important to establish whether a patient’s footwear style aggravated their forefoot symptoms. The NICE guidelines for neuroma advise that individuals who chose to wear narrow or tight fitting footwear, usually with a heel, often report that their footwear aggravates their symptoms, therefore health professionals should advise participants to modify their footwear (broader shoe style) (NICE, 2013). Some may argue that this is a treatment recommendation rather than a diagnostic method.

### 4.8 Strengths and Potential Limitations

This study design was able to assimilate current methods used for the clinical diagnosis of FFN. However the Delphi design has never been proved or disproved to significantly improve judgment in identifying or forecasting specific topic issues in healthcare, information technology or business, thus there is potential for the recommendations to not be precise (Rowe et al, 1999). There is an assumption that agreement between the participants would reduce the risk of outcomes being invalid (Hasson, Keeney and McKenna, 2000). One way in which the reliability of the recommendations were reviewed, was for the researcher (CD) to feedback the developing opinions at group level. It was anticipated that this would encourage disagreements or concerns to be raised. Hasson, Keeney and McKenna (2000) proposed the idea that if the panel members were not able to reflect or elaborate on their answers then this could be potentially seen as forced consensus. Therefore a section for “comments” was available for panel members to elaborate on their thoughts. Hasson, Keeney and McKenna (2000) also proposed that recommendations are strengthened when opinions are challenged anonymously, thus increasing validity. The ‘comments’ section provided insight and reflection for the researcher (CD) to check each panel members’ meaning, accuracy and consistency of a phrase throughout all 3 rounds.

Another potential study limitation could have been the participant sample recruited. The study was accessing participants who have a pre-existing interest in the topic, which in turn would increase content validity but could be affected by the response rate (Hasson, Keeney and McKenna, 2000). There is a risk that those invested in the study may modify their opinions to fit with the majority or with current clinical practice. To reduce this, Hsu and Sandford (2007) advise a qualitative and quantitative element to the Delphi design in

order to understand the priorities within the topic area. For the clinical diagnosis of FFN, the ranking of recommendations focused the panel members to vote for specific methods to identify this condition rather than a holistic approach.

### 4.9 Conclusion

Following the identification of 21 method recommendations, a core set of clinical diagnostic methods have been prepared as a clinical assessment protocol for the diagnosis of FFN. Based on expert opinion, the core set will assist clinicians in developing a clearer diagnosis of FFN.

# 5.0 Chapter Five

## Diagnostic Study

# The content validity and reliability of a novel expert derived clinical assessment protocol for the identification of FFN

### 5.1 Introduction

In clinical practice, diagnostic tools are integral to the identification of musculoskeletal pathology. For diagnostic tools to be used most effectively, they need to have established parameters to support clinical decision-making otherwise a diagnosis becomes inaccurate.

The development of the diagnostic forefoot neuroma clinical assessment protocol (FNCAP) tool was described in Chapter Five. There is a need to subsequently evaluate the FNCAP accuracy and consistency in clinical use. The results from this chapter address the aim to determine the content validity and reliability of an expert derived clinical assessment protocol for the identification of FFN. The diagnostic study method is presented, followed by the statistical analysis and interpretation of these findings in the context of forefoot musculoskeletal assessment in practice.

### 5.2 Chapter Abstract

**Background:** FFN is a change to the nerve as it passes between the metatarsal bones. Current methods of diagnosing FFN are varied and may include interpretations of participant reported symptoms, clinical observations or tests. However, similar approaches are used to diagnose other forefoot pathology such as bursitis, capsulitis or synovitis, with no clear differentiating factors. Currently, there is limited evidence to support a specific clinical diagnostic protocol specific to FFN. Previous work by the authors has led to the development of an expert-derived clinical diagnostic protocol for FFN. However, the repeatability and content validity of this protocol remains unclear.

**Aim:** To determine the repeatability and content validity of a novel expert-derived clinical diagnostic protocol for FFN.

**Method:** Ethical approval was obtained (IRAS ref: 14371). A prospective diagnostic study design was implemented over a 10-month period. Participants with forefoot pain and no peripheral neuropathy were recruited from a single UK NHS podiatry musculoskeletal service. The diagnostic protocol was used by the same podiatrist to determine the presence or absence of FFN. A second podiatrist, with a PGCert in foot and ankle ultrasonography, conducted a standardised forefoot ultrasound examination as the reference standard to determine the presence or absence of FFN. Both investigators remained blinded to each other's findings. A sub group of participants (n=9) were invited to attend a second appointment to determine intra-rater repeatability.

The data was analysed descriptively to define the population with FFN using percentage agreement, and sensitivity and specificity analyses. The intra-rater repeatability and content validity of the diagnostic protocol was evaluated using percentage agreement, Kappa analysis and Content Validity Ratio (CVR) analyses.

**Results:** Thirty participants were recruited to the study (18=female/ 12=male; mean age 58 years, range 37 to 81 years. Of these, 7 participants (6=female/1=male) had confirmed FFN via diagnostic musculoskeletal ultrasound and 8 were identified as having FNN from the clinical assessment protocol. The participant who was diagnosed with FFN using the diagnostic protocol was diagnosed as forefoot bursitis with ultrasound. Relative to ultrasound, the diagnostic protocol had a specificity score of 87.5% and a sensitivity score of 95.6%. The intra-rater repeatability was k0.58; 'moderate agreement'. Using the CVR formula, the most valid components of the diagnostic protocol were: burning (0.87), mulder's click (0.87) and paraesthesia (0.73) and the least valid were: no swelling (-0.47), clicking (-0.47) and diastasis (-0.47). The three items likely to be most useful in the identification of FFN are: clicking reported by patient, separating metatarsal heads: metatarsal dome, padding, off the shelf devices eases symptoms and shoe style: tight/narrow fitting footwear aggravates symptoms.

**Conclusion:** Overall there is evidence to suggest that the diagnostic protocol for FFN is repeatable and valid. Further analysis and refinement of the diagnostic protocol is required to confirm its clinical utility in practical settings.

## 5.3 Study Introduction

Currently, there are no published validated tools for the identification of FFN. There are a range of clinical tests and observations that are used to assess the forefoot although the accuracy and consistency of these to diagnose FFN is unclear. The FNCAP was created in order to address this diagnostic gap, as described in Chapter Four. In order to determine the accuracy and consistency of the FNCAP several factors were explored:

1. Content validity: to determine the extent to which the FNCAP represents all facets of the identification of FFN
2. Intra rater reliability: to determine the degree of agreement between the outcomes of the FNCAP after repeated use by the same podiatrist
3. Sensitivity: to assess whether the FNCAP can accurately identify individuals who do have FFN
4. Specificity: to assess whether the FNCAP can identify individuals who do not have FFN
5. Likelihood Ratios: to assess the value of the FNCAP in order to achieve a diagnosis

### 5.3.1 Study Aim and Objectives

The main aim of the study was to determine the content validity and reliability of FNCAP for the identification of FFN. To achieve this aim, several objectives were defined:

- To determine the content validity of each item in FNCAP for the identification of FFN
- To determine the mean content validity of FNCAP for the identification of FFN
- To determine the repeatability of FNCAP for the identification of FFN
- To determine the sensitivity of FNCAP for the identification of FFN
- To determine the specificity of FNCAP for the identification of FFN
- To determine the likelihood ratios of each item in the FNCAP for the identification of FFN
- To determine the items which are most likely to differentiate FFN from other forefoot pathology

Musculoskeletal ultrasound (MUS) was used as the comparative reference standard to the FNCAP.

### 5.3.2 Research Question and Hypothesis

The research question was as follows:

‘What is the content validity and reliability of an expert derived clinical assessment protocol for the identification of FFN (the FNCAP)?’

The hypothesis were as follows:

H1: The expert derived clinical assessment protocol will be valid and reliable in the identification of FFN.

H0: The expert derived clinical assessment protocol will not be valid or reliable in the identification of FFN

## 5.4 Methods

A prospective, cross sectional study design, that included participants for whom their foot health status was unknown, was used to compare the results of the index test (FNCAP) to a reference standard (MUS). In this instance the reference standard selected by the research team was MUS. Justification for the use of MUS as a reference standard has been previously discussed in Chapter Two, section 2.4.1, page 21.

### 5.4.1 Study Method

A diagnostic study design was used to understand and determine those individuals, within a specified population, who truly have the disease and/or condition to those individuals who do not from using the forefoot neuroma clinical assessment protocol (FNCAP). The reference standard or sometimes ‘gold standard’ is the diagnostic method set as the ‘truth’ (ref). Although the study design assumed MUS is 100% precise, the current evidence suggests a figure between 89 – 92% as previously discussed in Chapter Two, section 2.4, page 19. For this reason, multiple statistical tests are included to assess and cross reference the data collected (Mandrekar, 2017). Furthermore, the researcher completing the FNCAP was blinded to the results of the sonographer who was conducting the MUS examination in order to maintain objectivity and repeatability. There is evidence to suggest that test failure can be a result of identifying the wrong condition/disease or if the measurement error is too great. Therefore, as part of the study design, a subset of participants were invited to allow the researcher to repeat in order to determine intra-observer reliability. It was also important to develop thresholds to accept or reject outcomes from using the protocol and to ensure each method on the FNCAP was

clinically relevant and appropriate for the diagnosis of FFN. In order to do this, a population of participants with forefoot pain were used to determine if the protocol could exclude other forefoot pathology. The diagnostic study design seeks to determine the content validity and reliability of FNCAP.

### 5.4.2 Study Population

The study population included individuals with forefoot pain of unknown cause. Potential participants were identified upon referral into a single NHS podiatry service with symptoms of forefoot pain. Forefoot pain symptoms were defined as follows: shooting pain(s) in toe(s), aching sensation(s) in toe(s), tingling sensation(s) in toe(s), burning sensation(s) in toe(s), numbness in toe(s), sensation of walking on pebbles/stone (NHS Choices, 2014).

The inclusion criteria were as follows:

1. Individuals who were 18 years of age or above
2. Individuals who were able to complete a questionnaire and comply with the study protocol
3. Individuals who had uni/bilateral forefoot pain (as defined above)
4. Individuals who were referred to the podiatry department during the study recruitment period

The exclusion criteria were as follows:

1. Individuals who were not able or willing to give informed consent
2. Individuals who had rearfoot or midfoot pain

### 5.4.3 Sample Size

These calculations were conducted by the researcher (CD) and checked with the statistical support team; Faculty of Health Sciences, University of Southampton. Threshold values were discussed and determined a-priori by the researcher in light of previous work carried out by the researcher's PhD (CD) (Chapter Three) in 2014 investigating incidence and prevalence of FFN in Solent NHS Trust, podiatry service population (unpublished report completed 2014).

There is some evidence to suggest that the prevalence of FFN is around 30 to 33% in individuals who present with forefoot pain symptoms (Lee et al., 2007). On the other hand others have argued that no known figures exists to define the prevalence of this condition in the general population (Thomas et al., 2009). As the evidence describing the prevalence of FFN in a generalised population is unknown; a proportionate sample size

was used as an alternative to a power size calculation. This method was selected because the researcher wanted to avoid the risk of a type I or type II error. A type I error is said to have occurred when the null hypothesis is actually true but is rejected by the researcher (false positive). Whereas a type II error is said to have occurred when the null hypothesis is accepted by the researcher incorrectly as it is false (false negative).

A proportionate sample size calculation identified the number of participants in a selected population who have FFN and do not have FFN within a specified margin of error. A 95% confidence interval was used within the calculation to estimate the number of cases required to achieve the study aim. The formula used to determine the sample size indicated 126 participants would need to be recruited.

Therefore, following advice from our statistician, a proportional calculation was used in preference to a power sample size calculation. A 95% confidence interval was agreed to estimate the number of cases required to determine the sensitivity and specificity of FNCAP. The proportional calculation indicated that the total recruitment figure for this study would be 126 participants.

### 5.4.4 Recruitment Strategies

Within the recruitment window of 8 months, 30 participants were recruited onto the study. This meant that on average, 1 participant a week (2 weeks no participants) was seen on the research study. One potential reason for the low recruitment rate was that the local clinical commissioning groups (CCG's)(n=5) were reducing musculoskeletal services due to an annual review of service provision. These changes were confirmed and implemented shortly after ethical approval for the study was obtained. Two recruitment strategies were implemented to maximise opportunities to recruit participants within the planned time:

<u>Recruitment strategy one:</u>

A poster about the study was displayed in all the Solent NHS Trust podiatry clinical waiting areas across the Southampton region. Those individuals who wished to seek more information were able to contact the researcher directly to discuss the study further.

<u>Recruitment strategy two:</u>

Potential participants were identified at their initial podiatry assessment appointment that was part of the their routine NHS care. Podiatrists from the clinical team conducted the initial podiatry assessment in a number of health care sites across the Southampton region. When the podiatrists identified an individual as potentially eligible, to participate in

the study, they were issued an invitation pack. The invitation pack contained an invitation letter, a participant information sheet (PIS), reply slip and a stamped addressed envelope.

The podiatrist would have emphasised that a decision to take part or not will have no impact upon their on going clinical care and that they are not expected to make a decision on the day.  This gave the participant time to consider if they wished to take part in the study. Participants had a minimum of 24 hours to decide whether or not to take part in the study.

When the reply slip had been returned to the researcher (CD), a research appointment was booked by telephone. The research team did not contact potential participants who did not return the reply slip. Potential participants who did attend the appointment followed a standardised protocol. Figure 14 illustrates the referral process of recruitment strategy two.

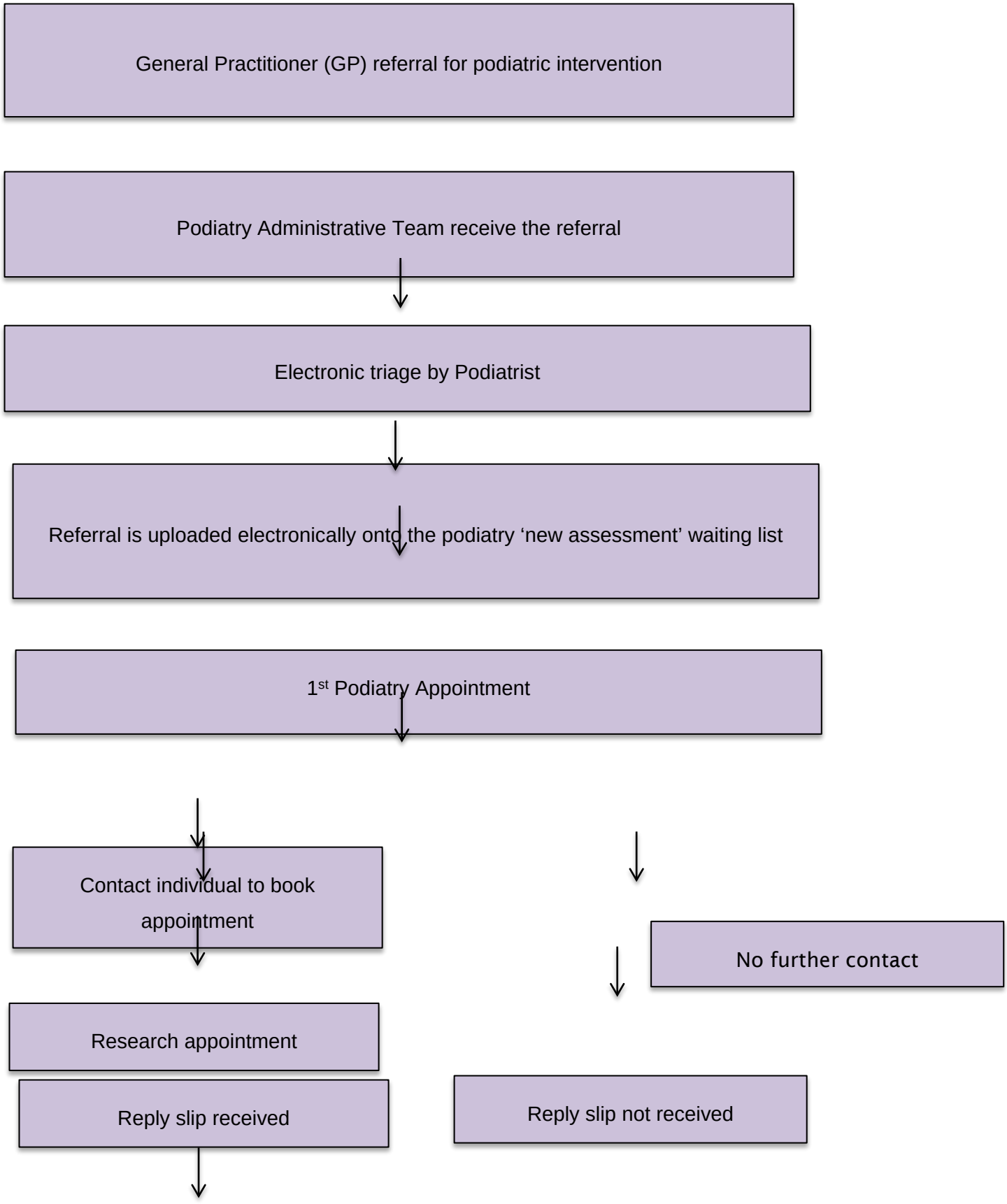



Figure 14: A flow diagram illustrating the podiatry referral and recruitment process.

### 5.4.5 Ethical Approval

Sponsor approval for this study was obtained from the University of Southampton, Faculty of Health Sciences, Ethics and Research Governance Online (ERGO) (ID reference: 14371). Using the integrated research application system (IRAS), both East Midlands - Nottingham 1 Research Ethics Committee (REC), Health Research Authority (HRA) and Solent Research and Development (Solent R&D) approval was given (IRAS ID: 178150; REC ref no: 16/EM/0268). All individuals enrolled onto the study provided written consent. All individuals who enrolled onto the study provided written consent to take part and for MUS image storage. Approval documentation can be found in the appendices (Appendix D).

### 5.4.6 Diagnostic Study Process

To review the accuracy of the index test (FNCAP) the results for the identification of FFN were dichotomised to positive (condition is present) or negative (condition is absent). Likewise, the reference standard also identified the presence or absence of FFN. The discrepancy between the results is assumed to arise from error in the index test. Both tests were conducted on each of the participants.

## 5.5 Standardised Procedure for Data Collection

A set data collection protocol was established. This was conducted on every study participant. This was to ensure that there was consistency in clinician behaviour and study process to reduce bias where possible. Biases will be discussed later in this Chapter, section 6.9, page 104.

### 5.5.1 Participant Screening and Consent

Potential participants attended their booked research appointment at a single community health centre. Potential participants were introduced to the researcher (CD). The researcher ensured that the participant had read and understood the invitation pack. If the potential participant raised no further queries, then written consent was obtained following the good clinical practice research standard (GCP) and the declaration of Helsinki Guidelines. Should the potential participant wish to decline consent at this time, they were made aware that they would still continue with their routine NHS clinical care and their clinical care would not be compromised in any way. All participants gave consent.

In accordance with confidentiality, pseudo-anonymisation was used in all research documentation. Participants were given a coded number so confidentiality of information was protected. If a participant was screened but no longer fitted the study criteria, CD discussed with the participant the reason why they were no longer eligible. To manage the participant's expectations, the 'participant information sheet' had highlighted this prior to consenting.

### 5.5.2 Participant Questionnaire

Participants were asked to complete a questionnaire about their demographics, foot pain and previous treatment details. This included: foot pain descriptors, history of steroid injection(s), surgery or previous imaging. This took approximately 10 minutes to complete.

### 5.5.3 Clinical Assessment

The FNCAP was derived by expert consensus through a Delphi technique. Assessment of the forefoot, using FNCAP, was conducted by a single researcher (CD) (Appendix F). CD completed each component of the FNCAP in the same order each time. The FNCAP required the participant to be observed weight bearing and non-weight bearing.

The FNCAP took approximately 10 minutes to complete and CD recorded the results. Once the FNCAP assessment was complete, CD left the room, and the second researcher (JB) introduced himself to the participant. JB conducted the MUS examination to reduce researcher bias. JB was blinded to CD's findings. Participants were aware that both researchers were blinded to each other results and therefore only answered direct questions about their foot pain.

JB is experienced in foot and ankle US and has a PGcert in 'Podiatry Ultrasound' via the AECC University College and is therefore a CASE (Consortium for the Accreditation of Sonographic Education) accredited sonographer.

### 5.5.4 Ultrasound Assessment

The participant was asked to sit on the clinical couch with their feet towards JB. JB demonstrated the ultrasound machine and discussed the MUS examination procedure. The ultrasound assessment took approximately 15 minutes.

A Flex Focus 400 EXP ultrasound machine was used (Make: Analogic Ultrasound). This unit is housed in the Solent NHS Trust, Podiatry department at the Adelaide Centre Southampton. Transducer size: High Frequency Linear Array 8870. Contact surface: 38.4mmx 3.5mm. Frequency (Hz) range: 18-6

From review of the literature in MUS there is general agreement within the field of sonography that FFN are defined as "…a hypoechoic mass either round or oval in shape that is proximal to the metatarsals heads or sits within the digital spaces." (Kankanala and Jain 2007, Quinn et al., 2000, Sharp et al., 2003, Zanetti and Weishaupt, 2005). This case definition was used to identify FFN in this study.

The forefoot ultrasound imaging scanning protocol was based upon the work of Bowen et al (2013) who utilised imaging of the forefoot to identify pathology in people with Rheumatoid Arthritis patients. The scanning protocol has been placed in the appendices (Appendix E). The researcher selected this scanning protocol because it assessed the anatomical structures in such a way that lesion size, location and doppler activity could be evaluated. Previous investigators have used similar scanning protocols as part of their data collection process, to interrogate the forefoot structures, as there is an appreciation that there is a wide range of normal anatomical variances (Kaminsky, Griffin and Milsap, 1997, Soo, Perera and Payne, 2010, Zanetti and Weishauipt, 2005). This would suggest that selecting a standardised method would ensure consistency in the data collection process thus reducing the potential risk of human error.

As part of the MUS examination, if FFN's were located then their size, location and appearance were documented. The majority of authors are in agreement that FFNs are frequently found within the third and less commonly second, IM spaces however appreciate that there is the potential for FFNs to be located in the first and fourth IM spaces (Sharp et al., 2003). The length and depth of FFNs were measured using the digital controls on the MUS machine. Current evidence hypothesises that the majority of symptomatic FFNs are larger than 5mm in length whereas a normal nerve is typically 1mm to 2mm at the level of the inter metatarsal heads (Quinn et al., 2000, Sharp et al., 2003). The researcher wanted to determine the lesion sizes in their population to assess whether these statements were still valid.

In addition to determining the lesion size and location, there is also a need to establish if there is an inflammatory response within the localised tissues of interest. The US machine controls can be used to detect pathological vascularisation within joints and peri-articular soft tissues thereby demonstrating the presence of active inflammation. This has been previously correlated to angiogenesis in Rheumatoid Arthritis participants (Schmidt, 2013). In the field of FFN, the evidence surrounding the presence of inflammation is unclear. Bencardino et al., (2000) suggested as a result of their study that FFNs showed no significant vascular flow (active inflammation) whereas Quinn et al (2000) hypothesised that bursa co-existing with neuroma are usually inflamed and therefore a positive doppler signal is visualised.

To determine the presence or absence of any inflammatory activity, the doppler signal was recorded. A semi- quantitative scoring system was used to grade the level of vascular activity within the doppler field (Taggart, Benson and Kane, 2011) (Table 9).

Table 9: Semi-quantitative scoring system for vascular activity with tissue under Ultrasound

| Grade | Description |
|---|---|
| **Grade 0** | No Doppler signal |
| **Grade 1** | Signal 10% less of the field |
| **Grade 2** | Signal present in 10% to 50% of the field |
| **Grade 3** | Signal is present in 50% or more of the field |

### 5.5.5 Image Capture, Reporting and Storage

Images were stored onto the machine hard drive and subsequently an encrypted memory stick. Any observations that were considered abnormal or needing further investigation were referred to radiology or a senior independent clinician for further action. This occurred in two instances; one participant had grade 3 bursitis and was in a lot of pain, one participant had grade 3 inflammation around previous surgically implanted metal fixation within the forefoot.

### 5.5.6 Study Summary for Participants

After the scans were saved by JB, he showed the participant their forefoot images. JB discussed the anatomical location of structures such as the metatarsal heads and skin however did not indicate to the participant if they had a neuroma present or not. JB saved images for each participant and completed an ultrasound examination report. These documents were both saved electronically and in paper form. The paper form was placed into the participants case report form (CRF).

Written consent was obtained by CD to use anonymised ultrasound images for future publications and presentations of the work and/or for this PhD thesis.

The participants then saw CD, who thanked them for their participation. A debrief letter was issued unless the participant had been booked for a second research appointment.

CD checked for any final questions or concerns. Results from the studies findings were sent to the participants once data collection and analysis was complete. This was set to take approximately 12 months.

Both clinicians, CD and JB, were blinded to each other's data findings at the time of the clinical visit. Data was inputted separately and participant data anonymised with the use of codes.

### 5.5.7 Repeated Clinical Assessments

The first 9 participants to complete the first research appointment were invited to return for a second research appointment. This involved the participant attending a 30 minute appointment for the researcher (CD) to complete the FNCAP for the second time.

The flow diagram below illustrates the protocol process for each participant on the study (Figure 15).

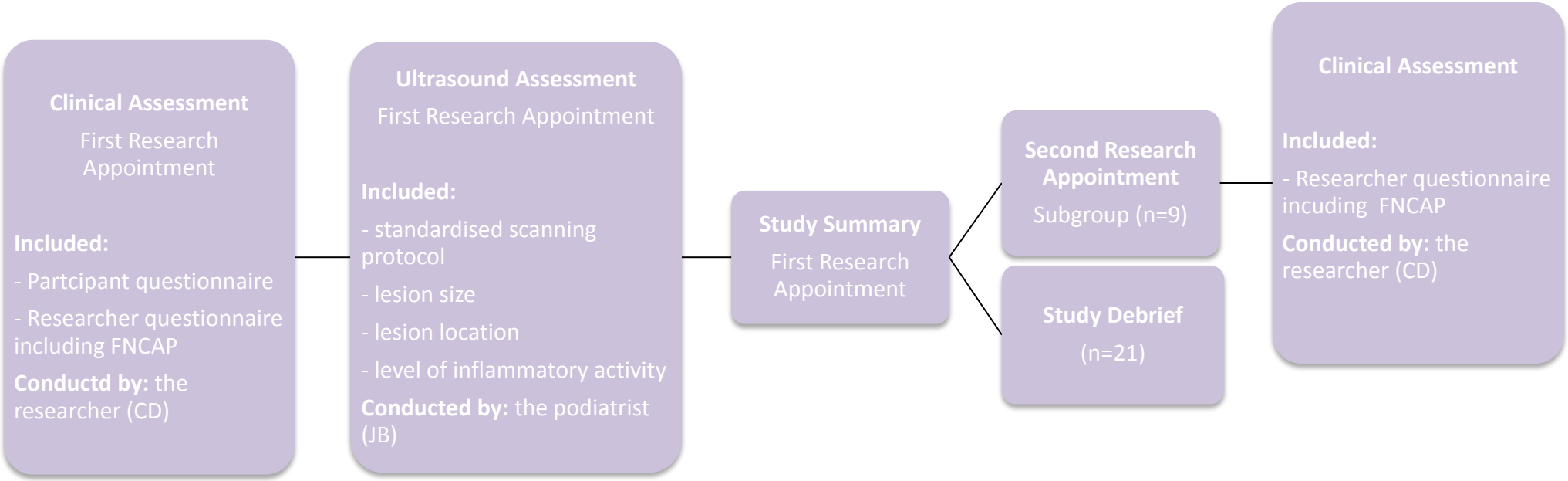



Figure 15: The protocol process for participants on the study

## 5.6 Data Analysis

The data collected was entered with a participant identification number into a Microsoft Excel spreadsheet (Version 14.6.1.1660122). The study data was checked for omissions or outliers and if noted, the original CRF reviewed.

### 5.6.1 Descriptive Statistics

Nominal demographic data for participants was collected for background information. The data was cleaned and analysed using IBM Statistical Packages for the Social Sciences (SPSS) Version 19.0 for Windows (SPSS Inc, Armonk, NY, USA) to determine: number of cases, median, mean and range. Questionnaires were used to explore qualitative themes in understanding the participant's previous medical history.

Participant reported descriptors about pain frequency; intensity and self-management were captured in free text questions. This was to verify context and meaning of the phrases used by participants in describing their symptoms associated with their foot pain.

### 5.6.2 Intra-rater Reliability

Reliability is defined as 'The quality of being trustworthy or of performing consistently well' (Oxford University Press, 2017). One aspect of reliability that was reviewed was to assess the intra-rater observer reliability that is defined as 'the degree of agreement among repeated administrations of the diagnostic test performed by a single rater' (Oxford University Press, 2017). To determine this, non-weighted Cohen's Kappa coefficient analysis was used to determine the agreement for categorical presence/absence of FFN between the first and second research appointment. The research team agreed an a-priori threshold criteria as "Substantial Agreement" on the majority of clinical assessment outcomes. The threshold values of agreement chosen by the researcher to use was adapted from Landis and Koch (1977).

Using the Cohen's Kappa formula, it was possible to determine the intra-rater reliability agreement of FNCAP. This was to determine if the researcher (CD) was consistent in determining the presence or absence of FFN from each item within the FNCAP under different circumstances. This was to explore if the researcher's (CD) judgements could have been influenced or altered by any external factors. In this incidence, external factors could have been the participant's activity levels, participant's perception of pain and use of self-management activities to reduce symptoms.

### 5.6.3 Sensitivity, specificity, positive predictive values and negative predictive values

To describe the relationship of FNCAP to the standard reference, several measures were required. These were:

Sensitivity: The proportion of people with the condition who have a positive test result

Specificity: The proportion of people without the condition who have a negative test result

Positive Predictive Value (PPV): The probability of the condition among persons with a positive test result

Negative Predictive Value (NPV): The probability of the condition among persons with a negative test result

To be able to complete the formulas a 2x2 table was used. This was used for each item within the FNCAP and for the protocol as a whole.

### 5.6.4 Likelihood ratios, pre test and post test probability

Likelihood Ratios (LR's) were used to measure and express diagnostic accuracy. LR's indicate how much an individual should shift their suspicion for a particular test result (Parikh et al., 2009). This is particularly helpful when deciding what tests help a clinician to 'rule in' or 'rule out' a disease. For LR's there is a positive likelihood ratio (LR+) and a negative likelihood ratio (LR-). A LR+ indicates how much to increase the suspicion of disease if the test is positive, while the LR- indicates indicate how much to decrease suspicion of disease if the test is negative. A LR greater than 1 indicates that the test is most likely to be associated with the condition whereas LR's less than 1 indicates that the test result is associated with the absence of the disease. Results above 10 and below 0.1 are considered to provide strong diagnostic evidence (McGee, 2002).

LR's could help indicate the potential thresholds a certain diagnostic test/item may have in a specified population rather than normal/abnormal. Unlike sensitivity and specificity values, LR's can indicate the probability of how stable the diagnostic test is in practical scenarios. When referencing 'stability' it's the probability that the diagnostic test is a true positive and not a false positive.  A false positive result could lead to clinicians making wrong clinical judgements if diagnostics tests are misleading or inaccurate. From sensitivity and specificity values alone, the understanding of how the diagnostic test would perform with variation is not clear whereas LR's are able to explore this concept. LR's values are able to demonstrate this because they use probability and odds to estimate variation.

Furthermore, LR's and post-test probability scores could support the FNCAP to sequence clinical tests to support clinical decision-making. In order to explore this option, LR's were used by the researcher to further understand what diagnostics tests could, if any, be of benefit for the identification of FFN. The values would also explore whether each item of FNCAP would support clinician decision making to 'rule in' or 'rule out' FFN. This was important in order to answer the overall research question (Chapter One, section 2.7, page 23). The researcher was interested in finding diagnostic items that could identify FFN.

Clinically, knowing this information could support clinicians in their initial assessment. Once the clinical history and assessment had been conducted the pre test probability may remain the same, increase or decrease. It is thought that clinicians intuitively action this; clinicians who are labelled 'experienced' are able to quantify their 'gut feeling'. By understanding how FNCAP could theoretically work in practice will define what further studies are required to evidence its use. The formulas for each are as follows:

LR+: Sensitivity/ 1-Specificity

LR-: Specificity/ 1-Sensitivity

Pre-test probability: prevalence of disease

Post-test probability:  post test odds/ (post test odds + 1)

Pre-test odds: pre test probability/ (1-pre test probability)

Post-test odds: pre test odds x LR

#### 5.6.5 Summary

By using a range of statistical methods the researcher has been able to understand how FNCAP and the single items within FNCAP could work in practice. The data analysis has started to consider FNCAP's value with regards to content validity and reliability for the identification of FNN.

#### 5.6.6 Statistical Guidance

Statistical support for the study was provided by Dr Sean Ewings, member of the Faculty of Health Sciences Statistical support network and/or the statisticians of the Southampton and Oxford Lower Limb Arthritis Research (SOLLAR) group.

## 5.7 Results

### 5.7.1 Descriptive Statistics and Qualitative Descriptors

The total number of participants and a subset group of participants with MUS confirmed FFN descriptive statistics were calculated as follows (Table 10):

Table 10: Simple sample descriptors

| Topic | Total Number of Participants | Mean | Median | Range |
|---|---|---|---|---|
| 12 males<br>18 females | 30 | 58 years of age | 60 years | 37 to 81 years |
| Foot Pain Duration | 30 | 3.8 years | 12 months | 2 months to 15 years |
| 1 male<br>6 females | 7 | 65 years of age | 60 years | 37 to 69 years |
| Foot Pain Duration | 7 | 4.7 years | 1 year | 2 months to 15 years |

The long term conditions participants documented managing were: Diabetes (type 1 and 2), Stroke, Chronic Obstructive Pulmonary Disease (COPD), Asthma, Osteoarthritis, Osteopenia, Depression, Migraines, Hypertension, Hyperthyroidism, history of knee or hip replacements, history of ankle fracture/sprains. 11 out of 30 participants reported having no long-term medical conditions. Participants reported if foot pain was unilateral or bilateral (Left foot: 9, Right foot: 8 and both feet: 13). All participants had tried self-management care for example; insoles, massage, stretching, footwear modifications and use of non-steroidal anti-inflammatory drugs (NSAIDs). Out of 30 participants, 23 had previously received insoles before their clinical appointment with the service. Participants provided additional detail by reporting their insoles had a range of prescriptions, for instance: rear foot correction, metatarsal bar, metatarsal pad and metatarsal domes to try to resolve symptoms. In some incidences participants reported these interventions initially worked, for others the pain had never resolved. Again, this was an additional detail participants described on their demographic questionnaire. None of the 30 participants had received a steroid injection, however, some participants did report previous hallux valgus surgery (n=1), lesser digits straightening (n=2), ankle plates (n=1) and an ankle fusion (n=1). Other pathology identified from using the FNCAP and diagnostic

musculoskeletal ultrasound were as follows: FFN, bursitis, degenerative joint changes, joint hypertrophy, capsulitis, ganglion cyst, synovitis, tendonitis, fat pad atrophy, fibroma. For some participants, no pathology was reported on clinical examination.

The participants, with a diagnosis of FFN, had their measurements tabulated. It was of interest to the researcher to determine if data was comparable to previous studies published. These results can be seen in Table 11 and MUS image reference in Figure 16.

Table 11: MUS measurements and descriptors from participants with MUS reported FFN.

| Outcomes | FN09 | FN14 | FN16 | FN19 | FN20 | FN23 | FN26 |
|---|---|---|---|---|---|---|---|
| **Pathology Location** | Left 3rd IM space | Right 3rd IM space | Left and Right 3rd and 4th IM spaces | Right 3rd IM space | Left and right 3rd IM spaces | Left 3rd IM space | Right 3rd IM space |
| **Shape** | Well defined circular appearance | Well defined mass | Ill defined | Ill defined and mixed echoic | Mass plantar to the transverse ligament | Well defined | Well defined oval shape |
| **Size** | 3.6mm x 3.5mm | 2.8mm in size | 5mm x 5mm | 5x4mm | 5mm x 4mm | 2.3mm – central mass | 5.4mm x 4mm |
| **Power Doppler Grade** | < Grade 1<br>Less then 10% vascularity | Grade 0<br>No vascularity | Grade 0<br>No vascularity | < Grade 1<br>Less then 10% vascularity | < Grade 1<br>Less then 10% vascularity | Grade 0<br>No vascularity | < Grade 1<br>Less then 10% vascularity |
| **Tissue description** | Hyper echoic mass centrally with hypo echoic halo | Hyper echoic mass with scattered hypo echoic masses positioned plantarly. Non-compressible under sonopalpation. Similar findings in the left 3rd IM space although less defined and asymptomatic | Loss of mixed echoic homogenous texture to fat pad and tissue at the IM spaces. | Compressible ill defined hypo echoic massed positioned in the IM space. | Non compressible hyper echoic mass with surrounding Ill defined hypo echoic mass | Non compressible hyper echoic mass with surrounding hypo echoic compressible mass As above with positive Mulders on assessment | Well defined hyper echoic mass deep to 3rd IM space. Scattered hypo echoic pockets within the fat pad suggestive of bursal changes. Mulders demonstrated movement of hyper echoic mass and no mass not compressible. |
| **Sonographer Impression** | Neuroma/bursa complex | Neuroma/bursa Complex | Neuroma/bursa complex | Neuroma/bursa – Clinical history and examination positive neuroma | Bilateral neuroma/bursa complex | Neuroma/bursa complex | Neuroma/bursa complex |

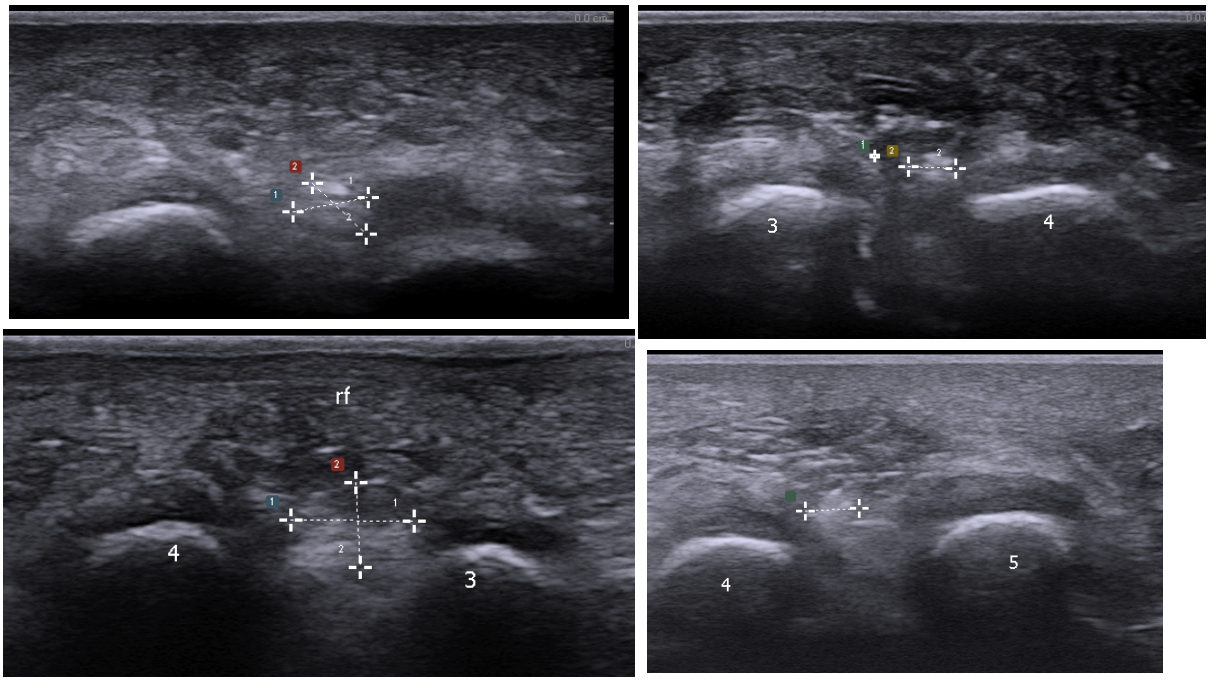



Figure 16: Ultrasound images of the plantar forefoot. Measurement tool indicates the size and location of FFN (authors own images, 2018)

### 5.7.2 Intra-rater reliability

From the subgroup of study participants (n=9), CD did not identify the same pathology as the MUS examination reports on 2 participant cases (Table 12). It was thought that this was a result of change to the answers following the FNCAP. In most incidences, CD was able to identify FFN using the FNCAP (Table 7). Overall, the total Cohen's Kappa score was 0.58 that in turn produced the threshold value of agreement to be defined as 'Moderate'. The percentage agreement values were also calculated to assess the likelihood of the rater achieving the outcome by chance (Table 15). The highest percentage agreement score was 100% for 'clicking reported by patient' and 'diastasis in the toes' (Table 13). This would suggest that there would be a minimal chance of variation when using these items to determine the presence or absence of FFN. Whereas, separation of the metatarsal heads, the presence of a Mulder's click and patients report of a 'burning sensation' varied between each individual at different time points. Thus, it is possible that correct identification (presence or absence) could have been down to chance so missed or wrong identification could potentially be more frequent.

Table 12: Forefoot pathology identification using FNCAP at two different time points.

| FN ID | CD Identification (appointment 1) | CD Identification (appointment 2) | Diagnostic Musculoskeletal Ultrasound Examination Findings |
|---|---|---|---|
| **FN01** | FFN and Capsulitis | Capsulitis | Bursitis |
| **FN05** | Bursitis and Capsulitis | Bursitis | Bursitis |
| **FN06** | Synovitis and Capsulitis | Synovitis | No pathology |
| **FN08** | Capsulitis | Capsulitis | Capsulitis and Bursa |
| **FN09** | FFN | FFN | FFN |
| **FN12** | Bursitis | Bursitis (possible Bursa/FFN complex) | Bursitis |
| **FN13** | Nerve entrapment (dorsal midfoot) | Nerve entrapment (dorsal midfoot) | Nerve entrapment (dorsal midfoot) as a result of a Ganglion cyst |
| **FN14** | FFN | FFN | FFN |
| **FN16** | FFN | FFN | FFN |

Table 13: Percentage agreement values from repeated FNCAP.

| Item | Percentage Agreement |
|---|---|
| Clicking reported by patient | 100 |
| Diastasis of toes | 100 |
| Pain located in 2nd/3rd inter metatarsal space | 88.9 |
| Paraesthesia radiating distally in toes | 88.9 |
| Participant reported pins and needles | 88.9 |
| Joint margins palpated: no reported pain | 88.9 |
| No swelling | 88.9 |
| Pain on lateral compression | 88.9 |
| Participant reported forefoot pain | 77.8 |
| Shoe style; tight/narrow fitting footwear aggravates symptoms | 77.8 |
| Participant reports shooting pain | 77.8 |
| Walking on pebbles/stone/lump in shoe reported by patient | 77.8 |
| No pain on movement of joint | 66.6 |
| Tenderness/pain on palpation of the inter metatarsal space (usually 2/3) | 66.6 |
| Pain on squeezing metatarsal heads | 66.6 |
| Mulders click (present) | 55.6 |
| Participant reported burning sensation | 44.4 |
| Separating metatarsal heads; met domes, insoles, padding eases symptoms | 44.4 |

### 5.7.3 Sensitivity, specificity, positive predicative values and negative predictive values

Using the FNCAP, 8 out of 30 participants were diagnosed with FFN. Using the reference standard, 7 out of 30 participants were diagnosed with FFN (7 participants were positively diagnosed using both approaches). Thus, using the FNCAP FFN was positively diagnosed in 1 participant but not using MUS. Using the FNCAP 1 participant was diagnosed with FFN when MUS confirmed bursitis. The sensitivity and specificity of the FNCAP was as follows:

Sensitivity: 7/(7=0) X 100 = 100%

Specificity: 22/(22+1) X100 = 95.6%

PPV: 7/(7+1) x 100 =  87.5%

NPV: 22/(22+0) x 100 = 100%

For each item in the FNCAP, the sensitivity and specificity values were calculated (Table 14).

Table 14: sensitivity, specificity, PPV and NPV values for each item in the FNCAP

| Theme | Item | Sensitivity Percentage (%) | Specificity percentage (%) | Positive Predictive Value Percentage (%) | Negative Predictive Value Percentage (%) |
|---|---|---|---|---|---|
| **Location of pain** | **Pain located in the 2nd/3rd IM space*** | **86** | **48** | **33** | **92** |
| | Participant reports forefoot pain | 100 | 13 | 26 | 100 |
| **Non weight bearing sensation** | **Paraesthesia radiating distally in the toes*** | **57** | **48** | **25** | **79** |
| | **Pins and needles reported by the patient*** | **86** | **43** | **32** | **91** |
| | Shooting pain reported by patient | 71 | 39 | 26 | 82 |
| | **Burning sensations reported by patient*** | **57** | **48** | **67** | **79** |
| | **Clicking reported by patient*** | **57** | **96** | **80** | **88** |
| **Weight bearing sensation** | Walking on pebble/lump or stone reported by the patient | 43 | 52 | 21 | 75 |
| | **Separating metatarsal heads: met dome, padding, off the shelf devices eases symptoms*** | **86** | **70** | **46** | **94** |

| | | | | | |
|---|---|---|---|---|---|
| | **Shoe style: tight/narrow fitting footwear aggravates symptoms*** | **86** | **57** | **38** | **93** |
| **Observations** | Joint margins palpated: no reported pain | 14 | 78 | 17 | 75 |
| | Diastasis of toes | 14 | 83 | 20 | 76 |
| | No pain on movement of joint(s) | 14 | 78 | 17 | 75 |
| | No swelling | 14 | 91 | 33 | 78 |
| **Tests** | Tenderness/pain on palpation of the IM space (usually 2/3) | 57 | 30 | 20 | 70 |
| | **Mulders Click (Not always Present)*** | **29** | **87** | **40** | **80** |
| | Pain on lateral compression of the forefoot | 14 | 78 | 17 | 75 |
| | Pain on squeezing metatarsal heads (lateral and direct compression) | 0 | 61 | 0 | 67 |

*Identified as having clinical utility for the diagnosis of FFN.

A threshold value of 70% or above was determined a-priori as being indicative of clinical utility when diagnosing FFN; this value was based upon other previous publications in diagnostic health care tool development. Separation of the metatarsal heads was the only item within the FNCAP to have sensitivity and specificity values over 70%. No items had values over 70% for PPV and sensitivity however items such as; pain located in the 2nd/3rd IM space and shooting pain reported by the participant had sensitivity values over 70% but the PPV value were under this threshold. This potentially suggests that participants who identified pain in the 2nd/3rd IM space or reported shooting symptoms did not always have a 'true' diagnosis of neuroma.

The following items; 'clicking reported by patient', 'separation of the metatarsal heads: met dome, padding, off the shelf devices eases symptoms', 'joint margins palpated: no reported pain', 'diastasis of toes', 'no swelling', 'Mulders click (not always present)' and 'pain on lateral compression of the forefoot' had specificity and NPV scores greater than 70% and can therefore be used to confidently exclude a diagnosis of FFN.

The study findings indicated that very few items reached or exceeded the 70% threshold. One reason for this could have been the small sample size (n=30) and a smaller proportion (n=7) were identified as having a true FFN diagnosis. The sample size might have not powered the data to accurately determine the items most useful for the diagnosis of FFN. The study data indicated that people with a positive test result such as, 'clicking reported by the patient', 'burning sensations reported by the patient' and 'paraesthesia radiating distally in the toes' tended to have FFN even if not all the people with FFN have these symptoms. Moreover, further analysis was required to explore the data.

In healthcare diagnostic development the alternative notions are considered when accepting an item for further study (Deeks and Altman, 2004):

1. Time taken to conduct the item

2. The cost implications to conduct the item

3. How invasive the item is to action

4. The skill level of the clinician required to gain a result

Some authors (Deeks and Altman, 2004, Kent and Hancock, 2016) believe a test cannot be determined by a single measure however it requires the consideration of a number of performance measures. Thus, the analysis also involved the exploration of likelihood ratios as well as pretest and posttest probability.

### 5.7.4 Likelihood Ratios

A pretest probability value was set at 30%. The 30% value was determined via previous published literature identifying FFN prevalence. The posttest probability positive and the posttest probability negative were both calculated (Table 15).

Table 15: The probability values of each item in FNCAP

| Item | LR Positive (P) | LR Negative (N) | Posttest probability (P) (%) | Posttest probability (N) (%) | Posttest probability difference |
|---|---|---|---|---|---|
| Pain located in the 2nd/3rd IM space | 1.6 | 0.3 | 40 | 11 | 29 |
| Participant reports forefoot pain | 114.9 | 761.5 | 98 | 100 | 2 |
| Paresthesia radiating distally in the toes | 1.1 | 0.9 | 31 | 29 | 2 |
| Pins and needles reported by the patient | 1.5 | 0.3 | 36 | 11 | 25 |
| Shooting pain reported by patient | 1.2 | 0.7 | 32 | 22 | 10 |
| Burning sensations reported by participant | 1.1 | 0.9 | 31 | 29 | 2 |
| **Clicking reported by patient*** | **11.4** | **0.5** | **82** | **16** | **66** |
| Walking on pebble/lump or stone reported by the patient | 0.9 | 1.1 | 27 | 32 | 5 |

| | | | | | |
|---|---|---|---|---|---|
| **Separating metatarsal heads: met dome, padding, off the shelf devices eases symptoms*** | **2.7** | **0.2** | **51** | **8** | **43** |
| **Shoe style: tight/narrow fitting footwear aggravates symptoms*** | **1.9** | **0.3** | **42** | **10** | **32** |
| Joint margins palpated: no reported pain | 0.6 | 1.1 | 21 | 32 | 11 |
| Diastasis of toes | 0.8 | 1.1 | 22 | 32 | 10 |
| No pain on movement of joint(s) | 0.6 | 1.1 | 21 | 32 | 9 |
| No swelling | 1.6 | 0.9 | 37 | 26 | 11 |
| Tenderness/pain on palpation of the inter metatarsal space (usually 2/3) | 0.8 | 1.4 | 23 | 36 | 13 |
| Mulders click (not always present) | 2 | 0.8 | 48 | 26 | 22 |
| Pain on lateral compression of the forefoot | 0.6 | 1.1 | 21 | 32 | 11 |
| **Pain on squeezing metatarsal heads (lateral and direct compression*** | **0** | **1.7** | **4** | **40** | **36** |

*Identified as having clinical utility for the diagnosis of FFN.

5.7.5 Data Summary

The results indicated that there is content validity for the items that form the FNCAP. The intra-reliability for the FNCAP demonstrated a 'moderate' threshold of agreement value. The sensitivity (100%) and specificity (95.6%) scores for the FNCAP were high and indicate the FNCAP could be useful for diagnosing FFN in most cases. LR's explored the diagnostic accuracy of each of the FNCAP items. The highest valued items for diagnostic accuracy are: 'Pain on squeezing metatarsal heads (lateral and direct compression', Shoe style: tight/narrow fitting footwear aggravates symptoms', 'Separating metatarsal heads: met dome, padding, off the shelf devices eases symptoms' and 'Clicking reported by patient'.

The three items most likely to be useful in the diagnosis of FFN are:

1. Clicking reported by patient
2. Separating metatarsal heads: metatarsal dome, padding, off the shelf devices eases symptoms
3. Shoe style: tight/narrow fitting footwear aggravates symptoms.

However items such as: Pain located in the 2$^{nd}$/3$^{rd}$ IM space, paraesthesia radiating distally in the toes, pins and needles reported by patient, burning sensations reported by patient, Mulders click and pain on squeezing metatarsal heads could potentially be of benefit for the diagnosis of FFN. These should also be considered in refining the FNCAP.

**5.8 Discussion**

This study has determined that 'clicking reported by patient', 'separation of the metatarsal heads; metatarsal dome, padding or off the shelf devices ease symptoms' and 'shoe style: tight/narrow fitting footwear aggravates symptoms' are most likely useful in the identification of FFN and thus these study findings have contributed to the field of clinical assessment for forefoot pathology. As part of this study, the content validity and some elements of reliability were explored to determine FNCAP's use of identifying FFN from other forefoot pathology in people with symptomatic forefoot pain. Panel members results from the Delphi study, Chapter Five had an agreement rate of over 50% suggesting that the items within the FNCAP were essential for the identification of FFN. The top three highest scoring agreements were: diagnostic musculoskeletal ultrasound, participant reported burning sensation and Mulders sign. The panel members valued these to be essential for the identification of FFN. The intra-rater agreement for the use of FNCAP was identified as 'moderate'. Overall, the FNCAP sensitivity (100%) and specificity (95.6%) scores were high.

In 1845, Lewis Durlacher was one of the first surgeon-chiropodists to describe the characteristics of his participants with suspected FFN (Pastides, El-Sallakh and Charalambides, 2012). Our study sample is relatively similar to the sample he first described. In our study sample, more women then men had FFN and age ranges were similar to previous studies (45 to 69 years of age) (Kankanala and Jain, 2007, Nery et al., 2012; Williams and Robinson, 2007).

The MUS reported comparable descriptors previously published in other manuscripts. In our study, all 7 participants had FFN located within the 3rd IM space and 1 participant had an additional FFN found in the 4th IM space. Koulouris and Morrison (2005) have previously reported that FNN is commonly found in the second or third inter metatarsal spaces. In this thesis, 2 out of 7 participants had multiple FFN located in one or both feet. On review of the lesion sizes, the range varied from 2.3mm to 5.4mm. Previous published evidence suggests symptomatic FFN are usually over 5mm (Quinn et al., 2000) however, in our sample this was not the case. When reporting the presence and grade of Doppler during the MUS examination, the results indicated no Doppler signal (grade 0) or less than 10% of the field with doppler signal (grade 1). Again, this is similar to evidence previous documented (Thomas et al., 2009). Those within our participant study group who had 10% to 50% Doppler signal of the field (grade 2) and 50% Doppler signal of the field (grade 3) had MUS confirmation of bursitis or surrounding tissue inflammation due to previous metal plating as a result of surgical intervention. Bossley and Cairney (1980) hypothesised that inflammation surrounding FFN was due to the presence of bursitis. Some of the MUS examination reports from the thesis did indicate the presence of FFN and bursae, occasionally referred to as a 'neuroma/bursa complex' (Cohen et al., 2016). This potentially suggests that FFN could co-exist with other forefoot pathology, thus be a potential reason why identification of this condition can be challenging.

Other authors researching this field have used a range of approaches to identify FFN. This means it is a challenge to compare others works to draw out reasonable conclusions. Consequently, minimal evidence is available to express how well these items perform in clinical practice. To the author's knowledge there is no published data looking into to sensitivity and specificity of the items stated in the FNCAP in other study samples, for instance individuals with rheumatological conditions, individuals seeking surgical assessments and individuals with neurological conditions. Despite this, it is possible to review other items within the FNCAP to other published studies. The most commonly documented clinical test for the identification of FFN is 'Mulders sign' sometimes referred to as "Mulders Click'. Mahadevan et al (2015) reported a specificity score of 62% and a sensitivity score of 61%. They also concluded that a positive Mulders sign was more likely to occur in participants with large FFN lesions. Whereas, Mulder's sign reported in the

thesis noted a sensitivity score of 29% and a specificity score of 87%, although, Owens et al (2011) has previously commented that Mulders sign is variant in its reliability (40% to 85%) thus it is possible that our study sample had smaller size lesions to which obtaining a ‘click’ consistently could have been more difficult.

Interestingly, both Owens et al (2011) (sensitivity 95%) and Madhadevan et al (2015) (sensitivity 96%) conducted tests that examined the IM spaces to which Madadevan et al (2015) found that this was the most sensitive screening tool for the clinical diagnosis of FFN. The thesis reported a sensitivity score of 57% when physically squeezing the IM space. One potential factor that might affect this is the characteristics of the participants who were recruited. The thesis study was based in a community MSK podiatry clinic whereas Owens et al (2011) and Mahadevan et al (2015) were based in surgical out patients and MUS clinics for surgical referral.  It might mean that those participants had symptoms that were more severe and well established for a longer period of time than those in a community setting where podiatry is their first access to receiving an assessment/management. This was not acknowledged in either study as a potential limitation.

Additionally, participants in the thesis were asked to draw on a foot diagram, in the participant questionnaire, where the origins of their pain were. The findings from this question corresponded to how participants with FFN verbally identified their pain ‘located in the second/third inter metatarsal spaces’. A sensitivity score of 86% was indicated, those with FFN could identify the IM space that was painful and where sensation changes were present.

Other studies looking at clinical tests for the identification of FFN have reported the use of plantar and/or dorsal percussion. Similar to the Mulder’s sign, variation has been acknowledged with sensitivity scores ranging from 37% to 61% (Owens et al., 2011 and Mahadevan et al., 2015). The development of FNCAP was through a rigorous Delphi technique. The panel members who formed the group were from an array of health professions. These tests were not initially identified and therefore not considered as part of the FNCAP development. It is unlikely that adding these perceived tests to the FNCAP would make any difference.

### 5.9 Strengths and Potential Limitations

There were a number of strengths when conducting the study. The first strength was the identification of the study sample. The inclusion criteria were set to include people with forefoot pain in order to capture those who did and did not have FFN. The study design ensured participant selection was from the usual clinical practice setting to ensure data was applicable to the service line pathway. Secondly, it was important to include

participants who had forefoot pain for a range of time. The data collected did not include participants who had a recent onset of symptoms to those participants who had been living with forefoot pain for a number of years as the study design was cross sectional rather than longitudinal. This was important to make sure the FNCAP could still identify FFN symptoms over time, although one limitation might be that the FNCAP was not tested in participants who had musculoskeletal conditions for example, those who have planned surgical intervention or those with a systemic rheumatological condition. It is possible these participants might present their symptoms differently. The study sample did have a few participants in each of these groups but the results are not sufficient enough to make generalised statements.

The second strength was the clarity around documentation of the data collection and analysis process. This ensured transparency in judgements when estimating values for analysis for example post-test probability. Likewise, it was important to describe how 'disease progression' was reduced. There could have been a potential bias if the time taken to conduct the index test was delayed from the reference standard. In this instance, both tests were conducted within the same appointment to ensure the disease state had little variation. However, there is potential for treatment paradox bias to alter the results within the sub group of participants who received a second research appointment. It is possible that those individuals within this group became motivated to conduct self-care management in between appointment one and appointment two. To try to reduce the risk of this, the second research appointment was 2 to 3 weeks after the first appointment.

Another strength is the application of the reference standard to all participants. This ensured that verification of the FNCAP result was conducted to ensure results were consistent. Also to reduce the potential reviewer bias, both CD conducting FNCAP and JB conducting the MUS examination were blinded to previous tests/imaging results in order to ensure external information did not impact the outcome of identifying FFN. Although it is possible that clinical review bias occurred as part of the study examination with the participant, the set up and environment of data collection was similar to 'routine' clinical practice and therefore is a bias most clinicians would encounter in day to day practice. As both CD and JB were blinded to each others results the study team have reduced incorporation bias via the use of one test result to inform the diagnosis of another. Part of this study also reviewed intra-rater agreement to assess observer variation. Subsequent studies in inter-rater agreement are required to determine the homogeneity of FNCAP between raters to identify FFN. As part of the study and participant care, if the diagnostic musculoskeletal ultrasound image was inconclusive or a second opinion required, then an onward referral to radiology was made. The outcome from their reported findings would be taken into consideration of the data analysis. During this study, one participant image

report required onward referral. The radiologist confirmed findings reported in the research diagnostic MUS examination. The radiologist report was reviewed after data analysis was completed as this could potentially overstate the effectiveness of the MUS examination and consequently alter data interpretation.

Although the study sample size was sufficient to feasibly review the data collected, the sample size was not large enough to make accurate associations between the study findings and previous published evidence. As a result, there is potential for the interpretation of these findings to accept the wrong hypothesis stated in Chapter Six, section 6.3.2. There is potential for a Type 1 error as findings from this study may not be true but alternatively are due to chance or random error.

### 5.10 Conclusion

With overall review of all the analysis conducted on each item within the FNCAP, there is more than 50% agreement in the content validity of the items that form the FNCAP. There is ‘moderate’ agreement with the intra-rater reliability of using FNCAP on participants with symptomatic forefoot pain. There is sufficient data to indicate good reliability for FNCAP to identify FFN from other forefoot pathology. There is acknowledgement that further studies using FNCAP are required to explore the use of the protocol and its impact in clinical practice over a period of time and within different populations. The results with the study sample size so far do suggest that the FNCAP is valid and reliable for the diagnosis of FFN with items in the FNCAP ruling in and ruling out this condition. This feasibility work does warrant further multi-site studies to determine the FNCAP’s validity and reliability with a range of clinical scenarios.

Innovatively, FNCAP has identified three potential questions that could be used by health professionals to influence their clinical decision-making when determining the presence or absence of FFN in people with symptomatic forefoot pain. A positive answer to any of these three questions indicate the likelihood that an individual may have FFN:

1. Does the participant report any clicking in the forefoot?

2. Does separating the metatarsal heads using metatarsal dome pads, padding or off the shelf devices ease symptoms?

3. Does a tight or narrow fitting shoe style aggravate forefoot symptoms?

A positive response to all three questions should increase suspicion of FFN being present. Knowing this, the impact on clinical practice will enable health professionals to discuss these questions with participants without necessarily needing a face-to-face consultation and/or examination. This could be conducted via telephone triage. With further evidence, it could be possible to develop an algorithm for this condition that clearly defines when individuals should carry out self-care activities and how long for before seeking additional services such as podiatry, orthopaedics and/or podiatric surgery for management so that in the future resources are allocated appropriately.

# 6.0. Chapter Six

## Discussions, Conclusions and Future Research

### 6.1 Introduction

The thesis programme has presented the methodological processes and theory used through three sequential studies that has led to the development of an expert derived clinical assessment protocol (FNCAP) for the identification of FFN. The overall research aim was to develop and provide a preliminary test of a novel expert derived clinical assessment protocol (FNCAP) to reliably diagnose forefoot neuroma in clinical practice. The results so far suggest that the FNCAP is repeatable, valid and therefore can facilitate timely diagnosis of FFN in clinical practice. Therefore, the overall conclusion is made that 'the FNCAP can diagnose FFN in clinical practice' and the alternative thesis hypothesis ''It is possible to develop an expert derived clinical assessment protocol for the diagnosis of FFN' outlined in Chapter One is accepted.

Chapter Six draws together the results of each chapter and has discussed the implications for clinical practice. The reliability issues surrounding this thesis programme of work and the challenges of conducting clinical research in practice are also discussed. The advancement in knowledge and contribution towards clinical practice made by the research programme is also considered. The generic limitations within the reported studies are acknowledged and recommendations for future research are proposed.

### 6.2 Defining the Starting Point

The thesis programme concentrated on the development of the author through the clinical academic pathway to be able to have the skills to study the acquisition of knowledge, to develop and understand robust research design as well as utilising philosophical paradigms to translate into clinical practice and teaching. First initial thoughts directed the author towards interventions for the treatment and pain management of FFN. This was driven from patient and health professional experiences however, through extensive reading, the need for reliable identification was paramount in order to build the knowledge and level of evidence within the field. Therefore this thesis programme started at the

beginning of the research continuum (figure 17) with the hope that future work will start to work along the research continuum.

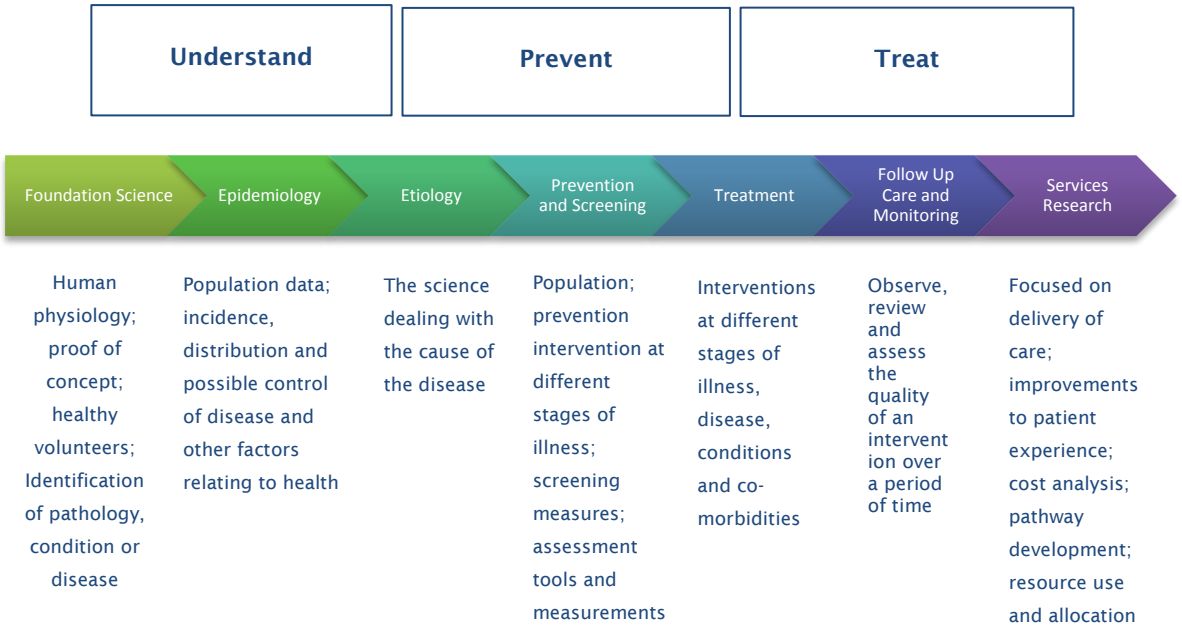



Figure 17: The Research Continuum (authors own image, 2018)

### 6.3 Progression of Knowledge

The author has designed and tested a novel expert derived clinical assessment protocol for the diagnosis of FFN. A semi-structured literature review was conducted (Chapter Two). Through mapping the published evidence, it was noted that no change in clinical assessment had occurred for a number of years. The author concluded that there are either a) a standard set of clinical tests that are unable to diagnose FFN, b) individuals are amending the clinical tests as a result of their own clinical experience and have not documented these in published literature or c) individuals are not conducting the clinical tests in a standardised order and thus generating different values such as false positives and false negatives which lead to incorrect diagnosis or continue to go undetected. It was thought that with the use of MUS as the reference standard, there would be a way to measure and review how effective our clinical assessments are and where improvement could encourage more timely diagnosis. Even with the development of new technologies such as MUS, the approach to forefoot clinical assessment was the same. For this reason, an in-house clinical assessment protocol was developed and tested using the new technology (MUS) to determine its applicability in clinical practice.

An intra and inter-rater agreement study was developed to review the agreement between a newly graduated podiatrist and a podiatric surgeon in the diagnosis of FFN. Unfortunately, due to ill health of the podiatric surgeon, the study was never completed yet this experience provided many opportunities; the author increased their surgical knowledge in FFN operative techniques, understood the logistics of setting up a study in the NHS and in the private sector plus understood the ethical principles of research when explored in a population who pay for treatment. Subsequently, the author developed and completed a service evaluation (SE) within a single NHS podiatry service to determine the incidence rate of FFN. The incidence rate was 2.5 per 1000 symptomatic persons and the prevalence was 3.4 per 1000 symptomatic persons. Results from the SE indicated that utilising the electronic data system for retrospective epidemiological data was difficult as a result of possible inaccurate reporting and uncertainty in a defined diagnosis from clinical examination alone. Nevertheless, the NHS podiatry service ascertains large quantities of demographical data from its service users that could potentially support epidemiological population studies. There is potential to use this information to review the clinical performance of pathways and teams that in turn could provide the evidence for commissioning specific services, invest in technology or provide guidance on where the clinical training needs are but this is currently not being utilised. This could be a result of skills to interpret the data, the ethical processes in place to use data at group level or the level of responsibility and time to manage a large data set. For the local podiatry service, of interest, the electronic templates were regularly changed to meet the operational team needs. Unfortunately, data could become invalid over time due to missed data sets and change in documenting outcome measures. At a local level, further insight was gained in understanding how the referral pathways were used. To the author, this highlighted that further investigations were required into the diagnosis of FFN. The idea for the second study was a result of considering the theory that inaccurate documentation could be a result of uncertainty in providing an accurate diagnosis.

The second study used a Delphi consensus design to develop a set of diagnostic criteria that has agreed expert consensus for the clinical diagnosis of FFN. A 21 item protocol was developed. Health care professionals initially identified reported symptoms, observations and tests associated with a forefoot assessment to ‘rule in’ or ‘rule out’ FFN. They were then asked to refine this to the items that they viewed ‘most influential’ in diagnosing FFN. 18 items were included in the resulting FFN clinical assessment protocol (FNCAP). By developing the FNCAP a standardised way of practice could be implemented for the clinical team to review, test and utilise, therefore developing a protocol that could improve and change practice whilst being adaptable and reliable.

There was an appreciation from the author that this would require multiple studies over time, using mix methodology to ensure the FNCAP was fit for purpose.

To explore if the FNCAP would be useful in clinical practice a diagnostic test study design was developed to determine the content validity and reliability of FNCAP for the clinical diagnosis of FFN. Relative to MUS, the diagnostic protocol had a specificity score of 95.6% and a sensitivity score of 100%. This suggests that the FNCAP has the potential to change practice for participants who have suspected FFN although further investigations are still required to demonstrate this. The intra-rater repeatability was k0.58; indicating there was 'moderate agreement' at two different time points on the diagnosis of participant's forefoot pain. There is also some evidence to potentially show that FNCAP could identify other forefoot pathology, however further investigations are required to demonstrate this. Using the CVR formula, the most valid components of the diagnostic protocol were: burning (0.87), Mulder's click (0.87) and paraesthesia (0.73) and the least valid were: no swelling (-0.47), clicking (-0.47) and diastasis (-0.47). The potential items considered most useful in the diagnosis of FFN are: clicking reported by patient, separating metatarsal heads and shoe style. Again, further investigations are required to determine the FNCAP's long-term impact and use in clinical practice.

There are some additional findings that were not anticipated at the beginning of this thesis. With the use of MUS as the reference standard a number of forefoot sonographic images were collected and compared. It was noted that a positive MUS doppler signal was present in participants who presented with FNN and active (inflamed) bursitis. Interestingly, the MUS examination reports documented possible 'neuroma/bursa complex'; however characterisation of these structures co-existing is not clearly defined in the literature. These findings have the potential to change how clinicians using MUS interpret their findings, but again, further investigations are needed to confirm and validate this. The need for further work investigating the MUS characteristics of foot and ankle pathology for clinical use was emphasised. There is an appreciation that there are large ranges or variation in 'normal' and 'abnormal' pathology except evidence for diagnosis is limited and usually hard to generalise as populations tend to be surgical or rheumatologic in nature. A specific imaging atlas could support clinical use to health professionals who are using MUS as an extended scope skill in practice. By having clarity and accurate characterisation of MUS forefoot structures, it is hoped that this will inform accurate diagnosis that will in turn lead to timely and effective management for participants with FFN. Overall, the thesis programme has provided data that has contributed to the body of knowledge and understanding of FFN diagnosis using a protocol.

## 6.4 Limitations

For each of the Chapters (Four, Five and Six) the specific research strengths and limitations have been discussed. There are, however, a number of limitations in the form of biases that are applicable to all the documented studies that warrant further comment.

Bias is defined as ‘any trend or deviation from the truth in the data collection, data analysis, interpretation and publication which could lead to the development of false statements’ (Simundic, 2013). Bias can occur intentionally or unintentionally and in most cases bias is nearly always present in research work. However, it is the responsibility of the researcher to be aware of the potential types of biases and where possible define what these are. For the studies in this programme of research the following biases were identified and were managed where possible:

### 6.4.1 Selection Bias

This is an error that can occur when the research team defines the study population and the process of participant selection is not random (Pannucci and Wilkins, 2010). There is a chance that the population of interest could be under or over represented in relation to the general population. Consequently, conclusions from the study would not have external validity. The sample population were symptomatic individuals with forefoot pain. The researcher is aware that participants with asymptomatic forefoot pathology were not represented. Although the study was interested in participants with symptomatic FFN, it was possible that participants with other symptomatic forefoot pathology could be enrolled onto the study. Also, at the point of enrolment, MSK diagnosis was unknown, thus participants were not able to decide whether they had symptomatic FFN.

### 6.4.2 Prevalence Incidence Bias

To increase recruitment chances, the researcher targeted incident cases of forefoot pain instead of prevalent cases. Incident cases are those with recent onset of symptoms compared to prevalent cases where the symptoms have been present with the individual for a period of time. In this case, participants who were recruited onto the study could have had varied symptom duration but are incident in as much as they were newly referred into the service to receive an assessment for symptomatic forefoot pain. It is thought that those who have had the condition longer will be more severe. The published evidence suggests severity is determined in pain descriptors (Morton, 1876) but what measures pain severity for FFN remains unclear. The results from the study indicated that participants reported pain frequency; pain type and ability to reproduce pain were hard to distinguish between those participants who’s onset was recent (3 months) from

participants who's pain had been present for longer (4 months plus). It is possible that different risk factors would affect these groups differently yet identification of the risk factors is still contested although gender, foot biomechanics and deformity have been suggested as observational comments but have never been extensively tested (Nissen, 1946 and Betts, 1940). Some authors have indicated mixing incident and prevalent cases could obscure the true relationship between study variables (Simundic, 2013). Limited evidence exists on the epidemiological data surrounding FFN and its effect on populations.

### 6.4.3 Recall bias

Recall bias is usually introduced at the data collection stage of an investigation. It can arise when there is intentional or unintentional difference in recall. Recall of information depends on memory which can often be unreliable and thus impact the internal validity and credibility of studies using self reported data (Simundic, 2013). As part of the data collection process in Chapter Six, self reported data was collected. By recruiting individuals with a new referral into the musculoskeletal service due to symptomatic foot pain it was anticipated that recall would be fairly accurate. Previous studies have shown that documenting details of an event reduce in accuracy over time to the extent that after five years detail becomes irretrievable (Smith and Noble, 2017). This information was important to capture in the questionnaire and as part of the Delphi design. The development and use of the FNCAP requires participant recall of symptoms and medical history to determine the presence or absence of FFN.

### 6.4.4 Reporting bias

It is possible that participants could have tried to collaborate with the researcher in order to develop answers they perceived to be of interest to support the study aim such as, simple gestures, over emphasis on certain questions or the researcher completing questionnaires on behalf of the participant. In order for this to be reduced, the researcher ensured sufficient time was allocated for participants to complete questionnaires; the researcher set the task and removed themselves from the environment so that participants had space/time to think. Furthermore, commonly asked questions had set answers to ensure consistency between participants who raised a query. For example, the majority of participants knew their body weight in stones rather than kilograms. The researcher would reply 'we have a set of scales set in kilograms. Would it be possible for you to stand on these so I can record your weight?'.

Interestingly, there is potential for conditions to be underreported or not disclosed. This usually arises when answers have poor connotations with regards to societal rules or current clinical evidence, for example, alcoholism, smoking, and recreational drugs (Smith and Noble, 2017). This is often referred to as social desirability bias (SDB) and is a form of systematic error on self-reported measures (Zerbe and Paulhus, 1987). The methods of reducing SDB are highly contested as minimal research has effectively evaluated this topic area however it is repeatedly reported the use of indirect questions encouraged participants to report the truth as the questions are not considered personal. Moreover, questions with a scale or pre-chosen items are more likely to reduce SDB as well as participants knowing the information is anonymised (Fisher, 1993). For our study in Chapter Six, there was a mixture of direct and indirect questions as well as pre chosen items and scales for participants to answer. It is possible that participants within this sample population could have miss-informed the researcher about their medical history. The participant sample was highly motivated; either retired or alternatively working in highly skilled job roles. Therefore, this population sample may not have been reflective of the overall population sample with FFN. Further consideration on using methods to minimise SDB is required and how SDB may be influenced by population demographics would need to be revised for future investigations.

### 6.4.5 The ‘Blue Sky Thinking’

The thesis programme has been a platform to review, critically evaluate and build evidence to problem solve a key issue in podiatry clinical practice, in this instance, the optimal clinical assessment diagnosis for FFN. If there were no financial constraints or time pressures the ideal studies to action would be to firstly conduct a large epidemiological study to determine the population distribution and associated risk factors to developing foot and ankle soft tissue pathology. Alongside this, further development of the FNCAP is required to determine its reliability and validity in clinical practice over a longer period of time. As technological advances continue to progress there is a need to establish a foot and ankle image atlas for ultrasound to understand the variances of ‘normal’ and ‘abnormal’ pathology to support clinical decision making in complex clinical scenarios. By detecting soft tissue characteristics, it would be hoped that this could help understand and explore the process of tissue healing and remodeling. Using imaging modalities it could be possible to evidence the soft tissue changes in response to insole therapy. Taking this one step further, building the links between inflammation, healing and other biomechanical factors such as stress, forces and torsion is required to understand how to rehabilitate tissues effectively by understanding when best to amend or change exercise programmes. By developing algorithms for prevention, rehabilitation and management of foot and ankle health, it is hoped that people with foot and ankle

musculoskeletal complaints will be able to remain fitter and more mobile for longer in pathways in both the private and NHS health sectors. Linking back to the research continuum model (figure 16 on page XX) the ongoing additions to the foundation science, epidemiology and prevention/ screening methods for FFN and other foot and ankle pathology could identify the plausible theories as to the aetiology of FFN and consider what future areas of research are required to manage this condition.

### 6.5 Implications for Clinical Practice

The completion of these sequential research studies has led to the development of FNCAP for the identification of FFN. From the findings within this research it is not possible to conclusively determine what specific items within the FNCAP are able to diagnose FFN from other forefoot pathology alone. However the results from the thesis do suggest that some items could aid clinician judgement in determining the presence or absence of this condition. As Nissen (1946) previously highlighted 'no one method is significant in the diagnosis of FFN but a combination of methods should make a clinician suspicious of FFN'. Further testing is required to determine the extent to which FNCAP can be of use in clinical practice.

The top three items that are most likely to distinguish FFN are participant recall questions; participant reported clicking, separation of the metatarsal heads and footwear style are noted by the participant to relieve foot pain symptoms. Originally it was thought by the researcher that clinician involvement would be required but in actual fact limited clinical skill is required to identify FFN using these items. To the researcher's knowledge, there are no current algorithms in place for the diagnosis of FFN. As these items stated above are based on recall, it is possible to suggest that these findings could start to formulate a self-management algorithm for people who present with symptoms suggestive of FFN. This would involve signposting the individual to services at specific time points dependant on the person's recall and self-care history. Published findings by Owen et al (2010) indicated that FFN diagnosis is predominately based on clinical history and assessment. It might be possible for people who have FFN to start a self-management intervention before accessing a health professional. This would be a unique way of providing the participant with information and care of their foot health. With the use of telemedicine it might be possible to implement this algorithm alongside clinical practice although further investigations would be need to determine its limitations for participants who may not have access to computer systems or the knowledge to use computer programmes to connect with clinical services (Pannucci and Wilkins, 2010). There is potential that as the knowledge base surrounding FFN develops, the algorithm could be extended or modified

to manage complex FFN pain cases or a range of participant scenarios such as surgery, steroid injection or systemic conditions such as Rheumatoid Arthritis (RA) and diabetes mellitus (DM).

Alternatively, following the use of the FNCAP, clinicians of mixed experience may be able to confidently diagnose FFN. By confidently diagnosing FFN it is hoped that further investigations looking into the treatment and management options of FFN will follow. Being able to demonstrate the accuracy of diagnosis would warrant the development of a policy, specific to the diagnosis of FFN, that could be adopted by health organisations nationally and internationally. Creating a policy document in FFN diagnosis would add to the evidence base of this condition. Building the evidence base in the diagnosis of FFN could provide the evidence to build into a clinical practice guideline for this condition. On an international scale this has the potential to impact upon how people with forefoot pain are identified and the options of care they could receive.

In order for this to be achieved, the FNCAP protocol would need to be published with clear descriptors of how to conduct each method to ensure standardisation of outcomes. This would require uniform terminology and further studies to review the protocols validity and reliability for clinical use. There is the option to develop a scoring system within the protocol. The score outcome could help standardise forefoot clinical assessment thus allowing future forefoot studies to be comparable and review accuracy on a large scale. This, in turn, could be modified into a prognostic tool to support clinical decision-making. Currently, there are no documented investigations looking into the predictive factors that are associated with FFN. The researcher has yet to find a published epidemiological study that has observed FFN populations. This might be because identification of FFN has been difficult to reliably diagnose in the past. There is, however, a need to review the inter rater observer agreement and to evaluate the impact of the FNCAP once implemented in clinical practice. Knowing this, the researcher has started to outline the questions in this field that still need to be studied.

### 6.6 Recommendations for Future Research

The identification and management of FFN requires further investigation. In order to continue to develop and refine the FNCAP, further programmes of study are required. There is a need to use a science implementation strategy to promote the uptake of FNCAP into clinical practice. Starting at a local level, the first phase of this strategy would be to provide training and feedback to the local clinical team on how to use FNCAP as part of their musculoskeletal forefoot assessment, with the view to reviewing its impact at

frequent time points. To determine the FNCAP impact, the service evaluation described in Chapter Four would be re run to review the number of appointments, the type of resources used and the outcome after podiatry intervention, for instance; onward referral to surgery, resolution of symptoms or an image request. The second phase of the strategy would look to evaluate the cost implications to using the FNCAP and the potential barriers of this working within clinical practice from an operations and business case perspective. In order to be of use, the FNCAP would have to demonstrate sustainability and cost effectiveness so that further justification for development can be reasoned or that change will be of benefit to the clinical and operational objectives set by the organisational boards on their promise to provide safe and effective care. The third phase of the strategy would look to explore the opinions of clinicians using the FNCAP, initially, to understand the benefits and potential limitations of the FNCAP on participants with foot pain symptoms, but to also consider the inter-rater observer agreement of using the FNCAP to support clinical decision making for the diagnosis of FFN. The fourth phase of the strategy would look to review the current clinical pathways that support participants who have suspected FFN. Strategies One, Two and Three would inform how the mapping of the pathway should function plus indicate what clinical and procedural components are required to provide safe and effective care to continue to allow participants to stay mobile for longer.

In order to continue to build upon the evidence on FNCAP, a further multi site diagnostic test study would look to assess the protocols ability to diagnose FFN in different population samples. Chapter Six demonstrated that the FNCAP has potential to diagnose FFN but the sample population was specific and the sample size small. Therefore, data collecting at different trusts/research sites would encourage diversity in sample populations which in turn would determine the generalisability of the protocols use in clinical practice. This could be undertaken nationally and/or internationally.

The FNCAP would also need to demonstrate reliability in participants with other conditions known to affect soft tissue processes such as RhA and DM. Many authors have documented the inflammatory mechanisms and responses of soft tissue in healing and preventing soft tissue injury (Taggart, Benson and Kane, 2011). It is possible those participants with a systemic condition might present symptoms differently compared to those who do not.  There is a need to determine if the FNCAP can still identify FFN when variations occur.

Another subgroup to consider would be those participants who have had previous forefoot surgery where tissue layers have been disrupted and in some cases metal work used to support structures in the foot. Likewise, understanding how FFN symptoms present in

services users who have had previous local steroid injection would also be important to acknowledge as both these treatments seek to make a change in the tissues/structures of the feet so that symptoms are reduced (Taggart, Benson and Kane, 2011). Understanding how this varies in those participants would be of benefit, to ensure the FNCAP could correctly identify FFN at onset, over a period of time and after interventions are implemented. By having a better understanding of how the FNCAP responds in different populations, it may be possible to develop a scoring system within the protocol which could determine condition severity and therefore inform clinical decision making as to interventions required to resolve symptoms or the best pathway to place participants on who present with specific symptoms. This could also support the need for epidemiological studies that evaluate and explore the possible risk factors surrounding the development of this condition. By being able to predict the likely course of FFN it is hoped that diagnosis and management will be evidence based practice and that prevention strategies could be implemented to reduce the incidences of FFN in the future. Consequently, people will be able to be mobile and independent for longer and not have to attend frequent health appointments to manage the condition.

As an adjunct, but an important development for health professionals using diagnostic MUS in practice, further clarification of the characteristics of sonographic FFN is required. Although multiple papers have published some guidance into what the sonographic structures of FFN should look like, there is still variation in interpretation of findings that in turn reduces confidence in diagnosing FFN (Cohen et al., 2016). Largely, this agreement has been concluded from publications using MUS on populations undergoing surgical excision of FFN (Cohen at al., 2016), although there is agreement between authors that variation in describing the sonographic appearance of this condition is varied and so is accepted as part of current practice (Gomez, Jha and Jepson, 2005).

### 6.7 Conclusion

The thesis programme set out to determine what the optimal clinical assessment protocol was for the diagnosis of FFN. Using all 18 methods in the FNCAP, the specificity (96.6%) and sensitivity (100%) scores are useful for the diagnosis of FFN. The key methods from the FNCAP that are most useful for the diagnosis of FFN are: clicking reported by patient, separating metatarsal heads and shoe style.

In order to determine this, three sequential studies were designed and delivered in order to assess the FNCAP use in clinical practice to diagnose FFN. The first study reviewed the number of people with diagnosed FFN in a NHS podiatry service. The second study

developed a forefoot clinical assessment protocol (FNCAP) specific for the diagnosis of FFN that had agreed expert consensus. The third study used the FNCAP (index test) in practice compared to MUS (reference standard) to determine aspects of validity, repeatability and reliability of the whole protocol as well as each of the methods within the protocol. The results identified three methods that were potentially useful to diagnose FFN. One contribution to the knowledge in this field is the development of a standardised procedure for conducting a forefoot clinical assessment. The second contribution to the knowledge in this field is the identification of methods specifically for the diagnosis of FFN.

Moving the topic area forward, the researcher has appreciated the need for further investigations to a) determine clinician feedback when using FNCAP in practice b) to determine if there is a change in practice (once implemented) and c) to determine if there are long term benefits to using FNCAP in practice in terms of participant experience and resource use. The thesis programme has set the foundations required to continue the development of the FNCAP to a diagnostic tool. With this in mind, the next steps for this thesis programme it to look to refine the protocol to ensure its use in practice is not time consuming, complex or costly. The ideas on future research will start to be incorporated into the researchers postdoctoral studies.

# 7.0 Chapter Seven

## The Clinical Academic Role

### 7.1 The Clinical Academic Role in Clinical Practice

A clinical academic is a person who is a clinically active researcher that strives to improve, maintain or recover health while parallel to researching new ways of delivering better outcomes for participants they treat and care for (NIHR., 2016). As part of the thesis programme, the researcher has uniquely contributed to Solent NHS Trust in supporting colleagues, changing the delivery of care to participants and contributing to the knowledge in the field of musculoskeletal podiatry. Clinically, the researcher has developed an extended skill set in clinical assessment, MUS and knowledge surrounding foot and ankle pathology. As part of this process, the researcher has been able to support other colleagues to acuquire skills in diagnostic MUS. As a result, four podiatrists within Solent NHS podiatry service have CASE accreditation in 'foot and ankle ultrasound training for podiatrists' completed at AECC University College. To continue to utilise these clinical skills, the researcher has worked with a senior clinical academic to submit a business plan for an income generation project to change service delivery. The aim of the business case is to review the use of MUS in podiatry to improve participant experience and to improve delivery of foot and ankle MUS imaging to participants with foot pain. Alongside this; the researcher has been disseminating the group's findings at local, national and international conferences, specific to podiatry and healthcare. This body of work was recognised and received an award at the College of Podiatry conference (2016) for 'Innovations in Science'.

Parallel to this, the researcher has been working with other academics to raise the awareness of clinical academics working in the field of musculoskeletal health. As a result, several articles have been published to evidence this role (Bowen et al., 2014 and Adams et al., 2015). In order to raise the profile of a clinical academic podiatrist a bursary scheme award (2015) allowed the researcher to attend the College of Podiatry conference to discuss the role and the possible career opportunities available. Working with the University of Southampton, there has been opportunity to supervise and mentor podiatrists from other NHS Trusts. Again working with local authorities such as the National Institute of Health Research (NIHR) and National Institute for Health Research Collaboration for leadership in Applied Health Research and Care (NIHR CLAHRC)

Wessex, it has been possible to network and be a part of the development process for outlining the national drivers and objectives set for clinical academic careers within Solent NHS Trust and Southern UK Region. The researcher has recently been awarded the 'Clinical Academic Transitional Award' to continue to build a postdoctoral fellowship application in order to continue her clinical academic career in musculoskeletal foot and ankle assessment.

As an adjunct, the role of a research podiatrist has encouraged the delivery of research to occur alongside and in some instances with clinical practice, thus providing participants with the option to partake in research and receive care that may not be available through normal NHS pathways. One benefit of this role has been to encourage the advancement of leadership skills, and in turn, opportunities to influence clinical and research operations via the invitation to managerial and clinical lead meetings. Providing this visible presence has ensured planning of research within the clinical team to continue future collaborations. Furthermore, the thesis has provided a platform for the researcher to demonstrate their ability to problem solve, develop and deliver a number of research studies using different research design methodology and governance approvals. Part of this has involved additional training for clinical colleagues in order to recruit, take consent and complete research paperwork. Now the clinical team actively recruits participants for clinically relevant studies that would not have happened if the clinical academic role were not imbedded in the service. This organisational cultural change has taken time and still requires evaluation to support its impact in practice. As a whole, the fellowship has supported the delivery of knowledge in the diagnosis of FFN and developed a clinical academic podiatrist with the skills to continue to explore and research topic areas within podiatry.

**Key Recommendations from the Thesis**

1. Clearer documentation is required by the clinical team(s) when documenting a specific diagnosis
2. The FNCAP requires further refinement to validate the key methods needed to determine a diagnosis of FFN
3. The FNCAP requires further investigations to determine the inter-rater observer agreement
4. The FNCAP requires further investigations involving multiple sites to determine its ability to diagnose FFN in a range of populations with variant geographical locations, ethnicity, systemic health conditions and socioeconomic status
5. The FNCAP could reduce the burden on clinical practice if adopted appropriately into clinical services
6. The three items most likely to be useful in the diagnosis of FFN are:
    a. Clicking reported by participant
    b. Separating metatarsal heads: metatarsal dome, padding, off the shelf devices eases symptoms
    c. Shoe style: tight/narrow fitting footwear aggravates symptoms.

# Appendices

**Appendix A**: Ethical Approvals for Study One, Two and Three

**Appendix B:** Additional File One, Delphi Study Round 2

**Appendix C** Additional File, Delphi Study Round 3

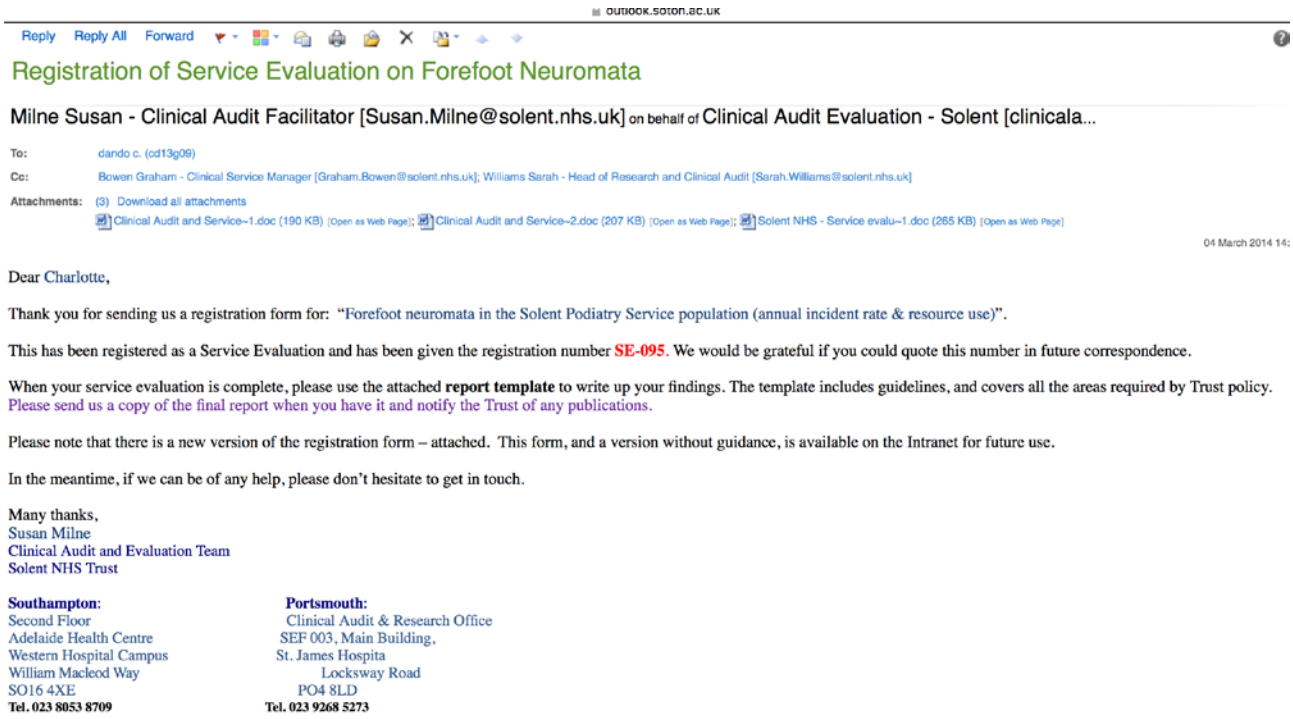
**Appendix D** Ultrasound Consent Form

**Appendix E:** Ultrasound Scanning Protocol

**Appendix F:** FNCAP Protocol

# Appendix A

### Study One: Service Evaluation Approval



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Reply Reply All Forward

Registration of Service Evaluation on Forefoot Neuromata

Milne Susan - Clinical Audit Facilitator [Susan.Milne@solent.nhs.uk] on behalf of Clinical Audit Evaluation - Solent [clinicala...

To: dando c. (cd13g09)

Cc: Bowen Graham - Clinical Service Manager [Graham.Bowen@solent.nhs.uk]; Williams Sarah - Head of Research and Clinical Audit [Sarah.Williams@solent.nhs.uk]

Attachments: (3) Download all attachments

Clinical Audit and Service~1.doc (190 KB) [Open as Web Page]; Clinical Audit and Service~2.doc (207 KB) [Open as Web Page]; Solent NHS - Service evalu~1.doc (265 KB) [Open as Web Page]

04 March 2014 14:

Dear Charlotte,

Thank you for sending us a registration form for: "Forefoot neuromata in the Solent Podiatry Service population (annual incident rate & resource use)".

This has been registered as a Service Evaluation and has been given the registration number SE-095. We would be grateful if you could quote this number in future correspondence.

When your service evaluation is complete, please use the attached **report template** to write up your findings. The template includes guidelines, and covers all the areas required by Trust policy. Please send us a copy of the final report when you have it and notify the Trust of any publications.

Please note that there is a new version of the registration form – attached. This form, and a version without guidance, is available on the Intranet for future use.

In the meantime, if we can be of any help, please don't hesitate to get in touch.

Many thanks,
Susan Milne
Clinical Audit and Evaluation Team
Solent NHS Trust

**Southampton:**
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### Study Two: ERGO approval email plus amendment

Documentation was submitted onto the Ethics and Research Governance Online (ERGO), University of Southampton on 09-06-2014 and agreed on 01-10-2014.

**Clinical Diagnosis of symptomatic forefoot neuroma in the general population: Delphi based Recommendations**

Submission ID:**10619**

**Submission Overview** | **IRGA Form** | **Attachments** | **Peer Feedback** | **History** | **Adverse Incident**

Approved by the Ethics Committee in **18 day(s)** on 1/10/2014

| Date | Activity | Comments | Attached Documents |
|---|---|---|---|
| 1/10/2014 1:18 pm | **Reviewed and approved** by the ethics committee | | |
| 23/09/2014 10:43 am | **Approved by supervisor** and sent to ethics committee | | |
| 23/09/2014 10:20 am | **Submitted** to supervisor Catherine Bowen (cjb5) | | |

On 19-03-2015 at 08.44am the amendment to the study was accepted.

**Clinical Diagnosis of symptomatic forefoot neuroma in the general population: Delphi based Recommendations (Amendment 1)**

Submission ID:14364

Submission Overview | IRGA Form | Attachments | Peer Feedback | History | Adverse Incident

Approved by the Ethics Committee in **1 day(s)** on 19/03/2015

| Date | Activity | Comments | Attached Documents |
|---|---|---|---|
| 19/03/2015 8:44 am | **Reviewed and approved** by the ethics committee | | |
| 17/03/2015 2:17 pm | **Approved by supervisor** and sent to ethics committee | | |
| 17/03/2015 8:26 am | **Submitted** to supervisor Catherine Bowen (cjb5) | | |
| 17/03/2015 8:19 am | Submission Amendment Created (14364) | | |

**Study Three: Research Ethics Committee (REC) Approval (subsequent HRA approval was sort)**

NHS
Health Research Authority
East Midlands - Nottingham 1 Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

21 June 2016

Dr Catherine Bowen
Faculty of Health Sciences, Building 45
University of Southampton
Burgess Road
SO17 1BJ

Dear Dr Bowen

| | |
|---|---|
| **Study title:** | **The content validity and reliability of an expert derived clinical protocol for the identification of forefoot neuroma.** |
| **REC reference:** | **16/EM/0268** |
| **Protocol number:** | **14371** |
| **IRAS project ID:** | **178150** |

Thank you for your letter of 21/06/2016. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 16 June 2016

# Appendix B

**Additional File 1** Round 2 votes of the accepted, rejected and re-voted methods for the clinical diagnosis of forefoot neuroma.

| **Accepted** | Patient reported the pain is sporadic | Lack of other pathology or differential diagnosis | Checking for nerve impingement |
|---|---|---|---|
| Weight bearing activity aggravates symptoms | Footwear removed relieves pain symptoms | Pain after weight bearing activity | Shoe style: tight fitting/narrow aggravates pain symptoms |
| Ultrasound (also used to confirm diagnosis) | MRI | X-ray (rule out other pathology/surgical planning) | Rule out radiculopathy/symptoms |
| Rule out MTPJ pathology | Mulders click/sign (not always present) | Pain on squeezing the metatarsal heads (lateral and direct compression) | Paraesthesia radiating distally in the toe(s) |
| Patient reports walking on pebbles/marble or stone | Tenderness/pain on palpation of the inter metatarsal space (usually $2^{nd}$/$3^{rd}$) | Pain on lateral compression of the forefoot | Pain in between the metatarsal heads and no directly upon them. |
| Patient reports tingling | Patient reports a shooting sensation | Patient reports a numbness | Pain extending to the toe(s) |
| Patient reports pins and needles | Patient reports a burning sensation | Patient reports electric shock(s) (feeling) | Abnormal sensation In the toe(s) |

| | | | |
|---|---|---|---|
| **Re-voted** | | Patient reports forefoot pain | Tightness or reduced space in the inter metatarsal space |
| Clicking reported by the patient | Cramps reported by the patient | Patient reports a sharp pain | No pain on movement of the MTPJ |
| Pain able to create the pain (yes + no) | Checking for constant or intermittent pain | Slightly vague or nebulous description of the pain and location | Visual Analogue scale |
| No heat/redness | Skin and tissue should look normal | Medication checked | Monofilament and peripheral sensation checked |
| Forefoot deformity | Diastasis of toes | Joint margins palpated: no pain reported | Light bulb effect: pain switching on and off |
| Separating metatarsal heads relieves symptoms | No swelling | Pulses normal with no warmth to the joint | Rule out tarsal tunnel |
| Pain located in the $2^{nd}/3^{rd}$ inter metatarsal space | Previous treatments failed | Undertaking new activities increases symptoms. | Diagnostic LA (plus or minus steroid injection) |
| Co-morbidities checked | Biomechanical alteration/difference to foot/ankle | General aggravating factors are established | General relieving factors are established |

| **Excluded** | Normal foot shape | Reduced mobility of MTPJ |
|---|---|---|
| Patient reports a ‘dislocating sensation of the toes’ | Pain in the lateral forefoot region | Temperature checked |
| Patient ‘unable to place a finger on it’ | Patient reports a popping sensation | Joint stiffness in the MTPJ |
| No pain on pressing the plantar forefoot region | No previous trauma or injury | No joint instability |

# Appendix C

**Additional file 2 :** Round 3 votes of the accepted, rejected and re-voted methods for the clinical diagnosis of forefoot neuroma.

| | | | |
|---|---|---|---|
| **Accepted** | Ultrasound (also used to confirm diagnosis) | Patient reports a burning sensation | Mulders click/sign (not always present) |
| Paraesthesia radiating distally in the toe(s) | Pain in between the metatarsal heads and no directly upon them. | Patient reports pins and needles | Rule out radiculopathy/symptoms |
| Patient reports a shooting sensation | Tenderness/pain on palpation of the inter metatarsal space (usually $2^{nd}/3^{rd}$) | Pain on lateral compression of the forefoot | Pain on squeezing the metatarsal heads (lateral and direct compression) |
| X-ray (rule out other pathology/surgical planning) | Lack of other pathology or differential diagnosis | MRI | Pain after weight bearing activity |
| Patient reports forefoot pain | Undertaking new activities increases symptoms. | No heat/redness | Checking for constant or intermittent pain |
| Diagnostic LA (plus or minus steroid injection) | Previous treatments failed | Patient reported pain is sporadic | Patient reports a sharp pain |
| Separating metatarsal heads relieves symptoms | Cramps reported by the patient | Skin and tissue should look normal | Joint margins palpated: no pain reported |
| No pain on movement of the MTPJ | Clicking reported by the patient | Diastasis of toes | Shoe style: tight fitting/narrow aggravates pain symptoms |

| | | | |
|---|---|---|---|
| Pain able to create the pain (yes + no) | Pain located in the 2nd/3rd inter metatarsal space | Patient reports walking on pebbles/marble or stone | Pain extending to the toe(s) |
| No swelling | | | |

| | | | |
|---|---|---|---|
| **Re-voted** | | Patient reports a numbness | Abnormal sensation In the toe(s) |
| Footwear removed relieves pain symptoms | Patient reports tingling | Weight bearing activity aggravates symptoms | Rule out MTPJ pathology |
| Checking for nerve impingement | Patient reports electric shock(s) (feeling) | General relieving factors are established | General aggravating factors are established |

| | | | |
|---|---|---|---|
| **Excluded** | Co-morbidities checked | Rule out tarsal tunnel | Light bulb effect: pain switching on and off |
| Medication checked | Monofilament and peripheral sensation checked | Pulses normal with no warmth to the joint | Slightly vague or nebulous description of the pain and location |
| Tightness or reduced space in the inter metatarsal space | Visual Analogue scale | Biomechanical alteration/difference to foot/ankle | Pain in the lateral forefoot area |
| Patient reports a popping sensation | No previous trauma or injury | No joint instability | Forefoot deformity |
| No pain on pressing the plantar forefoot region | Normal foot shape | Temperature checked | Reduced mobility of MTPJ |
| Patient ‘unable to place a finger on it’ | Joint stiffness in the MTPJ | Patient reports a ‘dislocating sensation of the toes’ | |

# Appendix D

**Ultrasound Image Consent Form**

**CONSENT FORM FOR ULTRASOUND IMAGES (V1)**

**Study Title: The content validity and reliability of an expert derived clinical protocol for the identification of forefoot neuroma.**

**Researcher name**: Miss Charlotte Dando
**Study reference**: 178150
**Ethics reference**: 16/EM/0268

I authorise that the ultrasound image(s) captured as part of the data collection may be used within published research or presentations by the researcher and her supervisors as part of the contribution towards her PhD thesis, which will be submitted to the University of Southampton.

I am aware that these image(s) will not be identifiable in any publications or presentations arising from this work.

Signed: .....

Date: ...../...../.....

# Appendix E

**Ultrasound Forefoot Scanning Protocol:**

*Plantar Transverse Scan*

- The participant was seated on a flatbed plinth, with their feet facing towards the researcher.
- The transducer was applied to the plantar forefoot region, at the level of the 1st metatarsal phalangeal head. Orientated in the transverse plane.
- The sonographer used the transducer to scan the forefoot at the level of the metatarsal head to the base of the proximal phalangeal joint (1st, 2nd, 3rd, 4th and $5^{th}$ IM spaces viewed).
- The transducer was then relocated medially to laterally (2nd, 3rd, 4th and 5th metatarsal phalangeal heads), with proximal to distal scan sequences repeated.
- The central portion of the transducer is positioned over the plantar metatarsal area. Transverse scans were completed for each IM space on both feet.

*Plantar Longitudinal Scan*

- The transducer is applied to the plantar forefoot region, at the level of the 1st metatarsal phalangeal joint region.
- Orientation was placed in the longitudinal plane with the transducer in alignment with the 1st metatarsal phalangeal joint space.
- The sonographer moved the transducer from the medial plantar forefoot region to the lateral plantar forefoot region to view the IM spaces.
- Longitudinal scans were completed for each IM space on both feet.

# Appendix F

**FNCAP Study Protocol:**

| Methods | Descriptor | Present/Absent |
|---|---|---|
| **Location of Pain** | Pain located in 2nd or 3rd inter metatarsal space | |
| | Patient reported forefoot pain | |
| **Non Weight Bearing Sensation** | Paraesthesia radiating distally in the toes | |
| | Pins and needles reported by patient | |
| | Shooting pain reported by patient | |
| | Burning sensations reported by patient | |
| | Clicking reported by patient | |
| **Weight Bearing Sensation** | Walking on pebbles/lump/ stone reported by patient | |
| | Separating metatarsal heads e.g. met dome, padding, off the shelf devices eases symptoms | |
| | Shoe style: tight/narrow fitting footwear aggravate symptoms | |
| **Observations** | Joint margins palpated: no reported pain | |
| | Diastasis of toes | |
| | No pain on movement of joint | |
| | No swelling | |
| **Tests** | Tenderness/pain on palpation of inter metatarsal space (usually 2/3) | |
| | Mulder's Click (Not always present) | |
| | Pain on lateral compression of the forefoot | |
| | Pain on squeezing metatarsal heads (lateral and direct compression) | |

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