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Somatosensory stimulation to improve lower-limb recovery after stroke

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Abstract

Introduction

Increasing lower-limb sensation could improve walking post-stroke but evidence for this is limited.

This thesis reports:

1) Review of published literature on somatosensory stimulation of the foot to enhance lower-limb function post-stroke.

2) Development of standardised intervention protocols for testing in a feasibility trial.

3) Feasibility trial of somatosensory stimulation interventions combined with functional activity.

Methods

1) Systematic review with narrative synthesis of somatosensory stimulation to the foot to improve balance and gait post-stroke.

2) Modified Nominal Group Technique with experienced therapists, informed by literature, to develop and seek consensus on three standardised therapy protocols.

a) lower-limb mobilization and tactile stimulation (MTS)

b) textured insole wearing (TI)

c) task-specific gait training (TSGT)

3) Mixed-methods, single-blind feasibility study explored: recruitment, participant characteristics, attrition, intervention and outcome measures acceptability (responses, feasibility, costs), sample size requirements, and participants' experiences. Adults 42–112 days post-stroke were randomized to either TIs+TSGT or MTS+TSGT. Lower-limb sensorimotor and functional outcomes were measured pre-randomization, post-intervention, and one-month later. Participants' experiences and acceptability of interventions and outcomes were explored in focus groups, with qualitative data analysed thematically. Quantitative feasibility outcomes were analysed using descriptive statistics, and within-group changes calculated.

Results

1) Seventeen trials included in the review confirmed that evidence for somatosensory stimulation to improve lower-limb function post-stroke is limited.

2) Validated trial intervention protocols for MTS, TIs and TSGT were developed, with consensus.

3) Thirty-four stroke survivors were recruited and completed the trial, with acceptable recruitment (48.57%) and attrition (5.88%) rates. Feasibility of outcomes, costs, delivery and acceptability of interventions and outcome measures were confirmed. Potential response to treatment was noted.

Conclusion

Somatosensory stimulation of the foot post-stroke warrants investigation. Feasibility of a larger trial of somatosensory stimulation interventions was confirmed. Participant characteristics, response over time, and variance of outcome measures will inform a future larger trial.

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List of abbreviations

5 or 10m/5MWT/6minWT	5 or 10 metre/5 metre walk test/6min walk test
ADL	Activities of daily living
AP	Anterior-posterior
BBS	Berg balance scale
CAHPR	Council for Allied Health Professions Research
CI	Confidence interval
CNS	Central nervous system
COFV	Centre of force velocity
CONSORT	Consolidated Standards of Reporting Trials
COP	Centre of pressure
CTU	Clinical Trials Unit
EMG	Electromyography
FA	Fast adapting
FAC	Functional Ambulation Classification
FG	Focus group
FTI	Force time integral
GCP	Good clinical practice
ICC	Intraclass correlation co-efficient
IQR	Inter-quartile range
LEMI	Lower Extremity Motricity Index
MAS	Modified Ashworth Scale
MCA	Middle cerebral artery
MD	Mean difference
ML	Medial-lateral
mNGT	Modified Nominal Group Technique
MRC	Medical Research Council
mRMI	Modified Rivermead Mobility Index
MS	Multiple Sclerosis
MSD	Mean standard difference
MTS	Mobilization and tactile stimulation
NHS	National Health Service
NIHR	National Institute for Health Research
NIHSS	National Institutes of Health Stroke Scale
OM	Outcome measure
PICOS	Population, Intervention, comparison, outcome, study type
PIS	Participant information sheet
PPF	Premature plantar flexor
PPIE	Patient and public involvement and engagement
PSL	Postural sway length
RASP	Rivermead Assessment of Somatosensory Performance
RCT	Randomized controlled trial
SA	Slowly adapting
SD	Standard deviation
Sig diff	Significant difference
SMV	Segmental muscle vibration
SRRR	stroke recovery and rehabilitation roundtable
SWIFT	Soft-Scotch Walking Initial FooT trial
SWM	Semmes Weinstein Monofilament
TENS/TES	Transcutaneous electrical (nerve) stimulation
TIDieR	Template for intervention description and replication
TSGT	Task-specific gait training
TUG	Timed up and go
WBV	Whole body vibration

Glossary of terminology used in the thesis

Attrition	Refers to the number of participants who withdraw or dropout from a trial (Cooper et al., 2018)
Central Nervous System (CNS)	This is the part of the nervous system which consists of the brain and spinal cord.
Compensation	Describes strategies aimed at addressing functional gain, rather than reducing impairment (Krakauer et al., 2012)
Chronic stroke	> six months post-stroke (Krakauer et al., 2012)
Dose	'Dose of exercise-based therapy is comprised of several components generally known as: intensity (effort); amount (quantity per session); frequency (number of sessions per day); and duration (number of weeks)' (Colucci et al., 2017, p.422).
Focus groups	Focus groups are a form of interview conducted with a few people who discuss topics, actively interacting with other group members and the moderator (Puchta and Potter, 2004).
Fidelity	Fidelity relates to the delivery of an intervention as planned, meeting the pre-arranged protocol criteria (Slaughter et al., 2015).
Mobilization and Tactile Stimulation (MTS):	A term given to a form of hands-on therapy treatment which is often delivered in conventional therapy, with an aim of mobilizing the area (e.g. hand or foot) and enhancing sensory input (feeling). It involves intensive tactile and proprioceptive stimulation combined with joint and soft tissue mobilization techniques (massage, passive movements, accessory movements, soft tissue stretching).
Recovery	Refers to a return to pre-stroke body function and structure and activity level (Bernhardt et al., 2017b)
Recruitment	Refers to the enrolment of people to participate in the trial.
Restitution	Refers to a return of structures and function to previous state (Levin et al., 2009)
Sensory	Pertaining to systems which enable input to the central nervous system e.g. the ability to feel following tactile stimulation.
Task-specific Gait Training (TSGT)	A form of therapy which involves repetition of various activities e.g. sitting to standing, stepping etc. with an aim of improving the ability to walk.
Textured Insoles (TIs)	Insoles made of material with projections. The aim of these peaks is to stimulate the sole of the foot, increasing sensory input.

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List of publications arising from this work

Aries AM, Pomeroy VM, Sim J, Read S, Hunter SM. 2018. **Sensory stimulation of the foot and ankle early post-stroke: a feasibility study (MoTaStim - Foot).** *International Journal of Stroke.* 13, 43.

Aries AM, Pomeroy V, Sim J, Read S, Hunter S. 2018 **MoTaStim-Foot, a Randomized, Single-blinded, Mixed-methods, Feasibility Study Exploring Sensory Stimulation of the Foot and Ankle Early Post-stroke.** *Journal of Neurorehabilitation and Neural Repair* 32(12) 1104

Aries AM. 2018. **'Our feet were made for walking' My 3-minute thesis experience.** *Journal of Academic Development and Education Student Edition*, 170-171.

Aries A, Pomeroy V, Hunter SM. 2017. **Developing physical therapy protocols for the lower limb post stroke utilising a modified Nominal Group Technique (mNGT).** *International Journal of Therapy and Rehabilitation*. 24, 164-165.

Aries A and Hunter S. 2016. **Characterising physical therapy for the lower limb post stroke: A modified Nominal Group Technique (mNGT).** *International Journal of Stroke*. 11, S59-S60.

1 CHAPTER ONE: INTRODUCTION

Every two seconds somebody in the world will experience a stroke. Currently, in the United Kingdom (UK), there are more than 1.2 million stroke survivors (Stroke-Association, 2018, p4). The consequences of stroke can be challenging (Patel et al., 2000), with the various impairments in bodily function impacting on independence (Rathore et al., 2002). Somatosensory impairment post-stroke is common, and has been reported to be experienced by between 65% (Feigenson et al., 1977b) and 85% (Kim and Choi-Kwon, 1996) of stroke survivors, with specific impairment relating to the lower limb found to be present in between 45% (Tyson et al., 2013a) and 56% (Gorst et al., 2018). The impact of a somatosensory impairment makes everyday tasks difficult (Patel et al., 2000; Tyson et al., 2013a) and decreases the potential for achieving independent walking following stroke. In the event of a pure motor deficit, the likelihood of achieving independent mobility is reported to be 87.5%, whereas if a somatosensory impairment is also present it is only 55.9%, and an extended period of rehabilitation should be expected. This percentage further decreases to just 30.8% achieving independent ambulation if hemianopia is also present (Sanchez-Blanco et al., 1999).

Regaining the ability to walk is a priority for many stroke survivors. Effective treatment to address mobility, exercise and fitness has been identified by the James Lind Alliance as one of the top ten research priorities for stroke (Pollock et al., 2014b). Diverse rehabilitation strategies may be used to address different deficits caused by stroke, with the aim of helping stroke survivors to return to functional walking.

The complex nature of therapy interventions has been acknowledged by the Medical Research Council (MRC) (Craig et al., 2006) and, due to this complexity, with many separate but inter-related constituents (Walker et al., 2017), developing an evidence base of complex interventions for stroke rehabilitation is challenging (Langhorne et al., 2011). However, there is now evidence to support the use of task-specific training to improve recovery of motor function after stroke, and some evidence emerging to support the use of sensory stimulation and retraining, particularly for the upper limb after stroke (Carey et al., 2011; Hunter et al., 2008; Winter et al., 2013).

Evidence based clinical guidelines exist to inform clinicians of interventions seen as best practice for implementation within stroke rehabilitation; however, these guidelines are not always followed. In a survey of 1755 clinicians (occupational therapists, physiotherapists and speech and language pathologists) undertaken by Rochette et al. (2007) it was found that, despite evidence indicating the importance of a family-related focus for stroke survivors, this approach was not implemented. This finding was concurred in Denmark where it was found that research-based evidence in its entirety was not delivered when the notes written by 13 clinicians (occupational therapists and physiotherapists) of 131 patients were analysed in an observational prospective cohort study (Kristensen et al., 2016). The main barriers cited relating to the delayed implementation of research into practice are staffing issues, challenges over time, education of staff, the therapists' selection of therapy strategies and prioritization of workload (Bayley et al., 2012).

Whilst clinical guidelines only recommend interventions for which robust evidence exists, clinicians may consider that other interventions are effective based upon their clinical experience. Conflicting expert opinion and evidence based guidelines can create tension for clinicians where evidence for an intervention does not currently exist (Grant, 2019). Nonetheless, this highlights the importance of researchers working closely with clinicians in order to create evidence which has clinical reality. Clinicians need to perceive the research as relevant to their practice in order to want to implement the findings i.e. research needs to be externally valid (Knottnerus and Dinant, 1997). Internal validity also needs to be maintained; pragmatic trials can be undertaken, aiming to make a difference for clinical practice (Knottnerus and Tugwell, 2017).

Retraining sensory impairment is an important, under-researched, strategy within stroke rehabilitation. It is known that afferent input can influence motor control (Chersi et al., 2011; Laaksonen et al., 2012; Rossignol et al., 2006); it therefore has the potential to improve motor control and optimize function which is clearly important following stroke (Abbruzzese and Berardelli, 2003). However, the use of somatosensory stimulation applied to the foot and lower leg to improve motor control and function, such as balance and walking, has not been well researched to date, despite it being used in clinical practice. Somatosensory stimulation can be delivered through hands-on physical therapy interventions, such as mobilization and tactile stimulation (MTS) (Hunter et al., 2008; Winter et al., 2013), which involves intensive proprioceptive and tactile stimulation; however, the effects of this have only been investigated on the upper limb after stroke. Other hands-off methods could include the use of

equipment, for example, textured insoles (TIs) (Christovão et al., 2013; Orth et al., 2013), the effects of which have been investigated through early phase research in healthy populations (Hatton et al., 2009; Hatton et al., 2011) and people affected by Multiple Sclerosis (Dixon et al., 2014).

A task-specific approach is recommended to retrain walking post-stroke (Wiener et al., 2018), with the National Guideline for Stroke, Fifth Edition (Rudd et al., 2016) advocating intensive, repetitive, task-orientated intervention; however, it is not known whether combining somatosensory stimulation with task-specific training would increase the effects of the training.

This thesis represents the beginning of a process of original investigation into the effectiveness of intensive somatosensory stimulation applied to the lower limb and foot, combined with task-specific gait training (TSGT), to improve balance and walking post-stroke.

1.1 Overview, outline and structure of the thesis

The thesis has been divided into eight separate chapters. Following this preliminary introductory chapter, chapter two will discuss the evidence for somatosensory loss after stroke and rehabilitative strategies to address it. Chapter three is a systematic review of the effectiveness of somatosensory stimulation for the lower limb and foot after stroke - Study 1. Chapter four will detail the aims and objectives of studies 2 and 3, which are also reported in this thesis, with an overview and justification of the methodologies. Chapter five, Study 2, involved the necessary development of intervention protocols that

were planned to be used in Study 3, a randomized, blinded, mixed-methods feasibility study, which is reported in full in chapter six. Chapter seven summarizes and interprets the findings of the research conducted. Finally, in chapter eight, conclusions are drawn, and recommendations made for further research.

A reference list follows the main body of the thesis and pertinent, relevant supporting documents relating to the studies are in the appendices, which are placed after the reference list.

2 CHAPTER TWO: BACKGROUND AND RATIONALE

2.1 Stroke

2.1.1 Definition and cause

Stroke is a common disease; indeed, every year 15 million people in the world experience a new stroke (Mackay and Mensah, 2004). Approximately 150,000 of these people reside in the UK (Townsend et al., 2012). The definition of stroke, widely recognized internationally, is: *"rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin"* (Hatano, 1976, p. 541). A stroke, usually caused by either ischaemic or hemorrhagic damage, alters brain function as a consequence of a lack of blood supply to a particular area, resulting in a contralesional upper motor neurone lesion (Kumar and Clark, 1998).

2.1.2 Clinical presentation

Clinical presentation of disturbed cerebral function may include a combination of sensorimotor dysfunction (Nudo, 2013), primarily affecting the contralesional side of the body (face, trunk, limbs), communication and speech disorders (Bonini and Radanovic, 2015), visual impairment (Ali et al., 2013), and/or higher cognitive dysfunctions (Bear et al., 2007). Common features of an upper motor neurone lesion can be classified as positive, negative (Burke, 1988; Goldstein, 2001) or adaptive. Negative features present as weakness, diminshed cutaneous reflexes, and a loss of dexterity, with early signs and symptoms identified as decreased muscle strength (Goldstein, 2001; Neckel et al., 2006)

and as the negative features occur as a result of ‘lost elements’ (O'Dwyer et al., 1996 p.1737) this would also include sensory loss. This results in poorly scheduled or graded tonic muscle activity (Olney and Richards, 1996). Later, positive features occur, when spasticity and its effects can be exacerbated by contractures (Ward, 2012). In addition, changes in the mechanical properties of the muscle (adaptive features) are seen, which further alter movement dysfunction (Dietz and Berger, 1984), and impact on independence in activities of daily living (ADL). Whilst the ability to undertake ADL, including functional walking, is something that most healthy people take for granted, 83% of stroke survivors have difficulty balancing and, therefore, walking after stroke (Tyson et al., 2006a). Sensorimotor dysfunction occurs when there is disruption to any of the systems (motor, sensory, perception) that integrate to enable the production of coordinated movement (Cohen, 1999), and is often significant following a stroke.

2.1.3 Balance and walking after stroke

Regaining the ability to walk is important for stroke survivors (Pollock et al., 2014b). Posture and balance are essential for independence in standing and walking (Shumway-Cook and Woollacott, 2012). Postural control is defined as ‘the act of maintaining, achieving or restoring a state of balance during any posture or activity’ (Pollock et al., 2000, p.404). Balance can be defined as ‘an even distribution of weight ensuring stability’ (Pearsall, 1999, p. 101) and is a complex multi-faceted process involving the coordination of sensory, motor and biomechanical aspects, with vision, vestibular and somatosensory inputs combining to enable balance to be achieved (Jacobson and Shephard, 2016).

Locomotion implies ‘movement or the ability to move from one place to another’ (Pearsall, 1999, p.833), ambulate ‘to move about’ (Pearsall, 1999, p.42), and to walk is to ‘move at a regular and fairly slow pace by lifting and setting down each foot in turn’ (Pearsall, 1999, p.1611). The term gait is defined as ‘a person’s manner of walking’ (Pearsall, 1999, p.579), and gait analysis is the methodical analysis of human walking (Whittle, 2007).

In a study where 40 older adults with hemiparesis were compared with 40 healthy older adults on the EquiTest system, it was found that a deficit in postural control predisposes stroke survivors to instability during balance, with 73% of the participants with stroke falling during the sensory organisation test (Marigold et al., 2004). Stroke survivors have an inherently high risk of falling (Beyaert et al., 2015), usually towards the contralesional side (Verma et al., 2012). In a cross-sectional observational study of 41 stroke survivors, over half of the participants reported falls and nearly 80% reported near falls, with 80% of the falls occurring in the home environment (Hyndman et al., 2002). Sometimes balance and walking are difficult because of loss of motor control, for example, difficulty in controlling foot placement during walking (Zissimopoulos et al., 2015). However, somatosensory dysfunction can also have a detrimental effect on balance and walking (Tyson et al., 2013a), which can be associated with poor integration and weighting of afferent input (Marigold et al., 2004).

A large prospective study of acute stroke survivors (n=804) living within the community reported that 50% became independently mobile following rehabilitation, although 18% were still unable to walk, 11% required assistance and 21% had died (Jorgensen et al., 1995). Further evidence from a systematic

review reported that 60% of stroke survivors (n=1373) who were managed in a rehabilitation unit, and still immobile at one month, did eventually achieve independent walking (with or without an aid, but with no assistance) (Preston et al., 2011). The ability to achieve this independent walking is associated with the type of impairment following stroke (Tyson et al., 2008); where both sensory and motor impairment occur together after stroke, the time to achieve independent walking is extended, reportedly more than five months longer than where there is just motor impairment (Sanchez-Blanco et al., 1999).

2.1.4 Sensory dysfunction after stroke

Sensory loss is a recognized feature of upper motor neurone lesions such as stroke (Feigenson et al., 1977a; Gorst et al., 2018; Kim and Choi-Kwon, 1996; Tyson et al., 2013a), although its assessment and treatment is frequently overlooked by clinicians (Carey, 1995). Somatosensory can be defined as ‘relating to or denoting a sensation which can occur anywhere in the body’ (Pearsall, 1999 p. 1367). Somatosensory function relates to the ability to detect, discriminate and recognize sensations and includes tactile sensation, vibration, pressure, proprioception, temperature and pain (Carey, 2012). Sensations can be received from stimuli external to the body, for example light touch, pain, pressure, vibration and temperature, whereas other sources of afferent stimuli are internal to the body, including information relating to position and movement of the limbs e.g. proprioception.

Reporting of the presence of sensory loss following stroke is limited and results are variable. Kim and Choi-Kwon (1996) reported that 85% of people post-

stroke experienced sensory loss as measured by two-point discrimination, point localization, position sense, stereognosis and texture discrimination; however, their study focused only on the upper limb. Feigenson et al. (1977a) reported that the prevalence of somatosensory dysfunction was 65%, but there are no details as to how or where this had been measured. Meyer et al (2016) conducted a cross-sectional observational study of stroke survivors (n=122) between 12 days and six months post-stroke (median 82 days) and found that somatosensory deficits are common within the subacute phase post stroke, and that somatosensory impairments are more strongly associated with motor impairments when visuospatial neglect is present.

Two studies have specifically reported the presence of somatosensory loss for the lower limb post-stroke: Tyson et al. (2013a) undertook a pooled analysis of data from 459 stroke survivors (tactile and proprioceptive loss), reporting that 55% had intact sensation. This meant 45% of stroke survivors had somatosensory dysfunction, which was reported to impact on functional activities such as balance and walking. Gorst et al. (2018) identified the presence of somatosensory impairment (measured using the Erasmus MC modified version of the (revised) Nottingham Sensory Assessment) in 56% of a cohort of 157 stroke survivors. Interestingly, although Tyson et al. (2013a) highlighted the detrimental effect of somatosensory loss on function, Gorst et al. (2018) did not identify this finding in their study.

Visual deficits have also been noted post-stroke (Ali et al., 2013), which can affect the interactions between the vestibular, somatosensory and visual

systems, resulting in loss of balance (Marigold et al., 2004). Thus, the complex nature of sensory loss inevitably contributes to making everyday tasks, such as balance and walking, difficult (Patel et al., 2000). The integration of sensory and motor information is key to enable controlled movement (Abbruzzese and Berardelli, 2003; Bolognini et al., 2016), and the importance of addressing sensory loss after stroke must not be underestimated.

2.1.5 Socio-economic impact of stroke

The often challenging personal implications for stroke survivors, and the global socio-economic effects of stroke throughout both developed and developing countries have been recognized (Wolfe, 2000). The ageing population means the financial burden of stroke is inevitably set to increase over and above the present high costs of providing long-term health and social care for stroke survivors; it is, therefore, imperative that care and rehabilitation strategies are effective, and further developed to reduce disability after stroke (Chevreul et al., 2013). As National Health Services (NHS) are becoming increasingly constrained, with the inexorable reduction of finances (Klein, 2013), it is essential that therapy time is optimized, to facilitate stroke survivors to reach their full potential.

2.2 Recovery from stroke

The recovery of brain function and the return of sensorimotor control is influenced by a process known as neuroplasticity, in response to the injury, and due to changing influences from the environment and altered patterns of use,

resulting in neurons adjusting their activity and even their morphology (Selzer, 2006). Neuroplasticity can result in altered size and arrangement of cortical areas that represent different body parts (Nudo and Milliken, 1996; Sens et al., 2012) on the motor and sensory homunculi (Penfield and Boldrey, 1937). These changes can occur extremely quickly, for example within one hour (Weiss et al., 2004). An enriched environment and engagement in therapeutic activities, with varying afferent input (Jenkins et al., 1990) is important for facilitating positive neuroplastic changes (Danzl et al., 2012), and it has been acknowledged that stroke rehabilitation requires interdisciplinary collaboration (Levin et al., 2009). Environmental stimuli are important to drive experience-dependent plasticity (Carey et al., 2019) and therefore rehabilitation potential can be further enhanced by adopting a 24-hour approach to rehabilitation after stroke (Aries and Hunter, 2014).

Re-organisation of cortical control can occur, for example via the contralesional primary motor cortex, bilateral ventral premotor cortex (Rizzolatti et al., 2002) and supplementary motor area (Rehme et al., 2012), which has been shown to play a role in the control of anticipatory postural adjustments (Jacobs et al., 2009). These normal anticipatory postural adjustments are reliant upon appropriate afferent information and are particularly dependent upon feedback from proprioceptors (Palluel et al., 2008a). Further, compensatory cortical control can involve ipsilateral control of movement via the transcallosal fibres (Boussaoud et al., 2005; Liu et al., 2002), which provide inhibition under voluntary control from one hemisphere to the other, or via other pathways, for example the reticulospinal fibres (Zaaimi et al., 2012), which are important for

control of muscle tone and rhythmic movements (Takakusaki et al., 2016), and the rubrospinal tract fibres (Belhaj-Saïf and Cheney, 2000), which are involved in the control of movement via spinal interneurons exciting flexor pathways and inhibiting extensor mechanisms via the 1a inhibitory neurons (Jankowska, 1988).

These changes to cortical representation may be facilitated by neuronal sprouting (dendritic or axonal growth) which, although generally inhibited after stroke, can be facilitated by molecular manipulation and behavioural activity, promoting plasticity and improving function (Overman and Carmichael, 2014). Furthermore, the extensive intracortical system allows for new routes of organisation within the cortex in response to appropriate cortical facilitation or inhibition (Nudo, 2013). Behavioural experience has therefore been shown to facilitate neuroplasticity and recovery post-stroke (Selzer, 2006) and this important principle for rehabilitation has emerged from a better understanding of motor control, the importance of afferent information, and the mechanisms of neuroplasticity after stroke.

2.3 The importance of afferent information for motor control

Afferent information from the periphery is important for motor control, particularly when performing a voluntary activity that requires good coordination and control (Chersi et al., 2011; Laaksonen et al., 2012; Rossignol et al., 2006). Afferent information guides the motor system, informing the conscious mind about both the external world (exteroceptive) and internal information (interoceptive) (Patel et al., 2014). Afferent pathways are directly linked to

motor areas in the cortex; elimination of input via the dorsal columns results in a severe motor deficit, indicating the importance of afferent input to enable coordinated voluntary activity (Asanuma and Arissian, 1984). Many bodily systems function in association with each other to control the body's position in space (Shumway-Cook and Woollacott, 2007), and sensorimotor integration plays an important part in the production of controlled movement (Campfens et al., 2015). An adaptable environment results in constant changes, and the interaction that occurs between ascending afferent input and descending goal-focused mechanisms can result in conscious experience (Squire et al., 2008). Information, which is selective to the particular receptor cell, travels to the central nervous system (CNS) via the posterior root ganglion and spinal cord, communicating with specific postsynaptic targets (Squire et al., 2008). Signals then continue through the brainstem to the thalamus before reaching the cerebral cortex (Bear et al., 2007), where sensory processes are analysed and compared with past experiences (Squire et al., 2008), and motor function is modulated, as required. An important sensory modality which is essential for balance and walking is proprioception.

2.3.1 Proprioception

Defined as 'the sensory processes involved in the conscious appreciation of posture and movement' (Cohen, 1999, p.111), proprioception enables the ability to sense the position of the limbs in space, with forces generated by the muscles, creating movement which is detected in the muscles, tendons, joints and skin (Cohen, 1999). Afferent information from the muscle spindles and Golgi tendon organs also provide proprioceptive information that is below

conscious awareness; this travels to the cerebellum (Moore, 2007), enabling facilitation of movement by making predictions relating to sensory function and controlled movement patterns (Therrien and Bastian, 2015). This process is essential to enable the cerebellum to compare feedforward prediction of movement with feedback information (Brownstone et al., 2015). The fact that anticipatory adjustments are modulated by cerebellar input (Takakusaki, 2017) indicates the important role proprioceptors play in control of posture.

2.3.2 Muscles and tendons

Golgi tendon organs provide information relating to the tension within muscles, and muscle spindles also contribute to proprioceptive functioning by monitoring and responding to length changes of muscles (Leonard, 1998). The Golgi tendon organs are mechanoreceptors in the musculotendinous junction, which send a signal to the spinal cord via 1b afferents, triggering inhibition of the alpha motor neurone which creates force within the muscle, resulting in reduced muscle activity; at the same time the antagonist muscle is excited via a process called reciprocal excitation (Tortora and Derrickson, 2011). This process serves to protect the muscle complex, preventing spontaneous small ruptures at the musculotendinous junction (Cohen, 1999).

Recording of muscle afferent activity (from muscle spindles and Golgi Tendon Organs) within the triceps surae via micro-electrodes has shown that stretch of a muscle during contraction, or application of a vibratory stimulus over the muscle, produces proprioceptive (stretch) reflexes. In an experiment by Burke et al. (1983), the Achilles tendon was percussed (1ms pulse duration and

frequency of 1Hz) with a tendon hammer triggering a light vibration response. It was found that the inevitable activity within other mechanoreceptors in the skin and other muscles, as a result of the percussion to the tendon, potentially affected the excitatory post-synaptic potential of motor neurones. The changes to the triceps surae muscles also resulted in a reciprocal increased ability to actively recruit the ankle dorsiflexors, which further contributed an inhibitory reflex effect on the motor neurones of soleus (Burke et al., 1983). Other sensory stimulation may, perhaps, have similar effects.

The important function of the proprioceptors at the ankle mediating activity of muscles during stance phase of gait was demonstrated in a study of 30 healthy volunteers (aged 22-38), using electromyography (EMG) to record the response to a perturbation of the plantar flexor muscles during treadmill walking (Grey et al., 2004). In this study, cutaneous afferent feedback was blocked by an anaesthetic nerve block in ten of the subjects. This nerve block did not influence the EMG from soleus in stance phase, and the authors concluded that it must be proprioceptive feedback, rather than cutaneous feedback, which facilitates the excitability of soleus in the late stance phase of gait. The afferent information to soleus is important in gait, ensuring swing phase does not commence until the extensor muscles are no longer loaded; there is continuous regulation of muscle tone in response to proprioceptive feedback during gait (Takakusaki, 2013).

Another important contributor to proprioception is the afferent information from joints and their surrounding structures particularly the articular capsules integral

within synovial joints, with free nerve endings and Ruffini endings detecting pressure. Also, acceleration and deceleration of joint movement is detected by small Pacinian corpuscles exterior to the capsule, and the ligaments also contain receptors comparable to Golgi tendon organs to detect extreme strain, effecting a reflex inhibition of the muscles concerned (Tortora and Derrickson, 2011).

Cutaneous mechanoreceptors in the glabrous (non-hairy) skin on the plantar surface of the foot relay afferent information to the CNS and are classified according to the speed with which they adapt to the stimulus and the area of the receptive field. There are four different types of receptor: fast adapting (FA), which are also known as rapidly adapting, of which there are two types (FA I and FA II), and slowly adapting (SA) Type I and II receptors (SA I and SA II) (Johansson and Vallbo, 1983; Vallbo and Johansson, 1984). The fast-acting receptors only provide information during onset and release of the deformation of the skin, whereas the slow-acting provide information from the time of stimulus application and throughout the time the stimulus is present; type I fibre types have small receptive fields, with a clear boundary, and type II receptors have large receptive fields (Cohen, 1999). FA I sensory units detect rapid skin displacement via Meissner's corpuscles, and FA II fibres detect high-frequency mechanical vibrations via Pacinian corpuscles. SA I fibres detect deformation of the skin via Merkel's discs, with SA II receptors detecting skin stretch and joint movement, by virtue of the large receptive area, via Ruffini endings (Cohen, 1999). Kennedy and Inglis (2002) explored the activity of the cutaneous mechanoreceptors in the glabrous skin of the plantar surface of the foot

identifying 104 mechanoreceptors, 59 of which were FA I (57%), 14 FA II (14%), 15 SA I (14%) and 16 SA II (15%), and they were widely distributed in the foot.

All the same types of mechanoreceptors present in the hand are also found in the foot (Hennig and Sterzing, 2009), enabling detection of both the position and velocity of the contact (pressure or indentation) made with the foot (Magnusson et al., 1990). The function of the foot is different from the intricate work required of the hand. The mechanoreceptors in the foot can modulate reflex activity facilitating muscle activity around the ankle joint (Fallon et al., 2005). To achieve this, there is a robust coupling of FA1 mechanoreceptors, followed by SA 1 mechanoreceptors. Important feedback from initial foot contact is detected by FA I mechanoreceptors (Fallon et al., 2005), and there is a predominance of this type of receptor under the foot (Kennedy and Inglis, 2002). However, key information relating to continuing contact of the foot on the supporting surface is received via SA I mechanoreceptors. This information from the SA I mechanoreceptors enables ongoing monitoring of ankle muscle activity, which is considered important when controlling posture, balance and gait during walking (Fallon et al., 2005; Hennig and Sterzing, 2009).

Sensory receptors, for example, those on the plantar surface of the foot, respond to specific stimuli and have particular features, enabling transfer of information into a signal recognized by neurons. Afferent information from the foot and ankle is therefore crucial for postural control and walking capacity (Smania et al., 2003).

2.4 The importance of somatosensory input for postural control and balance

Somatosensory input from the plantar surface of the foot is important for achieving and maintaining balance in upright standing. Stabilometry is commonly used in research to assess balance by measuring the dynamic changes of the body's centre of pressure (COP) migration (Degani et al., 2017). Increased stability would be observed if the movement of the COP is shown to decrease in either an anterior-posterior (AP) or mediolateral (ML) direction; conversely, an increase in the deviation of COP movement would indicate a loss of stability. Despite some methodological weaknesses (lack of blinding or control), a study of 10 healthy subjects aged 21–46 years suggested that the effect of forefoot anaesthesia on the COP exerted through the lower limb and foot on a force platform, when vision was occluded, was modest but significant ($p = 0.004$), resulting in a medio-lateral balance deficit during bipedal stance (Meyer et al., 2004). Further studies of somatosensory stimulation of the plantar surface of the foot, involving indentation of plantar skin via a fixed pin matrix, with pins protruding 1.5 mm through holes of a moveable plate (eight healthy participants, mean age (standard deviation (SD)) 36 (9) years and four people with vestibular dysfunction 35 (3) years) (Maurer et al., 2001), or shot-gun ball plates to alter pressure (n=16, healthy males mean age 24.5 years) (Watanabe and Okubo, 1981), reported increased control of body sway. Interestingly, it has also been shown that postural sway cannot be fully compensated for by visual or vestibular systems when there is even just a slight amount of somatosensory loss in the foot of healthy individuals (n=21, mean age 23 years) (Wang and Lin, 2008). The addition of afferent stimulation to the plantar surface of the foot

was also explored by Zehr et al. (2014) (healthy individuals, n=14), showing that afferent electrical stimulation delivered as five times 1.0 ms pulses at 300 Hz to discrete regions (five sites on the plantar surface of the foot) could steer foot positioning, altering the ankle trajectory and guiding foot placement. It is recognized that the research which has been undertaken relating to somatosensory input for postural control and balance is limited, with small numbers of participants, and the work has generally been undertaken in healthy participants.

Afferent information is important in the maintenance of upright posture and equilibrium during gait where the body's centre of mass needs to be maintained over the base of support (Dietz, 1996). A complex collaboration of bodily systems is required: sufficient muscle activity to counteract the forces of gravity in the upright position; higher level planning structures (motor cortex) and brain stem and spinal networks for coordination; along with internal representations and adaptive and anticipatory mechanisms (Shumway-Cook and Woollacott, 2007). Essential sensory information from visual, vestibular and somatosensory systems is integrated to enable the maintenance of postural stability, balance and prevention of falls (Cohen, 1999; Marigold et al., 2004), and is crucial for functional walking. Postural sway is the interaction between the changing forces acting on the body, resulting in decreased stability, and the ability of the body to correct these alterations during quiet standing, to prevent a loss of balance (Pavol, 2005).

One important way that upright posture and balance are achieved is through interlimb coordination, with automatic harmonisation of muscle action in both legs, which is necessary because the strength of muscle activity and timing of movements in one leg has a direct impact on the other leg (Dietz, 1996); however, independent operation of each of the legs is possible (Verma et al., 2012). Walking involves repeated loss of balance as the line of gravity continuously moves out of the base of support formed by the feet; this necessitates the placement of the swinging foot ahead and lateral to the centre of mass as it moves in a forward direction, to prevent a fall (Lugade et al., 2011; Shumway-Cook and Woollacott, 2012). There needs to be appropriate postural control to maintain stability upright against gravity; however, the purpose of walking is to move from one place to another, so dynamic stability of the moving body is required, and an ability to adapt to challenges within the environment (Shumway-Cook and Woollacott, 2012). Different levels of stability are required in accordance with the task being undertaken. Dynamic stability is required to control the body as it moves from behind the supporting foot to a position in advance of the supporting foot; therefore, as the limb is loaded, the extensor muscles at both the hip and knee are required to function to prevent the fall of body weight (Perry and Burnfield, 2010).

Sensory feedback is key during human locomotion, involving constant assessment of the length (by muscle spindles), and tension (by Golgi tendon organs) of muscles; the muscle spindles contribute via both a feedback process and also for feedforward control (Leonard, 1998). Proprioceptors within the hip are vital for controlling stance phase in gait (Takakusaki, 2013). When a muscle

is put on stretch, an example being the hip flexors at the end of stance phase, the muscle spindle is activated and transmits information in the 1a afferent, resulting in monosynaptic excitation of the hip flexors, facilitating activity in these muscles to initiate the swing phase of gait. The 1a afferents from the hip flexors also inhibit the antagonistic hip extensor muscles by virtue of synapsing with a 1a inhibitory interneuron (Leonard, 1998). Afferent information relating to the changing conditions is also sent to higher centres via the 1a afferents, with the premotor cortex key to the preparatory phase, during sequenced movement, responding to afferent feedback (Cohen, 1999), resulting in modification of gamma and alpha motor neurone discharge; hence, adaptation takes place, fulfilling the requirements of the feedforward mechanism (Leonard, 1998). The connectivity between the prefrontal and premotor areas is predictive of performance (Tsvetanov et al., 2018).

2.5 Normal gait

Within the scope of this thesis, it is not possible to highlight all the important components relating to normal and pathological gait and readers are directed to more specific published literature (e.g. Perry and Burnfield, 2010; Whittle, 2007). However, an overview and summary of some of the key aspects relating to control of movement, stability and somatosensory stimulation, in retraining balance and gait post-stroke, are presented.

Locomotion can arise in response to either volitional or emotional processing within the brain and occurs for a purpose - fulfilling a goal (Takakusaki, 2013). Volitional movement, including walking, is not simple; it involves a myriad of

components with integrated activity within the brain, spinal cord, peripheral nerves, muscles and joints (Whittle, 2007). Despite the complex nature of walking, it is remarkable how easy it appears as a task; this is because of connections between spinal interneurons, sensory input, locomotor areas in the brainstem and higher level cortical centres (Whelan, 1996). Walking necessitates maintenance of balance and upright posture while the body moves forwards as a result of repeated limb motions; where pathology is absent the resultant ‘normal’ gait is coordinated, efficient and effortless (Perry and Burnfield, 2010). Mobility is important for independence in many ADL; hence, focusing on therapy to achieve independent ambulation is imperative (Durward, 1998). Improving somatosensory function may be beneficial for helping stroke survivors return to independent walking.

Walking consists of periods of time when both feet are in contact with the ground (double support), followed by phases when only one foot is in contact with the ground and supporting the body weight; the other foot is moving above the ground at that point in time during swing phase (single support) (Durward, 1998). Stance phase occurs for approximately 60% of the gait cycle, with the swing phase accounting for 40% of the cycle, with values of 62% and 38% observed at the normal speed of walking of 82m/min (Perry and Burnfield, 2010). Figure 2.1 shows the different parts of the gait cycle: initial contact (heel strike), loading response, mid stance, terminal stance, pre-swing, initial swing, mid-swing and terminal swing.

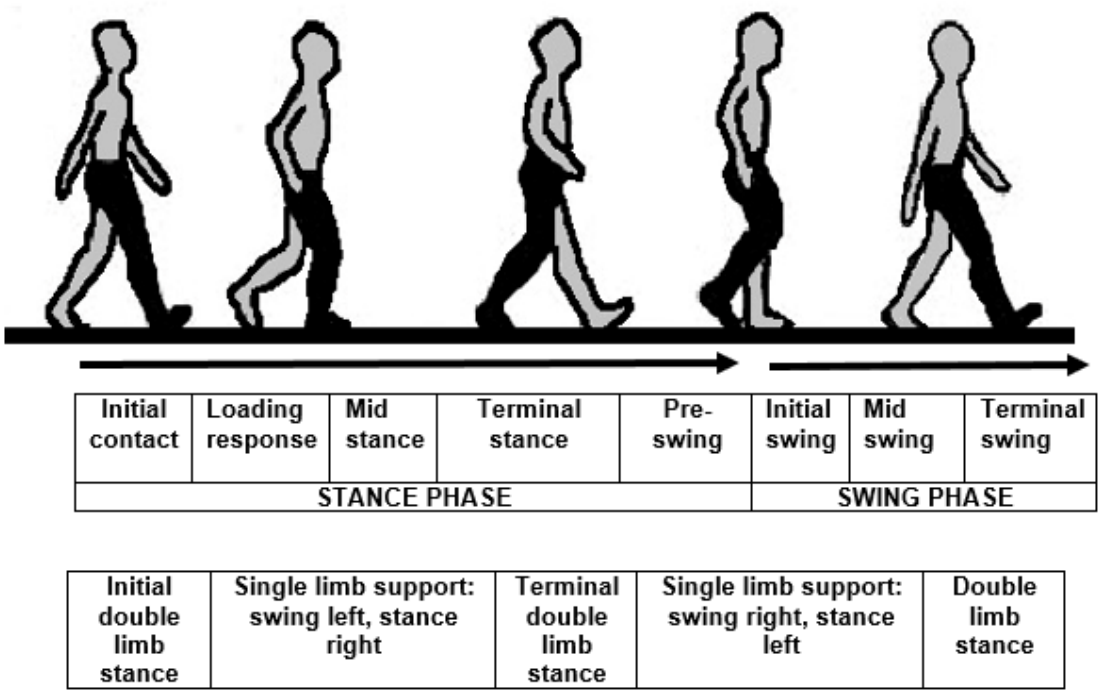


Figure 2.1 Subdivisions of stance and swing phase in gait (Perry and Burnfield, 2010) [Image provided by Paul Bailey and Aseel Aburub]

The control of walking has been studied in many ways, with much of the information relating to locomotion established in the 20th century by working with the decerebrate cat (Whelan, 1996). However, recent advances in medical science are beginning to enable real-life studies, and functional magnetic imaging resonance has been suggested as a useful tool for the future to study strategies for improving gait (Dobkin et al., 2004). Walking can either be a controlled process requiring input from the cortex or can occur on an automatic basis without higher levels of control (Schneider and Shiffrin, 1977). In automatic gait, utilisation of a learned sequence of events occurs, directed by the functions of the locomotor region in the midbrain in association with the central pattern generator (CPG) at a spinal level (Takakusaki et al., 2008).

The vestibular system plays an important role in balance, contributing to a stable, upright body posture by synchronising head and neck movements with trunk and body alignments (Cullen, 2012). Vestibular reflexes are active in dynamic activity, modulated by the differing demands of the task, neural pathways, muscle activity, and sensory feedback (Forbes et al., 2015). It works discreetly, combining with visual and proprioceptive inputs to detect motion; sensory integration is necessary to allow success in undertaking everyday activities, with triggering of appropriate postural responses as required, for example, if a trip occurs during walking or running (Cullen, 2012). The vestibular system works closely with the visual system during termination of gait to assist with the necessary slowing of the forwards centre of mass motion, and the ability to gain stability over the base of support (Perry et al., 2001). The vestibular system does not work in isolation; it works with the cerebellum enabling the production of coordinated voluntary activity, fine-tuning of sensorimotor information and promotion of plasticity (Manzoni, 2007). Input from brainstem areas is important for muscle tone regulation, with both excitatory and inhibitory influences counteracting each other; postural tone is increased as a response to the excitatory reticulospinal tract from the ventro medullary reticular formation but inhibited via an inhibitory area in the pedunculopontine tegmental nucleus (Takakusaki, 2013).

The extent of cortical control in human gait still requires further clarification (Koenraadt et al., 2014; Wang et al., 2008). Automatic actions of the CPGs are reported to be modified by information from the motor cortex, enabling ADL involving gait to be undertaken, for example when moving around an obstacle.

These supraspinal inputs are stated as being more important in humans than animals (Verma et al., 2012), evolving over time as a response to the complex behavioural requirements of human beings (Drew et al., 2008).

The cerebellum and basal ganglia work in conjunction with each other, and with the cerebral cortex. An essential role of the cerebellum is for the coordination of smooth movement, with it playing a role in preparation for movement, pre-setting the body ready for optimal function. The cerebellum is a regulator of both automatic and volitional movement influencing both the cerebral cortex and brainstem areas (Takakusaki, 2013). The cerebellum's important function relating to feedback during movement allows coordinated movement in a changing environment and also enables learning to occur; the cerebellum is, therefore, key for both the development and on-going monitoring of gait (Leonard, 1998). The basal ganglia contribute to motor control by maintaining a memory of movements which can later be reproduced as basic movement patterns (Whittle, 2007). In experiments involving monkeys, evidence was provided of the basal ganglia and cerebellum participating in several discrete loops with the cerebral cortex, involving connections with the premotor, oculomotor, prefrontal and inferotemporal areas of the cortex (Middleton and Strick, 2000). The caudate nucleus has been identified as being particularly involved in locomotion alongside the cerebellum (Pérennou and Hillier, 2014).

The thalamus is a significant structure essential for perceptual awareness. All the sensory systems in the body deliver information to the thalamus, which is imperative for conscious awareness of sensory experiences putting them into

context with emotional aspects and memories (Leonard, 1998). Therefore, it should not be forgotten when considering the importance of sensory information for function and gait.

Takakusaki et al. (2008) summarized the mechanisms involved in the neuronal control of bi-pedal locomotion from literature relating to both animal and human experiments. They identified three key elements for coordinated gait: firstly, extensive neural connections, such as the cortico-basal ganglia loop and basal ganglia-brainstem system; secondly, appropriate postural muscle activity and a synchronized musculoskeletal system; and lastly correct sensory processing. Furthermore, they highlighted that locomotion is dependent upon the locomotor (rhythm generating) system and the excitatory system creating appropriate muscle activity, with pathways descending from the midbrain locomotor region to the locomotor CPG in the spinal cord.

Figure 2.2 summarizes the multiple systems involved in voluntary, emotional and automatic processes, based on cat locomotor behaviours. Whilst it is acknowledged that figure 2.2 relates to cat behaviour systems, imaging of human supraspinal locomotor centres in the brainstem and cerebellum supports the view that supraspinal organisations are similar for both bipedal and quadrupedal mammals; multiple systems integrate to facilitate gait, including the motor cortices (enabling volitional control), the limbic system (emotional processing) and the many automatic processes that occur (Takakusaki et al., 2008).

2.5.1 Modular control of muscles

To control gait, interactions involving the whole of the musculoskeletal system and the nervous system are required (Takakusaki, 2013). In cats, groups of muscles work together to achieve a goal, initiated by one neural signal (Torres-Oviedo et al., 2006). These modular control mechanisms (or modules), originate centrally and coordinate appropriate movement in response to a specific task, enabling automatic postural adjustments to occur quickly by virtue of limited degrees of freedom at joints, and muscle activation with consistent features. Similar muscle synergies, defined as ‘a group of muscles activated in synchrony with fixed relative gains’ (Torres-Oviedo and Ting, 2007, p.2144), are also present in humans. EMG activity monitored sixteen muscles in the legs and lower trunk, and a maximum of six muscle synergies, similar in terms of both muscle activation and timing across individuals, were observed when postural responses for each participant were analysed. Combinations of synergies can occur to stabilize the centre of mass during motion; therefore, although movement patterns are constrained within the synergies, the differing amount of input from separate synergies working together enables variable responses to achieve stability and movement.

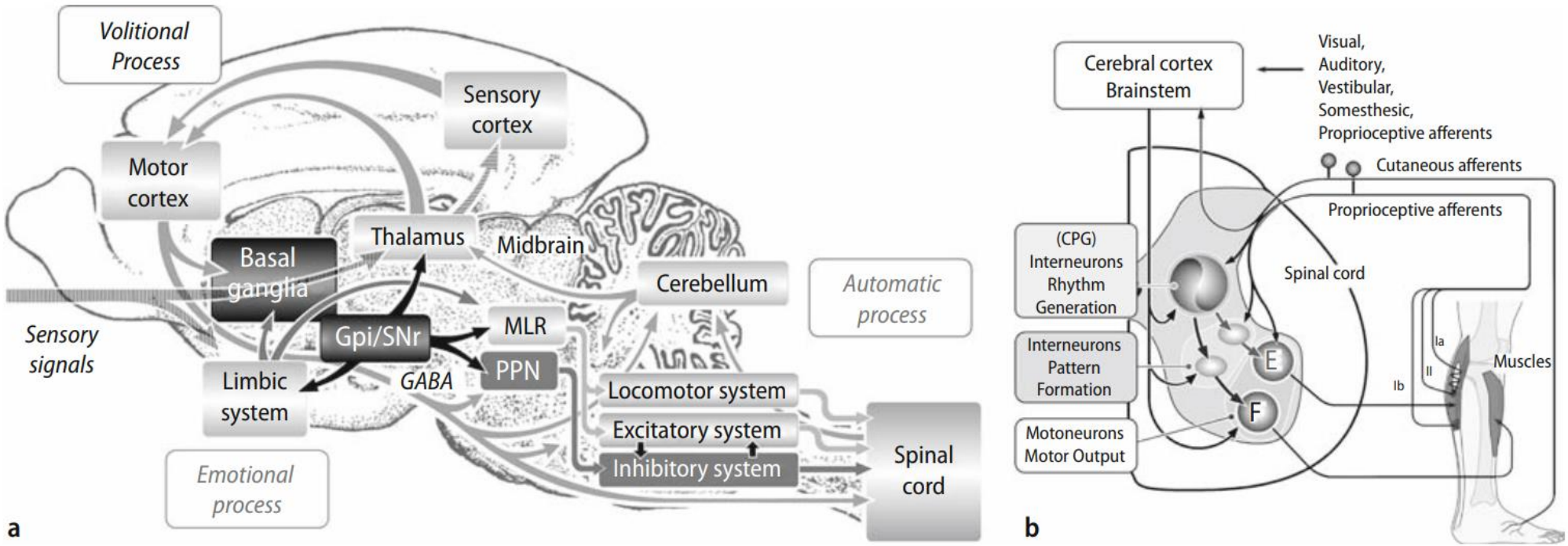


Figure 2.2 Framework of the cat locomotor behaviours. A - Signal flow involved in the volitional, emotional, and automatic processes of generating cat locomotor behaviours. B - Spinal locomotor network. Abbreviations: CPG, Central pattern generator; E, extensor motorneurons; F, flexor motorneurons; GPi, internal segment of globus pallidus; MLR, midbrain locomotor region; PPN, pedunculopontine pontine tegmental nucleus; SNr, substantia nigra pars reticulata; A is modified from Takakusaki, et al. (2006).

B is modified from Rossignol et al. (2006)

(Takakusaki et al., 2008) [reproduced with permission]

2.5.2 Automacy of gait and the importance of afferent input

Nielsen and Sinkjaer (2002) report two main roles for afferent information participating with the motor system to enable movement: the first method is via internal feedback influencing the output of neurones during volitional movement; and the second is a role in feedback to the CNS, enabling error correction. Automatic locomotor rhythmic activity, which enables walking without conscious input (Verma et al., 2012), is moderated in response to stimulation of proprioceptive and skin receptors, influencing motor output (Takakusaki et al., 2008). This modification occurs throughout all movements, as a result of both internal and external afferent changes (Leonard, 1998). Motor patterns are constantly modulated by sensory inputs, resulting in the dynamic sensorimotor interactions during gait (Rossignol et al., 2006). The primary somatosensory area in the parietal lobe has extensive connections with the frontal lobes (Bear et al., 2007), facilitating these sensorimotor interactions. Electroencephalogram readings in a study involving healthy individuals (n=10) showed activity within the posterior parietal lobe during gait and concluded that it plays a role in controlling the lower limb during gait (Bulea et al., 2015). This influence from sensory feedback occurs via a fast learning ability to reorganize the network, strengthening existing connections and weakening other pathways (Chersi et al., 2011).

2.5.3 Speed of gait

To achieve functional mobility, it is essential to be able to walk at a reasonable pace. Walking speed is the distance walked in a given time, usually measured in m/s (Perry and Burnfield, 2010; Whittle, 2007). In comparison to the average

speed of walking specified as 82m/minute (1.36m/s) for healthy adults (Perry and Burnfield, 2010), a speed of 0.8m/s (58.8% of the rate of normal walking) has been reported as being adequate for functional community ambulation (Perry et al., 1995). However, in one study it was found that, despite an average speed of walking of 0.898 m/s, 33% of stroke survivors were unable to walk without supervision in their community (Lord et al., 2004). It is acknowledged that functional ambulation involves many different aspects. A definition for community ambulation was derived following analysis of questionnaire results in a cohort of stroke survivors living at home (n=115); 'independent mobility outside the home, which includes the ability to confidently negotiate uneven terrain, private venues, shopping centres and other public venues' (Lord et al., 2004, p.236). Using voxel-based lesion-symptom mapping it has been shown that involvement of the insula, lateral and anterior putamen and external capsule have a detrimental effect upon walk speed response post-stroke (Jones et al., 2016a).

2.6 Kinematic deviations in gait after stroke

The changes that occur in gait after stroke are related to: the pathological effects of the stroke itself; resultant secondary problems, for example, shortening of muscles due to altered movement patterns; and the interactions of these issues within the complex motor control system. Alterations in gait pattern can, therefore, occur due to the original loss of motor control (negative features), sensorimotor dysfunction, for example, reduced power of the hip extensors, or because of the adaptation (adaptive features), for instance when

a muscle develops shortening due to a contracture, or as a compensatory strategy adopted to address muscle weakness (Moseley et al., 1993).

Common kinematic deviations can be observed during stance phase following a stroke. A seminal paper by Moseley et al (1993) provided an insight into hemiplegic gait biomechanics from a clinical perspective. Several aspects are presented in the paper. The importance of the position of other joints on the alignment of the ankle and foot is discussed; for example, that the degree of flexion/extension at the knee or hip will influence the alignment at the ankle and, therefore, alter the ability to be able to transfer the weight over the foot. Appropriate hip extension at the end of stance phase is important to allow weight to be transferred over the stance foot, promoting a more normal swing phase with better alignment at the foot and ankle. Reduced maximum hip extension has also been associated with reduced gait velocity (Cruz et al., 2009; De Quervain et al., 1996). Altered pelvic displacement (which can be associated with eversion of the foot during early stance) is another potential gait deviation, as well as reduced knee flexion/hyperextension, or increased knee flexion during stance, in addition to reduced ankle plantar flexion at toe-off (Moseley et al., 1993). Distal alterations also influence proximal movement: an adaptive shortening of the posterior tibial muscles, or inability of these muscles to work in a controlled manner eccentrically, will prevent the ability to transfer the weight appropriately over the foot, resulting in a kinematic deviation at the hip (Moseley et al., 1993). All these deviations will affect the contact of the plantar surface of the foot with the floor and the transition of weight over the foot during stance. If shortening or poor eccentric muscle activity of the plantar

flexor group of muscles exists, it will be difficult to transfer the weight forwards over the foot with adequate control (Moseley et al., 1993).

Consideration of how the deviations alter foot position is important. Hyperextension of the knee is associated with an equinus foot posture (a position of increased plantar flexion) at initial contact (Higginson et al., 2006), and this combination results in difficulty bringing the body weight over the foot during stance. Contralesional knee hyperextension during stance phase has been reported to be common, in 67% of stroke survivors (n=12) (Kim and Eng, 2004) and 65% of heterogenous stroke survivors (n=25) recruited between seven weeks and more than one year after the onset of stroke symptoms, with variable gait patterns and abilities (Knutsson and Richards, 1979). Again, the small sample sizes should be noted.

Reduced contralesional ankle plantarflexion at toe-off is associated with a lack of push-off, attributed to inappropriate activity of the plantar flexors at the beginning of stance phase (Burdett et al., 1988; Knutsson and Richards, 1979). Decreased activity of the tibialis anterior muscles to produce dorsiflexion, in preparation for initial contact, results in the foot being placed on the floor in a more plantar flexed position during loading; the result of this is premature plantar flexor (PPF) muscle activity, initiated by a stretch response. This strong contraction of the plantar flexors occurs at a point in time where the centre of mass of the body is behind the foot and, as a result, there is a backward thrust of the leg as inertia carries the body forwards, and hyperextension of the knee occurs. The result of this situation is that the plantar flexors are unable to propel

the body forwards at toe-off. Consequently, increased activity of the hip flexors is needed as a compensatory strategy to enable faster walking (Nadeau et al., 1999; Perry, 1993).

The causes of the PPF activity in gait were explored in an observational study (Fujita et al., 2018). A total of 31 independently mobile stroke survivors, at least six months post-stroke, with moderate degrees of spasticity (assessed using the Modified Ashworth Scale (MAS)) were recruited. Following assessment, the group was divided into two; those with PPF activity (n=13), and those without PPF (n=18). EMG results showed that the PPF group demonstrated significantly reduced activity in the tibialis anterior muscle during swing phase ($p < 0.05$), with significantly increased activity in both rectus femoris and biceps femoris muscles throughout swing phase ($p < 0.05$), with activity triggered significantly earlier than for the non-PPF participants ($p < 0.01$) and seen to continue during the loading response phase ($p < 0.05$). The authors suggest that rehabilitation plans to address weakness in the hip and knee extensors may help to reduce PPF. However, it must be taken into consideration that the sample size within this study was small. Addressing other aspects, for example, shortened posterior tibial muscles by using mobilizing and stretching techniques to enable a better foot position during stance, could perhaps also help to address PPF; however, this strategy has not been explored.

Varus deformity, ‘an inward angulation of the rearfoot and/or forefoot, generally measured in the frontal plane, which is the result of abnormal muscle activity and posturing,’ can also be observed after stroke (Reynard et al., 2009, p.69).

Gait analysis and EMG readings in stroke survivors who displayed varus deformity of the foot demonstrated an imbalance between tibialis anterior and extensor digitorum longus, with less activity (shorter and weaker) within the extensor digitorum longus and, therefore, an unopposed pull into inversion; this presentation tended to occur in conjunction with PPF activity, and varus deformity is associated with ankle plantar flexion and claw toes (Reynard et al., 2009). Furthermore, the patterning was suggested to be seen due to the presence of a primitive mass flexion synergy of hip flexion, abduction and lateral rotation associated with knee flexion and supination of the foot. This results in weight being taken on the lateral aspect of the foot during initial contact, with poor weight bearing under the 1st metatarsal head (Perry et al., 1978).

Different biomechanics following stroke result in altered sensory input from the foot and ankle during walking, in view of the importance of sensory feedback for regaining controlled motor function (Patel et al., 2014), this may be further compounding the issues of regaining the ability to walk after stroke. It is also interesting that hyperextension patterning of the knee has been observed not to occur when there was normal weight acceptance through the foot i.e. via the heel and not the forefoot (Kim and Eng, 2004). Foot position and activation is therefore important to address within therapy rehabilitation.

2.7 The potential for regaining the ability to balance and walk after stroke

Functional recovery of the upper limb after stroke has been extensively researched; however, limited knowledge exists relating to the recovery systems to restore lower limb function and walking after stroke (Peters et al., 2018). In a study utilising magnetic resonance imaging (MRI) and clinical motor assessments in stroke survivors (n=43) with an average age of 59.7 (11.2) years and time post stroke 64.4 (58.8) months, it was found that functional activity of the lower limbs is not so dependent upon an intact corticospinal tract; other pathways are involved to control lower limb movement and gait, such as the reticulospinal, rubrospinal and vestibulospinal tracts (Peters et al., 2018).

It is of interest to consider prognostic indicators for achieving functional walking after stroke, in order to contemplate who may benefit from enhanced sensory input strategies. Various prognostic indicators for independent walking have been identified. A prospective cohort study (n=101) explored predictive indicators within the first 10 weeks after stroke, finding that the age of the patient and the Barthel index were key factors (Kollen et al., 2006); however, sitting balance (identified using the Trunk Control Test) and strength of the hemiparetic leg (assessed by Motricity Index) have also been suggested as key measures for predicting the ability to walk in 154 first-ever ischaemic stroke patients (Veerbeek et al., 2011). Standing balance measured by the timed balance test or Fugl-Meyer balance test was also found to be a key determinant for recovering the ability to walk (Kollen et al., 2005). More recently a study undertaken by (Smith et al., 2017) found that a Trunk Control Test of > 40 and

hip extension strength of 3 or more on the Medical Research Council grading were an indication of the likelihood of regaining independent gait.

Cortical damage following stroke may affect the cortical control of walking; integration of sensory input and motor output, and somatosensory impairment all contribute to a reduction in automaticity of movement (Clark et al., 2014). A study by Chen et al (2000) of 55 hemiplegic patients assessed (by MRI) at one and six months post-stroke showed that the site and size of a lesion within the brain has a significant effect on the potential for motor recovery and function; for example, when a lesion affects the premotor cortex, there is an impact on walking disability post-stroke (Sullivan et al., 2009) and a loss of independence (Patel et al., 2000). Many people are unable to return to work or social engagements after stroke or may even require long-term support or care (Perry et al., 1995).

In a cross-sectional study, which compared 19 people with a right middle cerebral infarct and 20 people with a left middle cerebral infact with 108 controls, it was found that the severity of gait impairment following a stroke is associated with the integrity of gray matter in non-infarcted areas of the brain and not just the extent of the lesion itself (Chen et al., 2014). It has been shown that the potential for neuroplastic changes and the ability of the cortex to re-organise depends upon functional connections between the primary motor cortex and supplementary motor area of the ipsilesional hemisphere, with the red nucleus also being important (Peters et al., 2018). The red nucleus is important because it provides another potential method for controlling

movement via the rubrospinal pathways (Jankowska, 1988). In a study where participants were prospectively recruited for the **S**oft-Scotch **W**alking **I**nitial **F**oo**T** (SWIFT) trial, a multiple regression model showed that damage to the corticospinal tract was predictive of a poorer response as measured by changes to the results of both the Functional Ambulation Classification (FAC) (p=0.030) and modified Rivermead Mobility Index (mRMI) (p=0.024) following rehabilitation, but not associated with speed of walking (p=.060) (Jones et al., 2016a). This is perhaps due to the ability to retain control of walking on an automatic level.

A lack of automaticity of movement (Clark et al., 2014) is, however, increased in stroke survivors due to the nature of stroke being a disease predominant in the elderly; the ageing process itself may also contribute to impaired walking ability, and in this group even routine walking can be classed as a complex task, and is not controlled purely on an automatic level (Hausdorff et al., 2005). However, the spinal control of walking will remain unimpaired, and this may partly explain the higher levels of recovery of walking compared to the levels of upper limb recovery e.g. reach and grasp, which are under cortical control. Nevertheless, recovery of walking after stroke remains a challenge; in a group of stroke survivors (n=99) 78% still experienced problems walking three months after stroke (Algurén et al., 2010). Indeed, many stroke survivors report that difficulty walking affects their quality of life (Alguren et al., 2012).

Gait asymmetry has been correlated with a loss of balance (measured using the Berg Balance Scale (BBS)) (Lewek et al., 2014). In a cohort of 39 stroke

survivors, comfortable gait speed was significantly related to step length (r = -.55; *p* < .001), stance time (r = -.41; *p* = .010), and swing time (r = -.57; *p* < .001), which were used to assess for asymmetry. The BBS was negatively correlated with both step length asymmetry (r = -.61; *p* < .001) and swing time asymmetry (r = -.36; *p* = .025). The authors suggest that the asymmetry and loss of balance predispose stroke survivors to falls. It is not known whether some of the asymmetry could be attributed to altered sensation and a reluctance to weight bear on the contralesional side, or if increasing the somatosensory input from the foot and ankle may alter gait asymmetry, balance potential and risk of falls. Asymmetric gait pattern has been associated with lesions involving the inferior portion of the posterolateral putamen, potentially resulting in a loss of communication between the motor areas in the cortex and those in subcortical regions, when 17 chronic stroke survivors with a symmetrical gait were compared with 20 with an asymmetrical pattern of walking (Alexander et al., 2009).

2.7.1 Effect of lesion location on recovery of balance and walking

A slower gait with greater asymmetry, taking less weight for a shorter period of time on the affected side, is seen more often in right hemisphere strokes, particularly when the right middle cerebral artery (MCA) is involved (Chen et al., 2014). Also, when stroke survivors with a right MCA (n=17, mean (SD) age 65 (8) years, mean (SD) time post-stroke 7(6) years) were compared with stroke survivors with a left MCA infarct (n=20, mean (SD) age 65(8) years, mean (SD) time post-stroke 7(6) years) and controls (n=55, mean (SD) age 65(8) years), it was found that people with a right MCA lesion exhibited increased postural

sway in the absence of visual input, suggesting a reliance on vision to control postural sway (Manor et al., 2010). Perhaps this is due in part to a loss of afferent input on the contralesional side.

Chen et al. (2014) explored the effect of infarct hemisphere and non-infarcted brain volumes on locomotor performance following stroke and found a difference in gait speed between right and left MCA infarcts, with a correlation between speed of walking and volume of gray matter in the caudate nucleus ($r=0.57$, $p< 0.001$) and the cerebellum ($r=0.57$, $p=0.02$) noted in patients with right MCA infarct only. The authors suggested this was an indication of brain reserve that can be utilized within the locomotor control system following lesions; however, it has been shown that the right hemisphere is key for sensorimotor control with an influence on both the contralateral and ipsilateral sides (Hom and Reitan, 1982). This could be the reason behind the evident disadvantage for regaining the ability to walk following a right hemisphere stroke. It is not known whether addressing the loss of somatosensory control might improve the potential to walk after a right MCA stroke.

2.7.2 Influence of weak dorsiflexors and somatosensory impairment after stroke

Overall predictors for recovery of gait post-stroke have been discussed in section 2.7; distal influences will now be considered. In a study of 147 stroke survivors (mean (SD) age 55.5 (12.2) years), muscle strength and proprioception were proposed as the two most relevant impairments to be measured when assessing walking potential following stroke (Perry et al.,

1995). Weakness of dorsiflexors on the contralesional side was related to gait asymmetry and decreased velocity in 21 people more than six months post-stroke (Lin, 2005), and indications are that afferent information from the foot and ankle can influence balance and walking (Annino et al., 2015; Chien et al., 2017).

Whilst research exploring the contribution of proprioception to facilitate balance during gait is sparse in both healthy individuals and following a stroke (Mullie and Duclos, 2014), impaired proprioception in the ankle has been found in small studies of stroke survivors. Lee et al. (2005) reported significantly ($p<0.001$) reduced proprioception in the contralesional ankle of 11 ambulating survivors of chronic stroke compared to the ipsilesional ankle movement (sense of dorsi/plantar flexion movement was assessed using a linear servo-motor controlled by a variable ramp generator) and suggested that this loss of proprioception may affect foot placement and weight-bearing during ambulation. Although the sample size was small, the reliability of the assessment tool was reported to be moderate to high (ICC 0.58 to 0.76). Similarly, Yalcin et al. (2012) measured proprioception of the ankle using an isokinetic dynamometer and reported significant proprioceptive impairment in both the contralesional ($p<0.05$) and ipsilesional ($p<0.05$) ankles compared to healthy controls. These authors suggested that proprioceptive integration involves both cerebral hemispheres.

Impaired ankle joint position sense has been associated with altered step length in chronic stroke (n=68) (Lin, 2005), and with postural sway in acute and sub-acute stroke (n=30) (Niam et al., 1999). However, contrasting evidence

from a larger study of 147 stroke survivors (>3 months post-stroke, able to walk >6m), suggested that proprioception (a combined measure of the contralesional hip knee and ankle) was not correlated with the level of walking handicap (Perry et al., 1995). The categories of walking handicap ranged from unable and then physiological, with a mean (SD) walking velocity of 0.1 (0.05) m/s, to community walkers with a mean (SD) walking velocity of 0.8 (0.18) m/s. However, the findings from this study cannot be generalized to non-ambulatory stroke survivors and, therefore, it is unclear whether ankle proprioception is associated with inability to walk. Furthermore, the assessments of walking in these studies were on a floor or treadmill surface that was flat; however, it has been shown that afferent feedback is crucial during stepping on sloping surfaces (af Klint et al., 2008), where proprioceptive input modulates the motor response, a situation that more closely resembles real-life community ambulation over uneven ground.

Although balance and function have been shown to improve in healthy participants in response to afferent input, it is important to consider whether the findings are transferrable to stroke survivors. Stroke survivors themselves have indicated, in semi-structured interviews (n=13), that a loss of sensation within the foot does adversely affect function and the ability to walk, especially when coping with the challenge of walking over rough ground (Gorst et al., 2016). However, objective measurements from a cross-sectional observational study by the same authors (n=163 ambulatory chronic stroke survivors, mean (SD) age 67(12) years, mean (SD) time since stroke 29 (46) months), did not triangulate their qualitative study, and indicated a lack of correlation between

somatosensory impairment and the ability to walk (Gorst et al., 2018). One of the outcome measures (OMs) for this study was the 10-metre walk test (10MWT); it has been shown that it is only when walking speed is greater than 0.8 metres per second (m/s) that this measure is reflective of community ambulation (Taylor et al., 2006). Within the Gorst et al. (2018) study, the mean (SD) gait velocity for the stroke survivors was 1.1(0.6) m/s; therefore, some of the participants would not have been able to walk at the required speed to reflect abilities within a community environment.

Walker et al. (2014) explored foot placement in people who were at least six months post-stroke (n=12), finding that sensory stimulation at 30Hz electrical stimulation to the medial plantar nerve of the paretic foot, reduced medio-lateral targeting error (p=0.008). These authors advocate that the inclusion of somatosensory stimulation work to the foot in rehabilitation could enhance the ability to walk; however insufficient evidence exists presently to draw these conclusions. It must be considered that this was a small study with no randomization or blinding and a high potential for bias.

2.8 Rehabilitation of lower limb function after stroke

2.8.1 Rehabilitation strategies

The International Classification of Functioning, Disability and Health advises delivering holistic rehabilitation, addressing activity and participation, and not just bodily function (Bruyère et al., 2005). A 24-hour approach to rehabilitation in a stimulated, enriched environment is thought to be important in facilitating

recovery post-stroke (Aries and Hunter, 2014). Restoring sensorimotor connections and interactions is necessary to improve motor function, and interventions to target the retraining or reactivation of an impaired sensory system have been advocated (Bolognini et al., 2016). A selection of sensory modalities are encompassed when considering sensory interventions (e.g. somatosensory, vestibular, auditory and multisensory) (Schaaf and Case-Smith, 2014).

Pomeroy et al. (2011) proposed three important rehabilitation strategies to facilitate activity-driven motor cortex plasticity following stroke, promoting better function and independence: priming, augmenting and practice. Priming strategies involve techniques that prepare the sensorimotor system for motor function, specifically where there is limited or no volitional control of movement; augmenting techniques enhance somatosensation during activity, thereby improving motor output; and task-specific practice is recommended where the stroke survivor has the ability to repeat and practice movements (Pomeroy et al., 2011).

In relation to the foot, intensive somatosensory stimulation of foot and ankle proprioceptors as well as the cutaneous mechanoreceptors on the plantar surface of the foot could be considered to be a priming technique, which could enhance motor control and alignment of the foot, creating the ability to place and transfer weight over the foot, and permitting adaptation of the foot to different floor surfaces.

Once volitional activity is achievable, augmenting techniques can be used to improve voluntary control and muscle strength during functional activities facilitating better sensory awareness under the foot. Augmenting techniques could enhance the interaction of the foot with the supporting surface, which is important for functional activity; for example, sensory input through the heel during sitting to standing is considered to enhance activity of proprioceptors, facilitating activity within the lower limb muscles, promoting a more automatic patterning during sit to stand (Raine et al., 2009).

Practice and repetition of movement is then the most effective method of improving recovery of motor control following stroke, once sufficient muscle strength and voluntary control is available (Pomeroy et al., 2011). Practice is widely recognized as an important aspect of retraining sensorimotor function following stroke.

Consideration should be given to rehabilitation aims, and specifically whether the aim is to facilitate restoration of motor function by modification of underlying neural mechanisms, e.g. by encouraging repetition, or to adjust to a loss of neurological control by using adaptive interventions (compensatory strategies) as an alternative means of completing a task (Pomeroy et al., 2011). The stroke recovery and rehabilitation roundtable (SRRR) task force suggest that recovery ‘reflects the extent to which body structure and functions, as well as activities, have returned to their pre-stroke state’ (Bernhardt et al., 2017b, p794). However, compensation can be seen as the ‘patient’s ability to accomplish a goal through substitution with a new approach rather than using

their normal pre-stroke behavioral repertoire' and is a process that also involves learning (Bernhardt et al., 2017b, p794). With a better understanding of neuroplasticity principles, recovery is now often the aim in therapy rather than compensation strategies (Shumway-Cook and Woollacott, 2012), although a mixture of the two approaches may be necessary and is dependent upon time after stroke (McWain et al., 2012).

2.8.2 Therapy to the foot to improve balance and gait

Since some of the consequences of stroke directly impact on the biomechanics of the foot and ankle, the ability to balance and walk is affected (Fujita et al., 2018; Higginson et al., 2006; Reynard et al., 2009); see section 2.6. The foot and ankle play an essential part in enabling walking; consequently, any restriction to either passive or active range of movement can have a detrimental effect (Roy et al., 2013). Clearly, a kinematic alteration at any joint in the lower limb will have a direct effect on the other joints and the ability of the muscles to control movement appropriately. Therapy needs to be targeted at the underlying movement problem, whether it arises from the distal or proximal components of the limb, in order to improve foot alignment and placement during balance and gait.

The aims of therapy treatment in relation to the foot and ankle have been reported in the literature to be:

- prevent contractures (McWain et al., 2012) and, therefore, PPF by normalizing ankle motion from terminal swing to weight bearing during gait (Fujita et al., 2018);

- facilitate ankle strategy with better foot contact on the floor by optimizing length/tension of muscles, as well as strength (Raine et al., 2009);
- strengthen and promote selective control of muscles, especially dorsiflexors, which concentrically assist with foot clearance during swing and eccentrically control the fall of the forefoot on heel strike, and plantar flexors, which enable eccentric control of the shank of the leg over the foot during stance phase, and appropriate toe off at the end of stance (Raine et al., 2009).

Notable by its absence from this summary of aims is the retraining of sensory function in the foot and ankle. This is noteworthy since an exploratory study of therapists' experiences of conventional therapy for the lower limb post-stroke identified the attention given to sensory stimulation of the foot in routine practice. This focus group study, involving seven qualified clinicians identified that hands-on somatosensory stimulation of the plantar surface of the foot is frequently used, in conjunction with mobilization of joints and soft tissues in the foot and lower leg, to prepare the foot for standing and balance, prior to task-specific gait training (Aries et al., 2019).

A Cochrane review of 27 controlled trials (3423 participants) (Pollock et al., 2014a) found moderate quality evidence in support of physical rehabilitation to improve recovery of postural control and lower limb function, including gait, and achievement of independence in ADL, compared to no treatment (mean standard difference (MSD) 0.78 (95% confidence interval (CI) 0.58, 0.97) for independence in ADL) after stroke. However, no one specific physical therapy

approach was found to be more effective than another (Pollock et al., 2014a). Many of the included trials were of high or unclear risk of bias, and significant heterogeneity was an issue. The authors recommended that further research was still required to explore whether specific focused physical therapies applied to the lower limb and foot enhance recovery of balance and walking after stroke.

Subsequently, the Royal College of Physicians (RCP) stroke guideline (fifth edition) stated that ‘people with significant impairment of their balance and walking ability after stroke should receive progressive balance training, functional task-specific training, lower limb strengthening exercises and be considered for an ankle-foot orthosis’ (Rudd et al., 2016 p. 73). The guideline reported that electromechanical assisted gait training (Mehrholz et al., 2013) was supported by evidence, as well as the use of ankle-foot orthoses (Tyson and Kent, 2013) and functional electrical stimulation (NIHR, 2009) when there is limited ability to dorsiflex the foot. However, the section in the guideline relating to sensation is limited and stated that ‘there is no good evidence to support any particular passive or active intervention for sensory impairment after stroke’ (Rudd et al., 2016 p.82). When considering the literature that informs the guidelines, it is important to remember that “no evidence of effect” does not equate to “evidence of no effect” (Oxman, 1994: p650). Therefore, it must be remembered that a lack of evidence does not mean that sensory interventions are not effective. It simply indicates that the research relating to this aspect of stroke rehabilitation has not yet been undertaken.

The next sections will consider further the evidence for task-specific gait training and somatosensory stimulation of the lower limb to improve balance and gait post-stroke, since these have been highlighted by experienced clinicians to be components of routine stroke rehabilitation (Aries et al., 2019).

2.8.3 Task-specific gait training to promote improvement of balance and walking

Task-specific training is one aspect of therapy where there is general agreement regarding effectiveness following stroke (French et al., 2016(Rudd et al., 2016). The underlying mechanism of effect is facilitation of neuroplasticity (Kattenstroth et al., 2012), and repetition of skilled motor tasks is required (Nudo, 2013). The ability to transfer knowledge and skills from treatment to function is fundamental to enable independence in daily life (Geusgens et al., 2007) and task-specific training promotes this principle. Although high level of repetitions are not generally achieved in conventional stroke rehabilitation (Tyson et al., 2018), a proof-of-concept study has demonstrated the feasibility of stroke survivors achieving 300 repetitions in a single one-hour session of treatment (Birkenmeier et al., 2010).

There is strong evidence that task-specific gait training (TSGT) can be used to improve walking after stroke (Wiener et al., 2018). Addressing weakness, for example of the dorsiflexors, by strengthening through functional activities is important, and this can include stepping practice and facilitation of the ankle strategy to enhance balance (McWain et al., 2012). However, for those stroke survivors who have severe muscle weakness and are, therefore, unable to

engage in task-specific training and repetitive practice, other treatments are needed to prepare or enhance the sensorimotor system (Hunter et al., 2011), to help improve movement and function. Within conventional stroke rehabilitation, sensory retraining can be used as an adjunct to task-specific practice to enhance neuroplasticity (Kattenstroth et al., 2012).

2.8.4 Somatosensory stimulation as treatment post-stroke

Passive sensory stimulation consists of non-specific high-intensity stimulation, such as rubbing/icing or electrical stimulation without active muscle contraction (Schabrun and Hillier, 2009). In contrast, active stimulation involves conscious awareness and mechanisms to retrain sensory awareness, for example, practicing identifying different textures and detecting the position of body parts in space (Schabrun and Hillier, 2009). Active sensory retraining involves attentive training as the important element (Carey, 2012), for example, attending to an object or stimulus with vision occluded (Carey 1995), and use of feedback to enable learning and retraining of sensory perception. However, as some rehabilitation interventions include aspects of both passive and active stimulation, they may be difficult to categorize as one or the other.

Schabrun and Hillier (2009) systematically reviewed 14 studies (n=199 participants) involving passive and active sensory interventions for the upper and lower limb following stroke. Their findings supported the value of passive sensory training (electrical stimulation) for hand function (Jebsen-Taylor Hand Function Test). A meta-analysis of three studies (Celnik et al., 2007; Conforto et al., 2007; Wu et al., 2006) resulted in a total effect of 8.72 (95% CI 2.48,14.95)

in favour of the experimental groups. However, research related to active sensory training (education, localizing and discriminating sensations, sensory recognition, hardness discrimination and proprioceptive training) was found to be limited, with small sample sizes (n=3 to n=39), and a wide diversity of study designs and methodological quality. The findings of the review indicate that the evidence base for sensory stimulation post-stroke is confounded by a sparsity of research, heterogeneity of subjects, and unreliable OMs. There is a need for further high-quality research to determine the effectiveness of sensory training in stroke rehabilitation. Strengths of the review include clearly specified search terms and inclusion criteria, and the use of two independent reviewers when assessing methodological quality of studies. The Schabrun and Hillier (2009) review was updated by Serrada et al. (2019), with similar findings: there was some support for passive sensory interventions but limited evidence for active sensory interventions for upper and lower limbs following stroke.

A potential limitation of these reviews was the inclusion of sensory training for both the upper limb and the lower limb. These treatments may not be directly comparable in view of the neurophysiological differences relating to upper and lower limb control; it could be expected that there may be differences in relation to the outcomes from sensory retraining programmes. Voluntary movement in the upper limb is predominantly controlled by the primary motor cortex (M1) in the contralesional hemisphere of the brain, with direct corticospinal input enabling great dexterity of movement of the hand through monosynaptic corticomotoneuronal connections (Porter and Lemon, 1995). This differs from the control of walking, which can be more automatic with less input from higher

centres (Schneider and Shiffrin, 1977). An extensive neural network is present at spinal level which is able to facilitate inter-limb coordination following afferent input (Cohen, 1999), enabling walking which, in contrast to upper limb function, is much more automatic, with pattern-generating networks in the brainstem working in conjunction with the reticular formation and spinal cord, coordinating activity within the various muscle groups (Shumway-Cook and Woollacott, 2007). In the case of the lower limb, longer latency of response has been observed using EMG, between stimulation and muscle contraction (Cody, 1995), and this could have implications for the ability to control and change motor output in response to afferent input.

The other issue to consider is that the foot invariably receives sensory stimulation much earlier than the hand post-stroke, by being placed in contact with a surface (the floor) and it is further stimulated through compression in standing, since early mobilization is commonly advocated (Cumming et al., 2011). In contrast, the upper limb is often neglected in the early stages of stroke rehabilitation, and its relatively poor recovery is considered to be associated with learned non-use (André et al., 2004; Taub and Uswatte, 1999). These key differences mean the upper limb might receive less afferent input following stroke and this may affect results of studies, theoretically meaning that the upper limb has a greater potential to demonstrate change following subsequent additional experimental sensory stimulation compared to the lower limb.

Other aspects may also need to be considered when implementing sensorimotor training strategies, for example, it has been suggested that

different interventions may be necessary when working with stroke survivors with neglect (Meyer et al., 2016).

2.8.5 Somatosensory stimulation and re-training for the upper limb post-stroke

Sensory impairment in the upper limb is experienced by up to 80% of stroke survivors (Doyle et al., 2010). Given the similarity in cutaneous receptors in the glabrous skin of the hand and foot, it is of interest to briefly consider the evidence relating to sensory interventions for the upper limb.

A recent cross-sectional survey (SUPPLES-UK: Stockley et al., (2019) of current therapy delivered by UK therapists for the upper limb post-stroke identified that therapy for severe stroke included therapist-delivered and facilitated range of movement exercises. However, no interventions were reported for sensory loss or spasticity, and no technique adaptations for people with unilateral neglect were identified. A strength of the questionnaire was that it was designed with consideration of the UK stroke guidelines and the Template for Intervention Description and Replication (TIDieR) checklist. However, limited detail is presented in relation to the exact content of the therapy treatments or how treatments were adapted to address the heterogeneity of stroke. Furthermore, the overall response rate to the questionnaire is unknown and there is potential selection bias, which is acknowledged by the authors.

From various systematic reviews of sensory interventions for the upper limb, there is some promising but limited evidence in support of thermotherapy

(Doyle et al., 2010), intermittent pneumatic compression (Doyle et al., 2010), mirror therapy (Thieme et al., 2018), electrical stimulation (Veerbeek et al., 2014), biofeedback (Wattchow et al., 2018), and retraining of sensory discrimination (Turville et al., 2019). In contrast, Grant et al. (2018) found no evidence to support the use of sensory electrical stimulation or therapist delivered sensory stimulation (thermal stimulation, inflatable splint, and proprioceptive stimulation). However, it is important to note that the one study included in Grant et al. (2018) that involved therapist delivered (hands-on) proprioceptive stimulation of the hand (Hunter et al., 2011) was not an effectiveness study, but instead was a dose-finding study to identify the maximum feasible dose of therapy that could be delivered in an NHS ward-based service. Consequently, the conclusion drawn by Grant et al. (2018) about lack of effectiveness of therapist-delivered somatosensory (proprioceptive) stimulation is unfounded and inappropriate. Somatosensory (proprioceptive) function is important for upper limb function post-stroke (Meyer et al., 2014), and therapist-delivered intensive sensory stimulation and retraining of proprioception post-stroke should not be dismissed as being ineffective by a misunderstanding of the purpose and findings of the one study of this intervention (Hunter et al., 2008) included in a systematic review.

Whilst most systematic reviews of sensory interventions for the upper limb have included only RCTs or controlled clinical trials, there have been several other studies undertaken to explore the effects of sensory stimulation or retraining for the upper limb post-stroke using quasi-experimental and other designs. These comprise of replicated single-system studies using A-B (Carey et al., 1993;

Hunter et al., 2008; Winter et al., 2013), a cohort study (Carey and Matyas, 2005), controlled trial (Yekutiel and Guttman, 1993) and a cross over trial (Celnik et al., 2007). Whilst there are some possible limitations with these quasi-experimental designs, the single-system studies all indicate promising effects of either sensory re-training techniques, involving specific graded discrimination tasks and attentive exploration of stimuli with vision occluded (Carey et al., 1993), or mobilization and tactile stimulation (MTS) which involves intensive hands-on proprioceptive stimulation (Hunter et al., 2008; Winter et al., 2013).

2.8.6 Mobilization and Tactile Stimulation (MTS)

MTS is an intervention that involves application of a combination of physical therapy techniques (Hunter et al., 2006). It is a 'module' of conventional hands-on therapist-delivered physical therapy that was described and defined by experienced physiotherapists in a study that used consensus methodology (modified nominal group technique) (Hunter et al., 2006). Seven senior (Band 7) NHS physiotherapists were initially interviewed, individually, and asked to describe the treatment they would provide for an upper limb that was severely affected by stroke (Hunter et al., 2008). Data from the interviews were synthesized into a draft MTS upper limb treatment schedule, and following a series of iterations, reviewed and revised by the therapists individually; a final comprehensive treatment schedule was agreed through group discussion and piloted in clinical practice. Following the pilot, further feedback on the format of the treatment schedule was used to further refine the final schedule (Appendix 1).

The final MTS upper limb schedule comprised of all the interventions that the therapists identified. These were grouped into categories that included: joint and soft tissue mobilization and manipulation techniques (passive movements, accessory movements, massage, soft tissue stretch); active retraining of selective movements in the hand, wrist and forearm; sensory stimulation of mechanoreceptors (in joints/ligaments and the glabrous (non-hairy) skin, using touch, pressure, compression, stretch); and retraining of functional patterns of movement. MTS involves active and not passive sensory stimulation and retraining, since the patient is encouraged to attend to the limb and the afferent stimulation throughout the treatment.

MTS is considered to ‘prime’ the sensorimotor system, increasing excitability and preparing it for activity, through intensive stimulation of cutaneous mechanoreceptors in the glabrous skin of the hand, using touch, pressure, and stretch or cutaneous deformation, and proprioceptors in connective tissue, muscle and joints (Winter et al., 2013). The MTS upper limb schedule included the aims of MTS identified by the therapists: recover normal extensibility of the skin, muscle, connective tissues, tendons and joints; decrease hypersensitivity; reduce pain; increase awareness of movement and coordination of movement, normalizing afferent information during functional activity (Hunter et al., 2008).

Thus, MTS addresses muscle and soft tissue shortening, which is predominant in the limbs due to inactivity post-stroke. Chronic disuse results in altered afferent input and changes to the CNS, with subsequent development of a

vicious circle (Gracies, 2005). Cutaneous and proprioceptive stimulation techniques, such as MTS, facilitate motor activity by increasing excitability in the central nervous system; the mechanism is hypothesized to be as a result of the enhanced proprioceptive input decreasing pre-synaptic inhibition, with changes seen particularly in people severely affected by stroke (Hummelsheim et al., 1995). MTS is considered to work by reawakening the limb and preparing the motor system, prior to retraining motor activity and function, promoting facilitation of plasticity as a reaction to subsequent practice of tasks (e.g. through task-specific training) (Pomeroy et al., 2011).

Following the development of the MTS upper limb schedule, the intervention was validated using a postal survey of therapy for the upper limb, involving members of the Association of Chartered Physiotherapists in Neurology (ACPIN). The treatment schedule was sent to a random sample of ACPIN members (n=400) who were asked to review the content of the schedule and send comments back to the researchers about whether the content reflected their own practice of treating the severely affected upper limb post-stroke, and identify whether any additional interventions or techniques were missing from the schedule. The response rate 30% (n=120) and the overwhelming feedback was that the content of the MTS upper limb schedule reflected conventional hands-on physical therapy for the upper limb (Hunter et al. unpublished)[1].

The effects of MTS ,applied to the upper limb, on motor impairment (Motricity Index arm section – MI), functional capacity (Action Research Arm Test –

[1] Hunter, S.M., Coleman, C., Pomeroy, V.M. Generalisability of the MTS treatment schedule.

ARAT), and somatosensation (touch/pressure sensory thresholds) were investigated through replicated single system experimental studies, which employed an A-B-A design, in sub-acute (Hunter et al., 2008) and chronic (Winter et al., 2013) stroke. Having established a stable baseline, Hunter et al. (2008) used visual analysis of data plotted over the three phases (baseline, intervention, withdrawal) to identify changes in trend, level, slope and variability between the baseline and intervention phases, and appropriate statistical analysis accounting for autocorrelation and serial dependency of the data. Winter et al. (2013) randomized duration of the baseline phase, and analysed the plotted data using the same visual analysis, but also included randomization tests. Clinically significant improvements were seen in the ARAT (increase of 6 or more points) and MI during the intervention (B) phase compared with the initial A (baseline or control) phase in both studies.

In Hunter et al.(2008), all six participants showed a change in trend, level or slope of the ARAT scores between baseline (A) and intervention (B) phases, with a mean (SD) increase of 16.17 (8.28) points, which was statistically significant (p<.001) for three of the six participants: participant 2 scores increased from 16–33 points, participant 5 scores increased from 13–22 points, and participant 6 from 4–14. MI scores also increased (mean (SD) increase of 25.33 (16.88) points) with statistical significance (p<.001) reached for participant 2 (increased score from 57–68), participant 3 (increased scored from 33–57), participant 4 (increased score from 19–43), participant 5 (increased score from 58–74), and participant 6 (increased score from 42–54). In five of

the six cases, improvements were maintained during the two weeks following withdrawal of the intervention (the second A phase).

In Winter et al. (2013), the ARAT score increased for seven of the eight participants (one participant achieved full marks at baseline and therefore there was no opportunity for change); the other change scores ranged from 1–24 points, but did not reach a level of statistical significance. The MI scores improved for all the participants and the total change scores ranged from 9–37. The improvements were maintained indicating stability of the impairment and activity limitation, and clinically significant differences were achieved for the ARAT in four of the eight cases.

Whilst quasi-experimental studies are not considered to be as high a level of evidence as an RCT or controlled clinical trial, according to the hierarchy of research evidence, the methodology of these single system studies was robust and of high quality. This included replication of findings across more than three cases, valid and reliable OMs, regular and frequent collection of data points (>8) in all phases, and appropriate visual and statistical analysis of the data, all of which increased the internal validity of the studies. The evidence therefore supports the use of MTS as an effective sensory stimulation intervention to enhance recovery of the upper limb post stroke. Unfortunately, because of the quasi-experimental methodology, this evidence has not been included in systematic reviews of sensory interventions for the upper limb.

The benefits of MTS seen in sub-acute stroke (Hunter et al., 2008), replicated by Winter et al. (2013) in chronic stroke, demonstrate the potential for recovery even during the chronic stage of stroke, when stroke survivors would be unlikely to be receiving routine therapy, reducing confounding factors. Therefore, in the absence of other therapy, it can be assumed that the beneficial effects seen during the intervention (B) phase compared to the control or baseline (A) phase were due to the MTS intervention. The justification behind this assumption is inherent to the single system study design; participants were all stable at baseline, and as the only change in the intervention (B) phase was the introduction of the MTS intervention, it is possible to conclude that the MTS (the independent variable) produced the observed changes.

It has been identified in a focus group with experienced physical therapists (Aries et al., 2019), that MTS is an intervention that is also applied to the lower limb and foot in conventional stroke rehabilitation, to prepare the foot and lower limb for activity in standing. This is supported by another study that explored the content of physiotherapy interventions for acute stroke (Tyson et al., 2009), which showed that hands-on facilitation techniques are commonly used to facilitate postural control and walking and that specific mobilization techniques, such as those used in MTS, constituted 6% of the total interventions of routine physical therapy to prepare the foot and leg. Yet, to date, the effects of MTS applied to the foot and lower leg have not been investigated in research. However, despite the positive effects seen for the upper limb, the differing neurophysiological processes related to upper and lower limbs requires

consideration, and there is uncertainty as to whether the results are directly transferable to the lower limbs.

There is a move towards promotion of more ‘hands-off’ therapy approaches in the literature, based on the evidence in support of repetitive practice and a task-orientated approach (Veerbeek et al., 2014), the inclusion of unsupervised practice in rehabilitation (Stockley et al., 2019), and the ever increasing financial and time pressures of healthcare (Chevreul et al., 2013). Nevertheless, hands-on interventions continue to be utilized post stroke (de Almeida et al., 2015; Duncan et al., 2005), and it is important to investigate the value of therapist-led one-to-one treatments, such as MTS, which are resource intensive, but which represent clinical reality and conventional practice.

2.8.7 Somatosensory stimulation of the lower limb

A small number of studies have investigated the effectiveness of somatosensory stimulation applied to the lower limb (Goliwas et al., 2015; Hillier and Dunsford, 2006; Kim et al., 2015; Lynch et al., 2007; Morioka et al., 2009). Systematic reviews have reported effectiveness of placing textured materials beneath the foot to improve postural balance and control (Orth et al., 2013), and the use of different insoles to improve perceptual motor performance (Christovão et al., 2013).

Orth et al. (2013) reviewed 21 studies and two conference proceedings, with a range of study designs, involving somatosensory stimulation of the foot through standing on textured materials, to improve postural balance and control (n= 743

participants including young adults (18-51 years), and older adults aged 64.7-79.4 years), as well as healthy people and people with chronic ankle instability, falls, Multiple Sclerosis, Parkinson's, and plantar insensitivity. The Cochrane Risk of Bias Tool was used to assess methodological quality. Despite acknowledgement of significant heterogeneity (I^2 = 85.98%), meta-analysis was used to demonstrate effectiveness of textured materials in improving perceptual-motor function in young healthy individuals (MSD -0.28; 95%CI -0.46, -0.09). However, only six studies were included in the elderly group meta-analysis and further research was advocated for the elderly and clinical populations (MSD-0.31, 95%CI -0.66, 0.05). Greater detail regarding the search strategy for this review would have improved its quality.

Christovão et al. (2013) reviewed the evidence from 12 controlled trials utilising textured surfaces, involving 392 participants with a mix of populations including functional ankle instability, older adults, fallers, stroke and diabetic neuropathy. A variety of different insoles were included: vibrating; textured; quick-comfort (prefabricated orthotics); insoles with spikes; flat insoles with different Shore A hardness (which includes most rubber materials); insoles with wedges; and balance-enhancing insoles, which were designed to facilitate foot-plantar surface sensation. They used the PEDro scale to assess for methodological quality, utilising two blinded assessors. Three studies in this review support the benefits of using vibrating insoles to enhance balance and postural control (Hijmans et al., 2008; Priplata et al., 2006; Wang and Yang, 2012), which improved balance and oscillation velocity in an antero-posterior (AP) direction. These three studies included people with diabetic neuropathy (n=17) and

healthy controls (n=15) (Hijmans et al. (2008), people with diabetic neuropathy (n=15) and stroke (n=15) (Priplata et al. (2006), and elderly fallers (n=26) and healthy subjects (n=16) (Wang and Yang (2012). Textured insoles (TIs) or textured surfaces showed a decrease in mediolateral postural oscillations and facilitated activation of tibialis anterior in healthy subjects in four studies (Hatton et al., 2009; Hatton et al., 2011; Palluel et al., 2008b; Qiu et al., 2012). However, the search strategy and terms in this systematic review were not clearly stated, so the study would not be repeatable.

The wearing of TIs to provide somatosensory stimulation to the plantar surface of the foot can be considered a therapeutic strategy to augment somatosensory awareness. Simply standing on textured material or placing TIs in the shoes gives passive stimulation to the plantar surface of the foot. However, TIs are designed to stimulate and enhance afferent input during activity, for example when walking.

Different types of foot wear and insoles may have potential to alter sensory input and, consequently, the biomechanics of gait when walking. Walking barefoot or wearing shoes with differing levels of support has been shown to influence the degree of muscle activity required for walking in healthy adults: walking barefoot or in minimally supportive footwear decreases activity of tibialis anterior at initial stance due to placing of the foot in a more plantar flexed position at heel strike (Franklin et al., 2018). It is unclear whether this is due to the difference in support offered by the different footwear, a slower walking speed when barefoot, or perhaps the differing afferent input. Furthermore, it is

unclear whether these changes seen in healthy adults are also seen in stroke survivors. The enhanced somatosensory feedback from TIs has been found to decrease metabolic activity within the pre-frontal cortex in older adults with minor mobility issues (n=14, mean (SD) age 77.1 (5.56) years), suggesting that wearing the insoles results in more automatic control of gait, with less attention required, compared to walking in shoes without insoles (Clark et al., 2014). However, caution must be applied when interpreting this research in view of the small sample size.

Taking into consideration the importance of afferent information from the plantar surface of the foot to control balance (Kennedy and Inglis, 2002), other potential mechanisms of increasing plantar stimulation have been explored.

Although the central nervous system can be primed for activity using techniques such as MTS, or sensory information can be augmented, for example, by the use of TIs, the aim of these strategies is to influence motor activity and function. It is, therefore, common practice within therapy sessions to deliver combination treatments; for example: somatosensory electrical stimulation and task-specific training (Fleming et al., 2015); repetitive facilitative exercises plus an ankle-foot orthosis (Kazutoshi et al., 2017); or mirror therapy plus task-specific training (Hsieh et al., 2018). Developing evidence for complex hands-on therapy and applying the findings of research to practice within stroke rehabilitation is particularly challenging, due in part to a limited understanding and knowledge of therapy treatments (Langhorne et al., 2011), which involve many different aspects (Craig et al., 2006) and potential combinations.

2.8.8 Sensory re-training for the foot and ankle after stroke

Somatosensory stimulation of the foot and ankle after stroke has been investigated with the purpose of improving balance or gait in a small number of studies (Hillier and Dunsford, 2006; Kim et al., 2015; Lynch et al., 2007; Morioka and Yagi, 2003).

Hillier and Dunsford (2006) used a single-case repeated measures quasi-experimental design, with three subjects who had a right-sided stroke more than two years previously. A retraining intervention was delivered that included: education; practice in detection and localization; hardness, texture and temperature discrimination; and proprioceptive training. Measures were undertaken twice at baseline and twice post-intervention. All participants demonstrated a positive trend for improved tactile appreciation, with two reaching statistical significance (subject one p=0.01 for detection; subject three p=0.03 for detection and localization). Subject two recorded a significant change in duration of single leg stance (p=0.017), and one subject reported a 'sensory reawakening', stating '*thank you for helping me find my foot again*' (Hillier and Dunsford, 2006, p.240).

Lynch et al. (2007) and Morioka and Yagi (2003) both undertook randomized controlled pilot trials. Lynch et al. (2007) included 21 stroke survivors between 13 days and four months post-stroke, and compared a sensory retraining programme (the same as delivered by Hillier and Dunsford, (2006)), for the more affected lower limb with a sham intervention (relaxation). Significant

improvements (p=<0.05) were seen over time for light touch, postural control, timed gait and use of a walking aid. Morioka and Yagi (2003) investigated the effect of perceptual learning exercises for hardness discrimination on standing balance for stroke survivors (one to four months post-stroke) (n=26). They used feedback to enable learning, through an exercise to discriminate the hardness of sponge rubber placed under the plantar surface of the foot. They also reported improvements in postural control, with postural sway decreasing significantly (p< 0.01).

These promising results for all these studies were achieved within just two weeks. However, the result for Morioka and Yagi (2003) could possibly be attributed to increased time spent in standing for the experimental group over the control group, and not necessarily the sensory intervention. It is not known whether a change in sensory awareness contributed to the results, or perhaps just an increase in muscle strength associated with the extra standing practice.

Strengths of the Hillier and Dunsford (2006) study were the clearly stated inclusion and exclusion criteria, the use of a blinded assessor and testing of intra-rater reliability for OMs. Also, the inclusion of stroke survivors two years post-stroke, who were able to stand but not necessarily walk, means the work could be applicable to many stroke survivors; however, there is no justification offered as to why only participants with right-sided strokes were included. Nevertheless, due to the design of these studies, neither Hillier and Dunsford (2006) nor Lynch et al. (2007) can fully corroborate the benefits of sensory re-training for the lower limb post-stroke. Hillier and Dunsford (2006) included just

three single case studies, and Lynch et al. (2007) acknowledged a reduced power of the study, with recruitment of just 21 participants as opposed to the 32 stipulated by the power calculation; therefore, it was not possible to detect between-group changes. There was also no long-term follow up to allow assessment of the carryover effect of the intervention, and the inclusion criteria required participants to be able to walk 10 metres (10m), so many stroke survivors who may have benefitted from sensory re-training could potentially have been excluded. Strengths to note relating to Lynch et al. (2007) and Morioka and Yagi (2003) are randomization of participants to group allocation, and blinded assessment, both of which help reduce potential for bias. However, there is no statement relating to ethical approval in the Morioka and Yagi (2003) study. Also worth noting is that, although significant changes were reported for the BBS in Lynch et al. (2007), it is not clear whether the change reached the level of 5–7 BBS points, which is the necessary change to assure the changes were associated with the intervention (Stevenson, 2001).

Kim et al. (2015) concluded that even a single dose of somatosensory stimulation, involving stretching, distraction and compression to the foot and ankle, had a significant effect ($p<0.05$) on the BBS score of six stroke survivors who were independently mobile (MD 3.16) and six who were unable to walk unassisted (MD 7.33). This latter group reached the necessary 5–7 BBS point change, whereas the independently mobile group did not. This was potentially due to the higher functioning participants reaching the ceiling threshold that has been reported for the BBS (Blum and Korner-Bitensky, 2008).

It is important to consider the dose and intensity of the treatments delivered. A single dose of this same sensory intervention (n=14) was compared with 24 sessions given three times per week for eight weeks (n=16) (Kim, 2015). The trunk impairment scale was used to assess static and dynamic sitting balance and also trunk coordination (Verheyden et al., 2004). The author infers that the BBS measures static balance and reports that the scores for static balance did not reach significant levels for either group; contrary to this opinion, the BBS actually measures both static and dynamic balance (Blum and Korner-Bitensky, 2008). However, even the single dose of sensory intervention resulted in a significant change in dynamic balance as measured by the trunk impairment scale ($p<0.01$) and significant changes were seen for both dynamic balance and trunk coordination for the group who received eight weeks of intervention ($p<0.01$) (Kim, 2015). It must be remembered that the trunk impairment scale is only assessing changes to the trunk in sitting and, therefore, the noted changes in dynamic balance may not be transferrable to function, for example walking. Also, of note were small sample sizes, absence of consideration of the reliability of the OMs, neither of these studies included random allocation, and assessors were not blinded, so the possibility of bias cannot be ruled out. Again, the results of these trials should be interpreted with caution. Furthermore, there were no follow-up measurements undertaken, and it is not known whether any changes would have been maintained. In view of these major limitations it is not possible to draw relevant conclusions from these studies. Although a statement is included that the research ‘conformed to the ethical principles of the Declaration of Helsinki’ it is unclear whether specific ethical permission was granted for the study (Kim et al., 2015 p.1080).

2.8.9 TIs or textured surfaces as sensory stimulation

The influence of textured surfaces has been investigated, with some studies standing participants on a textured surface (Clark et al., 2014; Corbin et al., 2007; Hatton et al., 2009; Hatton et al., 2011; Hatton et al., 2012; Kelleher et al., 2010; Nurse et al., 2005) and others exploring the effects of wearing TIs in the shoe (Aruin and Kanekar, 2013; Baron et al., 2014; Dixon et al., 2014; Hartmann et al., 2010; Kalron et al., 2015).

In an observational study of 33 healthy adults (Corbin et al., 2007), balance was measured in three planes using the AccuSway PLUS Balance Platform; TIs were shown to improve postural control in standing when worn just for testing, with a significant interaction between vision and texture for COP deviation in bilateral stance ($F_{1,32}$ =5.11, p =0.03). Testing with the eyes closed without wearing the TIs resulted in a significant difference (increase) in COP deviation in comparison to the eyes open test; however, when the TIs were worn there was no significant difference in COP deviation between eyes open and closed.

When used with people with Multiple Sclerosis, both smooth and TIs resulted in improved spatiotemporal parameters of gait (measured with the GAITRite system), with mean stride increases of 3.5cm for the 46 participants (Dixon et al., 2014). This could perhaps be attributed to the fact that an insole (regardless of whether it was smooth or textured) provided a tighter fit of the shoe, giving a sense of greater stability, which itself had an effect on gait parameters.

Interestingly, Aruin and Kanekar (2013) applied a TI to the ipsilesional foot post-stroke, creating discomfort, with the aim of facilitating better weight transference to the contralesional side. They found that improved weight transference through this leg did occur. However, the results of this study need to be interpreted with caution, as it included a sample of just four stroke survivors, with no mention of how the sample was recruited; consequently, the potential for bias within the study is high.

The wearing of TIs, which provide sensory stimulation to the plantar surface of the foot, is not currently part of routine therapy post-stroke, despite them having been shown to improve both balance (Christovão et al., 2013) and gait variables in people with other neurological conditions affecting sensibility in the foot, such as Multiple Sclerosis (Dixon et al., 2014).

2.8.10 Vibration

The addition of increased afferent input via vibration has also been explored. One pilot RCT of 44 chronic stroke survivors applied low-amplitude segmental muscle vibration therapy at 120Hz, to the tibialis anterior muscle, exploring its effects on gait speed (Paoloni et al., 2010); and in a pre-experimental study of non-specified stroke duration (n=13), vibration was applied to the gluteus medius muscle and the anterior tibial muscle at 83Hz (Kawahira et al., 2004). Both studies reported significantly increased gait speed with the stimulation ($p<0.01$) and Paoloni et al. (2010) also reported increased activation of tibialis anterior, as monitored by surface EMG, in the experimental group. The methodology of Paoloni et al. (2010) was rigorous, in that it included

randomization, with strict inclusion criteria, and gait analysis was undertaken offline by an assessor blinded to group allocation. The results of Kawahira et al. (2004) should be interpreted with caution because there was no control group, no mention of blinding within the study and no summary data were presented; hence, there is the potential for a high risk of bias within this study.

Application of vibration at 80Hz and 1mm in amplitude, applied to the Achilles tendon, with the purpose of interfering with ankle proprioception, was also explored in a cross-sectional study (convenience sample) of ambulatory stroke survivors (both acute and chronic stroke, n=35) (Lin et al., 2012). Participants were grouped according to intact or impaired joint position sense; no significant effects were found for plantar sensitivity or leg muscle strength between the groups. The differences in stride characteristics were non-significant for both vibration and non-vibration conditions (p =.354). It should be noted that there was no blinding within this study for either assessments or analysis.

It has also been found that sub-sensory vibrations (with noise amplitudes set to 90% of sensory threshold, band-limited to 100Hz) applied to the feet of elderly recurrent fallers (n=18) and non-fallers (n=18) reduced the stride ($F_{1,45}$ = 9.85, p=0.003), stance ($F_{1,45}$ = 13.60, p<0.001 and swing phase ($F_{1,45}$ = 7.40, p=0.009) variability when walking (Galica et al., 2009). However, there were limitations to this study including small sample size, no randomization or blinding within the study and the fact that the sub-sensory threshold could not be set for some participants because they were unable to feel the vibrations from the insole on a maximum setting.

2.8.11 Combination treatments

Due to the heterogeneous nature of stroke, specific stand-alone rehabilitation treatments are rarely delivered, and combinations of different treatments form a regular part of conventional rehabilitation (section 2.8.7). An excellent example of a combination intervention for the upper limb post-stroke is the COMPoSE study, which combines both somatosensory and motor training delivered contemporaneously in a specific task, facilitating sensorimotor integration (Gopaul et al., 2018). However, the effects of combining a sensory intervention, to prime or augment motor activity and motor control, with repetitive task-specific practice has not yet been explored for the lower limb post-stroke.

2.9 Summary

This chapter has highlighted that various different sensory interventions have been explored in a range of different study designs, utilising a selection of different treatment interventions. Many of the reviews discussed relate to sensory stimulation or retraining for the upper limb post-stroke. It is also recognised that sensory information from other modalities e.g. vestibular, auditory and multisensory, influences movement (Schaaf and Case-Smith, 2014); nevertheless, it is not possible to explore these within the scope of this thesis. Sensory stimulation techniques are applied to the lower limb within clinical practice, and yet there is no systematic review or synthesis of the findings of somatosensory interventions for the lower limb to improve balance and gait post-stroke. Hence, this is the focus of this thesis. It is important that research for healthcare interventions is informed by best available evidence

from systematic reviews and patients' views and experience (Gopalakrishnan, 2013). To gain a more in-depth insight into the extent and quality of evidence already undertaken relating to somatosensory stimulation for the lower limb post-stroke, a systematic review was undertaken: Study 1 of this thesis.

3 CHAPTER THREE: STUDY 1 – EFFECTIVENESS OF SOMATOSENSORY STIMULATION FOR THE LOWER LIMB AND FOOT AFTER STROKE: A SYSTEMATIC REVIEW

This chapter comprises of the methods and results of Study 1 of this thesis: a systematic review relating to somatosensory stimulation for the lower limb and foot after stroke.

3.1 Research aims and objectives:

The research aim was:

To explore the evidence around somatosensory stimulation of the foot and lower leg to improve function after stroke.

Research objective:

1.1 To systematically review the published literature investigating the effectiveness of somatosensory stimulation applied to the lower leg and foot to improve balance and mobility after stroke.

3.2 Methodology for Study 1

3.2.1 Design

To address the research aim, a systematic review was undertaken, which involved identification of relevant literature related to somatosensory stimulation to the lower limb after stroke; extraction of pertinent data was undertaken, with appraisal of study designs. A systematic review enables synthesis of information from several separate studies (Green, 2005); rigorous methodology is important when assimilating the extensive amount of literature available, informing healthcare decisions (Clarke, 2007). Indeed, it has been suggested that no research should be initiated without first undertaking a systematic review of previous research; important design implications for future studies can be understood based upon preceding literature (Clarke, 2004).

It was not possible to simply update an existing review, because a review did not exist which solely focused on somatosensory stimulation to the lower limb. For example, Schabrun and Hillier (2009) included interventions for both the upper and lower limbs, categorising these interventions into active and passive sensory stimulation; it is not always possible to classify in this manner. Sensory interventions can include aspects to re-train sensation, and these can specifically involve active attention, for example discrimination of textures through touch (Carey et al., 2011); nevertheless, it may be that passive stimulation could also influence movement and function of the lower limb as it was shown to for the upper limb (Celnik et al., 2007; Conforto et al., 2007; Wu et al., 2006). Therefore, the decision was made to include all interventions

which could be referred to as sensory stimulation whether this was a passive intervention or active retraining in this current systematic review.

A systematic review of published literature (1st January 1997 to 28th November 2018) relating to effectiveness of somatosensory stimulation of the lower limb in stroke survivors to improve balance and gait was undertaken.

3.2.2 Search strategy

A search strategy was developed with support from a health librarian using the following key words linked with Boolean operators:

- “Cerebrovascular accident” OR CVA OR “acquired brain injury” OR “traumatic brain injury” OR “head injury” OR “TBI” OR “ABI” OR hemiplegia OR hemiparesis OR “upper motor neuron lesion”

AND

- Sens* OR stimulat* OR somatosens* OR propriocept* OR afferent OR mobilisation OR mobilization OR manipulat*

AND

- Foot OR leg OR “lower limb” OR “lower extremity”

AND

- Walk* OR gait OR mobil* OR step OR stance OR ambulat* OR “weight bear*”

AND

- Randomised controlled trial OR “randomised controlled trial” OR randomized controlled trial OR “randomized controlled trial”

NOT

- “Functional electrical stimulation” OR functional electrical stimulation OR FES

The full search strategy is presented in Appendix 2.

Using the EBSCO search engine, the following databases were searched on 28th November 2018: AgeLine, AMED, CINAHL PLUS, MEDLINE, PsycARTICLES, PsycINFO, SPORTDiscus. On the same date, Web of Science, Cochrane trials and PEDro databases were also searched. Important health databases were therefore included (Boland et al., 2017).

3.2.3 Inclusion/exclusion criteria

Inclusion of studies was based on PICOS (Population, Intervention, Comparison, Outcome, Study type) (Akobeng, 2005):

- Population: adult stroke survivors aged ≥18 years
- Intervention: somatosensory intervention involving sensory stimulation (mechanical or tactile, thermal, electrical for the purpose of sensory stimulation only, and proprioception) of the contralesional lower limb and/or foot
- Comparison: where applicable, standard care, routine/conventional therapy, or placebo (control)

- Outcome: valid and reliable outcomes related to gait and/or balance, for example, gait parameters, BBS
- Study type: RCTs, published in English language, with a clear statement of appropriate ethics approval.

Studies were excluded if they involved: participants with neurological conditions other than stroke; functional electrical stimulation and other interventions with the purpose of eliciting muscle contraction; sensory stimulation combined simultaneously with active or active assisted movement e.g. Proprioceptive Neuromuscular Facilitation (PNF); acupuncture; transcranial magnetic stimulation; transcranial direct-current stimulation; visual or auditory stimulation or feedback only, including visual biofeedback. Conference abstracts or other 'grey' literature, including unpublished studies and theses, were also excluded.

3.2.4 Procedures

Following the search, citations were exported to Endnote, where duplicates were identified and removed; this was checked manually for accuracy using a database exported from EBSCO and Web of Science.

The remaining titles and abstracts were screened independently by two researchers (AA, SH) according to inclusion and exclusion criteria; following discussion and subsequent agreement, non-relevant citations were excluded. The full texts of the remaining articles were retrieved and again screened independently by the same two researchers. Discussion and agreement about inclusion/exclusion of individual studies resulted in the final citations being

identified for review. A third researcher (VP) was also available in case of any disagreement. If uncertainty existed as to whether the electrical treatment delivered was of a sensory nature as opposed to creating a muscle contraction, authors were contacted via email for clarification to ensure the studies met the inclusion criteria of the systematic review. The reference lists of the included studies were hand-searched and any further citations that appeared to be appropriate for review were identified and screened by both researchers independently, according to the procedures above. Details are presented in the PRISMA flow diagram (Moher et al., 2009) (figure 3.1).

3.2.5 Data extraction and analysis

Data from included studies were extracted (by AA) using a data extraction tool (Appendix 3) to identify and summarize pertinent data: information about the study design, sample, interventions, OMs, results, and authors' conclusions were extracted and tabulated to facilitate narrative synthesis of findings (tables 3.2 and 3.3). Due to heterogeneity of studies, specifically populations/samples, interventions and outcomes, meta-analysis of data was not undertaken. However, where effect sizes were not stated, or had been calculated using an alternative method, these were calculated wherever possible. Prior to calculating the effect size, the pooled SD was calculated. The baseline SD, pooled over the two (or more) groups as the denominator (Sim and Wright, 2000), was used when calculating the effect size; this method was selected to enable the SD to be based on a larger sample size, and thus be more precise, than if only the SD of the control group had been used.

If both groups were the same size this was calculated using the equation below:

$$SD_{pooled} = \sqrt{\frac{SD_1^2 + SD_2^2}{2}}$$

However, if the group sizes differed, a weighted pooled SD was calculated using the following equation:

$$SD_{pooled} = \sqrt{\frac{SD_1^2 (n_1 - 1) + SD_2^2 (n_2 - 1)}{n_1 + n_2 - 2}}$$

The between-group effect size was then calculated by the following method:

$$\frac{\text{(post-intervention mean 1 - post-intervention mean 2)}}{\text{pooled SD at baseline}}$$

Effect sizes calculated from studies with a small sample were indicated by an asterisk in the table of results (table 3.5). A threshold of 30 (total sample for the study) was used to indicate a small sample. This was based upon the value that is suggested for the central limit theorem (Kwak and Kim, 2017). The principle of the central limit theorem is that as the sample size drawn from a population grows, its mean will more closely match the population mean, with less

variation in the results (Kwak and Kim, 2017).This process therefore enabled small studies (n≤30) with a potentially skewed distribution to be identified.

3.2.6 Assessment of methodological quality

Methodological quality of the studies was assessed by the researcher (AA) using the Cochrane Collaboration tool to assess risk of bias in RCTs (Higgins et al., 2011) (table 3.4). Assessment of quality was judged according to the Agency for Healthcare Research and Quality standards (Lohr and Carey, 1999), using the criteria in table 3.1.

Table 3.1 Thresholds for Converting the Cochrane Risk of Bias Tool to Agency for Healthcare Research and Quality Standards (Good, Fair, and Poor)

Quality level	Threshold
Good	All criteria met (i.e. low for each domain)
Fair	One criterion not met (i.e. high risk of bias for one domain) or two criteria unclear, and the assessment that this was unlikely to have biased the outcome
Poor	One criterion not met (i.e. high risk of bias for one domain) or two criteria unclear, and the assessment that this was likely to have biased the outcome, and there are important limitations that could invalidate the results, or two or more criteria listed as high or unclear risk of bias

3.3 Results of Study 1

The initial search identified 433 citations (details of number of citations identified from each database are available in Appendix 4), of which 144 duplicates were removed. Of the 289 studies screened from titles and abstracts, 254 were removed, leaving 35 studies for review from the full text. Of those, 24 were excluded[2] for the following reasons: not RCT (n=3), conference abstract only (n=1), thesis (2), balance and gait were not outcomes measured (n=1), intervention also included muscle contraction (n=11), not sensory

[2] (An and Jo, (2017); Bae et al. (2015); Chen et al. (2011); Cheng et al. (2010); Choi et al. (2013); Ertzgaard et al. (2018); Hsu et al. (2013); Knutson et al. (2013); Koseoglu et al. (2017); Kwong et al. (2018); Lau (2011); Lau (2013); Lee et al. (2016); Liang et al. (2012); Maupas et al. (2017); Morreale et al. (2016); Ng (2005); Okawara and Usuda, (2015); Park et al. (2015); Ribeiro et al, (2013); Spaich et al. (2014); Sungkarat et al. (2011); Xu et al. (2017); Yavuzer et al. (2016)).

stimulation/sensory stimulation not manipulated (n=4), sensory stimulation was visual or auditory not mechanical (n=1), no statement of appropriate ethics approval (n=1). Details of the studies that were excluded after reading the full texts, with reasons for exclusion, are given in Appendix 5. Figure 3.1, a PRISMA flowchart, summarizes the process and reasons for exclusion.

A total of 17 trials were included in the review. Further articles identified from manual searching of the reference lists of included studies, and their suitability for inclusion or exclusion (with reasons), are detailed in Appendix 6.

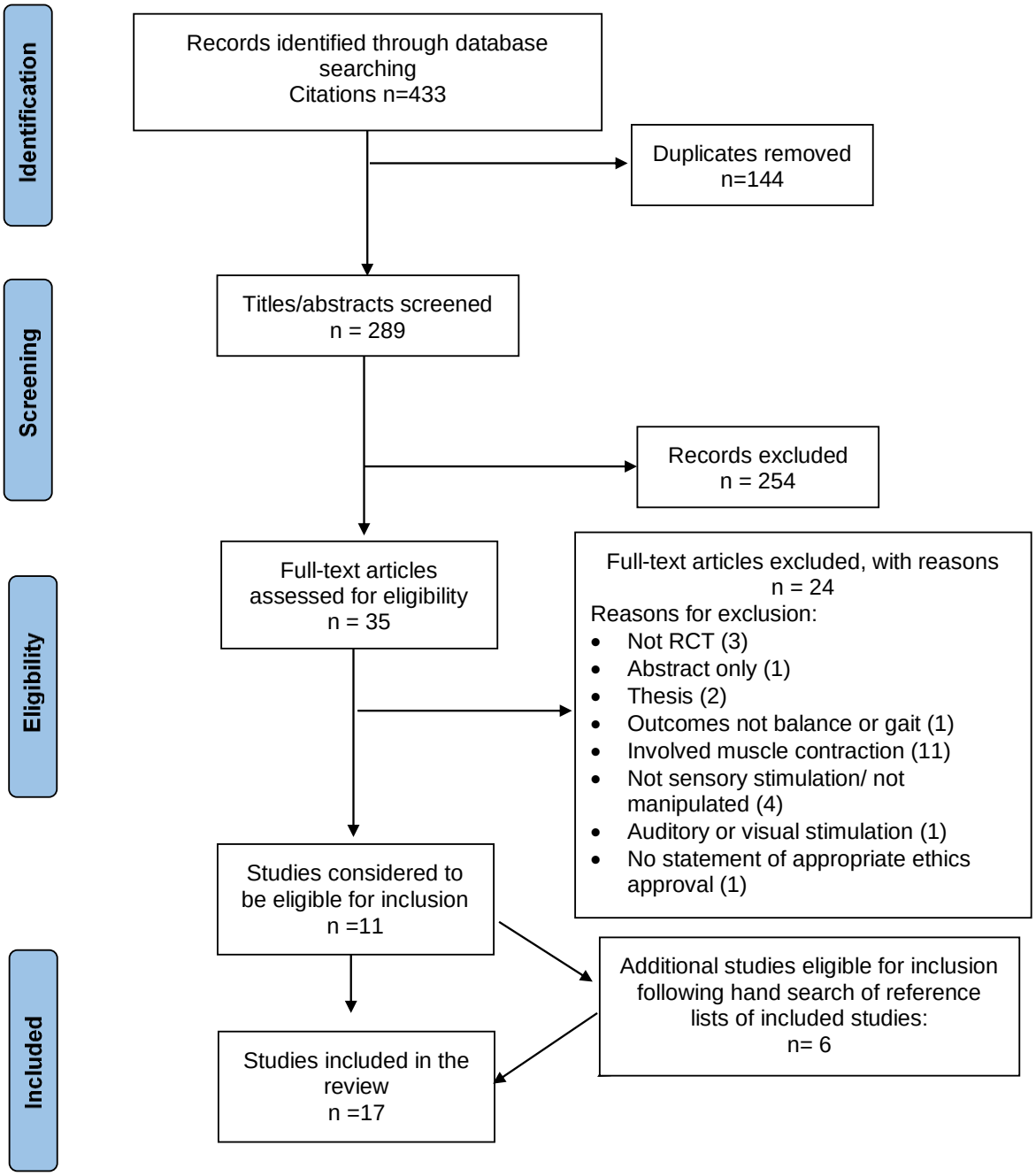


Figure 3.1 Flowchart of the data collection and screening process, based on 2009 PRISMA flow diagram

(Moher et al., 2009)

Table 3.2 Details of study participants and group allocation

Study	Study design/ sample size	Study group	No of partici-pants	Sex M/F	Side of paresis L/R	Age Mean (SD)	Mean (SD) time post-stroke	Type of stroke: Infarct/ haemorrhage	No. finished intervention
Bayouk et al. (2006)	Matched pairs RCT n=16	**Task orientated training (TOT), different surfaces proprioception feet/ankles and/or vision manipulated** (Total 16 hours)	8	6/2	6/2	68.4 (7.1) yrs	7.1 (12.5) yrs	Not stated	8
		TOT eyes open, hard surface	8	3/5	4/4	62.0 (4.6) yrs	5.7 (6.9) yrs		8
Brogårdh et al. (2012)	Double-blinded RCT n=31	**Whole body vibration (WBV) training** (Total 9 hours)	16	13/3	9/7	61.3 (8.5) yrs	37.4 (31.8) months	14/2	16
		Placebo vibrating platform (0.2mm amplitude)	15	12/3	7/8	63.9 (5.8) yrs	33.1(29.2) months	13/2	15
Cho et al. (2013)	Randomized placebo-controlled trial n=42	**TENS** (Total 1 hour)	22	14/8	Not stated	55.2 (11.49) yrs	15 (4.9) months	15/7	22
		Placebo TENS	20	13/7	Not stated	55.7 (8.6) yrs	13.9 (5.1) months	14/6	20
Ferreira et al. (2018)	RCT n=24	**Postural insoles** influencing muscle proprioception (3 months of insole use)	12	11/1	6/6	59.2(10.4) yrs	3.9 (1.5) yrs	10/2	12
		Placebo insoles, no corrective elements.	12	5/3	6/2	60.3(13.3) yrs	3.3 (1.1) yrs	6/2	8
Goliwas et al. (2015)	RCT n=27	Standard 6-week therapeutic rehabilitation programme + 15 or 20 mins (UNCLEAR) of **sensorimotor foot stimulation (SFS)** (Total approx. 22.5hrs)	13	5/3	2/6	62.3(9.4) yrs	4.4(3.1) yrs	8/0	8
		Standard 6-week therapeutic rehabilitation programme	14	7/8	5/7	67.7 (9.2) yrs	4.1 (2.8) yrs	12/0	12
Guo et al. (2015)	RCT n=30	**WBV training** (Total =53.33 hours)	15	Not stated	Not stated	53.8 (6.0) yrs	66.9 (42.9) days	10/5	15
		Placebo WBV (machine off)	15	Not stated	Not stated	54.3 (6.8) yrs	59.4 (61.4) days	12/3	15
Jung et al. (2017)	RCT n=41	**TENS to peroneal nerve** + Sit to stand (STS) training, 15 mins/day, 5x/week +	20	11/9	10/10	56.2 (10.4) yrs	6.5 (2.7) months	12/8	20

		therapy, 1 hour a day, 5x/week, six weeks (Total 37.5 hours)							
		Placebo TENS + same STS training therapy, 1 hour/day, 5x/week, 6 weeks	21	12/8	11/9	56.3 (10.2) yrs	6.6 (2.5) months	11/9	20
Kluding and Santos (2008)	Pilot RCT n=17	2/week therapy for 4 weeks involving functional training **+ Contralesional ankle joint mobilizations (5 minutes) 2x/week** (Total =2.67 hours)	8	4/4	4/4	55.5 (10.8) yrs	18.3 (11.8) months	Not stated	8
		2x/week therapy for 4 weeks involving functional training	9	5/3	7/1	56.1 (13.7) yrs	24.6 (15.7) months	Not stated	8
Lau et al. (2012)	Single blinded RCT n=82	**WBV training** 3x/wk for 8 wks, 24 treatments (Total 10 hours, but only 4.2 hours WBV)	41	26/15	20/21	57.3 (11.3) yrs	4.6 (3.5) yrs	20/21	38
		Same exercises on platform but with **no vibration.**	41	32/9	14/27	57.4 (11.1) yrs	5.3 (4.2) yrs	21/20	38
Lynch et al. (2007)	Pilot single-blind RCT n=21	Daily 1-hour group session: lower-limb strength, balance/cardiovascular fitness, + 30–60 minutes/day individual therapy session + **ten 30-minute sensory retraining sessions (2-week period)** (Total =12.5 hrs)	10	7/3	5/5	61.0 (15.8) yrs	48.7 (31.1) days	9/1	10
		Daily 1-hour group session: lower-limb strength, balance/cardiovascular fitness, + 30–60 minutes/day individual therapy session **+standing same time period (eyes closed) and 30 mins of relaxation techniques (supine, eyes closed)**	11	9/2	3/8	62.0 (12.3) yrs	47.8 (27.7) days	9/2	11
Ng and Hui-Chan (2009)	Randomized placebo-controlled clinical trial (4 groups) n=109	**TENS** + Exercise (Total 40 hours, 20 hours TENS and 20 hours exercise)	27	21/6	17/10	57.8 (7.3) yrs	4.7 (2.8) yrs	11/16	26
		TENS	28	24/4	18/10	56.5 (8.2) yrs	4.9 (3.9) yrs	13/15	25
		Placebo stimulation + Exercise	25	20/5	13/12	56.9 (8.6) yrs	4.7 (3.4) yrs	15/10	23
		Control	29	20/9	20/9	55.5 (8.0) yrs	5.0 (3.0) yrs	16/13	27
Paoloni et al. (2010)	RCT n=44	50 minutes physical therapy session, 3 x/week, (4 weeks) + **segmental muscle vibration**	22	19/3	11/11	59.5 (13.3) yrs	1.9 (0.59)	Not stated	22
		50 minutes physical therapy session, 3 x/week, (4 weeks) (Total = 10 hours)	22	20/2	10/12	62.6 (9.5) yrs	1.86 (0.61) yrs	Not stated	22

Park et al. (2014)	RCT n=34	30-min exercise with a physical therapist **+TENS** (Total = 30 hours, 15 hours TENS and 15 hours exercise)	17 (but characteristics for 15)	12/3	10/5	71.2 (3.46) yrs	18.7 (2.46) months	Not stated	15
		30-min exercise with physical therapist **+ placebo TENS**	17 (but characteristics for 14)	8/6	8/7	14 (3.8) yrs	18.6 (1.7) months	Not stated	14
Suh et al. (2014)	Single-blind RCT n=42	30 mins standard rehab + **Electrical stimulation**- 60 mins single session, interferential current (Total 1 hour)	21	15/6	Not stated	54.4 (12.1) yrs	15.05 (4.9) months	14/6 (? Why n=20, not n=21)	21
		30 mins standard rehab + **Sham electrical stimulation**- 60 mins single session, interferential current	21	14/7	Not stated	53.9 (12.4) yrs	13.9 (5.1) months	15/5 (? Why n=20, not n=21)	21
Tankisheva et al. (2014)	RCT n=15	**WBV training** (Total 9 hours)	7	4/3	3/4	57.4 (13.0) yrs	7.71 (8.6) yrs	6/1	6
		No additional training program; asked not to change lifestyle	8	6/2	4/4	65.3 (3.7) yrs	5.28 (3.6) yrs	4/4	7
van Nes et al. (2006)	RCT n=53	**WBV training** (Total 9 hours, 1.5 hours WBV)	27	16/11	13/14	59.7 (12.3) yrs	38.9 (9.2) days	16/11	27
		Exercise therapy on music (ETM), four sessions of 45 seconds stimulation 5x/week, 6 weeks. During ETM, patients adopted standing position as during the WBV.	26	14/12	15/11	62.6 (7.6) yrs	34.2 (11.1) days	22/4	24
Yan and Hui-Chan (2009)	Single blind stratified RCT n=56	Standard rehab (OT & PT) each lasting for 60 min + **transcutaneous electrical stimulation (TES)** (Total = 15 hours)	19	9/10	11/8	68.4 (9.6) yrs	9.2 (4.4) days	16/3	17
		Placebo stimulation	19	10/9	11/8	72.8 (7.4) yrs	9.9 (2.6) days	16/3	17
		Standard rehab (OT & PT) each lasting for 60 min	18	9/9	11/7	70.4 (7.6) yrs	8.7 (3.3) days	15/3	16

Abbreviations: Min minutes, SD Standard deviation, SFS Sensorimotor foot stimulation, STS Sit to stand, TOT Task orientated training, TENS/TES Transcutaneous electrical nerve stimulation, yrs=years, WBV whole body vibration, Wk=Week

Table 3.3 Outcome measures, results and effect sizes

Study	Study design	Intervention group and dose	Oms	Results	Effect size and (between-group effect size)
Bayouk et al. (2006)	Matched pairs RCT	**TOT, different surfaces proprio-ception feet/ankles and/or vision manipulated** 1 hour, 2x/week (8 weeks), 30 mins session aimed at improving static and dynamic balance, exercises executed while proprioception of feet and ankles and/or vision was manipulated.	**Timed 10m walking test** (10MWT) **Displacement of COP** (Matscan system) during double-legged stance and sit-to-stand (STS) tasks	**10MWT:** significant ↓ time (p<.05): 12.2%. **COP variability:** significant ↓ COP variability (p<.05) in ML (eyes open, firm surface) and AP directions (eyes open, soft surface). **COP total excursion for STS** under all 4 conditions: significant ↓ (p<0.05) COP total excursion, AP axis for eyes open/soft surface. No significant main effects of group x test interaction under other sensory conditions.	**10MWT:** *0.22 (0.12) $
		TOT eyes open, hard surface		**10MWT:** significant ↓ time (p<.05): 12% **COP total excursion for STS** under all 4 conditions: significant ↓ (p<0.05) COP total excursion, AP axis for eyes open soft surface condition. No significant main effects of group x test interaction with other conditions.	*0.24 (0.12) $
Brogårdh et al. (2012)	Double-blinded RCT	**Whole body vibration (WBV) training** Session ≤ 45 minutes Amplitude 3.75, frequency 25Hz. Standing, knee flexion 45–60˚. 12 sessions (2x/week for 6 weeks) WBV ↑ 40–60 seconds per repetition, number of repetitions from 4–12.	**Isokinetic and isometric knee muscle strength** (Biodex Multi-Joint System 3 PRO dynamometer) standard protocol **Modified Ashworth scale (MAS)**: hip adductors, hip and knee extensors/flexors, and ankle dorsi/plantarflexors **Berg Balance Scale (BBS)** **Timed Up & Go (TUG) test** **10MWT comfortable and fast gait speed (CGS and FGS) 6-minute Walk Test (6 minWT)** **Stroke Impact Scale (SIS)**	Adjustments made for between-group differences at baseline in TUG, 6minWT, and BBS. Non-significant differences in all OMs after training. Significant but small improvements were found within both groups after WBV training. Intervention group improved significantly in balance (4%; p<.05) and gait performance (TUG, 8%; CGS and 6minWT, 5%; p<.05).	**BBS:** 0.91 (0.09) $
		Placebo vibrating platform Amplitude 0.2mm, frequency 25Hz		Significant but small improvements found within both groups after training. Control group improved significantly in isometric knee extension strength in the paretic limb (12%; p<.05) and in gait performance (TUG and 6minWT, 6%; p<.05).	0.13 (0.09) $

Cho et al. (2013)	Random-ized placebo-controlled trial	**TENS to gastrocnemius** Frequency 100 Hz, pulse width 200 µs (2-3 times sensory threshold, 60 mins)	**MAS** Spasticity of ankle plantarflexor. **Handheld dynamometer (HHD)** to measure the **resistive force (kg) caused by spasticity** **Postural sway length (PSL)** while standing with eyes open, then closed, and on an unstable surface with eyes open	**MAS:** Spasticity ↓ by 29% **Handheld Dynamometer (HHD) resistance** ↓30% **Postural imbalance**: **Eyes-open: PSL** ↓16% **Eyes closed: PSL** ↓ significantly (*p*<.05) by 23%, the only condition with a significant difference (sig diff) between groups (*p*<.05) **Unstable surface/eyes open:** PSL ↓ by 16% Results: back at baseline values after a day.	No SDs presented; effect sizes could not be calculated
		Placebo TENS Same electrode placement; no electrical stimulation		**MAS:** Spasticity ↓ by 13% **Handheld Dynamometer (HHD) - resistance** ↓ 19% **Postural imbalance**: **Eyes-open: Postural sway length (PSL)** ↓ 9% **Eyes closed: PSL** ↓ significantly (*p*<.05) by 8. Only condition with sig diff between groups (*p*<.05) **Unstable surface eyes open:** PSL ↓ by 9% in control. Results back at baseline values after a day.	
Ferreira et al. (2018)	RCT	**Postural insoles** with pronating heel wedge (6 mm), a pronating band and metatarsal-phalangeal inlay to stabilize different segments of foot in neutral position, designed for equinovarus foot.	Evaluations on placement of postural insoles and after three months insole use (barefoot, self-selected pace over 10m). **Three-dimensional gait analysis** (SMART-D 140® system) 1) barefoot, 2) with habitual shoes 3) with habitual shoes + insoles Kinematic data with force plate (Kistler, model 9286BA): **COP displacement + time of contact between foot and surface of force plate**	**Gait analysis**: No statistical sig diff for gait velocity. **Kinematic aspects:** intra-group analysis. After three months of insole use, significant gains in ankle dorsiflexion (*p*=0.007), peak knee flexion (*p*=0.038) in comparison to the control group. No sig diffs found regarding the hip and pelvis.	**Mean velocity** *0.06 (0)
		Placebo insoles, no corrective elements.		**Gait analysis/kinematic aspects:** No significant changes observed.	*0.03 (0)
Goliwas et al. (2015)	RCT	Standard six-week therapeutic rehabilitation programme + 15 or 20 mins (UNCLEAR) of **sensorimotor foot stimulation (SFS)** 15 or 20 mins (UNCLEAR) of SFS (25 sessions)	**Zebris FDM-TDL treadmill with Win FDM-T software** (5,376 pressure sensors) measured **weight distribution on the feet.** Taken first and last day in rehabilitation facility. Eyes open/closed.	**Differences in weight distribution:** End test eyes open and closed – sig diff (*p*<0.05) between baseline and end, 30.6 ± 19.6% to17.8 ± 15.2% (p<.05), **Reduction of the differences in weight distribution:** Sig diff seen between experimental group (12.2 ± 12.9%, *p*<.05) vs control group, (2.4 ± 4.9%) with eyes open (*p*>0.05).	**Difference in weight distribution** *0.68 (0.05) $

		Standard 6-week therapeutic rehabilitation programme		**Differences in weight distribution:** End test with eyes open and eyes closed: 20.1 ± 18.4% 18.7 ± 18.2% (*p* >.05) **Reduction of the differences in weight distribution:** There were no sig diffs seen.	*0.07 (0.05) $
Guo et al. (2015)	RCT	**WBV training** (I-VIB5050, Body Green, Taiwan), Magnitude 6–10 Hz, amplitude 4.0mm (8 weeks). Semi-squat position, 60 secs vibration/10 seconds rest,10 rounds per set, eight sets per day… ? daily NOT CLEAR	**Before and after 8-week treatment:** **Fugl-Meyer (FMA-L)** for lower extremity assessment (17 items, total score 34 points), **10MWT** **Subjective observation of knee hyperextension**	**FMA-L score** improved significantly *p*=0.000, 95%CI [3.309,9.891]; **10MWT** *p*=0.000, 95%CI [5.214,11.39] **Times of knee hyperextensions** decreased significantly *p*= 0.000 95%CI [19.05,12.35].	**10MWT** 2.53 (0.86) $
		Placebo WBV (machine off) Same exercises/procedures, vibration machine off		**FMA-L score** improved significantly (*p*=0.000/, 95%CI [5.549,12.45] **10MWT:** *p*=0.000/ 95%CI [9.423,15.98] **Times of knee hyperextensions** decreased significantly (*p*= 0.000 95% CI [16.52,22.28].	1.65 (0.86) $
Jung et al. (2017)	RCT	**TENS to peroneal nerve** + STS training 15 mins/day, 5x/week + therapy, 1 hour a day, 5x/week, six weeks. TENS-7000, Koalaty Products Inc., USA used. Intensity – 2x sensory threshold, no muscle contraction. Pulse width 200 ms; frequency 100Hz.	**Wii Balance Board [WBB]) (force platform)** to assess postural sway. (eyes closed, eyes open) conditions. **Hand-held dynamometer (HHD)** (Model 01163, Lafayette Inc., IN, USA) measured isometric strength in extensors of hip, knee and ankle. **Composite Spasticity Score (CSS**) to evaluate spasticity of the ankle plantar flexor.	**Postural sway:** significant ↓ eyes open/closed (mean change, each 21.0 (16.2), 26.4 (19.9) cm), *p*<.05, **Muscle strength:** Muscle strength hip extensor significantly ↑ (*p*<.05), No sig diff in muscle strength knee and ankle extensors TENS vs placebo group. **CCS**: significant (mean change, 2.6 (0.8))	**Postural sway (distance cm)** 0.65 (0.50) $
		Placebo TENS + same STS training + therapy, 1 hour/day, 5x/week, 6 weeks		**Postural sway:** smaller, but significant ↓ eyes open/ closed (mean change, 8.8(13.1),13.1(13.0) cm), *p*<.05. **Muscle strength:** Muscle strength hip extensor significantly ↑ (*p*<.05) in placebo stimulation group.	0.27 (0.50) $
Kluding and Santos (2008)	Pilot RCT	2x/week therapy for 4 weeks involving functional training **+ Contra-lesional ankle joint mobilizations (5 minutes) 2x/week.** Grade I or II manual traction and gliding 1st session; grade III other sessions + 15 mins functional training	**Passive and active range ankle d/flexion** **Ankle kinematics and weight-bearing symmetry during functional activities (**3D Optotrak 3020[a] motion system): **Peak dorsiflexion during STS and stance phase**	**Goniometer: Passive and active ankle range:** Passive change: 5.7(3.1), 95% CI mean diff: 2.5° to 8.6° active:10.8 (7.5); 95% CI mean diff: 0.5° to 16.6°; **Ankle kinematics and weight-bearing symmetry during functional activities:** Peak d/flexion (STS): 1.88(4.72),95% CI: 7.95°,1.36°, Peak d/flexion (gait): 0.38(3.44), 95% CI: 9.27°, 4.97° **Peak weight-bearing diffs during STS** (%): -0.79(4.9) 95% CI 3.59, 29.37	**Effect sizes for peak weight-bearing diffs during STS:** * 0.03 (0.51) (in favour of **control group)**

			Weight-bearing differences during STS and static standing **Time to perform STS** **MAS:** passive resistance in ankle plantarflexors. **Rivermead Mobility Index (RMI)**	Average weight-bearing difference in STS 3.37(5.29) (%): 95% CI 3.26,19.46 **Total STS time:** Significant ↓ in experimental group compared to control: -0.82(0.91), 95% CI -1.9, -0.1s. Other measurements of function no diffs between groups. RMI score: 0.75(0.71), 95% CI: -0.84,1.09	
		2x/week therapy for 4 weeks involving functional training		**Goniometer: Passive and active ankle range:** Passive change: 0.2(6.2), 95% CI for mean diff: 2.5°, 8.6°; active: 2.3(7.6) 95% CI for mean diff: 0.5°, 16.6°; **Ankle kinematics and weight-bearing symmetry during functional activities:** Peak d/flexion (STS): 1.42(3.93) 95% CI -7.95°, 1.36°, Peak d/flexion (gait): 2.58(8.14) 95% CI -9.27°, 4.97° **Peak weight-bearing diffs (STS)** (%): -14.9(15.0) 95% CI 3.59, 29.37 Average weight-bearing diff in STS (%): -9.5(6.47), 95% CI 3.26, 19.46 **Total STS time:** Significant ↓ in experimental group compared to control: 0.17(0.77) 95%CI -1.9, -0.1s. Other measurements of function no diffs between groups. RMI score: Exp:0.75(0.71), control: 0.63(1.1) 95% CI: -0.84,1.09	*0.91 (0.51) (in favour of **control group)**
Lau et al. (2012)	Single blinded RCT	**WBV training** 3x/wk for 8 wks, 24 treatments Exercises while standing on platform. Vertical (synchronous) WBV signals (Jet-Vibe System). frequency range 20–30 Hz, amplitude 0.44–0.60 mm peak acceleration 9.5–15.8 mIsj^2 and g force of 0.97g–1.61g.	At baseline, after 24 sessions, + 1-month post-intervention. **Chedoke–McMaster stroke assessment Falls** last 3 mths. **BBS** **Limit-of stability (LOS) test (SMART balance system (NeuroCom, SMART EquiTest; NeuroCom Int, Inc., Clackamas, OR) Movement velocity (MVL)**; **average speed of COP movement** in degrees per second), end point excursions (**EPE); Distance COP travelled. Maximum excursion (MXE)**; maximum distance travelled by	ANOVA revealed a **significant time effect for the BBS score, 10MWT, 6minWT, isometric knee flexion and extension muscle strength, and ABC score** (P < 0.05). Interaction effects of time x group and group effects not significant for these variables (P >0.05). For the **LOS test**, a significant time effect identified for MVL, EPE, and MXE (P <0.05) but no time effect for DCL (P > 0.05). No significant time x group interaction or group effects for these variables related to the LOS test. Significant improvement immediately after training period in both groups (P <0.05) and values remained stable during 1-month follow-up period (P > 0.05;). No significant between-group difference in the incidence of	**BBS:** 0.22 (0.04) $
		Same exercises on platform but with **no vibration.**			0.002 (0.04) $

			COP **Directional control (DCL)**; comparison of amount of movement toward target with that away from it. **10MWT, 6minWT** **Cybex dynamometer Computer Sports Medicine, Inc., Stoughton,MA** for isometric knee flexion and (70°knee flexion). **Activities Specific Balance Confidence (ABC)** scale to evaluate fall-related self-efficacy. Falls logbook	falls, with three subjects in each of group reporting a fall during the 6-month follow-up period (Chi squared = 0.000, *p*= 1.000), also, no significant change found in the proportion of fallers before and after the treatment period in either group (McNemar test, *p* = 1.000.	
Lynch et al. (2007)	Pilot single blind RCT	Daily 1-hour group session: lower-limb strength, balance /cardiovascular fitness, + 30–60 minutes/day individual therapy session + **ten 30-minute sensory retraining sessions (2-week period).** Total treatment time divided evenly between education regarding sensation and sensory retraining; touch detection and localization at 7 points on soles of feet; hardness, texture and temperature discrimination: feet on various surfaces, sitting and standing with vision obscured; proprioception training (big toe and/or ankle); specific, graded stimulation tasks, emphasis on tasks subject able to do; attentive exploration of stimuli; prevention of visual dominance; comparison with ipsilesional side; quantitative feedback on performance. Daily 1-hour group session: lower-limb strength, balance/cardiovascular fitness, + 30–60 mins/day individual therapy session+relaxation techniques	**SWMs to assess light touch** at 7 points on soles of feet (big toe, little toe, 1st metatarsal, 5th metatarsal, lateral border of, medial border, and heel) **Distal Proprioception Test (DPT)** (out of 10) to assess **proprioception** of big toe. **BBS to assess postural control.** **Gait assessment**: time taken to walk the middle 10m of a 14-m walking track; **Iowa Level of Assistance Scale (ILAS) -** amount of therapist assistance and mobility aid.	**Light Touch:** Improved significantly at 3 points of affected foot: heel (*p*=.03), lateral border (*p*=.02), and big toe (*p*=.01). **Between-group differences** in sensation- not significant at these 3 points at any time points. Time had no significant effect on sensation at the remaining 4 points of the feet. Significant between-group difference in light touch sensation at **first metatarsal** at follow-up, with experimental group showing significantly improved detection of light touch compared to control group (*p*=.01); differences remained after 4-week period, even in the 3 points of the feet that had shown sig. improvements in sensation over time (Mann-Whitney *U* tests: big toe, *p*=.001, lateral border of the foot, p=.005; heel, *p*=.045). **DPT:** No sig diff over time in scores (*p*= .55); no significant between-group difference (*p*=.06). **Balance:** Within group significant diffs baseline to end of treatment for both groups (*p*<.005); no significant between-group diffs at end and follow-up. **Timed Gait:** No between-group differences found **Level of Assistance** No significant change observed over time or between groups.	*No SD presented so effect sizes could not be calculated.

Ng and Hui-Chan (2009)	Randomi-zed placebo-controlled clinical trial (4 groups)	**TENS** + **Exercise:** 20 sessions treatment 5 x/ week (4 weeks). 8 instruction sessions for home program. 60 mins TENS, via two pairs of electrodes placed on 4 acupuncture points of affected lower extremity: ST 36 (Zusanli), LV 3 (Taichong), GB 34 (Yanglinquan) and UB 60 (Kunlun), cathodes proximal. Pulses:100 Hz using a square pulse stimulator (pulse width 0.2 ms). Stimulus intensity approx 2x patient's sensory threshold + 60 minutes task-related exercises, involving 4 weight bearing and stepping exercises using wooden blocks of 2.5 or 5 cm in height: 1) loading affected leg; 2) stepping up with affected leg; 3) stepping down with unaffected leg; 4) heel lifts from a dorsiflexed position in standing. Also, functional training; 5) stand from chair, walk short distance, and return to chair; 6) walking with rhythmic auditory cues. Progression: higher wooden blocks and ↑ repetitions in 10 minutes. Walking progressed by ↑ speed.	**OMs:** Completed at baseline, after two weeks, after four weeks and at four weeks follow-up. **Gait velocity:** 4.6m long instrumented carpet (GAITRite). During testing, subjects walked with comfortable footwear at normal speed, and gait velocity calculated by GAITRite software**.** **6-minute walk test (6minWT):** Walking endurance **Timed up and go (TUG) test:** Functional mobility.	Participants showed significant improvements in **gait velocity** from week 2 (baseline: 47.9 (26.8), week 2 63.2(32.2) (*p*<0.01). Improvements maintained at follow-up, four weeks after treatment ended (70.2 (32.7)). When compared with the control group, the two exercise groups (TENS+exercise baseline 191.9 (89.4) to follow-up 245.5 (99.7) and placebo Stimulation + exercise (baseline: 175.9 (81.9) to follow-up 206.82 (85.8)) showed significantly greater absolute and percentage ↑ in average distance covered in the 6minWT (*p* <0.01) at follow-up. All three intervention groups showed significant decreases in their average TUG time scores (*p* <0.01) at week 4 compared with that of the control group, but only the two exercise groups (TENS + exercise and placebo stimulation + exercise) maintained improvements at follow-up. Compared with the control and TENS groups, only the combined TENS + exercise group covered significantly more distance in the 6minWT from week 2 onwards.	**Gait velocity:** 0.73 (0.22) $
		TENS: 60 mins identical TENS treatment, as described.			0.12 (0)
		Placebo stimulation + **Exercise:** 60 mins placebo stimulation + 60 minutes of same exercise program			0.39 (0.01)
		Control: No treatment, attended four assessment sessions			0.08

Paoloni et al. (2010)	RCT	50 mins physical therapy session, 3 x/week, (4 weeks) stretching, muscle strengthening, balance, and overground walking training **+ 30 mins segmental muscle vibration (SMV)** to contralesional tibialis anterior and peroneus longus. Low-amplitude SMV delivered by commercial acoustic wave vibratory device (commercial device: Horus; Akropolis, Rome, Italy); frequency 120 Hz; Vibration amplitude:10 mm. 30 mins stimulation in trains of 6 seconds divided by 1 second pauses.	**Gait analysis**: kinematic variables using ELITE stereophotogrammetric system (BTS, Milan, Italy), 8 infrared video cameras (TVC; BTS) **Time–Distance Data** Data collected paretic and normal sides: stride length (m); step width (m); step length (m); stance duration and swing velocity (m/s). Cadence and gait speed (m/s). Mean of 3 trials. **Kinematic Data** 3D marker trajectories during walking (Tracklab; BTS). **Electromyographic (EMG):** Surface EMG signal -TA and Gastrocnemius Medialis muscles, paretic and normal, (walking). Subjects instructed to walk at self-selected speed along a level surface 10 m in length; 5 trials.	**Time–distance gait parameters:** Significant treatment effect (2-way ANOVA *p*<.01) for gait speed: Significant effect (p<.01) also seen for: ipsilesional side swing velocity, stride length both sides, and toe-off percentage on ipsilesional side. Significant diff in kinematic evaluation (stance phase) for both ankle d/flexion angles at heel contact (2-way ANOVA *p*<.01); no significant changes in other parameters Significant diffs observed in max degrees of ankle d/flexion and plantarflexion - contralesional side swing phase, (2-way ANOVA; *p* <.01). Significant increase in surface EMG % activation of contralesional TA muscle pretreatment to posttreatment assessments (*p*<.01). Effect size .61 for max ankle d/flexion during contralesional swing phase.	**Gait speed:** 0.51 (0.4) $
		50 minutes physical therapy session, 3 x/week, (4 weeks), stretching, muscle strengthening, balance, and overground walking training.		No sig diffs observed	0.11 (0.4) $
Park et al. (2014)	RCT	30-min exercise with a physical therapist **+TENS,** 1:1 ROM exercise (10 min), mat exercise (10 min), gait exercise (10 min). Exercise program according to pre-set principles. 7 education/practice sessions in total. + **Two-channel TENS (TENS-7000, Koalaty Products Inc., USA).** Electrodes (5 cm^2)- affected lower extremity lateral and medial quadriceps and gastrocnemius Frequency:100 Hz; pulse width: 200µs. Stimulation 30 min, sub-sensory.	**MAS** **Good Balance (Metitur Ltd, Finland, 2008) device** to measure static balance with eyes open and closed for 30s; 3 times. Average used as an indicator of AP and ML postural sway, speed, and speed moment. **The TUG test** to assess dynamic balance. **A gait analyzer (OptoGait, Microgate S.r.l, Italy, 2010)** to test the gait pattern of patients and quantity of gait analysis. Temporal and spatial gait were measured.	**MAS** Significant reductions (*p*<.05) **Static balance:** A sig diff in eyes closed and opened, AP, ML postural sway velocity, and velocity moment observed in TENS group before and after test (*p*<.05), and in mean difference from pre- and post-test between the 2 groups (*p*<.05). **TUG:** Sig diff before/after test (*p*<.05), TENS group improved more than placebo TENS group (*p*<.05). **Gait analysis test:** Sig diffs in velocity, cadence, step length and stride length of paretic side in TENS group before and after test (*p*<.05) Greater improvements of cadence, step length of paretic side, and stride length of paretic side than placebo TENS group (*p*<.05).	**Gait velocity:** *0.4 (0.2) $
		Same 30-min exercise + **placebo TENS.** Two-channel TENS used in		Velocity showed a sig diff before and after test (*p*<.05)	*0.03 (0.2) $

		same manner, however, no stimulation given,patients were informed that the treatment would be imperceptible.			
Suh et al. (2014)	Single-blind RCT	Prior to intervention 30 minutes of standard rehabilitation based on the Bobath technique + **Electrical stimulation**- 60 mins single session, interferential current,via four electrodes to ipsilateral, medial and lateral gastrocnemius fibers (spastic muscle). Frequency:100Hz, approx. 2–3 x sensory threshold.	**MAS** to assess gastrocnemius spasticity. **Functional Reach Test and BBS** **TUG Test** **10MWT**	**MAS:** Significant ↓ in spasticity after therapeutic intervention; magnitude of ↓ significantly greater in the experimental group 41% (*p*<0.001) **Functional Reach test:** 19%, significant improvement *p*<0.001; **BBS:** 5%, significant improvement, *p*<0.001 **TUG:** Significant ↑ for experimental group -19% (*p*<0.001) **10MWT** improved by 16%(*p*<0.001).	**Effect size:** 0.44 (0.39) $
		Control group 30 minutes standard rehabilitation + **Sham electrical stimulation** 60 mins single session, interferential current. Electrodes attached, no stimulation applied.		**MAS:** Significant ↓ in spasticity 11% (*p*<0.002) **Functional Reach test:** 11% improvement; (*p*>.05) **BBS** 1% improvement, (*p*>0.05) **TUG: S**ignificant increase - 6% (*p*=0.006). **10MWT** improved by 4% *p*=0.011	0.12 (0.39) $
Tankisheva et al. (2014)	RCT	**WBV training** Vertical vibration platform (power plate) 3x/week for 6 weeks, minimum rest of 1 day between training sessions. Exercises: standing on toes, knee flexion of 50°–60° (high squat), knee flexion of 90° (deep squat), wide-stance squat, and 1-legged squat. Training intensity ↑ progressively by increasing the frequency (35 and 40Hz) or the amplitude (1.7 and 2.5mm) of vibration signal or increasing both. Vibration intensity gradually ↑ in first 12 sessions, more intensive in last 6 sessions. Training volume also increased systematically.	At baseline, after intervention and at 6 weeks follow-up. Standard clinical neurologic examination. **Barthel Index** **Functional Ambulation Classification (FAC).** **Brunnstrom-Fugl-Meyer test** (sensori-motor impairment). **Borg's perceived exertion scale.** **Ashworth scale** **Isokinetic dynamometer (Biodex System** **Dynamic posturography platform (Equitest)** **Sensory Organization Test (SOT)** (postural control via visual, vestibular, and proprioceptive information).	**Ashworth scale** – no sig diffs (*p* >.05). **Muscle strength (paretic leg)** significant between-group differences in favour of the vibration group only in isometric knee extension strength (paretic leg), baseline: 43.1 (10.1), follow-up: 48.1 (7.9), (*p*=.022) after 6 weeks of intervention and in isokinetic knee extension strength after a 6-week follow-up period (*p*=.005). **Postural control** improved after 6 weeks of vibration in the intervention group when the patients had normal vision and a sway-referenced support surface (*p*<.05).	**Postural control equilibrium score** *1.56 (0.57) $
		No additional training program; asked not to change lifestyle		**Ashworth scale** – no sig diff (p >.05). **Muscle strength** -significant between-group differences in favour of vibration group (isometric knee	*0.66 (0.57) $

				extension, paretic leg) Baseline: 30.5 (27.2), follow-up: 35.2 (25.7), not significant for control (*p*=.022) Isokinetic knee extension strength after a 6-week follow-up period not significant (*p*=.005).	
van Nes et al. (2006)	RCT	**WBV training –** each working day for 4 weeks + individualized treatment program (at least five 30-min individual sessions of physical therapy, five 60-min group sessions of physical therapy, and three 30-minndividual sessions OT augmented with speech and language therapy + psychologic treatment if nec). Four sessions of 45s WBV stimulation with 1-minute break between sessions. 120 treatment sessions in total. Vibration amplitude approx. 3 mm. Frequency: 30 Hz. Patients adopted a "squat", with hand support. Patients unable to stand independently were supported at their buttocks by a height-adjustable bench with their knees and hips in 45° flexion.	At baseline, after 6 weeks of WBV or ETM treatment, as well as after 6 weeks follow-up. At baseline: **Motricity Index and MAS, Somatosensory threshold of the affected leg, and the presence of hemineglect.** Somatosensory threshold determined for pressure sensitivity at tip of hallux using 5 calibrated monofilaments (2.83, 3.61, 4.31, 4.56, and 6.65). To determine the presence of neglect a computerized visual reaction-time task was used. **BBS, Barthel Index**, **Trunk Control Test, Rivermead Mobility Index,** **FAC** **The Motricity Index** **Somatosensory threshold affected leg.**	Both groups showed a main effect of time on the **BBS** (F [2,50] =56.67, *p*<0.01). An effect of time was also seen for the **Barthel Index** F [2,50] =97.12, *p*<0.01), **Rivermead Mobility Index** (F [2,50] =76.20, *p*<0.01**),** **Trunk Control Test** (F [2,50] =11.83, *p*<0.01), **FAC** score (F [2,50] =76.48, *p*<0.01), **Motricity Index (**F [2,50] =26.85, *p*<0.01) **Somatosensory threshold** (F [2,50] =3.92, *p*<0.05). Improvements most pronounced during the intervention period, but patients continued to improve during the follow-up period. There were no group time interactions, indicating similar recovery profiles for both treatment groups	**BBS:** 0.996 (0.03), in favour of control group.
		Exercise therapy on music (ETM) -4 sessions 45s stimulation 5x/wk, 6wks. In standing position as during WBV + same physical therapy, OT, SALT and psychologic treatment			1.04 (0.03), in favour of control group.
Yan and Hui-Chan (2009)	Single blind stratified RCT	Standard rehab (OT & PT) each lasting for 60 min + **TES** applied with 0.2 ms pulses, at 100 Hz in the constant mode within the subject's tolerance level, via (5 x 3.5 cm) electrodes over acupuncture points on affected lower extremity: St 36, Lv 3, GB 34, Bl 60. Treatment lasted 60 min per session, 5 days/ week for 3 weeks	**Composite Spasticity Scale (CSS) -** for assessing spasticity of affected ankle plantar flexors. **Maximum isometric voluntary contraction (MIVC)** of ankle dorsiflexor and plantarflexor muscles, recorded by torque and surface EMG, in supine.	**Composite spasticity scale** TES group showed less ↑ in muscle tone than other 2 groups over time. Sig diff in % participants with normal resistance between TES and control groups from week 1 onwards (Chi square test, *p*=0.001–0.013), and between TES and PS groups at week 3 (*p*=0.016). No sig diffs found between PS and control groups **Max Isometric Voluntary Contraction (MIVC)** Sig. ↑ (*p*<.05) in magnitude and % ↑ in ankle	**TUG*:*** TES 2.43 (1.65) $

		Standard rehab + placebo stim Same electrodes, locations and device, but circuit disconnected. Subjects told that they might or might not feel the simulation. 60 min per session, 5 days a week for 3 weeks	**TUG test –** to assess functional mobility when a subject could walk 7–8 m without personal assistance	dorsiflexion torque and ↓ in EMG co-contraction ratio in TES group compared to control group, from week 2 and 3. By week 8 post-stroke (5 weeks after TES stopped), magnitude and % ↑ in MIVC dorsiflexion torque in the TES group was sig. > those of the PS group (*p*<.05). Also, significantly greater ↓ in EMG co-contraction ratio during d/flexion (*p*<.01, at wk 8). No sig diff among 3 groups using the Chi square test.	0.93 (0.93) in favour of placebo stimulation group +exercise vs control
		Standard rehab (OT & PT) each lasting for 60 min			0.58

Abbreviations: 10MWT 10 metre walk test, BBS Berg balance Scale, CSS Composite Spasticity Scale, D/flexion dorsiflexion, EMG Electromyography, FAC Functional Ambulation Classification, HHD Hand held dynamometer COP Centre of pressure, MAS Modified Ashworth Scale, Mths Months, MVL Movement velocity,P/flexion Plantar flexion, OM Outcome measure, PSL Postural sway length RMI Rivermead Mobility Index, ROM Range of movement, s second, SFS Sensorimotor foot stimulation, SD Standard deviation, Sig diff Significant difference, STS Sit to stand TOT Task orientated training, TENS/TES Transcutaneous electrical nerve stimulation, WBV whole body vibration, Wk week. $ - in favour of experimental group * = sample size in study <30

3.3.1 Assessment of methodological quality - results

The results of the quality assessment and risk of bias within the studies are summarized in table 3.4.

Table 3.4 Quality assessment of included studies

	Selection bias		Reporting bias		Performance bias	Detection bias	Attrition bias
	Random sequence generation[1]	Allocation concealment[2]	Selective reporting[3]	Other sources of bias[4]	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data[5]
Bayouk et al. (2006)	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR
Brogårdh et al. (2012)	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Cho et al. (2013)	LOW	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	LOW	UNCLEAR
Ferreira et al. (2018)	UNCLEAR	UNCLEAR	LOW	LOW	LOW	UNCLEAR	LOW
Goliwas et al. (2015)	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	LOW	UNCLEAR	HIGH
Guo et al. (2015)	UNCLEAR	UNCLEAR	UNCLEAR	HIGH	LOW	UNCLEAR	LOW
Jung et al. (2017)	HIGH	UNCLEAR	UNCLEAR	LOW	UNCLEAR	LOW	UNCLEAR
Kluding and Santos (2008)	HIGH	UNCLEAR	LOW	LOW	HIGH	HIGH	UNCLEAR
Lau et al. (2012)	LOW	LOW	LOW	LOW	UNCLEAR	UNCLEAR	LOW

Lynch et al. (2007)	LOW	HIGH	UNCLEAR	UNCLEAR	LOW	LOW	LOW
Ng and Hui-Chan (2009)	LOW	LOW	LOW	LOW	LOW	UNCLEAR	LOW
Paoloni et al. (2010)	UNCLEAR	LOW	UNCLEAR	UNCLEAR	HIGH	LOW	LOW
Park et al. (2014)	LOW	LOW	LOW	LOW	UNCLEAR	UNCLEAR	UNCLEAR
Suh et al. (2014)	LOW	LOW	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	LOW
Tankishieva et al. (2014)	LOW	LOW	UNCLEAR	LOW	HIGH	HIGH	UNCLEAR
Van Nes et al. (2006)	LOW	LOW	LOW	LOW	LOW	UNCLEAR	LOW
Yan & Hui-Chan (2009)	LOW	UNCLEAR	UNCLEAR	UNCLEAR	HIGH	LOW	UNCLEAR

UNCLEAR – Insufficient information provided in the publication

[1]Describe the method used to describe the allocation concealment used to generate the allocation sequence in sufficient detail to allow the assessment of whether it should produce comparable groups

[2] Describe the method used to conceal the allocation concealment in sufficient detail to determine whether intervention allocations could have been foreseen in advance of or during enrolment

[3]State how the possibility of selective outcome reporting was examined by the authors and what was found

[4]Any important concerns not addressed above; if particular questions/entries were pre-specified in the studies protocol, responses should be provided for each question / entry

[5] Describe the completeness of outcome data for each main outcome including attrition and exclusions from the analysis, stated whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants); reasons for attrition/exclusions were reported

3.3.2 Sample size and chronicity of stroke

Sample sizes ranged from 16 (Bayouk et al., 2006) to 109 (Ng and Hui-Chan, 2009). The mean (SD) ages of the samples ranged from 54.04 (6.41) (Guo et al., 2015) to 71.17 (13.23) years (Park et al., 2014). The time post-stroke of participants in trials ranged from 9.27 (3.52) days (Yan and Hui-Chan, 2009) to 6.50 (6.41) years (Tankisheva et al., 2014). The chronicity of stroke in the trial samples is summarized in Appendix 7.

3.3.3 Interventions

Six trials involved sensory electrical stimulation. Five of those involved transcutaneous electrical nerve stimulation (TENS) (Cho et al., 2013; Jung et al., 2017; Ng and Hui-Chan, 2009; Park et al., 2014; Yan and Hui-Chan, 2009); one other involved interferential therapy (Suh et al., 2014). Six trials involved vibration, either whole body vibration (WBV) (Brogårdh et al., 2012; Guo et al., 2015; Lau et al., 2012; Tankisheva et al., 2014; van Nes et al., 2006) or segmental muscle vibration (SMV) (Paoloni et al., 2010). The other five trials used non-electrical interventions: task-oriented exercise with proprioception of the feet, ankles and/or vision manipulated under varying conditions (eyes open/eyes closed) and on different surfaces (firm/soft) (Bayouk et al., 2006), wearing postural insoles with a sensory effect on the soles of the feet, influencing muscle proprioception (Ferreira et al., 2018), sensorimotor foot stimulation (Goliwas et al., 2015), ankle joint mobilizations (Kluding and Santos, 2008), and a sensory retraining programme

(Lynch et al., 2007). A summary of the interventions and comparisons are presented in Appendix 8.

3.3.4 Outcomes

Various outcomes were measured across the studies, relating to spasticity, balance, gait, motor impairment and functional independence, including analysis of sit to stand, falls risk, and sensation. A table listing the range of OMs used across the studies is available in Appendix 9.

3.3.4.1 Spasticity

Three scales were used within the studies to measure spasticity: the MAS, which was used in six studies (Brogårdh et al., 2012; Cho et al., 2013; Kluding and Santos, 2008; Park et al., 2014; Suh et al., 2014; van Nes et al., 2006); the Ashworth Scale (Tankisheva et al., 2014); and the Composite Spasticity Scale (Jung et al., 2017; Yan and Hui-Chan, 2009). Of note, the Ashworth scale and MAS are measures of passive resistance and not spasticity, resistance being increased by the visco-elastic properties (stiffness) of the tissues (Pandyan et al., 1999). Inter-rater reliability of both the Ashworth scale and the MAS has been found to be poor when used as a tool for measuring the lower limb (Pandyan et al., 1999).

3.3.4.2 Analysis of balance

Balance or postural control was measured in seven studies (Bayouk et al., 2006; Cho et al., 2013; Goliwas et al., 2015; Jung et al., 2017; Lau et al., 2012; Park et al., 2014; Tankisheva et al., 2014). Postural sway/displacement of COP was measured in six studies using a variety of methods: Matscan (Tekscan) system (Bayouk et al., 2006); Zebris forceplate (Cho et al., 2013; Goliwas et al., 2015); Wii balance board (Jung et al., 2017); dynamic posturography platform, SMART balance system (Equitest) (Lau et al., 2012; Tankisheva et al., 2014); and the Good Balance (Meitur Ltd) device (Park et al., 2014). The BBS, which has been shown to be sensitive to change and able to reflect large effect sizes for change (English et al., 2006), was used in five studies (Brogårdh et al., 2012; Lau et al., 2012; Lynch et al., 2007; Suh et al., 2014; van Nes et al., 2006).

3.3.4.3 Sit to stand analysis

Sit to stand was analysed using ankle kinematics, weight bearing difference and timed sit to stand (Kluding and Santos, 2008).

3.3.4.4 Analysis of gait

Six studies used the 10MWT (Bayouk et al., 2006; Brogårdh et al., 2012; Guo et al., 2015; Lau et al., 2012; Lynch et al., 2007; Suh et al., 2014), and the TUG was measured in five (Brogårdh et al., 2012; Ng and Hui-Chan, 2009; Park et al., 2014; Suh et al., 2014; Yan and Hui-Chan, 2009). Walking speed was measured using a GAITRite mat (Ng and Hui-Chan, 2009), an ELITE stereophotogrammatic system

(Paoloni et al., 2010), and other gait kinematics were measured in three other studies (Ferreira et al., 2018; Paoloni et al., 2010; Park et al., 2014). Observation of gait was also reported by Guo et al. (2015); however, the subjectivity and reliability of this measure needs to be questioned as there is no mention of following a strict protocol during observation, or videotaping to aid analysis, which increases reliability when observing gait (Ferrarello et al., 2013). Walking ability and mobility function was measured using the FAC (Tankisheva et al., 2014; van Nes et al., 2006), the level of assistance scale (Lynch et al., 2007), the Rivermead Mobility Index (Kluding and Santos, 2008; van Nes et al., 2006), and walking endurance was tested using the 6 minute walk test (6minWT) (Brogårdh et al., 2012; Lau et al., 2012; Ng and Hui-Chan, 2009). Tankisheva et al. (2014) also measured endurance using the Borg's rating of perceived exertion scale.

3.3.4.5 Motor impairment and functional independence

Motor impairment was measured using the MRC scale (Jung et al., 2017), Fugl-Meyer (lower limb) scale (Guo et al., 2015), isometric muscle strength (Brogårdh et al., 2012; Lau et al., 2012; Yan and Hui-Chan, 2009), isokinetic strength (Brogårdh et al., 2012; Tankisheva et al., 2014), EMG (Paoloni et al., 2010), the Chedoke-McMaster Stroke Assessment (Lau et al., 2012), the Motricity Index (van Nes et al., 2006) and the Brunnstrom Fugl-Meyer Test (Tankisheva et al., 2014).

Functional independence was measured using the Barthel Index (Tankisheva et al., 2014; van Nes et al., 2006), which is a valid tool for measuring activities of

daily living and independence (Grau et al., 2015; Mahoney and Barthel, 1965). The scoring for the Barthel index indicates how much care someone requires, therefore, some may consider it to be a measure of carer burden; however, it was originally designed as a measure of function (Mahoney and Barthel, 1965). The Barthel index has been reported as having acceptable reliability from various studies, ranging from moderate to very good (*k*=0.41–1.00) (Quinn et al., 2011). Participation was measured with the Stroke Impact Scale (Brogårdh et al., 2012). The Trunk Control Test was also undertaken by van Nes et al. (2006).

3.3.4.6 Sensory threshold and proprioception

Only one study measured sensation in the foot (Lynch et al., 2007) using SWMs to record touch/pressure sensory thresholds, and the Distal Proprioception Test.

3.3.5 Comparison of interventions

3.3.5.1 Electrical nerve sensory stimulation versus placebo

All six trials exploring sensory electrical stimulation (Cho et al., 2013; Jung et al., 2017; Ng and Hui-Chan, 2009; Park et al., 2014; Suh et al., 2014; Yan and Hui-Chan, 2009) compared the stimulation to a sham or placebo stimulation. Ng and Hui-Chan (2009) and Yan and Hui-Chan (2009) also had groups which received no treatment at all. All of the studies recruited a sample size of more than 30, with the smallest sample size being 34 (Park et al., 2014) and the largest 109 (Ng and Hui-Chan, 2009). Mean age (SD) ranged from 54.13 (12.25) (Suh et al., 2014) to 71.17 (13.23) (Park et al., 2014). There was a range between the studies relating to time

post-stroke with Yan and Hui-Chan (2009) recruiting participants very early after stroke (9.28 (3.52) days), whereas, Ng and Hui-Chan (2009) recruited chronic stroke survivors 4.74 (3.4) years post-stroke. The other studies recruited participants in the sub-acute (6.55 (2.60) months; (Jung et al., 2017) to chronic stage post-stroke (18.62 (2.08) months; (Park et al., 2014). All studies delivered sensory stimulation without muscle contraction using a frequency of 100Hz; for all the studies using TENS the pulse width was also the same, reported as either 200 *μ*s (microseconds) or 0.2ms (milliseconds). The length of time of the interventions were either 30 minutes (Jung et al., 2017; Park et al., 2014) or 60 minutes (Cho et al., 2013; Ng and Hui-Chan, 2009; Suh et al., 2014; Yan and Hui-Chan, 2009). Two of the studies only applied the electrical stimulation once (Cho et al., 2013; Suh et al., 2014). The other studies all applied the TENS five times a week, for three weeks (Yan and Hui-Chan, 2009), four weeks (Ng and Hui-Chan, 2009), or six weeks (Jung et al., 2017; Park et al., 2014). The total number of hours of TENS (plus exercise, where appropriate) delivered ranged from 1 hour (Cho et al., 2013; Suh et al., 2014) to 40 hours (20 TENS and 20 exercise) (Ng and Hui-Chan, 2009). Three of the studies applied the stimulation to the gastrocnemius muscle on the affected side (Cho et al., 2013; Park et al., 2014; Suh et al., 2014), although Park et al. (2014) also applied the stimulation to quadriceps. Jung et al. (2017) placed the electrodes over the peroneal nerve on the affected side and both Ng and Hui-Chan (2009) and Yan and Hui-Chan (2009) attached the electrodes to acupuncture points on the lower extremity. All of the studies demonstrated a positive effect for the experimental group. Between-group effect at post

intervention ranged from a small effect (0.2) of TENS (100Hz, 200 μs, for 30 minutes, 5 times per week for 6 weeks) on gait velocity in chronic stroke (Park et al., 2014), to a very large effect (1.65) of TENS (100Hz, 200 μs , for 30 minutes, five times per week for 3 weeks) on timed up and go (TUG) in acute stroke (Yan and Hui-Chan, 2009) Interestingly, Suh et al. (2014) (n=42) delivered just a single session of electrical stimulation to the gastrocnemius for 60 minutes and demonstrated a between-group effect for the 10MWT of 0.39.

3.3.5.2 Whole body vibration (WBV) or segmental muscle vibration (SMV) versus no vibration

Of the studies involving vibration (either WBV or SMV), the sample sizes ranged from 15 (Tankisheva et al., 2014) to 82 (Lau et al., 2012) and the mean (SD) age of the participants ranged from 54.0(6.41) (Guo et al., 2015) to 62.53(7.32) (Brogårdh et al., 2012). There was also a large range in the time post-stroke with Guo et al. (2015) and van Nes et al. (2006) recruiting participants within the acute phase post-stroke (63.15(52.96) days and 36.59(10.18) days respectively), but Tankisheva et al. (2014) recruiting participants at 6.52(6.41) years post-stroke.

For the WBV, comparison interventions included sham/placebo vibration, with Brogårdh et al. (2012) comparing with a sham vibrating platform (amplitude of just 0.2mm) and other studies using vibration platforms that were not switched on (Guo et al., 2015; Lau et al., 2012). All three of these study controls involved participants undertaking the same exercises or standing position as the experimental group.

The control group in Tankisheva et al. (2014) were not involved in any additional training programme and were asked not to change their lifestyle, whereas, in van Nes et al. (2006) the control involved exercise therapy to music.

The training protocols varied between the studies: three involved six weeks of WBV, either twice per week (Brogårdh et al., 2012), three times per week (Tankisheva et al., 2014), or five times per week (van Nes et al., 2006). The other two involved eight weeks of intervention: although Guo et al. (2015) did not state how many treatments each week were undertaken, daily treatments were stated, so it can presumed this is likely to be five times per week (based on a normal 'working' week); Lau et al. (2012) delivered treatments three times per week. The total intervention times for the studies therefore ranged from 10 hours, but with just 1.5 hours of WBV in the intervention (van Nes et al., 2006), to 53.33 hours (Guo et al., 2015). The amplitudes used within the studies ranged from 0.44–0.60mm (Lau et al., 2012) to 4mm (Guo et al., 2015), and the frequencies from 6–10Hz (Guo et al., 2015) up to 50Hz (Lau et al., 2012). In summary, a different protocol was used for each of the studies investigating WBV.

The effect sizes for these studies ranged from experimental group 0.22, control 0.002 and between-group difference at post intervention 0.04 for the BBS following 24 sessions of WBV training (three times per week for eight weeks) at frequency 20–30Hz and amplitude 0.44–0.60mm, compared to sham WBV training (Lau et al., 2012), to experimental group 2.53, control group 1.65 and between-group

difference 0.86 following daily WBV training for eight weeks at frequency 6–10Hz and amplitude 4.0mm, compared to sham/placebo WBV training (Guo et al., 2015). Interestingly, Guo et al. (2015) used the lowest frequency (6–10 Hz) and the highest amplitude (4 mm) and demonstrated the greatest effect (0.86) for the 10MWT. Tankisheva et al. (2014) also demonstrated a medium effect size (0.57) for postural control; however, this result needs to be interpreted with caution because the control group received no therapeutic input at all and it could just have been the standing practice which had an effect. The other three studies (Brogårdh et al., 2012; Lau et al., 2012; van Nes et al., 2006) did not demonstrate any benefit from the WBV in relation to the BBS (effect sizes 0.09, 0.04 and 0.03 respectively). It is worth noting that the three studies that did not identify an effect following WBV (Brogårdh et al., 2012; Lau et al., 2012; van Nes et al., 2006) were of a better quality than the studies that showed an effect. However, the frequency and amplitude were different between the studies, which makes comparison difficult.

Paoloni et al. (2010) applied SMV three times a week for four weeks to the contralesional tibialis anterior and peroneus longus (amplitude 10mm and frequency of 120Hz), delivered in trains of six seconds divided by one second pauses. The control group just received the same therapy as the experimental group and no sham vibration. Effects sizes of 0.51 for the experimental group and 0.11 for the control group, with a between-group effect size of 0.4 in favour of the experimental group, were observed for gait velocity (cm/s).

3.3.5.3 Specific sensory input to the foot or ankle

Five studies applied specific sensory input to the foot or ankle via: manipulation of proprioception of feet, ankles, or vision, during task orientated training (Bayouk et al., 2006); a postural insole which was designed to have a sensory effect on the plantar surface of the foot (Ferreira et al., 2018); sensory motor foot stimulation, which involved 25 sessions of 20 minutes stretching soft tissues, facilitating sensory awareness and selective movement and function (Goliwas et al., 2015); ankle joint mobilizations (manual traction and gliding) (Kluding and Santos, 2008); or sensory training (discrimination and localization of touch, hardness, texture, temperature; graded proprioception training) (Lynch et al., 2007).

The sample sizes for these five studies were all <30, ranging from 16 (Bayouk et al., 2006; Kluding and Santos, 2008) to 27 (Goliwas et al., 2015). Mean (SD) ages of the participants ranged from 55.8(11.9) (Kluding and Santos, 2008) to 65.2(5.98) years (Bayouk et al., 2006). There was also a large variability of mean (SD) time post-stroke, which ranged from 48.23(29.36) days (Lynch et al., 2007) to 6.4(10.10) years (Bayouk et al., 2006).

Four studies (Bayouk et al., 2006; Goliwas et al., 2015; Kluding and Santos, 2008; Lynch et al., 2007) involved both groups undertaking an exercise programme of varying content and duration, with the intervention group receiving additional sensory stimulation, and the control groups either receiving just the exercise

programme or additional ‘placebo’ therapy. Bayouk et al. (2006 p.53) delivered a task orientated exercise programme, one hour per week for eight weeks (total 16 hours), performed under two different vision conditions (eyes open/eyes closed) and on different surfaces (firm/soft) for the intervention group; 30 minutes of the session was 'aimed at improving static and dynamic balance by executing exercises while the proprioception of the feet and ankles and/or vision was manipulated'. The control group undertook the same exercises, but just with the eyes open, on a hard surface. In the study by Lynch et al. (2007), all participants in both groups completed the same daily one hour group exercise programme (lower limb strength, balance, cardiovascular fitness) plus 30–60 minutes of individual therapy, over a 2-week period, amounting to between 12.5 and 20 hours in total. The intervention group also received a further 5 hours of additional sensory retraining (30 minutes per day, five days per week, over a 2-week period), and the control group stood with their eyes closed for the same period of time as the intervention group and then rested with eyes closed (in supine) for the rest of the 30-minute session, with guided relaxation techniques. The control groups in Goliwas et al. (2015) (total intervention 22.5 hours) and Kluding and Santos (2008) (total intervention 2.67 hours) just received the exercise programme and no additional therapy. In the fifth study, by Ferreira et al. (2018), the intervention group wore a postural insole with corrective elements for three months, and the control group wore a postural insole with no corrective elements.

In relation to the studies delivering specific sensory input to the foot or ankle, effect

sizes were calculated for all except Lynch et al (2007), which did not provide SDs. However, the effect sizes should be interpreted with caution in view of the small sample sizes. No effect was seen on mean velocity (m/s) for the insoles in the study by Ferreira et al. (2018) (experimental group 0.06, control group 0.03 and between-group effect size 0.0). Goliwas et al. (2015) did demonstrate an effect on difference in weight distribution (%): experimental group 0.68, control group 0.07; however, the between-group effect size was only 0.05. Effect sizes for the 10MWT were 0.22 (experimental), 0.24 (control) and 0.12 (between-group) for Bayouk et al. (2006), and for Kluding and Santos (2008), the between-group effect size was 0.51 in favour of the control group. However, it should be noted that the studies by Bayouk et al. (2006) and Kluding and Santos (2008) only included 16 participants.

3.3.6 Effectiveness of interventions

Effect size calculations for selected balance or gait OMs are presented in table 3.5, according to intervention. Two of the studies did not present SDs and therefore it was not possible to calculate effect sizes (Cho et al., 2013; Lynch et al., 2007). Four of the studies reported effect sizes (Kluding and Santos, 2008; Lau et al., 2012; Paoloni et al., 2010; Tankisheva et al., 2014); however, the methods of calculating the effect sizes were either inconsistent or not reported and therefore effect sizes for the 15 articles, for which it was possible to report a balance or gait effect size, were calculated using the pooled SD for both groups as the denominator. The selected OMs for which effect sizes could be calculated included gait assessments in the form of the 10MWT (Bayouk et al., 2006; Guo et al., 2015;

Suh et al., 2014), gait velocity or speed (Ferreira et al., 2018; Ng and Hui-Chan, 2009; Paoloni et al., 2010; Park et al., 2014), and the TUG (Yan and Hui-Chan, 2009). Balance was also evaluated by several studies with OMs including the BBS (Brogårdh et al., 2012; Lau et al., 2012; van Nes et al., 2006), postural sway or control (Jung et al., 2017; Tankisheva et al., 2014) and differences in weight distribution during stance (Goliwas et al., 2015), or on sitting to standing (Kluding and Santos, 2008). A total of seven of the 17 studies had sample sizes of ≤ 30 (indicated by an * in table 3.5), and therefore these effect sizes need to be interpreted with caution.

Calculation of effect sizes showed twelve of the studies demonstrating an effect in favour of the experimental group, with effect sizes ranging from 0.04 (Lau et al., 2012) to 1.65 (Yan and Hui-Chan, 2009). However, one study showed no effect (Ferreira et al., 2018), and two studies showed an effect in favour of the control group at 0.51 for Kluding and Santos (2008) and 0.03 for van Nes et al. (2006).

Table 3.5 Effect size for each group and between-group effect sizes according to intervention

Intervention	Author	OM	Effect size experimental group	Effect size control group	Effect size placebo stimulation group	Effect size other group	Between group effect size (post intervention)
Non-electrical	Bayouk et al. (2006) *	10MWT	0.22	0.24			0.12 $
	Ferreira et al. (2018) *	Mean velocity(m/s)	0.06	0.03			0
	Goliwas et al. (2015) *	Diff weight distribution (standing)	0.68	0.07			0.05 $
	Kluding and Santos (2008) *	Peak weight distribution difference STS (%)	0.03	0.91			0.51 (in favour of control group)
	Lynch et al. (2007) *		Results displayed in graphs only, no SDs presented				
Vibration, WBV or segmental	Brogardh et al. (2012)	BBS	0.91	0.13			0.09 $
	Guo et al. (2015)	10MWT	2.53	1.65			0.86 $
	Lau et al. (2012)	BBS	0.22	0.002			0.04 $
	Paoloni et al. (2010)	Gait speed (m/s)	0.51	0.11			0.4 $
	Tankisheva et al. (2014) *	Postural control: equilibrium score	1.56	0.66			0.57 $
	Van Nes et al. (2006)	BBS	0.996	1.04			0.03 (in favour of control group)
Electrical nerve stimulation	Cho et al. (2013)	Postural sway	No SDs given				
	Jung et al. (2017)	Postural sway	0.65	0.27			0.50 $
	Ng and Hui-Chan (2009)	Gait velocity (cm/s)	TENS + Ex 0.73	CONTROL 0.08	PLACEBO + EX 0.39	TENS 0.12	TENS+Ex= 0.22 $ TENS= 0
	Park et al. (2014) *	Gait velocity (cm/s)	0.40	0.03			0.2 $
	Suh et al. (2014)	10MWT	0.44	0.12			0.39 $
	Yan and Hui-Chan (2009)	TUG	TES 2.43	STANDARD REHAB 0.58	PLACEBO TES 0.93		TES=1.65 $ Placebo vs control=0.93 (in favour of placebo TES group)

* Indicates the sample size was < 30, $ indicates the effect was in favour of the experimental group

3.3.6.1 Assessment of quality of the included studies

Of the seventeen studies included, only three (Brogårdh et al., 2012; Ng and Hui-Chan, 2009; van Nes et al., 2006) were assessed as being of ‘good’ quality, according to the Agency for Healthcare Research and Quality standards (Lohr and Carey, 1999). Two were deemed to be of ‘fair’ quality (Lau et al., 2012; Lynch et al., 2007) and the other twelve studies of ‘poor’ quality (Bayouk et al., 2006; Cho et al., 2013; Ferreira et al., 2018; Goliwas et al., 2015; Guo et al., 2015; Jung et al., 2017; Kluding and Santos, 2008; Paoloni et al., 2010; Park et al., 2014; Suh et al., 2014; Tankisheva et al., 2014; Yan and Hui-Chan, 2009).

3.4 Summary of key findings

In terms of electrical stimulation, all the sample sizes were greater than 30 and there was consistency in relation to the frequency of the stimulation (100Hz) and the pulse width (0.2ms). However, there was great heterogeneity in relation to the mean (SD) time post-stroke, which ranged from 9.28(3.52) days to 4.74(3.40) years. There was also variability between the experimental protocols in relation to the positioning of the electrodes and number of sessions, with total time of the interventions ranging from just one hour (Cho et al., 2013; Suh et al., 2014) to 40 hours (Ng and Hui-Chan, 2009). However, it is important to note that all the studies demonstrated an effect size in favour of the experimental group.

In relation to the vibration interventions, there was a range of sample sizes from 15 (Tankisheva et al., 2014) to 82 (Lau et al., 2012). The protocols delivered varied

widely, with Brogårdh et al. (2012) delivering just 12 sessions and van Nes et al. (2006) including 30 sessions (although this did not mean greater WBV time); amplitudes ranging from 0.44–0.60mm (Lau et al., 2012) to 4mm (Guo et al., 2015) and frequencies from 6-10Hz (Guo et al., 2015) up to 50Hz (Lau et al., 2012). A range of between-group effect sizes were observed from 0.03, in favour of the control group (van Nes et al., 2006) to 0.86 in favour of the experimental group (Guo et al., 2015). The heterogeneity of the regimes makes comparison challenging.

The five studies that applied specific sensory input to the foot and ankle via differing mechanisms all had small sample sizes (<30) and there was a wide range of mean (SD) time post-stroke, from 48.23(29.36) days (Lynch et al., 2007) to 6.4 (10.10) years (Bayouk et al., 2006). None of the studies resulted in more than a small between-group effect size in favour of the intervention group, with 0.12 being the largest (Bayouk et al., 2006); one study found a medium sized between-group effect size (0.51) in favour of the control group (Kluding and Santos, 2008). In view of the heterogeneity of the treatment interventions, small sample sizes and range of group characteristics, the effect sizes for these studies should be interpreted with caution.

3.5 Discussion

The inferences of these findings from Study 1, along with strengths and limitations of the systematic review will be discussed in detail in chapter seven. It is perhaps

useful to highlight some of the differing results from this current systematic review in relation to the recently published systematic review undertaken by Serrada et al. (2019). The current review adopted a more focussed search strategy around sensory stimulation to the lower extremity with OMs relating to balance and gait and included only randomized controlled trials. Consequently, the search identified fewer citations for initial screening: 433 as opposed to 14,446 in Serrada et al., 2019. The current review included studies of interventions that involved specifically sensory stimulation, and so any intervention that also clearly included active movement was excluded. In contrast, Serrada et al. (2019) included studies of thermal stimulation that prompted the participant to actively move away from a noxious heat source (Chen et al., 2011; Hsu et al., 2013; Liang et al., 2012); similarly, a study involving electrical stimulation applied to stimulate muscle contraction (Yavuzer et al (2007), included in Serrada et al (2019, was excluded from this current study, as only electrical stimulation with a purely sensory effect was included. Further, Serrada et al. excluded whole body vibration as a sensory stimulation; yet, in the current review it was included because this stimulation was delivered through the plantar surface of the feet and, therefore, considered an appropriate sensory stimulation to the lower extremities. One paper which was included in both reviews may not at first glance be identifiable as being the same paper, because it appears to be by different authors: Jung et al. (2017) was incorrectly cited as In and Cho (2017) in Serrada et al. (2019). In addition, Morioka and Yagi (2009), included in Serrada et al. (2019), did not meet the inclusion criteria for this current review because there was no clear statement that ethical

approval had been granted for the study. Tyson et al. (2013b), also included in Serrada et al. (2019), was not included in the current review because it was a crossover trial and not a true randomized controlled trial. Finally, 26 of the 38 studies included in the Serrada et al. review related to sensory stimulation of the upper limb, and one to the trunk (Thielman, 2010), and not just to the lower limb, which was the focus of this current review. Of interest, there were two papers (Lee et al., 2013; Ng et al., 2016) in Serrada et al. (2019) which could have fulfilled the requirements for the current review but were not identified from the search for the current review. The reason for this is unclear.

Of the three studies included in both the Serrada review and the current review, there are some slight differences in quality assessment of the studies. Jung et al. (2017) stated that participants were randomly assigned using a selection envelope; presumably this procedure was undertaken by the researcher and may not be considered a rigorous method of randomization; the current review therefore assessed the risk of bias to be high, whereas, Serrada et al (2019) assessed this to be low risk bias for random sequence generation. Also, there was insufficient information relating to blinding of participants and personnel, and attrition; therefore, the risk of bias for these sections were assessed as unclear in the current review but assessed as low in the Serrada et al review. There was also some difference of opinion for the Lynch et al. (2007) study relating to selection and reporting bias. This may be accounted for by one of the authors for the Serrada et al review also being a co-author of Lynch et al. (2007), with greater insight into the procedures implemented within the study.

It is also important to highlight some implications for therapy treatment which have arisen from undertaking the review. The findings of this systematic review are similar to the findings of the systematic review undertaken by Schabrun and Hillier (2009), in which some support for passive sensory training was identified. There was no strong evidence to support the use of the sensory stimulation interventions included in the trials reviewed in this current systematic review, although there was some evidence to support using TENS. Evidence for use of electrical stimulation is the strongest from this review, and the promising use of electrical stimulation for retraining sensation has already been acknowledged in the fifth edition of the National Clinical Guideline for Stroke (Rudd et al., 2017). Nevertheless, a distinct lack of empirical studies supporting active sensory training was observed, and the interventions identified from both reviews do not accurately reflect all aspects of conventional physical therapy practice in preparing and retraining the lower limb for balance and gait following stroke; many hands-on somatosensory stimulation interventions are notably absent and clearly have not yet been investigated. However, clinicians have reported that they use hands-on techniques such as MTS, to provide somatosensory/proprioceptive stimulation to the foot (Aries et al., 2019), and so there is clearly a gap in the research and the literature, indicating that it is an area requiring further research. Similarly, evidence from other studies of other clinical populations has shown that wearing TIs has been effective in other clinical populations but not in stroke, hence the reason for them not having been not included in this review.

Based on this highlighted gap in the research literature, both MTS (to prime the motor system) and wearing of TIs (to augment the somatosensory input) were considered to be interventions that were worthy of further investigation. They were therefore justified as the chosen interventions to research, in conjunction with TSGT, which has an established evidence base, as combined interventions: MTS+TSGT and wearing TIs+TSGT. If the wearing of TIs is no less effective than MTS as an additional sensory stimulation combined with TSGT (to be evidenced in a subsequent randomized controlled trial), this could be recommended for use in clinical practice as a cost-saving but effective alternative treatment strategy post-stroke.

This systematic review has therefore informed the need for Study 2 (intervention modelling) and Study 3 the mixed methods, randomized, blinded feasibility study exploring somatosensory stimulation of the foot and ankle early post-stroke.

4 CHAPTER FOUR: METHODOLOGY

In Chapter two, the important role of afferent input, particularly proprioception, in control of movement was highlighted. Study 1, the systematic review, presented in chapter three identified the limited research presently available to support the effectiveness of somatosensory stimulation for the lower limb after stroke. Chapter four will summarize the research questions arising from the literature review, and the methodology of two further studies detailed in the rest of this thesis. The specific aims of the research and objectives of the studies that have been completed will be stated. Chapters five and six will then report the specific methods and findings of these two studies, respectively. The implications of the findings of all three studies will be discussed in chapter seven.

4.1 Rationale

Interventions that deliver intensive proprioceptive stimulation through hands-on physiotherapy, to prime the sensorimotor system, have been identified and described in previous studies, and given the collective name of Mobilization and Tactile Stimulation (MTS) (Hunter et al., 2006). However, the effects of MTS applied to the foot and lower leg have not been investigated. Similarly, the wearing of TIs has been shown to improve gait in people with multiple sclerosis (Dixon et al., 2014), but the effect of these on balance and gait post-stroke has not been explored. There is a body of evidence to support the use of TSGT to improve walking ability post-stroke. However, it is not known whether combining TSGT with

a sensory intervention is more effective than TSGT alone; furthermore, it is not known whether combining TSGT with a priming intervention might be more or less effective than combining TSGT with an augmenting intervention. Therefore, the benefits of priming the sensorimotor system prior to activity, such as TSGT, and augmenting the sensorimotor system during activities such as TSGT, warrant further exploration.

4.2 Research questions

An overarching research question evolved: is there a difference in outcomes of balance and gait post-stroke when comparing: a) TSGT alone, b) TSGT following a priming intervention (MTS), or c) TSGT augmented by wearing a TI?

Two potential null hypotheses need to eventually be addressed:

1. There is no difference in outcomes of balance and gait when TSGT alone is compared with priming the sensorimotor system using MTS prior to TSGT.
2. There is no difference in outcomes of balance and gait when TSGT alone is compared with augmenting the sensorimotor system by wearing TIs prior to and during TSGT.

However, before exploring the effectiveness of these combined interventions, more information is required relating to an appropriate dose and intensity of the three separate treatments: MTS, wearing TIs and TSGT. Consequently, exploratory, development research needed to be undertaken.

4.3 Evaluating complex therapy interventions

It has been acknowledged that therapy interventions are complex, often multifaceted, with many inter-dependent aspects (Walker et al., 2017) and applying the evidence to stroke rehabilitation is challenging (Langhorne et al., 2011). The MRC has recognized the difficulties relating to research and produced a framework for developing and evaluating complex interventions (Craig et al., 2006). This framework highlights the importance of taking time to develop and standardize complex interventions, making them repeatable, to enable rigorous analysis in future larger trials. Four distinct phases have been identified for the development and implementation phases of research; feasibility/piloting, evaluation, implementation and development as shown in figure 4.1 (Craig et al., 2006).

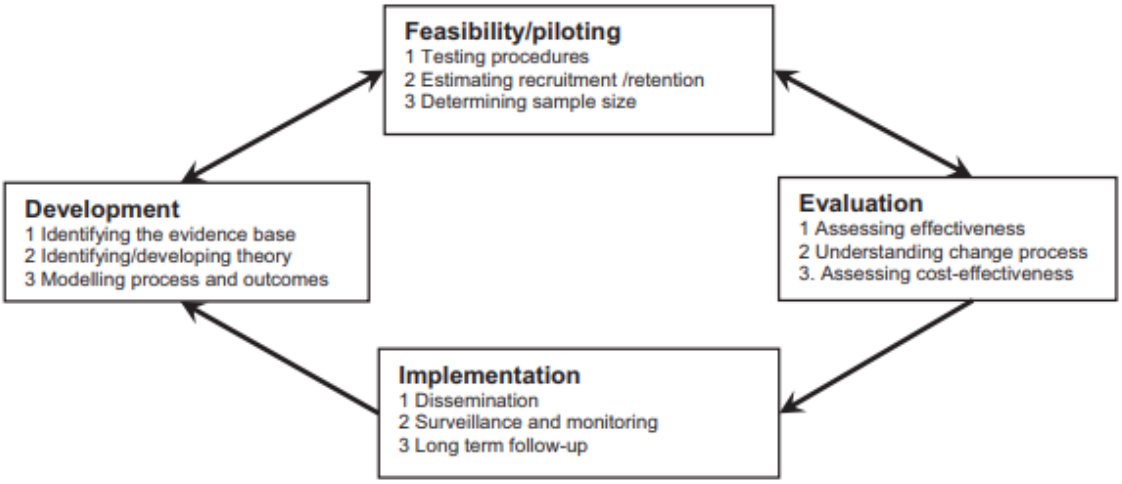


Figure 4.1 Key elements of the development and process of evaluating complex interventions. Reproduced with permission, (Craig et al., 2006)

Careful preliminary work is essential when researching complex interventions, and a feasibility or pilot study is advocated as an important step prior to proceeding to larger RCTs (Tickle-Degnen, 2013). Input at an early stage of research development should involve identification of the current evidence base and theories (Craig et al., 2006), as well as considering the opinions of clinicians to increase the external validity of the investigation (Samuel and Bucher, 2017), and input from patient and public involvement and engagement (PPIE) volunteers to ensure quality, relevance and importance of the research (Haywood et al., 2017). The intervention modelling study was undertaken following initial consultation at an early stage with clinicians and patient and public involvement advisors; time was dedicated to researching the evidence base, identifying and developing theory and integrating this information into the process of developing the interventions, as suggested in the development section of the MRC guidance (Figure 4.1). Consensus-based core recommendations have been developed from the SRRR to help improve the development, monitoring and reporting of research relating to stroke rehabilitation (Walker et al., 2017), and many of the suggested practices were followed in both the intervention modelling study and the feasibility study which were undertaken.

The development of standardized therapy protocols and subsequent evaluation of the effectiveness of the intervention are both important stages in the MRC framework; all therapy treatments involve many different components that interact and they can, therefore, be categorized as complex interventions (Craig et al.,

2006). Therapy interventions include talking to the patient as well as hands-on and independent techniques, and treatments could be influenced by the motivation and enthusiasm of the therapist and the patient; personalised treatment plans are common and communication and environmental issues are key (Tickle-Degnen, 2013). Indeed, the holistic nature of therapy interventions is referred to as a 'black box' of approaches and strategies, and a need for treatment to be individualised is acknowledged to meet the specific requirements of each stroke survivor, with a suggestion that rehabilitation is not a homogenous activity and can be influenced by multiple features (Ballinger et al., 1999). For this reason, it was important that the protocols within the MoTaStim-Foot trial enabled individualised treatment to also be delivered. When referring to the MRC guidelines, it was appropriate to undertake a feasibility study after the modelling study. This would allow for testing of the developed protocols, assessment of recruitment and attrition and collection of information to enable a sample size calculation.

Co-design has been defined as 'a collaboration between healthcare professionals and patients to develop clinical and educational interventions' (Green, 2018, p.50). It is a process which enables insight from the lived experience of a condition to be considered equally, along with professional expertise, empowering people to contribute to important issues (for example when developing rehabilitation interventions) that may directly affect them (Burkett, 2017). The importance of stakeholder involvement to enhance success when developing interventions is being increasingly recognized (Andersson, 2017). Healthcare professionals may

be considered the experts, with an ability to validate instruments and treatments; however, the importance of a patient who has experience of a particular condition is paramount, and was highly valued in relation to this study, because it has been described as being able to offer ‘the ultimate expert opinion’ (Hobart et al., 2004, p.9).

The feasibility and pilot stage of the MRC framework involves testing the acceptability of procedures, estimating probable recruitment and retention rates, and collecting data that can be used to calculate an appropriate sample size for a larger clinical trial (Craig et al., 2006). This study was undertaken early in the research process, and therefore a feasibility study was more appropriate than attempting to undertake a pilot study; OMs needed to be explored and a primary OM selected prior to a formal pilot which involves exact replication in a small form of the planned future study (NIHR, 2017). The National Institute for Health Research (NIHR) (2017, p.2) suggests the important question to be considered is ‘Can this study be done?’ and advises that feasibility studies should not involve evaluation of the effectiveness of the treatment intervention. As well as whether it is possible to undertake the trial, consideration needs to be given to whether the work should be taken forwards to a large trial (Horne et al., 2018).

A mixed-methods approach has been advocated, involving the collection of both qualitative and quantitative data to enhance knowledge relating to the suitability of the interventions and to explore any barriers to participation (Craig et al., 2006). In order to answer research questions, a methodological eclecticism approach can be

adopted using mixed methods, enabling the researcher to be a ‘connoisseur of methods’, selecting appropriate qualitative or quantitative approaches from the ‘toolbox’ (Teddlie and Tashakkori, 2012 p.777). Whilst there are a number of conceptual frameworks for research, quantitative methods sit under the umbrella of the positivist paradigm, whereas qualitative methods are encompassed within the constructivist (Tashakkori and Teddlie, 1998) and interpretivist paradigms which aid understanding of the social world (Chowdhury, 2014). Whilst ‘paradigm wars’ have existed over the years (Tashakkori and Teddlie, 1998), the compatibility of qualitative and quantitative methods has been advocated within the social and behavioural sciences; consequently, a different paradigm was suggested, named by some as pragmatism, with mixed methodologies emerging that combine both quantitative and qualitative approaches (Tashakkori and Teddlie, 1998).

Once feasibility has been established, evaluation of the complex intervention should take place in a larger trial. Even if the decision is made that the work should not be taken forwards it is still important to disseminate the findings to inform other research and potentially save any waste of valuable resources (Thabane et al., 2010). Dissemination of information, ideally at protocol stage, and when the results are available, is important, along with monitoring of the success of implementation of the techniques into clinical practice (Craig et al., 2006). When reporting the information from studies it is essential to include sufficient detail for replication of the work (Ioannidis et al., 2014), enabling synthesis of the information and facilitating implementation of the intervention (Craig et al., 2006). This whole process, from trial to implementation of findings into practice, has been suggested

as taking up to seventeen years (Grant et al., 2000) - known as the knowledge to practice gap - fostering a predominance of relying on clinical experience rather than evidence reported in the literature to support practice (Manns et al., 2015).

4.3.1 Implementation of evidence into clinical practice

Although global stroke evidence has been collated and disseminated through guidelines, this by itself is still insufficient to change clinical practice (Walker et al., (2013). Indeed, a cross-sectional, self-administered online survey of 172 occupational therapist and physiotherapist clinicians in Australia found that selection of treatment choices was mainly (‘often’ or ‘all the time’) based upon previous experience with similar conditions and presentations in the past (78%), or from colleagues (74%), whereas, only 42% of clinicians regularly used research literature for the basis of informing their clinical decision-making (Pumpa et al., (2015).

The challenges of implementation of research findings has been highlighted on many occasions; discussion often relates to bridging the evidence-to-clinical practice gap. As implied by the term ‘bridge’ this gap is a two-way phenomenon (Negrini et al., 2016). Not only does consideration need to be given to the fact that evidence needs to be implemented, but also to the issue that evidence for clinical practice may just not exist, even though the techniques appear to be effective to the clinicians involved i.e. no evidence of effectiveness is not evidence of ineffectiveness. This would account for the findings of Pumpa et al. (2015). The

relatively newly formed Cochrane rehabilitation group has acknowledged this issue and aims not only to apply evidence developed via Cochrane to rehabilitation, but also to identify the needs and specific aspects of rehabilitation that need to be researched to inform the clinical rehabilitation in the future (Negrini et al., 2018).

4.4 Research aims and objectives:

Hence, it was not appropriate to consider a large, powered RCT to investigate the effectiveness of the interventions of MTS and TI combined with TSGT until the development and feasibility stages had been completed. The decision was therefore made to undertake a feasibility study: the MoTaStim-Foot trial, the acronym arising from **Mo**bilization and **Ta**ctile **Stim**ulation to the **Foot** (post-stroke).

4.4.1 Research aims:

The first research aim of this thesis was:

1. To explore the evidence around somatosensory stimulation of the foot and lower leg to improve function after stroke. This was undertaken as Study 1 of this thesis, and the results have been presented in chapter three.

Study 1 led to the development of the null hypotheses presented in section 4.2; further aims were identified:

2. To develop standardized intervention protocols for sensory stimulation interventions for the lower limb (MTS, wearing TIs) and for TSGT, through co-design with expert clinicians, informed by the literature, which will be delivered in a trial.
3. To investigate the feasibility of delivering an RCT of sensory stimulation (MTS, TIs) combined with TSGT to improve balance and mobility following stroke.
4. To explore acceptability of the interventions and OMs to participants.

4.4.2 Research objectives:

Study 1: Systematic review of the literature (aim 1)

Objective 1.1: to systematically review the published literature investigating effectiveness of somatosensory stimulation applied to the lower leg and foot to improve balance and mobility after stroke.

Study 2: Intervention protocol development and co-design (aim 2)

Objective 2.1: in conjunction with expert clinicians and informed by the literature, develop and gain consensus on standardized treatment protocols for delivering: a) MTS for the lower limb, b) wearing TIs, and c) TSGT to stroke survivors.

Clinical trials often provide insufficient information for clinicians to understand the full details regarding the interventions explored and therefore translation into clinical practice is inhibited (Duff et al., 2010); in particular, details relating to duration and dose of treatment are often omitted (Glasziou et al., 2008). It was

important to ensure that the three protocols developed for this research were replicable. Details of how these protocols were developed is presented in chapter five. A detailed trial protocol is important so the rationale behind decisions and the methods are explicit; it describes how aspects of a trial should be carried out from the inception of the trial, through to the final reporting of the trial (Tetzlaff et al., 2012). Trial interventions need to be valid (supported by research), described in sufficient detail to enable replication (Schroter et al., 2012), and acceptable to patients in terms of the setting and specific treatment, as well as to clinicians who will administer the interventions (Sekhon et al., 2017). Development of clear, standardized protocols is imperative, enabling clinicians to interpret and consider them for clinical practice (Schroter et al., 2012); correct interpretation and replication of the findings of the research will aid translation into clinical practice where indicated, and permit other researchers to conduct further research relating to the specific intervention (Hoffmann et al., 2014) . The Consolidated Standards of Reporting Trials (CONSORT) 2010 Statement (Schulz et al., 2011) was consulted when developing the interventions for the MoTaStim-Foot feasibility study. This document highlights the importance of describing interventions in sufficient detail to enable them to be repeated. Further guidance is also offered within the CONSORT extension statement, the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guideline (Chan et al., 2013) suggesting content for trial protocols. This includes the development of rigorous treatment intervention protocols and treatment schedules for documenting the elements of the intervention undertaken. Although the development of a protocol

involves consideration of every individual aspect – for example, why, what, how, delivered by who and with what modifications etc. (TIDieR checklist, Hoffmann et al., 2014) – it is important to have a clear way of reporting exactly what has been undertaken in the intervention/treatment, and the development of a schedule facilitates this process. A schedule enables the recording of details relating to a treatment delivered and can be used to document completed therapy interventions (Jarvis et al., 2014). Development of treatment schedules is important to enable clinicians to be aware of the specific elements that have been evaluated (Hunter et al., 2006). Therefore, development of treatment schedules for MTS (lower limb), and TSGT was undertaken in this study, with the intention that the schedules would be used to standardize delivery of the interventions in a subsequent feasibility study (Study 2). A treatment schedule for TIs was not required as there was a simple wearing protocol which was followed (chapter five, section 5.3.4, table 5.3).

Study 3: Mixed-methods feasibility study (aims 3 and 4)

Objective 3.1: To determine feasibility of delivering a trial comparing MTS+TSGT with TIs+TSGT.

A 3rd group, exploring TSGT alone, was considered; however, this was not deemed necessary for this feasibility study. Evidence already exists that TSGT is effective and has already been delivered in previous trials (Blennerhassett and Dite, 2004; Dean et al., 2000; Monger et al., 2002; Salbach et al., 2004; Scianni et al., 2010). It was not the purpose of the feasibility trial to compare effects of

MTS+TSGT or TIs+TSGT with TSGT alone. Effectiveness will be explored in a larger trial in the future. Objective 3.1 was achieved through a number of more specific objectives:

3a Find out if recruitment methods were effective, by analysing the recruitment rate and associated data including number of people invited to participate, the number and proportion of those agreeing to consent to participate, and those eligible to participate.

3b Monitor and analyse the number of people who drop out of the trial (attrition rate).

3c Gain pertinent information to inform an appropriate and feasible sample size for a future study.

3d Explore participants' experiences of interventions and their views on the acceptability of the treatments and method of delivery as interventions for a future study.

3e Investigate whether daily diaries and focus groups (FGs) are suitable ways to capture and explore stroke survivors' experiences of the interventions.

3f Investigate feasibility (cost and acceptability to participants) of a battery of OMs for sensorimotor impairment and lower limb function and balance, to inform the choice of primary and secondary OMs for a future trial.

3g Explore responses to the interventions (MTS plus TSGT or TIs plus TSGT) over time and in relation to the number of treatment sessions delivered; this will help to determine the most appropriate duration of therapy in a future trial.

3h Generate information regarding the participants recruited i.e. participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk to ensure baseline characteristics of the two groups are comparable and to inform future studies.

Criteria for assessing feasibility:

- 3a - Recruit 34 participants within a period of 18 months, achieving a recruitment rate of >5%.
- 3b - Attrition rate <15%.
- 3c - Gain relevant data (e.g. standard deviation) to enable a sample size calculation to be undertaken prior to a future trial.
- 3d - Deliver the interventions to the participant safely (monitored by pain, fatigue and adverse events), in various venues (hospital/home) according to protocol (fidelity and adherence to dose).
- 3e - Focus groups (>n=17, 50% of total number of participants) are achievable to explore stroke survivors' experiences of the interventions and OMs
- 3f - OMs completed for all participants.

Criteria for assessing acceptability:

- 3d - Participants inform (from daily diaries or FGs) that the treatments (MTS, TIs and TSGT) and method of delivery as interventions are comfortable and acceptable.
- 3d - Venue (for example the home or hospital environment) for undertaking interventions and OMs is appropriate and acceptable to the participants.
- 3f -OMs are acceptable for participants to undertake.

4.5 Methodology for Studies 2 and 3

4.5.1 Study 2: Intervention modelling

Study 2 was an intervention modelling study in which standardized procedures for all three interventions (MTS, wearing TIs and TSGT) were developed. An intervention development study involves a rigorous, repeatable process at an early stage of research, between the original inception of an intervention and the point in time when it is ready for piloting, or formal feasibility or efficacy testing (Hoddinott, 2015). Decision-making processes should be transparent, and detailed information about the intervention, including training needs, should be developed (Hoddinott, 2015).

Study 2 addressed research aim 2 and involved a consensus methodology, utilising a modified Nominal Group Technique (mNGT) (Potter et al., 2004), for development and agreement of the treatment protocols. Consensus methodology involves seeking opinions of several neurological expert clinicians, with the aim of addressing specific problems, developing new concepts and deciding priorities (McMillan et al., 2016), and has been used in previous studies to identify interventions used in clinical practice (Taflampas et al., 2018).

NGT was first described and developed by Andre Delbecq and Andrew Van de Ven as far back as 1968 (Delbecq et al., 1975). The traditional format of NGT has

been developed from social-psychological research and is a group process involving a very structured meeting format with pre-arranged steps enabling thought processes, discussion, and due consideration to the problems and issues, with the facilitator also contributing to the process (Delbecq et al., 1975). It has been suggested that a mixture of both quantitative and qualitative methods is utilized within the NGT (Potter et al., 2004). An NGT allowed the use of an interacting group situation, enabling unstructured discussions, with members interdependent upon one another (Richards and Cuffe, 1972). One of the disadvantages of an interacting group could be that a few key dominant characters within the group do not enable others to express their independent thoughts, and this can restrict the generation of ideas, often resulting in the discussion of just one or two aspects (Delbecq et al., 1975); careful moderation is required.

The structure of an NGT meeting enables detailed consideration of each idea, and increases the opportunity for individual participation, ensuring everyone's ideas are taken forwards for discussion; this results in people feeling that they have contributed and makes them feel valued (Delbecq et al., 1975). The Delphi technique, which is also a consensus method was considered and it would also have offered the opportunity of generating new independent ideas; however, the Delphi technique requires a long period of time to complete, often as much as several weeks or even months (Delbecq et al., 1975; McMillan et al., 2016), due to the necessity for several rounds of assimilating opinions from the experts (Sim and Wright, 2000), and was deemed to not be feasible. The busy nature of the

clinicians' working lives was considered; although organization of an NGT requires a significant amount of time for the researcher to prepare (Delbecq et al., 1975), it traditionally involves participants for just a few hours and results are quickly evident (McMillan et al., 2016). An NGT has been described as a 'hybrid' of the Delphi method and the FG (Sim and Wright, 2000, p.79), suggested as suitable for use in physiotherapy research (Potter et al., 2004). Hence, in view of the many advantages of the NGT, this was the method selected for Study 2 of this feasibility study.

Five steps have been described for an NGT meeting (based on Potter et al., 2004):

1. Firstly, the facilitator welcomes the group and gives specific guidance relating to the format of the meeting.
2. After this, the participants sit in silence and consider their own responses to the problems or issues that need to be addressed, documenting them for sharing later.
3. Ideas are then collected and recorded on a flip chart. This is achieved via a round-robin process, with each participant given the opportunity to share an idea prior to moving on to the next person. All participants are therefore encouraged to participate equally.
4. Following clarification of any of the ideas presented, a group discussion takes place, with the facilitator ensuring all participants contribute to the discussion and comparable time is devoted to each idea, rather than focusing on one issue.

5. Finally, ideas are prioritized and a vote takes place, (usually not a public vote, to ensure independent thoughts are taken forwards, without influence from other participants (Sim and Wright, 2000)), resulting in immediate knowledge of the results of the study (Delbecq et al., 1975; Potter et al., 2004).

However, modifications were made to the above steps for Study 2 (discussed in detail in chapter five, section 5.3), to enable development of three distinct protocols, which needed to be achieved with just one face to face mNGT session. The NGT has been reported to be flexible (McMillan et al., 2016), and the traditional format has previously been adapted by some researchers; for example, Allen et al. (2004) included in their study a stage in advance of the NGT meeting, which involved sending a postal survey to the participants, collecting data that was used to inform the NGT meeting itself.

One of the modifications to the NGT in Study 2 involved undertaking scoping reviews relating to wearing TIs and TSGT in advance of the NGT meeting; the purpose was to enable an informed discussion of a summary of the information related to these interventions at the NGT meeting, facilitating development of protocols for these interventions at the mNGT meeting. Scoping reviews are a comparatively new method of reviewing the literature (Pham et al., 2014), allowing assessment of the evidence evolving in a subject area (Peterson et al., 2017). Research of various designs can be included, across wide-ranging topic areas,

with potentially a rigorous and transparent method; however, they do not formally assess the quality of the literature (Arksey and O'Malley, 2005).

The five steps were followed at the mNGT meeting, with a slight adaptation to step two. Part of step two (participants considering their own opinions) had been undertaken in advance of the meeting; and participants came to the meeting with ideas for discussion relating to the MTS protocol, in view of the work that had been conducted in advance of the meeting. The process will be discussed in detail in chapter five.

4.5.2 Study 3: Mixed-methods single-blind randomized feasibility study

In order to address research aims 3 and 4, and specific objectives *3a* to *3h* (see section 4.4.2.3), Study 3 involved delivering the interventions, modelled and agreed in Study 2, in a randomized, blinded mixed-method feasibility study (MoTaStim-Foot Trial), which included collection and analysis of both quantitative and qualitative data, as recommended by the MRC guidance (Craig et al., 2006).

It is widely acknowledged that an RCT methodology can reduce potential bias within a study (Boutron et al., 2007) and, although difficult to accomplish within research, blinding is a key element required to reduce this bias (Houweling et al., 2014). Randomization is also important, ensuring an equal chance of group allocation and comparability of the groups (Sim and Wright, 2000). Even though

the RCT is recognized as the ‘gold-standard’ methodology for undertaking research (Backmann, 2017), adoption of a mixed-methods design within an RCT offers advantages.

Exploratory research involving qualitative data offers a holistic insight (French et al., 2001), and can allow a detailed understanding of a person’s experience, within the context of their particular situation; experimental research involves the collection of numerical or quantitative data (Hicks, 2010). Implementation of mixed-methods research permits the collection of both these data types in a single study (Sockolow et al., 2016), enabling different aspects relating to the research question to be explored, making the study more complete (O'Cathain et al., 2007). It has been suggested that a pragmatic researcher who is willing to use both quantitative and qualitative techniques has an advantage, with the flexibility to address different types of research questions (Onwuegbuzie and Leech, 2005). Combining both methods in a single investigation enables different research strategies to address the research question, for example, allowing the participant’s voice to be heard, (which was an essential element of this feasibility study), as well as producing quantitative data, with the different methods complementing each other and potentially providing a more complete outcome from the research (Hicks, 2010), by triangulation of the findings (O'Cathain et al., 2010).

One important purpose of a feasibility study is to monitor and appraise recruitment strategies (Hubbard et al., 2015; O'Cathain et al., 2015) to inform any planned

large RCT (objective *3a* of this work). Evaluation of recruitment numbers and strategies, along with potential eligibility and screening to recruitment ratios is important to inform future trials, for example, how many sites will need to be included, how long the trial may take, and whether the inclusion criteria are suitable (El-Kotob and Giangregorio, 2018). Another essential role of the feasibility study is to explore the feasibility and acceptability of the interventions (O'Cathain et al., 2015) and OMs (objectives *3d* and *3f*). Acceptability involves many different aspects including: an ability to understand the intervention; perceived ability to participate (self-efficacy); effectiveness, as well as consideration of own perceptions of the intervention ('affective attitude'); burden, including necessary compromises to enable participation; and 'ethicality' (whether the intervention fits into the participant's value system) (Sekhon et al., 2017, p.8).

Assessment of acceptability was operationalized within the MoTaStim-Foot feasibility study by several mechanisms. The ability to understand the intervention would be assessed by independent observation of all research therapists and post hoc analysis of aspects of intervention that were delivered. The ability to participate, burden for the participants, and ethicality would be judged by the attrition rates and comments in the dairies and focus groups. An insight into potential effectiveness would be gained from the analysis of change scores from baseline to end of intervention and one month follow up, which would be undertaken to enable selection of a primary OM for future trials. Declaration of

researcher's assumption in advance of the study would be undertaken to address reflexivity in the study (affective attitude).

As part of the feasibility of delivering the interventions, fidelity of delivery should be monitored and explored (El-Kotob and Giangregorio, 2018). One particular consideration for this study was whether the participants would be willing to wear the TIs. By undertaking a mixed-methods design, with FGs and daily diaries, it was possible to capture participants' perceptions, identifying the acceptability of interventions and OMs delivered, as well as exploring the potential effect size and its variance, therefore meeting the aims and objectives of undertaking a feasibility study. Study 3 is presented in chapter six.

4.5.2.1 Focus Groups (FGs)

In order to address research aim 4 and research objectives *3d*, *3e* and *3f*, to explore the feasibility and acceptability of the interventions and OMs, FGs were undertaken (Sim and Snell, 1996; Tong et al., 2007). A FG is a form of group interview, ideally with a homogeneous group, which is led by a moderator who encourages interactive conversation and seeks opinions from the group, generating qualitative data relating to specific topic areas (Sim and Snell, 1996). A sample size of 9–12 is suggested as being ideal for generating a wide range of opinions in a group that is controllable (Allen et al., 2004). People who feel self-conscious or intimidated may be more likely to speak out in a FG situation than in an interview, and a variety of forms of communication can be utilized including

anecdotal stories, mocking and jokes (Kitzinger, 1995). A FG can provide a large quantity of rich data in a short period of time, allowing the researcher to find out 'what people really think and feel' (Krueger and Casey, 2000, p.7). Offering stroke survivors an opportunity to recount their experiences, and analysis of their personal accounts, has been suggested as essential to developing evidence-based practice within stroke rehabilitation (Merlo et al., 2013). The interaction between members of the FG is a strength, creating impulsivity, which adds another dimension to the data collection process, enabling triggering of ideas in response to comments within the group (Sim and Snell, 1996).

The inclusion of an additional member of the research team as observer and field-note taker during the FG provides additional insights and context behind the interactions of participants, providing investigator triangulation, reducing the bias associated with a single investigator (Archibald, 2016). In a seminal text, Lincoln and Guba (1985) discussed that credibility in qualitative studies can be enhanced by using different sources for the same information, introducing triangulation, helping to provide a more comprehensive representation of the issues being explored. Within the MoTaStim-Foot trial, triangulation of different data collection methods and researcher triangulation (Nowell et al., 2017) were used as a means of increasing credibility.

4.5.2.2 Daily diaries

Daily diaries were also used to address research objectives *3d, 3e* and *3f*. Asking participants to keep a researcher-driven diary, to inform the researcher of particular aspects relating to the interventions delivered and the OMs used (Elliott, 1997), enables the researcher to gain insights into the participants' experiences of the research (Mackrill, 2008). Use of a diary provides an opportunity to collect more precise information relating to the research and helps prevent issues relating to recall (Roghmann and Haggerty, 1972). However, there are challenges with the use of diaries, for example recall bias (Lyons and Pahwa, 2007; Papapetropoulos, 2012), poor compliance and diary fatigue (Papapetropoulos, 2012), or duplicate entries for the same date, as well as incomplete or illegible entries (Lyons and Pahwa, 2007). These are all issues that could threaten or bias the validity of the content.

4.6 Patient and Public Involvement and Engagement (PPIE)

Before designing the MoTaStim-Foot feasibility study, group stakeholder consultation was undertaken with both clinicians and PPIE volunteers on two occasions. Some early preliminary work occurred to explore the opinions of therapist clinicians (Aries et al., 2019), and those of stroke survivors and carers attending a local stroke club, as to whether the research being proposed was relevant and appropriate. Further insight from both clinicians and PPIE advisors was possible because of an NIHR Research Design Service (RDS) PPI grant, directly informing the research proposal for the feasibility study.

4.7 Summary

This chapter has summarized the aims and objectives of the work detailed in this thesis. Justification has been provided for the chosen methodologies for Study 2, an intervention modelling study, which will be presented in chapter five, and also the mixed-methods feasibility study (MoTaStim-Foot), Study 3, which is discussed in chapter six.

5 CHAPTER FIVE: STUDY 2 – INTERVENTION MODELLING

5.1 Purpose

Study 2 addressed the second aim of the work in this thesis, to develop standardized intervention protocols for sensory stimulation interventions for the lower limb that will be delivered in a trial. In line with the complex intervention development guidelines, the process of intervention modelling was a 'dynamic iterative process, involving stakeholders, and reviewing published research evidence, drawing on existing theories' (O'Cathain et al., 2019 p.1). The objective was, through co-design with expert clinicians and informed by the literature, to develop and gain consensus on standardized treatment protocols for delivering a) MTS for the lower limb, b) wearing TIs, and c) TSGT to stroke survivors.

The TIDieR guidelines (Hoffmann et al., 2014), Consolidated Standards of Reporting Trials (CONSORT) 2010 Statement (Schulz et al., 2011), and SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guideline (Chan et al., 2013) were followed or considered when developing the interventions for the subsequent MoTaStim-Foot feasibility trial. This was to ensure that rigorous treatment intervention protocols and treatment schedules for documenting the elements of the intervention undertaken were developed.

5.2 Ethics approval

Research ethics approval for Study 2 was obtained via the Keele University Ethics Review Panel (Appendix 10). Participants provided written informed consent and were asked to sign a statement in the consent form (Appendix 11) agreeing to maintain confidentiality regarding group discussions and participant attendance. Anonymity of all participants was maintained using participant numbers or pseudonyms when presenting the work and in any subsequent write-up and dissemination. A list correlating numbers with specific participants was kept in a password protected file accessible to the researcher.

Personal information of participants was only accessible to the researcher and the supervisor. Data were stored securely on a password-protected computer or in a locked filing cabinet within the School of Health and Rehabilitation, at Keele University. All data were collected and stored in accordance with the Data Protection Acts, 1998 and 2018 (Legislation.gov.uk, 1998; Legislation.gov.uk, 2018), and will be stored securely for ten years after the end of study declaration, in line with Keele University policy.

5.3 Design

An mNGT was undertaken - full details of the stages are documented in chapter four (section 4.5.1). As discussed in section 4.5.1 the NGT was modified (mNGT) in this study in three ways: firstly, by the inclusion of independent clinician activity

(by suggesting the changes required for the upper-limb MTS schedule and the first iteration of the lower limb MTS schedule) in advance of the mNGT meeting, to limit direct face-to-face time with the busy clinicians. Therefore, part of step two (participants considering their own opinions) had been undertaken in advance of the meeting; and participants came to the meeting with ideas for discussion relating to the MTS protocol. The upper-limb MTS schedule was to be adapted for a lower-limb MTS intervention and individual opinions of clinicians were important to ensure that all potential lower limb interventions were considered during protocol development, in readiness for discussion at the collaborative mNGT meeting. Details of the protocol development process are described in this chapter.

Secondly, in advance of the mNGT meeting, the researcher undertook scoping reviews of published literature relating to wearing TIs and TSGT, to inform the discussion in the meeting. The third modification related to the use of some small group work during the mNGT to develop the TSGT protocol. It was felt that the use of the small group work, within the mNGT meeting, prior to a full group discussion would enhance the depth of the discussions. A flowchart summarizing the process is available in figure 5.1.

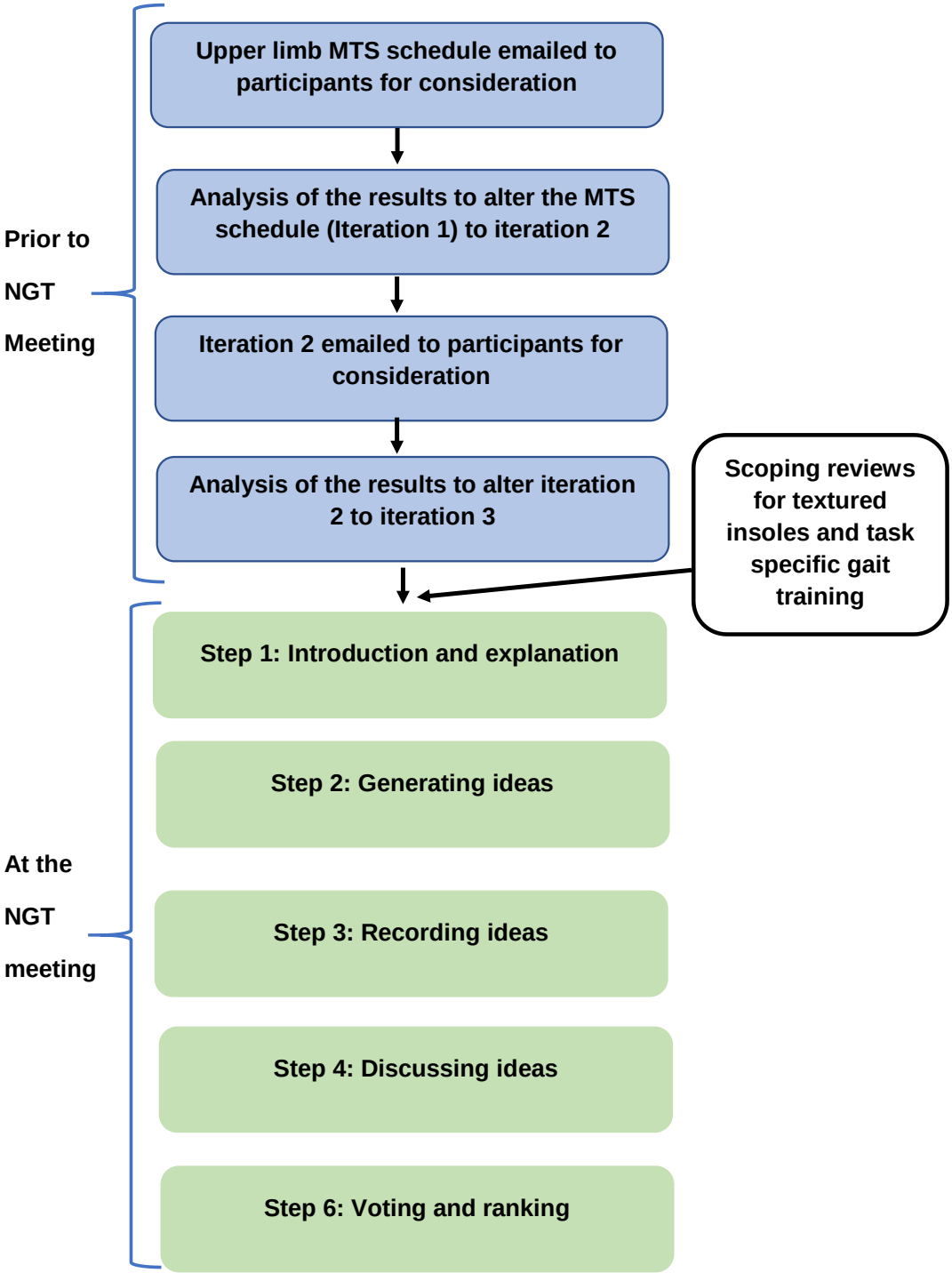


Figure 5.1 Stages of the modified Nominal Group Technique

5.3.1 Participants

A sample of 12 expert therapists (physiotherapists/occupational therapists) was recruited from NHS Trusts in the North Midlands, Staffordshire, and Shropshire through local networks: North Staffordshire Special Interest Group for Neurological Therapists, and the Keele Regional Hub of the Council for Allied Health Professions Research (CAHPR). Members of these groups were sent an email with a letter of invitation (Appendix 12), through the Special Interest Group for Neurotherapist's Chairperson and the CAHPR Keele Regional Hub Leader, outlining the project with an invitation to participate. Those who responded with a request for further information were sent a participant information sheet (PIS) (Appendix 13) and invited to ask questions of the researcher. The first twelve participants meeting the inclusion criteria and providing written informed consent (Appendix 11), either via email or in person prior to the commencement of the study, were recruited.

Inclusion Criteria

- Physiotherapists or occupational therapists working in the NHS at Band 6 or above
- At least two years of experience working in stroke rehabilitation
- Participants reported they had experience of hands-on sensory stimulation of the foot and ankle post-stroke, delivering MTS within conventional therapy
- Agreement to take part in all stages of the study

Exclusion Criteria

- Specialists in paediatric neurological therapy and, therefore, insufficient experience in applying sensory stimulation to the foot and ankle post-stroke in the adult population (≥ 18 years)

5.3.2 Systematic literature searches - scoping reviews

In preparation for the mNGT session, scoping reviews of the literature were undertaken relating to:

1) the use of textured surfaces as a rehabilitation intervention to improve gait and balance in standing
2) TSGT after stroke

The purposes of the scoping reviews were to: 1) provide an overview of the range of types and wearing protocols for TIs reported in the literature to enhance sensory input through the plantar surface of the foot; and 2) to provide a comprehensive summary of the content and dose of TSGT reported in published studies of TSGT for stroke, noting individual exercises and suggested ways for progression. It was not the purpose of the scoping review to provide a theoretical background relating to TIs; augmentation of sensation is discussed in the rehabilitation strategies section (section 2.8).

No scoping review was indicated for the MTS because there is already a theoretical backgound exisiting for sensory facilitation techniques (Hummelsheim et al., 1995) and the decision was made that it was appropriate to adapt the previously developed upper limb MTS protocol for the lower limb.

The databases searched were: Ageline, AMED, CINAHLplus with full text, Medline, PsycARTICLES, PsycINFO and SPORTdiscus with full text. For the TI scoping search, the databases were searched individually identifying all appropriate studies relating to either textured material or TIs. Searches relating to TIs were undertaken from inception to 27th September 2015. However, for the TSGT scoping search, the databases were searched together, with dates of search from January 1990 to August 2015. This was deemed to be appropriate as it would still highlight necessary pertinent information related to TSGT and fulfilled the purpose of the search.

Relevant studies were identified by reading titles and abstracts and accessing full texts where appropriate; reference lists were also checked, and any further suitable articles accessed. All types of research methodology were included, to ensure pertinent information was not missed. Articles were excluded if they were not written in English or were grey literature. Relevant information was extracted to inform the mNGT meeting participants and facilitate the development of standardized protocols, meeting research objective 2.1. Specific information extracted is detailed below in relation to the two different interventions.

5.3.2.1 Search terms and inclusion criteria for TI search

In relation to the TIs, specific questions to be addressed by the scoping search related to types of material, footwear worn, and duration and timing of wearing the TI or standing on the textured material. Therefore, the following search terms and strategy were used, summarized in table 5.1:

- 'Textur*' OR 'textured insoles' OR 'textured surface'

AND

- rehab* OR 'physical therapy' OR physiotherapy

AND

- Gait OR walk OR stand OR balance

Table 5.1 Search strategy for scoping review related to TIs

Search	Term
S1	Textur*
S2	Textured insoles
S3	Textured surface
S4	S1 OR S2 OR S3
S5	Rehab*
S6	Physical therapy
S7	Physiotherapy
S8	S5 OR S6 OR S7
S9	Gait
S10	Walk
S11	Stand
S12	Balance
S13	S9 OR S10 OR S11 OR S12
S14	S4 AND S8 and S13

5.3.2.2 Types of participants

To ensure all information relating to textured materials or TIs was accessed, the type of participants included: healthy young and older adults, older adults with self-reported history of falls, older adults with mild mobility and somatosensory deficits, survivors of acute or chronic stroke, adults with multiple sclerosis, adults with type II diabetes, or adults with Parkinson's disease.

5.3.2.3 Types of interventions and outcomes

Articles were included if they related to standing on textured surfaces or wearing TIs and referred to outcomes of balance or walking.

A flowchart representing the TI search is presented in figure 5.2. Summary data are presented in table 5.2 and full details, including OMs, results and author's conclusions are available in the table in Appendix 14.

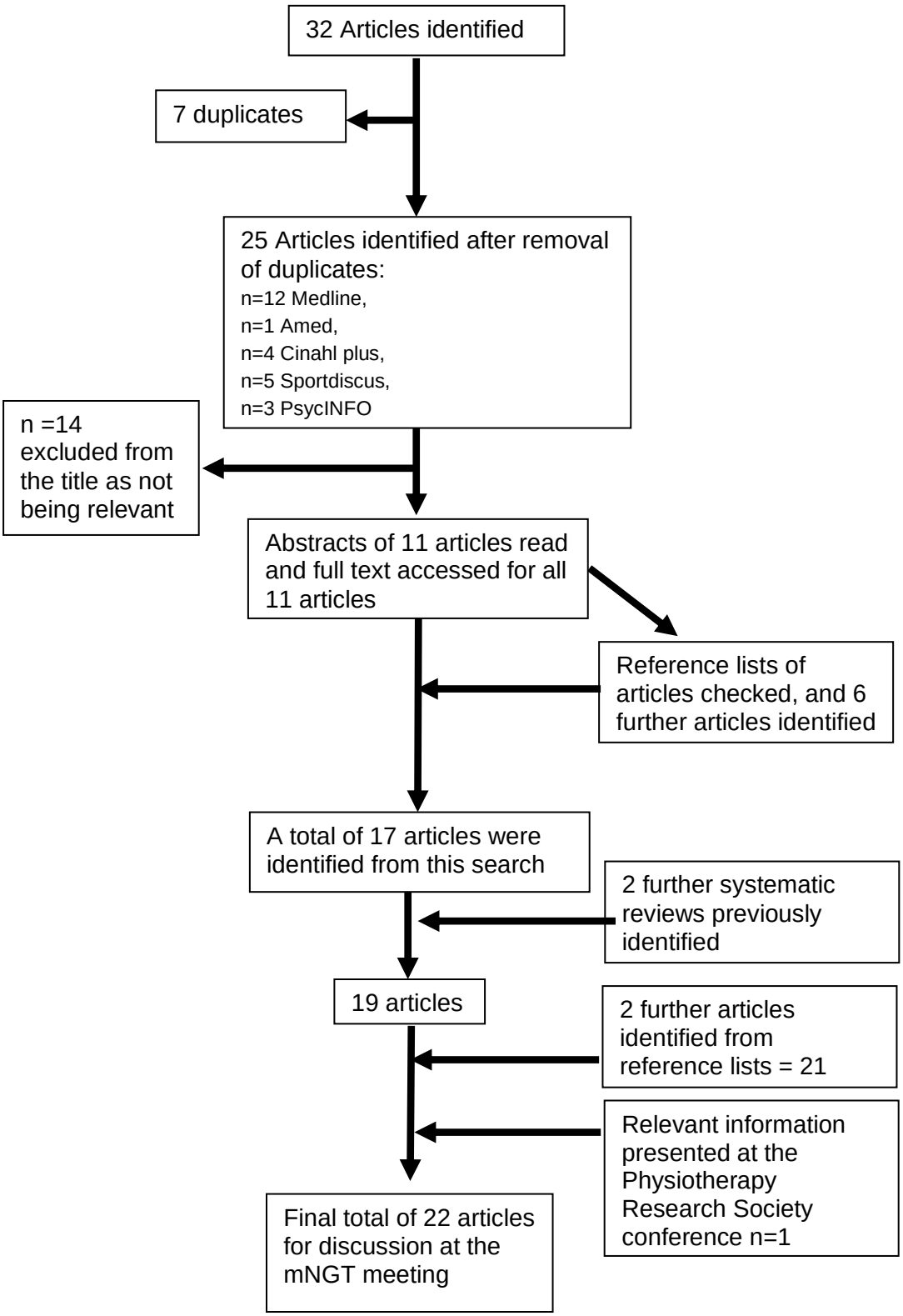


Figure 5.2 Flowchart of the process for identifying studies related to TIs

5.3.2.4 Characteristics of the included studies

A final total of 22 articles were included in the scoping review. Studies were included if they involved different textured surfaces under the plantar aspect of the foot, as not all studies used textured insoles per se.

Types of study included: RCTs (Hartmann et al., 2010); experimental designs with order of testing randomized (Dixon et al., 2014; Qiu et al., 2012; Qiu et al., 2013), and experimental designs (Aruin et al., 2000; Aruin and Kanekar, 2013; Clark et al., 2014; Corbin et al., 2007; Hatton et al., 2009; Hatton et al., 2011; Hatton et al., 2012; Kalron et al., 2015; Kelleher et al., 2010; Nurse et al., 2005; Palluel et al., 2008b; Palluel et al., 2009; Preszner-Domjan et al., 2012; Silva et al., 2015; Wilson et al., 2008).

Two other systematic reviews had been identified in earlier searches related to TIs (Christovão et al., 2013; Orth et al., 2013), so these articles were also included because they were deemed relevant for inclusion. A search of their reference lists identified two of the included studies which have been named above (Hartmann et al., 2010; Preszner-Domjan et al., 2012). A presentation given at the Physiotherapy Research Society highlighted additional relevant information (Baron et al., 2014), which was also included in the summary presented to the participants.

5.3.2.5 Descriptions extracted

Information extracted included: study objective, sample, study design, type of textured material or TI, details of the intervention or testing conditions, OMs, results and conclusions. Details of the interventions used in the literature were examined and protocols for the wearing of TIs synthesized, noting dose, how long the TIs were worn or whether they were only worn for testing (table 5.2). Whilst reviewing the literature relating to TIs information regarding the type of exercises undertaken in TSGT and how these were progressed was also extracted (tables 5.5 and 5.6).

5.3.2.6 Wearing time of the TIs

In nine experimental studies, participants simply stood on the textured material or wore the TIs during testing (Aruin et al., 2000; Aruin and Kanekar, 2013; Clark et al., 2014; Corbin et al., 2007; Hatton et al., 2009; Hatton et al., 2011; Hatton et al., 2012; Kelleher et al., 2010; Nurse et al., 2005). Four studies encouraged participants to wear TIs as much as possible while undertaking their usual functional activities (Baron et al., 2014; Dixon et al., 2014; Hartmann et al., 2010; Kalron et al., 2015).

Participants in Dixon et al., (2014) wore TIs for a mean of 11 (out of 14) days (SD 4, range 3–14); of the 14 participants in Hartmann et al., (2010), four wore insoles all day, four wore them for half a day, four for two hours per day, and two for less

than one hour per day. In contrast, participants in Kalron et al., (2015) reportedly wore TIs constantly throughout the day for four weeks.

5.3.2.7 Texture types

Different types of texture and insoles were used and these, along with the trial descriptions and sample sizes are presented in table 5.2. It should also be noted that Aruin et al (2000) and Aruin and Kanekar (2013) applied a shoe lift or a TI to the ipsilesional side, respectively, causing discomfort with the purpose of compelling weight shift through the contralesional side. The motive behind the use of these strategies is therefore different from the current MoTaStim-Foot feasibility study.

5.3.2.8 Synthesis of descriptions

Information gained from the scoping review of TIs was synthesized, summarized and presented to the participants, providing 22 pieces of research for discussion. The focus of the information presented included details of interventions, specifically types of textured material used, or TIs worn, and the protocols for wearing the TIs (table 5.2).

Table 5.2 Summary of the types of study, sample sizes and types of texture explored in the studies

Author and date	Sample	Study design	Textured material or insole
Aruin et al. (2000)	n=8, acute and chronic stroke n=5 subjects wore Ankle Foot Orthosis (AFO) (not during testing) n=1 6/52 therapy programme	(Pre-) experimental single group, pre- and post-intervention No blinding No random allocation	Lift put in shoe on the non-paretic side. Regular shoes worn. Just worn for testing. Although n=1 has a six-week therapy programme – insole worn all day and during all daily activities.
Aruin and Kanekar, (2013)	n=11 healthy subjects Pilot data from individuals with stroke n=4	(Pre-) Experimental (pre-post intervention, single group). No control, no blinding, no random allocation	Single TI, a D-insole made of polyvinyl chloride with small pyramidal peaks (3mm height and centre to centre distance 10mm), standardized footwear. Just worn for testing.
Baron et al. (2014) (conference proceedings)	n=46 Patients with Multiple Sclerosis (MS). Able to walk 100m	Exploratory (qualitative) study: Semi-structured interviews with participants on study exploring the effects of three different TIs	**Control:** smooth **Algeos TI -** Algeos Evalite Pyramid EVA, 3mm thickness, with small pyramidal peaks, centre to centre distances of approximately 2.mm **Crocs TI -** insoles with small nubs of approx. 1mm height Part of Dixon et al., (2014) trial – told to wear them as much as possible for two weeks
Christovão et al. (2013)	1) Controlled clinical trials 2 Intervention – insole, 3) Postural balance OMs 4) published 2005-2012 12 studies included (n=392) Mainly 'older volunteers'	A systematic review	Quick comfort insole, soft gel and hard insole, TI, vibrating insole, insole with spikes, insole with a wedge, balance-enhancing insole, flat insole
Clark et al. (2014)	n=14 older adults with mild mobility deficits and mild somatosensory deficits	Experimental study No blinding No random allocation	Made of thin semi-rigid plastic with firm raised (1.5mm) nodules 1.5 cm apart on a grid pattern. Just worn for testing.
Corbin et al. (2007)	n=33 healthy participants	A cross over trial No blinding No random allocation	TIs made from plastic floor matting purchased from local hardware store, with rounded plastic nubs, raised about ¼ cm off the plastic surface. Participants wore thin socks and their own athletic shoes for testing Just worn for testing
Dixon et al. (2014)	Part 1: n=46 Patients with MS, who could walk 100m unassisted or using one stick/crutch.	Design: 3 groups, within-session repeated-design with exploratory follow-up period. Blinding. Random allocation order of insole wearing.	1) Control (smooth surface) 2) Texture 1 - Algeos Evalite Pyramid EVA, 3mm thickness, with small pyramidal peaks, centre to centre distances of approximately 2.mm 3) Texture 2 - Crocs silver insoles with small nubs of approx. 1mm height Told to wear them as much as possible for two weeks.
Hartmann et al. (2010)	n=28 Independent living, or older adults aged 65 to 91 years	RCT pre/post-intervention. 3 groups: Insole plus training (IG) group Just training group (TG), Control group (no intervention), Random allocation No blinding	Med Reflex shoe insoles with raised projections to improve afferent feedback from the foot. Subjects asked to wear insoles as much as possible and use them during everyday life and during training sessions.
Hatton et al. (2009)	n =24 Young adults	Within-subject experiment Sequence of test condition randomized	Three different textured surfaces used: 1: Evalite to pyramid EVA 3 mm thickness, with small pyramidal peaks texture

		No blinding	2: Nora Luna soft mini non-slip 3mm thickness with convex circular patterning 3: control condition used a completely flat surface texture medium density Eva 3mm thickness. Just worn for testing
Hatton et al. (2011)	n=50 healthy older adults	Within-subject experimental Sequence of trials randomized / No blinding	**Texture 1:** Evalite to pyramid EVA 3mm thickness, with small pyramidal peaks **Texture 2:** Nora Luna soft mini non slip 3mm thickness with convex circular patterning. Just worn for testing
Hatton et al. (2012)	n= 30 older adults, with self-reported history of falls	Within subject experimental Sequence of textures worn, eyes open or closed. No blinding	**TIs:** Evalite to pyramid EVA 3mm thickness, with small pyramidal peaks. Centre to centre distance approx 2.5mm **Control** - completely flat surface texture medium density Eva 3mm thick. Just worn for testing
Kalron et al. (2015)	n=25 patients with relapsing-remitting MS	Within-subject experimental design with a four-week intervention phase No blinding No randomization	Insoles customized for left and right feet. Insoles 3mm thick and made of elastic rubber and fabric. Coarse texture of insole designed with miniature square pyramids organised in a grid pattern. Participants were instructed to wear the TIs throughout the day for four weeks and to continue their usual activities.
Kelleher et al. (2010)	n=14 patients with MS and 10 healthy controls	Experimental with control group No control healthy age-matched, no blinding. Trials with and without insoles were randomized.	Fine leather insoles were cut, Grade P80 wet and dry sandpaper adhered to leather base, ' considered sufficiently rough to provide sensory feedback but not so rough as to cause skin discomfort. For testing only
Nurse et al. (2005)	n=15 healthy participants	Experimental design No blinding No randomization	Two shoe insert conditions: 1) Control insert made from 3mm thick EVA foam (Shore C 60) 2) Textured insert 3 mm thick EVA foam insert cut from commercially available sandal; textured with semi-circular mounds with centre distances of 8mm. Worn for testing only
Orth et al. (2013)		Systematic review	
Palluel et al. (2008)	19 healthy elderly participants and 19 healthy young adults.	Within-subject experimental design No blinding No randomization	Footwear - Arena® NewMarco sandals (designed for pool activities). Entire insole had spikes made with semi-rigid PVC (density: 4 spikes/cm^2; height of a spike: 5 mm; diameter: 3 mm) and uniformly distributed under feet except on medial arch where spikes were bigger (density: 2 spikes/cm^2; height: 1 cm; diameter: 5mm). Just worn for 5 minutes each time during testing
Palluel et al. (2009)	n=19 healthy elderly, n=17 healthy young adults	Within-subject experimental design No blinding No randomization	Entire insole had spikes made with semi-rigid PVC (density: 4 spikes/cm^2; height of a spike: 5 mm; diameter: 3 mm) and uniformly distributed under feet except on medial arch where spikes were bigger (density: 2 spikes/cm^2; height: 1 cm; diameter: 5 mm). Just worn for 5 minutes each time during testing
Preszner-Domjan et al. (2012)	n=50 healthy young adults	Experimental study No blinding No randomization	Thin elastic layer of rubber with spiked layer (density 5 spikes/cm2, height of spikes 7mm, diameter of spikes 2mm), and it was placed onto the force plate. Just worn for testing.
Qiu et al. (2012)	10 younger and 7 older participants	Experimental study Order of insoles were randomized	Both insole surfaces (International Children's Orthotic Laboratory, Australia) were 1.5mm thick and had granulations with a diameter of 5.0 mm and a height of 3.1mm that were distributed evenly across the upper surface. Just worn for testing.
Qiu et al. (2013)	20 healthy elderly participants and 20 healthy young adults.	Within-subject experimental design No blinding No randomization	Insoles were 1.5mm thick and with soft insole material (270 density Ethylene Vinyl Acetate (EVA). The textured surface comprised granulations measuring 5.0mm in diameter and 3.1mm in height that were distributed evenly across the upper

			surface, accentuated by two raised compliant ridges measuring 3.1mm in height and 3.1mm in width which were located around the lateral perimeter of the insole and around the heel of the foot. The smooth insoles - same materials and had the same height and dimensions as the TIs, but without texture and raised ridges, ensuring a standard insole surface. Just worn for testing.
Silva et al. (2015)	n=12 with type II diabetes	Experimental design No randomization No blinding	13 stations with different textures one included proprioceptive balls with 8 cm diameter and external projections placed on the floor. Somatosensory training for 45 mins twice a week for 12 weeks.
Wilson et al. (2008)	Convenience sample of 40 healthy female subjects (Age 51.1 +/- 5.8 years)	Test-re-test prospective pilot single-blind randomized clinical trial	Control group (n=10) fitted with shoes with a standard Hotter shoe insole (Shore value A20 – soft) n=10 - shoes fitted with a flat, plain, and smooth surfaced foot orthosis (FO), made of three millimetres thick EVA. The shoes of the second intervention group n = 10 - a dimpled surfaced FO (1mm raised circles, with a diameter of 3mm spaced 5mm apart covering the entire surface of the FO). N=10 - raised grid pattern fitted into their shoes (1 mm raised square pyramid shapes, side length two-point 5 mm, peaks spaced 2.5 mm apart covering the entire surface of the FO). Subjects required to wear the shoes for 4 weeks, for a minimum of 6 hours per day

Abbreviations: AFO Ankle foot orthosis, EVA Ethylene Vinyl Acetate, FO Foot orthosis, PVC Polyvinyl Chloride, TI textured insole

5.3.3 Development of the textured insole (TI) protocol

At the mNGT meeting participants deliberated over the literature presented to them about TI wearing protocols and were given opportunity to ask questions of the facilitator, to discuss and assess commercially available textured materials, and to try out some TIs previously made by the researcher from sheets of textured material, making evaluations in relation to the different types of materials. Participants examined eighteen different types of textured material produced by Algeos.[3] Issues such as size, nature and type of texture, accompanying footwear, cost, and potential comfort/discomfort were all considered by the group, along with the length of time and activity involved during the gait-training phase of wearing the insoles.

All the materials tested had non-slip properties and a Shore value of A (indicating a softer material); however, these ranged from A45 (softer) to A90 (harder), with a thickness of the materials between 1.8mm and 8mm. Some materials had pyramidal or round peaks at varying distances and others were ribbed in differing widths. They were all made of compact rubber with differing degrees of flexibility and bounce.

Participants discussed the information in the literature related to the different types of textured materials and insoles used within studies, and the duration of wearing the insoles or standing on the textured material, as well as specifics related to

[3] Algeos UK Ltd: http://www.algeos.com/

footwear worn. One important point for discussion was whether the TIs should be worn on both sides, or just in the contralesional shoe, with a purpose of increasing stimulation on the contralesional side. Information from the scoping review was considered in relation to this aspect. A lengthy discussion ensued relating to the pros and cons of wearing the TIs on both sides or just the contralesional side; the facilitator gave all participants an opportunity to vote and agreement was reached.

5.3.4 Results

Consensus was attained regarding the choice of a textured material (details below), which was felt to have sufficient depth to the texture to increase the afferent input to the plantar surface of the foot, but not so rough as to cause friction and injury. The plan was that the insoles should then be cut to size for each participant.

One aspect debated, with conclusions drawn by the participants, related to the duration of wearing the TIs. Various suggestions were made by the participants:

- Trial participants should be in control of the duration of wearing the TIs each day; recording the actual wearing time would provide some insights into what might be a feasible dose for a future larger trial.
- TIs could be worn as much as the participants chose throughout the trial intervention period, an approach adopted by Dixon et al., (2014), who found improvements in gait in people with multiple sclerosis after a two-week

intervention period. Also, it was felt that giving control relating to the duration of wearing TIs to stroke survivors might increase their autonomy.

- Some stroke survivors may not physically be able to insert or remove the TIs from their shoes themselves without assistance from a therapist or carer. For those such trial participants, who perhaps do not have access to a carer to assist them, a research therapist would insert them into the shoe at the beginning of the TSGT session and remove them afterwards. It was therefore decided that, as a minimum, TIs should be worn during all sessions of TSGT, each lasting 30 minutes in duration.

Regarding whether a TI should be worn in the ipsilesional shoe as well as the contralesional shoe, or just in the contralesional shoe, there was an initial dichotomy in the group. Discussion and debate took place about the potential for a TI in the ipsilesional shoe to cause sensory extinction, where sensory stimulation of the contralesional side may not be perceived if stimulation is given simultaneously on both sides (de Haan et al., 2012). Following a vote, a decision was made that the TI should only be worn in the shoe of the contralesional side, but a smooth insole should be worn simultaneously in the ipsilesional shoe to ensure equal changes in shoe tightness or shoe sole thickness on both sides.

By the end of the mNGT meeting there was agreement on the following specific points relating to the insoles:

- an insole with a smooth surface (of medium density EVA, 3-mm thickness, Shore value A50, black, OG1304 manufactured by Algeos UK Ltd., Liverpool, UK[4].) should be worn in the ipsilesional shoe.
- A black TI, OG1549, (with small, pyramidal peaks, with centre-to-centre distances of approximately 2.5 mm Evalite Pyramid EVA, of 3-mm thickness, Shore value A50 manufactured by Algeos UK Ltd), should be worn in the contralesional shoe (figure 5.3).
- The insoles were to be participant specific and cut to size to fit well in each individual participant's shoes. The TI protocol is presented in table 5.3.

[4] Algeos UK Ltd (http://www.algeos.com/)

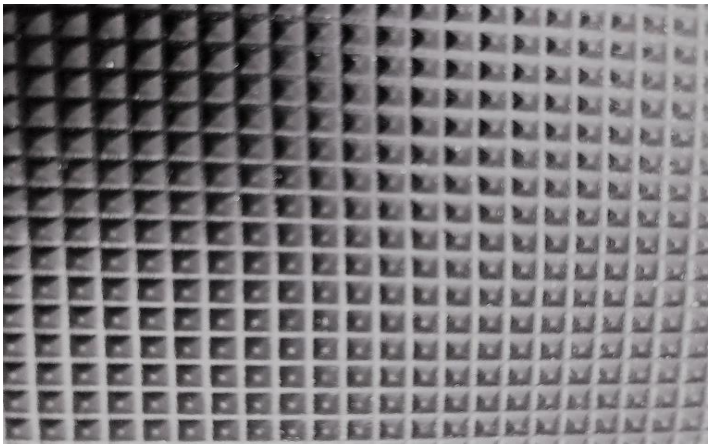


Figure 5.3 Smooth and TI, with a close-up of the pyramidal peaks of the textured material

Table 5.3 Protocol for the textured insole group (based on the Template for Intervention Description and Replication, TIDieR checklist)

1	**Name:**	Textured insole (TI) protocol for TI group
2	**Rationale:**	The plantar (sole of the foot) mechanoreceptors are key, sending information to the CNS, and plantar stimulation has been shown to result in increased control of body sway (Watanabe and Okubo, 1981). In view of the importance of cutaneous information from the plantar surface of the foot to control balance (Kennedy and Inglis, 2002), other potential mechanisms of increasing plantar stimulation have been explored. TIs have been shown to improve postural control in standing in healthy participants (Corbin et al., 2007), and to improve walking patterns for people with multiple sclerosis (Dixon et al., 2014). However, the combination of wearing TIs and task-specific gait training (TSGT) has not been evaluated to determine the benefits for balance and walking recovery early after stroke. The use of TIs in the shoes of stroke survivors involves a hands-off (therapist independent) approach, which may potentially be a more economical option for achieving increased sensory stimulation to the foot and is therefore important to investigate.
3	**Materials:**	Smooth and TIs will be used. The insole with the smooth surface will be of medium density EVA, 3mm thickness, Shore value A50, black, OG1304 manufactured by Algeos UK Ltd., Liverpool, UK. The TI has small, pyramidal peaks with centre-to-centre distances of approximately 2.5mm Evalite Pyramid EVA, 3mm thickness, Shore value A50, black, OG1549 manufactured by Algeos UK Ltd. The insoles will be patient specific and cut to size so they fit in the participant's shoe.
4	**Procedures:**	This group of participants will be encouraged to wear the TI on the hemiparetic side (and a smooth insole on the opposite side), as much as possible (to 'augment' the sensorimotor system), during the 4–6-week period of intervention, apart from when the outcomes are being assessed. In addition to wearing the TIs participants will also receive 20 sessions of TSGT (30 minutes for each session), during the intervention period. The specific content of each treatment session will be documented,

		and daily diaries will inform the researcher of the extent of wearing of the TIs. OMs will be undertaken without the participant wearing TIs, so it is the same conditions as the mobilization and tactile stimulation group, which is the other arm of the trial.
5	**Provided by:**	The participant will be responsible for wearing the textured/smooth insoles. If help is required to put the TIs into shoes and put on footwear (and no family support is available), a Research Therapist will assist, prior to TSGT.
6	**Mode of delivery:**	Participant controlled – wearing the TIs for as much as possible during the 4–6-week intervention period. The Research Therapist will help if required to put the TIs into shoes and put on footwear prior to TSGT if required. The participant will, therefore, wear the TIs a minimum of 30 minutes 4–5 times per week.
7	**Location:**	The participants will be encouraged to wear the TIs and receive the TSGT in their own environment, whether this is as an inpatient or their own home.
8	**When and how much:**	Time wearing the insoles will vary. Some participants may just wear them during the TSGT and others may wear them for long periods in the day. Participants will be encouraged to record the length of time insoles are worn on the daily diaries.
9	**Tailoring:**	As the participant is in control of how long they wear the insoles for, they can tailor the intervention to their own comfort and needs.
10	**Modifications:**	Any modifications to the TI protocol will be recorded.
11	**Intervention adherence and fidelity-planning:**	Intervention adherence and fidelity will be assessed. Strategies to improve fidelity and adherence include: research therapist training, encouragement and motivation regarding wearing of TIs by the research therapist delivering the TSGT and the keeping of daily diaries which will be collected weekly. A record of the length of time wearing the insoles will be included as a prompt in the simple diaries and this information will enable monitoring of adherence and fidelity. The information from the daily diaries will be analysed by the Chief Investigator, with guidance from her supervisors.
12	**Intervention adherence and fidelity - How well (actual):**	The analysis of the daily diary sheets will give an indication of adherence to the intervention. The FGs will enable further opportunity of assessing the adherence, fidelity and acceptability of the intervention.

5.3.5 Search strategy for scoping review related to task-specific gait training (TSGT)

The search terms below were used to access pertinent literature:

- ‘Lower limb’ OR ‘Lower extremity’

AND

- Stroke OR CVA OR ‘cerebrovascular accident’ OR ‘brain attack’

AND

- ‘task specific’ OR ‘task-specific’ OR ‘task orientated’ OR ‘task-orientated’ OR ‘Motor learning’ OR relearning

Table 5.4 Search strategy for scoping review related to task-specific gait training after stroke

Search	Term
S1	Lower limb
S2	Lower extremity
S3	S1 OR S2
S4	Stroke
S5	CVA
S6	‘cerebrovascular accident’
S7	Brain attack
S8	S4 OR S5 OR S6 OR S7
S9	‘task specific’
S10	‘task-specific’
S11	‘task orientated’
S12	‘task-orientated’
S13	‘Motor learning’
S14	Relearning
S15	S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16	S3 and S8 and S15

5.3.5.1 Types of participants

Only studies involving stroke survivors were included, in either the acute, sub-acute or chronic stage post-stroke.

5.3.5.2 Types of interventions and outcomes

Any studies of task-specific training to improve balance and gait were included. Two of the twenty full-text articles accessed focused on task-specific training for the upper limb (Donaldson et al., 2009; McDonnell et al., 2007); however, some useful information in these articles was used to inform the intensity and progression strategies for task-specific training. All training was based on repetitive, progressive exercises. Studies that included pertinent information relating to researched strategies for undertaking TSGT were included and individual exercises and ways of progressing the exercises were recorded.

5.3.5.3 Findings

A flowchart for identifying the TSGT literature is presented in figure 5.4. The searches identified 140 citations; after removal of 53 duplicates, 87 sources were left, of which 43 were excluded following reading the title: 14 were excluded because they were books (it was felt sufficient more current information was available within published journals), dissertations or government documents, and a further 10 were excluded after reading the abstracts. Full texts were accessed for 20 articles which were then read and pertinent information relating to TSGT was extracted. Information is summarized in Appendix 15.

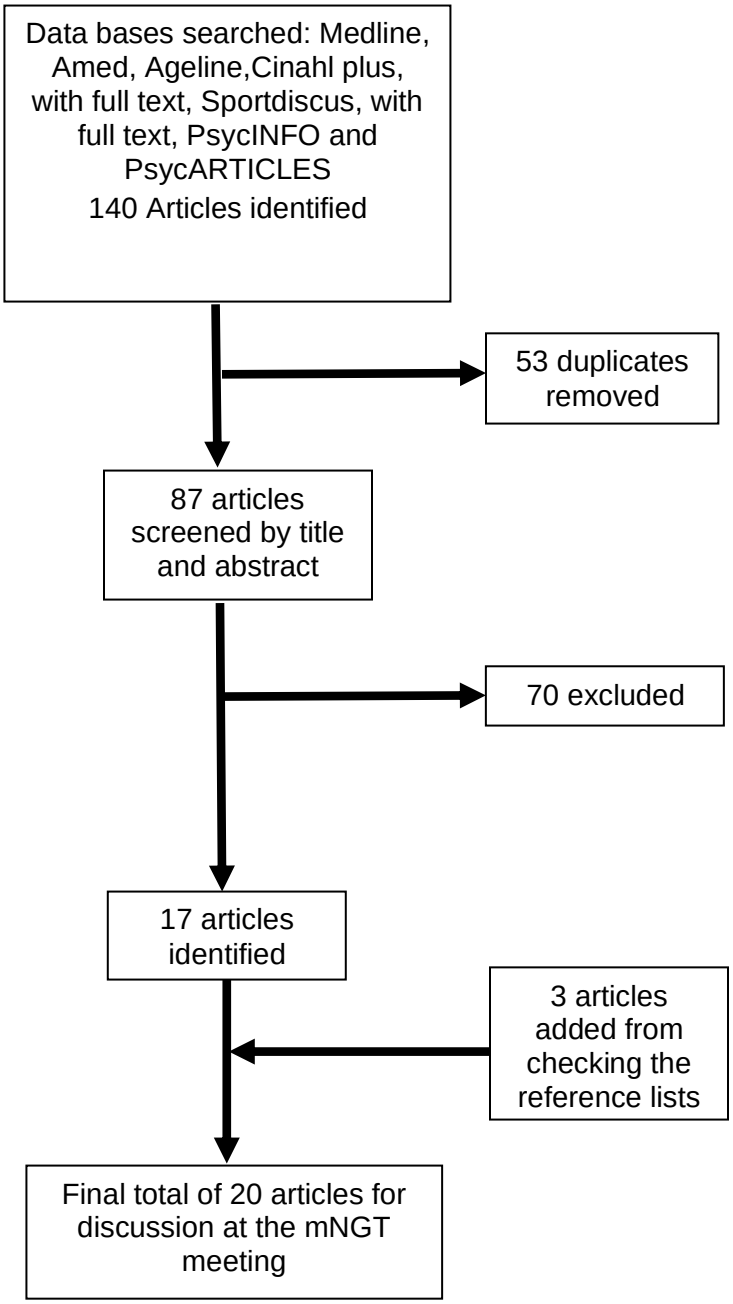


Figure 5.4 Flowchart of the process for identifying studies related to TSGT as an intervention

5.3.5.4 Characteristics of the included studies

Twenty studies were identified: twelve RCTs (Blennerhassett and Dite, 2004; Cooke et al., 2010b; Dean et al., 2000; Donaldson et al., 2009; Jonsdottir et al., 2010; McDonnell et al., 2007; Mead et al., 2007; Pang et al., 2005; Salbach et al., 2004; Scianni et al., 2010; van de Port et al., 2009; Yang et al., 2006), (although two were just protocols: Scianni et al., 2010; van de Port et al., 2009), one pre- post-test design (Monger et al., 2002), two randomized trials (with no control group) (n=22 and n=80) (Peurala et al., 2007; Sullivan et al., 2007), one repeated measures design (n=22) (Straube et al., 2014), and four systematic reviews (French et al., 2007; Pollock et al., 2014a; Pollock et al., 2007; Wevers et al., 2009). All of the articles involved TSGT being delivered to stroke survivors. Six of the studies delivered the intervention in a group situation and ten included individual treatments. This is an important consideration when considering potential costs during implementation of any study findings. Four of the sources included people following acute stroke, two sub-acute strokes, three a mixture of sub-acute and chronic stroke and seven chronic stroke survivors. The four systematic reviews all included people at any stage after stroke.

5.3.5.5 Exercises/activities reported

The types of exercises included in the studies are summarized in Appendices 15, 16 ,17 and table 5.5. Interventions included circuit training, progressive endurance and resistive training, and functional tasks. Duration of treatment ranged from 20 minutes (Monger et al., 2002) to 75 minutes (Mead et al., 2007). However, Mead et al. (2007) included tea and chat in that time. The

most common length of treatment was 60 minutes (Blennerhassett and Dite, 2004; Cooke et al., 2010b; Dean et al., 2000; Pang et al., 2005; Peurala et al., 2007; van de Port et al., 2009). Frequency of treatments ranged from twice a week (van de Port et al., 2009) to five times a week (Blennerhassett and Dite, 2004); and the number of sessions ranged from 18 (Salbach et al., 2004) to 57 delivered over a 19-week period (Pang et al., 2005). Information regarding intensity and progression of exercise was summarized (table 5.6).

Treatments were progressed by using repetition and increasing resistance, with the number of exercises graded to the ability of the participants. The planned TSGT protocol for the MoTaStim-Foot trial would not involve a formal progressive strength training regime; it was just planned to be a small part of the module of treatment enabling treatment to be individualised according to the participant's presentation on the day. The number of repetitions would be increased each treatment where possible, this approach for progression observed in the literature was noted and discussed with the clinicians at the mNGT meeting. A variety of exercises were researched within the various articles, but commonly the programmes included sit-to-stand practice, stepping, walking, squatting, standing on one leg, balance work, heel lifts and kicking a ball.

5.3.5.6 Synthesis of descriptions

A list of all potential TSGT exercises was formulated (table 5.5) and information summarized relating to exercise intensity and how exercises could appropriately be progressed (table 5.6).

Table 5.5 Summary of categories and tasks/activities involved in TSGT as reported in the literature

Category	Task / activity
Warm Up	Marching on-the-spot
	Arm lifts
	Ankle circles
	Stretching of the trunk, thigh, and calf muscles
Other	
Sitting Exercises	Sitting at a table and reaching in different directions for objects located beyond arm's length to promote loading of the affected leg and activation of affected leg muscles
Other	
Sit to stand to sit	Sit to stand from various chair heights to strengthen the affected leg extensor muscles and practice this task
Other	
Standing	Standing with the base of support constrained, with feet in parallel and tandem conditions reaching for objects, including down to the floor, to improve standing balance.
	Standing and reaching
	Heel lifts in standing to strengthen the affected plantar flexor muscles
	Reciprocal leg flexion and extension using the Kinetron in standing to strengthen leg muscles
	'standing balance'/balance control
	Standing with one foot in front of the other
	Kicking ball with either foot
	Balance beam - walking forwards, sidewards, and backwards between two parallel lines, 20 cm apart, progressing to using one line, to using a balanced beam, and finally to lateral stepping on the floor, feet crossing over in front or in back, and then alternating
	Stand on one leg
	Squat on one leg
	Stand on the paretic leg, then perform plantarflexion
Other	
Stepping	Stepping forward, backward, and sideways onto blocks of various heights to strengthening affected leg muscles.
	Stair climbing and descending exercise progressing from taking one step at a time to taking alternating steps, from using, then not using the handrail, and to achieving a greater number of flights

	Step ups progressed by increasing the height of the step or reducing arm support
	Step on block with the paretic limb
	Step on block with the non-paretic limb
	Step sideways on a block
Other	
Gait	Standing up from a chair, walking and short distance, and returning to the chair, to promote a smooth transition
	Walking on a treadmill
	Walking over various surfaces and obstacles
	Walking in different directions
	Tandem walking
	Walking over slopes and stairs, providing the opportunity for walking practice under variant conditions
	Inside and outside walking
	Sudden stops and turns during walking
	Walking on different surfaces (carpet, foam)
	Standing on foam, balance disc, or wobble board
	Walking through an obstacle course
	Speed walking
	Walk on foot prints
	Walk between lines
	Walking and picking up various objects from the ground
Other	
Functional Tasks	Bed mobility
	Turning
	Obstacle course e.g. stepping onto, along, and down from an aerobics step, walking over a mat, or a ramp, and returning, progressing by increasing the heights and number of obstacles, and from completing the course walking forwards to walking backwards.
	Walk and carry - continuous walking carrying a grocery bag, progressing to carrying a bag in each hand, to increasing the weight of the bag, to carrying a laundry basket, and to stopping on command.
Other	
Strengthening	Progressive-resistive exercise program for paretic hip flexors and extensors, knee flexors and extensors, and ankle dorsiflexors and plantar flexors.
	Partial squats: progressed by increasing movement magnitude
	Toe rises: progressed from bilateral to unilateral rises on either side
	Progressed by increasing number of repetitions (from 2 sets of 10 to 3 sets of 15), reducing arm support, or both
Other	

Table 5.6 TSGT information in the literature relating to intensity and progression:

Intensity (mins)	Frequency (days per week)	Duration (weeks)	Total time per week (mins)	Overall total time (mins)	Comments
60	5	4	300	1200	UL
60	4	6	240	1440	LL
60	3	4	180	720	LL
60	4	6	240	1440	UL
75	3	12	225	2700	Exercise management training based on falls exercise management study UL and LL
40	3	3	120		3-week home-based exercise programme of sit to stand
60	3	19	180	3420	Exercise programme. 3 stations: 1 Cardiorespiratory fitness* 2) Mobility and balance 3) Leg muscle strength

*10 minutes initially, with incremental increase of 5 minutes every week, up to 30 minutes of continuous exercise as tolerated per day (for cardio-respiratory fitness), intensity: started at 40% to 50% heart rate reserve (HRR), with increment of 10% HRR every 4 weeks, up to 70% to 80% HRR, as tolerated.

Treatment was progressed systematically using repetition and increasing resistance by, for example, changing the limb's relationship to gravity or increasing the range of motion or distance over which body weight was transported. Progression also included altering the height of the seat, reducing arm support, increasing the height of the step and increasing speed. Exercises were progressed as appropriate for the individual's ability. Some of the studies used equipment, and some studies used no equipment.

5.3.6 Development of the task-specific gait training (TSGT) protocol

5.3.7 Methods

The literature upon which the TSGT could be based (table 5.5), along with equipment, intensity, progression (table 5.6) and length of treatment sessions were discussed at the mNGT meeting. It is acknowledged that some reviews exploring task-specific training following stroke have previously been undertaken (Pollock et al., 2014a; Veerbeek et al., 2014). However, these reviews only included RCTs; it was important to be inclusive and comprehensive, capturing all possible interventions; hence additional scoping searches were undertaken, so all potentially suitable tasks and exercises could be presented to the group for the expert clinicians to discuss. It needs to also be recognized that it can be challenging to distinguish between specific functional task training and practice of an active movement (Pollock et al., 2014a). As the aim of this work was to develop clinically relevant protocols the experienced clinicians were given the autonomy to decide what they believed were exercises and strategies which should be included in the task-specific gait training protocol.

The NGT was modified (mNGT) to enable small group work (two groups, with four participants in each), facilitating discussion regarding which exercises should be included in the TSGT protocol (content of the TSGT). In their groups, participants discussed the information and decided upon the relevance of the different exercises and rehabilitation strategies for stroke survivors. The list of exercises and activities developed from the literature around TSGT for stroke

survivors (table 5.5) was analysed by the participants, and the suitability of each exercise or activity assessed. Participants were asked to consider the exercises they felt would be suitable for stroke survivors with different levels of capability (immobile, able to walk with assistance, or able to walk independently). This was to help the participants think carefully about relevant exercises for all stroke survivors. Furthermore, participants considered whether any other exercises should be added to the list.

The small groups each shared their views with the larger group and frank discussion ensued about which exercises should be included. Consensus was sought for inclusions rather than exclusions, enabling techniques to be included even when only a few participants felt the technique was important. The group then considered the summarized information from the literature about dose of TSGT, progression of activities, and equipment used in TSGT (table 5.6); further in-depth discussion took place, consensus was reached, and the final TSGT protocol developed (table 5.7).

5.3.8 Results

Following in-depth discussion, group consensus agreed that:

- the programme of TSGT exercises should be individualized for each participant.
- TSGT should be delivered at an appropriate intensity; in view of the heterogenic nature of stroke survivors, the intensity would be decided by the research therapist delivering the intervention; progression would be

within the limits of the participant's abilities. This reflects conventional therapy practice for stroke survivors. The TSGT schedule allowed for the recording of specific numbers of exercises undertaken and pertinent comments related to the exercise if required.

- A dose of 30 minutes of TSGT per day was appropriate.
- A total of 20 sessions of intervention was appropriate.

As co-design was utilized and the clinicians were given the autonomy to include all exercises that they felt would be appropriate in an inclusive intervention package of TSGT, the heterogeneity of the included exercises in the final TSGT protocol is justified. Some preparatory exercises are included (for example exercises in lying, lifting leg on/off a box), because the expert clinicians selected what, in their expert opinion, could potentially be used in gait training in clinical practice. This was, therefore, not the researcher's opinion, but a bottom-up design respecting expert clinical opinion.

A detailed protocol for the TSGT was agreed and is summarized in table 5.7. The recording sheet for the TSGT is presented in table 5.8.

Table 5.7 TSGT protocol based on the Template for Intervention Description and Replication (TIDieR) checklist

1	**Name:**	Task-specific gait training (TSGT) group.
2	**Rationale:**	Walking is a priority for many stroke survivors, confirmed by studies undertaken to define a national research agenda, which identified physical therapy to address balance and gait (walking) post-stroke within the top ten research priorities (James Lind Alliance, Pollock et al., 2014b). There is strong evidence that task-specific walking practice can be used to improve walking after stroke (Wiener et al., 2018).
3	**Materials:**	Based upon a review of the literature and a FG with experienced clinicians a few pieces of equipment will be required including theraband, football, chair, foam cushion, gym ball a stair or step and a wobble board.
4	**Procedures:**	30 minutes of TSGT will be supervised by the research therapist, with 20 sessions being delivered over a 4–6-week intervention period. The TSGT will be undertaken immediately after the Mobilization and Tactile Stimulation (MTS) for the MTS group. The TSGT will be undertaken whilst wearing a TI on the side affected by the stroke and a smooth insole on the other side, for the TI group
5	**Provided by:**	The TSGT will be delivered by a research therapist (Band 6), with experience of working with stroke patients. A log will be kept of which research therapist provides which treatment for each participant and this information will be analysed on completion of the trial.
6	**Mode of delivery:**	The research therapist will provide the TSGT in a 1:1 situation.
7	**Location:**	The TSGT will take place in either an inpatient clinical setting within an NHS organisation or a University research setting or the participant's own home.
8	**When and how much:**	All participants in BOTH groups/arms of the trial will receive 20 sessions of 30 minutes of TSGT within a 4–6-week period.
9	**Tailoring:**	Although a standardized protocol will be followed for the TSGT the research therapist will choose appropriate exercises and adapt them as required to suit the requirements of each individual participant, due to differences in presentation following a stroke. This reflects how TSGT would

		usually be implemented in conventional rehabilitation. Details of actual intervention delivered will be recorded on the treatment schedule.
10	**Modifications:**	Any modifications to the TSGT protocol will be monitored and reported appropriately.
11	**Intervention adherence and fidelity- planned:**	Intervention adherence and fidelity will be analysed. Strategies to improve fidelity and adherence include 1:1 intervention plus encouragement and motivation strategies by the research therapist during the TSGT, as in usual therapy rehabilitation. A log will be kept detailing, for each participant, which research therapist has delivered the TSGT.
12	**Intervention adherence and fidelity - How well (actual):**	The case report files completed by the research therapists will give an indication of adherence to the intervention. The FGs will enable further opportunity of assessing the adherence, fidelity and acceptability of the intervention.

Table 5.8 Task-Specific Gait (Walking) Training (TSGT) schedule for recording treatments delivered

NB Standard exercises for TSGT will be delivered (20 sessions of 30 minutes), however, they will be individualised for each participant according to need. It is essential that the research therapist liaises with the clinician responsible for routine therapy treatment for the participant, to ensure the participant does not become fatigued by the extra therapy.

Description	Task	Tick (If done)	Details
Warm Up	Stepping in sitting		
	Reaching/Rolling gymball forwards in sitting		
	Pelvic tilt – ant/post/lateral		
	Hip flexion/inner range quads		
	Ankle circles/dorsiflexion/plantar flexion/heel/toe		
	Stretching of the trunk, thigh, and calf muscles		
	Weight transfer in standing		
	Marching on-the-spot		
Other			
Lying Exercises	Lifting leg on/off block		
Sitting Exercises	Postural re-education		
	Sitting at a table and reaching in different directions for objects located beyond arm's length to promote loading of the affected leg and activation of affected leg muscles		
	Lifting leg on/off block		
	Heel lifts in sitting to strengthen the affected plantar muscles		
	Rolling ball with foot/kicking ball		
	Wobble board/balance exercises		
	Wobble cushion in sitting		
	Heel lift in sitting		
	Theraband/strengthening		
	Exercise bike		
Other:			
Sit to stand to sit	Sit to stand from various chair heights to strengthen the affected leg extensor muscles and practice this task		
	One leg stand/foot not affected by stroke in front/on step		
Other:			
Standing	Weight shift left/right		
	Standing and reaching		
	Standing with the base of support constrained, with feet in parallel and tandem conditions reaching for objects, including down to the floor, to improve standing balance.		
	Heel lifts in standing to strengthen the affected plantar flexor muscles		
	Reciprocal leg flexion and extension in standing to strengthen leg muscles		
	'standing balance'/balance control		

	Step standing		
	Kicking ball with either foot		
	Balance beam - walking forwards/sidewards/backwards between two parallel lines, 20 cm apart, progressing to using one line, to using a balanced beam, and finally to lateral stepping on the floor, feet crossing over in front or in back, and then alternating		
	Bilateral squats		
	Stand on one leg		
	Squat on one leg		
	Stand on the paretic leg, then perform plantarflexion		
Other:			
Stepping	Stepping forwards/backwards/sideways onto blocks of various heights to strengthening affected leg muscles.		
	Stair climbing and descending exercise progressing from taking one step at a time to taking alternating steps, from using then not using the handrail, and to achieving a greater number of flights		
	Step ups progressed by increasing the height of the step, reducing arm support		
	Step on block with the paretic limb		
	Step on block with the non-paretic limb		
	Step sideways on a block		
Other:			
Gait	Standing up from a chair, walking and short distance, and returning to the chair to promote a smooth transition		
	Walking on a treadmill		
	Walking over various surfaces and obstacles		
	Walking in different directions		
	Tandem walking		
	Walking over slopes and stairs providing the opportunity for walking of practice under various- conditions		
	Inside and outside walking		
	Sudden stops and turns during walking		
	Walking on different surfaces (carpet, foam)		
	Standing on foam, balance disc, or wobble board		
	Walking through an obstacle course		
	Speed walking		
	Walk on foot prints		
	Walk between lines		
	Walking and picking up various objects from the ground		
	Gait re-education with or without aids (please specify)		
Other:			
Functional Tasks	Bed mobility		
	Turning whilst walking		
	Obstacle course e.g. stepping onto/along/down from an aerobics step, walking over a mat, or a ramp, and returning, progressing by increasing the heights and number of obstacles, and from completing the course walking forwards to walking backwards.		
	Walk and carry - continuous walking carrying a grocery bag, progressing to carrying a bag in each hand, to increasing the weight of the bag, to carrying a laundry basket, and to stopping on command.		

	Stairs		
	Kitchen work		
	Personal care		
	Leisure/hobbies		
Other:			
Strengthening	Progressive-resistive exercise program for paretic hip flexors/extensors and ankle dorsiflexors/plantar flexors.		
	Progressive-resistive exercise program for paretic knee flexors and extensors		
	Partial squats: progressed by increasing movement magnitude		
	Toe rises: progressed from bilateral to unilateral rises on either side		
	Leg press		
Other:			
Stretching	Calf stretch - Standing with affected knee straight and extended arm/s resting on the wall: keeping the body straight, pivot the body forward at the ankles keeping heel on the floor until you feel the calf muscle is stretched. Hold for 2 minutes, relax, repeat 10 times.		
	Hamstring stretch in sitting		
Other:			
Endurance/ Aerobic	Bike (if available)		
	Treadmill (if available)		
	Brisk walking		
	Raising and lowering a 1.4-kg, 55-cm exercise ball (care taken of the shoulder)		
	Shuttle walking		
	Standing chest press		
Other:			

Progression

For specific strengthening - progress by increasing number of repetitions (e.g. from 2 sets of 10 to 3 sets of 10), according to the level of ability, and progress as they improve, also progress by reducing arm support. Other treatment progressions include increasing resistance e.g. in relation to gravity, increasing the range of movement or distance over which body weight is transported, changing weight of external objects, altering the height of seat/step and walking longer distances.

5.3.9 Developing the MTS protocol using an mNGT

It has been advised that research should consider existing evidence and build upon biological and physical rationales and theories (Walker et al., 2017). A scoping search relating to MTS was therefore not required because an upper limb MTS treatment schedule had already been developed by a rigorous process (Hunter et al., 2006). The development of this upper limb schedule involved firstly a systematic search of the literature, followed by semi-structured interviews with experienced neurotherapists (n=7); a detailed analysis was undertaken by two independent researchers, resulting in a preliminary list of interventions which were then discussed at a focus group meeting (n=6). This detailed development process enabled current therapy techniques to be evaluated resulting in the development of the upper limb MTS treatment sheet which was piloted and then has since been implemented in follow-up single system studies (Hunter et al., 2008; Winter et al., 2013). MTS is a module rather than a single intervention and therefore allows the flexibility to provide appropriate intervention to each patient within the confines of the module (Hunter et al., 2006). However, this published MTS schedule was specific to the upper limb and a decision was made to adapt this upper limb schedule to one that reflected MTS more specifically for the lower limb. An iterative cycle is advocated during intervention development (Jones et al., 2016b), and this is what occurred during the development of the lower limb MTS protocol; assessment of acceptability and feasibility of the intervention was possible as a result of the MoTaStim-Foot feasibility study (utilising both quantitative and qualitative aspects) as suggested by O'Cathain (2019).

The development of the MTS protocol for the lower limb involved three phases:

- **Phase one:** Alteration of the upper limb MTS protocol (iteration one) to create an MTS protocol for the lower limb (iteration two)
- **Phase two:** Refining iteration two, and development of iteration three
- **Phase three:** Ultimate refining of iteration three to enable development of the final standardized MTS schedule for LL.

Phases one and two occurred prior to the group meeting. All participants were sent an electronic copy of the upper limb MTS schedule by email and asked to consider, independently and without collaboration, how the different subsections of the upper limb schedule might be appropriately adapted as an intervention for the lower limb. Participants were asked to annotate the schedule according to how it should be modified to reflect current conventional therapy for the foot and ankle in preparation for standing and balance. In addition, they were asked to consider the aims, and rank (with 1 as most important and 9 as least important) the order of importance, and frequency of use, of each of the intervention subsections for application to the lower limb: passive movements through anatomical range; accessory movements; massage; soft tissue stretch; placing; isolated/selective joint movement; compression; specific sensory input; and patterns of coordinated movement underlying functional activity. Participants were asked to return the annotated schedule by email to the researcher, who collated and analysed all the responses, and developed a second iteration, based on those responses.

This second iteration of the modified schedule (Appendix 18) was returned by email to the participants, who were asked to independently review it, and provide feedback on how comprehensive the schedule was, and how accurately it reflected their experiences and practice of retraining somatosensation in the foot when preparing the foot for standing and for balance in standing. Feedback on this second iteration was returned to the researcher by email, who collated and analysed the responses and developed a third iteration (Appendix 19).

The third iteration was emailed to the participants prior to their attendance at a group meeting at Keele University. Again, the participants were asked to consider, in advance of the meeting, the applicability of the schedule.

The final phase of the mNGT, the group meeting, took place at Keele University. The plan for the session is available in Appendix 20. At the group meeting, the content of iteration three of the schedule was discussed, along with all other protocol considerations, such as appropriate treatment dose (intensity, frequency and duration). In-depth discussion continued until consensus on the content and format of the schedule and overall protocol for delivering MTS to the lower limb was achieved. The final schedule was then agreed.

To ensure that the final protocol was comprehensive, including all the interventions that the group considered to be relevant for inclusion in this

protocol, consensus was sought for inclusions rather than exclusions. This enabled techniques/interventions to be included even if only a few participants considered the technique to be important. For example, only one participant felt dissociation of gastrocnemius from soleus was an important technique to add. The protocol was designed so therapists could record, using tick boxes, just the techniques they felt were appropriate to apply to each individual participant; it was not intended that all the techniques would be delivered in one treatment session. Including all identified techniques in the schedule therefore allowed for flexibility and appropriate selection and accurate recording of all techniques applied. In chapter seven there will be further discussion relating to this aspect.

5.3.10 The mNGT meeting

One group meeting was held which lasted for just over three hours, with breaks built into the afternoon as required. The group facilitator (AA) provided a brief introduction, thanking the participants for their contribution to the study so far, and for attending the meeting. The purpose and content of the meeting were stated, and consent, confidentiality and anonymity discussed. The rationale underpinning the research was explained and it was made clear that the three protocols to be developed were MTS for the lower limb, TSGT, and wearing TIs. Participants were given an opportunity to ask questions or seek clarification on any matter relating to the study. With agreement from participants, discussion during the meeting was audiotaped.

During the group meeting, the facilitator (AA) ensured that individual responses were heard and prompted all group members to participate. Ideas from participants were then prioritized by the group, following the five-step strategy discussed in chapter four. All three protocols were finalized in one afternoon and it was important to keep the focus of the participants. Whilst the principles of the NGT were followed and all participants' views were respected and heard, its format was modified, as discussed in chapter four, to meet the study objective, 2.1. The mNGT created sufficient opportunities for individual ideas and opinions to be considered, enabling all to participate and feel valued (Delbecq et al., 1975), evidenced by quotations from the participants.

5.3.11 Results

Eleven physiotherapists and one occupational therapist were recruited. They were all skilled therapists with experience of working with stroke survivors; all were female, and worked in the NHS, within three separate trusts, in posts ranging from Band 6 to Band 8. The protocols for MTS and TSGT were developed by these experienced clinicians and therefore they were based upon current therapy practice. Examples of content and face validity are given in section 5.3.13 (quotations from participants) in relation to the protocols developed being aligned with current conventional therapy and rehabilitation techniques; the use of a mNGT facilitated the process of validation of the protocols. This, in turn, contributed to the external validity of the protocols for MTS and TSGT. The wearing of TIs is not standard practice within stroke rehabilitation, and it was not possible to assess external validity related to this aspect.

All 12 participants contributed to phase 1, providing feedback on how the upper limb MTS schedule could be adapted for the lower limb. A descriptive analysis of the results for this first stage is presented below.

5.3.12 Ranking sections of the upper limb MTS schedule for application to the lower limb (Iteration 1)

Table 5.9 shows the median, interquartile ranges, and range of rankings for each of the subsections of the upper limb MTS schedule, ranked on a scale from 1 (most important) to 9 (least important).

Table 5.9 Median, interquartile range, and range of rankings for subsections of the upper limb MTS schedule according to importance for inclusion in a lower limb MTS schedule

Subsection	Median	Interquartile range	Range
Soft tissue stretch	2	1.25, 3.75	1–4
Passive movements	2.5	1.00, 4.75	1–6
Accessory movements	4.5	3.00, 7.50	1–9
Massage	6.0	2.25, 8.75	1–9
Placing the foot	6.0	5.00, 8.00	4–9
Compression	6.5	3.25, 7.75	2–9
Specific sensory input	6.5	3.25, 7.75	2–9
Patterns of coordinated movement underlying functional activity	6.5	3.25, 7.75	1–9
Isolated selective movement	6.5	4.00, 7.75	2–9

5.3.12.1 Soft tissue stretch

All twelve participants agreed soft tissue stretch is important, giving scores between one and four; indeed, nine participants (75%) gave a score of either one or two, indicating a very high level of importance for soft tissue stretch, the mode was 2.

5.3.12.2 Passive movements through anatomical range

There was consensus from the participants that passive movements are important (mode was 1). All twelve participants gave a score of 6 or less with six (50%) of the participants giving a score of one or two; indeed, four (33.33%) ranked this component as number 1, indicating a high level of importance for passive movements to be included in the lower limb MTS schedule.

5.3.12.3 Accessory movements

There was a difference of opinion among participants regarding the importance of accessory movements, with six (50%) of the participants indicating they felt accessory movements were important by scoring this section 4 or less. However, six (50%) of participants scored it 5 or more indicating they felt it was less important, the mode was 3.

5.3.12.4 Massage

Again, no consensus was reached regarding massage. A dichotomy was seen; four participants (33%) scored the section 3 or less indicating a high level of

importance, whereas six participants (50%) scored it 7 or more, indicating a lower level of importance, the mode was 9.

5.3.12.5 Placing of the foot

There was consensus that placing of the foot is not so important, with no participants scoring the section with a 3 or less. The scores indicated a level of uncertainty relating to this section, the mode was 5.

5.3.12.6 Compression

The scores for this section ranged widely, indicating a difference of opinions relating to compression, the mode was 7.

5.3.12.7 Specific sensory input

Four participants (33%) scored this section 8 or 9 (the mode was 8), indicating a low level of importance. Two participants (16.6%) indicated they felt specific sensory input was very important to be included in the schedule by giving a score of one. No consensus was established at this stage.

5.3.12.8 Patterns of coordinated movement underlying functional activity

Most participants indicated that this category was not important, with nine participants (75%) giving a score of 5 or more. However, one participant (8.3%) graded it as the most important section. The mode was 7.

5.3.12.9 Isolated/selective joint movement

Ten participants (83.33%) ranked this section 4 or more (the mode was 7). Indeed, six of the participants (50%) ranked it 7 or more. Two participants (16.66%) ranked the section at 2. These results indicate that the isolated or selective joint movement was felt to be less important; however, there was some difference of opinion demonstrated.

5.3.12.10 Other issues raised by the participants

- Aims would easily be transferrable from the upper limb schedule to the lower limb schedule
- Include positioning of the patient for treatment
- A new subheading ‘joint mobilizations’ was suggested
- A new subheading ‘soft tissue mobilizations’ was suggested
- All joint names, movements and activities needed to be altered to reflect the lower limb, as opposed to the upper limb.

Following analysis of the comments (Appendix 21) and rankings provided by the participants, the second iteration of the lower limb MTS treatment schedule was developed (Appendix 18). The changes made to the schedule are summarized in table 5.10; the main changes were: to reflect treatment applied to the lower limb as opposed to the upper limb, for example altering the wording of the aims of the schedule and joints and muscles to reflect lower limb instead of upper limb; two of the sections, placing the hand on a flat surface or edge/corner, and the compression components that related to the upper limb, were also removed.

Table 5.10 Summary of main changes made to adapt the upper limb MTS schedule to formulate the lower limb MTS schedule (iteration two)

Subsection	Alteration made to adapt the schedule
Aims	Hypersensitivity and pain were put together in one bullet point, since stroke survivors rarely complain of foot pain, whereas hand pain is more prevalent
Passive Movements	A new subsection 'joint mobilizations' was included to encompass both these elements. Names of joints changed to reflect lower limb Anatomy
Accessory movements	
Massage	A new subsection 'soft tissue mobilization' was included, to encompass both massage and soft tissue stretch. Participants felt these aspects were often combined during treatments
Soft tissue stretch	
Placing of hand	Altered to 'creating an active foot in preparation for stance/gait' and compression was incorporated into this Section
Specific sensory input	Altered to reflect the foot and hot/cold stimulation added
Isolated selected movement	Descriptions altered to reflect application to the lower limb
Patterns of coordinated movement	Descriptions altered to reflect application to the lower limb

5.3.13 Phase two

All 12 participants commented on any alterations considered necessary to iteration two suggesting changes, which are summarized in table 5.11, and on the usability and appropriateness of the content of the lower limb schedule, indicating whether they felt it reflected clinical practice (Appendix 22).

Table 5.11 Changes made to iteration two to develop iteration three of the lower limb MTS schedule

Subsection	Changes made to schedule
1. Massage and soft tissue stretch	**Techniques added:** stretch of extensor hallucis longus; massage in between the toes and down the length of the toes; and dissociation of gastrocnemius and soleus.
2. Creating an active foot in preparation for stance/ balance	**Techniques added:** lumbrical exercises; compression through the lateral border of the foot. Correction of a typographical error. Also, additional space created for further details to be added in relation to the placing of the foot on different surfaces.
6. Patterns of coordinated movement underlying functional activity	**Techniques added:** heel raise; sit-to-stand was changed to sit-to-stand-to-sit; a functional mobility section including transfers, obstacle course and manoeuvring was added. Tick boxes were added for the position of sitting and standing and moving sideways in relation to weight transference, and to enable documentation of whether the person was walking independently or required assistance from a therapist to walk.

The alterations (table 5.11) were then clearly highlighted in iteration three (Appendix 19), which was sent out to the participants in advance of the mNGT meeting. Specific points were noted for discussion and clarification at the mNGT meeting, and clear objectives for the meeting were set around seeking agreement or consensus on:

i) whether the hip and knee should be placed in a specific position during passive movements

ii) dose and intensity of the intervention (Hoffmann et al., 2014), and of individual subsections of the intervention, such as number of repetitions of passive or accessory movements, and duration of soft tissue or joint stretch

iii) the range of movement to be achieved during passive and accessory movement

iv) who would deliver the treatments, and adherence to the intervention, in line with the TIDieR framework (Hoffmann et al., 2014)

v) Final content and format of the MTS schedule for the lower limb

Participant's comments (see below, with further examples in Appendix 22, presented with pseudonyms) in relation to iteration two, were extremely encouraging, confirming that the schedule was a) comprehensive, b) easy to use, and c) accurately reflected current clinical practice:

> "*The new schedule is very comprehensive and there doesn't seem to be anything missing"*. (Participant 10).

"Overall, in terms of the actual treatment carried out, I think it is pretty comprehensive and accurately reflects practice". (Participant 5).

"*The treatment schedule is great, very thorough" … "very detailed but easy to read and follow*". (Participant 1).

"The treatment protocol is very comprehensive and good that it is on one page. The aims of treatment section would cover my aims of treatment fully. The specific treatment sections also reflect my current practice". (Participant 6).

5.3.14 Phase three

Eight of the 12 participants who contributed to the pre-group activity attended the group meeting (participants 1, 2, 5, 6, 8, 9,10 and 12). There was a range of experience with NHS bands 6, 7 and 8 represented, and participants from two of the three trusts. The other four participants were unable to attend due to a car accident on the way to the meeting (participant 3), work commitments (participant 4), personal commitments (participant 7) and illness (participant 11).

All participants' views were considered in relation to Iteration 3 of the MTS schedule, and the specific objectives were addressed. Discussion took place concerning the hip and knee position during passive movements. There was

100% consensus that the specification of the hip and knee being in ‘alignment’, should be removed from the schedule. The rationale behind this decision was that participants felt it was important to individualize the passive movements, making them relevant for each individual patient; this may necessitate working with the hip and knee in different positions (objective i).

Detailed discussions took place with the eight clinicians at the mNGT meeting in relation to an appropriate length of time (intervention dose) for the MTS treatment. Based upon the information in the literature and their clinical experience as to what was likely to be required, a decision was made that an intervention length of time of 30-60 minutes would be appropriate, allowing for MTS to be delivered according to the needs of the individual participant. This reflected the optimum dose suggested by Hunter et al (2011) of 37–66 minutes (objective ii). It was important that the dose was feasible, for both the researchers and participants to facilitate adherence to the intervention (objective iv). Specific numbers of repetitions of dose and intensity of the intervention (Hoffmann et al., 2014), and of passive or accessory movement, and duration of soft tissue or joint stretch the range of movement would be participant-specific according to need (objectives ii and iii). It was deemed to be important that the research therapists delivering the MTS protocol have the expertise to be able to deliver it appropriately and should be appropriately trained to deliver standardized MTS treatments, individualized to the participant’s needs (objective iv). All the participants agreed with the content of the final MTS schedule for the lower limb (objective v), stating it closely

resembled techniques undertaken in clinical practice. The final agreed lower limb MTS schedule is presented in figure 5.5.

It is acknowledged that some of the rehabilitation strategies in the MTS protocol overlap with those in the TSGT e.g. stepping, sit to stand to sit; however, the way that these rehabilitation tasks would be undertaken are different, because MTS is hands-on therapy and TSGT is delivered as a hands-off approach.

The mNGT session was observed by a second researcher and a critique was undertaken; positive feedback in the report confirmed the success of the session (Appendix 23).

Treatment No:

TREATMENT SCHEDULE FOR MOBILIZATION AND TACTILE STIMULATION TO THE LOWER LIMB (MoTaStim-Foot) **FORM N (i)**

Date: Pt ID Position of patient: Length of session: Therapist:

AIMS (Please tick)

- ❑ Regain normal extensibility of skin, muscle, connective tissues, tendons and joints to enable foot to accept base of support
- ❑ Reduce hypersensitivity or pain
- ❑ Heighten awareness foot position and posture
- ❑ Normalize tempero-spatial activation of muscle during functional activity (accuracy, quality of movement, normalise balance reactions)
- ❑ Normalize afferent stimulation arising from functional activity
- ❑ Normalize performance parameters (smoothness, accuracy, co-ordination, reciprocal activation, strength) for movement, balance and gait.

JOINT MOBILZATIONS:

1a) PASSIVE MOVEMENTS THROUGH ANATOMICAL RANGE (NB NOTE ANY RESTRICTIONS)

- ❑ Knee flexion / extension
- ❑ Talo-crural (ankle) joint – dorsiflexion / plantarflexion
- ❑ Talocalcaneal (subtalar) joint – Supination – adduction, inversion and plantar flexion of calcaneus ☐
- ❑ Pronation – abduction, eversion and dorsiflexion ☐
- ❑ Metatarsophalangeal joints - flexion / extension / abduction / adduction
- ❑ Interphalangeal joints – flexion / extension
- ❑ 1st ray (hallux) – Flexion / extension

Comments:

1b) ACCESSORY MOVEMENTS (TICK AND INDICATE TYPE e.g. GLIDE, DISTRACTION, AND DIRECTIONS e.g. AP, PA, etc.)

- ❑ Talocrural (ankle) ☐ Sub talar ☐ Talonavicular
- ❑ Calcaneal glide – inversion / eversion (medial /lateral) / A-P glide, distraction
- ❑ Calcaneocuboid A/P
- ❑ Naviculocuneiform
- ❑ Cuboid – 4-5 metatarsal
- ❑ Tarsometatarsal
- ❑ Metatarsophalangeal Jts 1-5 A/P
- ❑ Interphalangeal Jts 1-5

Comments:

SOFT TISSUE MOBILIZATIONS:

2) MASSAGE AND SOFT TISSUE STRETCH (TICK AND NAME BODY PARTS MASSAGED / TISSUES STRETCHED)

- ❑ Effleurage for oedema management
- ❑ Gastrocnemius and soleus mobilization - kneading ☐ picking up ☐ dissociation of gastrocnemius from soleus ☐
- ❑ Deep soft tissue massage to the tendo Achillis
- ❑ Stretch to gastrocnemius
- ❑ Stretch to soleus
- ❑ Stretch to tendo Achillis
- ❑ Extensor hallucis stretch
- ❑ Anterior tibialis mobilization (kneading/ picking up)
- ❑ Abductor Hallucis mobilization (stretch / kneading/picking up)
- ❑ Abductor Digiti Minimi mobilization (stretch / kneading/picking up)
- ❑ Deep soft tissue massage to the plantar fascia (sole of foot)
- ❑ Sustained stretch – flexor digitorum
- ❑ Sustained stretch – flexor hallucis
- ❑ Massage in between and along length of toes
- ❑ Other (state)

Comments:

PREPARATION FOR FUNCTION:

3) CREATING AN ACTIVE FOOT IN PREPARATION FOR STANCE / BALANCE

- ❑ Compression - MTP joints
- ❑ Talocalcaneal compression
- ❑ Compression through lateral border of the foot and little toe
- ❑ Compression through shank of LL
- ❑ Placing the foot orientation to the floor, sitting ☐ perched standing ☐ standing ☐
- ❑ Placing the foot on different surfaces - Details.....
- ❑ Lumbricals strengthening
- ❑ Heel contact with floor
- ❑ Other (state)

Comments:

4) SPECIFIC SENSORY INPUT (TICK AND NAME OBJECTS OR BODY PARTS)

- ❑ Visual
- ❑ Tactile stimulation, use of different textures/surfaces, somatosensory input, varying speed and depth of contact, to stimulate and also desensitise
- ❑ Hot/cold stimulation
- ❑ Active touch (objects e.g. changing surfaces, uneven ground)
- ❑ Passive touch (objects e.g. rolling foot over a ball)

Comments:

5) ISOLATED / SELECTIVE JOINT MOVEMENT (TICK AND STATE DIRECTION OF MOVEMENT)

- ❑ Talocrural joint (Ankle) – dorsiflexion/ plantarflexion Passive ☐ Active assisted ☐ Active ☐
- ❑ Subtalar joint – inversion / eversion
- ❑ Toe flexion / extension

6) PATTERNS OF CO-ORDINATED MOVEMENT UNDERLYING FUNCTIONAL ACTIVITY

- ❑ Activities in sitting e.g. rolling foot over ball, facilitated heel strike, heel raise
- ❑ Sit to stand to sit
- ❑ Weight transference - in sitting ☐ standing ☐ medial / lateral ☐ Forwards / backwards ☐ sideways ☐
- ❑ Stepping (including toe off and heel strike) – forwards ☐ backwards ☐
- ❑ Functional mobility ☐ Transfers ☐ Obstacle course ☐ Manoeuvring ☐
- ❑ Stairs Assistance required ☐ Independent ☐
- ❑ Other (please state)

Comments:

2-15

Figure 5.5 Final treatment schedule for delivering MTS to the lower limb

The process and success of Study 2, the intervention modelling study, as well as strengths and limitations will be deliberated in the discussion chapter (chapter seven).

The findings from Study 2, including the standardized protocols for MTS, wearing TIs and TSGT were used to inform Study 3 MoTaStim-Foot – the mixed methods, randomized blinded feasibility study exploring somatosensory stimulation of the foot and ankle early post-stroke.

6 CHAPTER SIX: STUDY 3 - SENSORY STIMULATION OF THE FOOT AND ANKLE EARLY POST-STROKE: A FEASIBILITY STUDY (MoTaStim-Foot)

6.1 Introduction

Following the successful development, in Study 2, of protocols for the three interventions, MTS, TI wearing, and TSGT, the aim of Study 3 was to investigate the feasibility of a future adequately powered RCT of MTS plus TSGT compared to the wearing of TIs plus TSGT for the lower limb in stroke survivors. This chapter will consist of the methods and results for Study 3.

The objectives for the feasibility study were stated in chapter four, section 4.4.2.3, and for convenience are restated here. The purpose of a feasibility study is solely to explore the *feasibility* of delivering the study interventions (research objective 3.1), recruitment methods (objective 3a), attrition rates (objective 3b), acceptability of interventions (objective 3d), potential response to treatment (objective 3g) and suitability of OMs (objective 3f), these were, therefore, the aspects monitored. Examining the effectiveness of the chosen interventions was not an aim of this study.

Criteria for determining feasibility were: demonstration of the successful recruitment of stroke survivors meeting the inclusion criteria, and ability to deliver the interventions, as well as whether the interventions and OMs are acceptable to stroke survivors.

Objective 2.1 related to Study 2 and the development of the three standardized protocols, and objective 3.1 was to determine feasibility of delivering a trial comparing MTS+TSGT with TIs+TSGT. Objectives 3a-3h relate to Study 3, the MoTaStim-Foot feasibility study and were to:

3a Find out if recruitment methods are effective, analysing the recruitment rate and associated data including:

   i. number of people invited to participate.
   ii. number and proportion of those agreeing to consent to participate.
   iii. number of those eligible to participate.

3b Monitor and analyse the number of people who drop out of the trial (attrition rate).

3c Gain pertinent information to inform an appropriate and feasible sample size for a future study.

3d Explore participants' experiences of interventions and their views on the acceptability of the treatments and method of delivery as interventions for a future study.

3e Investigate whether daily diaries and FGs are suitable ways to capture and explore stroke survivors' experiences of the interventions.

3f Investigate feasibility (cost and acceptability to participants) of a battery of OMs for sensorimotor impairment (feeling/sensation and movement) and lower limb function and balance, to inform the choice of primary and secondary OMs for a future trial.

3g Explore responses to either intervention (MTS plus TSGT, or TIs plus TSGT) over time and in relation to the number of treatment sessions

delivered; this will help to determine the most appropriate duration of therapy in a future trial.

3h Generate information regarding the participants recruited i.e. participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk, to ensure baseline characteristics of the two groups are comparable and to inform future studies.

6.2 Research ethics approval

Research ethics approval for this study was obtained from the National Research Ethics Service (4/3/16), IRAS No: 171968 / REC Ref 16/WM/0080 (Appendix 24). The ISRCTN trial registration number is 13676183 and Central Portfolio Management System ID 30449. Keele University was the sponsor of the trial.

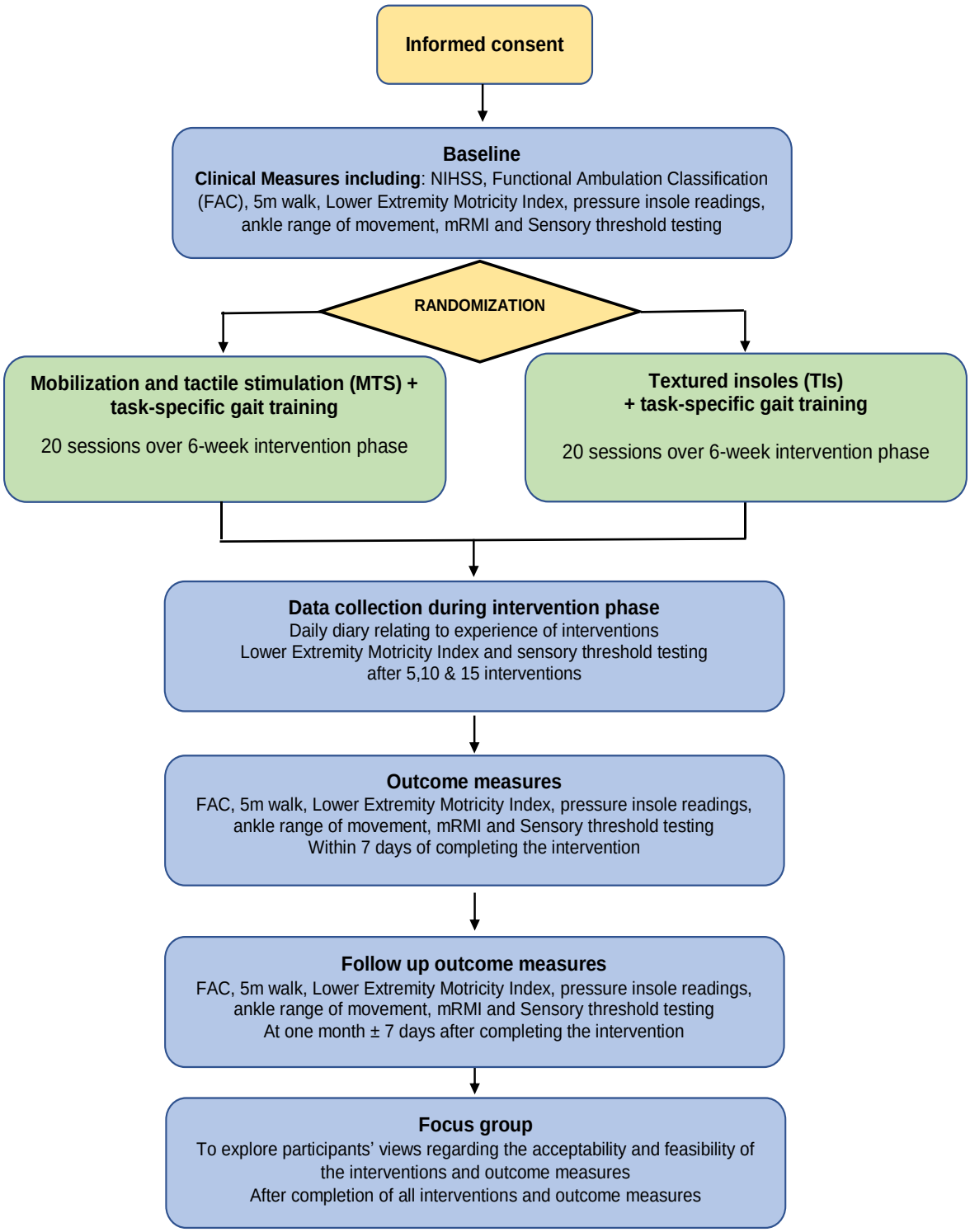
6.3 Methods

6.3.1 Trial design

A randomized, single-blinded feasibility trial was undertaken, using a mixed-methods design involving the collection of both quantitative (experimental) and qualitative (daily diaries and FGs) data. An overview of the trial is given in figure 6.1. Full details regarding the trial processes can be found in the MoTaStim-Foot trial protocol (Appendix 25), which was scrutinized and subsequently approved by the University of East Anglia Clinical Trials Unit Protocols Committee on 14/1/16.

The OMs were undertaken at baseline (prior to randomization), after twenty sessions of the intervention of either MTS+TSGT or TI+TSGT (delivered within a 6-week period, according to the agreed protocols reported in Study 2, chapter five), and at one-month follow-up. Inter-intervention phase OMs were also undertaken after five, ten and fifteen interventions, and participants kept a daily diary during the intervention phase. Post-trial, participants were invited to participate in a FG to explore the acceptability and feasibility of the interventions and OMs. If participants were receiving NHS therapy (usual care), this continued alongside the trial interventions and the dose and content of routine lower-limb therapy provided was recorded on a therapy treatment record (Pomeroy et al., 2005) by the clinicians delivering routine care (Appendix 26). A post hoc analysis of usual care will be undertaken as part of a separate research study.

As detailed in the MoTaStim-Foot protocol (Appendix 25) ethical approval was also granted for including blood flow studies to ascertain the effects of the treatments, endeavoring to develop the scientific basis behind the interventions, for example establishing if changes to sensation, movement and blood flow are seen following MTS, and also the wearing of TIs. However, the researcher who intended to undertake the blood flow studies was unable to dedicate the necessary time to data collection during the MoTaStim-Foot trial, and therefore this aspect could not be undertaken.



mRMI – modified Rivermead Mobility Index

NIHSS – National Institutes of Health Stroke Scale

Figure 6.1 Overview of the trial design

6.3.2 Rigour of the trial

The rigour of this feasibility study was improved by following the CONSORT 2010 statement: extension to randomized pilot and feasibility trials guidelines (Eldridge et al., 2016; Moher et al., 2012). As this was a mixed-methods design rigour needed to be considered for collecting both quantitative and qualitative data; a methodology was chosen for the feasibility study that increased the internal and external validity of the research. External validity relates to whether the findings from the study sample can be generalized to the population from which the sample was selected (Sim and Arnell, 1993), whereas, internal validity is dependent upon the design of the research enabling variations to be directly attributable to changes in the independent variable (Polgar and Thomas, 2000).

For quantitative research designs the terms internal validity, external validity and reliability are used when considering the rigour of the research design. Guba and Lincoln (1989, p.233-243) suggested alternative terminology when considering the rigour of qualitative research designs, advocating the use of the term ‘trustworthiness’, which consists of ‘credibility, transferability, dependability, and confirmability’, and it has been reported that it is the responsibility of the researcher to ensure rigour and trustworthiness (Nowell et al., 2017). A robust methodology enables credibility to be achieved, obtaining and analyzing appropriate data to address the research question (White et al., 2012). Transferability relates to the generalizability of the information to other cases, and dependability can be achieved by implementing a systematic audit trail, enabling an external person to understand how the researcher reached

their conclusions, with reflexivity (consideration and documentation of the researcher's opinions and biases) a key element (Tobin and Begley, 2004). In order to address reflexivity, consideration of the researchers own biases was essential, especially because the researcher was working as one of the research therapists in the study. This was achieved in several different ways:

After the first participant had been treated a detailed discussion took place between the researcher (PhD student/NIHR fellow) and her supervisors. The outcome of this meeting was a deeper understanding of how important it was to follow protocols strictly, ensuring influences relating to previous neurological therapy expertise were not utilised. The specifics and outcomes of the discussion were considered in greater depth by undertaking a detailed reflection. It was important to ensure none of the researcher's own opinions and biases influenced the implementation and analysis of the MoTaStim-Foot study. Other mechanisms built into the design to address reflexivity were the involvement of a PPIE advisor within the focus groups, who assisted with the final summary verifying the content of the discussions, helping to ensure any potential for researcher bias was addressed. The debrief meetings after each focus group enabled an opportunity for further analysis and discussion if any researcher bias had been present. Furthermore, the regular trial management group meetings ensured a rigorous overview of the trial was undertaken, involving many different independent people who could advise and oversee that researcher bias was not threatening the running of the trial.

Confirmability relates to whether the themes developed have resulted from the data itself, rather than the researcher's opinions and pre-conceptions (Tobin

and Begley, 2004). All these aspects were taken into consideration when designing the MoTaStim-Foot feasibility study, for example, triangulation occurred in relation to the use of more than one method of data collection and several researchers analysing the FG data, both enhancing credibility.

The OMs for the feasibility study were carefully selected. Psychometric properties of the measurement tools were considered to enhance the internal validity of the feasibility study. There are four distinct forms of measurement validity when considering quantitative data: face validity is present if the chosen tool or assessment measures the variable of interest; content validity is concerned with the ability of a tool to measure all the individual aspects of a domain (Sim and Wright, 2000); criterion-related validity exists when a measurement tool or instrument accurately represents the measurements that would be obtained when an accepted validated measure is used (Sim and Arnell, 1993); and construct validity depends upon the theoretical background within which a measure is used (Sim and Wright, 2000). Reliability of OMs was also researched prior to using them in the MoTaStim-Foot feasibility study.

Other aspects of the trial which increased the internal validity were randomization, which will be discussed in section 6.3.8 and blinding (section 6.8). Internal validity was also increaed by ensuring the research staff were suitably trained to enable standardization of procedures for delivery of both interventions and OMs, following strict protocols (reducing external factors and variables which may influence the results, (Hicks, 2010)). These aspects relating to Study 3 (the mixed-methods feasibility study) all increased the

internal validity within the trial (Downs and Black, 1998), an aspect which will be important for the future adequately powered RCT.

6.3.3 Population and sample

Participant inclusion and exclusion criteria

6.3.3.1 Inclusion criteria

(i) Adult stroke survivors (aged 18 years or older), with anterior or posterior circulation stroke, occurring 6–16 weeks (42–112 days) earlier.

(ii) Able to walk independently prior to stroke with or without a walking aid.

(iii) Able to follow simple commands and imitate actions, using the non-paretic upper limb.

(iv) Unable to step on and off a 7·5 cm high block more than 12 times in 15 seconds with either their paretic or non-paretic leg (Hill et al., 1996).

(v) Able to provide written informed consent.

Careful consideration was given to the time post- stroke for inclusion within the trial. The chosen timing aligns well with advice from SRRR (Bernhardt et al., 2017b) falling between the early subacute phase (seven days to three months) and the late subacute phase (three to six months) in a time-period where there is still potential for endogenous plasticity and improvement of impaired function. Furthermore, the most likely period for recovery of walking post-stroke is

between 4-7 weeks (Kollen et al 2006); in order to explore the effects of mobilization and tactile stimulation (MTS) / TIs – as opposed to natural, expected recovery – participants were recruited at the end of this period associated with best recovery.

The justification for including posterior circulation strokes as well as anterior circulation relates to the importance of the cerebellum for balance and gait, as discussed in chapter two (section 2.5). There will be further discussion relating to this aspect in chapter seven.

It was intentional that there were no inclusion criteria relating to specific sensory impairment; the inclusion criteria were kept intentionally wide, because part of the reason for the feasibility study was to explore the appropriateness of the inclusion criteria. Proprioceptive awareness occurs at both a conscious (Cohen, 1999) and subconscious level (Takakusaki, 2017) and therefore it was important to be inclusive, in order to inform selection of inclusion criteria for future studies.

6.3.3.2 Exclusion Criteria

(i) Pre-existing conditions affecting sensation (feeling) of the foot and lower limb e.g. diabetic neuropathy, polyneuropathy, peripheral nerve lesion, previous stroke affecting the sensation of the lower limb.

(ii) Fixed contracture of the tendo Achillis, assessed by being unable to achieve 90 degrees dorsiflexion at the ankle, either actively or passively, with the knee extended.

(iii) Pressure sores or ulcers on the foot or ankle (hemiparetic limb), due to the risk of infection.

(iv) Deep vein thrombosis, because some of the MTS techniques would be contraindicated.

(v) Other conditions that affect the blood supply to or from the foot, e.g. heart failure with peripheral oedema.

(vi) Botulinum toxin injection to the lower-limb in the previous six months, because it may have an impact on the results.

(vii) Pain sufficient to prevent delivery of treatments or outcomes.

(viii) Known HIV, hepatitis non-A or related condition (to meet sponsor requirements).

6.3.4 Sample size

The sample size for the quantitative element of the feasibility study was calculated as 34. A sample size of 30 has been suggested as the lower limit for calculating the number of participants that will be required for future studies in terms of an estimate of the standard deviation of values on a continuous OM (Browne, 1995). Recruitment of a sample of 34 participants was planned to account for approximately 10% drop out and enable potentially equal numbers (n=17) in each arm of the trial; this was the largest sample size considered to be feasible in the available time-period. Whilst it was not the aim of the feasibility study to demonstrate effectiveness, it is acknowledged that a sample

size of 34 is relatively small and could influence the results of the trial. Nevertheless, the sample size for a feasibility study just needs to be large enough to assess the aspects identified in the study's objectives (Thabane et al., 2010). It can, therefore, be argued that a sample size of 34 was adequate to meet the needs of this feasibility study.

As this was mixed-methods research, FGs were also undertaken, with all trial participants being invited to attend. Two FGs were conducted for each arm of the trial. A PPIE adviser was note taker, writing the field notes during each FG. Furthermore, the PPIE volunteer assisted the researcher with a summary at the end of each FG, helping to ensure the researcher had interpreted the participants' opinions appropriately, by offering a lay opinion from someone who has experience of stroke rehabilitation. In addition, the participation of three different researchers and a PPIE advisor when analyzing the data ensured investigator triangulation occurred, providing opportunities for individual opinions to inform a collective analysis enabling robust conclusions to be drawn (Carter et al., 2014).

6.3.5 Setting

The trial was set in a local NHS Trust hospital in which stroke rehabilitation occurred as an in-patient, or as part of the early supported discharge services, in conjunction with a community-based stroke team. The stroke team clinicians had been involved with other similar studies and were supportive of the research, which was an essential element since their assistance was required when identifying suitable participants. All treatments and assessments were

delivered either in the hospital or at the participant's place of residence in the community.

6.3.6 Recruitment

Adult stroke survivors meeting the criteria for the study, who were undertaking in-patient rehabilitation on the ward at the hospital or receiving treatment as part of the Early Supported Discharge team were invited to participate in the study. Potential participants were identified by research nurses or the multidisciplinary teams caring for the stroke survivors in keeping with Good Clinical Practice (GCP) and Data Protection Act standards.

A clinical team member or Clinical Research Network (CRN) research nurse initially approached potential participants to establish whether they would like to find out more about the trial. Oral consent was sought for a member of the research team to look at their medical notes. The screening and consenting processes are summarized below, and detailed in figures 6.2, 6.3 and 6.4 and in the MoTaStim-Foot protocol (Appendix 25).

6.3.7 Screening and consent

6.3.7.1 Stage one of the screening process

Stage one of the screening process (case note review) (figure 6.2) occurred to determine whether the stroke survivor was potentially eligible for the trial according to age, time since stroke and type of stroke, in accordance with inclusion criteria (i), and had a previous ability to walk independently (inclusion criteria ii).

If potential participants were interested but did not meet the inclusion criteria, a member of the research team met with the participant and thanked them for their interest and explained that, at the current time, they did not currently meet the criteria. If there was a chance the potential participant may become eligible in the future, for example, according to time after stroke or a healing wound, it was explained that they could be reassessed for the trial later. For interested potential participants who met the inclusion criteria, the purposes of the trial were explained by a member of the research team, clearly delineating what is research and what is clinical practice; explaining potential benefits and risks and going through the PIS (Appendix 27). PIS refers to the summary and full PISs, which were developed in collaboration with PPIE representatives; emails relating to their comments about the PIS information are available at Appendix 28. Any questions the potential participant had were answered, and the potential participant was left with a PIS to read and consider further. A record was kept of the contact and leaving of the PIS, and members of the clinical team were also informed either orally or in writing.

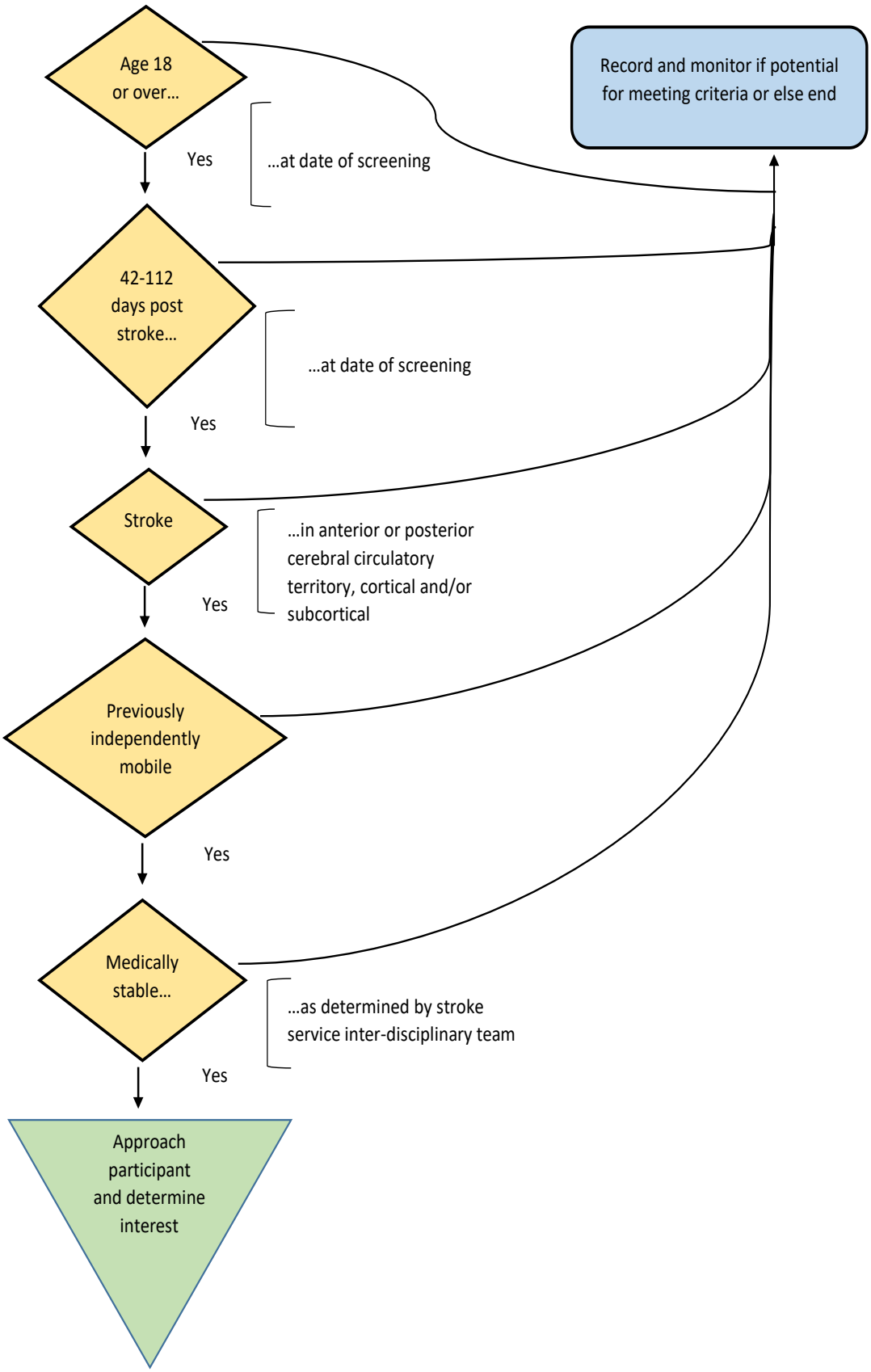


Figure 6.2 Initial screening process

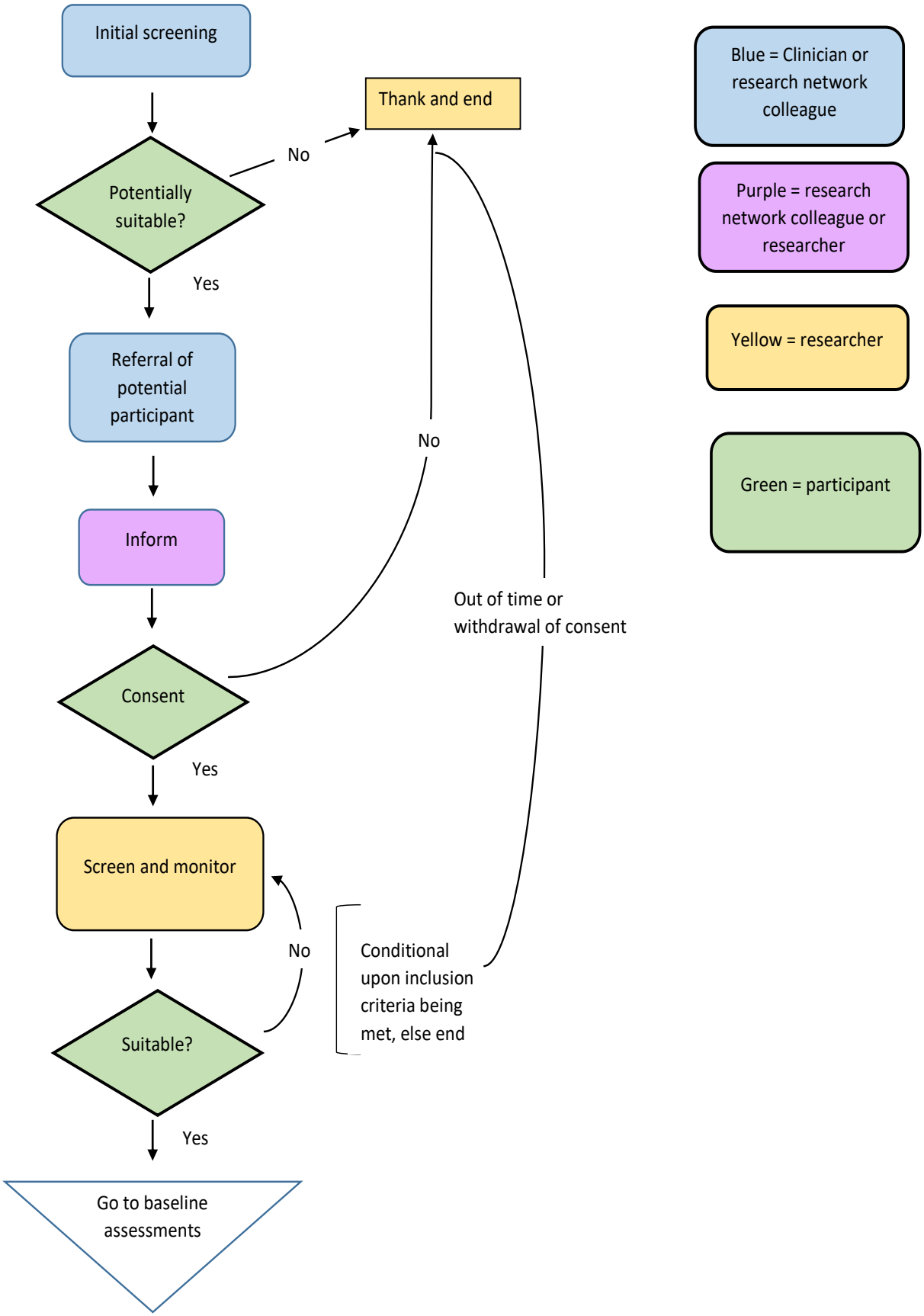


Figure 6.3 Participant eligibility pathway

Once participants had been given as much time as they needed, had any further questions answered, and established that they wished to take part in the trial, written informed consent was taken (Appendix 29). Details regarding consent to participate in the trial were then documented in the participant's medical notes and discussed with members of the clinical team.

In view of (a) the inclusion and exclusion criteria necessary for this trial (section 6.3.3), and (b) the wish not to create conflicts of interest or create extra work for the clinical team, further eligibility screening (Stage 2) (figure 6.4) of potential participants was required after participants had given consent. Participants were informed that, if they provided consent, there would be a few measures undertaken to check they met all the eligibility criteria for the trial.

6.3.7.2 Stage 2 of the screening process

Stage two of the screening process involved additional tests being explained to the participant and subsequently undertaken by a research therapist:

(i) Assessment for fixed flexion contracture of the tendo Achillis

(ii) The step test (Hill et al., 1996), which was used to avoid recruitment of stroke survivors who only had minimal lower-limb dysfunction. The number of steps in 15 seconds onto a 7.5cm step (>12 each leg) was decided upon after researching normal values in healthy patients and stroke survivors (Hill et al., 1996).

(iii) Ability to follow simple commands by imitating actions. Simple screening procedures were used, in the stage 2 screening process,

to make sure the potential participants could follow simple commands and undertake a task involving imitating actions.

If a participant did not meet the eligibility (inclusion and exclusion) criteria but indicated continuing interest, then he or she was followed up no more than three times a week (frequency depended on speed of recovery) until he or she either (i) withdrew consent, (ii) met all eligibility criteria, or (iii) reached the maximum time since stroke for recruitment into the trial.

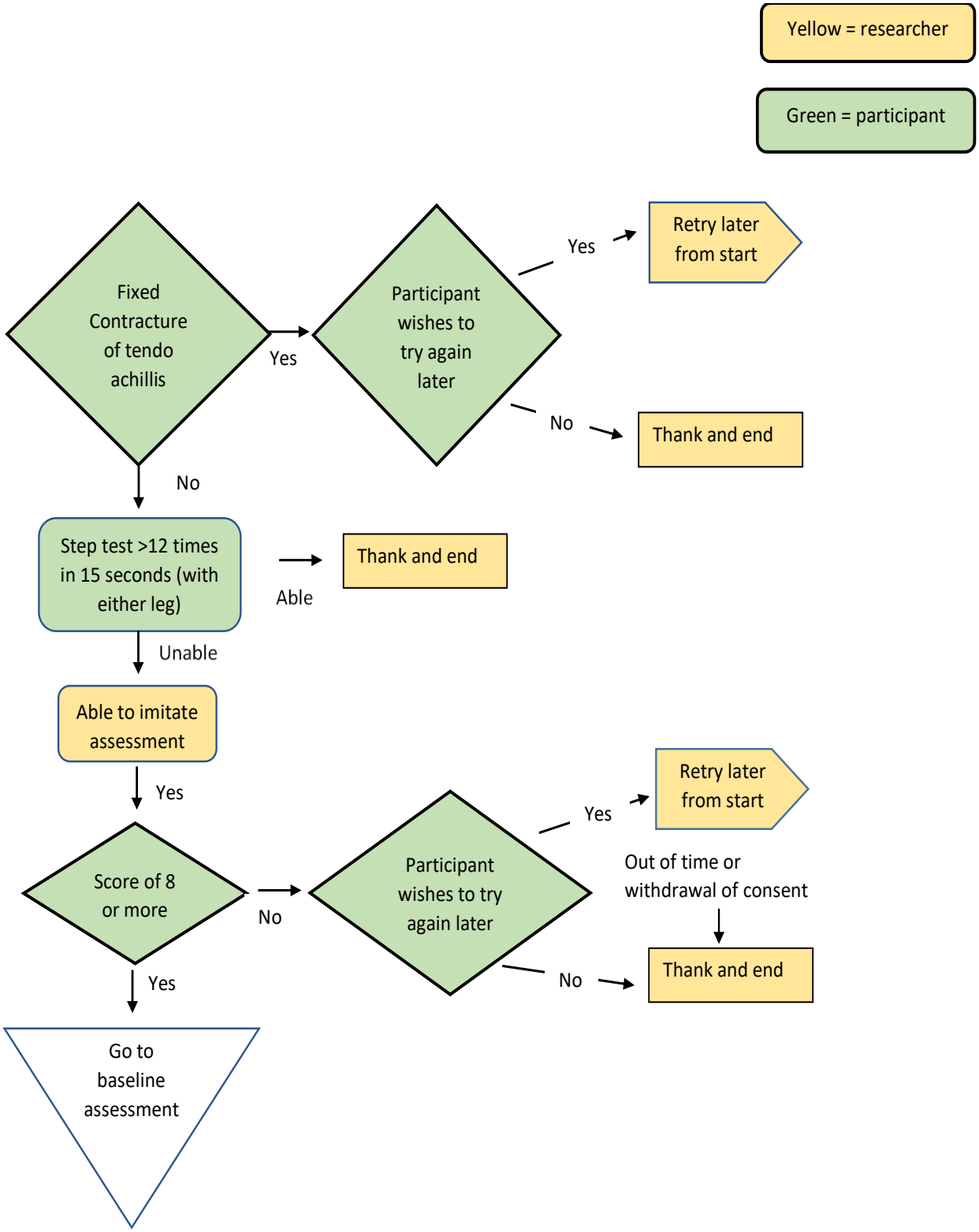


Figure 6.4 Stage 2 eligibility screening

Some stroke survivors have trouble making decisions. Before approaching a potential participant, the researcher discussed the decision-making capacity of individuals with the clinical team. If the clinical team believed that the communication impairment was too great to allow an individual to give informed consent, then the potential participant was not approached. If the clinical team conclusion was that informed consent was possible, albeit with the use of enhanced communication strategies, then the researcher approached the potential participant and adapted their communication strategies, as required, in relation to the provision of information relating to the trial. It was ensured that the participant understood the information about the trial and potential consequences of being involved in a trial before being asked to provide written informed consent.

At all times during the consent process, it was made explicit that the participant was free to refuse to participate in all or any aspect of the trial, at any time and for any reason, without incurring any penalty or affecting their treatment. Important aspects regarding consent were considered and consent was only taken by researchers who had completed GCP training and had a working knowledge of the Mental Capacity Act (2005). The important aspects of consent, include: (i) understanding the purpose and nature of the research; (ii) understanding what the research involves, its benefits (or lack of benefits), risks and burdens; (iii) understanding the alternatives to taking part; (iv) able to retain the information long enough to make an effective decision; (v) able to make a free choice; and (vi) capable of making this particular decision at the time it needs to be made (NIHR, 2016).

Some participants had dominant arm weakness and difficulty signing the form, or speech problems. If this was the case, an independent witness signed the consent form, if required, on behalf of the participant. This was either a family member or one of the clinical team working with the patient, but not a member of the trial team.

6.3.8 Randomization

After providing informed consent and undertaking the baseline measures, participants were randomized to receive one of the two study interventions. The randomization procedure was in a 1:1 ratio, with stratification by left or right stroke. Stratification aimed to ensure an equal number of right-and left-sided strokes in each treatment group. This was achieved using permuted block randomization in blocks of four and two. The decision to stratify in accordance with side of the stroke was made because it has been reported that the rehabilitation potential for people with right and left-sided strokes may differ. Alexander (1994) demonstrated that there was significantly less reported change for people with a right-sided lesion than a left (p =.0354) when the Functional Independent Measure was assessed at admission and discharge.

The randomization sequence was generated before the trial commenced and Professor Julius Sim, the statistician for the trial, provided the randomization order to Norwich Clinical Trials Unit (CTU). The allocation order was concealed from the research team (Clark et al., 2016) by using a 3rd party randomization service (Norwich CTU). The order was revealed to the research therapists

after baseline measures were made for a participant by an automated computer randomization system.

6.3.9 Baseline characteristics

To meet objective 3h, information was collected regarding the participants recruited – i.e. participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk. The National Institutes of Health Stroke Scale[5] (NIHSS) (Appendix 30) and FAC (Appendix 31) were used to characterize the clinical presentation of the participants.

The FAC is a six-point scale used to assess walking ability and categorize functional walking according to basic motor skills, resulting in ordinal data. It has been found to be valid and responsive, with excellent intra-rater reliability (Cohen *k*=.950) and inter-rater reliability (*k*=.905) in stroke survivors (Mehrholz et al., 2007). The assessments were standardized by ensuring appropriate training of the assessors, and if any issues relating to recording of scores arose, discussions involving the Chief Investigator took place until consensus was reached.

The NIHSS is an established, valid, widely used assessment tool that provides a quantitative measure of stroke-related neurologic deficit (Meyer and Lyden, 2009). The maximum total is 42; however, due to the inherent design of the

[5] http://www.nihstrokescale.org/

scale, even a patient in a coma can only reach a maximum score of 39 (Lyden, 2017); a lower score indicates less impairment, with the optimum score being 0 (no impairment). Also, the weighting within the NIHSS is organized such that someone with a left hemisphere lesion with stroke and speech and language difficulties will score four additional points over and above someone with a right-sided lesion (Lyden, 2017). It was designed for use in trials involving stroke participants (Brott et al., 1989) with overall interobserver reliability >.98 reported for physicians and study coordinators following training (Goldstein and Samsa, 1997). Although responsiveness of the NIHSS is not as high as the Stroke Impairment Assessment set and the Canadian Neurological scale (Seki et al., 2014), this was not considered to be relevant in this study since the assessment of clinical presentation of the participants was only undertaken at baseline. The NIHSS assessment is relatively quick to undertake (less than ten minutes) (Brott et al., 1989), and on-line training is now readily available, which has been shown to be useful for standardization of assessment scales (Lyden et al., 1994). This was deemed to be an important resource for ensuring appropriate training of the research therapists in this trial. Consequently, all research therapists and assessors undertaking the NIHSS in this trial were trained in this way, being required to complete the online NIHSS training and therefore be certified prior to assessing any participants.

6.3.10 Outcome measures

To address study objective 3f, (sections 4.4 and 6.1), a range of OMs were included in this study. As this was a feasibility trial, one of the objectives was to identify which measure should be the primary OM for future trials.

Consequently, each OM used was evaluated according to acceptability for participants (from the information in the daily diaries and FGs), clinical relevance (from evidence in the literature and FG analysis), ease of use (feedback from research therapists and assessors and also from the FGs), quality of data collected (from analysis of the results), validity and reliability (from information in the literature). The outcomes evaluated are summarized (including their psychometric properties) in table 6.1 and described in more detail within this chapter.

6.3.10.1 Consideration of alternative outcome measures

When deciding the measures that should be used to screen participants, screening for unilateral spatial neglect was also considered; however, a decision was made that as this was a feasibility study it was important to be as inclusive as possible. When designing the trial, the inclusion of a quality of life measure was also considered. However, quality of life is a multi-faceted construct, influenced by, for example, age, gender, marital status, socioeconomic status, level of education, extent of disability after stroke**,** depression or anxiety, cognitive impairment, incontinence and other comorbidities, as well as social factors and self-management strategies (Wang and Langhammer, 2018); it was not the purpose of the feasibility study to explore issues relating to quality of life. Any quality of life issues directly relevant to the trial experience could be explored through the daily diaries and FGs. Other outcome assessments such as the Nottingham Extended Activity of Daily living were also considered; however, as some of the participants were to be in a hospital setting when receiving the research interventions, it was felt not

to be the most appropriate functional OM, and the mRMI was selected instead. Gait speed was deemed essential as an OM for the trial, so results can be compared to other studies and since it links with assessment of potential as a functional ambulator (Perry et al., 1995).

6.3.11 During intervention phase experience

Throughout the intervention period, participants were asked to keep a written or audio daily diary to help them 'focus their thoughts' (Jacelon and Imperio, 2005, p.993), providing qualitative data contemporaneously, relating any changing perceptions of their lower-limb, and experiences of the interventions and outcomes. The format of the diary involved spaces each day to record aspects, for example, whether their foot felt hot or cold, whether the MTS, TIs or TSGT were comfortable or uncomfortable etc., as well as space for comments relating to the various aspects (Appendix 32 and 33).

As this was a feasibility study it was important to explore whether participants perceived any variations to their foot (feeling and movement) or function (standing, balancing and walking); any changes, or comments about the treatment interventions could be documented in the daily diary sheets, contributing a fuller understanding of the comfort and acceptability of the interventions and outcome measurements. The use of diaries during the six-week intervention period, therefore, facilitated a better insight into the participants' trial experience; an important aspect towards meeting objective 3e.

Table 6.1 Summary of outcome measures for the feasibility study

Outcome		Measurement tool	Frequency of measurement	Additional information
Sensorimotor impairment	Ankle range of motion – dorsiflexion/plantarflexion Inversion/eversion	Electrogoniometer attached to lower leg (lateral border) of contralesional foot	Baseline Post-intervention One-month follow-up	Provides ratio-level data (cm) Intra-rater reliability r = 0.979 (Bronner et al., 2010).
	Touch/pressure sensory threshold of plantar skin - under heel, hallux,1st metatarsal phalangeal (MTP) joint and 5th MTP joint	Semmes Weinstein Monofilaments (SWMs)	Baseline After 5, 10 and 15 treatments, Post-intervention One-month follow-up	Provides ordinal data; filaments are numbered 1-20. One represented the smallest force (0.008g, 1.65) and 20 the largest force (300g, 6.65). Intra-rater reliability has been reported to be an r value of >0.9 when a specific protocol was followed (Tracey et al., 2012).
	Motor impairment (strength) of hip flexors, knee extensors and ankle dorsiflexors	Lower Extremity Motricity Index (LEMI)	Baseline After 5, 10 and 15 treatments, Post-intervention One-month follow-up	Provides interval level data, for individual actions (ankle dorsiflexion, knee extension and hip flexion) and all actions combined, Pearson correlations - good to excellent (r = 0.78–0.91), significant (p < 0.001), and of high power (≥99%) (Cameron and Bohannon, 2000). Excellent test-retest intra-rater reliability of the Lower Extremity Motricity Index (LEMI) as a measure of strength (ICC= 0.93) (Fayazi et al., 2012).

Lower limb function and balance	Walking ability	Functional Ambulation Classification (FAC)	Baseline Post-intervention One-month follow-up	Provides categorical/nominal data. Valid and responsive, with excellent intra-rater reliability (Cohen *k*=.950) and inter-rater reliability (*k*=.905) in stroke survivors (Mehrholz et al., 2007).
	Walking speed	5-metre walk test (5MWT) (videoed)	Baseline Post-intervention ne-mnth follow-up	Provides ratio-level data (seconds). 5MWT was shown to have a standardized response mean (95%CI) of 1.22 (.93–1.50) at a comfortable pace and 1.00 (.68–1.30) at a maximum walking pace (Salbach et al., 2001).
	Pressure under the feet during stance phase of walking	TEKSCAN pressure insoles to record force-time integral (FTI) and centre of force velocity (COFV) in an AP direction	Baseline Post-intervention One-month follow-up	Provides ratio-level data force time integral (FTI) (N/sec) and (COFV) (cm/sec). Foot Scan pressure insole systems have been found generally to provide reliable force and pressure data (ICC > 0.75) (Low and Dixon, 2010). Pressure insoles have shown a very strong degree of association when measuring COP in an AP direction with Pearson's correlation coefficients - greater than 0.90 for 67/67 trials (100%) (Chesnin et al., 2000).
	Functional mobility	Modified Rivermead Mobility Index (mRMI)	Baseline Post-intervention One-month follow-up	Provides ordinal level data. Inter-rater reliability excellent = 0.98; (p<0.001) (Lennon and Johnson, 2000). The minimal clinically relevant difference is 4.5 points.

Participants' perceptions of the acceptability of the interventions and Oms	Daily diaries and FGs	Information recorded daily throughout the intervention period. Attendance at an FG on completion of all the interventions and measures	FGs were used to provide an insight into the participants' trial experiences (Krueger and Casey, 2000). Interview schedules were used. A PPIE advisor assisted with note-taking and summarizing the information discussed at the end of each FG. Braun and Clarke's (2006) six-stage process for thematic analysis was broadly followed.

Abbreviations: 5MWT Five metre walk test, AP Anterior-posterior, Cm Centimetres, COFV Centre of force velocity, COP Centre of pressure, FAC Functional Ambulation Classification, FG Focus group, FTI Force time integral, ICC Intraclass correlation co-efficient, LEMI Lower Extremity Motricity Index, N/sec Newtons per second, SWMs Semmes Weinstein Monofilaments.

6.4 Assessment of sensorimotor impairment

6.4.1 Ankle range of motion (dorsiflexion and inversion)

Ankle range of movement was measured during stance phase, using an electrogoniometer[6] attached to the lateral border of the lower leg, collecting ratio data (degrees). The sensor was set up in accordance with figure 6.5, and the data log acquisition unit was calibrated (zeroed) with the participants standing in a neutral position (Moriguchi et al., 2007). Dorsiflexion was taken to be positive (meaning that movement of the foot up towards the shin resulted in a positive reading from the goniometer and plantar flexion was taken as a negative reading); the maximum range of dorsiflexion and inversion movement at the ankle was recorded during the 5-metre walk test (5MWT). Data were extracted from the Biometrics programme and run through a Matlab programme by a technician to achieve the results in degrees of movement. Reliability of the electrogoniometer for the ankle has been established, with intra-rater reliability r = 0.979 (Bronner et al., 2010).

[6] http://www.biometricsltd.com/gonio.htm

Figure 6.5 Set up for placement of the goniometer

6.4.2 Touch/pressure sensory thresholds (plantar surface of the foot)

SWMs measure touch/pressure threshold. They comprise a set of 20 filaments[7] that deliver a range of forces, from 0.008g to 300g, when applied perpendicular to the skin. The touch test sensory evaluator (table 6.2) was used for the MoTaStim-Foot trial.

Table 6.2 Touch-test sensory evaluator[8]

SWM Number	SWM Code	Target Force (grams)	Threshold
1	1.65	0.008	**Normal plantar threshold**
2	2.36	0.02	
3	2.44	0.04	
4	2.83	0.07	
5	3.22	0.16	
6	3.61	0.4	
7	3.84	0.6	**Diminished light touch**
8	4.08	1	
9	4.17	1.4	
10	4.31	2	
11	4.56	4	**Diminished protective sensation**
12	4.74	6	
13	4.93	8	
14	5.07	10	**Loss of protective sensation**
15	5.18	15	
16	5.46	26	
17	5.88	60	
18	6.10	100	
19	6.45	180	
20	6.65	300	**Deep pressure sensation**

[7] Patterson Medical Ltd.
[8] Sensory evaluator chart, Adapted from North Coast Medical, Inc. (2000)

SWMs are the most common method of identifying loss of protective sensation (Mayfield and Sugarman, 2000); the assessment involves touching the plantar skin using a nylon filament that exerts a specific force when bowed into a C shape against the skin for 1 second, as shown in figure 6.6. Intra-rater reliability has been reported to be an r value of >0.9 when a specific protocol was followed (Tracey et al., 2012), and these filaments have been used previously to record sensation in the feet of stroke survivors (Hillier and Dunsford, 2006).

The Nottingham Sensory Assessment was considered; however, it has been suggested it is more of a screening tool rather than a detailed somatosensory assessment (Connell et al., 2008). The Rivermead Assessment of Somatosensory Performance (RASP) (Winward et al., 2002) was also considered as an alternative tool for measuring various aspects of sensation (sharp/dull, surface localization, temperature, proprioception, sensory extinction and two-point discrimination, as well as touch sensation). However, the RASP can take up to 30 minutes to complete, and in view of the large battery of OMs already included within the trial, it was felt this would be too burdensome for the participants to include. Furthermore, the ability to feel touch and pressure was considered to be more relevant to this trial, than for example, temperature perception, as the interventions were designed to improve awareness of the sensations important for balance and gait. Also, the force delivered by the RASP tool for testing pressure is not calibrated or standardized, whereas the force delivered by the SWMs is, and therefore is more consistent/repeatable (Bell-Krotoski and Tomancik, 1987).

6.4.2.1 Testing site

Identification of the minimum pressure/force required to accurately identify touch/pressure sensation was measured at four different points on the plantar surface of the foot, under the: heel; pad of the hallux; 1st metatarsophalangeal (MTP) joint; and 5th MTP joint (figure 6.7). There is no agreement regarding the optimum areas to test on the plantar surface of the foot and tailoring of sites to the disorder has been suggested (Collins et al., 2010); areas of the foot that are important for weight bearing during gait were therefore selected.

Figure 6.6 Demonstrating SWMs used to test the touch/pressure sensory threshold

Figure 6.7 Points tested with SWMs:

1. Under the heel, in the midline of the foot, 1 cm forwards of the back of the heel.
2. Under the pad of the hallux
3. Under the 1st metatarsal joint
4. Under the 5th metatarsal head

Diagram of the foot drawn by P Bailey (2017)

6.4.2.2 Testing protocol

There is no consensus relating to the number of monofilaments to use when assessing the feet, but the use of all twenty monofilaments is discouraged due to the time involved to implement the testing (Collins et al., 2010). In view of this, and following consultation of related literature, a strict protocol was developed for the MoTaStim-Foot trial (Appendix 34). This protocol took into account that Tracey et al., (2012) demonstrated that a three-down-one-up rule was more reliable than a two-down-one-up rule, because people were able to differentiate better with a larger difference between the forces produced by the SWMs; similarly, the 4-2-1 stepping algorithm, designed by Snyder et al., (2015), was considered. This protocol was rejected in relation to concerns regarding commencing with SWM number 12, (4.74, 6g/mm). This force is aligned with diminished sensation (table 6.2), and not normal plantar threshold sensation; starting at this force could sensitise the area being tested, affecting the results. Merkel cells (which detect deformation of the skin) are extremely sensitive to the position and velocity of a stimulus (Abraira and Ginty, 2013); therefore, this could influence the results of subsequent SWM testing. A starting point of SWM number 4 (2.83, 0.07g/mm) was decided upon because it is at the midpoint of the normal threshold for plantar threshold normative touch-pressure data. Other protocols commenced using the number 12 (4.74,6g/mm) SWM (Snyder et al., 2015), or a 4.5g/mm SWM (SENSELab Aesthesiometer, Hörby, Sweden) (Tracey et al., 2012), but no justification was offered as to why this level was used as a starting point. In view of the fact that stimulation of a site with a SWM with more force than necessary could

enhance the next response – that is, it would potentiate synaptic transmission (Izhikevich, 2006) – it was deemed to be important to commence testing at a level with less force.

When a level was tested and the participant was able to feel the SWM, the testing ensured that the next SWM assessed was at least 3 steps downwards, and the 3 down one up rule as tested by Tracey et al., (2012) was basically followed. However, to ensure all possible SWMs were tested, on two occasions the protocol necessitated a jump down of 5 SWMs (due to the larger spread of the normal plantar threshold and loss of protective sensation sections).

6.4.2.3 Recording results

In order to record the results, the SWM code, e.g. 4.31, was documented in the case report forms. This code represents a log value of the actual force delivered by the monofilament (e.g. 2g for the 4.31 coded filament). For the purpose of analysis, the results were graded from one to twenty, with one representing the smallest force (0.008g, 1.65) and 20 the largest force (300g, 6.65) required to achieve the threshold of sensation, resulting in ordinal data. It was decided this was the optimum way to record the data. Many researchers consider the SWMs to give ratio-level data; however, the force produced by the SWMs does not increase in a way that means the increments between each SWM are equal.

If a participant was unable to feel any stimulation this was noted, and if the research assessor felt the participant's response was unreliable, this was also recorded appropriately.

6.4.3 Lower Extremity Motricity Index (LEMI)

The Motricity Index is quick to undertake and is a valid scale for measuring motor impairment in the upper and lower limbs after stroke, according to a 6-point scale (0–5), based upon the MRC grading (0–5) of muscle strength (table 6.3) (Collin and Wade, 1990). It does not assess the quality of movement. Motricity Index scores are weighted, taking into consideration the difficulty experienced by patients when progressing from one MRC grade to the next, with scores ranging from 0 (no movement) to 33 (full strength) for each of three joints tested in a limb, i.e. hip, knee and ankle; a final one point is added so it can be scored out of 100 (Collin and Wade, 1990). Scores can be treated as interval data (Cameron and Bohannon, 2000).

6.4.3.1 Reliability and validity

The Motricity Index has been found to possess criterion-related validity in a group of stroke survivors (n=15), with individual joints (ankle dorsiflexion, knee extension and hip flexion) and all actions combined; Pearson correlations were good to excellent ($r = 0.78–0.91$), significant ($p < 0.001$), and of high power (≥99%) for both the individual joint scores and the total scores showing good to excellent correlations with hand held dynamometer readings (Cameron and Bohannon,

2000). A further study with stroke survivors (n=20) also demonstrated excellent test-retest intra-rater reliability of the LEMI as a measure of strength (ICC= 0.93) (Fayazi et al., 2012).

In the MoTaStim-Foot trial, the LEMI was used to measure motor impairment (loss of muscle strength) in the hip flexors, knee extensors and ankle dorsiflexors. Trial research therapists (for monitoring fatigue) and assessors (for blinded assessment) were trained prior to undertaking the LEMI. Opportunities were created to practice using the LEMI, to improve the reliability of the measurements, particularly in relation to differentiating between a score of 25 (full movement against gravity but weaker than the other side) or 33 (normal power). A standardized protocol was developed and followed to further increase reliability (Appendix 35).

Table 6.3 Lower extremity weighted scores for muscle strength using the Motricity Index, compared to MRC unweighted scores

Quality of muscle contraction	Motricity Index score	MRC grade
No movement	0	0
Palpable contraction in muscle, but no movement	9	1
Visible movement, but not full range against gravity	14	2
Full range of movement against gravity, but not against resistance	19	3
Full movement against gravity, but weaker than the other side	25	4
Normal power	33	5

(Demeurisse et al., 1980)

6.5 Assessment of lower limb function and balance

6.5.1 Pressure under the feet during stance phase of walking

Force-time integral and centre of force velocity (COFV) in AP direction, including centre of force trajectory were measured via pressure insoles, using the F-Scan system developed by Tekscan,[9] which collects interval data relating to the vertical ground reaction force.

The Tekscan F-Scan pressure assessment system uses thin resistive sensors that can be inserted into the shoe (figure 6.8) and records ongoing plantar forces during gait. Each sensor has 960 separate pressure sensing cells arranged in rows and columns. The top and bottom layers of the sensor are 0.02mm thick and made of a sheet of polyester, which is laminated (0.076mm) to aid handling of the sensor. Pressure insole systems can be portable (MacWilliams and Armstrong, 2000), flexible, and are worn in the shoe; they measure the contact between the foot and the inside of the shoe (Razak et al., 2012), and can provide detail relating to abnormal biomechanics within the foot (MacWilliams and Armstrong, 2000).

The only contact between the body and the floor surface when walking independently is via the plantar surface of the feet (Ofek et al., 2018; Razak et al., 2012), and measuring the pressure or force under the feet can give an indication of how well the feet are making contact with the floor. The ground reaction force is

[9] https://www.tekscan.com/products-solutions/systems/f-scan-system

equal in size but in the opposite direction to the force created by the weight-bearing limb, and can be discussed as a vector with both magnitude and direction (Perry and Burnfield, 2010). The combined COP_{net} of both feet is situated at the site of the ground reaction vector (Winter, 1995). The ground reaction force waveforms during gait correlate with the COP_{net} (Winter, 1995).

6.5.1.1 Reliability and validity

Foot Scan pressure insole systems have been found to provide reliable force and pressure data (ICC > 0.75) (Low and Dixon, 2010), and have been advocated as a suitable method for measuring ground reaction forces, as the COP movement over time will correlate with the ground force reaction vector (Winter, 1995). However, this conclusion was drawn from analyzing Pedar® insoles which contain 85-99 capacitive sensors, whereas, Tekscan F-Scan insoles work with resistive sensors (Koch et al., 2016). Nevertheless, a study that compared a Parotec insole (which has 24 separate resistive sensors, which is the same type as the Tekscan F-scan system) data to a force plate, also found a very strong degree of association when measuring COP in an AP direction, with Pearson's correlation coefficients greater than 0.90 for 67/67 trials (100%) (Chesnin et al., 2000).

A validated method involving inverse dynamics to calculate the complete ground reaction force components from the vertical ground reaction force (both force and moment) from the motion data measured with pressure insoles has been developed (Forner Cordero et al., 2004). This method was used by Fong et al.

(2008) to explore the correlation of pressure insole readings with force plate data; excellent levels of correlation in an AP direction (correlation coefficient=0.928) and vertical direction (correlation coefficient=0.989) were established, and moderate correlation in a medial-lateral direction (r=0.719) (Fong et al., 2008).

Although early studies challenged the validity and reliability of the Tekscan F-Scan in-shoe system (McPoil and Cornwall, 2006), the system has been subjected to rigorous assessment by Giacomozzi (2010) including a whole-surface static pressure test, local static pressure tests (5 areas), sinusoidal test (5 areas) to measure hysteresis, creep (5 areas) and COP estimation (5 areas). The Tekscan unit demonstrated high linearity (R^2=0.995), moderate spatial variability, low creep, low hysteresis, high correlation with sinusoidal loading, as well as good accuracy and precision of the COP estimations. The benefit of an in-shoe system is that there is continuous collection of data with every step taken (MacWilliams and Armstrong, 2000).

6.5.1.2 Recording results

When deciding what pressure insole measurements to record, informal discussions took place with some stroke survivors/service users, regarding their concerns in relation to their walking pattern and asymmetry of gait; therefore, a decision was made to record the force-time integral (FTI) (which takes into account the length of time spent on the hemiparetic foot as well as the force through the plantar surface), and the centre of force velocity (COFV) in an AP direction (to give

an indication of how well participants transferred their weight forwards over their affected leg).

Figure 6.8

Set up for MoTaStim-Foot trial: Tekscan F-Scan™ pressure insoles and photo of pressure insole which was cut down to size and placed in the shoe. Electrogoniometer is also shown insitu

6.5.1.3 Testing procedure

Pressure insole readings were undertaken during a timed 5MWT. Calibration of the insoles prior to each measurement being undertaken was built into the protocol for the pressure insole assessments. This involved doing a step calibration, which required participants to stand on one leg for up to two seconds, and then change to stand on the other leg. On commencement of the study, it was anticipated that this would not be possible for the participants to do, so it was written into the protocol that a researcher of a similar weight could calibrate the insoles for the participants if required, as recommended by a representative from Tekscan, the company who made the insoles.

6.5.2 Walking speed 5-metre walk test (5MWT)

Walking speed gives an indication of the overall walking ability of stroke survivors (Olney et al., 2006). A 5MWT was used to assess walking speed (seconds), producing ratio level data for analysis, and meaningful results of gait speed that can be compared to published gait speeds post-stroke (Salbach et al., 2001).

6.5.2.1 Reliability and responsiveness

The 5MWT has been found to be reliable for use with stroke survivors (Collen et al., 1990). The 5MWT has been recommended as the most appropriate OM for both researchers and clinicians to select when measuring a change in walking ability post-stroke, when compared to the 10MWT, Stroke Rehabilitation Assessment of Movement, BBS, Barthel Index and the TUG (Salbach et al., 2001).

When the standardized response mean and 95% CIs were analysed the 5MWT was shown to have the best responsiveness at 1.22 (.93–1.50) at a comfortable pace and 1.00 (.68–1.30) at a maximum pace; this compared to .92 (.64–1.18) and .83 (.52–1.12) for the 10MWT. Although the 10MWT has also been shown to be reliable (Wade et al., 1987), the 5MWT was selected because many of the assessments were to be undertaken in the community and therefore it was felt the 5MWT would be more practical.

6.5.2.2 Testing procedure

A 5-metre distance was marked out on the floor and participants were asked to walk at a self-selected speed, as fast as they could walk comfortably and safely; the time to walk 5-metres was recorded by using the timer on an iPhone. At the point when the first foot crossed the 5-metre line, the timer was stopped. In addition to quantifying variables such as walking speed for the 5MWT, an observational analysis of the quality of gait was undertaken and whether walking aids or support were required was noted, as is common practice in therapy rehabilitation; the 5MWT was videoed using a web-cam, attached to a computer. It is acknowledged that using an aid to walk could influence the validity of the results; it was possible that someone could walk faster with an aid or assistance at baseline than they did at the end of intervention if they were walking independently. However, this does reflect clinical practice, with stroke survivors altering their need for use of an aid or assistance as they progress.

6.5.3 Modified Rivermead Mobility Index

The mRMI (Lennon and Johnson, 2000) was developed from the Rivermead Mobility Index (Collen et al., 1991), It involves eight tasks:

1. Turning over in lying
2. Lying to sitting
3. Sitting balance
4. Sitting to standing
5. Standing
6. Transfers from plinth/bed to chair
7. Walking indoors
8. Stairs

A stopwatch, tape measure, chair and access to a bed (at a height of 45 cm) and a flight of stairs, are required. Participants are requested to perform each item as independently as possible with both sides assessed, towards the ipsilesional side first (when rolling or transferring), with the score towards the contralesional side reported separately. A limitation of this measure is that the exact number of stairs is not specified.

Ordinal data are produced, with a rating given relating to the amount of assistance the person required, either physical assistance from the assessor or from an aid e.g. pulling on the edge of the bed when rolling. The total score possible is 40

points, with each item allocated a potential five points from 0 (unable to perform) to 5 (independent).

6.5.3.1 Validity and reliability

The mRMI is valid (face and content validity established via a consensus exercise), reliable in a population of stroke survivors (Intraclass correlation co-efficient (ICC) was calculated to explore inter-rater reliability and found to be excellent = 0.98; $p<0.001$), and responsive (effect size = 1.15) as a measure of mobility in the early stages of stroke rehabilitation; the degree of measurement error was found to be 4.46 using an ANOVA to calculate the variance within the patients (Lennon and Johnson, 2000). Use of effect sizes to indicate responsiveness of a clinical measure has been advocated by Kazis et al. (1989), and an understanding of the measurement error is important when calculating the minimal clinically important difference (Rai et al., 2015).

The mRMI was selected for use within MoTaStim-Foot because of its psychometric properties and the fact it is relatively quick to complete (10–15 minutes), a valid tool for assessing mobility following a stroke, and good reliability can be established with minimal experience (Lennon and Johnson, 2000).

6.5.3.2 Testing procedures

For full details and instructions regarding the mRMI assessment see Appendix 36. Training was provided to all assessors to ensure a standardized approach; any

uncertainties were addressed by discussions within the team until a consensus relating to the correct scoring was reached.

6.6 Focus groups

All participants from both arms of the trial were invited to an FG, on completion of the intervention and all follow-up OMs The purpose of the FGs was to provide an insight into the participants' individual trial experiences (Krueger and Casey, 2000). All participants were approached using a personalized telephone call (Krueger and Casey, 2000), and this was followed up with a letter addressed to the individual concerned, with details of the FG they were invited to attend (Appendix 37). Two FGs, aiming for a sample of 6–8 participants in each group, which has been suggested as being an ideal size to promote discussion in a FG (Krueger and Casey, 2000), were conducted for each arm of the trial.

An FG interview schedule, with open-ended questions (Kitzinger, 1995), for both the MTS + TSGT group (Appendix 38) and the TI + TSGT group (Appendix 39, was developed in advance by the researcher and members of the supervisory team, with input from PPIE advisors. The interview schedules were developed with a researcher who was not a physiotherapist to further reduce the chance of data collection bias (Carter et al., 2014), and decreasing the influence of the researcher's personal beliefs (Smith and Noble, 2014). Objectives 3d and 3f of the feasibility study were: to explore participants' experiences of the interventions and the battery of OMs, and their views on the acceptability of the treatments and

method of delivery as interventions for a future study, and to explore perceived responses to the interventions over time. Open-ended questions were used to facilitate a greater understanding of the participants' experiences, enabling the participants to take a lead with the information shared (Krueger and Casey, 2000). Specific topics relating to the acceptability of the interventions and the OMs, and perceived changes in the leg or in lower-limb functions of standing, balancing and walking following intervention were explored.

The FGs were moderated by the researcher (AA) actively participating in the research process and facilitating discussion (Morgan, 1996); an independent PPIE volunteer took field notes during the discussions, noting any relevant interactions between group members. The final question of the FG asked participants to summarize in one word, or one sentence, their opinion on being involved within the trial, enabling reflection upon this important aspect, as suggested by Krueger and Casey (2000). The moderator (AA) summarized the discussions at the end of the group (with assistance from the PPIE advisor) and sought validation of her understanding of the issues from the participants (Krueger and Casey, 2000).

All the FGs were audio-taped with consent from participants, and transcribed verbatim, with analysis occurring as the study progressed, ensuring each FG was listened to, transcribed and analysed prior to the next FG specific to either MTS or TIs, so that any emerging ideas could be included in subsequent discussions if required (Kisely and Kendall, 2011).

Debrief meetings were held involving the PPIE volunteers, supervisor and the group facilitator (AA) after each FG; this enabled discussion relating to the main topic areas and emergent themes (Boysen et al., 2016), and identification of missing topic areas (McMahon and Winch, 2018), that should be considered for exploration in future FGs. Another purpose of the debriefing involves evaluation of the moderator's role and consideration of researcher reflexivity increasing the trustworthiness of the data (McMahon and Winch, 2018). The researcher's assumptions prior to undertaking the FGs were considered (Appendix 40). Bracketing of these ideas and thoughts continued throughout the data collection and analysis phases, as recommended by Fischer (2009). Another purpose of the debriefing meetings was to offer psychological support in case of unpredictable emotional response (Copeland and Liska, 2016); this was important because the PPIE volunteers may have been affected by comments made within the FG.

6.7 Interventions

Research therapists delivered all the interventions, MTS and TSGT, as well as encouraging the participants in the TI group to wear their insoles. A log was kept detailing, for each participant, which therapist delivered the treatment. Standardization of treatment intervention delivery was facilitated by the development of the standardized protocols, which were followed by all the research therapists.

6.7.1 Mobilization and Tactile Stimulation (MTS) for the lower limb

Each participant in the MTS group received 30–60 minutes of standardized MTS treatment to the lower limb, described fully in Study 2, to prepare the sensorimotor system prior to TSGT. The actual treatment techniques delivered were recorded by ticking boxes on the MTS treatment schedule (figure 5.5, section 5.3.14). In view of the heterogeneity of stroke and specific needs of the participants, treatment was individualized for each participant. The specific content of each treatment session was adapted according to need, e.g. to address foot hypersensitivity, and to take into account the tolerance of each technique.

Research therapists (experienced Chartered Physiotherapists, NHS Bands 6 and 7 equivalent) selected and delivered appropriate combinations of pertinent techniques from the MTS treatment schedule for each session. It was not necessary, or appropriate, to include all the techniques in the schedule; selections and combinations were based upon the clinical decisions of the research therapists delivering the treatment. MTS was delivered with no medium, such as aqueous cream, whenever possible (except for example, if the participant's skin was particularly dry and fragile), to ensure there was maximum stimulation of the cutaneous mechanoreceptors.

The research therapists were all trained in delivering MTS, to ensure they were delivering the interventions to protocol. To assess fidelity to protocol, the research therapists were observed by a research supervisor (SH) at various points in the

research trial to ensure they were complying with working to protocol. A report relating to these observations is provided in Appendix 41.

6.7.2 Wearing the textured insole (TI)

Participants were encouraged to wear the insoles daily, with one TI in the contralesional shoe, and a smooth insole in the ipsilesional shoe (details of insoles are reported in section 5.3.4, chapter five). Advice was given to the participants that they should gradually build up the time wearing the insoles; however, they had the autonomy to choose how long they wore the insoles each day during the 4–6-week period of intervention, apart from when the outcomes were assessed. This was in accordance with the TI wearing protocol developed in Study 2 (chapter five), provided in section 5.3.4. The insoles were individually made, participant-specific, and cut to size to fit in the participant's shoes. The purpose of the TI was to 'augment' the sensorimotor system by providing sensory feedback from the plantar surface of the contralesional foot. The duration of wearing the insoles was recorded by the participant in the daily diary (Appendix 32).

6.7.3 Task-specific gait training (TSGT)

Thirty minutes of TSGT was delivered to both groups, either immediately following 30–60 minutes of MTS treatment (MTS group), or whilst the participants wore TIs (TI group). The specific content of each gait training session was documented using the comprehensive list of interventions identified in Study 2, the intervention modelling study, described in the TSGT protocol (chapter five, section 5.3.8).

6.8 Observer-blinding of outcome assessment

Research therapists were employed specifically and suitably trained as blinded assessors for the MoTaStim-Foot trial, undertaking a battery of OMs with participants. These therapists had experience of working in the NHS, in a relevant field. Research therapists or the blinded assessor undertook the baseline assessments, prior to randomization. However, all OMs in which observer bias could occur (the FAC, LEMI, sensory threshold testing with SWMs and the mRMI) were undertaken by assessors who were blinded to treatment group allocation. Measures were employed to enhance blinding, for example, all participants within the trial were given a pair of TIs (even if they were in the MTS group), so a chance observation of insoles in the home would not unblind the assessor. Also, participants were asked not to disclose to the blinded assessor which group they were in, and the case report forms were hidden from the blinded assessor. At the one-month follow-up, the blinded assessor was asked to indicate to which group they thought the participant had been allocated; this allowed for assessment of the success of the observer blinding procedure.

6.9 Statistical analysis of quantitative data

All data from the trial were entered into the database and checked systematically for accuracy by two independent researchers. Baseline characteristics were summarized according to the intervention group. Count variables were presented as frequencies and proportions, ordinal variables as medians and interquartile ranges, and numerical variables as means and SDs (or medians and interquartile

ranges, if data were skewed). When analyzing the results of the pressure insole readings, a blinded assessor selected the representative steps to analyse (according to clearly defined criteria) from the force-time curve on the Tekscan (pressure insole) software.

As this was a feasibility study, no formal hypothesis testing was undertaken. Instead, point estimates, with 95% CIs for within-group changes (using medians and interquartile ranges), were calculated for key OMs (where appropriate). The variance of scores for OMs was calculated, providing information for the sample size calculation for a subsequent main trial. The distribution of outcome variables was also assessed, to further inform the sample size calculation and guide the choice of analysis in the main study. The number of eligible patients recruited, and the proportion of those recruited who were lost to follow-up at one-month were also calculated.

Research objective 3d (sections 4.4 and 6.1) also included informing the choice of primary and secondary OMs in readiness for a future trial. In order to facilitate these choices, such aspects as clinical relevance, validity, reliability, floor and ceiling effects, as well as acceptability were explored. It was not the purpose of the study to consider the effectiveness of the interventions, and therefore no between-group analysis was undertaken. However, to inform the choice of primary and secondary OMs for the potential subsequent study (objective 3f), some within-group analysis was undertaken to indicate the responsiveness of the OMs and

potential efficacy of the interventions, and to identify any issues relating to floor or ceiling effects with the OMs. Medians and IQRs were produced through IBM SPSS statistics, version 24 and CIs were generated through the Confidence Interval Analysis (CIA) program (Gardner et al., 1991).

To fulfil objective 3g of the feasibility study (sections 4.4 and 6.1), relating to responses to the interventions over time, within-group analysis was undertaken exploring changes from baseline to end of intervention, from baseline to one-month follow-up, and also from end of intervention to one-month follow-up. Differences between the medians and 95% CIs were calculated; these were approximate CIs, because the programme used to calculate non-parametric CIs does not always produce CIs at the exact confidence level specified.

Consideration was given to analysing the extent of clustering of observations by each therapist, using an intra-cluster correlation coefficient to assess the extent to which outcomes are correlated (clustered) within therapists. This analysis would have given greater insight into whether specific experience in neurological skills or a particular personality had an influence upon the outcomes within the trial. However, as the research therapists were all part-time and, on many occasions, more than one therapist was involved in delivering each participant's interventions, this analysis was deemed to be neither possible nor appropriate. Moreover, the sample size would have given extremely imprecise estimates of the intra-cluster correlation.

A detailed statistical analysis plan was drawn up prior to beginning data analysis (Appendix 42).

6.10 Collection and analysis of qualitative data

Daily diaries were collected weekly from the participants, comments were extracted, and subjected to thematic analysis, with consideration given to whether they were appropriate to address the objectives of the trial; the data from the daily diaries was also presented in two word-clouds (one for each of the intervention groups) giving a visual insight into the main aspects discussed in the diaries.

The analysis of the diaries was mainly a content analysis (Krippendorff, 2013). However, inductive thematic analysis was utilized for the daily diaries comments and also the FGs; coding was data-driven without consideration of how the ideas developed may fit with pre-existing theory or the researcher's pre-conceptions (Braun and Clarke, 2006). The researcher played an active role in generating the themes (Richards and Hemphill, 2018).

The primary purpose of the analysis was to explore the feasibility of the interventions and OMs and understand participants' experiences on the MoTaStim-Foot trial. *A priori* topics relating to the interventions and participation within the study, as well as changes in functional ability, were developed, which informed the FG schedules (Appendix 43), ensuring pertinent issues were discussed. Therefore, there was an element of theoretical analysis driven from the

researcher's analytical curiosity (Braun and Clarke, 2006) relating to the possible changes that may occur when somatosensory stimulation is delivered.

Braun and Clarke's (2006) six-stage process for thematic analysis of qualitative data was followed:

Step 1: Familiarisation with the data

Step 2: Generation of initial codes

Step 3: Searching for themes

Step 4: Reviewing themes

Step 5: Defining and naming themes

Step 6: Production of the final report

However, other resources and methods were utilized too. Once initial coding for the FGs had taken place, the management of the data was facilitated using NVivo qualitative data analysis (Software QSR International Pty Ltd. Version 11, 2016), which is useful to assist coding processes and aid retrieval of pertinent information (Woods et al., 2016). Organisation and familiarisation of data and the codes that were produced were also enhanced by the process of using the one sheet of paper method (Ziebland and McPherson, 2006). Examples with and without quotations are available (Appendix 44).

Qualitative data collected from both the FGs and diaries were subjected to a thematic analysis. Thematic analysis is a flexible, valuable research tool, not aligned with a particular epistemological or theoretical perspective, but appropriate to elicit richness residing in the data (Braun and Clarke, 2006), putting aspects into context and discovering meaning behind individual conditions and circumstances (Maguire and Delahunt, 2017). The thematic analysis was principally inductive, primarily at a semantic level, identifying explicit meanings from the data based on the participants' responses (Braun and Clarke, 2006). However, some aspects relating to life before and after involvement in the trial were explored. There was, therefore, further analysis at a latent level, considering ideas and assumptions at a deeper level (Braun and Clarke, 2006). Nevertheless, the purpose of the study was not to develop understanding behind what it meant to the participants to have a stroke or discover detail about any differences in their quality of life.

6.10.1 Coding

The researcher (AA) coded the data in the transcripts and subsequently discussed codes, themes and sub-themes with two other members of the research team (SH and SR), who had also reviewed and analysed the transcripts independently, identifying preliminary themes for discussion with the researcher.

6.10.2 Identifying themes

Provisional themes for the qualitative data were shared and discussed in a group consisting of supervisors and an independent PPIE representative (PB), who had

also read the four FG transcripts, enabling development and progression or maturation of themes. Any differences of opinions were highlighted and discussed; the researchers and PPIE advisor collectively looked for conceptual relationships within and across the FGs, and final themes were identified. A table of themes from the daily diary comments (table 6.7) and the final themes from the FGs were produced (table 6.9). An audit trail was kept of how the themes were developed and matured (Appendix 45), enhancing transparency (Richards and Hemphill, 2018).

6.11 Data collection

6.11.1 Data management

All data were collected and stored in accordance with the Data Protection Acts, 1998 and 2018 (Legislation.gov.uk, 1998; 2018). Data that could identify individuals were stored separately from anonymous data and the linking information was accessed only by members of the research team on a need to know basis. All data by which individuals may be identified were kept in a lockable storage facility within the research offices. Any electronic data by which individuals could be identified were placed in a password protected secure space on hard drives. Personal names and information were not transferred via email. Use of personal addresses, postcodes, faxes, emails or telephone numbers was restricted to the minimum number of people necessary to ensure the efficient and safe running of the trial. Participant numbers were used to anonymize data.

On transcription of the FG information, pseudonyms were used to maintain anonymity, prior to being stored on password protected computer or laptop. Faces were blanked out on the 5MWT videos for dissemination and the videos were stored on a password protected computer. In writing up the findings of the study, all direct quotations were anonymous, and no individual is identifiable.

Research therapists were appropriately trained in issues relating to confidentiality of personal data as part of their induction on commencement of their post. Only anonymous data (by means of issuing each participant a unique trial number) was shared with other organisations. All data will be stored securely for ten years after the end of study declaration, in line with Keele University policy.

6.12 Adverse events and reactions

Adverse reactions of pain and fatigue were of clinical interest in informing the results of the trial and the acceptability of the interventions (research objective 3d). There was a small possibility that either the MTS or TSGT could be associated with an overuse syndrome as expressed by a participant's experience of pain or fatigue. Fatigue was accounted for as it would normally be in usual therapy rehabilitation and both pain and fatigue were monitored throughout the intervention period by the research therapist. Monitoring of pain and fatigue by using standardized OMs such as the Short Form 36 Health Survey Questionnaire (SF-36) (Brazier et al., 1992) and the Functional Assessment of Chronic Illness

Therapy Fatigue Scale (FACIT-F) (Tennant, 2019) was considered; however, the practicalities of completing these (approximately ten minutes each) with participants, almost daily, meant this was not feasible. Therefore, a pragmatic decision was made to monitor pain verbally (by asking the participant) and visually (by observing participants' behaviours), and to monitor fatigue by assessment of strength using the LEMI. The method used successfully in other trials, for example the FAST INdiCATE trial (Hunter et al., 2018) was, therefore, followed.

Participants were observed for signs of pain at every visit and a record of the response noted. The LEMI was undertaken prior to delivery of the interventions to monitor for any potential fatigue (Appendix 35). The motricity index has been shown to be an important predictor of fatigue (p=0.01) (Kim et al., 2012) and has been used successfully in other studies too (Hunter et al., 2018) and therefore was deemed to be an appropriate measure to use for this purpose. Fatigue was considered to be an adverse reaction if (i) a participant demonstrated a decrease of two levels in the LEMI score on four consecutive therapy sessions and (ii) the therapist and clinical team were unable to account for this in any other way than involvement in this trial. Murphy and Niemiec, (2014) report fatigability as the degree of fatigue experienced during activities and suggest modification of activities or adaptation of daily routines using pacing strategies. Alternatively, acute fatigue may be improved by resting (Egerton, 2013). In the event of a participant reporting pain or fatigue, the therapist would adjust the therapy as appropriate or, if indicated, stop the interventions on either a permanent or a

temporary basis. In the event of fatigue, rest periods were increased, or the number of prescribed exercises and length of treatment reduced as required.

Pain was considered to be an adverse reaction if: (i) a participant reported the onset or increase of paretic lower limb pain (verbally or behaviourally); (ii) the pain was sustained over four consecutive therapy sessions; and (iii) the research therapist and clinical team were unable to account for this in any other way than involvement in this trial. If required this would be addressed by the research therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction would be recorded as the date of the fourth consecutive therapy session after pain or fatigue was first noted. Pain and fatigue were recorded on a case report form within the MoTaStim-Foot feasibility study (Appendix 46).

6.13 Trial management

The trial team was led by the Chief Investigator (AA). A trial protocol (Appendix 25), Standard Operating Procedures, intervention protocols and case report forms were developed prior to commencing the trial, approved by the Norwich CTU.

6.13.1 Trial management group

A trial management group was set up, chaired by the Chief Investigator (AA), to assist with developing the design, co-ordination and strategic management of the

trial. The membership, frequency of meetings, activity (including trial conduct and data review) and authority were explicit within the trial management group terms of reference (Appendix 47). The trial management group consisted of: the Chief Investigator (AA); the researcher's supervisory team, who have experience in clinical trials with stroke participants, qualitative and quantitative research methods, and statistics; a consultant stroke physician with experience in running clinical trials; the senior clinician (physiotherapist) working on the ward where recruitment of some of the participants took place; the senior clinical trials operations manager from the CTU involved with the study; and a PPIE representative (PB). The research delivery manager at the study recruitment site was also invited to be part of the trial management team because she would be able to advise on the day to day management of the trial. Since this was a small-scale feasibility study, a decision was made that a trial steering committee and data monitoring committee were not required. The responsibilities of a trial steering committee and data monitoring committee were undertaken by the members of the trial management group.

6.13.2 Research therapists

Two part-time research therapists were employed over a fifteen-month period at a Band six level (15 and 14 hours per week), one of whom had extensive neurological experience and the other who had primarily a musculoskeletal background. The costings for these two research therapists were based upon one full-time therapist for 12 months; however, in view of anticipated issues relating to

recruitment, it was decided to employ the therapists over a longer period. Having two part-time therapists added to the flexibility within the trial, giving greater ability to cover annual and sick leave. For the last two months of the trial, an additional research therapist was employed at a Band six level, on a casual basis, completing a total of 46 additional hours to ensure the participants could complete all the interventions.

A researcher assessor, who was an HCPC registered occupational therapist, was employed at Band 5, for six hours per week, over an eighteen-month period, to undertake the observer-blind assessments. A further blinded researcher assessor (Chartered Physiotherapist) was trained and involved on an occasional basis to cover annual leave of the research assessor.

All members of the trial team completed GCP training. All research therapists and the research assessor were appropriately trained by relevant members of the trial team (AA, SH), to ensure that they were competent prior to undertaking interventions and assessments.

6.14 Results of study 3

All the feasibility study objectives were successfully achieved and detailed in the following sections.

6.14.1 Objective 3a, relating to recruitment and flow of participants

The information relating to recruitment and attrition is summarized in the CONSORT diagram (figure 6.9).

In total, 70 stroke patients were assessed for eligibility over 18 months, of whom 5 (7.14%) were not interested in the trial and declined an approach by the research team; 15 people (21.43%) declined to participate after reading the PIS. A further eight people did not meet the inclusion criteria (inappropriate diagnosis n=3; not 42-112 post-stroke n=2; medically unstable n=1; out of area n= 2). The remaining 42 (71.43%) provided informed consent and undertook the post-consent screening process. Seven of these (16.67%) were subsequently found to be ineligible to participate; three had skin lesions, three failed the step test, and one was experiencing heart failure. One participant withdrew before completing the baseline assessment.

A total of 34 participants (48.57% of those screened) were, therefore, randomized to one of the two interventions, demonstrating a successful recruitment strategy. Following randomization, the group sizes were not completely equal, with 19

people randomized to the MTS+TSGT (MTS) group and 15 to the TI+TSGT (TI) group.

6.14.2 Objective 3b, relating to attrition

The attrition rate was 5.88% at both end of intervention and one-month follow-up, due to two participants being withdrawn from the TI group; one participant received a botulinum toxin injection to his contralesional lower limb prior to completing the first treatment session, the other developed a problem with the ipsilesional foot (as opposed to the contralesional foot, which was the one in contact with the TI).

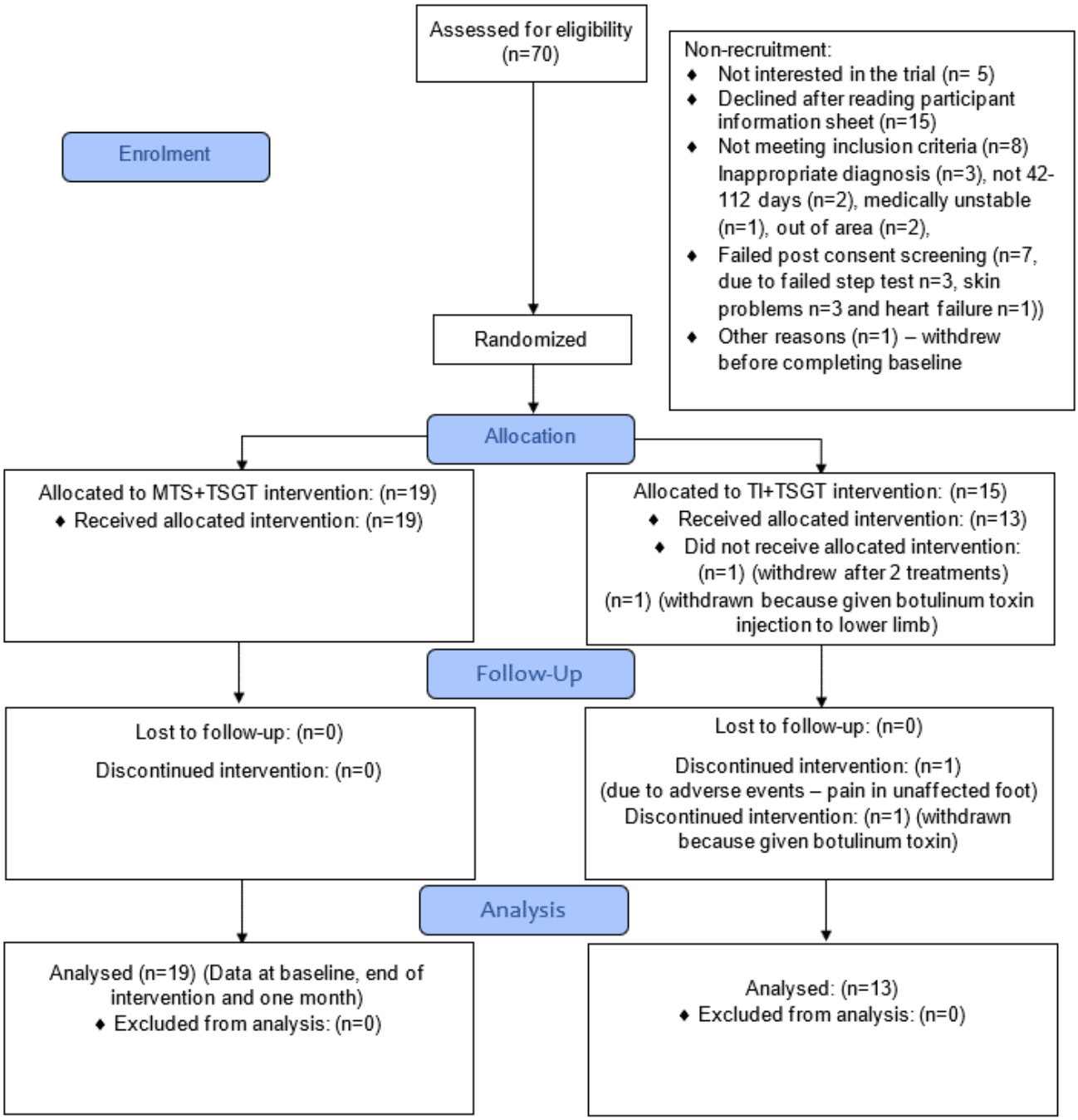


Figure 6.9 CONSORT diagram for the MoTaStim-Foot feasibility study

6.14.2.1 Baseline characteristics of participants (Objective 3h)

The baseline characteristics for the groups are presented in table 6.4. The mean (SD) age for the two groups was similar (MTS: 73.84 (14.09) years; TI: 72.40 (9.79) years), the proportion of males to females was slightly different in each group with 47% males in the MTS and 60% males in the TI group. This imbalance could be accounted for by the small sample size. There were slightly more ischaemic strokes in the MTS group (89.47%) than the TI group (80%); however, the mean (SD) number of days post-stroke was comparable for both groups, at 58.5 (18.13) and 54.64 (12.46) days, respectively. To give an indication of the level of functioning prior to the stroke, the percentage of people able to walk over one mile prior to the stroke is also presented in table 6.4, with a slightly higher level noted for the TI group (73.33%), compared to the MTS group (68.42%). The NIHSS results for the two groups were similar with a median of six in the MTS group and five in the TI group and are presented in figure 6.10. Interquartile-range (IQR) is also presented. There was, an even spread across the groups in relation to speech and language difficulties, with three participants affected in the MTS group and two in the TI group.

Table 6.4 Participant characteristics and demographics at baseline

		MTS (n=19)	TI (n=15)	All (n=34)
Age (years)	Mean (SD)	73.84 (14.09)	72.40 (9.79)	73.21 (12.23)
Sex	Male (%) Female (%) (M: F)	47.4 52.6 (9:10)	60 40 (9:6)	52.9 47.1 (18:16)
Type of stroke	Ischaemic (%) Haemorrhagic (%)	89.5 10.53	80 20.00	85.3 14.71
Side of brain	Left (%) Right (%) (L: R)	57.9 42.11 (9:10)	60 40.00 (6:9)	58.8 41.18 (15:19)
Days after stroke	Mean (SD) Range	59.47 (18.12) 43–106	53.87 (12.38) 43–95	57 (15.88) 43–106
Walking prior to stroke	% able to walk more than 1 mile prior to stroke	68.4	73.3	70.57
NIHSS	Median (IQR) Range	6.00 (4.00, 7.25) 1–11	5.00 (4.00, 7.00) 3–16	5.00 (4.00, 7.00) 1–16

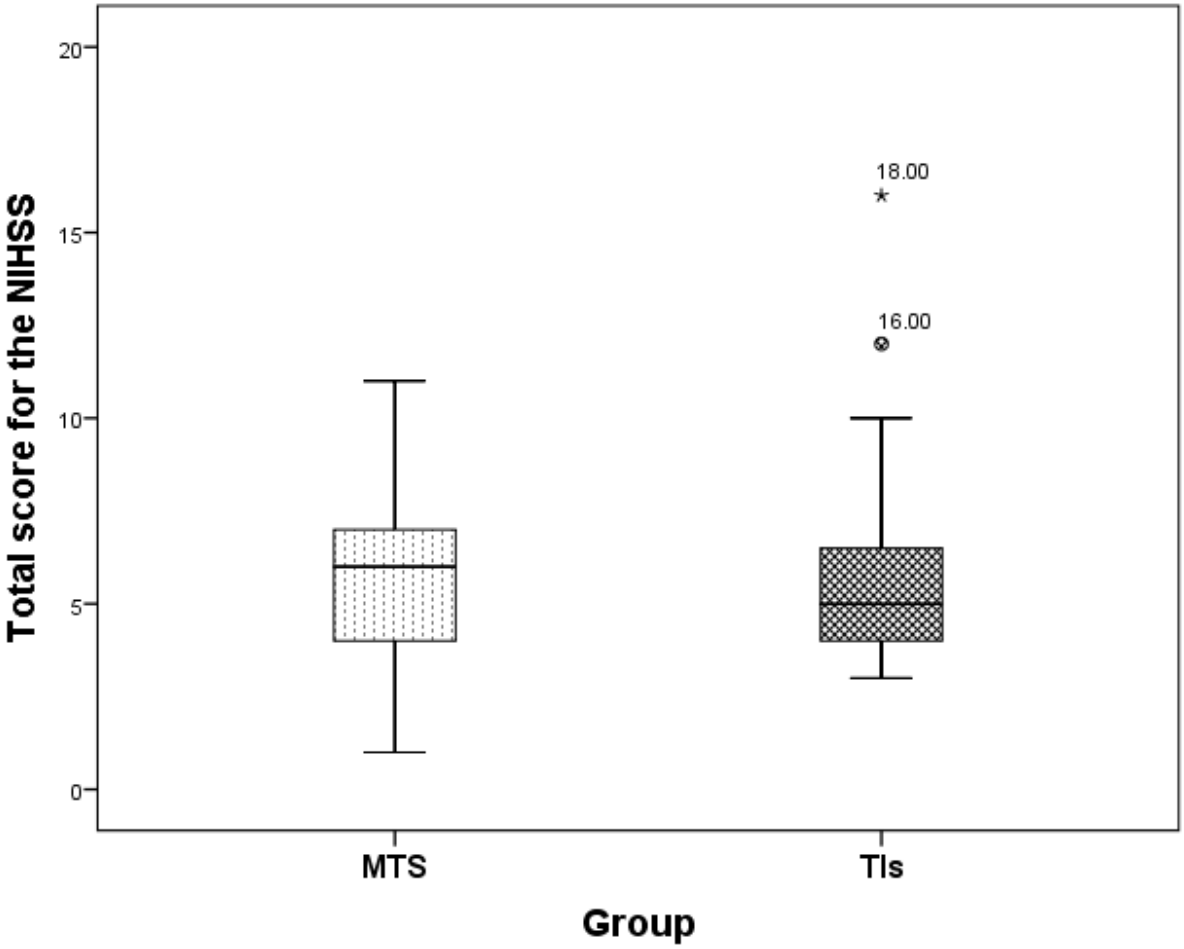


Figure 6.10 Boxplot of NIHSS results for both groups

6.14.3 Objective 3d, relating to acceptability of the interventions

6.14.3.1 Serious adverse events, adverse events and adverse reactions

This type of therapy intervention trial is considered low risk for adverse events and reactions. Within this feasibility study, there were no adverse reactions to report, indicating that no participant reported pain or fatigue related to the trial interventions or a reaction to the TIs.

There were three serious adverse events, which were all reported to the Norwich CTU/Research and the Research Governance Department at Keele University. None of these were related to participation in the trial: one participant suffered a further stroke, between completion of all the interventions and OMs and the FG; another had a fall and attended the Accident and Emergency department although, after one week, was able to resume interventions; and a third was admitted overnight to hospital with a suspected chest infection and after a short break of a few days continued in the trial.

In addition, there were twenty-seven adverse events documented (Appendix 48), 14 of which were reported from participants in the MTS group and 13 from the TI group. These consisted of: falls n=16; neck pain n=1; back pain n=2; heel pain (ipsilesional side) n=1; viral infection n=1; atrial fibrillation n=1; pressure sore n=1; scratch on dorsum of foot n=1; and a report of feeling tired with swollen painful ankles n=1, urinary tract infection n=1, hip and knee pain n=1. These were all

discussed with an independent assessor to ensure they were not considered to be related to the trial.

6.14.3.2 Delivery of trial interventions

All of the participants in both of the groups (except for the two who were withdrawn from the TI group) received all twenty sessions and it was clearly demonstrated that it was possible to deliver the interventions and OMs.

6.15 Analysis of the daily diary sheets (Objectives 3d, 3e and 3f)

All of the participants completed the daily diary sheets either independently or with support from a family member – or with assistance from the research therapist, if required, to just document the participant's comments or ticks in the relevant sections. Only one participant attempted to use the audio diary method; however, they struggled with this and changed to using the paper diaries.

There was inconsistency between the participants regarding the number of comments written on the diary sheets (17/19 in the MTS group, and 10/14 of the TI group made comments). The section relating to whether the foot felt sensitive or not could have been interpreted in different ways and is therefore not reported in detail here but will be debated in chapter seven, the discussion section. The number of participants ticking each of the sections is reported in table 6.5 for the MTS group, and table 6.6 for the TI group. In general, the interventions were well tolerated over the main six-week intervention period. As participants were able to place a tick in each box daily (seven days a week for the duration of the intervention), a range of responses to each section was possible. The weekly average number of ticks was calculated for each section.

6.15.1 Comfort of the MTS

The box titled MTS was *not* uncomfortable was 'ticked' by most participants (range 79.0%–94.7%) and when there was discomfort this was reported generally as not lasting a long time (figure 6.11). Only one participant ticked the 'discomfort lasted a

long-time section'; this participant was suffering from chronic neuropathic pain following his stroke, this aspect will be discussed in chapter seven.

Table 6.5 Number of participants for each aspect ticked on the MTS diary sheets

Aspect	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Foot feels cold	3	8	4	2	3	3
Foot feels warm	16	18	18	17	18	7
Foot feels sensitive	12	13	11	9	6	5
Foot does not feel sensitive	9	13	13	10	11	4
There is no change in the foot	5	9	7	11	7	4
Unable to feel as much	1	2	2	1	0	0
Can feel more	15	16	13	11	14	3
MTS was uncomfortable	8 (42.11%)	7 (36.84%)	6 (31.58%)	6 (31.58%)	3 (15.79%)	4 (21.05%)
Discomfort lasted long time	0	0	0	1	1	1
Discomfort did not last long	6	6	6	6	2	4
MTS was not uncomfortable	15 (78.95%)	18 (94.74%)	17 (89.47%)	15 (78.95%)	16 (84.21%)	8 (88.89%)
TSGT was uncomfortable	3	5	3	3	2	2
TSGT was not uncomfortable	18	17	18	19	19	9
Outcome measurements were uncomfortable	0	0	0	0	0	0
Outcome measurements were not uncomfortable	0	6	10	7	3	0

* There were 19 participants in the MTS group. One participant completed the interventions within four weeks, nine in five weeks,15 in six weeks, 18 in seven weeks. Due to adverse events and the Christmas period one participant took nine weeks to complete the interventions. Just the results of the first six weeks are presented because this is when the majority of the participants completed the interventions. NB By week six 10 participants had already completed the 20 interventions so the results for that week are based upon just nine participants.

Table 6.6 Number of participants for each aspect ticked on the TI group diary sheets

Aspect	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Foot feels cold	4	2	3	1	2	1
Foot feels warm	13	12	11	10	9	6
Foot feels sensitive	4	2	3	2	1	1
Foot does not feel sensitive	12	12	9	6	6	3
There is no change in the foot	12	7	8	7	8	4
Unable to feel as much	1	1	0	0	1	0
Can feel more	7	6	6	6	3	4
Not worn the TIs	1	3	1	2	1	1
Worn TIs less than 1 hour	5	3	2	1	2	1
Worn TIs 2-4 hours	3	6	2	3	3	1
Worn TIs more than 5 hours	8	11	11	11	12	8
Actual time worn specified	Ave 6.01 hrs	Ave 8.05 hrs	Ave 8.02 hrs	Ave 7.86 hrs	Ave 7.72 hrs	Ave 8.55 hrs
TIs uncomfortable	1	1	0	0	0	0
TIs NOT uncomfortable	13	12	12	12	13	9
TSGT was uncomfortable	0	0	0	1	1	1
TSGT was not uncomfortable	13	12	12	10	10	7
Outcome measurements were uncomfortable	0	0	0	1	1	0
Outcome measurements were not uncomfortable	3	3	5	2	4	2

* There were 14 participants who commenced interventions in the TI group, one withdrew after the first week. Four participants completed the interventions in five weeks, 12 in six weeks and all 13 had completed within seven weeks.

Weeks 2, 3 and 5 were not applicable for one participant. Week 4 was not applicable for two participants. Week 6 was not applicable for five participants.

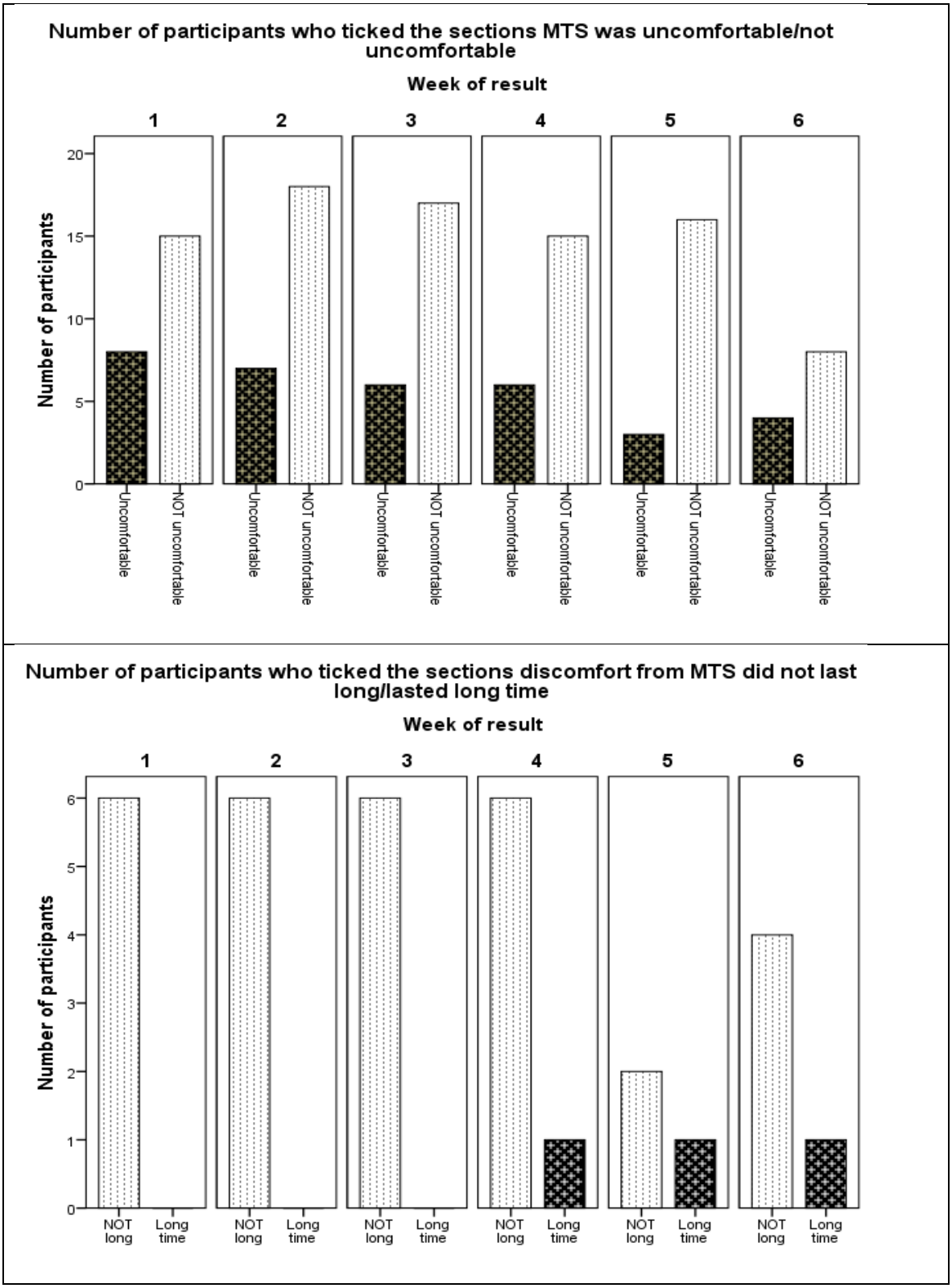


Figure 6.11 Comfort/discomfort of the MTS according to the number of participants (calculated from the number of ticks), and how long the discomfort lasted (n=19)

6.15.2 Comfort of TIs

The TIs were tolerated well, with only one person reporting some discomfort. Most of the ticks were in the ‘TIs not uncomfortable’ section, often with 100% of participants agreeing (figure 6.12).

Participants were in control of how long they chose to wear the insoles each day, and the diary sheets were a useful way of recording the number of hours participants wore the TIs. The mean (SD) number of hours the TIs were worn each week were, week one 6.01 (3.79) week two 8.05 (3.46); week three 8.02 (3.18); week four 7.86 (3.34); week five 7.72 (3.41); and week six 8.55 (3.84). Thus, overall, the mean length of time wearing the TIs was 7.70 hours per day (SD 0.80, range: 0.5–12 hours), which is a good indication that the majority of participants found the TIs comfortable (figure 6.13). One participant was unable to ‘don’ and ‘doff’ the TIs without assistance, and therefore only wore the TIs during the 30 minutes of TSGT each day, with assistance provided by the research therapist.

6.15.3 Comfort of the TSGT

The TSGT was also found to be well-tolerated in both groups, with most participants ticking the ‘TSGT was not uncomfortable’ section, indicating the intervention was comfortable, range in MTS group: 89.47–100% and TI group: 76.92–100% (figure 6.14).

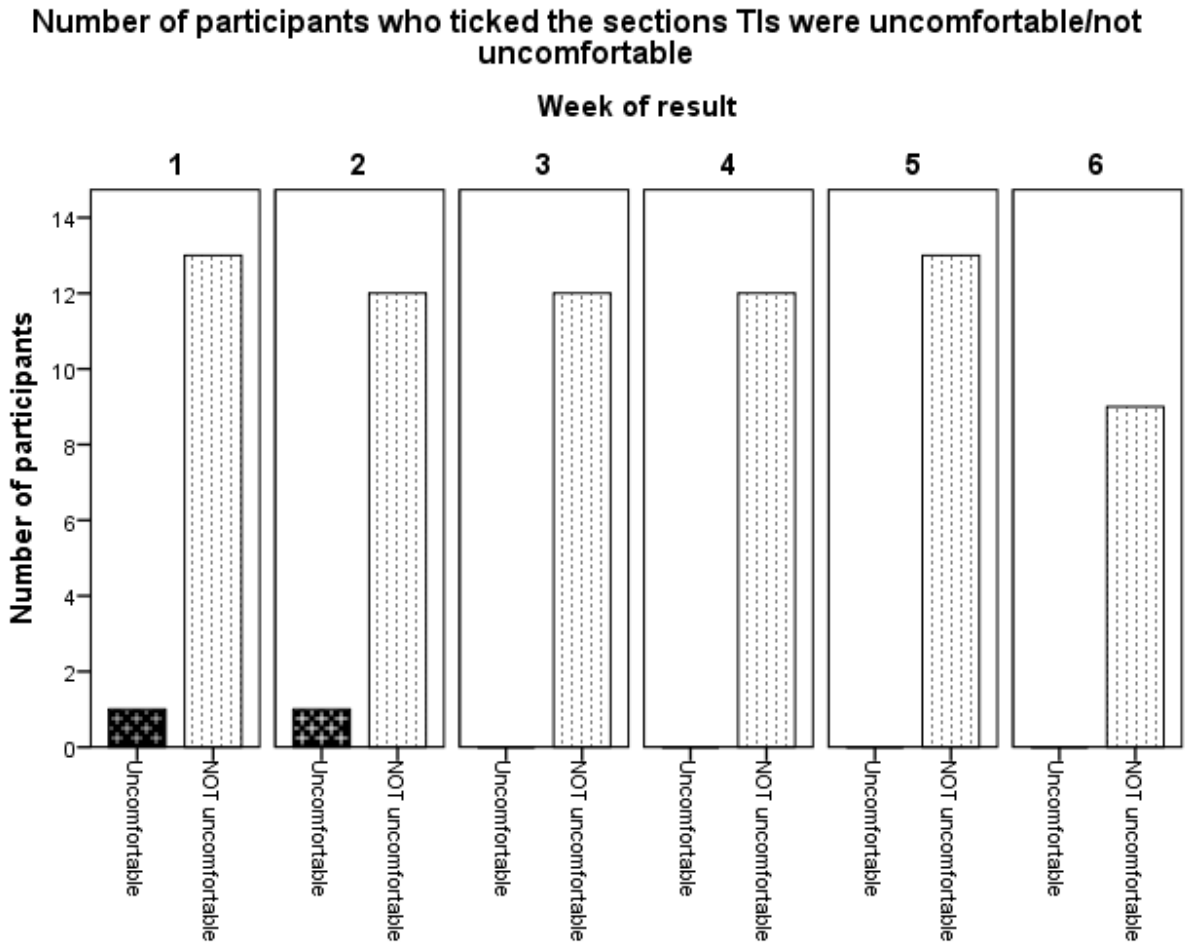


Figure 6.12 Number of participants ticking TIs were uncomfortable or not uncomfortable (n=13)

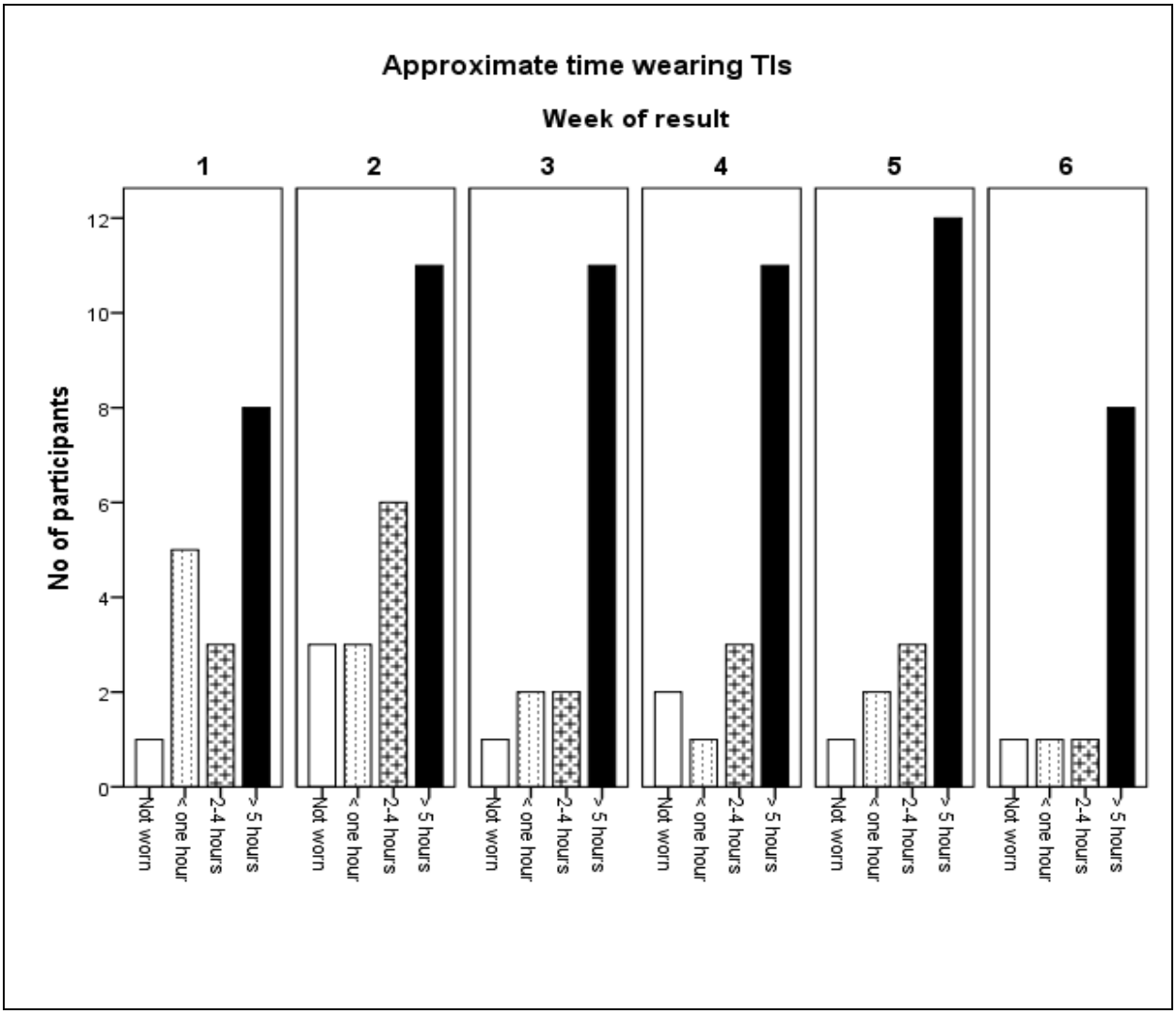


Figure 6.13 Number of participants and average time wearing TIs according to the number of ticks on diary sheets

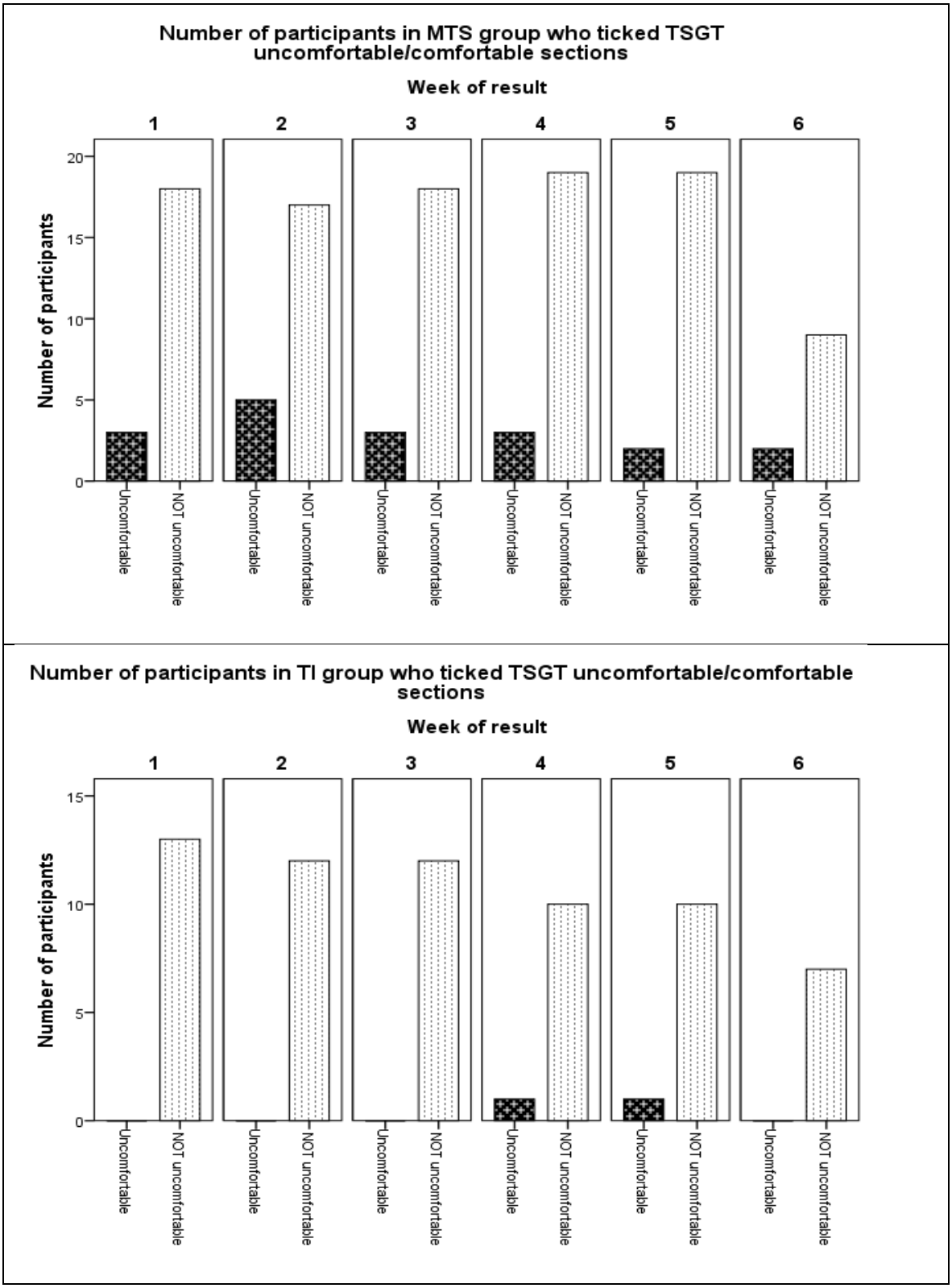


Figure 6.14 Number of participants in the MTS and TI groups who ticked the TSGT was uncomfortable/not uncomfortable sections

6.15.4 Comfort of the outcome measures

Participants' experiences of the OMs were also very positive, with no participants in the MTS group and only 4.23% in the TI group stating that having the OMs undertaken was uncomfortable (figure 6.15).

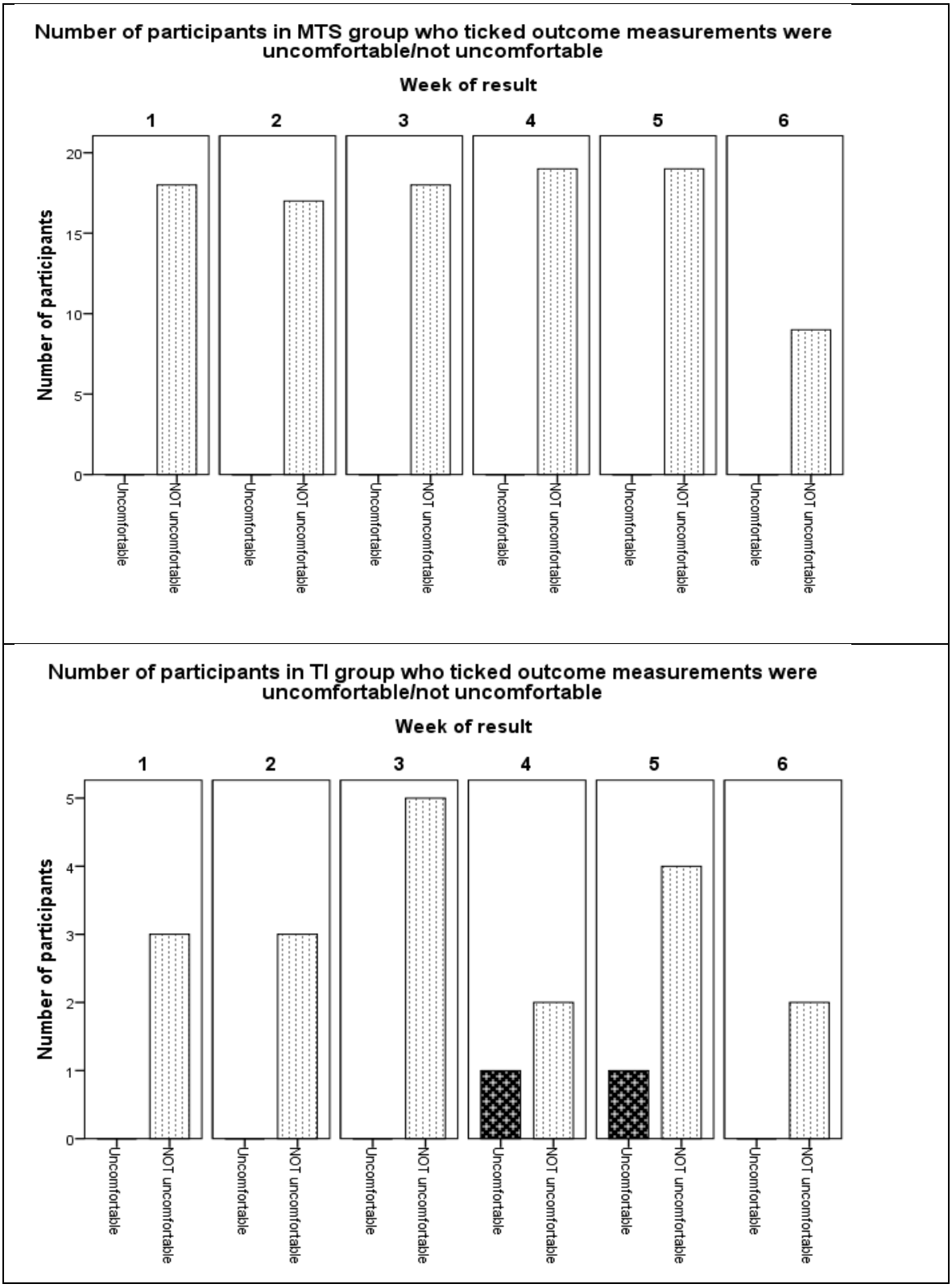


Figure 6.15 Comfort/discomfort of the outcome measurements according to group, analysed by the number of ticks

6.15.5 Thematic analysis of the daily diaries (Objectives 3d, 3e, 3f and 3g)

Comments made in relation to the MTS interventions, wearing TIs, and the TSGT intervention suggest the interventions were acceptable to the participants, addressing trial objective 3d. The MTS was described as being *"quite intense"* and *"a little uncomfortable";* however, the discomfort was described as *"only lasting very little time"* and *"stopping immediately when the massage discontinued"*. The TIs occasionally caused some discomfort *"due to shoe tightness",* with hot weather exacerbating this issue, but they were generally felt to be comfortable and participants suggested they helped them to feel more in their foot; *"could feel insoles more than yesterday"*. The TSGT was described as *"hard work"*, *"challenging", "tiring"* and even *"scary"* at times; however, it was also described as *"enjoyable"* and it appeared that many of the participants found it rewarding, reporting that it *"helped with balance"* and *"greatly improved"* mobility. Almost no negative comments were made relating to the OMs, just one person said it could be *"tiring"*.

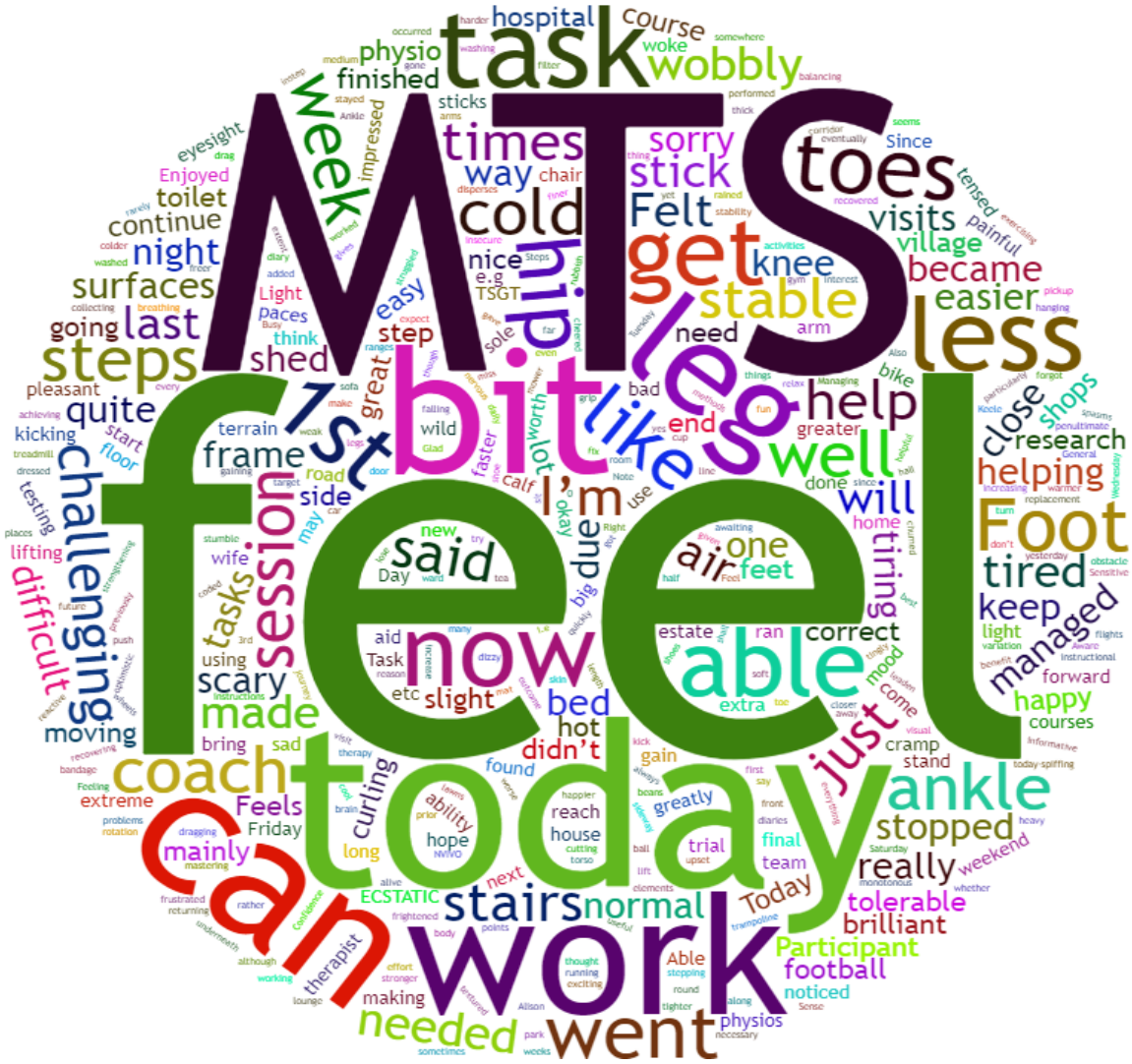
Trial objective 3e related to the suitability of the daily diaries and FGs for exploring stroke survivors' experiences of receiving the treatments. Although there are limitations and drawbacks to the use of diaries in research, which will be discussed in chapter seven, it is clear a great deal of useful information has been drawn from the daily diaries, assisting in the decision-making process relating to whether the interventions and outcomes are acceptable interventions for stroke survivors.

Table 6.7 Topics and themes identified from the daily diaries

MTS group	
Topic	**Theme**
MTS treatment	Uncomfortable/intense Increased flexibility Better function Benefits
Changes in feeling in foot/lower limb	Temperature Sensitivity Able to feel foot more Sense of belonging/increased awareness Stability Better movement Foot feels freer
General	Valued treatment Progress Activities of daily living (ADL)
TSGT	Uncomfortable Tiring Challenging Scary Enjoyable Improved balance Improved mobility Ability to walk unaided
Sense of achievement	Increased confidence Increased strength Independence with personal care Ability to walk again Ability to run again Improved balance Returning to normal daily activities: - Car transfers - Kitchen skills - Stairs - Outdoor mobility

TI Group	
TIs	Comfortable Discomfort: - Tightness in shoe - Smooth insole Difficult: - Hot weather/swelling Forgot to wear them Awareness of insoles
Change in feeling of the foot	Increased feeling Foot feels ticklish Increased awareness of foot Pain Swelling Temperature
Comments relating to lower limb	Increased confidence Control Stability
TSGT	Uncomfortable 1st class physio Helpful Enjoyable Balance work/cushion hard Increased confidence Tiring Hard work Challenging Improved movement and balance
Sense of achievement	Greater independence Better walking Increased movement and flexibility Improved balance Returning to normal daily activities: - Outdoor mobility - Steps - car transfers
Outcome Measures	Tiring

To give an overview of the words used in the daily diaries for each group word-clouds have been created too:


MTS
feel
today
can
work
went
needed
stairs
ankle
able
now
bit
leg
hip
toes
task
less
get
stable
cold
times
stick
Felt
sorry
wobbly
hospital
physio
finished
week
steps
challenging
difficult
session
coach
made
moving
scary
said
help
well
will
Foot
tired
keep
managed
helping
research
close
shops
became
easier
visits
village
knee
stopped
really
tolerable
brilliant
Participant
football
noticed
physios
Today
normal
bed
slight
hot
didn't
just
tiring
correct
one
air
feet
frame
terrain
shed
last
going
surfaces
night
continue
toilet
Enjoyed
eyesight
impressed
way
chair
since
course
woke
sticks
quite
pleasant
kicking
lifting
testing
tasks
using
wife
Feels
Friday
mainly
extreme
therapist
curling
ability
hope
long
reach
house
trial
final
team
greatly
found
bring
sad
Task
aid
etc
estate
ran
extra
happy
courses
forward
stand
cramp
gain
making
ECSTATIC
next
frightened
Able
thought
running
exciting
round
tighter
along
Sense
Allison
park
weeks
sometimes
necessary
weekend
Saturday
monotonous
whether
elements
trampoline
useful
points
body
effort
stronger
lounge
although
working
underneath
returning
rather
frustrated
Confidence
brilliant
mastering
problems
rotation
dragging
Feeling
bandage
recovering
reactive
strengthening
lifting
testing
places
dressed
treadmill
floor
start
kicking
pleasant
achieving
collecting
breathing
going
last
surfaces
night
continue
toilet
Enjoyed
eyesight
drag
rarely
colder
washed
finer
diary
added
Light
paces
Busy
think
shed
step
expect
ranges
sole
easy
TSGT
e.g
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steps
Interest
activities
arm
need
bad
end
greater
done
since
calf
faster
worth
lot
great
wild
Glad
terrain
weak
road
door
side
may
car
target
gaining
Note
use
okay
due
big
new
Day
ward
tea
Right
awaiting
Feel
half
Given
tiring
home
mood
come
extra
toe
closer
away
soft
skills
dizzy
increase
reason
aid
Task
etc
slight
bed
hot
didn't
found
sad
bring
therapy
visit
kick
always
beans
happier
happy
courses
forward
stand
cramp
gain
greatly
trial
final
team
Today

Figure 6.17 Word-cloud formed from the comments in the daily diaries from the participants in the TI group

6.16 Focus group (FG) findings (Objectives 3d,3e,3f and 3g)

All 32 participants who completed the study were invited to attend a FG. Details of numbers of participants invited and attending the FGs are given in table 6.8. Four FGs were held, two for the MTS group (FG1 n=5; FG3 n=8) and two for the TI group (FG2 n=5; FG4 n=2)

Table 6.8 Number of participants invited and attending the FGs

	MTS group	TI group	TOTAL
No of participants invited	19	13	32
No of participants attended	13	7	20
% of participants attended compared to invited	68.4	53.8	62.5

In total, 62.5% of participants attended one of the FGs, with 68.4% of the participants in the MTS group and 53.8% of those in the TI group attending. Although the intended sample size for each FG was 6–8, the actual numbers of participants attending ranged from 2–8.

6.16.1 Results of the thematic analysis of the FGs

Some a priori topics relating to the feasibility study objectives had been identified (Appendix 43); however, several other themes and sub-themes were identified from analysis of the FG transcriptions. Some of the themes were observed from more than one FG. The themes from the initial analysis are presented in Appendix 43, and summarized using the one sheet of paper technique (Ziebland and McPherson, 2006) (Appendix 44). The themes, which were developed over time with several iterations, are summarized in Appendix 45, creating an audit trail, and the final themes are presented in table 6.9.

Table 6.9 Final themes summarized

Theme	Sub-theme
Acceptability of the interventions	Comfort Perceived benefits/effects Dose intensity, frequency and duration Difficulties/challenges
Acceptability of the outcome measures	Comfort Perceived benefits Difficulties/challenges
Use of daily diaries	Ease of completion Difficulties/challenges Perceived benefits
Overall trial experience	Environment Confidence Improved function The beneficial and challenging effects of being involved in an intensive therapy trial End of trial

Other aspects were also discussed within the FG relating to life after stroke, for example, fear of the unknown, fear of falling and feeling self-conscious. Several participants also discussed regaining control of their life again and developing self-management strategies, which led to increased confidence and a sense of achievement, as well as independence and autonomy. Whilst these aspects do fit within the theoretical framework of acceptability, with increased confidence and self-efficacy being important in relation to the participants' assessment of the acceptability of the intervention following completion of the intervention (Sekhon et al., 2017), it was not possible to explore these issues in any depth given the time

scheduled for these focus groups in this study. However, these were valuable, interesting discussions to be taken forwards in post-doctoral study.

6.17 Summary of themes

There were four main themes that developed and fifteen sub-themes, which can be seen in table 6.9. These themes related to the trial experience, and will be discussed, with ideas and concepts supported by quotations from the FGs. Pseudonyms have been used to maintain participants' anonymity.

6.18 Acceptability of the interventions (Objective 3d)

6.18.1 Comfort/discomfort of the interventions

6.18.1.1 Mobilization and tactile stimulation

Three participants found aspects of the MTS to be painful or uncomfortable, particularly when the massage needed to be slightly deeper, using the thumb to mobilize tight tissues.

> *"Some parts of it were painful … sticking your thumb in"* (Edward, FG3, L124-125).

Although this discomfort was described as lasting *"only a few seconds" (Edward, FG3, L129)*

Some participants found it to be uncomfortable only early on in the treatment, but it was tolerable:

> *"Painful for the first couple of sessions, after that it was okay"* (L131, Evelyn, FG3).

> *Mine was only [uncomfortable] for the first couple of times but I tolerated it"* (L195, Michelle, FG3).

Others disagreed and felt the MTS treatment was not uncomfortable at all and it was even reported to be enjoyable:

> *"Mine was never painful"* (L132, Dennis, FG3).

> *"Mine wasn't [painful] ever"* (L133, Nancy, FG3).

> *"I enjoyed it"* (L636, Jackie, FG3).

6.18.1.2 TIs

Participants generally felt that the insoles were surprisingly comfortable to wear, describing them as being easy to take from shoe to shoe. The appearance of the texture of the insole itself provided an initial impression of being quite uncomfortable to wear, although this turned out not to be the case:

> *"I felt surprised actually because when I first saw them I thought "oh dear these are going to be prickly", and they weren't".* (L56, Olivia, FG4).

"they were more comfortable than uncomfortable, aren't they? Yes. so, they're all right" (L155-156, Brian, FG2).

Surprisingly, some participants preferred the sensation of wearing the TI rather than the sensation of the plain insole in the ipsilesional shoe:

"especially … the textured one on the left foot, when you got used to it, it's more comfortable than the plain one in the right foot." (L106-107, Brian, FG2).

Participants generally liked wearing the insoles, and wore them as much as possible throughout the day, some even wearing them all day:

"once they was in the shoes they stopped there till I went to bed" (L189, Isaac, FG2).

*"I transferred it from different shoes that I was wearing, I even put it in my slippers" (*L225-226, Nadine, FG2).

6.18.1.3 TSGT

The TSGT was not reported as being uncomfortable; however, it was perceived to be challenging at times and this will be discussed in relation to challenges of the interventions (section 6.19.4).

6.18.2 Perceived effects (Objective 3g)

Some people clearly felt that the MTS trial intervention, particularly the massage component, had made a difference to them. Participants observed that the MTS changed the feeling within the leg, and increased the flexibility of the muscles and soft tissues:

> *"it woke it up, it woke your leg up in the morning"* (L101-102, Michelle, FG3)

> *"I loved the massage* (L104) … *Well, it kept it flexible"* (L109, Phoebe, FG3)

> *"It made everything more flexible."* (L172 -174, Michelle)

Nancy was very clear that the MTS had been of great benefit to her, commenting on the fact that the treatment affected not only her foot but the whole of the lower leg, up to the knee. She described the effect of the MTS on the movement of her lower limb, but she had also recognized that the change in her ability to feel her foot had actually improved her walking:

> *"It* [MTS] *helped me enormously, with my feet especially because I couldn't move my right foot at all, and it's helped me enormously…it's made a difference to my right leg as well, up to the knee... because that was all weird, couldn't move it very much, and*

*it has made a difference with that…I can feel it more than I could, I know when I'm lifting it now, whereas I didn't before, … and that makes walking easier it does… it's helped me enormously in moving the leg up and down. My right leg, where I had all the massage and what-have-you, is better than my left one!" (*Nancy, FG3, L152–212).

Two participants in the MTS group reported a change within the feeling of the foot or lower limb, frequently insinuating that the body part now belonged to them:

"Well, I'd like to say that…I found that…it was part of me…part of my other leg, you know? It was…" (L34), "*… like…knowing I've got two legs instead of one"* (L37), *"It brought them together"* (L39, Harry, FG1).

"I think it is my brain realising that it's got a left side to the body and I think the treatment has brought that on" (L72-74) ... *"I could feel that I've got a left side I didn't realise"* (L88, Frank, FG1).

Indeed, Frank said it now felt the same as the other foot:

"I noticed, er, textures beneath my foot I couldn't feel that" (L681, Frank, FG1) … "*They're both the same" (L704, Frank, FG1).*

This was corroborated by accounts from other participants, who also acknowledged the importance of being able to feel the foot in order to walk and a sense that being able to feel the foot made them want to walk:

> *"My foot had woken up, I felt better for walking"* (Michelle, FG3, L886).

> *"I'd like to say the treatment [the MTS], it made you feel as though you wanted to walk."* (Harry, FG1, L158-159).

Progress with rehabilitation was attributed to the massage and encouragement from the research therapists:

> *"I think I've got more movement in my foot"* (L668) … *"seems to move more freely now"* (L670) … *"I think my left leg now, foot, is as strong as my right one; there's not much difference in them"* (L708) … *"I can rely on it now, where I couldn't before"* (L712-713, Harry, FG1).

Several of the participants appeared to attribute walking again and improved function to receiving MTS combined with TSGT, and participation in the MoTaStim-Foot trial:

"I couldn't walk... I've learned a lot, I can walk now right, I don't walk with any aid in the house. I've come on leaps and bounds, that's what has happened. Leaps and bounds." (L83-86, Evelyn, FG3).

"The treatment's given me the ability to walk with my partner. To get myself from A to B which is great." (L125-127, Frank, FG1).

"It helped me enormously…. I can walk now with my sticks…I couldn't… couldn't walk at all when it started. (L152-155, Nancy, FG3).

"I get out of bed some mornings and I don't need sticks I walk round the bedroom" (L162-163) … *"sometimes I feel like I can run. Honestly, I feel like I can run again"* (L243-244, Keith, FG1).

6.18.2.1 Textured Insoles

The stability provided by wearing an insole appeared to be a factor in participants feeling an effect from wearing an insole, whether textured or plain:

"In fact, since I had a stroke, I've taken to wearing insoles inside the shoes, um..., white insoles that you buy, padded insoles, but I much prefer to wear the trial insole…because of the design of the insoles your foot wasn't

flapping up and down mm, did you notice that? your foot was more stable" (*L159*–164, Nadine, FG2).

"Yes, the insole made the shoe a bit more rigid." (L165, Henry, FG2).

Loss of sensation following a stroke has an impact on the ability to feel the floor under the foot, and to move appropriately to function. Nadine explained the changes in feeling relating to her foot and function clearly:

"before I had the textured insole … when I used to put my foot on the floor, … the sole of my foot it just felt like a plank of wood... if that makes any sense?" ... *there's no feeling of movement in the foot and the toes wouldn't move, … when I was wearing the textured insole it gave me better movement in the foot, … I could feel the foot more"* (L49-56, Nadine, FG2).

Participants chose to wear the insoles because they felt they were having a good effect, although this feeling was not instant:

"I preferred to wear the insole because I felt as though I was getting benefit from it" (L233-234, Nadine, FG2).

"when I first wore it, it was a sensation I wasn't familiar with, and it took me 4 or 5 days to become familiar with the sensation, and then after 4 or 5

days, maybe a week later I could feel the texture of the insole affecting the foot" (L38-40, Nadine, FG2).

"At first you didn't think it was making much difference, but it was, it was a gradual build up" (L79-80) ... *but after wearing the insole for a period of time that's the feeling I had... that someone was tickling me … which was good"* (L90-93, Nadine, FG2).

Others could also feel the TI and perceived benefits of wearing the insoles, describing an ability to feel changes within the foot, which in some cases were clearly long-lasting effects:

"my left foot went from virtually no sensation … to being downright ticklish" (L87) *"still feels different now, weeks after taking the insole* out" (L1147-1148) … *"in sensitivity"* (L1150) …*"me foot is tingling at the moment"* (1153, Henry, FG2).

"the trial helped me to gain more feeling, more control, over my right foot which was the affected foot, it's made a huge impact on me and it's helped me recover even quicker" (L1459-1462, Nadine, FG2).

The importance of the sensation from the plantar surface of the foot was recognized:

"*what's the first thing you do when you're walking, when you stand up? It's your feet, it's the sensation in the sole of your foot" … "This trial helped us to gain the sensation back in the sole of the foot, it's had a major impact"* (L1414-1418, Nadine, FG2).

"this morning when I got out of the car, there was lots of loose pebbles on the ground, and and I could feel it through my left foot" (L1419-1420, Henry, FG2).

Isaac was unable to feel the TI and felt it made no difference to him:

"I don't think it made any difference wearing it with or without" (L62) *"normally I just wear my lambs wool insoles"* (L122) *…" and there was no difference"* (L124) … *"there was no difference from start to finish for me"* (L1542, Isaac, FG2).

However, a change in sensation was linked to improved movement and function by some of the participants after wearing the TIs and receiving TSGT:

"I got to be able to control my knee" (L1366) …. *"and have confidence to put weight on my left leg"* (L1368) … *"I could feel the muscle just above my knee (pause) going tighter and holding my knee in place"* (L1374-1379) … *"well if you know you've got control over your leg, as you can lock it up and*

it isn't going to cave in beneath you... that's marvellous" (L1405-1406, Henry, FG2).

Nadine was aware of the insole while undertaking the tasks in the TSGT session. She even referred to becoming dependent upon the insoles because she felt they were beneficial. She describes a change in feeling of her whole leg, which increased her confidence walking again, making her able to put weight through the side which was affected by her stroke:

"all the time when I was using the side step I could feel the insole in the shoe" (L287-288, Nadine, FG2).

"it feels the same as what the gentleman said it's like a ticklish feeling, ...I'd look forward to getting up in the morning and putting that textured insole in the shoe, because it was giving me that ticklish feeling, and … gradually over a period of time, I found myself, wearing the insole all the time. And I didn't take the insoles off until I was getting ready undressed and going to bed and um..., um... yep I became dependent upon the insole because it was bringing me sensation back into my foot". L112-120, Nadine, FG2).

"it gave me, more feeling in the right leg to walk without thinking that this leg is weak, it gave me a sense of power back" (L1359, Nadine, FG2).

Describing it as a *"minor miracle"* (L86, Olivia, FG4), Olivia felt wearing the TI contributed to her foot being straighter:

> *"it gradually got straighter and it's still straight now"* (L78).

Afferent feedback is important for walking, assisting with moving the foot and leg, as well as stepping and placing the foot during gait. Nadine describes her awareness of the importance of somatosensory feedback to facilitate the movement in her foot and her ability to walk again, summarizing well the overall benefits she felt from wearing the TIs:

> *"I've got more control over my foot since wearing the insole ... as I explained before, the only way I can describe it is having this foot and it didn't move, I felt as though it didn't move. But when I wore the insoles I could feel the feet moving I could actually move the foot, and I've got more control over the foot, I can actually... the brain ... my... I can use my brain to tell the foot to move it a bit, and that only happened with wearing the insole, I can send a signal to the brain to move the foot"* (L1158-1165, Nadine, FG2).

6.18.2.2 Task-specific gait training

Participants valued the TSGT they received, indicating it had helped them to gain control over their body, improving their balance, walking and confidence, and assisting them to achieve functional activities.

> *"the walking training helped me a lot, to go outside the home environment"* (L371, Jackie, FG3).

> *"It's [the TSGT] definitely helped because to start with er..., the foot had got a mind of its own, er it tended to want to go a different way (laughs) but after so long with the textured insoles and the training and all the rest of it, got more confidence."* (L226-230) ... *"it (the TSGT) was very useful for me"* (L378-379, Olivia, FG4).

> *"I liked the balancing"* (L263) *… "that's what seemed to have helped me more than anything. I don't seem to fall... I also don't seem to ever trip up"* (L265-267, Phoebe, FG3).

The participants clearly felt the time which had been dedicated to the TSGT and the hard work and effort they had put in had made a difference to them personally, with several participants even indicating that they did not think they would have walked again or managed the stairs after their stroke, without the trial intervention:

"I wouldn't have been able to walk without it" (L250, Michelle, FG3).

"it made a huge difference" (L319... *"improved us tremendously"* (L326, Nadine, FG2).

Participants indicated that they found the TSGT worthwhile, even though it was hard work, because they could see results; the motivational element of working one to one with a therapist may have helped:

"it was helpful because it got me motivated" (L476, Nancy, FG3).

"I wouldn't have been anywhere like I am now without these lot, you know with...your determination" (L79-80, Dennis, FG3).

One of the participants indicated that without his participation in the trial he would still be in a wheelchair rather than walking, and another suggested they would not have been able to go on their holiday:

"made me do things...I'd still have been in my bloody chair if I hadn't have done that...you know, it was really good" (L 318-320, Dennis, FG3).

"she got me to Lanzarote, she told me on day one I would go" (L187, Michelle, FG3).

6.18.3 Dose intensity, frequency and duration (Objective 3d)

The interventions took place regularly, often daily, and participants' opinions were sought regarding this issue. All the participants except Trevor were happy having such regular treatments and many even wanted more sessions:

> "*no, never too much*" (L424, Marie, FG3)
>
> "*you could have come to my house every day*" (L426, Dennis, FG3)
>
> *"it went so quick. If we had twice as many sessions, I think I would have been further advanced than what I am now."* (L534,536, Brian, FG2).

However, Trevor (a young stroke survivor in his fifties) suggested that an intensive daily rehabilitation programme over a three-month period, to which the trial intervention had contributed, had become a burden from which he was ready to be relieved, even though the intensity of the trial intervention was acknowledged to have been *"about right"* (L1011, Trevor, FG1)*:*

> *"but after three months of day in day out I was probably thinking it was enough" (*L334, Trevor, FG1).

However, Trevor did feel the length of each treatment session (approximately 30 minutes of MTS, plus 30 minutes of TSGT) was appropriate:

> *"I would say that an hour was about right"* (L998, Trevor FG1).

Due to the intense nature of the TSGT, it was important to find out whether the timing that was chosen (30 minutes) was acceptable to the participants. Although some of the participants wanted a longer treatment period and felt they *"could be doing a bit more"* (L480, Dennis, FG3), others felt the chosen intervention time was appropriate: *"it was just enough for me"* (L485, Nancy, FG3), "*it was all right what I did but er no longer"* (L 439, Isaac, FG2).

6.18.4 Difficulties/challenges

Several of the participants clearly found the TSGT challenging in various ways, with five people describing it as "*hard work*" (Brian, FG2; Edgar, FG4, Henry FG2, Nadine, FG2, Trevor FG1):

It was also perceived by four people as being tiring at times, requiring recovery time afterwards, with the fatigue even manifesting itself the following day:

> *"I did need to rest afterwards"* (L476-477, Nancy, FG3).
>
> *"I used to feel tired the next day"* (L447, Phoebe, FG3).

Nadine also felt it was *"confusing at times"* and two of the participants said at times they had found it frightening (Dennis, FG1 and Keith, FG1).

6.19 Acceptability of the outcome measures (OMs) – Objective 3f

6.19.1 Comfort of outcome measures

There was a generalized acceptability of the need to participate in the OMs, with participants clearly understanding what they had agreed to when they consented to be part of the trial. One person said she thought the OMs could be *"challenging, … but that's part and parcel"* (L504, Olivia, FG4) and another said *"as long as we all knew what they were doing, I think we were all quite happy to go along with it because it was part of the trial we signed up for"* (L790-791, Michelle, FG3).

6.19.2 Perceived benefits of outcome measures

The OMs were clearly useful to some of the participants, and this perhaps made them more acceptable, despite the time it took to undertake them. For example, Henry found the visual feedback on the computer screen useful:

> "*you know the pressure sensors that you put in the er in the shoe...and then on the computer screen showing equal pressure on both feet I thought that was amazing" (*L727-734*),* Henry, FG2).

It seemed that some of the participants were encouraged and motivated by the positive results they saw in relation to the OMs:

"I thought to myself this is measuring the outcome of the progress that I have made and I was quite happy with that" (L740-742, Nadine, FG2).

"you showed me the clip of me walking three months ago and I couldn't believe it was me, I couldn't believe it was me, and it had changed dramatically how you're moving; well, one was just moving just through the room and, er it was quite remarkable to see the, the knee and this walking" (L456-460, Trevor, FG1).

6.19.3 Difficulties/challenges

Generally, the participants did not have any major problems with the OMs, although the wires from the Tekscan pressure insole set up were occasionally an issue:

"The first time it was quite difficult because I felt as though the wires were dragging a bit, but the last time it was brought in I was quite all right. I could walk down and walk back again" (L714-716, Nadine, FG2).

"you've got to beware haven't you of tripping?" (L 538, Edgar, FG4)

One participant (Dennis, FG3) suggested a wireless system would be more suitable, and for others the wires were not seen as a problem:

"I wasn't particularly bothered about the wires" (L717, Henry, FG2).

"it was fine because obviously there was someone there watching what... where you were putting your feet etc. so you can't ask for more than that" (L555-556, Olivia, FG4).

6.20 Use of daily diaries (Objective 3e)

6.20.1 Ease of completion

In the main participants did not have any problems completing the daily diaries, stating they were *"very easy"* (L559, Trevor, FG1, L896, Edward, FG3) and also that they *"wish all the forms were that easy"* (L874, Isaac, FG2) and *"no it wasn't difficult"* (L889 Henry, FG2) and also *"no it wasn't a burden" (L654, Frank, FG1)*.

6.20.2 Difficulties/challenges

Phoebe's poor eyesight made it a little more challenging; she had to wait for assistance to complete the diary and therefore her ability to recall what she had felt or achieved was potentially reduced:

"*well, I'd have found it would have been a lot easier if I could have seen so that I could have wrote it as I felt it. Oh, but waiting for somebody to come and fill it in, it had gone". (L914-916, Phoebe, FG3).*

Other participants were honest about the fact they sometimes forgot to complete it:

> *"I just kept forgetting" (L1276, Evelyn, FG3).*

6.20.3 Perceived benefits of daily diaries

There was a perceived value in using the daily diaries to note progress:

> *"because I was progressing you see with everything"* (L906-907, Nadine, FG2).

6.21 Overall trial experience

6.21.1 Environment

Many of the participants received their treatments in their own home environment and this was not seen to be an issue at all; indeed, there was unanimous agreement that this was preferable, and no-one reported that they felt it was intrusive, they just reported the benefits:

> *"I felt comfortable because it was in my own house and felt as though I'd got more control over it as well"* (L775-776, Nadine, FG2).

“it was ideal I felt more confident in my own surroundings” (L565) ... “*so, it gave you the confidence to do that bit more because you were secure in your surroundings”* (L559-560, Michelle, FG3).

Participants indicated that it was easier for them to have the therapist travelling to their house, and one participant said she would not have completed the full course of treatment if it had been necessary for her to travel to receive it.

“without you coming to the house I don’t think I would have completed the course because I would think oh, it’s too much trouble to go and get ready and go out” (L568-570, Jackie, FG3).

Some participants would, however, have been happy to travel to receive the treatment:

“I would still have gone [to the hospital], even though, but it’s convenient you coming at home” (L 815-816, Dennis, FG3).

Some people did receive their treatment while they were still in the hospital, but again this was not perceived as a problem.

6.21.2 Confidence

The treatment on the trial was reported as contributing to an increase in confidence and independence:

> *"It gave me the confidence to go out, back out, and to walk with a stick"* (L112-113, Jackie, FG3).

> *"Well it gave me confidence; you said to me one…one day you're going to walk now without your stick" and I said to you "I can't do it" …and you said to me "I've been in this job long enough to know that you can do it"…and I did it! I went from the kitchen into the living room, and I was REALLY surprised at that!"* (L263-267, Harry, FG1).

The value that the participants placed upon the treatment they received could perhaps in part be attributed to the skilled therapy they received, and this would, in turn, have made the treatments more acceptable to the participants.

> *"having someone who knows what they're talking about, that helps when you have no idea yourself and it does help with confidence"* (L363-367, Olivia, FG4).

"After you lot coming around and giving it all you're doing right, you know what you are doing" (L651-652) … *"You know every bone in the body"* (L654, Dennis, FG3).

The confidence instilled in the participants from the research therapists was also discussed:

"My wife isn't the same as you standing there. You do give me confidence" (L771-772)..."*as soon as you dropped off, my confidence dropped"* (L767, Harry, FG1).

6.21.3 Improved function

All the participants perceived benefits from being part of the MoTaStim-Foot trial, with many different comments made about it being enjoyable, useful, and beneficial in helping them to achieve their goals:

"it's helped me to achieve my goal and more um because I'm now trying things that I wouldn't have tried before" (L1297-1298) ... "*yes, it has absolutely without a doubt. I am even walking, walking on my own now without a walking stick"* (L1301-1302, Nadine, FG2).

"Well, if it weren't for that treatment I wouldn't be walking now" (L193-194) "*My wife thinks the same... if it wasn't for you…I wouldn't be walking now, I should be static"* (L195-196, Harry, FG1).

"Well, life after the trial has been good, because I'm able to get up and move about a bit on my own, transfers, (L1023-1024) *so I'm not a burden on somebody else."* L1026, Henry, FG2).

6.21.4 The beneficial and challenging effects of being involved in an intensive therapy trial

The trial involved a great deal of effort and time commitment on behalf of the participants. It was evident that the trial had not only had an impact on the participants but also on their families:

"it made a big, big impact on my daughter and my husband because they could understand what I was going through and what was happening with the trial" (L1258-1259, Nadine, FG2).

"yes, yes it has had an impact" (L1257) … *me Dad still shouts "stand tall!" (laughs)" …. "don't stick your bum out, stand tall" (*L1264–1267, Henry, FG2).

Two of the participants felt that their participation in the trial had helped prevent them having falls:

> *"Knowing that I'd got control of my knee meant there was no fear of falling, and I haven't fallen."* (L1385-1386, Henry, FG2).

> *"Where I would have gone down… now I find my balance a lot easier. That's what I have found one of the biggest benefits to me".* (*L*269-270, Phoebe, FG3).

However, the intense nature of almost daily treatments, often alongside NHS therapy was challenging for some participants:

> *"Many people are interfering with your life"* (L290, Frank, FG1).

> *"I felt it was a bit stress … stressful, a bit 'oh no, she's coming again" … "every day, for it to be every day it seemed too much"* (L285-295, Trevor, FG1).

6.21.5 End of the trial

Some of the participants found it challenging when the trial finished and described a sense of disappointment or loss:

“After the trial finished…. I experienced a sense of loss” (L1341, Nadine, FG1).

“let down” (L582, Brian, FG2).

“when it all finished I felt like bloody hell, what am I going to do now?” (L642-643, Dennis, FG3).

“it feels a whole lot better but I’m gutted you’ve left” (L970, Evelyn, FG3).

“I felt sorry it had finished because I felt it was doing me good” (L633-634, Jackie, FG3).

However, by the time the trial finished many of the participants had developed sufficient movement and ability to undertake functional activities unaided or with their families and several participants were demonstrating self-management skills.

The qualitative aspects of this trial have added value, and will inform the future RCT in many ways: ethically, it has been possible to ensure that recruitment and communication strategies take into account the needs of participants, ensuring being part of the trial is a positive experience, interventions are deemed suitable and appropriate for both the participants and the research therapists, internal validity is increased by confirming that appropriate OMs are employed.

Furthermore, the qualitative aspects have the potential to improve the success of the trial and facilitate future implementation of techniques (O'Cathain et al., 2013). For example, it has been possible to reflect upon the fact that such regular input (almost daily) leaves little time for participants to be involved in other activities and this can be an important aspect, particularly for younger stroke survivors.

Whilst most of the feedback from the participants has been positive, when considering the analysis of the information from the FGs the issue of social desirability must not be forgotten; for example, the participants may have a tendency to report positive aspects that they consider the researcher and other participants may like to hear (Zerbe and Paulhus, 1987).

In order to address objective 3g, exploring the responses to the interventions over time, detailed within-group analysis was undertaken for each OM. As this was a feasibility study, between-group analysis was not appropriate and therefore not undertaken.

6.21.6 Outcomes

6.21.6.1 Five-metre walk test (5MWT)

The 5MWT was undertaken at baseline, end of intervention and one-month follow-up. The outcome was relatively quick to undertake, with very minimal cost implications, for example requiring use of just a timer. As the data were not normally distributed, median and IQR, range, within-group differences between medians (baseline and end of intervention, and baseline to one-month follow-up) and 95% CIs were calculated and are summarized in table 6.10. The box plots show a representation of the results of the 5MWT (figure 6.18).

A reduction in time taken to complete the 5MWT was seen in both groups at end of intervention and at follow-up. For the MTS group, median (IQR) change in time from baseline to end of intervention was 10.18 (4.67,16.27) seconds (95% CI -15.52 to -5.45), and it was 11.49 (2.34,16.79) seconds (95% CI -22.90 to -1.40) for the TI group. The change in time from baseline to one-month follow-up was 10.33 (6.12,18.60) seconds (95% CI -17.89 to -6.15) for the MTS group, and 13.17 (6.12,18.60) seconds (95% CI -26.08 to -0.39) for the TI group.

Table 6.10 Results of 5MWT, at baseline, end of intervention, and one-month follow-up, including change from baseline to end and baseline to follow-up, showing median (IQR) and range of times (seconds), and 95% CIs

Group		Baseline	End of Intervention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS group (18)	Median (IQR)	23.80 (17.53, 31.13)	13.43 (8.70, 17.30)	-10.18 (4.67,16.27)	11.41 (6.80, 15.75)	-10.33 (6.12,18.60)
	Range	12.08–71.00	6.50–34.80	14.57–43.19	5.59–37.66	-25.58–56.20
	95% CI			-15.52 to -5.45		-17.89 to -6.15
TI group (11)	Median (IQR)	27.65 (16.91, 39.78)	14.51 (11.79, 21.19)	-11.49 (2.34,16.79)	14.79 (13.64, 22.47)	-13.17 (3.58,19.07)
	Range	12.30–80.00	9.44–48.47	-6.32–56.00	11.33–44.80	-2.49–38.06
	95% CI			-22.90 to -1.40		-26.08 to -0.39

CI=Confidence interval

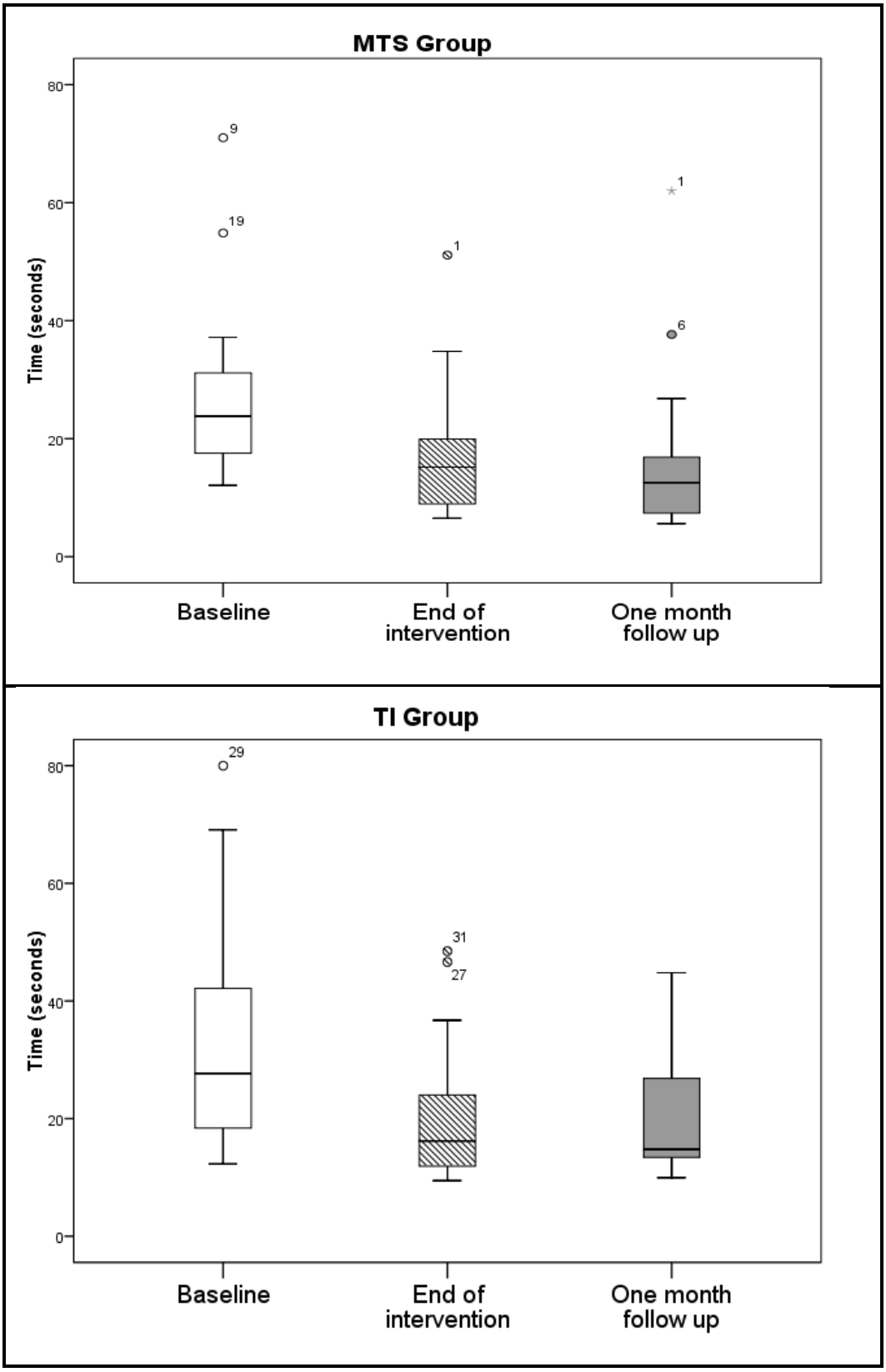


Figure 6.18 Box plots for all three time-points for the 5MWT according to group

6.21.6.2 Functional Ambulation Classification (FAC)

The FAC was undertaken at baseline, end of intervention and one-month follow-up, was quick to undertake and required no financial resources. Assessment and change scores are summarized in table 6.11.

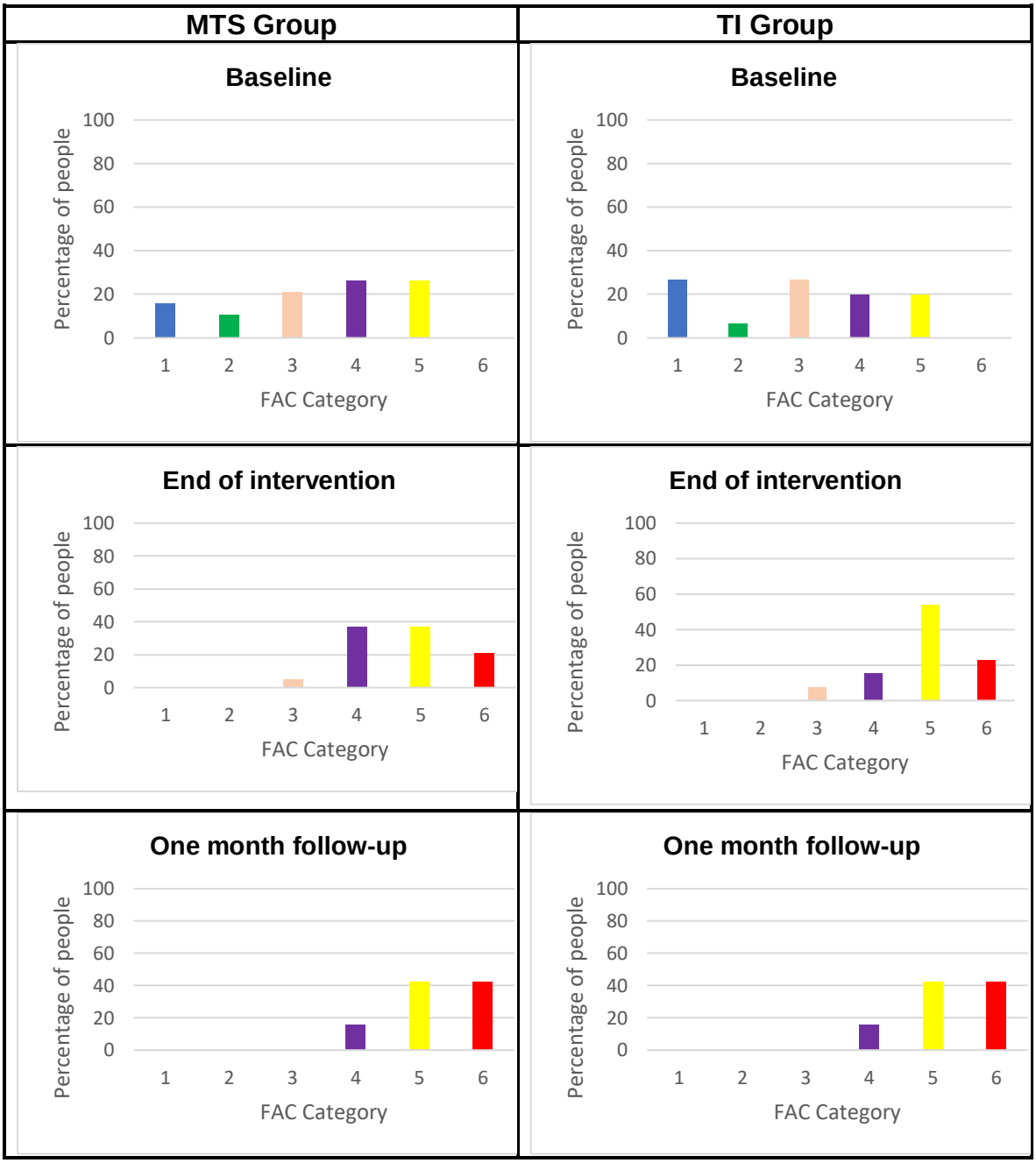
At baseline, the median (IQR) score for the MTS group was 4.0 (2.0, 5.0). However, at the end of intervention and one-month follow-up assessments, the median (IQR) score was 5.0 (4.0, 5.0) and 5.0 (5.0, 6.0) respectively. In the TI group, the median (IQR) score was 3.0 (1.0, 4.0) at baseline, 5.0 (4.5, 5.5) at end of intervention and 5.0 (5.0, 6.0) at the one-month follow-up.

A visual representation of the results is displayed in figure 6.19, with each of the two groups represented separately. This clearly shows the change where many of the participants at baseline were dependent upon others, and in some cases non-ambulatory, to cohorts in both groups who were much more independent ambulators.

Table 6.11 FAC scores at baseline, end of intervention, and one-month follow-up, including change from baseline to end and baseline to follow-up, showing median (IQR) and range of FAC categories

Group		Baseline	End of Intervention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS group	**Median (IQR)**	4.0 (2.0, 5.0)	5.0 (4.0, 5.0)	1.0 (1.0, 2.0)	5.0 (5.0, 6.0)	2.0 (1.0, 3.0)
	Range	1.0–5.0	3.0–6.0	0.0–3.0	4.0–6.0	0.0–4.0
TI group	**Median (IQR)**	3.0 (1.0, 4.0)	5.0 (4.5, 5.5)	2.0 (1.0, 3.0)	5.0 (5.0, 6.0)	3.0 (1.0, 3.0)
	Range	3.0–6.0	3.0–6.0	0.0–4.0	4.0–6.0	0.0–4.0

MTS group n=19 TI group n=15 at baseline; n=13 at end and one-month follow-up



Key:

- Non-functional (unable to ambulate)
- Dependent Level II (requires continuous manual contact of one person)
- Dependent Level I (requires intermittent manual contact of one person)
- Dependent, supervision (level surfaces only, no manual contact required)
- Independent, level surfaces only
- Ambulation independent on unlevel surfaces, stairs and inclines

Figure 6.19 FAC results displayed as bar charts for each group at baseline, end of intervention, and one-month follow-up

6.21.6.3 Goniometer readings – maximum dorsiflexion and maximum inversion for the contralesional side

The goniometer readings were undertaken at baseline, end of intervention and one-month follow-up. The costs for initially purchasing the goniometry equipment need to be taken into consideration (£4,611). For each group, change in median (IQR) scores were calculated from baseline to end of intervention, and from baseline to one-month follow-up. The results are represented in table 6.12 and visually in the box plots in figures 6.20 and 6.21.

6.21.6.3.1 Dorsiflexion

Changes in median (IQR) scores from baseline to end of intervention were 0.10 (-2.2, 5.6) (95%CI -2.20 to 6.70) for the MTS group, and -0.45 (-2.18, 6.25) (95%CI -9.50 to 6.70) for the TI group, and from baseline to one-month follow-up were 0.20 (-5.40, 4.25) (95%CI -4.90 to 3.00) for the MTS group, and -2.65 (-5.93, 1.13) (95% CI -6.00 to 1.50) for the TI group.

6.21.6.3.2 Inversion

Changes in medians (IQR) from baseline to end of intervention, were -0.85 (-3.05,1.33), (95%CI -6.30–8.60) for the MTS group and 1.80 (-2.60, 3.50), (95%CI -7.50 to 4.70) for the TI group and for baseline to one-month follow-up were 0.25 (-3.03, 1.38), (95%CI -3.20 to 1.60) for the MTS group and -0.19 (-6.58, 3.05), (95%CI -6.80 to 4.10) for the TI group.

A few extreme values were noted. In the absence of a clear reason for these extreme values, the reliability of the goniometer measurements was questioned. This issue will be further discussed in chapter seven.

Table 6.12 Goniometer readings for maximum dorsiflexion and inversion at baseline, end of intervention, and one-month follow-up, including change from baseline to end and baseline to follow-up, showing median (IQR) and range movement (degrees)

Group		Baseline	End of Intervention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS group Maximum dorsiflexion	**Median (IQR)**	9.9 (5.05, 12.35)	9.85 (6.50,12.70)	0.10 (-2.2, 5.6)	8.5 (7.20, 11.50)	0.20 (-5.40, 4.25)
	Range	2.40–24.30	2.30–41.50	-13.70–26.30	2.90–29.20	-17.16–19.30
	95% CI			-2.20 to 6.70		-4.90 to 3.00
TI group Maximum dorsiflexion	**Median (IQR)**	9.45 (7.30, 9.80)	10.10 (8.90, 11.70)	-0.45 (-2.18, 6.25)	5.80 (4.60, 11.30)	-2.65 (-5.93, 1.13)
	Range	2.20–18.60	3.70–15.30	-13.70 – 6.25	3.20–11.90	-7.8–5.60
	95% CI			-9.50 to 6.70		-6.00 to 1.50
MTS group Maximum inversion	**Median (IQR)**	8.30 (5.85, 10.8)	6.15 (4.55, 11.40)	-0.85 (-3.05,1.33)	8.20 (5.95, 9.80)	0.25 (-3.03, 1.38)
	Range	2.80–19.00	1.10–14.10	-6.30–8.60	1.20–13.40	-7.20–9.10
	95% CI			-3.10 to 1.80		-3.20 to 1.60
TI group Maximum inversion	**Median (IQR)**	7.0 (3.40, 11.50)	7.70 (6.60, 11.10)	1.80 (-2.60, 3.50)	6.10 (4.50, 8.10)	-0.19 (-6.58, 3.05)
	Range	2.80–19.00	2.40–17.00	-5.00–7.10	1.60–20.20	-8.30–15.90
	95% CI			-7.50 to 4.70		-6.80 to 4.10

MTS group n=16 TI group n=10

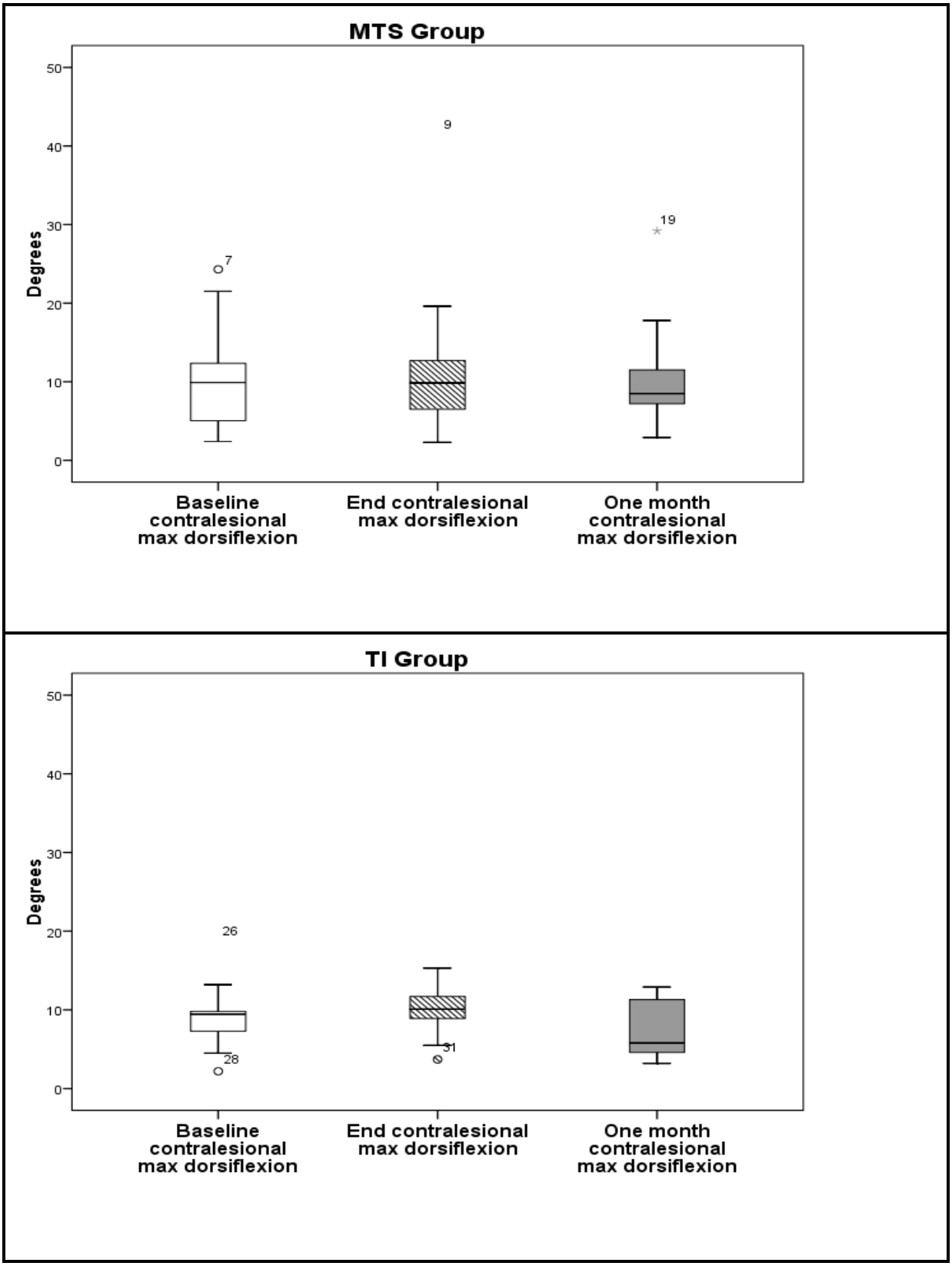


Figure 6.20 Box plot of maximum dorsiflexion results at baseline, end and follow-up

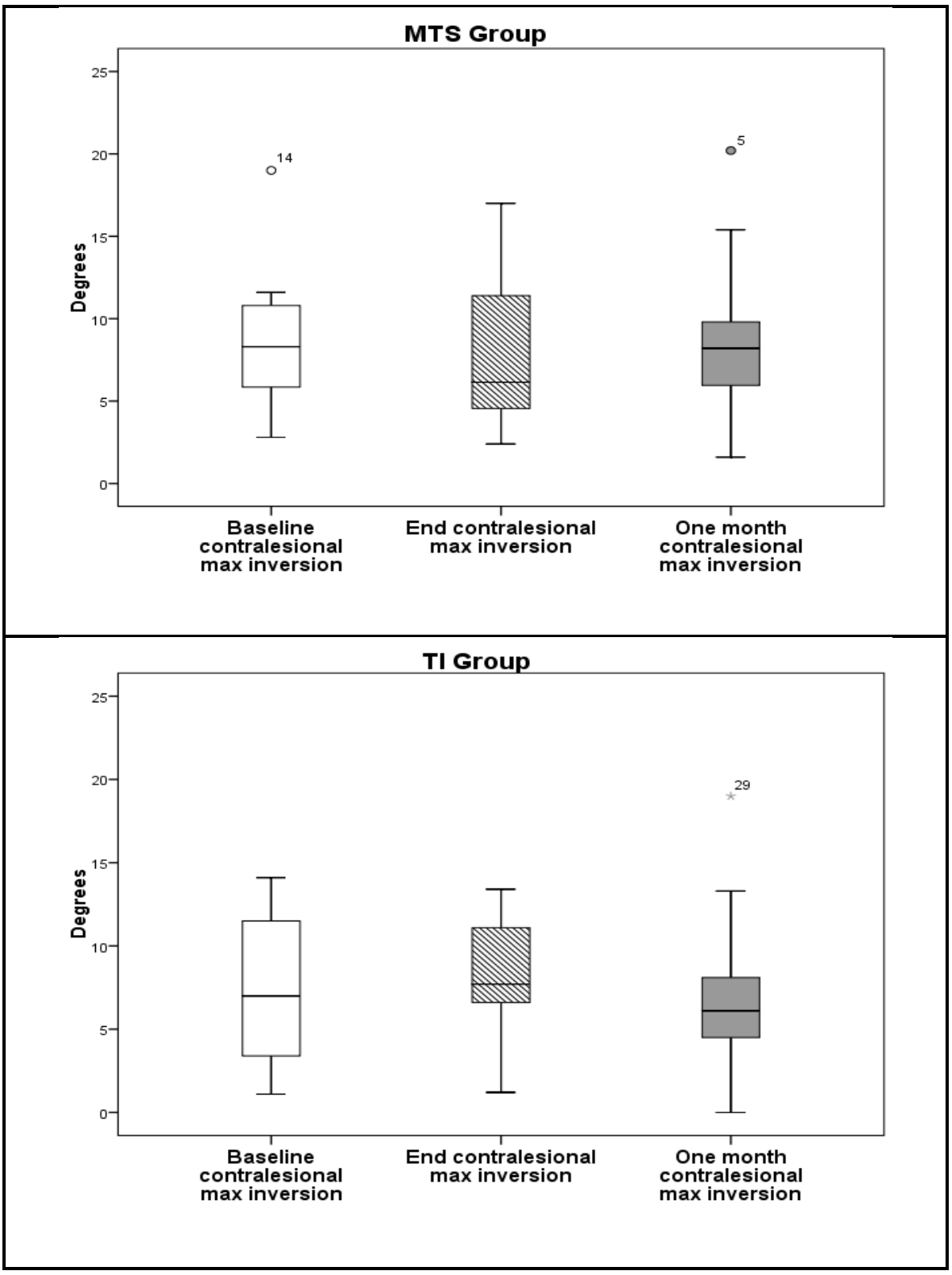


Figure 6.21 Boxplot of maximum inversion at baseline, end and follow-up

6.21.6.4 The modified Rivermead Mobility Index (mRMI)

The mRMI was undertaken at baseline, end of intervention and one-month follow-up. There were no costs associated with implementation of the mRMI. Results are presented in table 6.13. The mRMI is usually scored out of 40; however, an issue arose in that it was not possible standardize the number of stairs participants were assessed on, in view of the multiple venues used for testing, and that some participants in their home environment did not have access to a flight of stairs. It was, therefore, impossible to assess this section in these cases. To ensure parity between the scores, a pragmatic decision was made to remove the stairs score from all the participants, scoring the mRMI for all participants out of 35 instead.

The mRMI score increased for both groups from baseline to end of intervention. Towards the ipsilesional side, there was a change in median (IQR) score from 33 (29, 34) to 34 (33, 35) in the MTS group, and from 23.5 (20, 33) to 34 (33,34) for the TI group. Towards the contralesional side: there was a change in median (IQR) score from 33 (28, 33) to 34 (34,34) in the MTS group, and from 24.5 (20, 31) to 34 (33,34) in the TI group.

The range of scores for both groups decreased, from 19–34 (ipsilesional) and 14–34 (contralesional) at baseline to 26–35 (ipsilesional) and 21–35 (contralesional) at end of intervention for the MTS group; and from 12–34 (ipsilesional) and 12–35 (contralesional) at baseline to 26–35 (ipsilesional) and 25–35 (contralesional) for

the TI group, as can be seen in table 6.13 and visually represented in the boxplots in figures 6.22 and 6.23.

Table 6.13 mRMI at baseline, end of intervention, and one-month follow-up, including change from baseline to end and baseline to follow-up, showing median (IQR) and range of scores

Group		Baseline	End of Intervention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS group towards ipsilesional side	**Median (IQR)**	33 (29, 34)	34 (33, 35)	3.24 (0.00, 4.50)	34 (34, 35)	3.94 (1.00, 6.00)
	Range	19–34	26–35	-3.00–14.00	32–35	-2.00–15.00
TI group towards ipsilesional side	**Median (IQR)**	23.5 (20, 33)	34 (33, 34)	7.5 (1.00, 14.25)	34 (31, 35)	8.2 (1.00, 13.25)
	Range	12–34	26–35	1.00–15.00	28–35	1.00–20.00
MTS group towards contralesional side	**Median (IQR)**	33 (28, 33)	34 (34, 34)	2.00 (1.00, 5.50)	34 (34, 35)	2.00 (1.00, 6.50)
	Range	14–34	21–35	0.00–20.00	31–35	-2.00–20.00
TI group towards contralesional side TI group	**Median (IQR)**	24.50 (20, 31)	34 (33, 34)	6.00 (2,50, 11.75)	34 (31, 34)	9.00 (1.50, 12.00)
	Range	12–35	25–35	0.00–15.00	29–35	0.00–17.00

MTS group n=17 TI group n=10

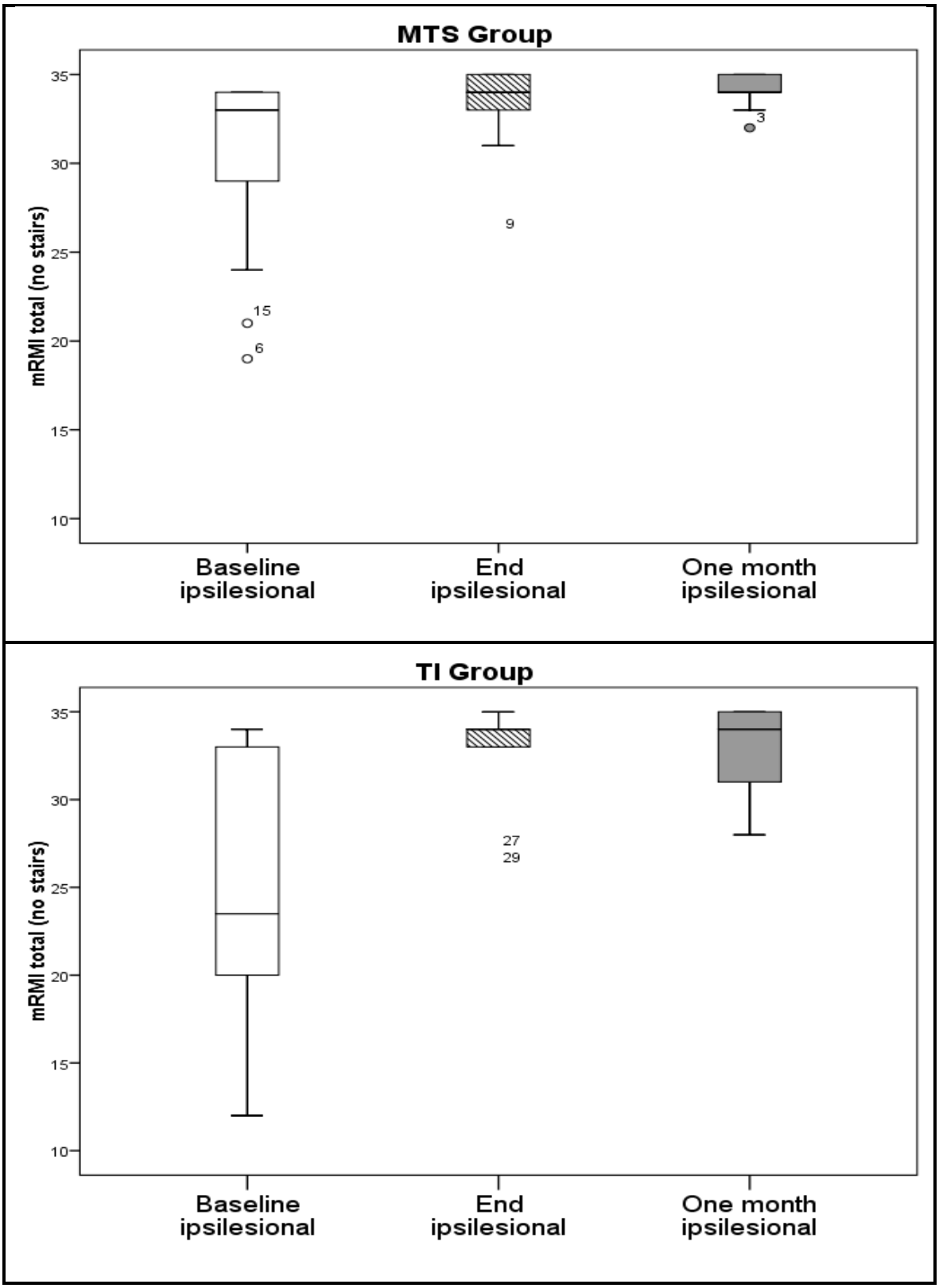


Figure 6.22 Box plot for all three time-points according to group for the mRMI on ipsilesional side

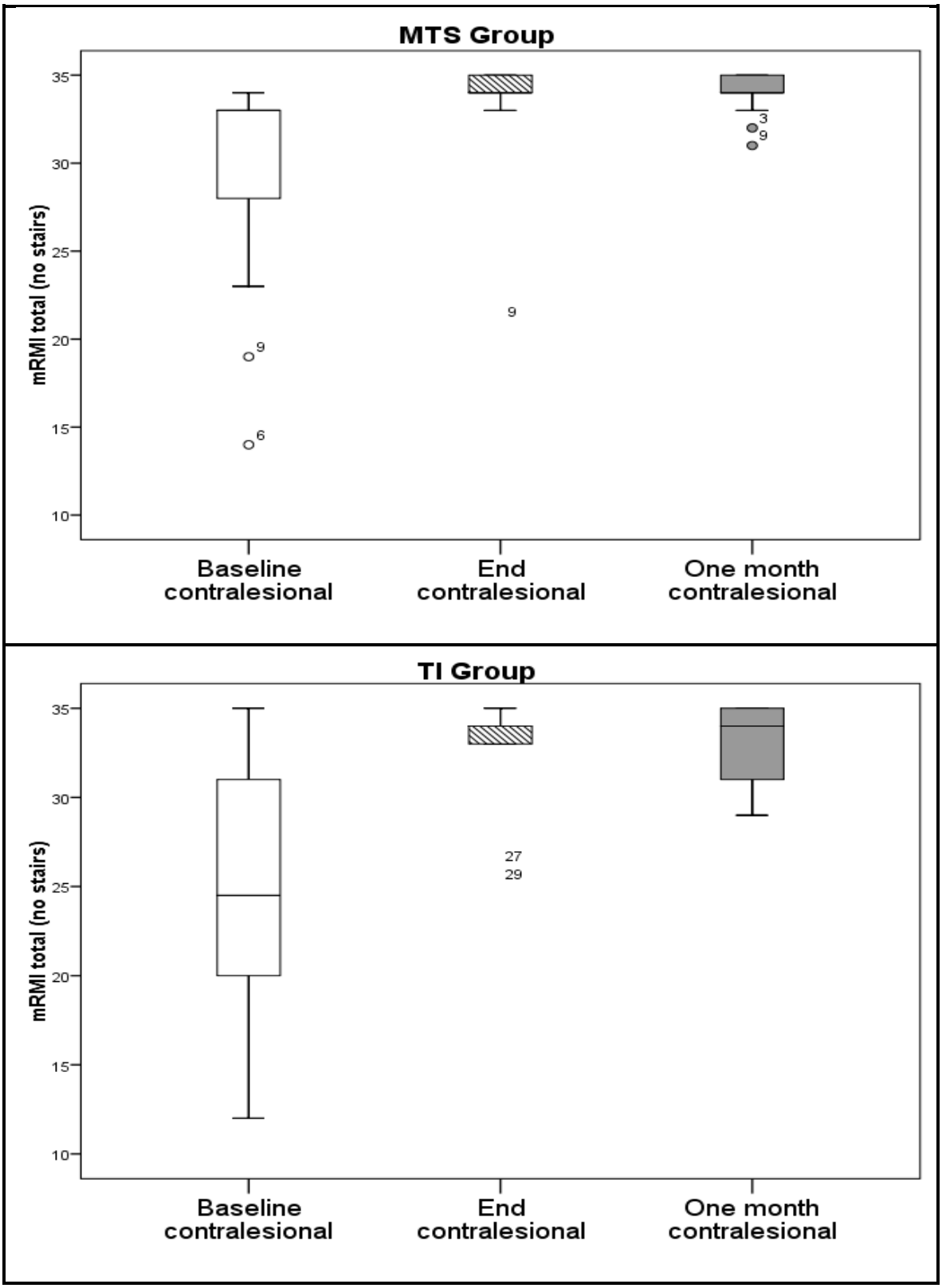


Figure 6.23 Boxplot for all three time-points according to group for the mRMI to contralesional side

6.21.6.5 Pressure insole readings

The pressure insole measurements were undertaken at baseline, end of intervention and one-month follow-up. There were large costs involved with the purchase of the Tekscan (F-Scan) equipment (approximately £14,000). The two aspects analysed were: (i) FTI, and (ii) mean COFV in an AP direction. The differences between medians and 95% CIs from baseline to end of intervention, and from baseline to one-month follow-up were calculated.

Most participants were able to calibrate their own insoles, with the assistance of a vertical surface (for stability only and not for putting weight through), and assistance of a researcher, if required. It is acknowledged that this may have affected the total weight taken through the one leg; however, in view of the significant impairment of many of the participants it was necessary to take a pragmatic approach to the calibration procedure and this was another important aspect for analysis as part of the feasibility study.

For FTI: The 95% CI for the differences between medians from baseline to end of intervention were -292.37 to 178.92 for the MTS group, and -66.78 to 181.28 for the TI group; and from baseline to one-month follow-up -211.62 to -34.82 for the MTS group and -245.87 to 318.84 for the TI group.

For COFV: The 95% CI for the differences between medians from baseline to end of intervention, were -1.40 to 4.60 for the MTS group and -0.30 to 3.40 for the TI group and for baseline to one-month follow-up were -1.00 to 5.50 for the MTS group and -0.50 to 3.60 for the TI group.

The results are presented in tables 6.14 and 6.15 and in the box plots in figures 6.24 and 6.25, and an example representation of the presentation of the pressure under the feet at baseline, end of intervention and one-month follow-up is shown in figure 6.26.

Table 6.14 Force time integral (FTI) from pressure insole readings from contralesional foot at baseline, end of intervention, and one-month follow-up, including change from baseline to end and baseline to follow-up, showing median (IQR) and range of results (Newtons/sec)

Group		Baseline	End of Intervention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS	Median (IQR)	756.39 (564.06, 928.30)	500.02 (467.78, 724.75)	-102.04 (-292.37,178.92)	554.74 (377.70, 748.90)	-105.98 (-238.59, -36.01)
	Range	32.70–1555.79	355.93–1387.43	-461.82–323.23	319.52–1438.23	-508.51–471.57
	95% CI			-292.37 to 178.92		-211.62 to -34.82
TI	Median (IQR)	585.44 (440.95, 766.92)	672.97 (535.20, 848.43)	71.14 (-62.80,176.48)	707.96 (431.62, 876.15)	6.74 (-210.40, 284.92)
	Range	374.34–1125.25	334.51–1927.57	-246.52–1019.23	306.77–996.93	-418.05–622.59
	95% CI			-66.78 to 181.28		-245.87 to 318.84

MTS group n=18 TI group n=12

Table 6.15 Mean centre of force (AP) velocity from contralesional foot at baseline, end of intervention, and one-month follow-up, including change from baseline to end and baseline to follow-up, showing median (IQR) and range of results (cm/sec)

Group		Baseline	End of Intervention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS	**Median (IQR)**	3.45 (1.30, 6.80)	2.10 (2.30, 8.00)	0.80 (-1.40,4.60)	3.35 (0.40, 9.40)	1.35 (-1.15, 5.55)
	Range	0.00–13.90	0.20–13.50	-7.60–7.00	0.00–13.90	-6.80–9.50
	95% CI			-1.40 to 4.60		-1.00 to 5.50
TI	**Median (IQR)**	1.90 (1.10, 3.55)	3.90 (1.55, 6.15)	1.30 (-0.23, 3.40)	2.15 (1.60, 5.90)	0.35 (-0.45, 3.38)
	Range	0.00–7.5	0.5–10.90	-1.70–5.30	0.40–14.20	-1.90–6.70
	95% CI			-0.30 to 3.40		-0.50 to 3.60

MTS group n=18 TI group n=12

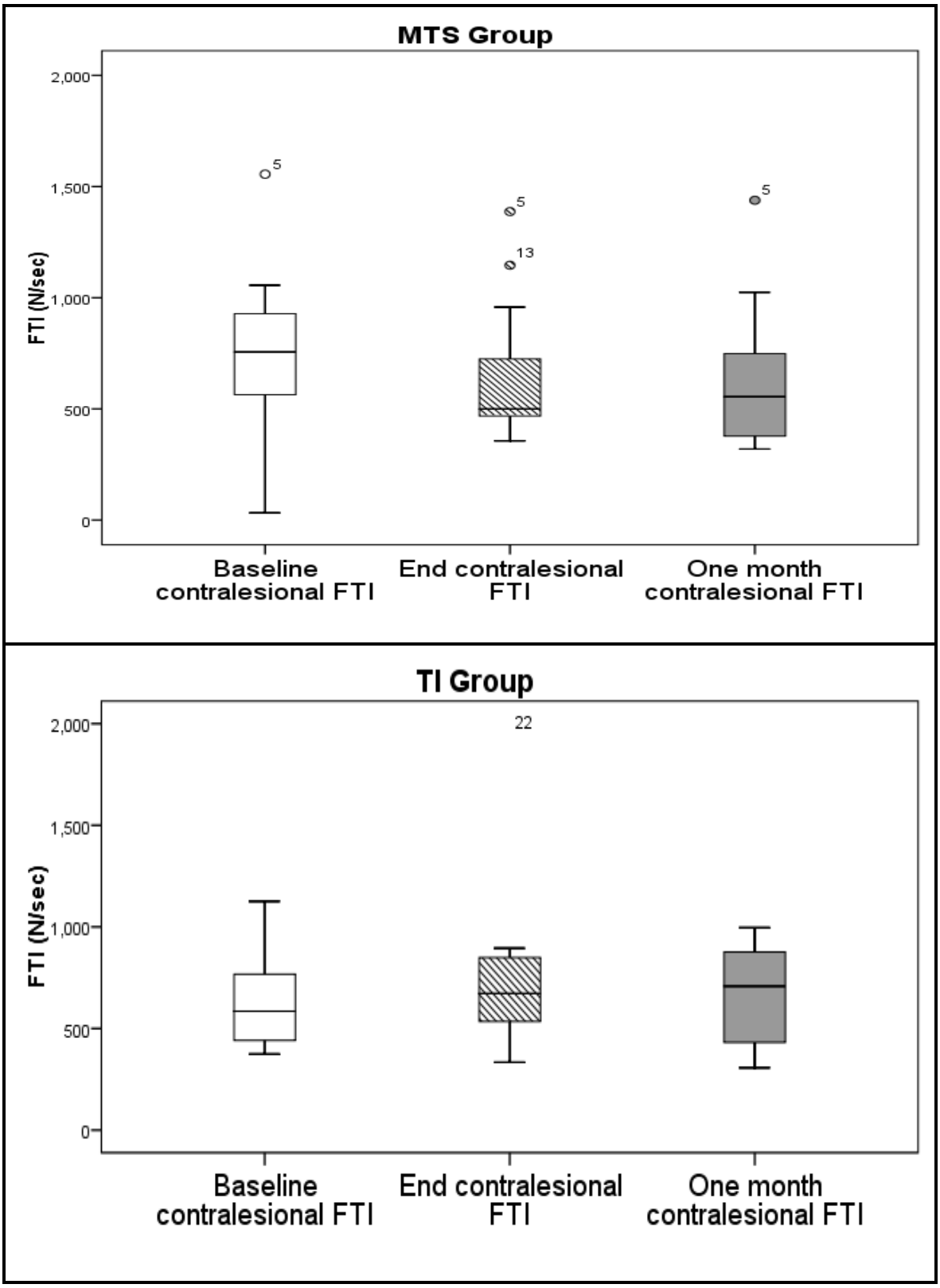


Figure 6.24 Boxplot of contralesional force time integral (FTI)

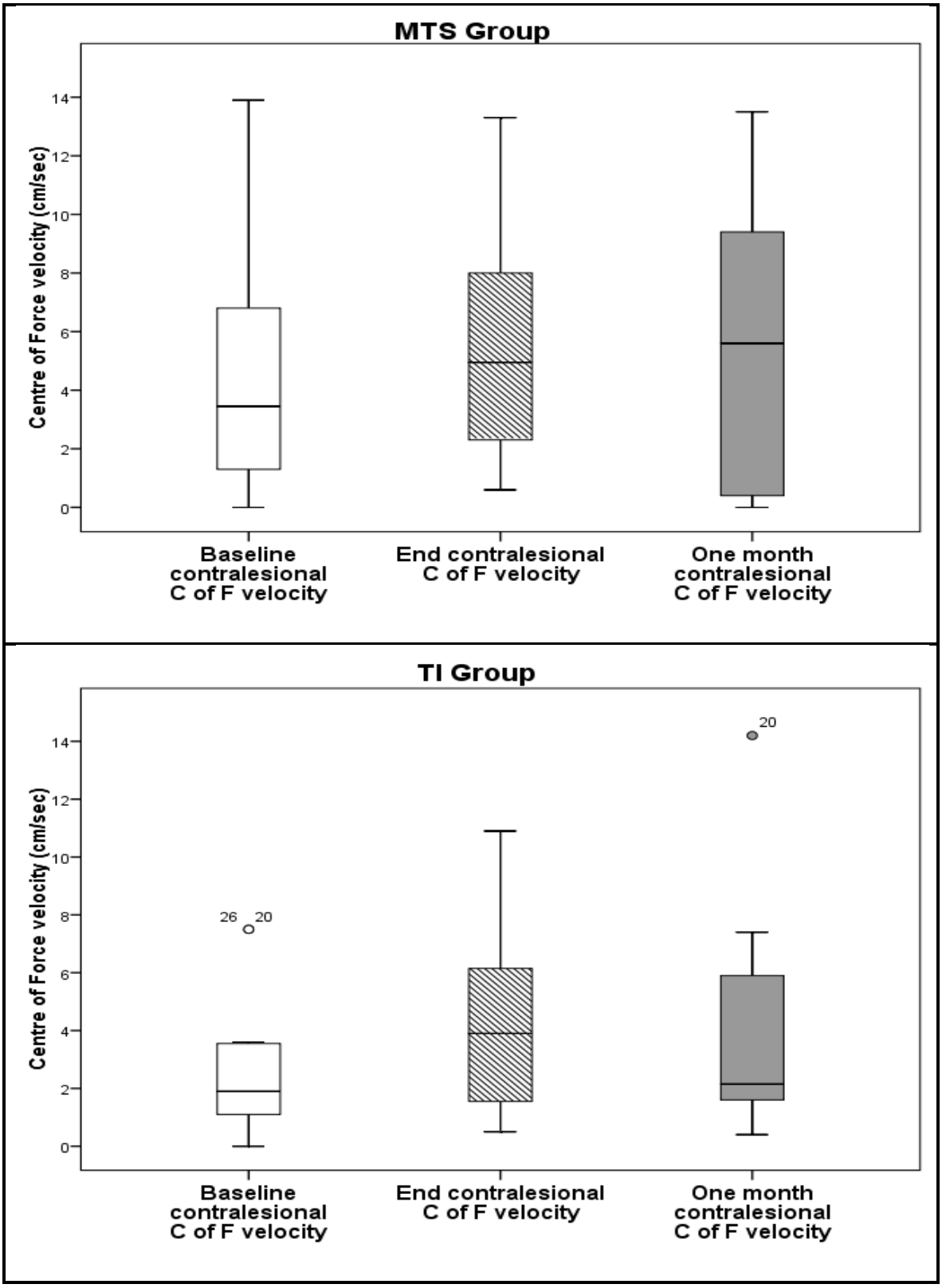


Figure 6.25 Boxplot of mean centre of force velocity for the contralesional side

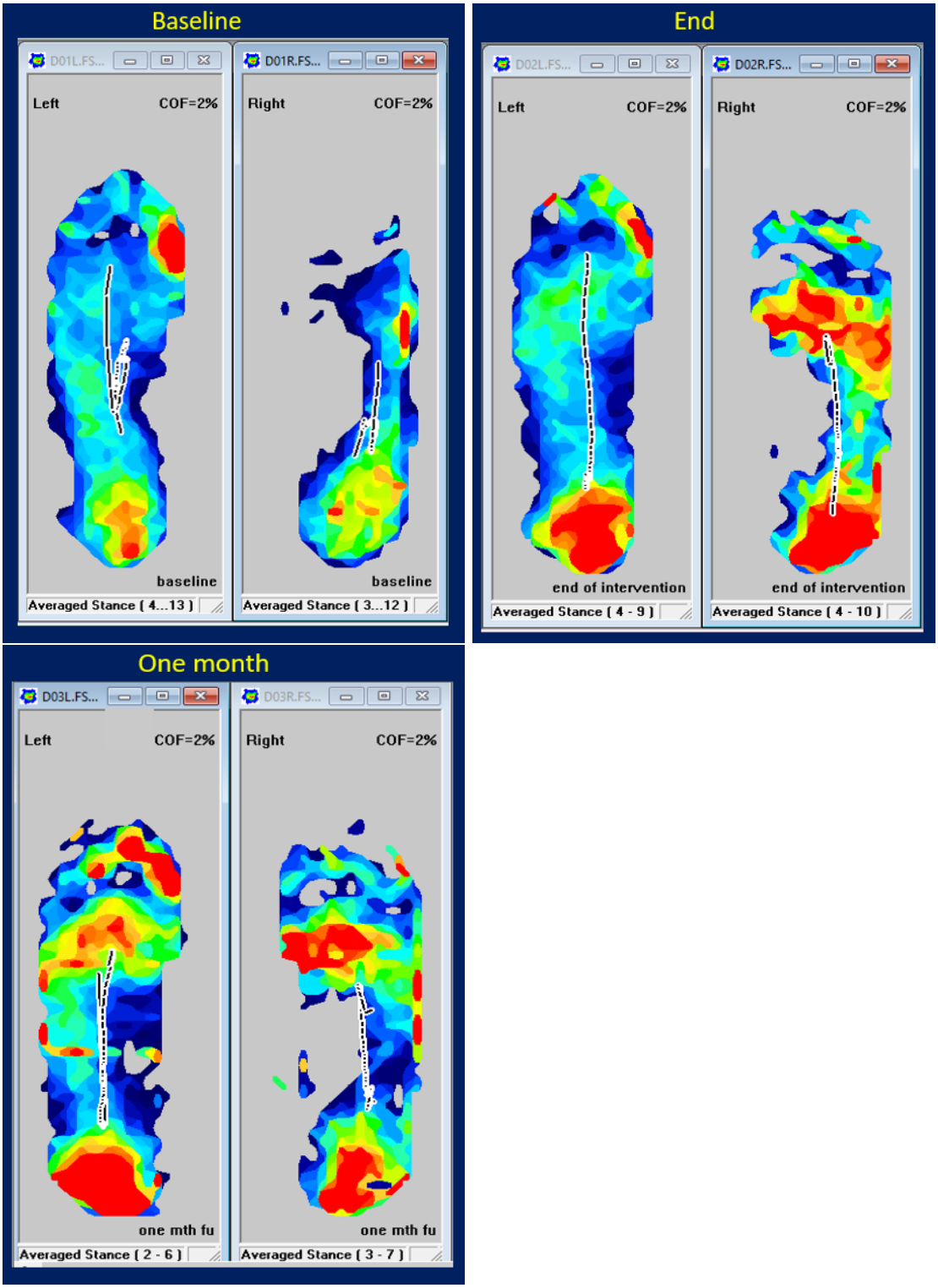


Figure 6.26 Example of the representation of pressure under the feet and centre of force trajectory: baseline, end of intervention and one-month follow-up

6.21.6.6 Lower Extremity Motricity Index (LEMI)

LEMI measures were undertaken regularly: at baseline; after five, ten and fifteen interventions; after all twenty interventions (end of intervention); and at one-month follow-up. This was to ascertain more clearly when any changes occurred, if indeed change did occur. No costs were involved in the use of this OM.

The differences between medians (IQR) and 95% CIs from baseline to end of intervention were 16 (0,19), (95% CI 0 to 19) for the MTS group and 12 (2, 24), (95% CI 19 to 25) for the TI group; and from baseline to one-month follow-up were 16 (0, 24), (95% CI 0 to 24) for the MTS group and 16 (2, 20.75) (95% CIs 0 to 21) for the TI group.

The results are presented in table 6.16. The changes are presented in the boxplots shown in figures 6.27 and 6.28. A line graph is also presented for the LEMI (figure 6.29) to give a visual representation of changes over time.

It is of interest to note that there was an instant increase in median score by 8 points in the MTS group, from baseline to interim 5 (which was then maintained at end of intervention and actually increased by the one-month follow-up); however, there was no change in median score in the TI group until the end of intervention assessment. This fits with the experiences of the participants in the TI group, who reported it taking a few weeks to feel any benefit from the TIs.

Table 6.16 LEMI scores at baseline, end of intervention, and one-month follow-up, including change from baseline to end, and baseline to follow-up, showing median (IQR), range and 95% CIs

MTS group n=19 TI group n=15 at baseline; n=12 at end and one-month follow-up

Group		Baseline	Interim 5	Change baseline to Interim 5	Interim 10	Change baseline to interim 10	Interim 15	Change baseline to interim 15	End of Inter-vention	Change from baseline to end	One-month follow-up	Change from baseline to follow-up
MTS	**Median (IQR)**	76 (59.5, 88)	84 (59.5, 96)	4 (0,16)	84 (70, 92)	6 (0,16)	84 (73, 92)	4 (0,20)	86 (76, 96)	16 (0, 19)	92 (84, 100)	16 (0, 24)
	Range	33–100	43–100	-12–27	34–100	-17–32	29–100	-22–39	48–100	-14–33	49–100	-8–39
	95% CI									0 to 19		0 to 24
TI	**Median (IQR)**	76 (43.5, 84)	76 (48, 88)	8 (-6,14)	76 (62, 92)	8 (-.5,16.75)	84 (64.5, 96)	9 (2,24.75)	84 (67, 96)	12 (2,24)	84 (65, 96)	16 (2, 20.75)
	Range	0–100	15–100	-23–17	15–100	-18–26	29–100	-12–45	24–100	19–25	20–100	-8–24
	95% CI									0 to 24		0 to 21

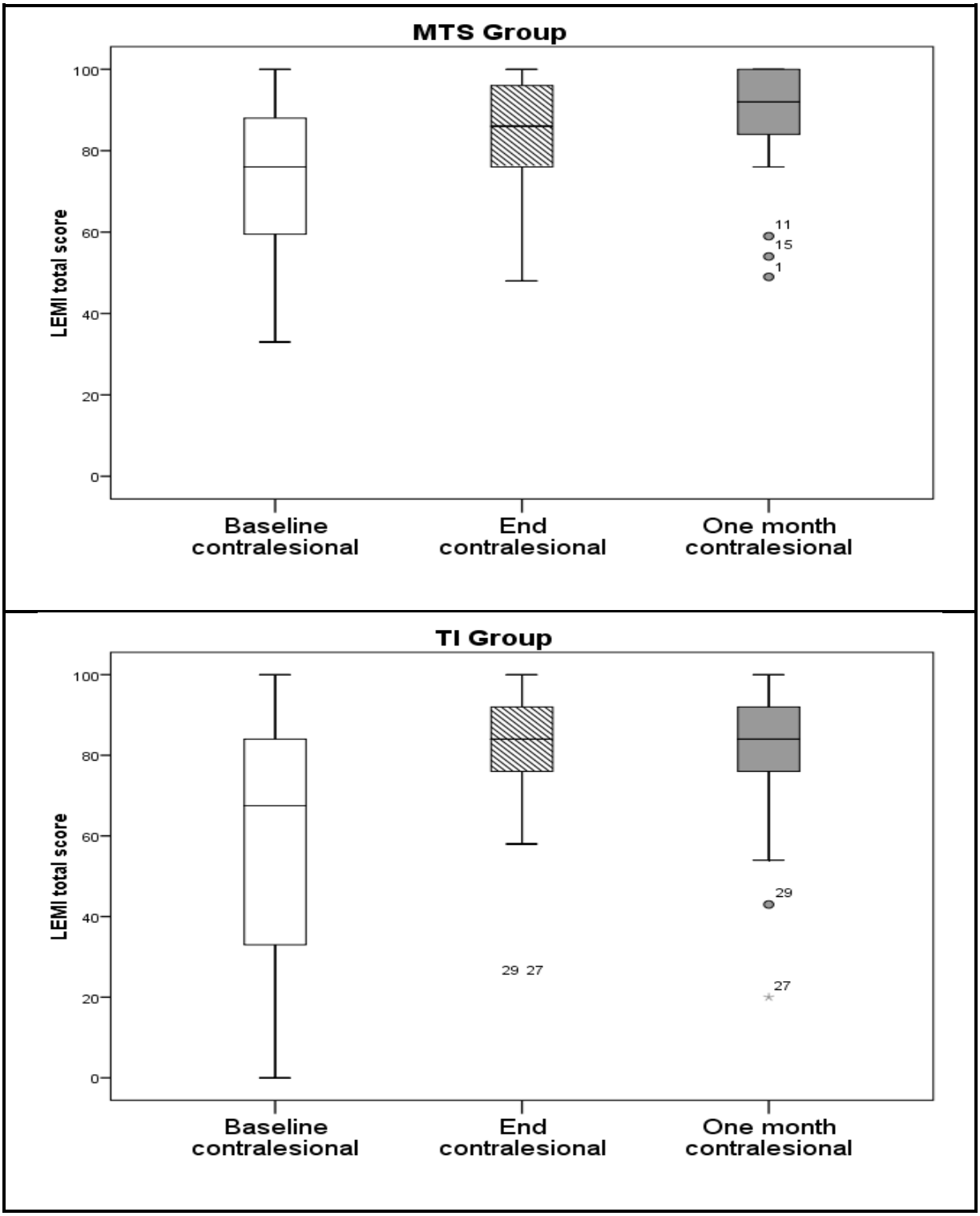


Figure 6.27 Box plot of LEMI results, both groups baseline, end and follow-up only

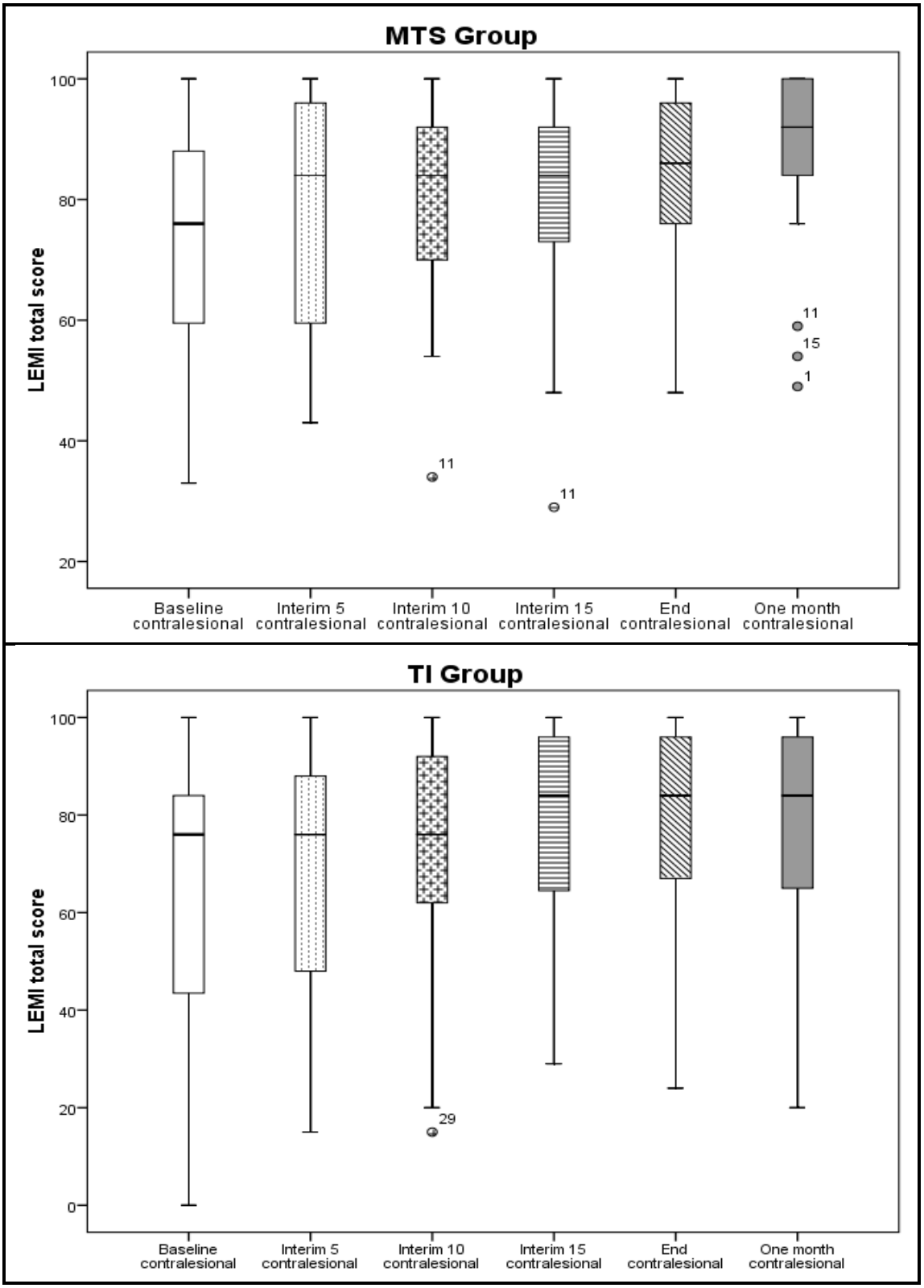
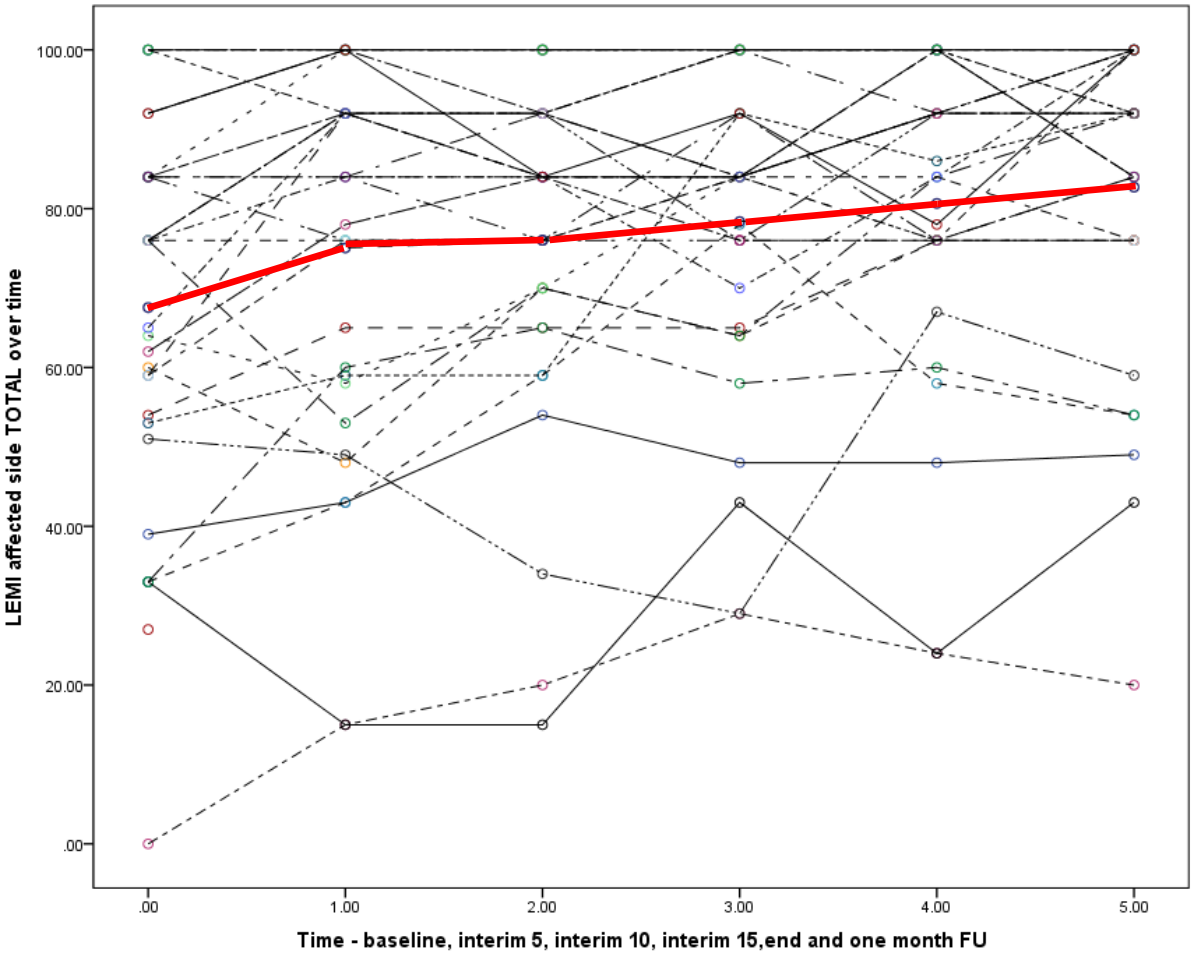


Figure 6.28 Box plot of LEMI results for all six time-points according to group



The red line represents the average scores for all the participants

X axis represents order of assessments, not actual temporal spacing:

.00 represents baseline, 1.00 – interim 5, 2.00 – interim 10,

3.00 – interim 15, 4.00 – end of intervention and

5.00 – one-month follow-up.

Figure 6.29 Line graph of the LEMI results over time for all participants

6.21.6.7 SWM sensory threshold testing

The SWM measures were also undertaken regularly: at baseline; after five, ten and fifteen interventions; after all twenty interventions (end of intervention); and at one-month follow-up. This was to ascertain more clearly when any changes occurred, if indeed change did occur. There were initial costs for purchasing the SWMs (approximately £240). Both the contralesional and ipsilesional sides were tested, with the results reported separately. Four separate points were tested (for full details please see the methodology section 6.4.2). The points tested were under the heel, pad of the hallux, 1st MTP joint and 5th MTP joint. For ease of reporting, these points will just be referred to as heel, hallux, 1st MTP and 5th MTP.

Contralesional side

The results are presented in table 6.17 and figures 6.30, 6.31, 6.32 and 6.33, and a line graph is presented for the hallux point for all participants (figure 6.34) giving a visual representation of changes over time. It can be seen from the line graph that there is a steady increase in the ability to feel the SWMs at the hallux point over time up until the end of intervention assessment. There is then a decline observed in the ability to detect the SWMs between the end of intervention and one-month follow-up.

From the box plots, it is also possible to observe that the median score for the MTS group increases steadily over time, whereas the TI group median is variable over time. Also, of note, is that the median scores in the MTS group were higher

than the median scores in the TI group. Indeed the 5th MTP score on the contralesional side reached a median of 14.5 (11,16) which is very close to the threshold for normal plantar threshold sensation (15 and above). The other three points were also very close to achieving a level equating with diminished sensation (11–14), as opposed to diminished protective sensation (8–10). Whereas, in the TI group, the heel median score aligned with the loss of protective sensation category (2–7), and 1st MTP score was in the range of the diminished protective sensation category. However, both the hallux and 5th MTP results achieved a level of diminished light touch (11–14). The categories are explained in table 6.2, (section 6.4.2) in a sensory evaluation chart for sensory assessment. The implications of these findings will be discussed in chapter seven.

Ipsilesional side

The sensory threshold level for the ipsilesional side was also measured on two occasions (baseline and end of intervention) as a comparison to the contralesional side. The results are presented in table 6.18 and figure 6.35.

Table 6.17 Results for sensory threshold testing of the contralesional foot with SWMs at baseline, after 5, 10 and 15 treatments, and at end of intervention and one-month follow-up, showing median (IQR) and range of scores

Group/point assessed		Baseline	Interim 5	Interim 10	Interim 15	End of intervention	One-month follow-up
MTS							
Heel	**Median (IQR)**	6 (4,11)	6.5 (5,10)	9 (6,11)	10 (6,11)	10.5 (5,11)	10.5 (5,11)
	Range	0–17	2–17	2–16	1–15	4–19	1–13
Hallux	**Median (IQR)**	10.5 (6,14)	11 (5,16)	11.5 (6,15)	11 (7, 16)	10.5 (6, 12)	11 (9, 14)
	Range	0–18	2–17	4–18	0–19	4–20	4–18
1st MTP	**Median (IQR)**	11 (9,12)	12 (9, 17)	11 (10,16)	12.5 (8,17)	12.5 (9,16)	11.5 (10,16)
	Range	0–18	4–18	5–20	4–20	3–19	4–18
5th MTP	**Median (IQR)**	10 (6,13)	11 (9,15)	11 (10,13)	12.5 (11,17)	14.5 (11,16)	13 (11,16)
	Range	4–18	5–18	4–18	3–20	5–19	4–17

TI							
Heel	**Median (IQR)**	4 (3, 7)	6 (4, 10)	4 (1, 11)	6 (4, 11)	4 (4, 10)	4 (4, 10)
	Range	0–11	0–11	0–12	0–17	0–17	0–15
Hallux	**Median (IQR)**	5 (2,11)	11 (4, 12)	9 (5, 11)	13 (6, 17)	12 (11,16)	9 (5, 11)
	Range	0–15	0–16	0–18	0–18	3–18	0–18
1st MTP	**Median (IQR)**	6 (4,10)	11 (5,13)	7 (3,15)	13 (5,16)	10 (3,15)	10 (4,14)
	Range	0–11	0–19	0–18	0–17	0–17	0–18
5th MTP	**Median (IQR)**	7 (5,10)	11 (7,11)	11 (6,16)	11 (4,15)	11 (4,14)	11 (4,13)
	Range	0–11	0–15	0–17	0–17	0–17	0–17

MTS group n=19 for all assessments except interim 15, n=18. TI group baseline, n=15, all other assessments n=13

Table 6.18 Results for sensory threshold testing of the ipsilesional foot with SWMs at baseline, after 5, 10 and 15 treatments, and at end of intervention and one-month follow-up, showing median (IQR) and range of scores

Group/point assessed		Baseline	Interim 5	Interim 10	Interim 15	End of intervention	One-month follow-up
MTS							
Heel	**Median (IQR)**	11 (7.5,12)				11 (6.5,12.5)	
	Range	4–18				4–20	
Hallux	**Median (IQR)**	16 (11,17)				12 (10,17.5)	
	Range	6–20				5–19	
1st MTP	**Median (IQR)**	14 (9.5,17)				16 (10.5,18)	
	Range	2–18				1–20	
5th MTP	**Median (IQR)**	12 (10.5,16)				13 (11,16)	
	Range	16–18				5–18	

TI							
Heel	**Median (IQR)**	6 (5,11)				8 (6,11)	
	Range	0–19				0–19	
Hallux	**Median (IQR)**	12 (10,15)				11 (10,18)	
	Range	0–20				0–18	
1st MTP	**Median (IQR)**	10 (6,15)				12 (6,17)	
	Range	0–18				0–20	
5th MTP	**Median (IQR)**	11 (6,11)				11 (9,15)	
	Range	0–17				0–20	

MTS group n=19 for all assessments except interim 15, n=18. TI group baseline, n=15, all other assessments n=13

NB Sensory threshold testing only undertaken for ipsilesional side at baseline and end of intervention.

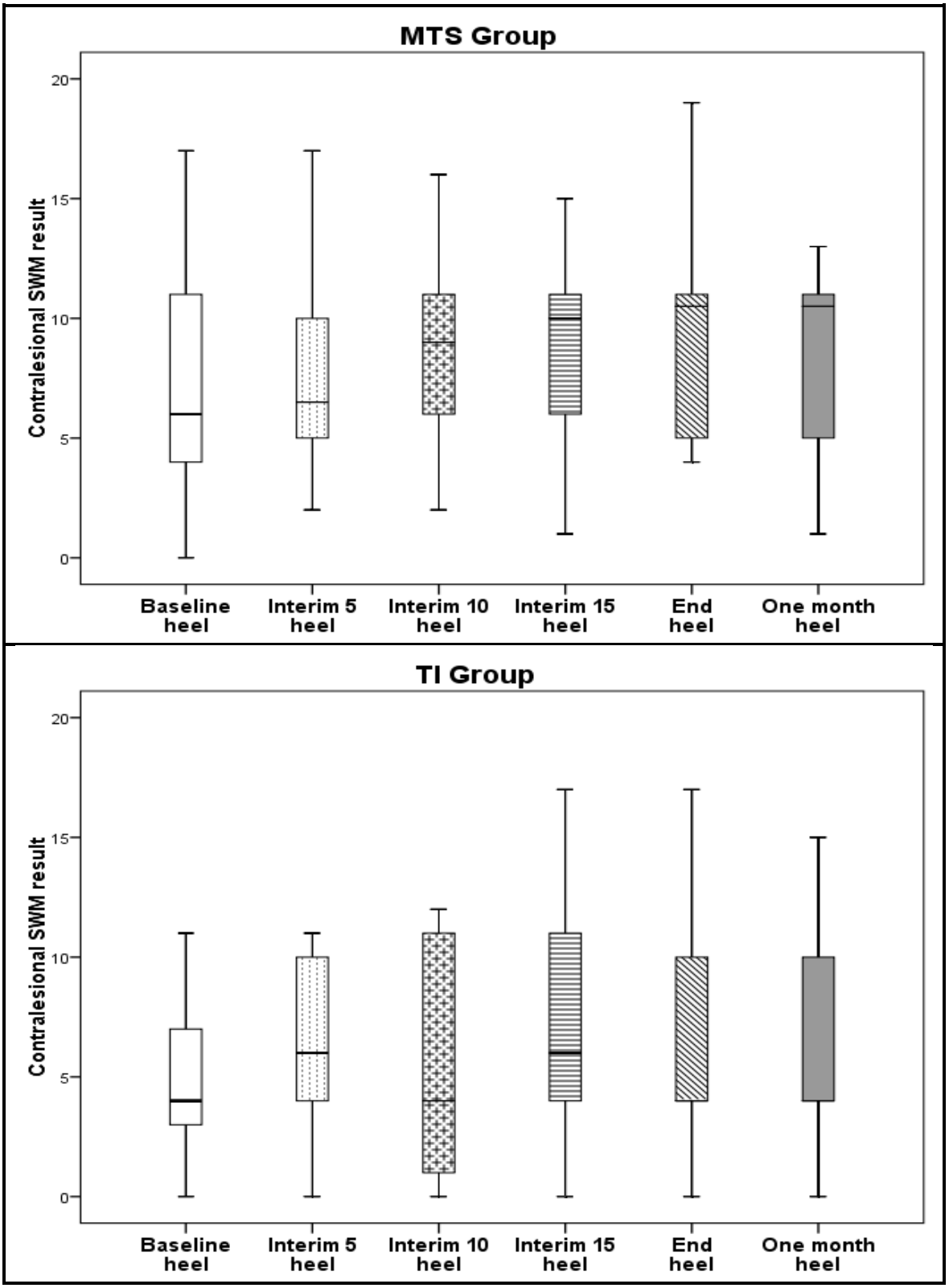


Figure 6.30 Box plot of SWM results for the contralesional heel

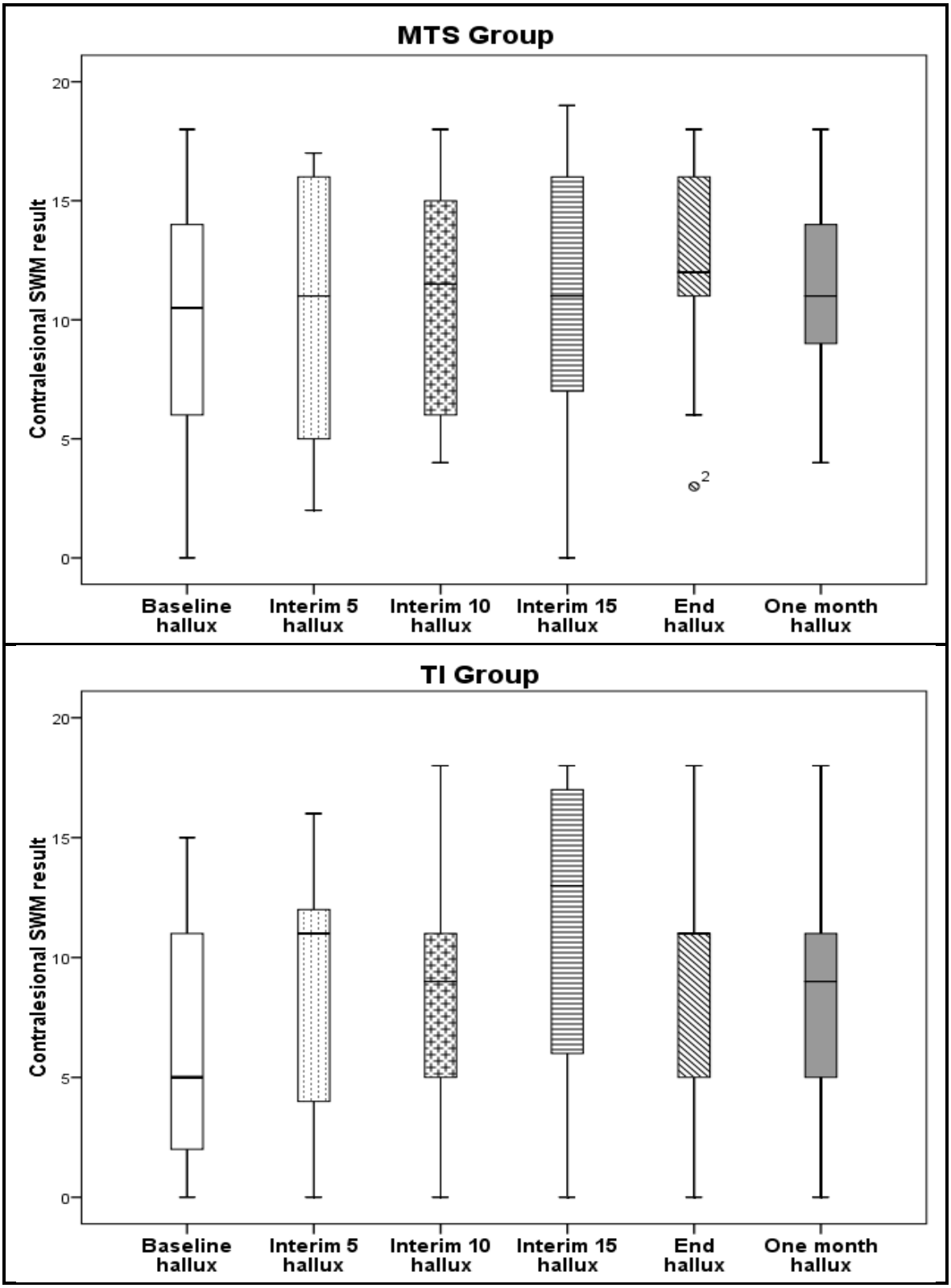


Figure 6.31 Box plot of SWMs results for contralesional hallux

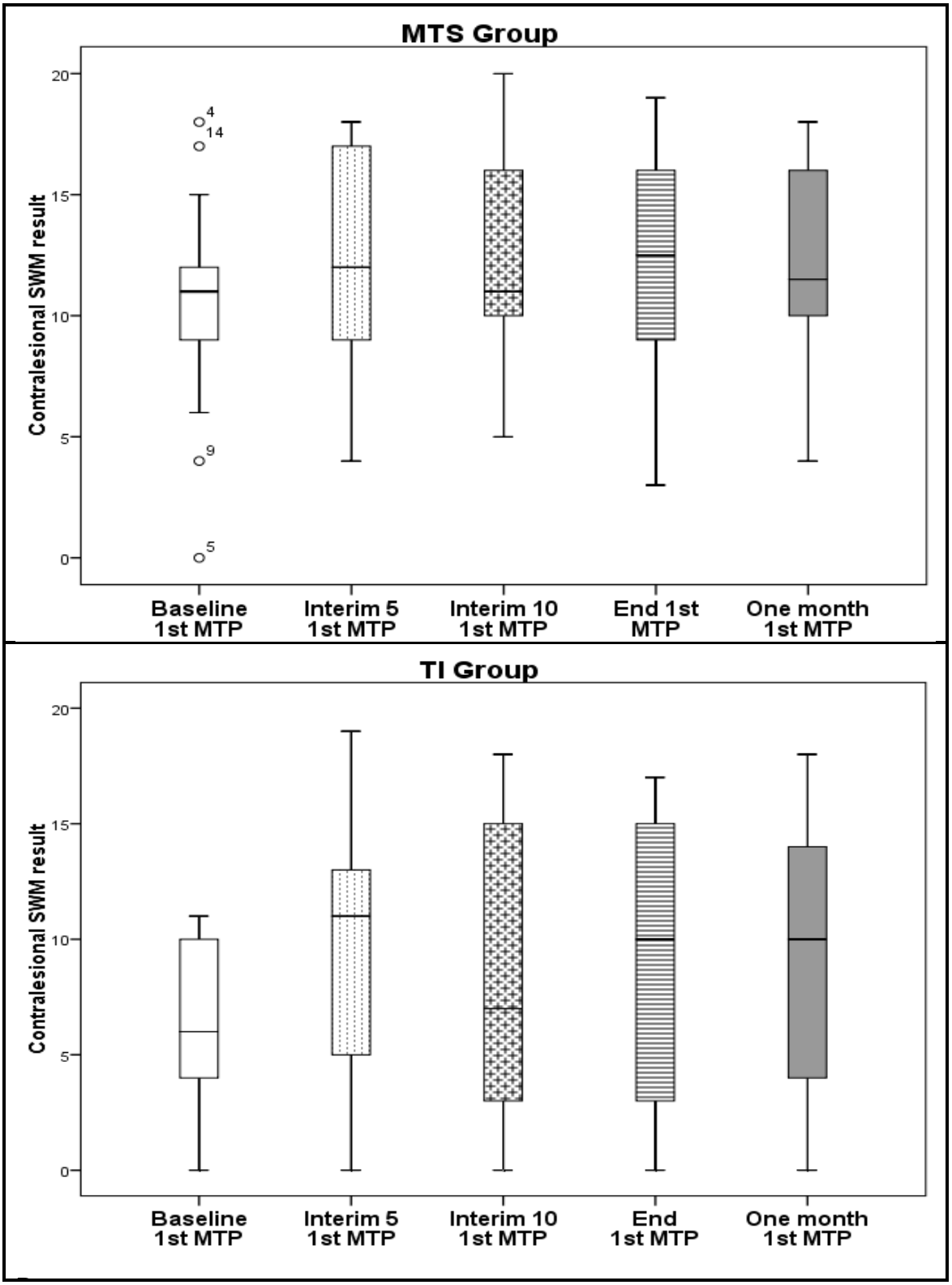


Figure 6.32 Boxplots of SWMs results for the contralesional 1st MTP

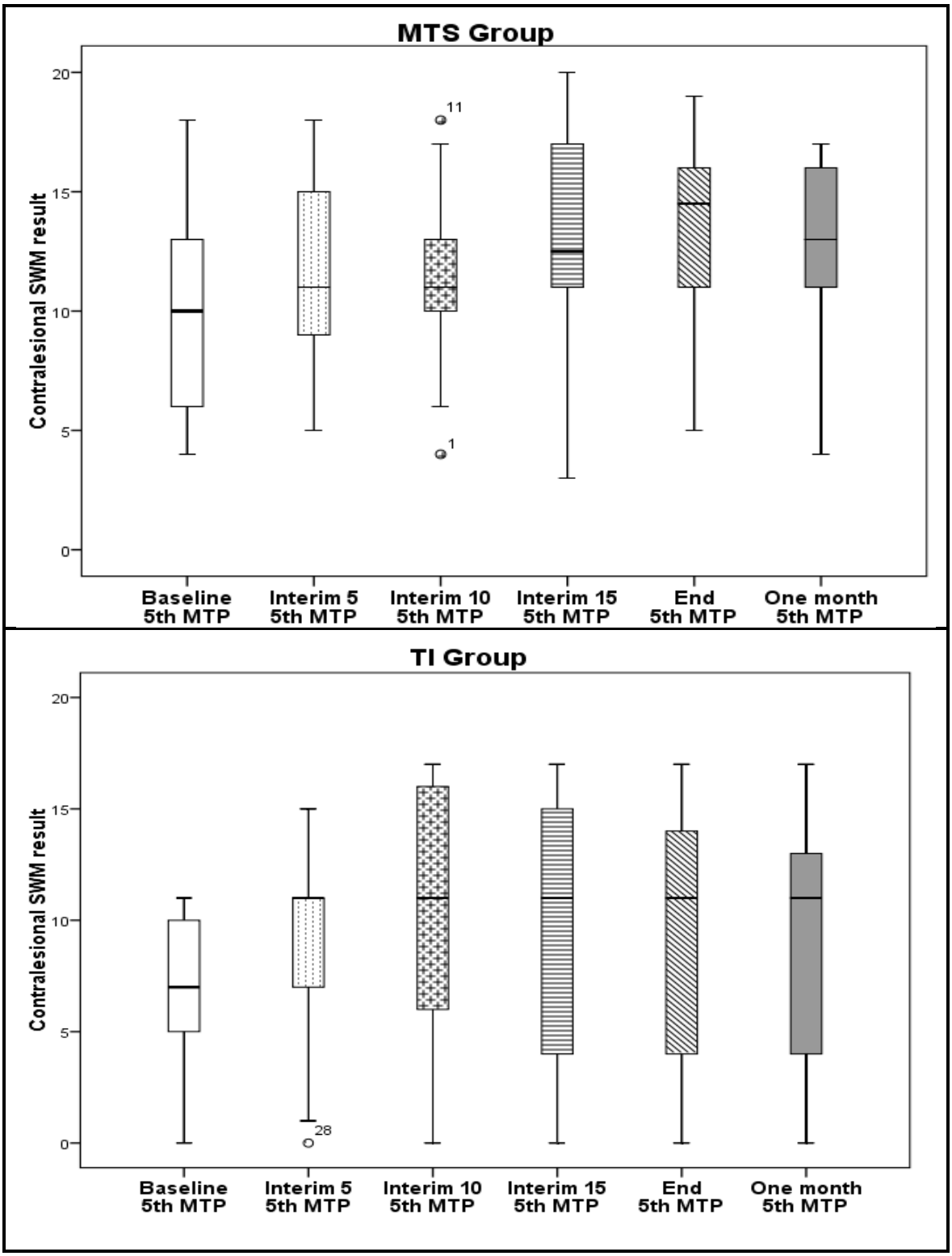
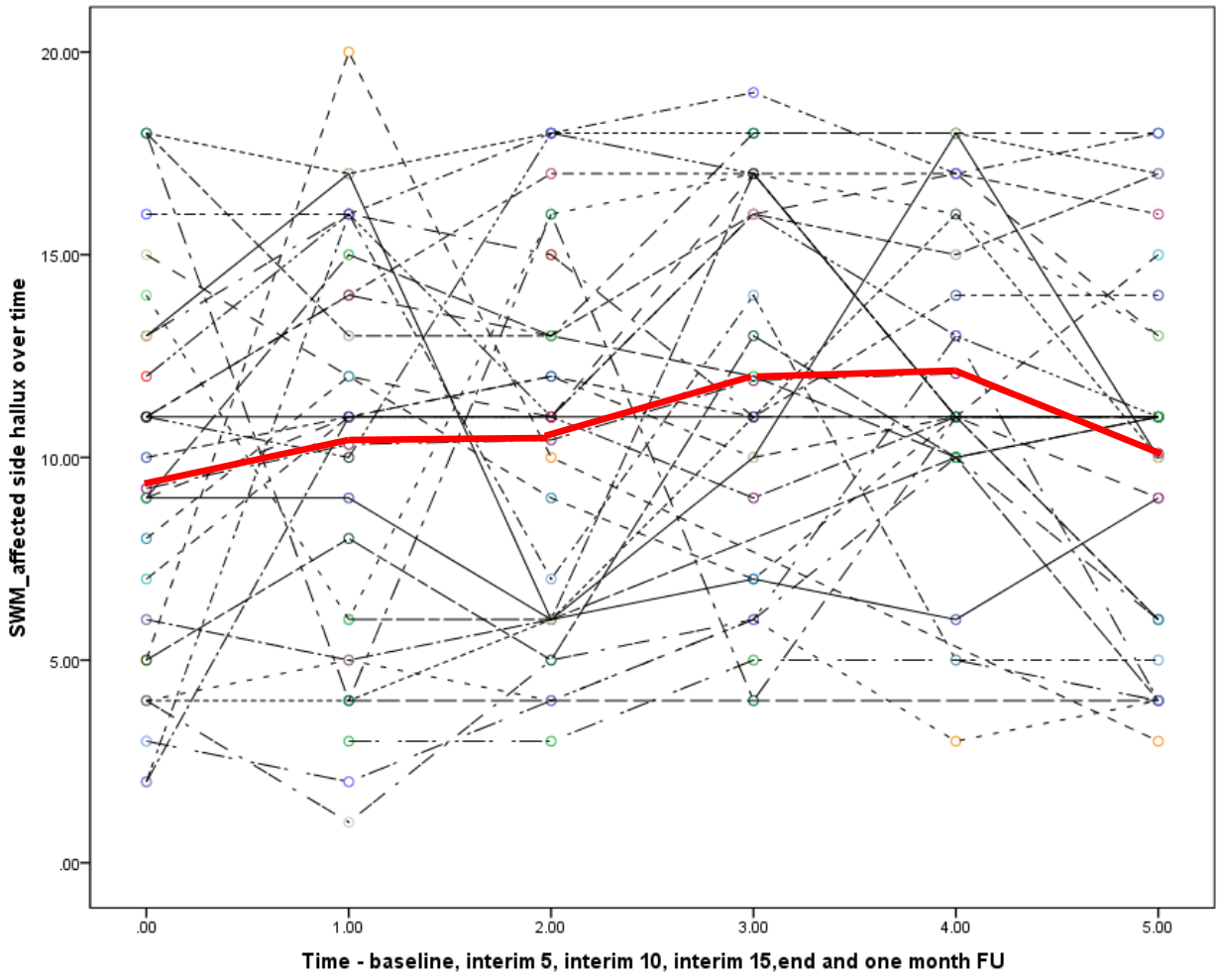


Figure 6.33 Boxplots of SWMs results for the contralesional 5th MTP



The red line represents the average scores for all the participants

X axis represents order of assessments, not actual temporal spacing:

.00 represents baseline, 1.00 – interim 5, 2.00 – interim 10, 3.00 – interim 15,

4.00 – end of intervention and 5.00 – one-month follow-up

Figure 6.34 Line graph of SWMs results for the contralesional hallux

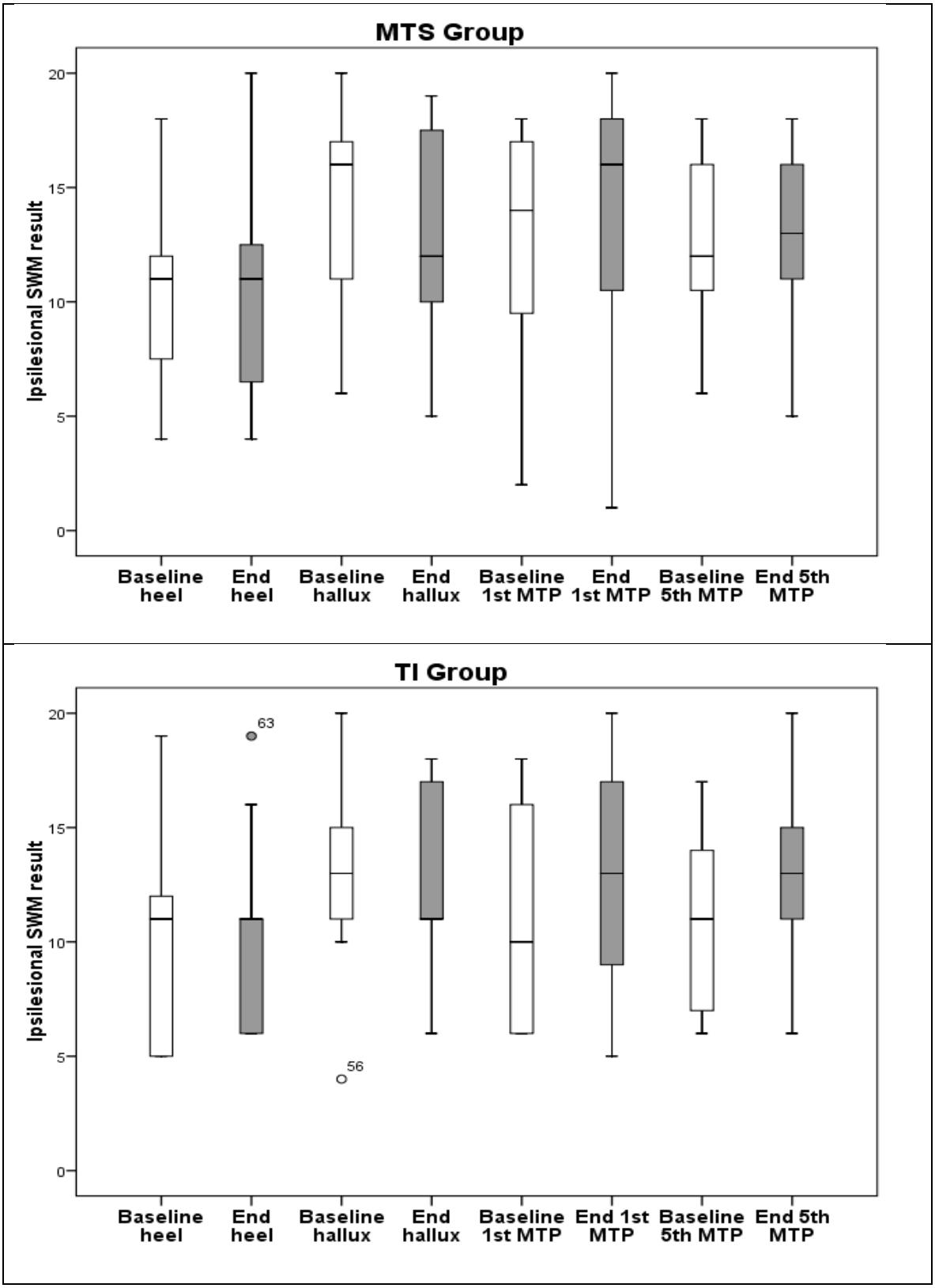


Figure 6.35 Boxplots of SWM results for the ipsilesional side

6.22 Success of blinding

In order to assess whether blinding was successful in the study, the blinded assessor was asked to give their opinion as to what group they thought the participant was in at the one-month follow-up. The blinded assessor was unsure in 29 out of 32 cases (91%). The blinded assessor accurately guessed the group allocation correctly of just three participants (9%). The results are shown in table 6.14.

Table 6.19 Blinded assessor rating for group allocation

Description	Assessor's recording
Confident MTS+TSGT	1/32
Maybe MTS+TSGT	0/32
Unsure which group	29/32
Maybe TI+TSGT	1/32
Confident TI+TSGT	1/32

6.22.1 Feasibility study objectives

Objectives 3a-3h related to Study 3 the MoTaStim-Foot feasibility study were met:

3a Find out if recruitment methods are effective, analysing the recruitment rate and associated data including:

i. number of people invited to participate.
ii. number and proportion of those agreeing to consent to participate.
iii. number of those eligible to participate.

3b Monitor and analyse the number of people who drop out of the trial (attrition rate).

3c Gain pertinent information to inform an appropriate and feasible sample size for a future study.

3d Explore participants' experiences of interventions and their views on the acceptability of the treatments and method of delivery as interventions for a future study.

3e Investigate whether daily diaries and FGs are suitable ways to capture and explore stroke survivors' experiences of the interventions.

3f Investigate feasibility (cost and acceptability to participants) of a battery of OMs for sensorimotor impairment (feeling/sensation and movement) and lower limb function and balance, to inform the choice of primary and secondary OMs for a future trial.

3g Explore responses to either intervention (MTS plus TSGT, or TIs plus TSGT) over time and in relation to the number of treatment sessions delivered; this will help to determine the most appropriate duration of therapy in a future trial.

3h Generate information regarding the participants recruited i.e. participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk, to ensure baseline characteristics of the two groups are comparable and to inform future studies.

6.22.2 Summary of results

Following a successful recruitment strategy, 34 participants were randomized and 32 received all twenty of the interventions, whether MTS+TSGT or TIs+TSGT. The interventions were found to be acceptable to the participants and possible to deliver for the research therapists. OMs were also both appropriate and acceptable. The mixed-method approach enabled detailed insight into the perceptions of the participants via daily diaries and FGs. Feasibility was therefore established. The specific criteria relating to feasibility and acceptability of the MoTaStim-Foot trial will be considered in chapter seven; further information from Studies 2 and 3 will be also be discussed prior to drawing conclusions.

7 CHAPTER SEVEN: DISCUSSION CHAPTER

In chapters one and two, the subject of somatosensory stimulation of the foot and ankle after stroke was introduced, and pertinent literature relating to the topic area was discussed; chapter 3 reported Study 1, a systematic review of the literature relating to somatosensory stimulation of the foot after stroke. The aims and objectives of the studies, and details of methodology were presented in chapter four. In chapters five and six, the intervention modelling study (Study 2), and the MoTaStim-Foot feasibility trial (Study 3) were presented, explained and justified. This chapter will involve a discussion concerning the findings of all three studies, putting them into context within existing literature. Strengths and limitations of the study methodologies will be highlighted, along with pertinent findings; finally, suggestions for future research will be made.

Summary of findings in relation to stated objectives:

7.1 Study 1 - Effectiveness of somatosensory stimulation for the lower limb and foot after stroke: a systematic review

Research objective:

Research objective 1.1 was to systematically review the published literature investigating the effectiveness of somatosensory stimulation applied to the lower leg and foot to improve balance and mobility after stroke

7.1.1 Discussion relating to the findings of Study 1

The regaining of optimal functional movement post-stroke is based upon appropriate integration of both sensory and motor information (Bolognini et al., 2016). Facilitation of afferent input can be undertaken by various methods, and the systematic review highlighted evidence relating to the effectiveness of some of the different types of sensory stimulation. The indications from this systematic review are that sensory electrical stimulation can influence balance or gait parameters effectively, post-stroke, supporting the neurophysiological principles discussed in section 2.2. Sensory electrical stimulation selectively excites large diameter, low threshold non-noxious afferents (A-beta) (Johnson, 2007). A combination of TENS and subsequent task-related exercises resulted in a significant increase in the distance walked over the 6minWT, and increases in gait velocity in one study (Ng and Hui-Chan (2009); this study delivered the greatest amount of treatment (TENS 20 hours and exercise 20 hours), was assessed as being of good quality and included the largest sample (n=109) in the systematic review. These results corroborate previous findings by Levin and Hui-Chan (1992) who applied 15 sessions of daily TENS treatment within a three week period and demonstrated that TENS (but not placebo TENS) significantly reduces and also delays stretch responses, with a resultant decrease in clinical spasticity, measured by the Composite Spasticity Score ($p<0.05$). In the Levin and Hui-Chan (1992) study an increased vibratory inhibition of the soleus H reflex ($p=0.02$) was noted and a phenomenal increase of 820% in the force of dorsiflexion following TENS was observed, which is clearly clinically relevant.

Explanations have been proposed for these positive effects of TENS treatment. It is proposed that the improved strength of dorsiflexion can be attributed to TENS increasing pre-synaptic inhibitory input of the soleus muscle, reducing stretch reflex thresholds, resulting in a reduction in excitability and decreased co-contraction (Levin and Hui-Chan, 1992). This in turn, via neuroplastic changes (taking 2-3 weeks), facilitates a disinhibition of underlying neural pathways associated with dorsiflexion (Levin and Hui-Chan, 1992).

As discussed earlier there is the potential to alter post synaptic potential of motor neurons following percussion to a tendon (Burke et al., 1983), and it would be expected that this neurophysiological mechanism could also be applied to the application of vibration, with expected beneficial effects post-stroke; however, it has not been possible to draw this conclusion from this systematic review. Two of the studies exploring WBV were assessed as being of good quality (Brogårdh et al., 2012; van Nes et al., 2006) and both concluded that there was no benefit from WBV as assessed by BBS. The study by Brogårdh et al. (2012) recruited a sample of just 16, and one of the inclusion criteria was an ability to walk >300 metres. As the BBS is known to have a ceiling effect, particularly in higher functioning stroke survivors (Salbach et al., 2001), this could be a reason why beneficial effects were not demonstrated. van Nes et al. (2006) recruited 53 stroke survivors, however, some caution should be applied to the conclusions drawn from the study by van Nes et al. (2006), in view of the fact that this study recruited stroke survivors in the acute stage post-stroke at just 36.59 (10.18) days; it is therefore impossible to know how much of the improvement was due to spontaneous recovery. Also, only

1.5 hours WBV was delivered over the six weeks and this may also help explain the results. A control group received ‘exercise therapy on music’, however, group sizes of just 27 and 26 are perhaps not sufficiently large to draw definitive decisions when there is such an extensive heterogeneity of clinical presentations seen in stroke (van Nes et al., 2006 p.2332).

Proprioceptive stimulation was provided by standing on different surfaces (hard or soft) with eyes open and closed (Bayouk et al., 2006); wearing postural insoles (Ferreira et al., 2018); sensorimotor foot stimulation (Goliwas et al., 2015); ankle joint mobilizations (Kluding and Santos, 2008), or sensory training (Lynch et al., 2007). There is insufficient evidence at this point in time to support effectiveness of these other interventions on the 10MWT (Bayouk et al., 2006), mean gait velocity (Ferreira et al., 2018), difference in weight distribution in standing (Goliwas et al., 2015) or peak weight bearing difference during STS (Kluding and Santos, 2008). The sample sizes for these five studies were small (<30), with 27 being the largest (Goliwas et al., 2015) but still with just 13 in the experimental group. None of these studies would therefore have been adequately powered to establish effectiveness of these interventions. It should also be noted that in the study by Kluding and Santos (2008) the total number of hours of intervention was just 2.67.

A meta-analysis by Kwakkel et al., (2004) concluded that at least 16 hours of augmented therapy time must be delivered after stroke (over and above that received in the control group) for an effect to be seen, and a more recent

systematic review and meta-analysis concurred with this view suggesting that 17 hours extra therapy were required over a 10 week period (Veerbeek et al., 2014). Excluding the study by Ferreira et al., (2018) which involved wearing insoles for three months and no other additional intervention, only six of the included studies (37.5%) implemented a total intervention time of greater than 16 hours, and only two of these studies achieved a difference in treatment time of >16 hours between the experimental group and the control group (Jung et al., 2017; Ng and Hui-Chan, 2009). Interestingly, both of these studies demonstrated positive effect sizes (0.65 and 0.73 respectively). It has to be questioned whether studies exploring rehabilitation strategies post-stroke, and in particular these studies exploring sensory stimulation are actually delivering the interventions at an adequate dose and intensity for an effect to be expected, and this aspect will be discussed later in this chapter.

Study 1, the systematic review highlighted the insufficient numbers of studies that are adequately powered to enable appropriate conclusions to be drawn about the benefits of this type of sensory input or training. The potential benefits of electrical sensory stimulation have been highlighted and should be considered for application in clinical practice and indeed they have been included in the fifth edition of the National Clinical Guideline for stroke (Rudd et al., 2016). It may also be possible to apply the neurophysiological principles behind the actions of TENS to the other interventions included in this systematic review. It should be remembered that within this systematic review the majority of studies included had

small sample sizes, and many of the studies were not adequately powered or were assessed as being of poor methodological quality.

7.1.2 Conclusions from Study 1, the systematic review

Implementing evidence-based practice within stroke rehabilitation is challenging, due to an insufficient understanding and knowledge underpinning therapeutic interventions (Langhorne et al., 2011), and their complex nature (Craig et al., 2006). Rehabilitation strategies to address the impact of sensory impairment on motor activity and function have not been thoroughly investigated (Carey et al., 1993), and there is a lack of research related to sensory dysfunction of the feet post-stroke (Lynch et al., 2007). This systematic review has highlighted promise for electrical stimulation to facilitate balance and gait following stroke by an expected decrease and delay in stretch responses, resulting in reduced spasticity, and a potential improvement in dorsiflexor activity. The receptors stimulated by electrical stimulation are not the mechanoreceptors that provide proprioception. There is very limited research about the effects of intensive proprioception (this could be any stimulus that is received by the mechanoreceptors in the glabrous skin – so Merkel's disks, Pacinian corpuscles, Ruffini endings, or Meissner's corpuscles – which respond to pressure, stretch, touch, and vibration – or muscle (muscle spindle) joints and ligaments (Ruffini endings)). TENS, on the other hand, delivered at a frequency and pulse width to initiate sensory input stimulates non-noxious large diameter afferents, which is not proprioception.

Research objective 1.1 was completed. The review identified a distinct lack of good quality, rigorous research (with sufficiently large sample sizes, delivering an adequate dose of intervention) exploring the effects of sensory stimulation of the foot/lower limb on balance and gait post-stroke. It is not known whether application of somatosensory input which primes or augments normal afferent input facilitates a change in balance or gait or not. There is a need for further research in this area to be conducted.

7.2 Study 2 – Intervention modelling study

Research objective:

The objective of Study 2 (objective 2.1) was, in conjunction with expert clinicians and informed by the literature, to develop and gain consensus on standardized treatment protocols for delivering a) MTS for the lower limb, b) wearing TIs, and c) TSGT to stroke survivors.

7.2.1 Discussion relating to Study 2

The mNGT was a successful method for developing standardized interventions, which enabled consensus regarding the protocols to be achieved in a relatively short period of time. However, it must be remembered that it is human nature to be hopeful and, therefore, it is a possibility that the therapists in the mNGT possessed optimistic bias (Weinstein, 1980) because they may have wanted the therapeutic interventions to be suitable and could have been optimistic that they will be helpful for stroke survivors in the future. Another issue to consider is the possibility of group think, whereby the participants of a group take a unified approach and are reluctant to upset the harmony in the group (Janis, 1991). However, various strategies were employed to reduce the risk of group think, for example, participants' individual views were sought in advance of the mNGT meeting, and also at the meeting, by following the stages advocated by (Potter et al., 2004).

The method allowed for full participation from the involved therapists, but part of the work was undertaken via email communication limiting the face-to-face contact time for the busy clinicians to just one afternoon. Another potential limitation, which must be acknowledged, is that the number of participants involved in the initial stages of the mNGT work was small (n=12) and only eight clinicians attended the final mNGT meeting, and they were all from a similar geographical area in the UK. Other methodologies such as a Delphi study would have enabled greater insight from different regions who may be less familiar with MTS as a therapy intervention. This would have made the results more generalizable.

Reporting of intervention development is notoriously poor within published studies (Duff et al., 2010; Glasziou et al., 2008), hence, the need for documents such as the TIDieR guidelines (Hoffmann et al., 2014). Study 2 was one of the few studies in which the interventions are reported according to the TIDieR guidelines. It was deemed to be important that adequate time and care was taken when developing the interventions for the MoTaStim-foot feasibility study. The mNGT was an appropriate method for developing and validating the three protocols: MTS to the lower limb, TSGT and wearing of TIs. It was a rigorous method, drawing upon information, summarized from the literature, which was considered in conjunction with the opinions of expert clinicians. However, limitations of the study need to be acknowledged, in that there was a relatively small number of primary participants (n=12) and it is also not known if the work is generalizable to other services.

Nonetheless, a key strength is that the interventions described can be replicated in subsequent research and are transferable to other stroke rehabilitation services.

7.2.2 Conclusions from Study 2

The mNGT enabled discussion and debate, facilitated by the researcher; achievement of 100% consensus from the participants relating to the three developed protocols was possible. Three valid protocols were, therefore, developed in readiness for evaluation in Study 3, the randomized, single-blinded, mixed-methods feasibility trial.

7.3 Study 3, Sensory stimulation of the foot and ankle early post-stroke: a feasibility study (MoTaStim-Foot)

The research objectives for Study 3 were associated with the undertaking of a feasibility study, relating to the overall feasibility of a future large RCT of MTS+TSGT compared to the wearing of TIs+TSGT.

Research objectives:

Objective 3.1 was to determine the feasibility of delivering a trial comparing MTS+TSGT with TIs+TSGT. This was achieved through a number of specific objectives within the feasibility study:

3a Find out if recruitment methods were effective, by analysing the recruitment rate and associated data including number of people invited to participate, the number and proportion of those agreeing to consent to participate, and those eligible to participate.

3b Monitor and analyse the number of people who drop out of the trial (attrition rate).

3c Gain pertinent information to inform an appropriate and feasible sample size for a future study.

3d Explore participants' experiences of interventions and their views on the acceptability of the treatments and method of delivery as interventions for a future study.

3e Investigate whether daily diaries and FGs are suitable ways to capture and explore stroke survivors' experiences of the interventions.

3f Investigate feasibility (cost and acceptability to participants) of a battery of OMs for sensorimotor impairment and lower limb function and balance, to inform the choice of primary and secondary OMs for a future trial.

3g Explore responses to the interventions (MTS plus TSGT or TIs plus TSGT) over time and in relation to the number of treatment sessions delivered; this will help to determine the most appropriate duration of therapy in a future trial.

3h Generate information regarding the participants recruited i.e. participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk to ensure baseline characteristics of the two groups are comparable and to inform future studies.

7.3.1 Recruitment and attrition (Objectives 3a and 3b)

7.3.1.1 MoTaStim-Foot findings

The successful recruitment of all 34 stroke survivors, as planned, indicated success in relation to the recruitment methods (objective 3a). The rate of recruitment for MoTaStim-Foot was 48.57%, calculated as the percentage of people recruited out of the number assessed for eligibility. The attrition rate (objective 3b) within MoTaStim foot, was low, at both the end of intervention and one-month follow-up (5.88% at both time-points). From these comparisons, it is clear to see that from a point of recruitment and attrition, feasibility was achieved in the MoTaStim-Foot trial. Greater insight has been achieved regarding the number

of potential participants who may need to be approached, and the number likely to drop out, as well as expected adverse events and serious adverse events, and these aspects will be important for informing a prospective study.

7.3.1.2 Comparison of MoTaStim-Foot results with other trials

The rate of recruitment for the MoTaStim-Foot trial (48.57%) compares well with other rehabilitation trials. Recruitment for therapy trials can be challenging. In a trial comparing functional strength training with movement performance therapy for the contralesional upper limb post-stroke, the FAST-INdICATE trial, the recruitment rate was only 5.7% of those screened (Hunter et al., 2018); for the FeSTivaLS trial, exploring functional strength training for both upper and lower limbs post-stroke, it was just 4.6% (Mares et al., 2014), and for the SWIFT cast trial (Pomeroy et al., 2016) it was similar at 4.59%. Within the MoTaStim-Foot feasibility study both groups received extra therapy and there was no control group. It is possible that this was an influencing factor in relation to the better recruitment levels because stroke survivors understand the value of physical activity to assist them to gain functional recovery (Morris et al., 2015), and regaining the ability to walk is important for stroke survivors (Pollock et al., 2014b). Another feasibility study included twelve community-dwelling stroke survivors who all received nine 40-minute sessions using a virtual-reality gaming system (Warland et al., 2018), and they also had high recruitment levels (37.5%); again, there was no control group. However, other reasons may exist for the high levels of recruitment in MoTaStim-Foot. The feasibility study was only undertaken at a

single site and the therapists there (who were identifying suitable participants for the trial) were extremely pro-research. Other trials, for example, the FAST-INdICATE trial were multi-site trials with different recruitment strategies, for example, use of the Clinical Research Network. Also, the inclusion criteria for the MoTaStim-Foot feasibility study were kept purposefully wide, for example the inclusion of posterior circulation strokes as well as anterior. These aspects may have been influencing factors in the high recruitment rate for MoTaStim-Foot. Other trials have reported higher levels of attrition: within the FAST INdiCATE trial, an attrition rate of 12.5% at outcome and 27.8% at follow-up (six months after stroke) was reported (Hunter et al., 2018); in the FeSTivaLS trial a rate of 15.5% was reported (Mares et al., 2014), and in the SWIFT Cast trial the attrition rate post-intervention was 19.4%, and 19.9% at six months (Pomeroy et al., 2016). However, it must be remembered that the sample size for MoTaStim-Foot was only small and this could have affected the attrition levels, because if a sample size is larger more adverse events predisposing to attrition would be likely. Nevertheless, this is not always the case; a small sample size also means that even if only a few people drop out there can be a large effect on the attrition rates, as seen in the trial by Warland et al. (2018), where the rate was 16.7%. Another consideration is that the MoTaStim-Foot trial only had a one-month follow up where other trials, e.g. FAST INdICATE, had a six-month follow up.

7.3.1.3 Implications for a future RCT

A total of 18 months was required to complete recruitment in this feasibility study, equating to an average of just under two participants per month (1.89). Recruitment rate was limited because of the capacity of the team of research therapists; the time available to deliver the interventions to participants in various locations, e.g. hospital and community, was fixed per day. Consequently, the maximum feasible capacity for the team had to be calculated accordingly, and this limited the number of participants that could be enrolled in the trial at any one time. This will need to be considered again for a larger trial and careful forward planning of recruitment and enrolment carried out, according to the sample size calculated, with consideration of how many sites would need to be identified, and how many therapists would be required. There is a clear cost implication for this. The recruitment site for MoTaStim-Foot had previously been involved in other rehabilitation trials, and the clinicians were very supportive of the research. It is not known if the same levels of recruitment would apply to other sites, further multi-site piloting is needed to test this out.

7.3.2 Evaluating the selected screening tools

7.3.2.1 MoTaStim-Foot findings

The screening tools selected for the MoTaSTim-Foot feasibility study were found to be quick and effective in screening out participants who did not meet the eligibility criteria. The step test (Hill et al., 1996) was appropriate for excluding three potential participants with minimal disability to the lower limbs after stroke.

Participants were also screened for their level of understanding of simple instructions, to ensure they would be able to complete informed consent and cooperate with instructions within the interventions. No participants were excluded following this test; all the participants recruited possessed a sufficient level of understanding to comply with instructions within the treatment sessions.

7.3.2.2 Comparison of MoTaStim-Foot results with other trials

The step test (Hill et al., 1996), was also used in the FeSTivaLS trial (Mares et al., 2014), and the screening process used for MoTaStim-Foot was the same as the one that had been successfully used in FAST INdICATE (Hunter et al., 2018).

7.3.2.3 Implications for a future RCT

The findings suggest that both of these screening tools would be appropriate to take forward to a subsequent RCT.

7.3.3 Inclusion/exclusion criteria

7.3.3.1 MoTaStim-Foot findings

Both anterior and posterior circulation stroke lesions were considered to be appropriate for inclusion in this feasibility study, and justification for this was provided in the methodology section. The wider trial team was consulted in relation to this aspect and a decision was made to include people with a posterior circulation stroke, on the basis that between 10–15% of people admitted to the

local stroke service are diagnosed with posterior circulation stroke. It was felt that for this feasibility study it was important to be as inclusive as possible. Indeed, Tao et al. (2012) have shown that the symptoms of both anterior and posterior strokes can be very similar. The opinions of expert clinicians were also sought and there was agreement; it was felt that because the cerebellum (which is supplied by the posterior circulation) is key for balance and important in automatic walking it would be appropriate to include people with a posterior circulation stroke. Clinicians also reported that they may use MTS for people following a posterior circulation stroke as well as people with an anterior circulation stroke (Email, from participant 1 in the mNGT work, Appendix 49).

The timing chosen post-stroke falling between the early subacute phase (seven days to three months) and the late subacute phase (three to six months), in a time-period where there is still potential for improvement of impaired function, was appropriate (evidenced by the response to interventions); however, the challenges of this time period are discussed in section 7.5.4.

It should be noted that there was no sensory assessment to ascertain if the stroke survivors had sensory impairments on recruitment to the MoTaStim-Foot trial. This was intentional to ensure that the inclusion criteria could be kept wide; as this was a feasibility study, it was important to include as many people as possible, enabling exploration of who might respond to the interventions. However, this is an aspect that warrants further consideration when moving forward to a future study, and the

reason for this is highlighted in section 7.3.5.4. Further post-hoc analysis will inform decisions as to whether presence of somatosensory impairment should be one of the inclusion criteria for future studies.

The exclusion criteria for the trial were generally appropriate and effective; however, the exclusion criterion related to having botulinum toxin needs to be reviewed. Also, the ceiling threshold was reached for the mRMI for some of the participants. A further screening tool, in addition to the step test, to exclude higher functioning stroke survivors should be considered if the mRMI is to be used in a future study.

7.3.3.2 Comparison of MoTaStim-Foot results with other trials

Some other rehabilitation trials have not included posterior circulation trials, e.g. FAST-INdICATE trial, which explored functional strength training for the upper limb post-stroke (Hunter et al., 2018). Others have included both anterior and posterior circulation strokes e.g. the FeSTivaLS trial, which explored both upper and lower extremity rehabilitation post-stroke (Mares et al., 2014). The differences in neurophysiological control of the upper limb and lower limb were discussed in chapter two (sections 2.6 and 2.8.3). Control of balance and gait can involve many different systems and is more automatic than control of the upper limb which is dependent upon the corticospinal system; in view of these differences it is a logical decision that including posterior circulation strokes is appropriate for lower limb trials analyzing balance and gait but would not be indicated for upper limb trials.

Only one study in the systematic review reported in this thesis also excluded anyone who had received a botulinum toxin injection in the previous six months (Ferreira et al., 2018).

7.3.3.3 Implications for a future RCT

A challenge arose in relation to the issue of including participants with a posterior circulation stroke; during the randomization process, to allocate participants to one of the two groups in the MoTaStim-Foot trial, an ‘affected side’ had to be stipulated enabling stratification for the side of the lesion. For those participants with anterior circulation stroke lesions, the ‘affected’ side was the contralesional side, and this was the expected scenario when the randomization procedure was set up. However, there were three participants with posterior circulation stroke lesions, which were located in the cerebellum in two cases; consequently, either the ipsilesional side or both sides of the body were ‘affected’. When required, a consultation took place with the participant’s NHS therapist, their opinion was accepted in relation to identifying the side which was more affected. This was a useful finding of this feasibility study and must be considered carefully when planning a larger trial.

There was a rationale for exclusion of participants who had received botulinum toxin injections, in that it could be a confounding factor, so it would be impossible to know whether any changes were due to the trial intervention or the effects of the injection. This was not a major concern for this feasibility study because efficacy of

the treatments was not part of the remit of the study; however, it could be an important consideration for a future trial. The senior clinician who was part of the trial management group had concerns regarding this exclusion criterion because the use of botulinum toxin to manage spasticity is increasing with stroke survivors, and she felt this may be an issue when recruiting to future trials. Interestingly, there was one participant who was considered for botulinum toxin after she had received just a few of the trial interventions. The participant chose not to have the injection at that point in time. Her foot control improved, and she was pleased with the progress she made during her time on the trial, particularly when her 5MWT time decreased from 54.9 seconds at baseline to just 6.2 seconds at the one-month follow-up. There are clearly pros and cons to having botulinum toxin as an exclusion criterion; this aspect will need further exploration with experienced clinicians and PPIE volunteers prior to undertaking future trials.

7.3.4 Feasibility of delivering the interventions (Objective 3d)

7.3.4.1 MoTaStim-Foot findings

It was important to establish if it was feasible to deliver the interventions to the stroke survivors. The successful delivery of all 20 sessions to all the participants completing the trial indicates that it is possible to deliver these treatments. The effective delivery of the treatment interventions to protocol was also ascertained by the findings of the independent reviewer (Appendix 41) who observed all the different research therapists within MoTaStim-Foot and confirmed that it was possible to deliver the interventions following the standardized protocols. The

detailed schedules allowed for specific documentation of the combined interventions that were selected and delivered in both the MTS and TSGT interventions for each participant. Additional post-hoc analysis of this information has been undertaken[10] and will inform future studies; this is discussed further in section 7.5.1. However, an acknowledged limitation of the study is that formal feedback was not obtained from the research therapists involved; this would have enabled an understanding of their opinions regarding fidelity of delivering the interventions. This will be even more important to build into future trial designs, when effectiveness of interventions is investigated.

It should be noted that there were differences in dose of the somatosensory stimulation between the two groups. The MTS group received 20 treatment sessions lasting between 30-60 minutes per day, over the 6 week period; however, the TI group could potentially wear the TIs for anything up to 12 hours per day for the 4-6 weeks they were receiving the TSGT. When developing the trial protocol, these differences were discussed in detail. This final trial design was chosen because it was acknowledged that the two interventions aim to stimulate in different ways: MTS is a priming intervention, given prior to retraining motor activity, whereas TIs augment sensory feedback during the retraining of motor

[10] Samuel, E., Hunter, S.M., Aries, A.M. (2019) Analysis of the content and dose of mobilization and tactile stimulation (MTS) and task-specific gait training (TSGT) for the lower limb after stroke delivered as part of the MoTaStim-Foot feasibility trial. (unpublished).

activity. Thus, both interventions (MTS+TSGT, and TIs+TSGT) were delivered in a way that had the optimal potential to achieve their purpose, and to be effective.

7.3.4.2 Implications for a future RCT

The protocols which were developed were successfully delivered and will be appropriate to take forwards to a future RCT.

7.3.5 Acceptability of the interventions (Objective 3d)

7.3.5.1 MoTaStim-Foot findings

In order to successfully deliver the interventions participants had to be willing to participate in therapy, often working hard within sessions, on a daily basis. The information extracted from the daily diaries clearly indicated that the interventions were acceptable to the participants with 85.72% stating that the MTS was not uncomfortable, and 96.49% of the people in this group stating that the TSGT was not uncomfortable either. The TIs were also well accepted with unanimous agreement: 100% of participants stated they were not uncomfortable. Indeed, the analysis showed that only 2.58% of the participants had any discomfort with the TIs at any point in time during the six-week intervention period. The TSGT in the TI group was also well received with 90.96% of people saying it was not uncomfortable. The findings of the FGs corroborate the general acceptability of the interventions. Information regarding acceptability of interventions is imperative to decide whether a larger future study is feasible and appropriate. The MRC guidance advises that it is important to evaluate the impact of the interventions and

understand participants' responses to intervention (Moore et al., 2015), and this aspect was therefore important for achieving objective 3d, confirming the acceptability of the interventions to the participants. The perception by the participants of perceived benefits would be likely to make the treatments more acceptable, despite the fact the participants had to put significant effort into the TSGT.

7.3.5.2 TSGT

TSGT is an intensive form of rehabilitation involving repetition of functional activities such as sitting to standing, stepping, squats etc. (French et al., 2016). Numerous repetitions are required to facilitate neuroplastic changes within the CNS (Birkenmeier et al., 2010; Nudo, 2011) and it was important to find out whether this level of intense rehabilitation was acceptable to the participants. Level 1a evidence already exists supporting TSGT as an appropriate therapy intervention post-stroke. However, it is not known whether potential enhancement of sensorimotor activity via priming with MTS or augmentation via wearing TIs will improve stroke survivors' response to TSGT and increase rehabilitation potential still further or not. The decision to include TSGT for both arms of this study was based upon the known and agreed benefits of TSGT. In conventional therapy, MTS may be implemented to mobilize joints and soft tissues and facilitate the activity of the foot and lower limb; however, it would then be followed by TSGT, putting any additional range and control of movement into functional activities.

When TIs have been worn within studies, normal function is usually encouraged. Hence, the decision to use TSGT within the MoTaStim-Foot trial.

Four participants (20%) reported in the FGs that they found the TSGT tiring, with the other 16 (80%) reporting it to be comfortable, despite the fact that the research therapists pushed the participants quite hard, ensuring multiple repetitions of exercises in line with the recommendations in the literature to facilitate function and neuroplastic changes (French et al., 2016; Lang et al., 2009). The acceptability of the interventions for the participants would be expected to increase if the participants felt they were gaining something from taking part in the trial (Baron et al., 2014). Several participants stated that they felt that if it was not for the treatment, they would not have ever walked again, and the benefit was attributed to both the sensory stimulation (MTS or TIs) and the TSGT.

7.3.5.3 Implications for a future randomized controlled study

Tailoring of the TSGT to individual participants was necessary in view of the heterogeneity of stroke and differing levels of functional ability; however, it was also important to standardize the TSGT delivered, which was achieved via rigorous protocol development in conjunction with the expert clinicians who participated in the mNGT involved in Study 2. One aspect that was addressed through training of research therapists was that the TSGT was primarily a ‘hands-off’ therapy treatment and did not involve facilitatory techniques. The independent observation of the research therapists, built into the MoTaStim-Foot methodology (Appendix

41), confirmed the fact that research therapists were adhering to protocol when delivering the TSGT. Appropriate training for research therapists in relation to how the TSGT protocol should be undertaken and tailored for individual participants must be built into plans for a future trial.

7.3.5.4 Mobilization and tactile stimulation

Two participants in the trial did report severe discomfort or pain during the MTS intervention. One of these participants reported that the pain did not last long and that, after approximately three or four treatments, the MTS was no longer painful, and he then had an increased awareness of his left side. An experienced physiotherapist with extensive neurological skills was involved in the treatment of this participant. The hypersensitivity was purposefully addressed by handling and desensitization work. This finding corroborates with the work of Hunter et al., (2006) who advocate MTS as a means of decreasing hypersensitivity in the upper limb post-stroke.

A second participant also complained of pain and discomfort in response to the MTS treatment, reporting that the discomfort lasted a long time (although the actual time was not specified on the diary sheets). This participant regularly complained of pain and discomfort (not just as a response to the MTS), although this was not of sufficient consistency for it to be considered an adverse reaction. It may have been that this participant was also suffering from an additional disorder, such as complex regional pain syndrome. However, although it may not have been

possible to deliver the full 30–60 minutes of treatment on every occasion for this participant, the pain was never at a level that prevented participation within the study; indeed, he was happy to complete the full course of twenty sessions of intervention on the trial. Interestingly, this participant was treated by a research therapist with more limited neurological rehabilitation handling skills, and it is not known whether this had any influence on the outcome.

The mechanism of how somatosensory stimulation may have an effect needs to be considered. Physiotherapeutic facilitation techniques applied to the upper limb, including methods to facilitate afferent input, have been shown to influence the frequency of muscular response potentials, increasing amplitude as well as reducing the latency of response, measured using single transcranial magnetic stimuli (Hummelsheim et al., 1995). Although direct muscular contraction of the wrist extensors instigated the maximum response in the study by Hummelsheim et al. (1995), it was also found that cutaneous and proprioceptive stimuli had an excitatory effect in severely affected people with stroke. It is not known whether these principles are also applicable to sensory stimulation of the foot and lower limb.

It is anticipated that the techniques within the MTS protocol will deliver a similar effect via the mechanoreceptors to the lower limb, with rapid skin displacement stimulating the quickly adapting mechanoreceptors (discussed in chapter two, section 2.3.2), from the massage and soft tissue mobilization, exciting Meissner's

corpuscles and SA Merkel's discs, as well as passive and accessory movements stretching the skin and stimulating the Ruffini Endings (Vallbo and Johansson, 1984).

Participants reported in both the daily diaries and FGs that the foot felt different following MTS, and this could be due to improved proprioceptive awareness of the foot, through the intrinsic feedback given during the MTS treatment. This increase in afferent feedback can influence the activity within cortical circuits (Ridding and Rothwell, 1999) increasing the muscular response potential (Hummelsheim et al., 1995; Laaksonen et al., 2012). It is therefore proposed that MTS is expected to have an effect by mobilizing and activating the foot, optimizing contact of the whole foot, including the heel with the floor and preparing it for standing and walking, together with assisting with the ability to move the tibia over the stabilized foot during the stance phase of gait. The increased activity within the foot and lower extremity following MTS is therefore expected to facilitate functional activity because MTS is a priming technique, which enhances the excitability of the motor system (Pomeroy et al., 2011). It has been demonstrated that MTS can alter activity and motor impairment in the upper limb in sub-acute (Hunter et al., 2008) and chronic stroke (Winter et al., 2013). Further research is required in relation to MTS delivery to the lower limb post-stroke.

An alternative hypothesis for a mechanism of potential effect for MTS is that it may have similar effects to TENS described by Levin and Hui-Chan (1992) influencing

pre-synaptic inhibitory input and reducing stretch reflex thresholds; a resultant decrease in excitability of the soleus muscle would enable dorsiflexion with reduced antagonistic resistance, thereby facilitating activity of tibialis anterior and selective dorsiflexion. Some potential for efficacy related to MTS treatment has been noted within the MoTaStim-Foot trial, so there is a possibility, that afferent input has a direct effect upon motor control resulting in balance and gait changes; however, these concepts need to be explored in a larger, powered RCT.

It should be noted that Hummelsheim et al. (1995) found that the physiotherapeutic techniques including tapping/rubbing of the skin and weight-bearing, actually had an inhibitory effect on healthy individuals, but a beneficial effect (increasing muscular response potentials) in severely affected stroke patients. It would, therefore, be useful to undertake further post hoc analysis looking into whether there was a link between NIHSS score, or in particular, the lower limb section of the NIHSS/LEMI score too, and any in-group changes observed for the OMs to inform inclusion criteria for future studies.

7.3.5.5 Implications for a future RCT

The skill level of the research therapists needs to be considered carefully for any subsequent trial: hands-on therapy requires skill in terms of assessing the condition, extensibility, and range of movement in soft tissues and joints, in order to determine the appropriate intensity of application for each patient; and although it may be possible to delegate components of MTS to a less qualified or even non-

qualified therapist or carer, it is not known if this approach to delivery would be as effective as treatment delivered by a skilled qualified therapist. This clearly warrants further investigation to explore the feasibility and potential effectiveness of alternative methods of delivering an intensive therapist-dependent intervention that has resource implications. Stroke survivors' opinions of what they feel could be delegated to an assistant or carer, and which aspects require specialist therapy handling, have been explored via a focus group undertaken after the MoTaStim-Foot study was completed.[11]

7.3.5.6 Wearing of TIs

The concept that the TI and smooth insole used within MoTaStim-Foot was acceptable to the participants can be confirmed in view of the unanimous agreement of the participants. Not only did the participants find the insoles comfortable, but they also reported that they had an influence on the feeling within the foot and their ability to balance and walk. Some of these findings are in contrast to those of (Baron et al., 2014), who undertook an exploratory study in a cohort of people with multiple sclerosis, which was embedded within a RCT. Participants in her study wore a smooth insole or a TI (made from the same material, from the same manufacturer as that used in the MoTaStim-Foot trial). Perceptions relating to wearing TIs were explored using semi-structured FGs and

[11] Barwell, K., Aries, AM., Hunter, SM 2019 Stroke survivors' perceptions and opinions of receiving aspects of hands-on physical therapy interventions from a trained carer or other health professional (UK Stroke Forum)

1:1 interviews. Baron et al. (2014) reported that participants' perceptions of both the comfort and potential efficacy of the TIs varied amongst the 13 participants in the qualitative study. A willingness to wear the TIs was found to be linked with participants perceptions of the potential efficacy associated with wearing TIs. These different findings (a lack of consensus) may perhaps be linked to working with people with multiple sclerosis as opposed to stroke, in view of the potential for people with multiple sclerosis to relapse, which could have influenced the results. However, the texture of the insoles used in the MoTaStim-Foot trial are considered to be acceptable for further study with stroke survivors.

The choice of material for the TIs proved to be suitable with many participants able to perceive the TI underfoot and commenting on the difference in feeling. However, it was interesting to hear that it sometimes took a period of time of adjustment (approximately a week to feel the TI, and four to five weeks to notice a change in sensation). Another reflection of the appropriateness of the TI selected is that there were no adverse reactions related to the TI throughout the whole trial period. This was an initial concern of the researcher in case of rubbing/reaction to the insole. It is difficult to compare this issue with other studies because they have not included this information, so a comparison is not possible (Dixon et al., 2012; Kelleher et al., 2010).

Participants in the MoTaStim-Foot trial also reported that wearing a TI increased the sense of stability in the shoe. This is an interesting and important point for

consideration, as it is unclear whether the perceived benefits were simply from the increased stability created by inserting an insole into a shoe, thus providing a general sense of compression around the whole foot, or from the sensation arising from textures stimulating the plantar surface of the foot. Including a smooth insole in the ipsilesional shoe was done to eliminate a feeling of left and right shoes feeling different according to compression and height.

7.3.5.7 Implications for a future RCT

The perceived benefits by the participants and the lack of adverse reactions within MoTaStim-Foot, would seem to support the fact that these specific TIs would be suitable to take forward to a larger study. A decision was made that the insoles should be removed before undertaking the OMs. In view of the potential for augmentation, facilitating sensorimotor control while wearing the TIs, it was important that they were removed to enable parity between the groups, and this should be undertaken in future trials.

A further aspect worth exploration is whether wearing a TI had a different effect on balance and walking than wearing a smooth insole post-stroke. This has not been explored yet.

Inserting the insoles into the shoes was challenging for only one participant out of the 34 (3%). Nevertheless, the ability to insert insoles should be considered

carefully when planning inclusion/exclusion criteria for a larger trial in order to increase standardization of the dose.

7.3.6 Acceptability and use of the selected outcome measures (Objective 3f)

7.3.6.1 MoTaStim-Foot findings

Research objective 3f related to the feasibility of a battery of OMs for sensorimotor impairment. Various issues related to the OMs will be discussed. The battery of OMs was chosen with consideration given to appropriateness of each OM for measuring sensorimotor impairment or lower limb function and balance, as well as attention to validity (George et al., 2000), reliability (Hicks, 2010) and responsiveness to change (objective 3g) (Sim and Wright, 2000), which are required for rigorous clinical research. Several of the OMs were expected to assess change at an impairment level (SWMs to ascertain sensory threshold, LEMI for motor impairment, and electrogoniometer for range of movement). This would give an indication of changes representing restitution i.e. return of structures and function to their previous state (Levin et al., 2009). Other OMs were selected to establish functional changes (5MWT, FAC, pressure insoles and mRMI) and it was anticipated these would give an indication of recovery i.e. returning to pre-stroke body function and structure, and activity level (Bernhardt et al., 2017b). However, it must also be considered that these functional measures may show changes as a result of compensation utilising other strategies to achieve functional gain, rather than reducing impairment (Krakauer et al., 2012).

Most of the OMs were shown to be valid, reliable and responsive to change, however, some (mRMI, electrogoniometer) did have their limitations, which will be discussed; all were acceptable to the participants. The timings of the OMs were found to be appropriate with all outcomes assessed at baseline, end of intervention and one-month follow-up. The LEMI and SWMs were measured more frequently (after five, ten and fifteen treatments).

7.3.6.2 LEMI

Interestingly, the strength observed at end of intervention for the LEMI was maintained at follow up (chapter 6, figure 6.29), perhaps because the participants' functional level was maintained, and repetitive practice continued, for example, by walking and practicing sitting to standing etc.

Although strict protocols were followed when undertaking the OMs, there was one issue which arose with the LEMI testing for one participant that had not been anticipated. It was noted that if she wore shoes, she could achieve dorsiflexion; however, if she was in bare feet she was unable to achieve even a flicker of activity from the dorsiflexors. This could perhaps have been because of sensory stimulation from the shoe. Following discussions between the chief investigator and research therapists, it was decided that all participants should be tested without their shoes on. This was a useful finding of the feasibility study to inform protocols for future studies. The LEMI was an appropriate OM to use in the MoTaStim-Foot trial and is valid, reliable (Cameron and Bohannon, 2000; Fayazi

et al., 2012) and responsive, as well as quick to administer and would be a suitable secondary OM to use for future studies.

7.3.6.3 Sensory threshold testing using SWMs

The contralesional side was measured for sensory threshold, using the SWMs at baseline, after five, ten and fifteen interventions, as well as end of intervention and one-month follow-up. The line-graph for the sensory threshold of the contralesional hallux (chapter 6, figure 6.34) showed an upward trajectory until the end of intervention (although not as steep as for the LEMI, chapter 6, figure 6.29). However, changes observed at end of intervention were not carried over to the one-month follow-up; it is not known if the results would have continued to increase if a greater number of sessions had been delivered. Although participants may have been continuing functional activities between end of intervention and the one-month follow-up it was unlikely they were receiving the same degree of afferent stimulation as they were during the intervention phase.

Another point to consider in relation to the SWM is that measuring of sensory thresholds in four locations in one assessment is time-consuming, and this needs consideration for future trials. Repeated testing of sensation has the potential to increase testing fatigue, or alternatively to enhance sensibility of the area being tested. Using an algorithm for SWM testing in this trial (Appendix 34) decreased the burden of testing for participants by reducing the number of filaments that needed to be used at each location on the foot. Further consideration needs to be

given to the testing site, and whether just one site should be tested (if assessment at this site indicates either fully intact or absent sensation) (Busse and Tyson, 2009), in accordance with the rationale that if one site is affected by stroke, it is likely that all sites will be affected due to the nature of stroke being an upper motor neurone lesion rather than a peripheral nerve lesion, in which dermatomal distributions might be differentiated in sensory testing.

Decreased sensation, for example at the level of loss of protective sensation increases the potential of injury (Boulton et al., 2008), and any loss of sensation in the foot can make balance and walking difficult, predisposing the person to falls (Perry, 2006). It was perhaps surprising that greater changes were not observed for the SWMs results for any of the four points on the plantar surface. However, it must be remembered that the participants in the FGs reported that it took time to feel the TIs, perhaps six weeks was too short a time to see changes in sensory threshold. Also, the dose of the treatment delivered could have been an influence. As discussed in section 7.1.1, trials investigating rehabilitation often do not deliver the intervention at a sufficient dose (frequency, duration and number of sessions); at least 16 hours of additional therapy is required over and above what is delivered in the control group (Kwakkel et al., 2004). This feasibility study was not looking at effectiveness, however it is essential that dose is taken into consideration for a larger trial in the future. From the systematic review undertaken (reported in chapter three, and discussed in section 7.1) it is evident that most of the studies exploring sensory stimulation post-stroke have not delivered the interventions at an

adequate intensity, indeed only two (Jung et al., 2017; Ng and Hui-Chan, 2009) of the studies in the systematic review achieved the suggested additional 16 hours of intervention in the experimental group. This is in agreement with the findings of another systematic review exploring dose of therapy interventions (Cooke et al., 2010a).

However, a study which did report a clinically meaningful change for the 10MWT was undertaken by Renner et al., (2016). This study explored delivery of an intensive daily rehabilitation programme for sub-acute stroke survivors with moderate to severe disability, delivering 45 hours of therapy over a six-week period (over double the amount delivered in the MTS group and over four times that delivered in the TI group). The results from this study by Renner et al., (2016) not only question the intensity of rehabilitation required to see a clinically meaningful effect, but it also raises the issue relating to severity of disability post-stroke and who may respond best to different types of therapy, because they only included stroke survivors who were moderate to severely affected. It is acknowledged that delivering a trial of purely task orientated training is not the same as delivering a sensory stimulation intervention (priming or augmenting) combined with TSGT. However, it would be valuable to analyse the MoTaStim-Foot results in relation to the NIHSS and sensory threshold changes to see if perhaps stroke survivors with greater sensory loss respond differently from higher functioning stroke survivors with intact sensation. It could then be considered whether an inclusion criterion should be added related to only including people

with somatosensory loss. This would be in alignment with the work undertaken by Hummelsheim et al., (1995) discussed in section 7.3.5.4.

It must also be considered as to whether the touch sensory threshold is the most appropriate OM to use. Cutaneous tactile assessment in a non-weight bearing position may not reflect sensory input requirements during standing; integration of other afferent information, for example, from ankle proprioceptors, may decrease the importance of cutaneous input from the plantar surface of the foot during balance (Marigold et al., 2004). Although MTS results in cutaneous input, an important aim of the technique is to provide intensive proprioceptive stimulation (Hunter et al., 2006). Perhaps measurement of proprioception would be more relevant; inter-rater reliability of the Erasmus version of the NSA and the sensory section of the Fugl–Meyer Assessment have been advocated for clinical application, although careful standardized testing procedures is necessary (Connell and Tyson, 2012). Some additional piloting relating to this aspect would also be valuable.

7.3.6.4 Electrogoniometry

Bronner et al., (2010) demonstrated excellent intra-rater reliability (r = 0.979) of the electrogoniometer for the ankle. However, there is generally a deficit of literature exploring the inter-rater reliability of the electrogoniometer. Despite following a strict protocol for the goniometry assessment within MoTaStim-Foot, with the data acquisition log calibrated to zero as recommended by Moriguchi et al.

(2007), and standardization of the positioning of the goniometer, concerns arose relating to reliability. During the assessments some participants mentioned that there was discomfort over the lateral side of the ankle due to the pressure of the shoe pressing on the electrogoniometer, although no-one mentioned this issue in the FG discussions. The pressure from the shoe may have resulted in slight movement of the goniometer which may have affected the validity and reliability of the results, due to a possible malalignment of the equipment. These issues may be able to account for the fact there were several extreme outliers noted for the electrogoniomery assessments. The other aspect to consider is that Bronner et al., (2010) tested the goniometer in a group of dancers, as opposed to stroke survivors, who may have altered alignment due to adaptive shortening or spasticity. Further reliability studies would perhaps be appropriate prior to using an electrogoniometer to measure ankle range of movement in future studies.

7.3.6.5 Implications for a future RCT

The burden of undertaking the battery of OMs must be considered when designing a future trial. Undertaking this feasibility trial has enabled a detailed insight into potential burden of each OM for both the participants and the research assessors. The extra burden on the participants and research therapists of the interim assessments (LEMI and SWMs) is an important consideration. At the commencement of the trial, the pressure insole measures, goniometry and 5MWT were also undertaken after five, ten and fifteen interventions, but this was quickly found to be too much of a burden and an amendment to protocol had to be sought

to decrease these assessments to just baseline, end of intervention and one-month follow-up. This was another useful finding of the feasibility study.

7.3.7 Measures of balance and gait

7.3.7.1 MoTaStim-Foot findings

The 5MWT, FAC and mRMI were responsive to change in both groups, reflected in improvements in function and the ability to balance and walk.

7.3.7.2 mRMI

A concern with the mRMI was that a potential ceiling effect was observed (Johnson and Selfe, 2004), with many participants reaching top scores by end of intervention/one-month follow-up. Another issue relating to the mRMI was access to stairs. The validated OM involves allocation of five points for a stair assessment (total score of 40). However, there was inconsistent access to stairs for participants, many of whom were in their home environment, with several living in bungalows. In view of this issue, to enable consistency and parity across the cohort of participants, the stairs assessment results were removed from the final score and a score out of 35 was used, rather than a maximum possible score of 40, eliminating the score for stairs. It must be remembered that this may have affected the validity of the measure. This aspect will require further consideration prior to moving forward with future trials and is an indication that the mRMI may not be suitable as a primary OM for a future trial.

7.3.7.3 5MWT

For this feasibility study, there was no primary OM. It was one of the objectives of the feasibility study (3f) to identify an appropriate primary OM for future trials (Lancaster et al., 2004). Various aspects need to be considered when selecting a primary OM, including the acceptability for the participants, clinical relevance, psychometric properties of the tool e.g. validity, reliability, floor and ceiling effects, responsiveness, and the level of measurement.

7.3.8 Implications for a future RCT

The 5MWT has been shown to be reliable (Collen et al., 1990), and responsive to change in walking ability after stroke (Salbach et al., 2001), which was demonstrated within the MoTaStim-Foot trial, and it clearly has clinical relevance. It was also quick and easy to set up and measure. After due consideration of these characteristics, the 5MWT was considered to be the most appropriate tool to take forward as the primary OM for future trials. It needs to be acknowledged, however, that since this trial ended, the SRRR guidelines for research have been published (Kwakkel et al., 2017) and these guidelines advocate the use of the 10MWT. Nevertheless, whichever of these OMs is taken forwards it will be necessary to consider the environment for undertaking the assessment and standardization of the measure. Suzuki et al. (1990) advocated a 3 metre lead up and Salbach et al. (2001) advised 2 metres to allow acceleration and a further two metres at the end for deceleration. Working in people’s homes this space was not available in the MoTaStim-Foot trial. In order to allow further standardization for future trials a

larger space in an appropriate location in the university or the hospital will need to be identified.

7.3.8.1 FAC

The FAC has been found to be valid and reliable in stroke survivors (Mehrholz et al., 2007), is quick to undertake, and was clearly responsive to change within MotaStim-Foot; it is deemed suitable as a secondary OM for future trials.

7.3.8.2 Pressure insoles and implications for future studies

Setting up and recording measurements with the pressure insoles was challenging at times. In order to achieve accurate measurements from the pressure insoles, it was necessary to calibrate the insoles prior to each measurement being undertaken; this was an issue for some of the participants, and, the process of calibrating the insoles could be extremely time-consuming; this should be built into planning, if the pressure insoles are to be used within future studies. Also, the system used within MoTaStim-Foot necessitated a great deal of time to set up and extreme care with the wires while undertaking the measurement was required. Although participants' safety was maintained at all times, some of the participants said in the FGs that they thought a wireless system would be better. However, this has additional cost implications that need to be considered if the pressure insoles were to be used in a further trial.

Also, the specific aspects of the pressure insole information that were chosen in the MoTaStim-Foot trial for data analysis (FTI and COFV) did not demonstrate a change correlating with the improvements in gait observed for the 5MWT. Further consideration needs to be given as to what information would be most clinically useful in future studies. For example, the centre of force trajectory (Figure 6.26) represents well the ability to transfer weight forwards over both the ipsilesional and contralesional feet during gait, giving a useful visual representation of changes, and would be worth considering for future studies.

7.3.8.3 Response of outcome measures over time (Objective 3g)

Research objective 3g related to whether the OMs demonstrated a response to treatment. It was not the purpose of the feasibility study to demonstrate the effectiveness of the interventions; however, the results do indicate that a potential efficacy was demonstrated for several of the OMs, for both groups. This aspect (in relation to choosing a primary OM for the subsequent trial) will be discussed. The purpose of regular LEMI and SWM measurements was to enable a more detailed understanding of potential changes occurring in relation to the number of sessions delivered, to inform regarding intervention requirements for a future trial. These regular measurements did meet their purpose.

7.3.8.4 LEMI

The combined LEMI scores for all 34 participants clearly showed a trend of continued increasing strength throughout the intervention period. No plateau in

strength was observed and the indications are that at least the full twenty treatments are required to aim for optimum change for the participants.

It is possible that greater benefit may have been seen if more than 20 sessions were undertaken. A large trial in America (n=347) explored the response to therapy in stroke survivors receiving locomotor training (gait training on a treadmill with bodyweight support and over ground training) or strength and balance training, as a secondary analysis of the Locomotor Experience Applied Post-Stroke (LEAPS) RCT (Rose et al., 2017). Participants received 36 sessions (3 times per week for 12 weeks) for 90 minutes in duration and OMs were undertaken after 12, 24, 30 and 36 interventions. The participants in both groups were still showing responses to treatments even after 36 sessions; however, the improvement slowed down between 25 and 36 sessions. To put into perspective the amount of therapy delivered within the LEAPS trial compared to MoTaStim-Foot, after just 12 sessions of 90 minutes duration the participants in the LEAPS trial had received 18 hours of treatment, and by the full 36 sessions, they received 54 hours of treatment. In MoTaStim-Foot the MTS group received approximately 20 hours of treatment (MTS+TSGT) and the TI group just 10 hours of TSGT (although they did benefit from being able to wear the TIs as much as they wanted during their daily activities). This brings into question whether additional sessions in MoTaStim-Foot may have resulted in greater within-group changes; this should be taken into consideration for future trials. However, the LEAPS trial investigated training rather than the effect of combining sensory stimulation (priming or augmenting) with training; it is not known whether the results are directly applicable.

7.3.8.5 Implications for a future RCT

In view of the fact that no plateau was observed for the LEMI results it is not known whether delivering more than 20 treatments would have enabled participants to achieve greater muscle strength and function. Hence, there is a need for some further piloting in advance of a large trial.

7.4 Adverse events

7.4.1.1 MoTaStim-Foot findings

Some adverse events within a trial are expected, both serious and non-serious complications occur (Johnston et al., 1998). It is well known that mobility and balance are affected after a stroke (Sullivan et al., 2009; Tyson et al., 2006b), and the rate of falls within the population of people post-stroke is high. It is, therefore, unsurprising that 16 of the 27 (59.3%) adverse events within MoTaStim-Foot were due to a fall; ten participants reported falling, representing 29.4% of the cohort of 34 participants.

7.4.1.2 Comparison of MoTaStim-Foot results with other trials

This result for the MoTaStim-Foot trial is similar, but less, than a cohort of 41 stroke survivors of whom over half had reported experiencing a fall, and 80% admitted to near fall events (Hyndman et al., 2002).

7.5 Feasibility methodology

The chosen methodology for this thesis enabled a systematic review of current literature (Study 1), and dedicated time to be devoted to developing standardized protocols for the three interventions to be delivered within the MoTaStim-Foot trial (MTS, wearing TIs, and TSGT) (Study 2). This is in alignment with the stages advocated within the MRC framework (Craig et al., 2006). Study 3 of the trial allowed for exploration relating to acceptability and feasibility of delivering the interventions, with qualitative aspects complimenting the quantitative study, and enabling the question 'can this study be done' (NIHR, 2017, p.2) to be answered. As this study was undertaken early in the research process, the design as a feasibility study was more appropriate than attempting to undertake a pilot study where a miniature replica of the main study is undertaken (NIHR, 2017). It was important to explore the OMs for feasibility and acceptability and to choose a potential primary OM for the future trial.

7.5.1 Assessment of the success of the MoTaStim-Foot feasibility trial

The MoTaStim-Foot trial can be judged as being successful because it met most of the criteria relating to feasibility and acceptability (section 4.4.2). All 34 participants were recruited within the 18-month period, achieving a recruitment rate of > 5% and an attrition rate of <15%. The interventions were delivered in various venues according to protocol.

An analysis was undertaken of the aims and content of the MTS and TSGT interventions delivered.[12] The most commonly used aim of the MTS intervention was to heighten awareness of foot position and posture; normalizing performance parameters, afferent stimulation and temporo-spatial activation, as well as regaining extensibility of the foot were also regularly used. Reducing hypersensitivity and pain was not such a common aim of treatment (Figure 7.1).

[12] Samuel, E., Hunter, S.M., Aries, A.M. (2019) Analysis of the content and dose of mobilization and tactile stimulation (MTS) and task-specific gait training (TSGT) for the lower limb after stroke delivered as part of the MoTaStim-Foot feasibility trial. (unpublished).

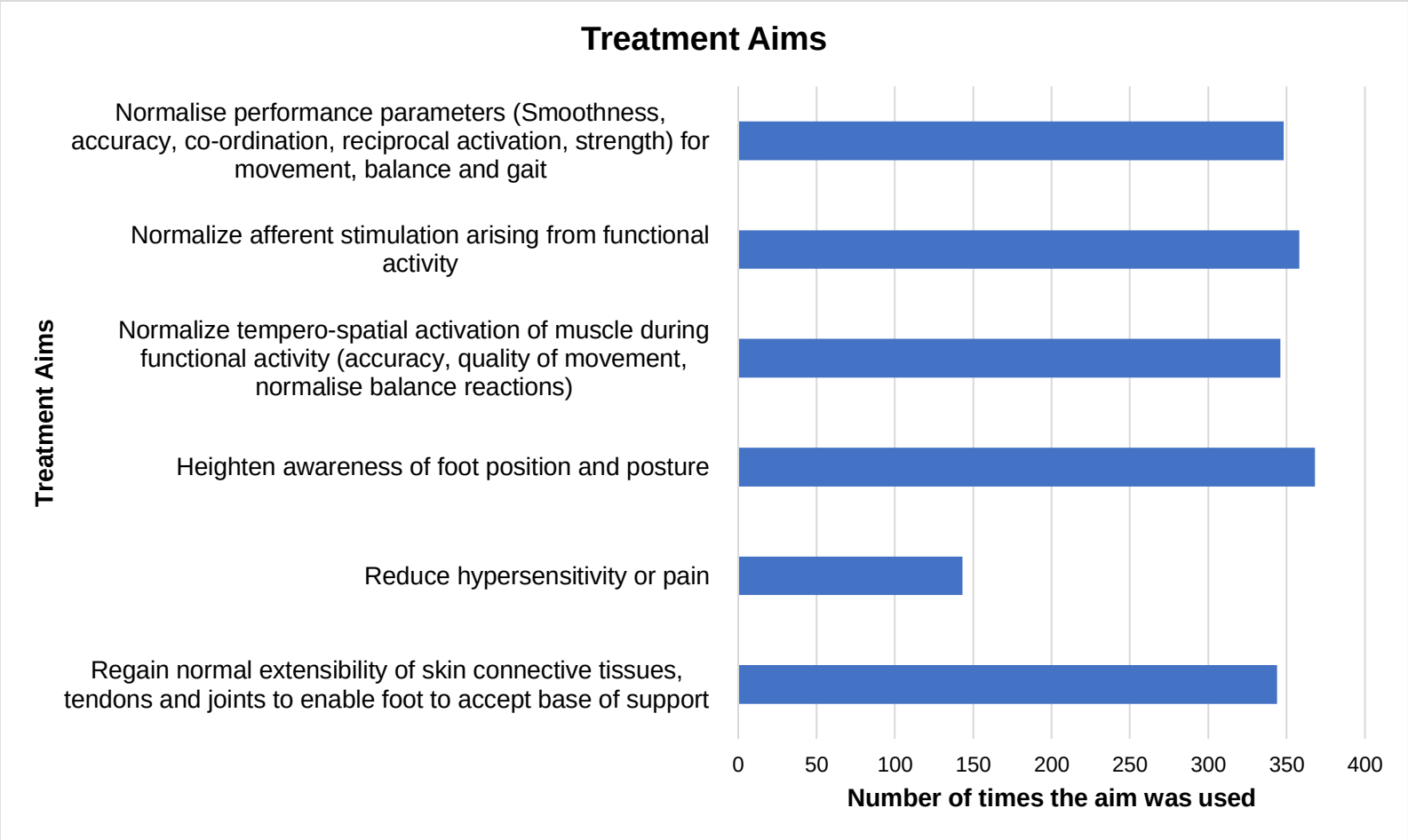


Figure 7.1 Number of times each aim of MTS treatment was selected

Analysis of fidelity relating to the interventions identified that the overall mean duration of MTS treatment delivered was 31.13 minutes, (standard error (SE) 1.94) with 84% of the participants in the MTS group receiving the full 30–60 minutes. All the MTS treatment options were used; however, passive movements (metatarsophalangeal joints flexion/extension/abduction/adduction; talocrural joint dorsiflexion/plantarflexion) and massage/soft tissue stretch (deep soft tissue massage to the tendoachiles; deep soft tissue massage to the plantarfascia; gastrocnemius and soleus mobilization) were the treatments most commonly selected by the research therapists to apply. The least commonly applied were patterns of coordinated movements underlying functional activity which included stair practice, obstacle course, manoeuvring, transfers and functional mobility. Figure 7.2 gives a visual representation of the treatments selected.

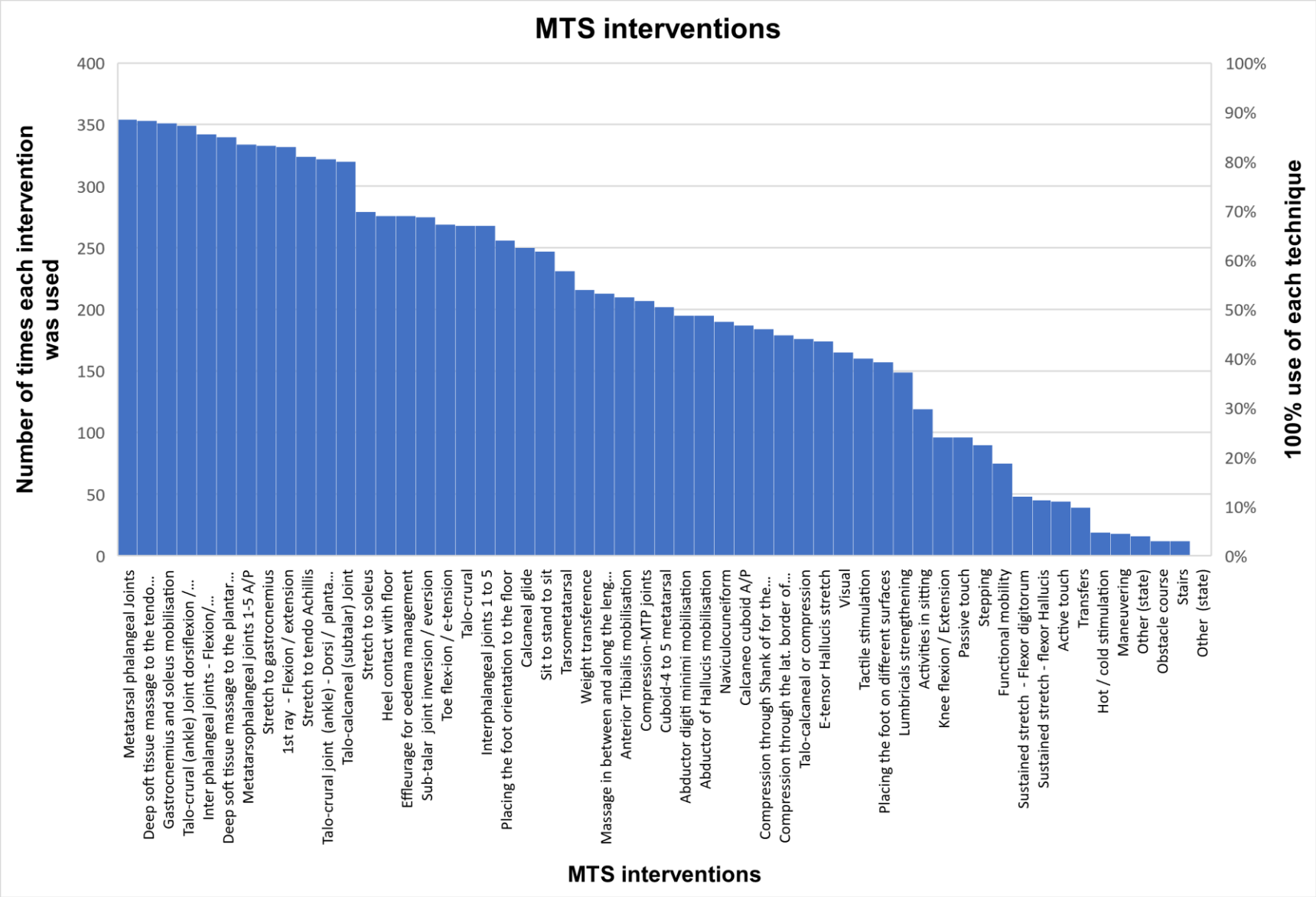


Figure 7.2 Number of times each MTS intervention was used

The content analysis of the TSGT (Figure 7.3) showed that the most commonly used interventions included gait re-education with or without aids (all participants, except two), standing balance/balance control, and sit to stand. During the TSGT there were several interventions that were not used at all including leisure/hobbies, leg press, raising and lowering a 1.4kg; 55cm exercise ball, shuttle walking, and standing chest press. This indicates that a review of the TSGT protocol is required prior to the next study being undertaken.

The mean duration of TSGT was 29.49 minutes (SE 2.10). A few of the participants, therefore, did not receive the full expected amount of MTS or TSGT; this was due to tiredness or fatigue on some occasions, however, reasons were not always stated. Data from the daily diaries and FGs demonstrated acceptability of both interventions and OMs for the participants, and >50% of participants attended an FG. OMs were completed for all participants, although there was some missing data, particularly at the beginning of the trial. Research therapists struggled initially to collect the goniometer, pressure insole and 5MWT contemporaneously; however, appropriate data were collected to enable a sample size calculation to be undertaken prior to a future trial.

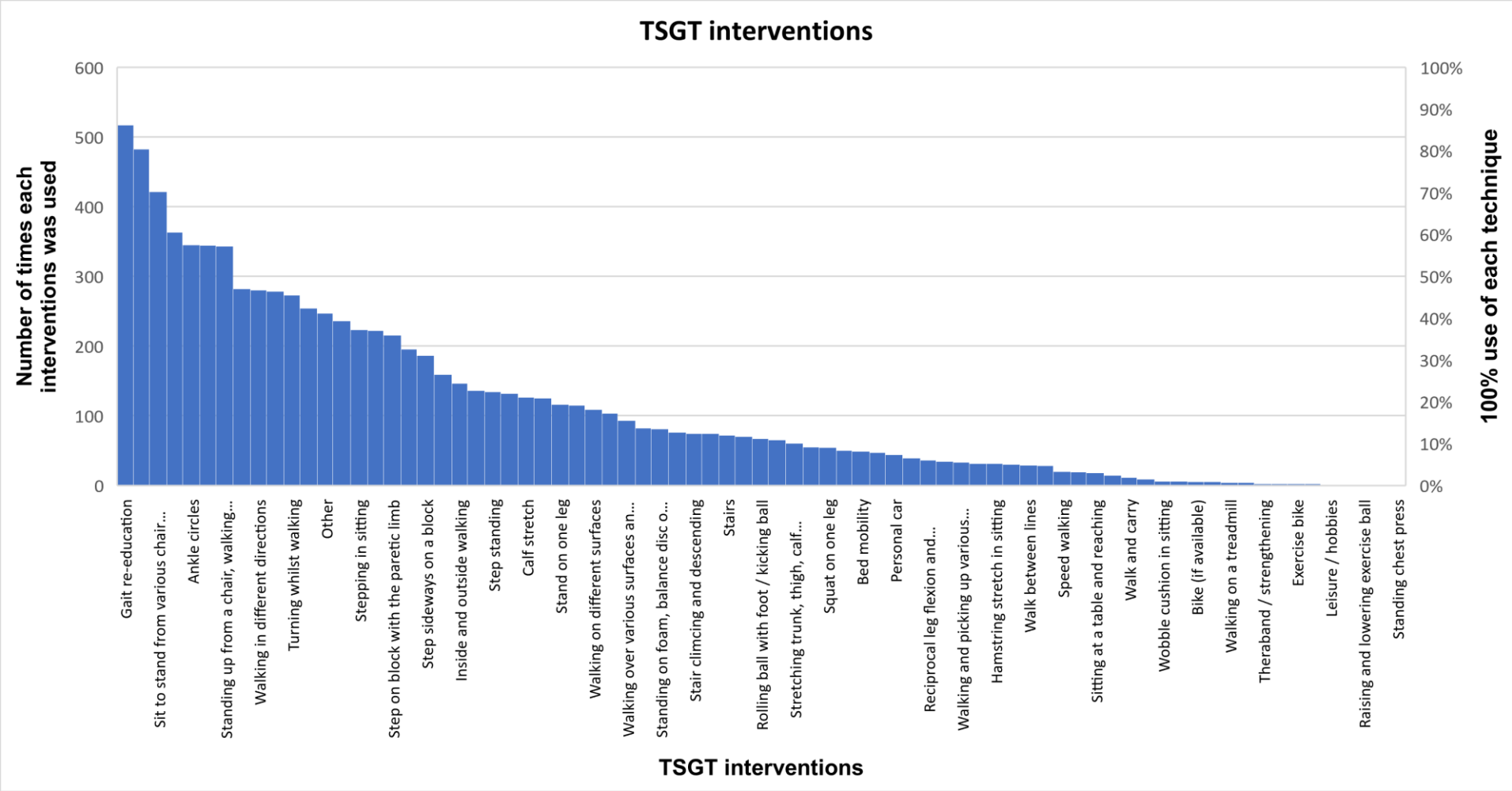


Figure 7.3 shows the frequency and 100% use of each of the interventions included in the TSGT treatment schedule.

7.5.2 Pros and cons of delivering a trial in the community (Objective 3f)

Most of the interventions were delivered in the home environment (81.46%) with just 18.54% delivered in a hospital environment (ward or gymnasium). There were advantages and disadvantages associated with delivering the MoTaStim-Foot trial within the community setting. As alluded to, one of the main disadvantages was the lack of space in some people's homes. Finding a stretch longer than five metres was often challenging, and invariably there was no opportunity for two metres before and after the five-metre stretch, which would have enabled recording of a steady gait pattern without acceleration or deceleration. The lack of access to stairs was another issue in some people's homes affecting the results of both the mRMI and the FAC assessments.

Travel costs and time commitments must also be considered when travelling to people's homes. A pragmatic decision early on in MoTaStim-Foot had to be made to exclude two geographical areas of Stoke-on Trent which were too far away and involved nearly one hour each way travelling time for the research therapist delivering the intervention. Not only would this have been time consuming, but potentially overly costly in terms of travel expenses for the trial. This needs careful consideration in planning the next study, as this will have implications for the funding application and overall trial costs.

A concern of the researcher at the start of the trial was that it may be perceived as intrusive to be visiting participants in their own home on an almost daily basis.

However, this concern was unfounded, and it generally worked well to treat the participants in their own environment. Participants reported feeling secure in their own home and liked the convenience of the therapist travelling to them. Indeed, in the FGs, some of the participants suggested they would not have continued with the full course of treatment if they had a need to travel to receive the interventions. In view of these findings it would be appropriate to deliver interventions (sensory stimulation plus TSGT) in the participant's own environment in future trials.

There are many principles upon which neurorehabilitation should be based and these include 'use it or lose it', specificity, repetition and intensity (Kleim and Jones, 2008, p.S227). Task-specific training encompasses these features and principles, and along with occupational adaptation (which focusses on the importance or value of the task in hand), make the home environment ideal for implementing task-specific practice (Rowe and Neville, 2018b). Therapy goals can be set collaboratively and put into context in the home environment (Rowe and Neville, 2018b) and this ownership of goals by the stroke survivor increases motivation and self-efficacy; the home environment can therefore facilitate progress, enhanced by encouragement from others (Rowe and Neville, 2018a).

7.5.3 The challenge of completing 20 sessions in a six-week period (Objective 3d)

For many of the participants it worked well treating them almost daily and they were happy to have regular treatments; most participants completed the twenty

sessions in approximately five weeks. However, some participants, particularly the younger stroke survivors found that it did not offer much flexibility for undertaking other activities; increasing the period of time when the treatments need to be delivered should be considered for future trials. Greater flexibility would also assist with working around any other therapy commitments of the participants. However, if the duration of time for delivering the interventions is extended this will mean a reduction in the frequency of the treatments (times per week) and the implications of this in terms of potential effectiveness requires careful consideration. In the first few weeks after stroke, brief but regular treatments have been found to be most beneficial (Bernhardt et al., 2017a). There are indications that a higher dose of therapy enhances recovery of movement, and in a dose finding study for the upper limb, higher intensity learning-based sensorimotor training resulted in better outcomes (Byl et al., 2008). Literature relating to this aspect is limited and further dose-finding studies are required (Cooke et al., 2010a). Several of the participants in the MoTaStim-Foot trial reported that it took several weeks to perceive changes to plantar sensation, therefore, extending the time for delivery of the interventions may potentially optimize opportunity to see a change in effect. This issue requires further discussion with expert clinicians and PPIE volunteers prior to undertaking the future trial.

7.5.4 The timing of recruitment post-stroke (Objective 3a)

Several of the participants were still receiving early supported discharge care under the NHS when they were recruited into the trial. This complicated the

arrangements for research therapy and, although a record was kept of the additional treatment received, it did add a confounding factor. The purpose of this feasibility study was not to investigate effectiveness of treatment; however, for future studies, the timing post-stroke for recruitment should be considered. If participants were perhaps recruited slightly later, for example, between 10-20 weeks post-stroke, instead of 6-16 weeks, they would still have the potential for good recovery but would be less likely to still be under the care of the NHS therapists, eliminating a potential confounder.

7.5.5 Daily diaries and FGs (Objective 3e)

Research objective 3e related to exploring whether the daily diaries and FGs are suitable ways to explore stroke survivors' experiences (Mackrill, 2008) of receiving the treatment. The FGs clearly met their purpose, and the daily diaries brought a different perspective to the study, enabling participants' daily thoughts to be documented, sharing information about the lived experience of participating in the trial. Much of the data collected from the daily diaries was analysed at a semantic level, for example, whether a participant's foot was hot or cold (and this could be affected by issues such as a change in weather), or if there were any changes relating to the feeling within the foot, or for how long the participants wore the TIs. The participants' acceptance of treatment and OMs (trial objectives 3d and 3f) was difficult to assess from the tick box sections of the diary sheet, but thematic analysis (see tables 6.7 and 6.9 for themes) of the daily diary comments and FGs,

gave an insight into both acceptance and response to the interventions (objective 3g).

Diaries are said to help prevent issues related to recall (Roghmann and Haggerty, 1972); however, some of the participants reported that they occasionally forgot to complete them on the day, and therefore there could have been recall bias, introducing error within the study (Hufford and Shiffman, 2003). Nevertheless, there was a great deal of useful information extracted from the daily diaries, although it would have been helpful to have included greater clarity in relation to the sections ‘Today my foot felt sensitive’ and ‘Today my foot did not feel sensitive’. It was not possible to ascertain from the diaries whether the sensitivity was a good indication i.e. able to feel more generally in the foot, or a problem, for example, a foot that is hypersensitive and potentially perceived as painful. On analysis of these sections, it appears that participants have interpreted the requirements of some of these sections in different ways. Several of the diary sections were, therefore, perceived as being inconsistent in view of the differing interpretations and the findings from these sections have not been reported within this thesis. It was, nevertheless, useful to establish that the recording of the daily diaries was not felt to be a burden to the participants, and therefore they could be used for future studies, if appropriate, but they would need to have a specific purpose.

Another point worth noting is that although participants were all invited to an FG, this could have been several weeks after completing their intervention; this may have affected both take up of the offer to attend, and the ability to remember events accurately.

7.5.6 Participant characteristics (Objective 3h)

In line with research objective 3h, it has been possible to understand the likely participant demographics and clinical characteristics including time since stroke, type of stroke and previous impairment affecting the ability to walk, again this information will be used to inform a future study. The sample was representative of the stroke population. The mean age (SD) for participants in MoTaStim-Foot (MTS: 73.84 (14.09) years; TI: 72.40 (9.79) years), which is slightly lower than the median age 78 years, (IQR 69–86) identified from Sentinel Stroke National Audit Programme data based upon 2584 admitted to a Gloucester Royal Hospital between 2014 and 2017. However, it is similar to other rehabilitation trials: CIRCIT trial, mean (SD) 69.9 (12.7) years (English and Hillier, 2011), and the FAST INdiCATE trial, Mean (SD) 72.2 (12.5) years) (Hunter et al., 2018), for example. Within the MoTaStim-Foot trial were 52.9% male participants and this value is slightly lower than some other trials, such as the CIRCIT trial (59%), FAST INdiCATE trial (64.6%) and FeSTivaLS trial (67.3%), differing perhaps due to the small sample size.

7.6 Strengths of the three studies

7.6.1 Strengths of the systematic review (Study 1)

There were several strengths to the methodology undertaken for the systematic review. The search strategy was robust, with clear terms and would be repeatable. The inclusion and exclusion criteria were clearly specified. Two researchers (AA, SH) screened the results and checked articles against the inclusion and exclusion criteria. Any discrepancies were discussed, and authors of the articles were contacted if further clarification was required. A third researcher (VP) was available in case of any disagreements, but this was not required. A rigorous analysis of the included articles was undertaken, synthesizing and evaluating the information. Effect sizes were calculated for all but two of the articles (where SD was not available). Also, a valid, reliable tool was used for quality assessment, the Cochrane Collaboration tool to assess risk of bias in RCTs (Higgins et al., 2011).

7.6.2 Strengths of the intervention modelling study (Study 2)

Study 2 followed a methodology involving a mNGT. A rigorous approach was adopted, enabling development of standardized protocols for all three interventions (MTS, wearing TIs and TSGT), formulated in conjunction with 12 experienced clinicians. The process itself allowed for both face and content validity of the protocols to be established, with comments from the clinicians to support this notion. The standardized protocols developed allowed for consistency of techniques to be applied in each intervention and were representative of clinical

practice. However, they enabled adaptation on an individual basis (as would be done in conventional therapy rehabilitation), with progression strategies built in, which had been discussed during the mNGT process, adding to the transparency of the methodology for the study.

There were numerous strengths to Study 2. These include: use of detailed, systematic, repeatable scoping reviews to inform the discussion, involvement of expert clinicians with the skills to inform the protocol development phase, and consideration of the aspects contained in the CONSORT 2010 and 2013 guidelines (Chan et al., 2013; Schulz et al., 2011) and the TIDieR guidelines (Hoffmann et al., 2014). The mNGT enabled consideration of the views of all the participants involved and was a transparent process, which could be replicated. The mNGT session was observed by a second researcher and a positive critique of the session recorded (Appendix 23).

7.6.3 Strengths of Study 3, the MoTaStim-Foot feasibility study

Study 3, the randomized, single-blinded mixed-methods feasibility study, followed an equally rigorous methodology. The protocol for MoTaStim-Foot was developed in conjunction with Norwich CTU. The randomization process was set up in advance with a statistician from Keele University collaborating with a statistician from Norwich CTU. The members of the research team delivering the interventions or OMs had no influence upon the randomization method. Participants were

stratified according to the side of the stroke lesion to help take into account potential differences in response to rehabilitation, balancing the groups.

There were several ways in which internal and external validity were addressed within this feasibility study. For example, randomization (Altman, 1991) and blinding (Armijo-Olivo et al., 2017; Eldridge et al., 2016) were implemented and importantly successful, as well as the use of standardized interventions and OMs (Bodner, 2018); the methodology was rigorous for both the randomized trial and the qualitative aspects of the research design. The inclusion and exclusion criteria were carefully selected and were applicable to many stroke survivors, increasing the external validity of the trial. Stroke survivors with aphasia were included within the MoTaStim-Foot trial, providing they were able to consent and follow simple instructions. This increases the clinical validity of the study findings (Brady et al., 2013).

The recruitment procedures were clearly effective, demonstrated by the successful recruitment of all 34 participants in the allocated time-period. The OMs used within MoTaStim-Foot were selected carefully, with consideration of validity and reliability.

Within therapy practice, clinicians work to improve weight-bearing through the hemiparetic (contralesional) side, gaining a better transfer of weight throughout the stance phase and thereby increasing the symmetrical pattern of gait, so the choice

of pressure insole measures aligned well with clinical practice. This decision to consider a measure aligned with asymmetry of gait was corroborated by some of the quotations within the FGs, with one participant feeling that how he walked was an issue to him and he reported feeling that people stared at him when he was out in public.

7.6.4 Training of trial therapists

The comprehensive training of research therapists and blinded assessors assisted in ensuring standardized protocols were followed for both treatments and OMs; the independent assessment of research therapists to ensure standardized protocols were being implemented also enhanced the study. All staff were GCP trained and required to be competent prior to undertaking assessments and treatments. As an example, all staff were required to complete the online competencies for the NIHSS prior to undertaking a baseline assessment with participants.

7.6.5 Triangulation of findings through mixed-methods

The use of daily diaries and FGs to explore participants views relating to the acceptability of the interventions enabled triangulation of methods (Polgar and Thomas, 2000). Diaries have been used successfully in a similar way to give an indication of compliance with intervention (Askim et al., 2018).

7.6.6 Rigorous documentation

A further strength of the study was the rigorous documentation of all aspects related to both Study 2 and Study 3 of the MoTaStim-foot trial. The Chief investigator worked closely with both Research Governance at Keele and Norwich CTU. This included quality assurance processes, for example, the monitoring of correct processes in relation to informed consent within the trial. However, there was a burden to the research therapists in completing all the case report forms and electronic documentation should be explored prior to undertaking another study.

7.6.7 Patient and Public Involvement and Engagement (PPIE)

The value of PPIE in health research has been increasingly recognized, with the NIHR and stroke research networks embracing strategies to increase PPIE input (Ardron and Kendall, 2010). The involvement of PPIE volunteers at all stages of the MoTaSTim-Foot feasibility trial was another strength. This involvement began at an early stage when initial research ideas were considered. PPIE advisors also assisted with both the fellowship and ethics applications, offering invaluable input into the lay summary for the study and development of the PIS, ensuring that suitable language was used that would be understandable to the participants. A further PPIE workshop was funded by a Research Design Service grant prior to submitting the fellowship application and this enabled further discussion relating to details about the intervention and final decisions regarding appropriate OMs. Clinicians were also involved at this early stage to finalize the research design for MoTaStim-Foot. PPIE advisors have been an integral part of the MoTaStim-Foot

team, throughout the research process, with advisors sitting on the trial management group and participating in meetings, as well as assisting with note taking in the FGs. Indeed, PPIE advisors have been a constant source of support and advice throughout, from inception of the research ideas to implementation of the trial and dissemination of the work.

Their input was exceptionally useful in relation to the FGs, taking on a valued role as note taker to document the field notes, and assisting with summarizing the themes at the end of each FG, adding credibility to the findings (Krueger and Casey, 2000). Furthermore, involvement of a PPIE advisor (PB) in the thematic analysis of the FGs was important, enabling confirmability of the findings of the study. FG transcripts were shared with PB and he worked in partnership with the other researchers (Baines and Regan de Bere, 2018); he agreed that the identified themes fitted with his understanding of the content of the FGs, from his original involvement as notetaker, and also from reading the transcripts. His role was viewed as essential in the methodology, with him contributing to the discussions relating to the themes, which evolved from each individual FG, and also the overall themes that were finally developed from the data relating to all of the four FGs. Analysis of the field notes recorded by the FG observer (PPIE advisor) also provided additional insights and context behind the interactions of participants and was important to enhance the rigour of the qualitative aspects of the feasibility study. One PPIE advisor (PB) also assisted with providing images for this thesis

and with dissemination of the work relating to the MoTaStim-Foot feasibility study at the UK Stroke Forum.

7.7 Limitations of the studies

7.7.1 Limitations of the systematic review (Study 1)

It would have been valuable to have two researchers extracting the data, assessing the quality of the literature and synthesizing and evaluating the findings of this systematic review to increase the rigorous nature of the methodology.

7.7.2 Limitations of the intervention modelling study (Study 2)

One possible limitation is that although participants were included from three different trusts, the experts were all from the same region, and therefore it is not possible to be sure that their views would be generalizable to clinicians in other regions. The small number of participants (n=12) is also a limitation.

7.7.3 Limitations of Study 3, the MoTaStim-Foot feasibility study

Some limitations to the MoTaStim-Foot study are also acknowledged. The randomization within the study resulted in uneven groups. Block randomization was used in blocks of four and two. A situation may have occurred where, fortuitously, the randomization was halfway through both blocks, in the two strata, with the first two subjects in each block allocated to the MTS group. The discrepancy between the groups perhaps reflects the small numbers in the

feasibility study. The result of this was the maximum difference possible in number between the two groups with 19 people in the MTS group and 15 people in the TI group. It was then unfortunate that a further two people were withdrawn from the TI group too.

As discussed in section 7.3.4.1, formal feedback was not obtained from the research therapists involved; this would have provided opportunity for gaining insight into and understanding of the research therapists' perspective relating to the fidelity of delivering the interventions.

Measuring knee range of movement in addition to ankle range of movement could have been undertaken in this study. The degree of dorsiflexion of the ankle is altered if the angle of the knee changes. It may, therefore, have been advantageous to measure the range of movement at the knee too to enable comparisons with normal gait during analysis.

The 5MWT was successfully implemented within MoTaStim-Foot. However, there were restrictions in relation to space on many occasions, because the OMs were undertaken in participants' homes. Consequently, whilst five metres was made available in each location by moving furniture and other obstacles in the participants' homes, it was not generally possible to have a two metres lead up and run out, before and after the marked out five-metre walkway. This might have

affected the reliability of the 5MWT data and should be considered prior to taking this OM forward to a future trial.

Measurement of light touch/pressure of the feet has been found to be related to activity OMs (Connell and Tyson, 2012) and, therefore, SWM sensory threshold testing was selected as an OM in the MoTaStim-Foot trial. However, within the literature review, discussed in chapter two, stimulation of mechanoreceptors is also reported to occur with somatosensory interventions, and alignment of the foot and ankle is highlighted as an important aspect to enable normal balance and gait. Therefore, it would also have been useful to assess proprioception, perhaps of the ankle joint. Proprioception deficits post-stroke have been found to be more prevalent than tactile sensory loss (34-64% as opposed to 7-53%) (Connell et al., 2008). When this is considered, in conjunction with the importance of proprioception to enable controlled movement, it can be speculated that analysis of proprioception, as opposed to touch/pressure sensation, may have been more appropriate within the MoTaStim-Foot trial. This requires further consideration prior to a future trial and indicates that it would be more appropriate to measure proprioception in addition to tactile sensory loss in future trials.

The sensory threshold testing with the SWMs was undertaken using a newly developed protocol. This protocol was developed following consultation with the literature, and it was successfully used within MoTaStim-Foot following training of the assessors. It would, nevertheless, have enhanced the rigour of the study if

reliability of the protocol had already been established. This is currently being explored and will inform protocols for the future.

It was appropriate to be inclusive and include people with aphasia in the MoTaStim-Foot trial; however, although participants were briefed prior to the focus groups and the facilitator specifically ensured that people with aphasia were able to contribute to the FG discussion and communicate their opinions as well, the degree of interaction for some of the participants was limited. People with aphasia use various different communication strategies, for example, non-verbal communication, picture books and environmental props (Luck and Rose, 2007) and therefore video recording, rather than simply audio recording, the focus groups may have captured more input from people with aphasia, and should be considered for further studies.

Another aspect to consider is that this study was only undertaken at one site. This site had been involved in other trials relating to aspects of therapy interventions previously and therefore some prior knowledge may have existed. The results of this feasibility study may, therefore, not be transferrable to other sites and regions. Further piloting at different sites is recommended before undertaking a phase III trial.

7.8 Aspects to take forward to a future study

This feasibility work justifies the importance of further investigation of somatosensory interventions to improve function of the lower limb after stroke, with a view to bridging the practice-to-evidence gap (Negrini et al., 2016). Prior to finalizing plans for a future study, consideration needs to be given to the challenges relating to implementation of evidence into clinical practice. This is important to optimize the potential of implementing any relevant research findings.

Following a successful feasibility study, meeting all the objectives, the intention is now to plan to take this work forwards to a large multi-centred RCT, to test two hypotheses:

1. There is a difference in outcomes of balance and gait when TSGT alone is compared with priming the sensorimotor system using MTS prior to TSGT.
2. There is a difference in outcomes of balance and gait when TSGT alone is compared with augmenting the sensorimotor system by wearing TIs prior to and during TSGT.

This study would need to include a third group receiving just TSGT as the control, or possibly a fourth group too receiving usual care. This design would enable exploration of whether TSGT following sensory stimulation (either priming the system using MTS or augmenting by wearing a TI) is more effective than TSGT alone or solely conventional therapy.

Prior to undertaking a definitive clinical trial, it would be valuable to complete some further piloting. MoTaStim-Foot has only been implemented within one local NHS Trust, and the clinicians at this site are familiar with MTS as a technique and supportive of the research. It is anticipated that recruitment would be more challenging across multiple sites. It is also not known whether the interventions would be so well accepted at different sites. Additional piloting would also give better insight into which participants in terms of the level of disability/type of stroke may potentially benefit from the interventions, and an opportunity to monitor the number of participants injected with botulinum toxin, helping to ensure optimum inclusion criteria in a future study. Standardization of the 5MWT (or 10MWT) with acceleration and deceleration space included could also be established. Several other aspects would benefit from further piloting, including consideration of a change in time post-stroke to perhaps 10–20 weeks, or later, as opposed to 6–16 weeks. Although the largest improvement is observed in the first 30 days post-stroke (Duncan et al., 1994), the potential for further recovery continues for six months (Bonita and Beaglehole, 1988). This would still align with the late subacute phase post-stroke (3–6 months) at a point in time when there is still potential for motor recovery and response to therapy intervention (Bernhardt et al., 2017b) but would mean fewer clashes with NHS therapy, reducing the confounders. Further exploration in relation to a potential increase in the number of sessions delivered would also be valuable, in view of the fact that changes were still occurring after twenty sessions. It should also be considered as to whether proprioception should be assessed in a future trial.

A traffic light system (Meijel et al., 2015; Sheron et al., 2012) could be applied when considering which aspects of the MoTaStim-Foot feasibility study to take forward to a future trial, and which should not be taken forwards. Table 7.1 shows the aspects of this feasibility study which should not be continued (red), could be continued but some changes are required (amber) or could be taken forward to the main study without any changes (green).

Table 7.1 Planning a future trial: Feasibility study aspects considered within a traffic light system

Traffic light colour	Aspect of feasibility trial	Considerations/changes required
	Outcome measures: mRMI	Ceiling effect with mRMI is a concern, as well as access to stairs – unlikely to meet the requirements for the next trial.
	Outcome measures: Ankle range of movement measured with a goniometer	Electrogoniometry - not to be used unless there is further reliability testing. It is inappropriate to measure just the ankle and not the knee ankle. Use of the tibia to vertical angle (Kerr et al., 2019) may be more clinically useful and could be piloted for further studies.
	Daily diaries	Unlikely to be required for the future trial.
	Trial Management group	This worked well; however, for future trials independent steering and data monitoring committees will be required.
	Case report forms	Although the case report forms worked well it should be considered whether there would be greater efficiency if the forms are electronic for future trials.
	Recruitment procedures	Although recruitment was successful within MoTaStim-Foot it was extremely time-consuming for the trial staff. It would be useful to involve the Clinical Research Network to assist in recruitment for future studies if possible.
	Exclusion criteria	Consider whether botulinum toxin should be an exclusion to the trial or not.
	NIHSS	People with left hemisphere stroke score 4 points less than people with right hemisphere stroke, this is just a consideration, although the NIHSS worked well in MoTaStim-Foot. Training of staff is essential – must be competent to undertake the assessment.
	Randomization procedures	Need to consider whether posterior circulation strokes should be included or not and how they would be dealt with during randomization.

	Monitoring length of time wearing TIs		If daily diaries are not used in a future trial, there needs to be a mechanism for recording the length of time TIs are worn.
	Outcome Measures	Protocols for undertaking OMs	LEMI – must specify removal of footwear prior to testing.
		LEMI	Suitable and quick to administer but need to consider standardization – no footwear.
		FAC	Need to consider access to stairs and inclines to ensure the ability to score accurately.
		Pressure insole measurements	Need to consider the purchase of a wireless system to increase the safety of participants and speed of conduction of the testing. Need to build in time for setting up the equipment and calibrating the insoles.
		Sensory threshold testing with the SWMs	Due to the lack of significant results for all but the hallux point in the TI group and the fact that the SWMs take considerable time to test, consideration needs to be given as to whether this OM should be used in further trials or not, and alternatives explored.
	Proprioception		Plan to include an OM for assessing proprioception in future trials
	Patient and public involvement and engagement		The PPIE within MoTaStim-Foot was thorough and beneficial. This level of PPIE should also be sought for future studies.
	Screening tools	Step test for screening	This worked well, screening out stroke survivors who functioned at too high a level.
		Ability to follow simple commands screening test	This served its purpose. All participants recruited had capacity to consent and could follow instructions for therapy.
	Interventions	MTS protocol	Thorough training must be undertaken for research therapists to ensure adherence to protocol.
		TI protocol	
		TSGT protocol	

	5MWT or 10MWT	Videoing of the 5MWT was useful to enable assessment of whether the participant required assistance to walk or an aide. Consider whether it would be possible to have 1-2m at the start and end of the 5MWT/10MWT.
	Blinded Assessment	This worked well and should be continued for future trials
	Therapy treatment record (to record conventional therapy taking place alongside the trial treatments	It is important to keep a record of the NHS therapy intervention received.
	Pain/fatigue assessment process and form	This is important to use to monitor pain and fatigue.
	Use of FGs to explore participants perceptions of their trial experience	This will allow the participants' opinions to be heard which is an important in relation to a therapy trial because they play an active part in rehabilitation. It also allows for triangulation of methods.
	FG schedules	Will need to be adapted as required for a future trial.
	Thematic analysis	The use of thematic analysis for the FGs was successful in giving an insight into the participants' trial experiences.

Suggestions and reasoning for further studies relating to sensory stimulation of the foot and ankle post-stroke are summarized in table 7.2. Also, the estimates of standard deviations, attrition and missing data obtained in this study can be used to calculate an appropriate sample size for the primary OM in a main trial (Objective 3c), which is planned in the future.

A power calculation was undertaken (Figure 7.4) using the data from the 5MWT and the suggested meaningful gait speed improvement during the first 60 days post stroke i.e. the minimal clinically important difference, which was found to be 0.16m/s x60 = 9.6m/min (Tilson et al., 2010). Based upon these calculations with a significance level of 0.5, for a power of 0.8, 35 people would be required in each arm of the trial, whereas, for a power of 0.9, 47 people would need to be recruited in each of the two arms of the trial.

Z score for significance level

Z score for power

Pooled standard deviation for the 5MWT change scores baseline to end

A minimum number of participants in each group, rounded up

$$n \geq \frac{2(\mathrm{Za} + \mathrm{Zb})^2 \text{ x } \sigma^2}{\delta^2}$$

Minimum clinically important difference – the difference in population means deemed important to detect

Alpha (α) 0.5, Power 0.8

$$n \geq \frac{2(1.960 + 0.842)^2 \text{ x } 14.22^2}{9.6^2}$$

$$n \geq \frac{2(2.802)^2 \text{ x } 14.22^2}{9.6^2}$$

$$n \geq \frac{15.702 \text{ x } 202.21}{92.16}$$

$$n \geq \frac{3{,}175.10}{92.16}$$

$$n \geq 35$$

Alpha (α) 0.5, Power 0.9

$$n \geq \frac{2(1.960 + 1.282)^2 \text{ x } 14.22^2}{9.6^2}$$

$$n \geq \frac{2(3.242)^2 \text{ x } 14.22^2}{9.6^2}$$

$$n \geq \frac{21.022 \text{ x } 202.21}{92.16}$$

$$n \geq \frac{4{,}250.86}{92.16}$$

$$n \geq 47$$

Figure 7.4 Power calculation based on the 5m walk change scores from baseline to end of intervention using a pooled standard deviation

Table 7.2 Suggestions and reasoning for further research

Suggestion for future research	Purpose
Further studies exploring effects of sensory stimulation.	Studies with larger numbers are required so subgroup analysis can be undertaken to determine the characteristics (e.g. in terms of disability, and whether stroke survivors with more severe disability respond differently from those who are mildly affected). This will help inform inclusion criteria for future studies.
Exploration of whether MTS could be delivered by a carer or an assistant.	It needs to be understood whether skilled handling is essential when undertaking MTS, or whether carers and assistants can be trained to undertake MTS with the same effect. This has cost implications for implementation of MTS within the NHS in the future.
Comparison of a smooth insole with a TI in stroke survivors.	This is to ascertain whether the perceived benefits of wearing the TIs in MoTaStim-Foot are related to increased plantar sensation or the feeling of improved stability.
Reliability studies for ankle electrogoniometry in healthy participants and stroke survivors.	This will inform a decision as to whether or not ankle electrogoniometry should be considered for further studies.

7.9 Summary

Within this chapter, the findings from the studies have been discussed, along with potential neurophysiological changes associated with the interventions. The strengths and limitations of the studies have been presented accompanied by plans for how this research can be taken forwards in the future. The following, final chapter will include concluding remarks from this body of work.

8 CHAPTER EIGHT: CONCLUSIONS

8.1 The importance of afferent input and development of the protocols

The importance of afferent input to facilitate balance and mobility has been discussed in detail, utilising pertinent literature. A systematic review has been undertaken and two sensory stimulation intervention protocols, MTS to prime the CNS, and wearing of TIs to augment the system, have been developed, along with a TSGT protocol for the lower limb. A rigorous process involving a consensus methodology and twelve experienced clinicians was implemented for developing the protocols. All three of the interventions have been delivered as two separate treatment combinations (MTS+TSGT and TIs+TSGT) in a randomized, single-blinded, mixed-methods feasibility study.

8.2 Success of the feasibility study and plans for the future

The MoTaStim-Foot feasibility study has been completed successfully, demonstrated by recruitment to time and target of the planned number of stroke survivors meeting the inclusion criteria, and delivery of the interventions, which have been found by the participants to be acceptable. The mixed-methods design enabled insight into participants' perceptions of the interventions and the overall trial experience.

In conclusion, the chosen methodology was appropriate to meet the objectives of the feasibility study. The importance of sensory stimulation post-stroke has been highlighted and a necessity for further research exploring the effectiveness of MTS+TSGT and TIs+TSGT in a large, adequately powered RCT has been established. Based upon the findings of the MoTaStim-Foot feasibility study other potential areas for investigation are summarized in table 7.2.

A critique of all three studies has been undertaken describing their strengths and limitations. Following the MoTaStim-Foot feasibility study, suggestions have been made for further piloting of certain aspects prior to undertaking a large phase III RCT; other studies relating to somatosensory stimulation of the lower limb post-stroke deemed important for undertaking in the future have also been highlighted (table 7.2).

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Appendix 1 Upper limb mobilization and tactile stimulation (MTS) schedule

Date:	Length of session:	Pt.ID:	Therapist:

AIMS (TICK)

- ☐ Regain normal extensibility of skin, muscle, connective tissues, tendons and joints
- ☐ Reduce hypersensitivity
- ☐ Reduce pain
- ☐ Heighten awareness of hand position and posture
- ☐ Normalize tempero-spatial activation of muscle during functional activity
- ☐ Normalize afferent stimulation arising from functional activity
- ☐ Normalize performance parameters (smoothness, accuracy, co-ordination, reciprocal activation) of upper limb movement,

PASSIVE MOVEMENTS THROUGH ANATOMICAL RANGE: (NOTE ANY RESTRICTIONS)

- ☐ Radio-ulnar pronation / supination
- ☐ Wrist flexion / extension
- ☐ Wrist radio-ulnar deviation
- ☐ Thumb MCPJ flexion / extension
- ☐ Thumb IPJ flexion / extension
- ☐ Thumb abduction / adduction
- ☐ Thumb opposition
- ☐ Finger MCPJ flexion / extension
- ☐ Finger IPJ flexion / extension
- ☐ Finger abduction / adduction

ACCESSORY MOVEMENTS: (TICK AND INDICATE TYPE e.g. GLIDE, DISTRACTION, AND DIRECTIONS e.g. AP, PA, etc.)

- ☐ Radio-ulnar joint
- ☐ Wrist joint
- ☐ MCPJ1
- ☐ MCPJ2-5
- ☐ IPJ1
- ☐ PIPJ2-5
- ☐ DIPJ2-5

MASSAGE (TICK AND NAME BODY PARTS MASSAGED)

- ☐ Effleurage
- ☐ Circular kneading
- ☐ Picking up
- ☐ Wringing
- ☐ Other (state)

SOFT TISSUE STRETCH (TICK AND STATE WHICH TISSUES)

- ☐ Longitudinal
- ☐ End of range
- ☐ Transverse
- ☐ Diagonal
- ☐ Sustained
- ☐ Other (state)

PLACING THE HAND ON

- ☐ Flat surface
- ☐ Edge / corner

ISOLATED / SELECTIVE JOINT MOVEMENT (TICK AND STATE DIRECTION OF MOVEMENT)

- ☐ Radio-ulnar
- ☐ Wrist
- ☐ MCPJ1
- ☐ MCPJ2-5 (lumbrical action)
- ☐ IPJ1-5

COMPRESSION

- ☐ MCP joints
- ☐ Palm
- ☐ Wrist
- ☐ Other (state)

SPECIFIC SENSORY INPUT (TICK AND NAME OBJECTS OR BODY PARTS)

- ☐ Visual
- ☐ Auditory
- ☐ Active touch (objects / body parts)
- ☐ Passive touch (objects / body parts)

PATTERNS OF CO-ORDINATED MOVEMENT UNDERLYING FUNCTIONAL ACTIVITY

- ☐ Reach – with / without object (please circle)
- ☐ Grasp and release – with / without object (please circle)
- ☐ Fine finger activity – with / without object (please circle)
- ☐ Weight-bearing through limb
- ☐ Other (please state)

Appendix 2 Full search strategy for systematic review (Study 1)

Search	Search term
S1	CEREBROVASCULAR ACCIDENT
S2	stroke
S3	“cerebrovascular accident”
S4	“CVA”
S5	“acquired brain injury”
S6	“traumatic brain injury”
S7	“head injury”
S8	“TBI”
S9	“ABI”
S10	hemiplegia
S11	hemiparesis
S12	“upper motor neuron lesion”
S13	ACQUIRED BRAIN INJURY
S14	TRAUMATIC BRAIN INJURY
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10
S16	FOOT
S17	LEG
S18	“lower limb”
S19	“lower extremity”
S20	S16 OR S17 OR S18 OR S19
S21	sens*
S22	stimulat*
S23	somatosens*
S24	propriocept*
S25	afferent
S26	mobilisation
S27	mobilization
S28	manipulat*
S29	SOMATOSENSORY STIMULATION
S30	PROPRIOCEPTION
S31	S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30

S32	WALKING
S33	GAIT
S34	WEIGHT BEARING
S35	walk*
S36	gait
S37	mobil*
S38	step
S39	stance
S40	ambulat*
S41	“weight bear”
S42	S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41
S43	Randomised controlled trial
S44	“Randomised controlled trial”
S45	RANDOMIZED CONTROLED TRIAL
S46	“Randomized controlled trial”
S47	RCT
S48	S43 OR S44 OR S45 OR S46 OR S47
S49	Functional electrical stimulation
S50	“Functional electrical stimulation”
S51	FES
S52	S49 OR S50 OR S51
S53	S15 AND S20 AND S31 AND S42 AND S48
S54	S53 NOT S52

Limiters: English language

Thesaurus terms are shown in capital letters

Appendix 3 Data extraction form for systematic review (Study 1)

Somatosensory stimulation of the lower limb and foot – systematic review

Data Extraction Form

General Information	
Date of extraction	
Author	
Title	
Source, year, volume, page numbers	
Methodological Quality of study	
Design of study	
Quality assessment	This has been documented in separate table.
Population Characteristics & Treatment Setting	
Recruitment procedures	
Sample characteristics: • inclusion/exclusion criteria • baseline characteristics	
Number of participants in each group	

Were intervention and control group comparable?	Yes/No
Treatment setting	
Experimental & Control Interventions	
Content of intervention (duration, delivery mode, type of constraint, amount and description of 'practice')	
Content of control (duration, delivery mode, type of therapy)	
Outcomes	
Outcomes measured at baseline	
Outcomes measured after intervention	
Outcomes measured at follow-up (state timing of follow-up)	
Who completed measurements? (Blinded?)	
Analysis	
Statistical measures used	
Attrition rate	

Was attrition adequately dealt with?	Yes/No
Quantitative results	
Sub-group analysis	
Qualitative analysis	
Conclusions	
Study author's conclusions	
Additional Comments	

Appendix 4 Details of the number of citations from each database

Database	No. of citations
Ageline	0
Amed	12
Cinahl Plus	61
Medline	64
PsycArticles	0
PsycINFO	9
SPORTdiscus	30
Web of Science	249
Cochrane Library trials	8
PEDro	0
TOTAL	433

Appendix 5 Studies excluded after reading full texts and reason for exclusion

Author and date of publication	Reason for exclusion
An and Jo (2017)	Involved muscle contraction
Bae et al. (2015)	No clear statement of appropriate ethics approval
Chen et al. (2011)	Involved muscle contraction
Cheng et al. (2010)	Involved muscle contraction
Choi et al. (2013)	Not sensory stimulation
Ertzgaard et al. (2018)	Involved muscle contraction
Hsu et al. (2013)	Involved muscle contraction
Knutson et al. (2013)	Involved muscle contraction
Koseoglu et al. (2017)	Not an RCT
Kwong et al. (2018)	Sensory stimulation not manipulated
Lau (2011)	Thesis
Lau (2013)	Abstract only
Lee et al. (2016)	Involved muscle contraction
Liang et al. (2012)	Involved muscle contraction
Maupas et al. (2017)	No gait or balance outcome measure
Morreale et al. (2016)	Involved muscle contraction
Ng (2005)	Thesis
Okawara and Usuda (2015)	Not an RCT
Park et al. (2015)	Not an RCT
Ribeiro et al. (2013)	Involved muscle contraction
Spaich et al. (2014)	Involved muscle contraction
Sungkarat et al. (2011)	Auditory stimulation
Xu et al. (2017)	Not sensory stimulation and involved FES
Yavuzer et al. (2006)	Not sensory stimulation – involved muscle contraction

Appendix 6 Articles identified from reference lists and indication for inclusion or reason for exclusion

Author	Included or not	Reason for exclusion
Brogårdh et al. (2012) (from Tankisheva et al., 2014)	√	
Chan et al. (2012) (from Guo et al., 2015)	X	No clear statement of ethical approval
Cho et al. (2013) (from Suh et al., 2014)	√	
Cordo et al. (2009) (from Paoloni et al., 2010)	X	Not an RCT
Geiger (2001) (from Goliwas et al., 2015)	X	Involved visual feedback
Lau et al. (2012) (from Tankisheva et al., 2014)	√	
Lee et al. (2013) (from Guo et al., 2015))	X	Both groups had FES
Magnusson et al. (1994) (from Goliwas et al., 2015)	X	Acupuncture and muscle contraction
Morioka and Yagi (2003) (from Lynch et al., 2007)	X	No clear statement of ethical approval
Ng and Hui-Chan (2007) (from Jung et al., 2017)	X	No clear statement of ethical approval
Ng and Hui-Chan (2009) (from Suh et al., 2014)	√	
Park et al. (2014) (from Jung et al., 2017)	√	
Tyson et al. (2013b) (from Goliwas et al., 2015)	X	Not an RCT
van Nes et al. (2006) (from Tankisheva et al., 2014)	√	

Appendix 7 Chronicity of stroke in trial samples

Authors	Stroke chronicity
Bayouk et al., 2006	Mean (SD) time post-stroke: 6.3 (9.7) years
Brogårdh et al., 2012	Mean (SD) time post-stroke: 35.3 (30.5) months
Cho et al., 2013	Mean (SD) time post-stroke:14.5 (5.0) months
Ferreira et al., 2018	Mean (SD) time post-stroke: 9.1 (1.3) years
Goliwas et al., 2015	Mean (SD) time post-stroke: 4.3 (3.0) years
Guo et al., 2015	Mean (SD) time post-stroke: 63.2 (52.2) days
Jung et al., 2017	Mean (SD) time post-stroke: 6.6 (2.6) months
Kluding and Santos, 2008	Mean (SD) time post-stroke: 21.4(13.8) months
Lau et al., 2012	Mean (SD) Time post-stroke: 5.0 (3.9) years
Lynch et al., 2007	Mean (SD) time post-stroke: 48.7(31.1) days
Ng and Hui-Chan, 2009	Mean (SD) time post stroke: 4.7(3.4) years
Paoloni et al., 2010	Mean (SD) time post stroke: 1.9 (0.59) years
Park et al., 2014	Mean (SD) time post stroke: 18.6 (2.1) months
Suh et al., 2014	Mean (SD) time post-stroke: 14.5 (5.0) months
Tankishieva et al., 2014	Mean (SD) time post-stroke: 6.5 (6.1) years
van Nes et al., 2006	Mean (SD) time post-stroke: 36.6 (10.2) days
Yan and Hui-Chan, 2009	Mean (SD) time post-stroke: 9.3 (3.4) days

Appendix 8 Summary of interventions and findings

Authors	Intervention	Main finding
Bayouk et al., 2006	**Task-oriented exercise** under varying conditions (eyes open/eyes closed) and on different surfaces (firm/soft) 1hr/wk x8 wks Total=16hrs	**10m walk test:** Both groups significantly decreased time (p<.05): 12.2% for experimental group (EG) and 12% for control group (CG). No significant main effects or group x test interaction. **COP variability:** EG significantly reduced COP variability (p<.05) in ML (eyes open, firm surface) and AP directions (eyes open, soft surface).
Brogårdh et al., 2012	**Whole body vibration (WBV) Training.** All participants underwent 12 sessions of WBV training (twice weekly during 6wk) Total=9 hrs	Significant but small improvements were found within both groups after the WBV training. EG improved significantly in balance (4%; *p*<.05) and in gait performance (TUG, 8%; CGS and 6minWT, 5%; *p* <.05). Control group improved sig. in isometric knee extensor strength (paretic limb) (12%; *p* <.05) and gait performance (TUG & 6 Minute Walk Test, (6minWT) 6%; *p* <.05). The differences in all OMs after the training were nonsignificant.
Cho et al., 2013	In addition to physical therapy based on the Bobath-concept for 30 min before TENS application: **Experimental group:** TENS stimulation (frequency 100 *Hz*, pulse width 200 *µs*, with 2 to 3 times the sensory threshold) applied gastrocnemius for 60 min. Total=1 hr	**Spasticity (MAS)** Spasticity reduced by 29% in EG and by 13% in CG; **HHD-based resistance measurement**: reduced by 30% (EG) and by 19% (CG) (p<.05) and difference between groups was significant (p<.05); **Postural sway length (PSL)** reduced by 54.3cm, and the postural imbalance of the placebo-TENS group was reduced by 9% after the intervention. All results for both groups returned to the baseline values after a day. **Postural imbalance**: **Eyes-open condition**: PSL reduced by 16% (from 64.5cm to 54.3cm) in EG, and by 9% in CG. Both groups returned to baseline values after one day **Eyes closed condition**: PSL decreased significantly (p<.05) by 23% (from 89.8cm to 69.1cm) in the EG, and by 8% (from 85.3cm to 78.2cm) in CG. Both groups returned to baseline values after one day. **Unstable surface eyes open:** PSL decreased by 16% (from 209.4cm to 174.6cm) for the EG but returned to the pre-application values after one day. PSL decreased by 9% (from 218.3cm to 197.5cm) in CG and returned almost to baseline values after one day.
Ferreira et al., 2018	Postural insoles with pronating heel wedge, a pronating band and MTP inlay for the stabilization of the different segments of the foot in the neutral position (3 months of insole use)	A tendency was found toward improvements in spatiotemporal gait variables in the EG immediately following the placement of insoles. However, the differences did not achieve stat. sig. After three months of insole use, sig. improvements were found in the gain of ankle dorsiflexion, peak knee flexion as well as range of motion of the ankle and knee in comparison to the CG.

Goliwas et al., 2015	Standard programme of rehabilitation 5x/week, 45 mins for control group and 30-minute sessions + 15mins (or 20 mins – UNCLEAR) sensorimotor foot stimulation (SFS) Total =22.5 hrs	**EG: For differences in weight distribution:** End test with eyes open and eyes closed – significant difference (p<0.05) between baseline and end, Exp group: 30.6 ± 19.6% to 17.8 ± 15.2% (p<.05), Control group: 20.1 ± 18.4% 18.7 ± 18.2% (p>.05) **Reduction of the differences in weight distribution:** Significant difference seen between the EG (12.2 ± 12.9%, p<.05 vs CG, which was 2.4 ± 4.9% with eyes open (p>0.05). **CG:** No sig. differences seen at all
Guo et al., 2015	Whole body vibration (I-VIB5050, Body Green, Taiwan) with a magnitude of 6~10Hz and amplitude of 4.0mm. For 8 wks ? 5 x/wk 8 sets per day (80mins) **(Total=53.33hrs WBV)**[a]	The Fugl-Meyer lower extremity score and 10m max walking speed test of both groups were improved sig (*P*=0.000/*P*=0.000, d=1.500/d=1.952, 95%CI [3.309, 9.891]/ 95%CI [5.549,12.45]; *P*=0.000/*P*=0.000, d=2.015/d= 2.952, 95%CI [5.214,11.39]/95%CI [9.423,15.98]), and the times of knee hyperextensions decreased significantly (*P*= 0.000/*P*=0.000, d=3.537/d=5.108, 95%CI [19.05,12.35]/95% CI [16.52,22.28]; Compared with the CG after treatment, the WBV's 10 m maximum walking speed and times of knee extension had significant statistical differences (*P*=0.001, d=1.345, 95%C I[1.896,6.704]; *P*=0.000, d=1.749, 95%CI [2.915,7.285])
Jung et al., 2017	TENS and sham groups had sit-to- stand training. The training lasted for 15 min a day, 5x/wk for 6 weeks. Prior to training sessions, subjects in the TENS group received electrical stimulation for 30 min (two times the sensory threshold without muscle contraction). Pulse width of 200 ms /frequency 100 Hz. (Total=37.5 hrs)	Results table difficult to interpret; however, text states: the training caused a more significant decrease in postural sway when subjects stood with their eyes open and eyes closed in the TENS group (mean change, each 21.0 (16.2), 26.4 (19.9) cm) than in the placebo stimulation group (mean change, each 8.8 (13.1), 13.1(13.0) cm). After training muscle strength of hip extensors was sig. inc. in the TENS group than in the placebo stimulation group. No sig. difference was found in muscle strength of knee & ankle extensors between TENS and placebo stimulation groups. Spasticity score sig. decreased in the TENS group (mean change, 2.6 (0.8) score) compared with the placebo stimulation group (mean change, 0.7 (0.8) score), p<.05.
Kluding and Santos, 2008	Ankle joint mobilisations + functional training + activity vs functional training + activity **(Total 2.67hrs)**[b]	Joint mobilisations + functional training may increase ankle ROM (passive ROM 95%CI 2.5°, 8.6°, effect size .88, active ROM 95%CI 0.5°, 16.6°; effect size .72) and improve speed of sit→ stand (95%CI -1.9, -0.1s, effect size = .6), and sig. increase peak weight-bearing during sit→stand (95% CI 3.59, 29.37, effect size =.85) more than functional training +activity alone
Lau et al., 2012	WBV training (frequency 20-50Hz) 3x/wk for 8 wks. Each session included 15 min of warm-up exs. in the sitting position. (Total 10 hrs, 4.2 were WBV)	The addition of the present WBV protocol to the dynamic leg exercise program confers no supplementary benefits for improving neuromotor performance and reducing falls when compared with leg exercise alone in chronic stroke patients with mild to moderate motor impairments.
Lynch et al., 2007	Sensory training + standard care vs standing with eyes closed and relaxation + standard care (Total 12.5 hrs)	Sensory retraining programme of the feet + standard care was no more effective than standard care + standing with eyes closed + relaxation

Ng and Hui-Chan, 2009	20 sessions over 4 weeks. **TENS group**: 60 mins TENS, on four acupuncture points (100 Hz /pulse width 0.2 ms) at twice each patient's sensory threshold. **TENS and exercise group**: 60 minutes, same TENS protocol plus 60 minutes of task-related exercises. (Total = 40 hrs, 20hrs TENS and 20 hrs exercise) **The placebo stimulation exercise group** - 60 mins of the same exercise after receiving 60 mins of placebo stimulation. **Control group:** No treatment - just attended four assessment sessions	Only the members of the TENS +exercise group demonstrated sig improvements in gait velocity from week 2 onwards (baseline: 47.9 (26.8), week 2 63.2(32.2)) (p<0.01). the improvements were maintained at follow-up, four weeks after treatment ended (70.2 (32.7)). When compared with the control group, the two exercise groups (TENS+exercise baseline 191.9 (89.4) to follow up 245.5 (99.7) and placebo Stimulation + exercise (baseline: 175.9 (81.9) to follow up 206.82 (85.8)) showed significantly greater absolute and percentage increases in the average distance they covered in the 6minWT (p <0.01) at follow up. All three intervention groups showed significant decreases in their average TUG time scores (p <0.01) at week 4 compared with that of the control group, but only the two exercise groups (TENS + exercise and placebo stimulation + exercise) maintained the improvements at follow-up. Compared with the control and TENS groups, only the combined TENS + exercise group covered significantly more distance in the 6 Minute Walk Test from week 2 onwards.
Paoloni et al., 2010	SMV therapy + general care vs general care (Total = 10 hrs)	SMV + general care may improve gait in pts with foot drop secondary to chronic stroke more than general care alone
Park et al., 2014	TENS + exercise (30 mins) A frequency of 100 Hz and a pulse width 200 µs were used. Participant pre-stimulation threshold was measured from 0.01 mA and stimulated by 90% amplitude using the sub-sensory threshold. Control, placebo TENS + ex 30 m (Total =30 hrs, 15 hrs TENS and 15 hrs exercise)	Exercise therapy with TENS improves spasticity, balance, and gait in chronic stroke patients TENS group showed more reductions of MAS than the placebo TENS group (p <.05) **Static balance:** A sig. difference in eyes closed and opened, AP, ML postural sway velocity, and velocity moment was observed in the TENS group before and after the test (p<.05), and in mean difference from pre- and post-test between the 2 groups (p<.05). **TUG:** A sig. difference in before and after the test was observed in the TENS group (p<.05) and the TENS group was more improved than the placebo TENS group (p<.05). **Gait analysis test:** Sig. difference in velocity, cadence, and step length and stride length of the paretic side were observed in the TENS group before and after the test (p<.05), but in the placebo TENS group, only velocity showed a sig. difference. before and after the test (p<.05) and the TENS group showed more improvements of cadence, step length of the paretic side, and stride length of the paretic side than the placebo TENS group (p<.05)
Suh et al., 2014	ES (interferential therapy) + standard care vs sham ES + standard care (Total 1 hour)	ICT + standard care applied to spastic gastrocnemius reduced spasticity and improved gait in chronic stroke compared to sham ICT + standard care or standard care alone

Tankisheva et al., 2014	Training program on a vertical vibration platform (Power Plate) 3 times a week for 6 weeks. CG were not involved in any additional training programme. (Total 9 hrs)	Ashworth scale – no sig. differences (*p* >.05). Muscle strength - sig. between-group differences in favor of the vibration group only in isometric knee extension strength (paretic leg) (WBV baseline: 43.1 (10.1), follow up: 48.1 (7.9), Control: baseline: 30.5 (27.2), follow up: 35.2 (25.7) , (knee angle, 60˚) (*p* =.022) after 6 weeks of intervention and in isokinetic knee extension strength (velocity, 240˚/s) after a 6-week follow-up period (*p* =.005), both for the paretic leg. Postural control improved after 6 weeks of vibration in the intervention group when the patients had normal vision and a sway-referenced support surface (*p* <.05).
Van Nes et al., 2006	Whole body vibration (WBV) on each working day during 6 weeks of their admission in the rehabilitation centre. Four sessions of 45 seconds stimulation with 1-minute break between each session. A total of 120 treatment sessions were given per patient (Total = 9 hrs,1.5 hrs were WBV)	Both groups showed a main effect of time on the Berg Balance Scale score (F[2,50]=56.67, *P*<0.01) as well as the Barthel Index F[2,50]=97.12, *P*<0.01), Rivermead Mobility Index F[2,50]=76.20, *P*<0.01), Trunk Control Test (F[2,50]=11.83, *P*_0.01), FAC score (F[2,50]_76.48, *P*<0.01), Motricity Index (F[2,50]=26.85, *P*<0.01), and somatosensory threshold (F[2,50]=3.92, *P*<0.05). Improvements were most pronounced during the intervention period, but patients continued to improve during the follow-up period. There were no group time interactions, indicating similar recovery profiles for both treatment groups
Yan & Hui-Chan, 2009	TES with electro-acupuncture to LL + standard care vs Placebo TES acupuncture to LL + standard care vs standard care alone (Total =15 hrs)	TES with electroacupuncture to LL + standard care reduced spasticity and increased strength of dorsiflexion compared to placebo TES + standard care or standard care alone

[a] Largest dose [b] Smallest dose

Abbreviations: 6minWT 6 minute walk test; AP Anterior-posterior; Cm Centimetres; CG Control group; CGS Comfortable gait speed; COP Centre of pressure; EG Experimental group; ES Electrical stimulation; HHD Hand held dynamometer, Hr hour; ICT Interferential current therapy; LL Lower limb; MAS Modified Ashworth Scale; ML Mediolateral; MTP Metatarsal phalangeal; PSL Postural sway length; ROM Range of movement; SFS Sensorimotor foot stimulation; sig Significant; SMV Segmental muscle vibration; stat sig Statistically significant; SWMs Semmes Weinstein Monofilaments; TENS/TES Transcutaneous electrical (neuromuscular) stimulate; TUG Timed up and go; vs Versus; WBV Whole body vibration; Wk week.

Appendix 9 List of outcome measures used according to study

Outcome	Outcome measure	Authors
	Ashworth Scale	Tankisheva et al., 2014
Passive resistance / spasticity in spasticity:	Modified Ashworth Scale	Brogårdh et al., 2012, Cho et al., 2013, Kluding and Santos, 2008; Park et al., Suh et al., 2014, van Nes et al., 2006
	Composite Spasticity Scale	Jung et al., 2017, Yan & Hui-Chan, 2009
	Hand-held dynamometry	Cho et al., 2013,
Motor impairment / muscle strength (LL)	MRC scale 0–5	Jung et al., 2017
	Fugl-Meyer (LL)	Guo et al., 2015
	Maximum isometric voluntary contraction	Brogårdh et al., 2012, Yan & Hui-Chan, 2009 (with EMG)
	Cybex dynamometer Computer (isometric muscle strength)	Lau et al., 2012
	Isokinetic knee muscle strength	Brogårdh et al., 2012
	Isokinetic dynamometer (Biodex System)	Tankisheva et al., 2014
	EMG	Paoloni et al., 2010
	Chedoke–McMaster stroke assessment.	Lau et al., 2012
	Motricity Index	van Nes et al., 2006
LL function	Brunnstrom-Fugl-Meyer test	Tankisheva et al., 2014
ROM e.g. d/flex	Goniometer	Kluding and Santos, 2008
Walking speed	Timed 10m walk	Bayouk et al., 2006, Lynch et al., 2007; Suh et al., 2014;
	GAITRite mat	Ng and Hui-Chan, 2009
	ELITE stereophotogrammetric system	Paoloni et al., 2010
Functional independence	Barthel Index	Tankisheva et al., 2014, van Nes et al., 2006

Participation	Stroke Impact Scale	Brogårdh et al., 2012
Walking ability and mobility function	Functional Ambulation Category (FAC)	Tankisheva et al., 2014, van Nes et al., 2006
	Timed up and go (TUG)	Brogårdh et al., 2012, Ny and Hui-Chan, 2009, Park et al., 2014, Suh et al., 2014; Yan & Hui-Chan, 2009
	Level of Assistance Scale	Lynch et al., 2007
	Timed sit→stand	Kluding and Santos, 2008
	Rivermead Mobility Index (RMI)	Kluding and Santos., 2008, van Nes et al., 2006
	10MWT	Guo et al 2015, Lau et al., 2012, Lynch et al., 2007
	10MWT at comfortable and fast gait speeds	Brogårdh et al., 2012,
	6 Minute walk test (6minWT)	Brogårdh et al., 2012, Lau et al., 2012, Ng and Hui-Chan, 2009
Exertion	Borg's perceived exertion scale	Tankisheva et al., 2014
Balance / postural control:	Berg Balance Scale	Brogårdh et al., 2012, Lau et al., 2012, Lynch et al., 2007, Suh et al., 2014, van Nes et al., 2006
	Centre of pressure displacement	Bayouk et al., 2006
	Postural sway length	Cho et al., 2013,
	Anterior-posterior and medial-lateral postural sway, speed, and speed moment	Park et al., 2014
	Dynamic posturography platform (Equitest)	Tankisheva et al., 2014
	Weight distribution on the feet using the Zebris FDM-TDL treadmill	Goliwas et al., 2015
	Functional Reach Test	Suh et al., 2014
	Limits of stability	Lau et al., 2012

	Ability to maintain postural control - Sensory Organization Test (SOT)	Tankisheva et al., 2014
	Force platform (Wii Balance Board)	Jung et al., 2017
	Balance confidence (ABC) scale to measure falls efficacy	Lau et al., 2012
Trunk control	Trunk control test	van Nes et al., 2006
Sensory impairment (light touch and proprioception)	Semmes-Weinstein Monofilaments (SWM)	Lynch et al., 2007
	Somatosensory threshold (monofilaments)	van Nes et al., 2006
	Distal Proprioception Test	Lynch et al., 2007
Gait observation	Subjective observation of knee hyperextension	Guo et al., 2015
Gait analysis	Gait analyzer (OptoGait, Microgate S.r.l, Italy, 2010) sensed and transmitted through the infrared ray sensor, collecting temporal and spatial variables	Park et al., 2014
Gait kinematics	Step length	
	% stance phase	
	Kinematics of hip, knee, ankle	
	Cadence (ELITE stereophotogrammetric system)	Paoloni et al., 2010
	Time-distance data (ELITE stereophotogrammetric system)	Paoloni et al., 2010
	3-dimensional gait analysis on 10m walkway: Displacement from the center of pressure and the time of contact between the foot and force plate.	Ferreira et al., 2018
Sit to stand analysis	Ankle kinematics – WB symmetry during functional activity – 3D motion analysis	Kluding and Santos, 2008
	Timed sit→stand	Kluding and Santos, 2008
	Weight-bearing – peak dorsiflexion during sit→stand; weight bearing difference during sit→stand and in static standing	Kluding and Santos, 2008

Appendix 10 Keele University ethics approval for mNGT work (Study 2)

RESEARCH AND ENTERPRISE SERVICES

ERP1230
10th April 2015
Alison Aries
School of Health and Rehabilitation, MacKay Building
Keele University
Dear Alison

Re*:* Development and initial evaluation of the efficacy of afferent reawakening treatment of the foot on lower limb function after stroke: A feasibility study

Thank you for submitting your application for review. The proposal was reviewed at the Ethical Review Panel meeting on Thursday 2nd April. The Panel would like to commend you for a clear and well produced application and I am pleased to inform you that your application has been approved by the Ethics Review Panel. However, the Panel would like to make the following recommendations for consideration: -

Application Form

Section A

The section entitled *status* should be revised to state 'Post Graduate Research Student' only and the details for the School of Health and Rehabilitation should be removed from section entitled *Research Institute or School if not in a Research Institute*. This information should also be amended accordingly throughout all the study documentation.

Summary Document

Within the information about the sample it stated that '…. recruited from NHS Trusts in the North Midlands, Staffordshire and Shropshire.' It is recommended that this is revised to read '…. Recruited from NHS Trusts in Staffordshire and Shropshire.'

Information Sheet

Under the heading *How will information about me be used* it is recommend that a line space is inserted between the following two sentences; 'However, individual therapists and trusts involved in this study will not be identified.' And 'Personal information such as contact details …… group meeting.'

Consent Form

It is recommended that the asterisk in point 5 is deleted and that the document is formatted as appropriate so that it does not exceed one page.

If you revise any study documentation, please send a copy of the revised documents to uso.erps@keele.ac.uk for our records.

Research and Enterprise Services, Keele University, Staffordshire, ST5 5BG, UK Telephone: + 44 (0)1782 734466 Fax: + 44 (0)1782 733740

RESEARCH AND ENTERPRISE SERVICES

The following documents have been reviewed and approved by the panel as follows:

Document	Version	Date
Summary Document	1	19/03/2015
Letter of Invitation	1	19/03/2015
Information Sheet	1	19/03/2015
Consent Form	1	19/03/2015
Consent Form (for use of quotes)	1	19/03/2015
Appendix 1 Principles of the Nominal Group Process	1	19/03/2015
Appendix 2 Final treatment schedule for the upper limb	1	19/03/2015

If the fieldwork goes beyond the date stated in your application **30th November 2015**, you must notify the Ethical Review Panel via the ERP administrator at uso.erps@keele.ac.uk stating **ERP1** in the subject line of the e-mail.
If there are any other amendments to your study you must submit an 'application to amend study' form to the ERP administrator stating **ERP1** in the subject line of the e-mail. This form is available via http://www.keele.ac.uk/researchsupport/researchethics/
If you have any queries, please do not hesitate to contact me via the ERP administrator on uso.erps@keele.ac.uk Stating **ERP1** in the subject line of the e-mail.

Yours sincerely

pp N. Leighton

Dr Jackie Waterfield
Chair – Ethical Review Panel
CC RI Manager

Research and Enterprise Services, Keele University, Staffordshire, ST5 5BG, UK Telephone: + 44 (0)1782 734466 Fax: + 44 (0)1782 733740

Appendix 11 Consent form for mNGT work (study 2)

Keele University

CONSENT FORM

Title of Project: Development and initial evaluation of the efficacy of afferent reawakening treatment of the foot on lower limb function after stroke: A feasibility study. Phase 1 – protocol development.

Name and contact details of Principal Investigator:
Alison Aries
National Institute for Health Research (NIHR) Research Fellow
School of Health and Rehabilitation
MacKay Building
Keele University
ST5 5BG
Email: a.m.aries@keele.ac.uk
Tel: 01782 734418

Please tick box if you agree with the statement

1. I confirm that I have read and understood the information sheet dated 20/5/15 (version no.2) for the above study and have had the opportunity to ask questions ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time ☐
3. I agree to take part in this study. ☐
4. I understand that data collected about me during this study will be anonymised before it is submitted for publication. ☐
5. I understand that, although data will be anonymised, it may be possible that I could be identifiable in reports and publications because of my professional role ☐
6. I agree to the nominal group technique discussion group being audio recorded ☐
7. In the discussion group (Nominal Group Technique):
   I agree to keep the issues discussed within the discussion group confidential and, in particular, to avoid identifying any of the participants in relation to any issues/individual comments made during the session ☐
8. I agree to allow the dataset collected to be used for future research projects ☐

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Researcher	Date	Signature

For nominal group technique discussion group:
If you consent to participate in this study, it should be drawn to your attention that the researcher has a professional obligation to act upon any aspects of poor practice and/or unprofessional behaviour that may be disclosed during the research activity. Researchers should use the appropriate reporting mechanisms if they have witnessed or experienced poor practice and/or professional behaviour.

CONSENT FORM
(for use of quotes)

Title of Project: Development and initial evaluation of the efficacy of afferent reawakening treatment of the foot on lower limb function after stroke: A feasibility study. Phase 1 – protocol development.

Name and contact details of Principal Investigator:
Alison Aries
National Institute for Health Research (NIHR) Research Fellow
School of Health and Rehabilitation
MacKay Building
Keele University
ST5 5BG
Email: a.m.aries@keele.ac.uk
Tel: 01782 734418

Please tick box if you agree with the statement

1. I agree for my quotes to be used ☐

2. I do not agree for my quotes to be used ☐

Name of participant	Date	Signature
Researcher	Date	Signature

Appendix 12 Letter of invitation for mNGT work (Study 2)

8/5/15

Re: Invitation to participate in research relating to stroke rehabilitation

I am writing to invite you to take part in some research that is being held in the School of Health and Rehabilitation at Keele University.

The title of the project is: Development and initial evaluation of the efficacy of afferent reawakening treatment of the foot on lower limb function after stroke: A feasibility study. Phase 1 – protocol development.

You have been invited to take part in this study because you are a clinician (physiotherapist or occupational therapist) working in the NHS with experience in neurological rehabilitation. Participation is completely voluntary and if you do not want to take part it will have no impact on your future involvement with the University.

The researcher is Alison Aries, a National Institute for Health Research (NIHR) Fellow. The plan is to undertake a feasibility study within the next three years, exploring the possibility of evaluating sensory stimulation to the foot / lower limb post stroke. In preparation for this it is important to develop standardised protocols for the treatments which will be explored. These include mobilization and tactile stimulation (MTS), use of textured insoles (TIs) and task-specific gait training (TSGT), which is often used in clinical practice following preparatory stimulation techniques.

This phase of the project will use a modified nominal group technique (full details of which will be available in the information sheet): a total of nine to twelve experienced clinicians will be recruited and invited to comment on two versions of the MTS protocol being developed for the lower limb (it is expected this may take approximately 30-45 minutes), and then to attend a group discussion (lasting no longer than three hours) to finalise the protocols for MTS, TIs and TSGT.

You can choose whether you would like to take part or not, and you can withdraw at any point in time. Should you decide you are interested in participating in the research then please let us know (contact details below), by the 18th May 2015. If you are not interested in participating, please disregard this letter. For further information or to express an interest, please email Alison Aries on a.m.aries@keele.ac.uk or telephone on 01782 734418.

Yours sincerely

Alison Aries

Contact details

Any questions or concerns the please contact us on the contact details below.

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Supervisor
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Tel: 01782 733809

Appendix 13 Participant information sheet for the mNGT (Study 3)

Information Sheet

Study Title: Development and initial evaluation of the efficacy of afferent reawakening treatment of the foot on lower limb function after stroke: A feasibility study. Phase 1- protocol development

Aims of the Research

Sensory stimulation techniques to the foot and ankle are commonly used in rehabilitation following stroke, and are often applied prior to activities to retrain standing balance and walking. In the near future a study is to be undertaken as part of a doctoral fellowship to explore the feasibility of a randomised controlled trial investigating sensory stimulation techniques post-stroke. Prior to undertaking the feasibility study it is necessary to develop intervention protocols for sensory stimulation and balance/gait retraining that closely resemble current conventional therapy.

The objective of this phase is to develop the standardised post-stroke intervention protocols informed by literature and expert opinion of experienced therapists for the delivery of:

a) a module of Mobilisation and Tactile Stimulation (MTS) for the foot and ankle

b) enhanced sensory stimulation during activity (sensory augmentation) using a textured insole (TI)

c) task-specific gait training (TSGT) to the lower limb (LL) post-stroke.

Invitation

You are being invited to consider taking part in this first phase of a research project entitled: Development and initial evaluation of the efficacy of afferent reawakening treatment of the foot on lower limb function after stroke: A feasibility study. This project is being undertaken by Alison Aries (National Institute for Health Research (NIHR) Research Fellow). Before you decide whether or not you wish to take part, it is important for you to understand why this research is being done and what it will involve. Please take time to read this information carefully and discuss it with friends and relatives if you wish. Please ask us if there is anything that is unclear or if you would like more information (contact details at the end of the document).

Why have I been invited?

You have been invited to take part in this study because you are a clinician (physiotherapist or occupational therapist) working in the NHS, with experience in neurological rehabilitation.

Do I have to take part?

You are free to decide whether you wish to take part or not. If you do decide to take part you will be asked to sign two consent forms, one is for you to keep and the other is for our records. You are free to withdraw from this study at any time and without giving reasons.

What will happen if I take part?

Following receipt of this information sheet, and appropriate time allowed for consideration as to whether you wish to participate, please contact Alison Aries, Principal Investigator (details at the bottom of this sheet) if you would like more information or if you would like to take part. You will have an opportunity to ask the research team any questions you may have about the project. You will then be asked to complete a consent form either via email or in person.

You will be involved in the development of the three separate protocols: a) MTS; b) TIs; and c) TSGT.

This will be done in several stages:

Stage 1.

a) Prior to a consensus meeting, you will be sent a copy of the MTS schedule previously developed for the upper limb (UL) post-stroke and asked to consider, independently and without collaboration with colleagues, how the subsections of the UL schedule might be appropriately adapted as an intervention for the LL. You will be asked to annotate the schedule according to how it should be modified to reflect current conventional therapy for the foot and ankle, in preparation for standing and balance. In addition, you will be asked to rank the order of importance / frequency of use of each of the intervention subsections (it is anticipated this process will take no longer than 15-30 minutes), and then return the schedule with your comments to the research team, who will collate all the responses.

b) You will subsequently receive a second iteration of the modified schedule and be asked to independently review this second draft and provide feedback (anticipated to take no longer than 15 minutes) on: a) how comprehensive the schedule is; and b) how accurately it

reflects your experiences and practice of retraining somatosensation in the foot and preparing the foot for standing and balance in standing. You will return this feedback to the research team who will collate and draft a third version of the schedule.

Stage 2

You will be invited to attend a group discussion meeting with the other nine to twelve clinicians involved in the study (lasting no longer than one morning or afternoon), within the School of Health and Rehabilitation at Keele University. This meeting will be audio-taped to ensure accurate information is recorded. Group members will be asked to consent to maintaining confidentiality regarding group membership and any discussion that takes place within the group. The purpose of this group meeting will be to discuss the proposed protocols for MTS, TI and TSGT.

a) Version three of the MTS schedule will be discussed and modified until consensus is attained on the content and format of the schedule.

b) A selection of commercially available TIs will be considered, discussed and evaluated in order to seek agreement by the group; issues such as size, nature and type of texture, accompanying footwear, cost, and potential comfort/discomfort will all be considered, along with the length of time and activity involved during the pre-gait training phase of wearing the insoles. A TI protocol will be developed and agreed by the group.

c) The group will also be asked to consider and discuss the protocol for TSGT which will be adapted from the protocol developed by Dean et al (2000), and agree on an appropriate TSGT protocol for the feasibility trial. TSGT will be delivered in addition to the sensory interventions (MTS or TI).

What are the benefits (if any) of taking part?

There are no direct benefits to you in taking part but you will be assisting with the development of standardised protocols which will be used in further research to evaluate therapy for stroke.

What are the risks (if any) of taking part?

There are no expected risks involved with your participation. However, as the final discussions will take place in a group situation though there is always the potential that you feel your opinion is not heard. The group facilitator will ensure everyone has the opportunity to participate in the discussions. If you have any concerns or queries after the discussions the facilitator will be available to discuss these issues with you.

How will information about me be used?

Some demographic information will be collected i.e. age/date of birth, gender, profession and NHS band, along with information about how long you have been qualified, your professional background and experience and any post-registration training. It will be used to

provide a summary of the expertise of the group overall. However, individual therapists and trusts involved in this study will not be identified.

Personal information such as contact details will be used only to make contact with you, to send you the various iterations of the MTS schedule, and to arrange for you to attend the group meeting.

Who will have access to information about me?

Personal information will only be accessible to the researcher and the supervisor and will be anonymised and stored securely on a password-protected computer or in a locked filing cabinet at Keele University, in accordance with the requirements of the sponsor (Keele University) and the Data Protection Act (1998). On completion of the project, all personal information of participants will be deleted.

Please note, however, that it is necessary to work within the confines of current legislation over such matters as privacy and confidentiality, data protection and human rights and so offers of confidentiality may sometimes be overridden by law. For example in circumstances whereby I am concerned over any actual or potential harm to yourself or others I must pass this information to the relevant authorities.

Who is funding and organising the research?

This research is funded by the National Institute for Health Research (NIHR) as part of a Clinical Academic Fellowship doctoral study. Keele University is the sponsor for the research.

What if there is a problem?

If you have a concern about any aspect of this study, you may wish to speak to the research team who will do their best to answer your questions. You should contact Alison Aries on a.m.aries@keele.ac.uk or Tel: 01782734418. Alternatively, if you do not wish to contact Alison, the Principal Investigator, you may contact the supervisor for the research, Dr Susan Hunter, on s.m.hunter@keele.ac.uk or 01782 733809.

If you remain unhappy about the research and/or wish to raise a complaint about any aspect of the way that you have been approached or treated during the course of the study please write to Nicola Leighton who is the University's contact for complaints regarding research at the following address:-

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Appendix 14 Table of data extracted from textured insoles (TI) articles

Author and date and sample	Objective	Study design	Type of TI	Details of inter-vention	Outcome measures	Results	Conclusions	Comments
Aruin et al., 2000 n=8, acute and chronic stroke (0.16 – 5 years) All subjects ambulatory with assistive device. n=5 subjects wore AFO (not during testing) n=1 had a 6/52 therapy programme)	Explore 1) symmetry of weight bearing in stroke survivors with shoe lift on non-paretic LL 2) compelled weight bearing from shoe lift + targeted exercise helps to overcome learned non-use of hemipareti c limb.	(Pre-) experimental single group, pre- and post inter-vention No blinding No random allocation	Lift put in shoe on non-paretic side. Regular shoes worn. Just worn for testing. Although n=1 has a six-week therapy programme – insole worn all day and during all daily activities.	n=8 Just wore the shoe lift for testing n=1 had a 6/52 therapy programme, with a shoe lift in situ all day and for exercises	Weight bearing on paretic side- quiet standing, and compelled weight shift with Balance Master computerised force platform system Fugl Meyer Balance Scale n=1 Timed 5MWT in motion analysis lab	Symmetry of weight bearing increased gradually with increasing lift height, reaching almost 50:50 weight distribution at 10 mm lift condition. Authors claim: Significant results (p<0.05) achieved for all three lift heights. Carry over seen when weight bearing was measured without a lift insitu (after the testing with lifts).	Authors suggest it helps overcome learned disuse of the affected side. They claimed there was an increase in weight to the affected side after the lift was removed from the unaffected limb.	No mention of how the sample was recruited Likely bias high NOT TIs – not really relevant to my study. Student's t test is used for a small sample n=8, no discussion as to whether data was normally distributed. Only n=8 – not appropriate to use students t-test
Aruin & Kanekar, 2013 n=11 healthy subjects Pilot data from individuals with stroke n=4	Investigate effect of a novel discomfort-induced approach on the alteration in symmetry	(Pre-) Experimental (pre-post intervention, single group) No control No blinding No random allocation	Single TI, standardised footwear. Just worn for testing.	Novel discomfort-induced approach. No control group but participants were tested without an insole too NB – only wore TIs for testing	GaitRite system SMAR Equi Test (balance) TIs only worn for testing	Significant immediate effect seen for static (weight bearing), and dynamic (weight symmetry index, strength symmetry) balance tests. Static balance: ANOVA revealed significant side insole interaction for the % Wt bearing $F_{9,2}$ =50.44, p<0.001) Dynamic: Effect of D-insole – when considering in right shoe	Results indicate that a TI can significantly modify symmetry of stance and gait in healthy individuals. Pilot data from individuals with stroke showed a reduction in asymmetry of gait	No mention of how the sample was recruited ANOVA and t test used when sample size was just 10 (should have been Kruskal-Wallis (not ANOVA) and

	of gait and balance					/ left shoe statistically significant for large ($F_{9,2}$ =47.3, p<.001 / $F_{9,2}$ =58.65, p<.001), medium ($F_{9,2}$ =43.8, p<.001 / $F_{9,2}$ =41.92, p<.001) and small ($F_{9,2}$ =30.2, p<.001 / $F_{9,2}$ =28.79, p<.001) perturbations. Gait velocity – no significant difference (p = 0.6). Significant side-insole interaction was observed for swing phase ($F_{10,2}$ = 15.3, p <.0001) and stance phase phase ($F_{10,2}$ = 16.6, p <.0001)	when walking with single TI in shoe of unaffected side.	Mann- Whitney U not t-test. Likely bias high
Baron et al., 2014 (conference presentation PRS 2014) n=46 Patients with MS. Able to walk 100m	To explore perceptions of people with MS on the effect and comfort of two different TIs: a qualitative study.	Exploratory Semi-structured interviews with participants on study exploring the effects of three different TIs	Control: smooth Algeos TI Crocs TI Part of Dixon et al. (2014) trial – told to wear them as much as possible for two weeks	26 wore insoles daily, 13 wore them frequently and 7 wore them infrequently	N/A	**Croc insoles**: 81.82% said they would wear again, 13.64% said they would not wear them again, 4.5% said they would possibly wear them again **Algeos insoles:** 62.5% said they would wear again, 33.33% said they would not wear them again, 4.17% said they would possibly wear them again	Subjective experiences of wearing TIs are highly individual. Acceptability and efficacy were linked to perception of benefit.	Some useful information for my study, relating to comfort of TIs
Christovão et al., 2013 1) Controlled clinical trials 2)intervention – insole, 3) OM related to postural balance 4) published 2005-2012 12 studies (n=392) Majority included 'older volunteer	Systematic review of literature on effect of different insoles on postural balance	Systematic review	Quick comfort insole, soft gel and hard insole, TI, vibrating insole, insole with spikes, insole with wedge, balance enhancing insole, flat insole	N/A	Articles used force plates, EMG, gait disturbance protocol, electronic version of the Romberg test + camera on motion analysis	Quality assessed with PEDro scale – papers scored at 3 or 4	Insoles have benefits which favour better postural balance and control.	Papers evaluated by 2 blinded researchers Insufficient details given regarding the participants in each study to assess the relevance of this review to my study. Few stroke patients (n=15), mainly older adults.

Clark et al., 2014 n=14 older adults with mild mobility deficits and mild somatosensory deficits	Determine if enhancing somatosensory feedback can reduce controlled processing during walking, as assessed by prefrontal cortical activation	Experimental study No blinding No random allocation Used functional near infra-red spect-roscopy, quantifying cortical activity by measuring tissue oxygenation index (TOI)	Made of thin semi-rigid plastic with firm raised (1.5mm) nodules 1.5 cm apart on a grid pattern. Just worn for testing.	Just worn for testing. Treadmill walk and overground with & without shoes and walking with a TI and while dual tasking. Metabolic activity L & R prefrontal cortices assessed with fNIRS monitor	A split belt treadmill with embedded force plates and GAITRite walkway – used to acquire spatiotemporal gait measures. SWMs	Primary finding: is enhanced somatosensory feedback during walking reduced metabolic activity of prefrontal cortex. (Left hemisphere: TOI = -0.85+/- 0.35, p=.01, right hemisphere: TOI = -1.19 +/- 0.46, p=.01) The prefrontal cortex is important for attention, this indicates that walking became more automatic with increased somatosensory input with TIs - only seen for treadmill walking and not overground walking.	'Our findings support the hypothesis that enhanced somatosensory feedback of the feet reduces prefrontal metabolic activity. This finding is consistent with lower utilization of attention-demanding controlled processing during walking in older adults'	Data is presented for 11 of the 14 participants but the other 3 are not accounted for. No raw data is given
Corbin et al., 2007 n=33 healthy participants	To compare postural control measures between different balance conditions, with and without TIs.	A cross over trial No blinding No random allocation Just worn for testing	TIs of plastic floor matting, with rounded plastic nubs, raised about ¼ cm off the surface. Participants wore thin socks and own athletic shoes for testing	Subjects performed 24, 10 second bipedal and unilateral stance balance trials eyes open/closed, with and without TIs	Average velocity and area of COP excursions using the Accusway PLUS Balance Platform	Significant interaction between eyes and texture for COP area measures in bilateral stance (p=0.03) Significant differences in area and velocity of COP excursions observed during bilateral stance only when subjects not wearing TIs (t_{32} = -2.9, p =.008). No significant difference when wearing TIs (t_{32} = -0.53, p =.60).	Increased afferent information from TIs improves postural control in bilateral stance. Postural control improved while subjects wore TIs during bilateral, eyes-closed stance.	Crossover design meant subjects served as their own control. TIs were only worn for testing
Dixon et al., 2014 Part 1: n=46 with MS, who could walk 100m unassisted or using one stick / crutch.	To investigate immediate effects of TIs on balance and gait in people with MS and explore any effects after 2 wks	Design: 3 groups, within-session repeated-design with exploratory follow up period. Blinding.	1) Control (smooth surface) 2) Texture 1 - Algeos Evalite Pyramid EVA, 3mm thickness, with small pyramidal peaks, centre to centre distances	Part 1 – testing with the three different insoles (randomised order) Part 2 – 2 weeks wearing of a TI randomly allocated. Participants encouraged to wear insoles as	Double limb stance measured using Kistler force platform COP velocity Level overground walking measured using GAITrite system	Balance: significant increase observed in AP range during double-limb standing with eyes open, with texture 2 insoles. (p<.05) The mean difference was 4.5 (95% confidence interval (CI) 0.6,8.4mm) Effects of 2 wks wear: Stride length in both legs increased significantly in both	Partial evidence of immediate increase in AP sway when wearing texture 2 insole. After 2 wks of wear, no effects on standing balance. Gait: increased stride and step length. Authors suggest that TIs may	Details written regarding the insoles used – helpful for my study. Order of testing was randomised Blinded assessor used. Rigorous methodology,

	of wear (mean no of days reported as 11)	Random allocation of order of insole wearing.	approximately 2.mm 3) Texture 2 - Crocs silver insoles with small nubs of approx. 1mm height and 2mm diameter.	often as possible, but actual wear was at the discretion of participant.		the TI groups relative to control conditions:	provide sensory-motor training effect, giving improvement in walking, which is still exhibited without the TIs, rather than just a mechanical effect**.**	useful study for informing my study.
Donzé, 2015 NO details given re literature search strategy or numbers of articles identified etc,	To study what is new in rehab approach to balance and impairment in people with MS	Literature review	No details stated – just states TI are used to increase plantar stimulation	N/A - Review	N/A		Effectiveness of TIs not been demonstrated by large RCT but TIs could represent a complementary service to other PT technique in specific indications	No details given regarding search terms and methodology. Not reproducible
Hartmann et al., 2010 n=28 Independent living, or older adults aged 65 to 91 years	Investigate effects of physical exercise combined with wearing MedReflex shoe insoles on gait performance and muscle power in older adults	RCT pre/post intervention. 3 groups: Insole plus training (IG) group Just training group (TG) CG (no intervention) Random allocation No blinding	Med Reflex shoe insoles with raised projections to improve afferent feedback from the foot Subjects asked to wear insoles as much as possible and use them during everyday life and during training sessions.	n=14 Insole group (training plus wearing insoles during everyday life and during training sessions) n=14 training session: aerobic exs, progressive resistance strength training and stretching exercises twice per week for 12 weeks. Control group had no exercise or insoles	Falls efficacy scale, gait analysis and muscle power measurements of knee and ankle joints pre- and post-training. Spatio-temporal gait parameters determined using DynaPort (trunk triaxial accelerometer) During usual walking speed gait evaluated in 4 conditions: 1.On gym floor 2.Gym floor + dual task 3.On soft foam rubber walkway	Significant time x group interactions All subjects: (Walking speed: $F_{3,156} = 6.59$, $p<.001$, Cadence: $F_{3,156} = 12.71$, $p<.001$, step duration: $F_{3,156} = 12.42$, $p<.001$, step length: $F_{3,156} = 0.71$, $p<.55$) The IG and TG group did not differ significantly in their improvements. The CG showed a trend to deterioration.	Significant improvements in gait performance and muscle power after conventional training programme in independent living, older adults. However, no additional effect of long-term adaptation of gait caused by wearing insoles concurrent to physical training	Subjects wore insoles as much as possible. Four subjects wore the insoles all day, four subjects wore them half a day, and two less than 1 hour per day. There was no mention of blinded assessors.

					4.Soft walkway + dual task			
Hatton et al., 2009 n =24 Young adults	In to investigate whether textured surfaces alter postural stability and lower limb muscle activity during quiet bipedal standing balance with eyes open.	Within subject Experiment Sequence of test condition randomized No blinding Just worn for testing	3 different textured surfaces: 1: Evalite to pyramid EVA 3 mm thickness, with small pyramidal peaks texture 2: nora Luna soft mini non-slip 3 mm thickness with convex circular patterning 3: control condition -flat surface medium density Eva three mm thickness.	Participants randomized to three conditions: 1) control surface 2) texture one and 3) texture two	AP and ML or so sway variables and intensity of EMG activity in the eight dominant lower limb muscles collected synchronously over 30 seconds.	Under specific conditions of this study, with young, healthy participants, texture did not affect either postural sway or lower limb muscle activity in static bipedal standing. From the repeated measures ANOVAs there were no statistically significant differences among the three conditions for any of the postural sway variables: AP SD ($F_{2,21}$ = 2.366, p = 0.105), AP ($F_{2,21}$ = 1.583, p = 0.216), ML SD ($F_{2,21}$ = 0.406, p = 0.669) and ML range ($F_{2,21}$ = 0.021, p = 0.957).	Results of study point to three areas of further work including: 1) effect of textured surfaces on postural stability and lower limb muscle activity under more vigorous dynamic balance tests 2) post –fatigue 3) in older adults presenting age related deterioration.	Participants only stood on the textured surfaces for testing
Hatton et al., 2011 n=50 healthy older adults	To explore effects of standing on textured surfaces on double-limb balance in older adults and changes in muscle activity as possible mechanis m of effect	Within subject experimental Sequence of trials randomised / No blinding	Texture 1: Evalite to pyramid EVA 3 mm thickness, with small pyramidal peaks Texture 2: nora Luna soft mini non slip 3 mm thickness with convex circular patterning.	Eyes open and closed on two different textured surfaces and a smooth surface control.	ML and AP sway and COP velocity measured on a force platform. LL muscle activity collected using surface EMG.	ANOVA calculated for each variable. The ML range with eyes closed showed a statistically significant effect of texture ($F_{2,47}$= 3.840, p=0.033). Texture 1- mean diff for ML range was -1.7 (-3.3, -0.2) and for texture 2 -1.1 (-2.3,0.1)	Effect of standing on textured surfaces on ML sway in older adults, supporting therapeutic benefits of textured surfaces as intervention to improve balance. Effects with texture 1 but not texture 2 shows that texture type important e.g. shape, thickness, density, spacing or contouring affecting deformation of plantar skin and	Good details given regarding textured surfaces Only stood on textured surfaces for testing.

							stimulation of mechanoreceptors.	
Hatton et al., 2012 n= 30 older adults, with self-reported history of falls	To investigate immediate effects of wearing TIs on gait and double limb standing balance in older fallers.	Within subject experimental Sequence of textures worn and eyes open or closed Randomized No blinding	TIs: Evalite to pyramid EVA 3 mm thickness, with small pyramidal peaks. Centre to centre distance approx. 2.5mm Control - flat surface texture medium density Eva three mm thickness.	No intervention as such, insoles just worn for testing	Level ground 10 m walk with Gait Rite System, and double-limb standing with eyes open and closed over 30 seconds using Kistler force platform under two conditions: wearing TIs (intervention), and smooth (control) insoles in usual footwear.	2-way ANOVAs were calculated as within subjects' differences. Wearing TIs caused significantly lower gait velocity (p=0.02), step length (p=0.04) and stride length (p=0.03) compared with wearing a smooth insole. No significant differences were found with the balance parameters F statistics and CIs are not stated.	Gait velocity, step length and stride length significantly reduced when wearing TIs Plantar surface of the feet remained in contact with indentations of the TI. This may have stimulated slow adapting mechanoreceptors which are reported to respond to maintained and prolonged skin indentation.	Again, good detail given regarding the TIs No blinding The effects of prolonged wear of TIs remain to be investigated.
Kalron et al., 2015 n=25 relapsing remitting MS patients	1. Determine whether TIs have immediate effects on postural control and spatiotemporal parameters of gait and plantar sensation in people with MS 2. Explore effects of four weeks	Within subject experimental design with a four-week intervention phase No blinding No randomisation	Insoles customised for left and right feet. Insoles 3mm thick and made of elastic rubber and fabric. Coarse texture of insole designed with miniature square pyramids organised in a grid pattern	Participants instructed to wear TIs constantly throughout the day for four weeks and continue with usual activities	Spatiotemporal parameters of gait and centre of pressure excursions during static postural control using the Zebris FDM-T treadmill. Light touch and pressure sensation thresholds using Semmes Weinstein monofilaments	Data was normally distributed according to the Kolmogorov-Smirnov test. Spearman rho correlation analysis to assess relationship between postural control parameters and sensory evaluation measurements, plus paired sample t tests. Examination during the eyes closed task demonstrated an immediate reduction in the COP path length (298.4 mm, SE = 49.7 mm, versus 369.9 mm, SE = 56.3 mm; *p* = .04) and sway rate (12.0 mm/s, SE = 1.4 mm/s versus 15.1 mm/s, SE = 1.6 mm/s, *p* = .03) after insertion of TIs compared to wearing casual shoes without	Although there were improvements in some aspects of balance, efficacy of TIs in the MS population remains unclear	Good justification for why insoles were 3mm thick with coarse texture with miniature square pyramids organised in a grid pattern. – 'provide sensory feedback, yet not too rough enough to cause skin discomfort'. Treadmill used - not the same as over ground walking. Sample size at follow-up relatively small but I could

	wearing, and whether immediate effects maintained over time.					insoles. TIs did not alter static postural control parameters when examined with eyes open. Examination during eyes closed task demonstrated immediate reduction in COP path length. Findings maintained at termination of four-week intervention.		not find how many dropped out.
Kelleher et al., 2010 n=14 patients with MS and 10 healthy controls	To inspect effect on gait patterns in a group of patients with MS	Experimental with control group No control healthy age matched / No blinding Trials with and without insoles were randomised.	Fine leather insoles were cut, Grade P80 wet and dry sandpaper adhered to leather base, 'considered sufficiently rough to provide sensory feedback but not so rough as to cause skin discomfort'.	Participants tested with and without TIs. TIs only worn for testing, no actual intervention. Pts asked to walk 6m at a self-selected walking velocity. Data collected from first heel strike on force platform.	Plantar sensation using SWMs. Kinematic and kinetic EMG data. Eight Vicon 612 cameras and two Kistler force plates. Details given regarding methodology used. EMGs measured for tib ant, gastrocs and soleus	Wilcoxon Signed Ranks test used. Significant reduction in sensation in MS group compared to control group (p<.05), especially at medial forefoot. Maximum dorsiflexion angle increased whilst wearing TIs (p<.05). Significant increase in knee extension at heel strike whilst wearing TIs. Max knee flexion also increased significantly. Whilst wearing TIs there was significant increase in accelerating (max AP) ground reaction force (GRF), getting closer to values recorded for controls.	Slight ↑ in velocity + ↑ braking and acceleration GRF's, Also 'relationship between increases in gait velocity and max and min AP GRFs is a positive indication of benefits of using TIs to alter gait patterns in MS by enhancing afferent feedback from sole of foot'. Authors suggest that 'by changing the texture in contact with the sole of the foot, it may be possible to alter gait patterns, thus supporting theories that sensory feedback from the plantar surface of the foot is important in determining movement strategies during human locomotion'.	NB Gives details regarding SWMs used for measuring sensory threshold. Good description of methodology throughout. Immediate effects of TIs not measured, all participants walked approx 15m whilst wearing TIs before data was collected. Some useful info in this study which I can use for my study.

Nurse et al., 2005 n=15 healthy participants	Determine effects of textured footwear on lower extremity muscle activity, limb kinematics and joint kinetics while walking	Experimental design No blinding No randomisation	Two shoe insert conditions. Control insert made from 3mm thick EVA foam (shore C 60) Textured insert 3 mm thick EVA foam insert cut from commercially available sandal; textured with semi-circular mounds with center distances of 8 mm. For testing only	N/A	3-dimensional lower extremity kinematics and EMG Three spherical reflective markers attached to right limb segments of interest, rear-foot, shank, and thigh. Analysis of movement data using KinTrak software. Emg of soleus, medial gastrocnemius, tibialis anterior, vastus medialis, rectus femoris, and biceps femoris	Wilcoxon Signed Ranks test used to analyse muscle data and paired t test to analyse kinematic and kinetic data. NB raw data not provided. Significant decrease in total tibialis anterior energy (13% less) for entire stance phase while wearing textured insert.	Changing only texture of shoe insert resulted in significant changes in EMG activity of both ankle flexor and extensor muscles, ankle joint kinematics, and moments generated at knee joint. There is strong indication that changes in gait patterns were due to change in sensory feedback from plantar surface of the foot. This supports the theory that sensory feedback from cutaneous receptors in the plantar surface of the foot is important in determining movement strategies during human locomotion.	No randomisation, no blinding but OMs used perhaps did not require blinding.
Orth et al., 2013	To evaluate the efficacy of textured materials for enhancing perceptual motor functionality	Systematic review		N/A - Review		23 eligible - 21 published peer reviewed research articles and two published conference proceedings. Two distinct age groupings identified (young from 18 to 51.1 yrs and,elderly, from 64.7 [to 79.4 yrs) which could be further characterized by presence of ailment (with or without)	Forest plot summarizing the of textures clearly suggests a trend toward improved perceptual-motor performance Methodological quality assessed independently	' unequivocal' support for utilising textured materials in young healthy populations for improving perceptual-motor performance. In elderly and ailing further research required

							by lead author and research assistant using Cochrane risk-of–bias tool.	
Palluel et al., 2008 19 healthy elderly participants and 19 healthy young adults.	Explore contribution of plantar cutaneous inputs induced by spike support surface to control of stance	Within subject experimental design No blinding No randomisation	Footwear consisted of Arena® NewMarco sandals Entire insole had spikes made with semi-rigid PVC (density: 4 spikes/cm2 ; height of a spike: 5 mm; diameter: 3 mm) and uniformly distributed under feet except on medial arch where spikes were bigger (density: 2 spikes/cm2 ; height: 1 cm; diameter: 5 mm)	Both groups came for two sessions - one standing and one walking and were tested with and without spikes	COP motion processed through mean COP location (in mm), surface area (in mm^2), mean speed (in $mm.s^{-1}$), root mean square (RMS in mm) and median frequency (Hz) on the AP and ML axes.	In the elderly, post-hoc analysis showed improvement of postural control in both sessions. In standing session, there was decrease of COP surface area and AP RMS between t0' and t5' of spike condition (p =0.001, p=0.003, respectively) and between t5' of both conditions (p =0.001, p = 0.004, respectively). Significant difference of mean speed in spike condition between t0' and t5' of condition (p =0.005), with lower values occurring at t5' (10.6% of improvement in standing session and 3.9% in walking session	Results provided evidence that wearing sandals with spike insoles can contribute, at least temporarily, to improvement of unperturbed stance in elderly with relatively intact plantar cutaneous sensation, and also in young adults. standing or walking for 5 min with these spike sandals led to a significant improvement of balance in both groups for AP and ML planes. In the elderly, effects were more pronounced in standing than in walking session	Limitations acknowledged: Potential limitations of the experiment pertain to the subjects' selection, the quantification of postural performances, and statistical analyses. Did not randomise order of testing so there could have been a learning effect
Palluel et al., 2009 n=19 healthy elderly, n=17 healthy young adults	To explore lasting effects of tactile sensitivity enhancement induced by spike insoles on control of	Within subject experimental design No blinding No randomization	Entire insole had spikes made with semi-rigid PVC (density: 4 spikes/cm^2 ; height of a spike: 5 mm; diameter: 3 mm) and uniformly distributed under feet except on medial arch	Participant exposed to standing and to walking sessions, counterbalanced across participants. In both sessions, postural responses assessed during unperturbed	COP of foot motion calculated through surface area (i.e., 90% confidence ellipse area, in mm, mean speed (mm.s1), root mean square (RMS) on AP RMS and ML RMS axes (mm). Mean of three trials calculated at t1, t2,	ANOVA with repeated measures. Adjustments of p values for the violation of the spherical assumption were made with a multivariate test (Hotelling-Lawley Trace). Three-way interaction of age x session x time was significant for CoP surface (p= .028) and the AP root mean square (RMS) (p < .001). In elderly subjects, post hoc analysis	Results confirmed reorganization of hierarchy of sensory inputs and inability of elderly people to rapidly reconfigure postural set when sensory context is modified.	Did not randomise order of testing so there could have been a learning effect. Even 5 mins wearing the spike insoles was uncomfortable. Placed control insoles on top of

	stance in elderly		where spikes were bigger (density: 2 spikes/cm^2 ; height: 1 cm; diameter: 5 mm)	stance (Equi, model PF01, Aix les Bains, France) force platform. Eyes closed	t3, and t4 for standing and walking sessions, respectively.	showed improvement of CoP surface and AP RMS after standing for 5 minutes (t2) with spike insoles, compared to t1 (p < .001 and p = .048, respectively). When spike insoles were removed (t3), benefits were immediately lost for both variables (p < .001) with values returning to baseline. In walking session, decrease of CoP surface and AP RMS not significant between t1 and t2 (p = .26 and p > .99, respectively), but higher values observed immediately after removing insoles (t3; p <.001) and after rest of 5 minutes (t4) for CoP surface, only (p < .001) Raw data not provided		spike insoles for testing
Preszner-Domjan et al., 2012 n=50 healthy young adults	Investigate effect of different types of mechanical stimulation of sole on standing postural stability in healthy, young adults	Experimental study No blinding No randomisation	Thin elastic layer of rubber with spiked layer (density 5 spikes/cm2, height of spikes 7 mm, diameter of spikes 2 mm), and it was placed onto the force plate	Displacement of COG, subjects stood on stable platform Measurements performed in three sessions (3 9 10 s) in open & closed eyes. Then supporting surface altered from the firm to foam with added spiked layer, first open eyes and then closed eyes. Spiked layer affected sole just during	COP - sway paths, AP & ML Static balance parameters were measured before and after manual stimulation. The baseline measurement of the static postural stability without any stimulation served as a control condition. Participants were asked to stand up for 20 s after the stimulation, in this way the negative	Wilcoxon Signed Ranks test used to compare tactile threshold medians of left and right feet with normal though threshold. Two-way ANOVA used to analyse sway data. Sway paths increased significantly in both directions and in both surface conditions when there was no visual input. Standing on foam surface significantly increased the sway path in both directions, in both eye conditions compared with standing on firm surface. A main effect of vision was observed in both directions	'Activation of plantar mechanoreceptors by 10-minute manual stimulation can partially compensate subjects for the absence of visual input and the lack of accurate pressure information'	To investigate the effect of different types of mechanical stimulation of the sole on standing postural stability in healthy, young adults Just for testing

				posturographic measure Baseline measurement of static postural stability without stimulation served as control.Manual technique -static and glide pressure focus on supporting surfaces of sole, especially heel and metatarsal heads. 10 mins. Stimulation performed simultaneously both feet	effect of sudden standing up was avoided. Manual stimulation was applied at least 30 min after the stimulation of the spiked layer.	(AP $p<0.001$; ML $p<0.001$) in the baseline measurement: the absence of visual input (EC) caused a significant increase in the sway path, however, these changes disappeared in the AP and ML directions after manual stimulation, and on the spiked layer in ML direction. Results showed a significant two–way interaction of vision x stimulation for the sway path in both AP ($p<0.001$) and ML ($p<0.001$) directions on firm surface. The main effect of manual stimulation was observed in both AP ($p=0.001$) and ML ($p<0.001$) directions when subjects stood on firm platform with closed eyes compared to baseline data, i.e., the sway paths decreased significantly. We noticed an additional main effect of stimulation, the spiked layer caused significant decreased sway path in both AP ($p<0.001$) and ML ($p<0.001$) directions in EC condition. In ML direction, this effect was more prominent, thus, subjects were fully compensated by the spiked layer for the missing visual information. No raw data presented.		
Qiu et al., 2012 10 younger and 7 older participants	Study investigated the effects of textured	Experimental study Order of insoles were randomised	Both insole surfaces (International Children's Orthotic	Participants were tested under two vision conditions (eyes open, closed) on two	Centre of pressure measurements included the range and standard deviation of AP and	A mixed model ANOVA comparing young with old and also within participant factors (insole surface, vision and standing surface), Post hoc	These findings suggest that textured insole surfaces can reduce postural sway in	Anecdotally participants reported that the harder insoles were

were randomly selected from a database of healthy older adults.	insole surfaces on postural sway in ten younger and seven older participant s performing standing balance tests on a force plate under three insole surface conditions: (1) barefoot; (2) with hard; and (3), soft textured insole surfaces		Laboratory, Australia) were 1.5 mm thick and had granulations with a diameter of 5.0 mm and a height of 3.1 mm that were distributed evenly across the upper surface	standing surfaces (firm, foam). Four 30 s trials were collected for different combinations of insole surface, standing surface and vision.	ML displacement, path length and the 90% confidence elliptical area.	comparisons with Fisher's least significant difference test. Results revealed a significant Group*Surface* Insole interaction for five of the dependent variables (90% confidence elliptical area, path length, AP and ML sway and ML standard deviation) (p<.05). Compared to younger individuals, postural sway was greater in older people on both standing surfaces in the barefoot condition (p<.05). However, both textured insole surfaces reduced postural sway for the older group especially in the eyes closed condition on a foam surface (p<.05). Raw data not provided.	older people, particularly during more challenging balance tasks	uncomfortable over an extended period of time
Qiu et al., 2013 20 healthy older adults (controls) and 20 participants with Parkinson's Disease (PD)		Experimental study Order of testing was randomised No blinding	Insoles 1.5mm thick with soft insole (270 density Ethylene Vinyl Acetate (EVA). Textured surface - granulations measuring 5.0mm in diameter and 3.1mm in height distributed evenly across	Participants performed standing tests, on two different surfaces (firm and foam), under three footwear conditions: 1) barefoot; 2) smooth insoles; and 3) TIs	Standing balance was evaluated using a force plate yielding data on the range of anterior-posterior and medial-lateral sway, as well as standard deviations for anterior-posterior and medial-lateral sway.	A mixed model ANOVA with one between -participant and 3 within-participant factors. Greatest benefits were observed in the PD group while wearing the TIs, and when standing on the foam surface with eyes closed. Relative to the barefoot and smooth insole conditions, the PD ppts demonstrated significantly reduced ML postural sway while wearing the TIs (Fisher's least	Demonstrated that TIs provide a passive intervention that is an inexpensive and accessible means to enhance the somatosensory input from the plantar surface of the feet, which may provide a low-cost means of improving postural stability in	No blinding – potential for bias

			upper surface, accentuated by two raised compliant ridges measuring 3.1mm in height and 3.1mm in width located around lateral perimeter of insole and around heel Smooth insoles - same materials height and dimensions			significant difference test: textured v barefoot: p =.040, textured vs smooth: p=.001)	high falls-risk groups, such as people with PD	
Silva et al., 2015 n=12 with type II diabetes	To evaluate the effects of somatosensory training on the mean amplitude of the COP in the upright position and the sustained benefits after 6-months	Experimental design No randomization No blinding	13 stations with different textures. 1st) 10 cm thick foam with high density; 2nd) wooden box with beans; 3rd) 2 cm thick mat, with a density lower than the station foam; 4th) wooden box with cotton; 5th) 2 cm thick mat; 6th) balance board to train mid-lateral balance; 7th) participants sat down and grabbed a towel spread on the floor using their	Somatosensory training for 45 mins twice a week for 12 weeks. A circuit was composed of 13 stations with different textures. The participant was instructed to remain for 2 min at each station, following the rhythm of slow-paced and fast-paced songs.	SWMs The balance evaluation was performed through COP analyses, which were obtained in bipodal position under two conditions: eyes open and eyes closed. No details are given regarding the equipment used to perform the assessment.	Kolmogorov-Smirnov test used to determine the consistence of the stabilographic data, followed by the analysis of variance (ANOVA) and the Tukey- Kramer Multiple Comparisons Test Eyes open: The results showed a significant decrease (p < 0.001) in the AP oscillation of the COP comparing the initial (2.17–0.72 cm) and after 12 weeks (0.62–0.42 cm). Significant difference was found (p < 0.01) between the initial and after 6-month follow-up (1.34–0.68 cm) Eyes closed: The results obtained with eyes closed showed significant differences (p < 0.001) in the anterior-posterior oscillation of the COP between the initial (2.47 _ 0.75 cm) and after	The somatosensory training reduced the mean amplitude of the AP oscillation with sustained benefits after 6-month follow up in elderly individuals with type II diabetes mellitus	No randomisation, no blinding and insufficient reporting of methodology to allow the study to be reproduced. Potential for a high level of bias is noted

			toes (foot strengthening exercise); 8th) 10 cm thick foam; 9) proprioceptive balls with 8 cm diameter and external projections placed on the floor for somatosensory stimuli in different regions of the foot; 10th) wooden box with millet; 11th) 2 cm thick mat; and 13th) sandpaper (abrasive mineral) to slide the feet for somatosensory			12 weeks (0.84 _ 0.61 cm). The comparison between the initial and after 6-month follow-up (1.22 _ 0.79 cm) showed significant difference ($p < 0.01$). Raw data not provided. F-statistics from ANOVA not provided.		
Wilson et al., 2008 Convenience sample of 40 healthy female subjects (Age 51.1 +/- 5.8 years)	To develop a standard-ised methodology and evaluate the clinical effectiveness of four differently textured foot orthoses on static and dynamic	Test-re-test Prospective pilot single-blind randomised clinical trial	Subjects wore shoes for 4 weeks, minimum 6 hrs per day Control group (n=10) fitted with shoes with a standard Hotter shoe insole (Shore value A20 – soft) n=10 - shoes fitted with a flat, plain, and smooth surface, made of 3mm	Postural stability was assessed on a Kistler force platform (Model 9286AA, Kistler, Alton, UK) by recording the differences between the maximum and minimum ranges of centre of pressure (COP) in the ML and AP directions. Subjects stood on	Medial / Lateral and anterior -/posterior postural stability: No significant differences found between groups at either baseline or post intervention. Base of support: No significant differences seen either at baseline or post intervention	2 x 4 repeated measures ANOVA to assess postural stability. Dynamic postural stability was measured using a repeated measures ANOVA. Data from 37 subjects were available for final analysis. Three subjects withdrew from the study during the 4- week period (one from the control group and two from the dimple FO group). Data from 37 subjects were available for final analysis. No significant differences found between groups at	'Static balance and in our 30-m walk, there were no decrements or improvements in postural or walking stability over a 4-week period of continuously wearing any of the shoes with any of the FO'	Limitations:'Our findings may have limited application to an older, frailer female population, as we sampled a relatively healthy middle-aged female population recruited from the staff and student community. There is therefore the possibility of sample bias. Each of the FO groups

	balance variables in an older female population		thick EVA. 2nd intervention group n =10 – shoes- dimpled surface (1 mm raised circles, with a diameter of 3 mm spaced 5 mm apart covering the entire surface n=10 - raised grid pattern fitted into their shoes (1 mm raised square pyramid shapes, side length two point 5 mm, peaks spaced 2.5mm apart covering the entire surface	the force platform wearing the shoes and FO. Base of support was evaluated during walking using the GAITRite system		either baseline or post intervention. Medial / Lateral (F=0.273, p=0.605) and with foot orthosis (FO):(F=0.677, p=0.572) and no significant interaction of visual conditions and FO: (F=0.590, p=0.626) Anterior -/posterior postural stability: (F=3.029, p=0.091), FO conditions: (F=0.567, p=0.641) and no significant interaction of visual conditions and FO: (F=0.213, p=0.887) Base of support: No significant differences seen either at baseline or post intervention (F=0.019, p=0.892) or for FO conditions: (F=1.481, p=0.238) and no significant interaction of visual conditions and FO: (F=0.265, p=0.850)		contained only 10 subjects. This raises the possibility of type II sampling errors, and erroneous acceptance of the null hypothesis

Abbreviations: 5MWT 5 metre walk test; AFO Ankle foot orthosis; AP Anterior-posterior; CI Confidence Interval; COP Centre of pressure; EMG Electromyography; EVA Ethylene Vinyl Acetate; FO Foot orthosis; GRF Ground reaction force; LL Lower limb; ML Mediolateral; MS Multiple Sclerosis; OM Outcome measure; PD Parkinson's Disease; PT Physical therapy; PVC Polyvinyl Chloride; SWMs Semmes Weinstein Monofilaments; RMS Root mean square; TI textured insole; TOI Tissue oxygenation index.

Appendix 15 Study details relating to TSGT including type of study, sample size and details of intervention

Study type, author and sample size	Details of intervention
Blennerhassett and Dite (2004) Prospective randomized single-blind clinical trial (n=30)	Participants randomized to either the upper limb or mobility training group. Additional task-related practice for 1 hour a day, five days per week for four weeks. Each session consisted of a circuit of ten 5-minute work stations, with up to four subjects in each session. All activities were customised and progressed to suit the individual subjects. Mobility group activities included warm up and endurance tasks using stationary bikes and treadmills, followed by functional tasks such sit to stands, step ups, obstacle course, walking, standing balance, stretching is required and strengthening using traditional gymnasium equipment.
Cooke et al (2010) Phase 1 RCT (n=102)	Intensity: Up to 1 hour per day, 4 days a week for 6 weeks (24 hours) The content of functional strength training focused on repetitive, progressive resistive exercise during goal-directed functional activity. The emphasis was on producing appropriate muscle force for the functional activity being practiced. Treatment progressed systematically using repetition and increasing resistance by, for example, changing the limb's relationship to gravity, increasing the range of movement or distance over which body weight was transported, and changing the weight of the external objects used to provide resistance. Treatment activities progressed systematically from light to heavy loads and from few to many repetitions. Participants performed the repetitive exercise of functional tasks such as sit to stand to sit, stair climbing /step ups, inside and outside walking, transfer training, bed mobility and treadmill training with and without the use of a body weight support system.
Dean et al (2000) A randomized, controlled pilot trial (n=12)	Intervention: exercise classes three times a week for four weeks (one-hour task-related training). The exercise class for the experimental group focused on strengthening the affected lower limb and practicing functional tasks involving the lower limbs, while the control group practice upper limb tasks. There were 10 workstations incorporated into the circuit. The work stations were designed to strengthen the muscles of the affected leg in a functional way and provide for practice of locomotor-related tasks: 1. Sitting at a table and reaching in different directions for objects in the of the located beyond arm's length to promote loading of the affected leg and activation of affected leg muscles 2. Sit to stand from various chair heights to strengthen the affected leg extensor muscles and practice this task

	3. Stepping forward, backward, and sideways onto blocks of various heights to strengthening affected leg muscles. 4. Heel lifts in standing to strengthen the affected plantar flexor muscles 5. Standing with the base of support constrained, with feet in parallel and tandem conditions reaching for objects, including down to the floor, to improve standing balance. 6. Reciprocal leg flexion and extension using the Kinetron in standing to strengthen leg muscles. 7. Standing up from a chair, walking and short distance, and returning to the chair to promote a smooth transition 8. Walking on a treadmill 9. Walking over various surfaces and obstacles 10. Walking over slopes and stairs providing the opportunity for walking of practice under variant conditions
Donaldson et al (2009) Randomized phase two study (n=30)	Although lower limb is mentioned in the article the functional strength training was for the upper limb – not appropriate
French et al (2007) Systematic review (Randomized/quasi-randomized trials)	Fourteen trials with 17 intervention-control pairs and 659 participants were included (adults, post-stroke). Interventions included an active motor sequence performed repetitively within a single training session, aimed towards a clear functional goal, and where the amount of practice could be quantified
Jonsdottir et al (2010) RCT (n=20)	20 sessions of 45 mins each. Electromyographic bio feedback applied in a task orientated approach based on principles of motor learning to increase peak ankle power of the affected leg and gait velocity in patients with chronic mild to moderate hemiparesis. In sufficient detail is given in relation to the intervention it would not be repeatable, and it is not helpful for the current study.
McDonnell et al (2007) A pilot RCT (n=20)	Nine sessions of task-specific physiotherapy training over three weeks. To determine whether combining appropriate afferents stimulation with task-specific training resulted in greater improvements than training alone in patients with impaired upper limb function in the sub-acute phase following stroke. NB for upper limb – not appropriate
Mead et al (2007) RCT (n=66)	Each session lasted 1 hour 15 minutes (including ‘‘tea and chat’’ after the interventions). Interventions were held three times a week for 12 weeks randomized exploratory trial comparing exercise training (including progressive endurance and resistance training) with relaxation (attention control). Mode of exercise, initial exercise level, and rate of progression were based on the Falls and Exercise Management Study to reduce

	falls in older frailer participants. The endurance component began in Week 1 as a circuit of cycle ergometry, raising and lowering a 1.4-kg, 55-cm exercise ball, shuttle walking, and standing chest press performed consecutively. Between each circuit station, patients walked or marched in place to ensure continuous movement. A stair climbing, and descending exercise was added in Week 4. The circuit duration increased from 9 minutes to 21 minutes by Week 12. Cycling intensity was increased weekly by small increments in pedalling resistance, cadence or both while maintaining perceived rate of exertion in the range of 13 to 16. The resistance training included upper back strengthening and triceps extension exercise, both performed seated using elastic resistance training bands and progressing from four repetitions using the lowest-resistance band to 10 repetitions using the highest-resistance band by Week 12; a pole-lifting exercise performed standing, progressing from four repetitions with a 0.22-kg pole to 15 repetitions with a 3.6-kg pole by Week 12; and a sit-to-stand exercise, resisted by body mass, progressing from four to 10 repetitions by Week 12 and becoming more difficult by introducing pauses during lowering into the chair and then increasing the frequency and duration of the pauses and increasing the angle of the knee bend and the upper body levers (i.e., the arms).
Monger et al (2002) A pre-test, post-test design	Three-week home-based exercise programme. The task-specific training protocol was supervised by one of the investigators who visited the subjects in their homes three times weekly. Subjects were also asked to practise on their own each day for approximately 20 minutes. Each supervised exercise session was of 20 minutes duration. The number of repetitions and intensity of each exercise was graded to subject's level of ability and progressed as they improved. Subjects were encouraged to exercise as hard as possible and to perform their maximum number of repetitions without pause, repeating three times. Seat and step heights were set at a level to encourage force generation in the affected lower limb. Exercises were progressed in difficulty in several ways including decreasing the height of the seat, increasing the height of the step, increasing speed and increasing the number of repetitions. Verbal feedback, e.g. about weight distribution and speed, as well as encouragement were provided. Subjects were given a copy of the protocol, a diagram of the step-up exercises and a diary in which to record the number of repetitions done each day. The daily exercise protocol: **Sit-stand–sit** 10 times (or maximum number up to 10 that can be performed without a rest). Repeat 3 times (30 repetitions in total). Move feet backward, look straight ahead, swing trunk forward at the hips and stand up with weight evenly distributed through both feet. Do not use your arms. **Step-ups** Standing, affected foot on 8-cm block, step up and down with other leg (a) to shift body mass forward on to affected leg and (b) to shift body mass sideways on to affected leg. Exercise near furniture to

	steady yourself if necessary. Do 3 sets of 10 repetitions (or maximum number up to 10 that you can perform without a rest). **Calf stretch** Standing with affected knee straight and extended arm/s resting on wall: keeping body straight, pivot the body forward at the ankles keeping heel on the floor until you feel the calf muscle is stretched.
Pang et al (2005) A randomized, controlled trial (n=63)	1-hour sessions, three sessions/week, for 19 weeks. The intervention group underwent a fitness and mobility exercise (FAME) program designed to improve cardiorespiratory fitness, mobility, leg muscle strength, balance, and hip bone mineral density. The control group underwent a seated upper extremity program.
Peurala et al (2007) Randomized trial (n=22)	Patients spent a daily maximum of 1hr therapy time to obtain 20 min of walking. Additional physiotherapy was also provided during the 3 wk therapy period. Patients spent a daily maximum of 1hr therapy time to obtain 20 min of walking. Additional physiotherapy was also provided during the 3 wk therapy period. Each patient also received other gait-oriented physiotherapy for 55 minutes each day, according to individually set goals.
Pollock et al (2007) **Systematic review** (randomized/quasi-RCTs)	Twenty trials (1087 patients) were included in the review related to physiotherapy treatment approaches aimed at promoting postural control and lower limb function
Pollock et al (2014) Cochrane review included randomized trials	To review the evidence of the effectiveness of interventions aimed at improving sit to stand ability after stroke. 13 studies with 603 participants met the inclusion criteria for the review and data from 11 of these studies were included within the meta-analysis.
Salbach et al (2004) RCT	Subjects in both groups attended sessions three times a week for six weeks. The experimental intervention comprised of 10 functional tasks designed to strengthen the lower extremities and enhance walking balance, speed and distance. The interventions: subjects in both groups participated in 18 sessions of task orientated training, given three times a week for six weeks in a rehabilitation or hospital setting. The mobility intervention inspired by Dean et al. (2000) was a standardised programme supervised by a or physical or occupational therapist, of 10 walking related tasks designed to strengthen the lower extremities and enhance walking balance, speed and distance in a progressive manner. * For components of the intervention see table (Appendix4.7)
Scianni et al (2010) Randomized trial – protocol only	The experimental group would undertake task-specific walking training, plus targeted strength training three times per week over 10 weeks, while the control group will only undertake task-specific walking training. $ For details of proposed intervention see table (Appendix 4.8)

Straube et al (2014) Repeated measures (n=22)	Practice of multiple stepping tasks was provided in variable environments or contexts at high aerobic intensities for >40 sessions over 10 weeks.
Sullivan et al (2007) A phase II, single-blinded, randomized clinical trial (n=80)	Exercise sessions were four times a week for for 6 weeks (total of 24 sessions). The exercise interventions consisted of body-weight-supported treadmill training, limb-loaded resistive leg cycling (CYCLE), LE muscle-specific progressive resistive exercise (LE-EX), and upper-extremity ergometry (UE-EX). Lower extremity exercise: Progressive-resistive exercise program for paretic hip flexors and extensors, knee flexors and extensors, and ankle dorsiflexors anti plantar flexors. **Training Parameters Exercise selection and resistance:** Participant attempts the baseline exercise for each muscle group. The baseline exercise position for each muscle group specifically targets the isolated muscles and requires the participant to move in an antigravity range deviating from synergy. If the participant cannot perform the baseline exercise movement, deviating from synergy a decrease in progression is made incorporating movement patterns within synergy. If the participant can complete the baseline exercise, the exercise is continued, or progressive resistive loading is initiated until the 10-Repetition maximum (RM) load is determined. **Repetitions: 10** Sets: 3 (for each muscle group). **Exercise selection and resistance:** Determined by the participant's success in completing 10-RM. If the participant is able to perform 10 repetitions with ease. then a progression is applied (increase exercise level or resistance). If the participant is able to complete only 8 repetitious in each set but can complete 10 repetitions with ease when the load is decreased, then the current exercise level or resistance is maintained. If the participant is able to do less than 8 repetitions in each set. then the exercise is decreased (either in exercise level or resistance). **Repetitions: 10 Sets: 3**
Van der Port et al (2009) Multicentre single-blinded randomized trial (n= 220) [Protocol only]	Task-oriented circuit class training (CCT) two times a week for 12 weeks Primary aim of the FIT-Stroke trial is to evaluate the effects and cost-effectiveness of a structured, progressive task-oriented CCT programme, compared to usual physiotherapeutic care during outpatient rehabilitation in a rehabilitation centre. The task-oriented CCT will be applied in groups of 4 to 6 patients. Patients assigned to the intervention group (two participants or more) will receive a 90-minute structured progressive task-oriented CCT programme twice a week over a twelve-week period (24 sessions). The programme includes 4 stages: (1) warming up (5 minutes), (2) circuit class training (60 minutes), (3) evaluation and a short break (10 minutes) and (4) group game (15 minutes).

	The training programme includes 8 different workstations, intended to improve meaningful tasks related to walking competency, such as balance control, stair walking, turning, transfers and speed walking. The eight workstations incorporated in the circuit are: (1) standing and reaching; (2) stair walking including transfer; (3) walking and picking up various objects from the ground; (4) kicking a ball; (5) stepping up and down; (6) walking course with obstacles; (7) transfers (lying to standing and sitting); and (8) speed walking. Graded progression will be achieved by (1) increasing the difficulty of the task; (2) adding weights; or (3) increasing the number of repetitions. No special (fitness) equipment is needed to perform the tasks. Each workstation will be done for 3 minutes, followed by 3 minutes of rest and 1 minute to change to the next workstation. The participants will complete the exercises in pairs, where one does the exercise while the 'partner' has a rest period and helps the other by keeping track of the number of repetitions and stimulates him/her to perform at their best. Time will be kept by the supervisors. The precise composition of the treatment package for each patient, in terms of appropriate selection of type of workstation, number of repetitions and intensity, will be determined at baseline, based on patients' profiles in terms of muscle strength, physical fitness and mobility status. All patients will keep an activity log in which they record the number of repetitions at each workstation during the sessions, which they will then use as feedback in the next session. The one-hour session of workstation training will be followed by a 15-minute group game, in which the whole group performs a game to improve walking competency. Games will vary across the sessions. Options include a game in which walking tasks are combined with a cognitive task, or a game consisting of fast walking and changing directions. Ball games can, of course, be used as well, as long as they serve to train walking performance. ***Control group:*** Received regular care.
Wevers et al 2009 (Systematic review of RCTs)	To systematically review randomized, controlled trials of task-oriented circuit class training on gait and gait-related activities in patients with stroke. Six of the 445 studies screened, comprising 307 participants, were included.
Yang et al (2006) Single-blind, RCT (n=48)	Subjects in the control group did not receive any rehabilitation training. Subjects in the experimental group were put on a four-week task-oriented progressive resistance strength training.

Abbreviations: CCT Circuit class training; Hr Hour; LE-EX Lower extremity exercise; UL-Ex Upper extremity exercise

Appendix 16 Details from Salbach et al (2004): Components of the mobility intervention

Task	Target	Description and progression
Warm up	Range of movement and flexibility	Marching on-the-spot, arm lifts, ankle circles, stretching of the trunk, thigh, and calf muscles.
Step ups	Balance	5 minutes of placing each foot alternately on a step, progressing to stepping onto a step (step ups), to a higher step, and to decreasing upper extremity support; time divided evenly between leading with right vs. left foot
Balance beam	Balance	5 minutes of walking forwards, sidewards, and backwards between two parallel lines, 20 cm apart, progressing to using one line, to using a balanced beam, and finally to the lateral stepping on the floor, feet crossing over in front or in back, and then alternating
Kicking ball	Balance	5 minutes of kicking a ball against a wall, progressing to decreasing upper extremity support, to increasing the distance from the wall, to kicking to a target, and to dribbling the ball around pylons; time divided evenly between kicking with right verses left foot
Stand up and walk	Balance lower extremity strength walking	With four standard on chairs placed at four corners of a square, five minutes of repeatedly standing up and walking to the chair directly in front, sitting, then standing up and walking to the chair on the left, etc. progressing from using the arms to not using the arms, and to decreasing the seat height
Obstacle course	Walking balance	5 minutes of stepping over an obstacle, stepping onto, along, and down from an aerobics step, walking over a mat, or a ramp, and returning, progressing by increasing the heights and number of obstacles, and from completing the course walking forwards to walking backwards.
Treadmill	Walking endurance	10 minutes of walking pattern comfortable pace, progressing from using arms to not using arms, by the increasing treadmill speed, and by adding an inclination
Walk and carry	Walking balance	5 minutes of continuous walking carrying a grocery bag, progressing to carrying a bag in each hand, to increasing the weight of the bag, to carrying a laundry basket, and to stopping on command.

Speed walk	Walking endurance	5 minutes of continuous walking at maximum speed, progressing to running
Walk backwards	Walking	5 minutes of continuously walking backwards, progressing from receiving physical assistance to receiving no assistance
Stairs	Lower extremity strength	5 minutes of going up and down a flight of stairs, progressing from taking one step at a time to taking alternating steps, from using then not using the handrail, and to achieving a greater number of flights

Appendix 17 Details from Scianni et al (2010): Walking activity characteristics of the task-specific walking training

Activity	Type	Practice	Progression
Step on block with the paretic limb	Segmented	Swing	Diminishing hand support and increasing speed Step on block with nonparetic limb
Step on block with nonparetic limb		Stance	Diminishing hand support
Stand on one leg (paretic leg)		Stance	Diminishing hand support
Squat on one leg		Stance	Diminishing hand support and increasing speed
Stand on paretic leg, then perform plantarflexion		Stance	Diminishing hand support
Step sideways		Lateral movement	Diminishing hand support and increasing speed
Step sideways on a block		Lateral movement	Diminishing hand support
Walk on footprints	Complete	Whole task	Increasing stride length
Walk between lines		Whole task	Decreasing stride width
Speed walk		Whole task	Increasing speed

Strength Training:

Grade 1
Focus on the mid-range of muscle length
Decrease the effects of gravity
Decrease friction
Decrease the lever arm

Grade 2
Focus on range of motion
Sustain contractions and increase speed
Begin to add resistance at mid-range

Grade 3 and 4 Resistance exercises using weight machines, free weights and body weight (initial load: 50% of 1 RM; then 80% of 1 RM)

Appendix 18 2nd iteration of the lower limb MTS protocol

TREATMENT SCHEDULE FOR MOBILIZATION AND TACTILE STIMULATION TO THE LOWER LIMB – ITERATION 2

Date: Pt ID Position of patient: Length of session: Therapist:

AIMS (Please tick)
❑ Regain normal extensibility of skin, muscle, connective tissues, tendons and joints to enable foot to accept base of support ❑ Reduce hypersensitivity or pain ❑ Heighten awareness foot position and posture ❑ Normalize tempero-spatial activation of muscle during functional activity (accuracy, quality of movement, normalise balance reactions) ❑ Normalize afferent stimulation arising from functional activity ❑ Normalize performance parameters (smoothness, accuracy, co-ordination, reciprocal activation, strength) for movement, balance and gait.
JOINT MOBILZATIONS:
1a) PASSIVE MOVEMENTS THROUGH ANATOMICAL RANGE (WITH HIP AND KNEE IN NEUTRAL ALIGNMENT, NB NOTE ANY RESTRICTIONS)
❑ Knee flexion / extension ❑ Talo-crural (ankle) joint – dorsiflexion / plantarflexion ❑ Talocalcaneal (subtalar) joint – Supination – adduction, inversion and plantar flexion of calcaneus ☐ ❑ Pronation – abduction, eversion and dorsiflexion ☐ ❑ Metatarsopharangeal joints - flexion / extension / abduction / adduction ❑ Interphalangeal joints – flexion / extension ❑ 1st ray (hallux) – Flexion / extension
1b) ACCESSORY MOVEMENTS: (TICK AND INDICATE TYPE e.g. GLIDE, DISTRACTION, AND DIRECTIONS e.g. AP, PA, etc.)
❑ Talocrural (ankle) ❑ Sub talar ❑ Talonavicular ❑ Calcaneal glide – inversion / eversion (medial /lateral) / A-P glide, distraction ❑ Calcaneocuboid A/P ❑ Naviculocuneiform ❑ Cuboid – 4-5 metatarsal ❑ Tarsometatarsal ❑ Metatarsophalangeal Jts 1-5 A/P ❑ Interphalangeal Jts 1-5
SOFT TISSUE MOBILIZATIONS:
2) MASSAGE AND SOFT TISSUE STRETCH (TICK AND NAME BODY PARTS MASSAGED / TISSUES STRETCHED)
❑ Effleurage for oedema management ❑ Gastrocnemius and soleus mobilization (kneading/ picking up) ❑ Deep soft tissue massage to the tendo achillis ❑ Stretch to gastrocnemius ❑ Stretch to soleus ❑ Stretch to tendo achillis ❑ Anterior tibialis mobilization (kneading/ picking up) ❑ Abductor Hallucis mobilization (stretch / kneading/picking up) ❑ Abductor Digiti Minimi mobilization (stretch / kneading/picking up) ❑ Deep soft tissue massage to the plantar fascia (sole of foot) ❑ Sustained stretch – flexor digitorum ❑ Sustained stretch – flexor hallucis ❑ Other (state)
PREPARATION FOR FUNCTION:
3) CREATING AN ACTIVE FOOT IN PREPARATION FOR STANCE / BALANCE
❑ Compression - MCP joints ❑ Talocalcaneal compression ❑ Compression through lateral border of little toe ❑ Compression through shank of LL ❑ Placing the foot orientation to the floor, sitting ☐ perched standing ☐ standing ☐ ❑ Placing the foot on different surfaces ❑ Heel contact with floor ❑ Other (state)
4) SPECIFIC SENSORY INPUT (TICK AND NAME OBJECTS OR BODY PARTS)
❑ Visual ❑ Tactile stimulation - use of different textures/surfaces, somatosensory input, varying speed and depth of contact, to stimulate and also desensitise ❑ Hot/cold stimulation ❑ Active touch (objects e.g. changing surfaces, uneven ground) ❑ Passive touch (objects e.g. rolling foot over a ball)
5) ISOLATED / SELECTIVE JOINT MOVEMENT (TICK AND STATE DIRECTION OF MOVEMENT)
❑ Talocrural joint (Ankle) – dorsiflexion/ plantarflexion ❑ Subtalar joint – inversion / eversion ❑ Toe flexion / extension
6) PATTERNS OF CO-ORDINATED MOVEMENT UNDERLYING FUNCTIONAL ACTIVITY
❑ Activities in sitting e.g. rolling foot over ball, facilitated heel strike ❑ Sitting to standing ❑ Weight transference medial / lateral ☐ Forwards / backwards ☐ ❑ Stepping (including toe off and heel strike) – forwards ☐ backwards ☐ ❑ Stairs ❑ Other (please state)

Appendix 19 3rd iteration of the lower limb MTS protocol

TREATMENT SCHEDULE FOR MOBILIZATION AND TACTILE STIMULATION TO THE LOWER LIMB – ITERATION 3

Date: Pt ID Position of patient: Length of session: Therapist:

AIMS (Please tick)

- ❑ Regain normal extensibility of skin, muscle, connective tissues, tendons and joints to enable foot to accept base of support
- ❑ Reduce hypersensitivity or pain
- ❑ Heighten awareness foot position and posture
- ❑ Normalize tempero-spatial activation of muscle during functional activity (accuracy, quality of movement, normalise balance reactions)
- ❑ Normalize afferent stimulation arising from functional activity
- ❑ Normalize performance parameters (smoothness, accuracy, co-ordination, reciprocal activation, strength) for movement, balance and gait.

JOINT MOBILZATIONS:

1a) PASSIVE MOVEMENTS THROUGH ANATOMICAL RANGE (WITH HIP AND KNEE IN NEUTRAL ALIGNMENT, NB NOTE ANY RESTRICTIONS)

- ❑ Knee flexion / extension
- ❑ Talo-crural (ankle) joint – dorsiflexion / plantarflexion
- ❑ Talocalcaneal (subtalar) joint – Supination – adduction, inversion and plantar flexion of calcaneus ☐
- ❑ Pronation – abduction, eversion and dorsiflexion ☐
- ❑ Metatarsopharangeal joints - flexion / extension / abduction / adduction
- ❑ Interphalangeal joints – flexion / extension
- ❑ 1st ray (hallux) – Flexion / extension

Comments:

1b) ACCESSORY MOVEMENTS (TICK AND INDICATE TYPE e.g. GLIDE, DISTRACTION, AND DIRECTIONS e.g. AP, PA, etc.)

- ❑ Talocrural (ankle) ☐ Sub talar ☐ Talonavicular
- ❑ Calcaneal glide – inversion / eversion (medial /lateral) / A-P glide, distraction
- ❑ Calcaneocuboid A/P
- ❑ Naviculocuneiform
- ❑ Cuboid – 4-5 metatarsal
- ❑ Tarsometatarsal
- ❑ Metatarsophalangeal Jts 1-5 A/P
- ❑ Interphalangeal Jts 1-5

Comments:

SOFT TISSUE MOBILIZATIONS:

2) MASSAGE AND SOFT TISSUE STRETCH (TICK AND NAME BODY PARTS MASSAGED / TISSUES STRETCHED)

- ❑ Effleurage for oedema management
- ❑ Gastrocnemius and soleus mobilization (kneading ☐ picking up☐ dissociation of gastrocnemius from soleus ☐)
- ❑ Deep soft tissue massage to the tendo achillis
- ❑ Stretch to gastrocnemius
- ❑ Stretch to soleus
- ❑ Stretch to tendo achillis
- ❑ Extensor hallucis stretch
- ❑ Anterior tibialis mobilization (kneading/ picking up)
- ❑ Abductor Hallucis mobilization (stretch / kneading/picking up)
- ❑ Abductor Digiti Minimi mobilization (stretch / kneading/picking up)
- ❑ Deep soft tissue massage to the plantar fascia (sole of foot)
- ❑ Sustained stretch – flexor digitorum
- ❑ Sustained stretch – flexor hallucis
- ❑ Massage in between and along length of toes
- ❑ Other (state)

Comments:

PREPARATION FOR FUNCTION:

3) CREATING AN ACTIVE FOOT IN PREPARATION FOR STANCE / BALANCE

- ❑ Compression - MTP joints
- ❑ Talocalcaneal compression
- ❑ Compression through lateral border of the foot and little toe
- ❑ Compression through shank of LL
- ❑ Placing the foot orientation to the floor, sitting ☐ perched standing ☐ standing ☐
- ❑ Placing the foot on different surfaces - Details.....
- ❑ Lumbricals strengthening
- ❑ Heel contact with floor
- ❑ Other (state)

Comments:

4) SPECIFIC SENSORY INPUT (TICK AND NAME OBJECTS OR BODY PARTS)

- ❑ Visual
- ❑ Tactile stimulation, use of different textures/surfaces, somatosensory input, varying speed and depth of contact, to stimulate and also desensitise
- ❑ Hot/cold stimulation
- ❑ Active touch (objects e.g. changing surfaces, uneven ground)
- ❑ Passive touch (objects e.g. rolling foot over a ball)

Comments:

5) ISOLATED / SELECTIVE JOINT MOVEMENT (TICK AND STATE DIRECTION OF MOVEMENT)

- ❑ Talocrural joint (Ankle) – dorsiflexion/ plantarflexion Passive ☐ Active assisted ☐ Active ☐
- ❑ Subtalar joint – inversion / eversion
- ❑ Toe flexion / extension

6) PATTERNS OF CO-ORDINATED MOVEMENT UNDERLYING FUNCTIONAL ACTIVITY

- ❑ Activities in sitting e.g. rolling foot over ball, facilitated heel strike, heel raise
- ❑ Sit to stand to sit
- ❑ Weight transference - in sitting ☐ standing ☐ medial / lateral ☐ Forwards / backwards ☐ sideways ☐
- ❑ Stepping (including toe off and heel strike) – forwards ☐ backwards ☐
- ❑ Functional mobility ☐ Transfers ☐ Obstacle course ☐ Manoeuvring ☐
- ❑ Stairs Assistance required ☐ Independent ☐
- ❑ Other (please state)

Comments:

Appendix 20 Plan for the mNGT session

Nominal Group Technique session - Wednesday 30th September 2015

Plan for the afternoon:

1pm start please - do feel free to bring your lunch. Drinks and light refreshments will be provided.

1pm: Welcome and introduction
AA

1.15pm: Nominal Group Technique work related to the Mobilization and Tactile Stimulation (MTS) protocol.
ALL

2pm: Discussion related to textured insoles
ALL

2.30pm: Tea / coffee

2.45pm: Group work to develop the Task-Specific Gait Training (TSGT) protocol
ALL

3.30pm: Practical work related to the MTS protocol (please bring shorts!)
ALL

4pm: Summary
AA

4.15pm: FINISH

Appendix 21 Comments from participants relating to the 1st iteration

AIMS

- 1. Regain normal extensibility of skin, muscle, connective tissues, tendons and joints to enable the foot to accept a base of support, ensuring optimum contact with the floor
- Improve strength and activation of p/f and d/f
- 2. Reduce hypersensitivity (wearing of socks and shoes, BOS)
- 3. Reduce pain (importance for weight bearing), but removed by one person
- 4. Heighten awareness of foot position and posture (improve stance leg, increase orientation, automatic gait, ankle strategy. Neutral foot posture important for balance and afferent stimulation ('ready to go') also proprioception
- 5. Normalize temporo-spatial activation of muscle during functional activity (accuracy, quality of movement) Normalise balance/ righting reactions
- 6. Normalize afferent stimulation arising from functional activity (Improve automatic balance and gait)
- 7. Normalize performance parameters (smoothness, co-ordination, selective activation) of lower limb movement.

Comments:

Consider – in what position patient would be? Sitting, supine, Prone….

- The aims from the UL schedule would appear appropriate and could easily be transferred to the foot and ankle

1-4 &6 – same aims for foot.

- Not sure about:

- Normalize temporo-spatial activation of muscle during functional activity

- Foot position is required for foot contact and normal gait cycle
- Increased hypersensitivity is bad to decrease foot contact and poor gait cycle, same for pain – leads to change in gait cycle
- Pain inhibits weight-bearing and normal movement / gait cycle
- Posture is essential to assist balance / gait speed
- Normal feedback leads to more normal gait
- Aims 1-6 will lead to the last aim (7) being achieved. Normalising performance parameters requires that most of the aims 1-6 are already in place and gait would be the end point.
- All aims relate to falls risk, speed and distance, function and safety.
- Patients do not normally complain of foot pain, whereas this is much more prevalent in UL
- One therapist ticked all the aims for the UL but suggested they were linked to a specific goal - ? state that working towards standing / mobility

? NEW SUB HEADING: JOINT MOBILISATIONS:

PASSIVE MOVEMENTS THROUGH ANATOMICAL RANGE (with knee and hip in neutral alignment): (NOTE ANY RESTRICTIONS)
Knee flexion / extension
Talo-crural (ankle) joint – dorsiflexion / plantarflexion
Talocalcaneal (subtalar) joint – Supination – adduction, inversion and plantar flexion of calcaneus
Pronation – abduction, eversion and dorsiflexion
Metatarsopharangeal joints - flexion / extension / abduction / adduction
Interphalangeal joints – flexion / extension
Hallux – Flexion / extension
Comments

– consider positive support reaction / flexor withdrawal

- Change to reflect normal foot movements, which are required for stability
- Movements may be more general i.e. plantar flexion, dorsiflexion, pronation / supination
- Foot movements are less specific in function and passive movements would reflect this and would be done with an element of stretch if indicated by stiffness
- One person suggested hip flexion / extension, ab/adduction, rotations and lumbar rotation
- - another suggested need to check knee and hip and neutral alignment
-

ACCESSORY MOVEMENTS: (TICK AND INDICATE TYPE e.g. GLIDE, DISTRACTION, AND DIRECTIONS e.g. AP, PA, etc.)
- Distal fibula
- Talocrural (ankle)
- Sub talar
- Talonavicular
- Calcaneal glide – inv / eversion (med/lat) /AP glide, distraction
- Calcaneocuboid AP
- Naviculocuneiform
- Cuboid – 4-5 metatarsal
- Tarsometatarsal
- Metatarsophalangeal Jts 1-5 AP
- Interphalangeal Jts 1-5

Comments:

- Rotation – feel this is an important aspect of sensory stimulation!

Plan for new sub heading:
SOFT TISSUE MOBILISATION

MASSAGE (tick and name body parts massaged)
Comments:

- Abductor halluces - picking up
- Kneading - draw out lateral border / 'scoop out'

- Abductor digiti minimi, I feel working on this is very important, but links in with soft tissue stretch. Gaining length and rotating it out.
- This section is very specific and often mobilisation is more overall with joint movement.
- This would be used for oedema management to gain range
- Muscles - effleurage - gastr/ tibial is muscles, peroneus brevis/ longus, circular
- kneading - anterior tibialis, picking up – gastrocnemius
- Effleurage - for fluid (all other sections crossed out)
- Effleurage and picking up kept (other sections crossed out - massage to gastrocnemius and soleus
- If it is just ankle and foot, then some of the massage techniques are irrelevant eg picking up
- I also use heel deep pressure massage, deep foot sole massage with forefoot stretch (arch)' trigger points
- Effleurage up low leg, only ok,If there is swelling.
- Picking up to accentuate the arches of the foot
- Other - deep soft tissue massage to plantar fascia and Achilles' tendon. Both often tight

SOFT TISSUE STRETCH (tick and state which tissues)

Comments:

- Soleus stretch, gastro said stretch, abductor dig min
- TA very important. Gaining length and rotating it out (or was this comment relating to abductor digits minimi?)
- TA stretch, gastroc length - longitudinal, end of range, transverse
- Passive movements and soft tissstretches would often be combined to gain position and the specific soft tissue manipulation used to gain extra length. This would also extend up to the knee including gastrocnemius and soleus.
- Longitudinal extensor - Hallucis longus, extensor digitorum
- End of range - gastroc/ soleus
- Sustained - flexor digiti
- diagonal crossed out - plantar fascia, gastroc, soleus for two people
- After a period of massage to decrease sensitivity I then work on this I find it very important
- Massage - same as upper limb

PLACING THE FOOT ON

Comments:

- Foot to floor contact
- Edge/ corner crossed out and just flat surface left for four people
- Would still place the foot on the floor or a mat to gain interaction
- Placing barefoot on floor or carpet to increase sensory awareness
- One person originally left this out stating they would work in a more dynamic position. Is placing the foot the same as stepping activities?

- Placing on a flat surface - plantar surface, edge / corner - proximal mets
- Placing foot on an even rough surface, balancing board
- One person added bed/floor stating it was important
- This I do in bare feet on a mat, sitting if possible patient perched to progress
- Place foot on flat surface or spiky ball
- Floor contact, toe contact, toe activity, orientation to surface/ floor, talocrural, calcaneal

ISOLATED /SELECTIVE JOINT MOVEMENT (tick and state direction of movement)

Comments:

- Ankle, metatarsopharangeal, interphalangeal
- Ankle, MCP Jt 1, MCP Jt 2-5, IP Jt -5
- Ankle, metatarsals, phalanges
- Change to reflect the foot- toe flexion/ extn, pronation, supination, dorsiflexion, plantarflexion, tends to be done more as a group to reflect loss of selective nature of foot and function
- Dorsiflexion, plantar flexion, prox met ext., prox met flex, eversion
- Ankle selective d/f and p/f, selective toe flex and ext , MTP
- Ankle d/f and p/f, toe MTP flex/ ext
- True ankle joint, subtalar, interphalangeal and metatarsopharangeal
- Adapt to foot/lower limb

COMPRESSION

Comments:

- Compression into metatarsal joints ('shorten' feet)
- MTPs IP jts
- plantar aspect of foot
- Number two as I would put it with number one. Would this be just put in with accessory movements for the foot?
- Ankle d/f/ plantar flexion, metatarsals, phalanges
- Crossed out and not initially numbered by one therapist
- calcaneus, MTP
- palm and wrist crossed out, MCP jts ticked, lateral border of foot/little toe, calcaneum
- MTP, calcaneum
- compression is good together with distraction (traction) in all foot joints
- adapt to foot /lower limb
- I do compression at MTPs if tone in the foot is low

I would do this through stretching or accessory movement, or it would be around weight-bearing/gait, not specific compression

SPECIFIC SENSORY INPUT (TICK AND NAME OBJECTS OR BODY PARTS)

Comments:

- tactile stimuli - use of different textures/surfaces somatosensory input vary speed,
  depth of contact etc.
- same as for upper limb
- Active touch object/body parts crossed out - I don't think I'd use active touch for the foot
- Visual, active touch, passive touch
- Floor surfaces for desensitisation and foot mobility
- Hot /cold bathing, proprioception/texture work
- Visual ticked auditory crossed out
- Visual, different surfaces, hot /cold, socks shoes on/off
- I think this is very important re somatosensory input. Could a picture of the foot/lower limb with areas shaded, to illustrate specific areas to be managed be used?
- stepping, standing, gait, swing phase, stance phase, steady stance, adaptation to changing surfaces, stairs, uneven surfaces

PATTERNS OF CO-ORDINATED MOVEMENT UNDERLYING FUNCTIONAL ACTIVITY

COMMENTS:

- stepping, standing, gait, swing phase, stance phase, steady stance, adaptation to changing surfaces, stairs, uneven surfaces
- coordination of movement, e.g. Ball under foot, break down gait cycle, facilitate patterns of weight transfer, varying the degree of weight bearing? %, uneven surface/balance ball, increase proprioceptive stimuli
- ? Use FES as an adjunct I.e. Prepare foot/ ankle prior to standing/ gait, sensory feedback, soft tissue stretch
- weight bearing/ weight transfer, squat/ sit to stand, facilitated step, prone standing, step up
- sit to stand, forward step, backward step
- facilitated heel strike in perch sitting, banging heel on floor
- weight bearing through limb, PNF patterns- distal activation to initiate proximal control/ activity
- weight transference, lateral (weight bearing), weight transference AP (weight bearing), heel raise, toe off, heel strike, step forward and back practice
- weight bearing through limb ticked by 6 people
- heel raises, gastroc propulsion, stepping in sitting or standing, forwards, backwards, sideways
- seated or standing, foot placement multidirectional, heel raises
- dorsiflexion, inversion, eversion, rolling ball forward and back (foot on top of ball), swiping tissue from one side to another with foot (hip and knee in

neutral position), grasp and release tissue with toes, can use static pedals, wobble board, trampoline, steps, ball, TES

- after a period of weight bearing I sit the patient down and spend some time on active movements at ankle and foot- d/f and p/f, then stand again and work on stepping or stance phase.
- p/f, d/f, toe wiggling, heel to toe tip toes

ADDITIONAL GENERAL COMMENTS:

- I feel the protocol should start with somatosensory input (of which I would put the first 3 (Sensory input, Massage, Compression within this scope) then I would move onto different types of movement (the next 4 -Soft tissue stretch, Passive movements, Accessory movements ,Isolated selective joint movement would fit within this scope).
- I'm a little lost where to put placing the foot (I've put it at no.8)– it seems reasonable to put it after passive / active movements before moving onto function but am not quite sure as my second thought would be to put it before movement as in testing acceptance of different types of surfaces before moving onto movement patterns.
- I would recommend categories for:

Position: Details regarding position of patient – are they sitting / lying / standing? If working within on all three or just one / two this could be added as separates categories

Previous restriction / injuries / pain – This would greatly impact on aims

Aims - Could these be linked with goal? Do we need to state here that aim would be to work towards standing / mobility if appropriate as our patients can vary greatly within these areas

I would have separate categories for: (listed below in order that I would assess in) however I may not act in this order when I am treating if that makes sense). See sheet attached for comments

ASSESSMENT:

1.Patient awareness:

- how aware is the patient of their lower limb / foot?

2. Observation:

- How does lower limb and foot present to observation, what does it look like, i.e. colour / oedema / flaccid / high tone?How does it react to the floor / bed as in accepting surfaces? What position is it in? What position / placement do you want it in?

3. Range of movement available:

- range of active movement initiated by patient
- passive and active movements (could include accessory movement and isolated movements) within these sections and could be broken down as on your form

4.Somatosensory input:
- level of sensation?
    - Within that you could then list the areas of sensory input and how needed:
        Massage / stretching / compression etc.

5. Patterns of movement (including functional activity) wanted:
- heel to toe / tip toes etc.

If treating I would probably list it in order of: 1 / 2 / 4 / 2 & 4 again then 3 & 5
If this were a protocol would it be helpful and sure this is what you are doing to have a guide as to completion and to the categories listed.
On a personal note as an OT, I am fully aware that our anatomical knowledge is not as technical as physio's in relation to lower limb / foot and that reliance on technical terms may be off putting to OT's or they may lack a level of understanding / knowledge of the terms. I think this may have some relevance for use of the protocol if wanting it to be a multi-disciplinary tool between OT/PT. Ideally I would like to think of this as being a tool that could be used together or by either profession.

<u>Conventional therapy to prepare foot and ankle for standing.</u>

1) B.O.S.: Alignment and acceptance of B.O.S. is required for lower limb to act effectively as a support in order to allow standing /transferring/gait. We need mobility in the foot as well as stability. Ensure that foot is accepting the B.O.S.
2) (+) Reaction in the foot/Flexor withdrawal.
3) Handling /desensitisation of foot.
4) Stretching/Mobilisation of foot.
5) Length of soft tissue gastroc .
6) Oedema.
7) Pain/in growing toe nails.
8) Muscle Power.
9) Tone.
10) Perception/cognition/proprioception
11) ROM.

Principles of Treatment

Low Tone: Brisk movement, small ROM, loud voice, Small BOS, higher COG.
High Tone: Slower Movements, Supportive inhibitory Handling, Larger BOS, lower COG, Calm voice, quieter, slower and encouraging.

I think I left them out (placing the foot and compression) because I would do the work in a more dynamic position on that basis placing the foot would be 8 although I would do more placing foot but in context of stepping. I wasn't sure if placing in stepping activities was the same as placing the foot or whether it came under gait; then I would put compression as 9 but having thought about it this would come in on mobilisation dorsiflexion/stretching but not distinct on its own

Appendix 22 Comments from participants relating to the 2nd iteration

NGT work: details of comments made relating to 2nd Iteration:

Daisy - 'the treatment schedule is great, very thorough' Only thing Daisy could think of extra was working on the 'lumbricals' of the foot (using your toes to scrunch up a towel which has been placed under the foot). Daisy thinks this could come under section 3 or 6. Other than that Daisy felt it is 'very detailed but easy to read and follow'.

Debra - Comment on:
Section 2 - May also stretch extensor hallucis, although if consistent issues botulinum toxin would be used, especially if interfering with therapy / progress.
Section 3 - CORRECTION MTP NOT MCP joints!
Section 6 - Add in sideways on stepping section.? also add in walking obstacle course / manoeuvring, transfers / functional mobility.
Further comment: One of the things which is not mentioned is stabilisation splinting and use of electrical stimulation, as both stimulation and muscle activation technique. Patients have exercise stimulators which they use to gain muscle activation.

Grace - Section 3: Specify which for continuity (in relation to placing foot on different surfaces)
Section 6: Is the weight transference medial / lateral / fwds bkwds in standing or seated?

Isabelle - Section 2: In point 2 - ? add dissociation of gastrocs and soleus
Section 3: In relation to point 3 (compression through lateral border of little toe) add lateral border of the foot.

Lydia - 'Overall in terms of the actual treatment carried out, I think it is pretty comprehensive and accurately reflects practice. I guess the only thing I was thinking was is further detail required to quantify the amount of input given i.e. number of repetitions, duration of stretch, range achieved. Maybe this is something which needs further discussion. I guess it depends how the protocol is used. Particularly in a clinical setting if a patient was having treatment from different staff of different grades, greater documentation of dosage would be helpful, as well as clearly highlighting markers to monitor progress. '

Rachel - 'The treatment protocol is very comprehensive and good that it is on one page. The aims of treatment section would cover my aims of treatment fully. The specific treatment sections also reflects my current practice'.

I was just wondering if there is a reason the passive movements have to be done with the hip and knee in neutral alignment? I am assuming this means in anatomical position so patient would need to be lying down. I would sometimes do this with the patient supine but more generally I would do it with the patient in

sitting on the side of the plinth and I raise the plinth up so their head is approximately where it is when they are standing.

I also wondered where massage in between the toes and down the length of the toes would fit in? Does it need its own bit in the massage section rather than just going under the other box? Or would it go in section 4 under the tactile stimulation box? I think it is quite an important part of stimulating the foot and perhaps needs its own heading in the massage section.

Hazel - Section 2: other (state) - illiotibial band, gluteal, piriformis stretches
Section 6: Other (please state) - weight bearing/pressures applied to the foot in supine towards the head.

Olivia - 'All looks good just little comment to add. In sections 3,5 and 6 we need to specify how much assistance was given or if the patients performed all movements independently. Hope in September we can go through the treatment protocol practically to see how straightforward it is and if we all assess the same'.

Nicola - 'Looks very good, must say pretty technical for me and would need some training but covers everything that you'd need I think'

Kelly - 'The new schedule is very comprehensive and there doesn't seem to be anything missing'.

The practicality of all of these things being done in one treatments session is probably not what happens in reality however it would be the ideal!

The only difference to the schedule in our practice is that we do use electrical stimulation and also taping (Kinesio) as preparation to aid sensory stimulation/feedback and muscle length/facilitation. I don't know whether this is appropriate to add but thought it was worth a mention.

I would say that on observation of practice over the years there is much more effort made on preparing the hand before tasks/activities than the foot, however as more people go on courses etc. there is a definite change in practice towards preparing the foot more.'

Tracy - 'I am not sure whether we have to comment on sub part of each section or collectively just comment?
Looking at the treatment schedule there are quite few things that I don't do as I don't know. Hopefully after my Bobath course I will be able to do all these techniques.
Like accessory movements – I don't do all of them, not in that detail i.e. Calaneocuboid AP,Talonavicular.
Joint mobilisation: all except? 1st ray (hallux) flex/ext. Do the flex/ext of the big toe if that's the same thing?

Soft Tissue mobilisation: Again not on that much detail specially Abdutor hallucis mobilisation, abductor digiti minimi,or the sustained stretch.

Prepration for the function: do practise all of them.
Sensory input: all of them.
Isolated joint movement: all of them.
Patterns of coordinated movement: all of them.
I hope I am on the right track if not please let me know.'

Terry - Section 3: 'Does this include less affected side' e.g. working on overactivity? Add prone stand
Section 6: 1st point add 'heel raise'
2nd point add 'stand to sit

Appendix 23 Critique of the mNGT session

Observation of Alison Aries facilitating group discussion (n=8 experienced clinicians) as part of NGT

Alison was very well prepared for the session - she had sent out clear information to all participants in advance, detailing the timed plan for the afternoon, car parking and directions etc. She had also arranged for refreshments to be available and had booked appropriate rooms for the tasks. She had also brought two audio-taping devices, with one as a back-up.

Alison had prepared some overhead slides to summarise some of the background, and to highlight important points. On some of the slides, the text was rather small and there was a lot of information; but on others this was not the case. All slides were clear and easy to read - Alison had chosen a blue background with yellow text which made the text stand out clearly.

At the start, Alison revisited issues around consent, timings, audiotaping, confidentiality, and explanation of what to expect of the afternoon. She went on to set the context for the meeting, with a review of what had been done so far (participants had previously been invited to comment on drafts of the MTS schedule and feed back their comments to Alison individually). This provided a clear update and context for the afternoon session.

During the discussion, Alison was inclusive and encouraged all participants to contribute and to voice their individual opinions. She addressed each participant around the table to ask for their view. She provided reassurance about the project where this was needed (e.g. that the therapists involved in delivering the intervention would be given training), and she gave clear explanations for why some ideas of interventions that had been fed back to her from the drafts (e.g. FES, splinting) had been subsequently removed or omitted from the draft schedule. Consensus was actively sought with regards to any further inclusions/omissions/change to wording (eg. “in neutral alignment”) and sought agreement from the group.

The literature around TIs and TSGT was summarised for the group with a clear explanation about which literature had been reviewed (search terms stated clearly etc). Voting was used to determined the level of agreement in response to the question about whether Tis should be provided for both feet, or just one foot (affected foot), or whether textured and non-textured should be used for affected and non-affected respectively; 100% agreement was attained with clear rationale for why this decision was made.

Finally, the group was split into two smaller groups of 4 and asked to discuss and rank the TSGT activities. Small groups specifically included therapists from different work bases / Trusts. On completion of the small group discussion, there was a whole group plenary with in-depth discussion about how the study will sit alongside conventional therapy services. Alison had some specific questions for the group and pursued agreement on the appropriate answer.

Alison ended the discussion group with an expression of her gratitude for the participants’ input to the whole NGT process, and the offer of practice of some of the techniques. She answered final questions competently and clearly.

Appendix 24 Approval for Study 3, the MoTaStim-Foot feasibility study

NHS
Health Research Authority

West Midlands - Solihull Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

04 March 2016

Mrs Alison M Aries
NIHR Research Fellow
Keele University
School of Health and Rehabilitation
MacKay Buidling, Keele University
Keele, Staffordshire
ST5 5BG

Dear Mrs Aries

Study title:	**Sensory stimulation of the foot and ankle early post-stroke: A feasibility study(MoTaStim-Foot)**
REC reference:	**16/WM/0080**
Protocol number:	**2013-338**
IRAS project ID:	**171968**

Thank you for your letter of 2 March 2016, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Joanne Unsworth, nrescommittee.westmidlands-solihull@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS

research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [2015 TWIMC Professional Indemnity]	3rd August 2015	03 August 2015
Letter from funder [LetterOfIntent-CDRF_2014_05_065]		01 December 2014
Other [8-12-15_Protocol for the Task Specific Gait Training]	Version 1	08 December 2015
Other [Final MTS_iteration 1-12-15.]	Version 1	01 December 2015
Other [protocol 8-12-15_TI protocol]	Version 1	08 December 2015
Other [FINAL _MTS DIARY 18-12-15]	Version 1	18 December 2015
Other [Final_DAILY DIARY - TI group_18-12-15]	Version 1	18 December 2015
Other [Focus Group Schedule - version 1__18-12-15]	Version 1	18 December 2015
Other [Response to REC: Sensory stimulation of the foot and ankle early post stroke: A feasibility study (MoTaStim-Foot)]	Version 1.0	01 March 2016
Participant consent form [FINAL_CONSENT FORM -Version 1.1]	Version 1.1	22 January 2016
Participant information sheet (PIS) [18.12.15_Full_PIS]	Version 1	18 December 2015
Participant information sheet (PIS) [Summary_PIS_18-12-15]	Version 1	18 December 2015
REC Application Form [REC_Form_27012016]		27 January 2016
Research protocol or project proposal [MoTa-Stim - Foot_Final Protocol 8.1.16]	Version 1.0	08 January 2016
Summary CV for Chief Investigator (CI) [AA_CV_updated_for_IRAS Application 3.12.15]	Version 1	03 December 2015
Summary CV for student [AA_IRAS_CV_signed]	Version 1	16 December 2015
Summary CV for supervisor (student research) [SH_CV August 2015 for IRAS]	Version 1	17 September 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Appendix 25 MoTaStim-Foot trial protocol (Study 3)

Staffordshire and Stoke on Trent Partnership NHS Trust

NORWICH CTU

Sensory stimulation of the foot and ankle early post-stroke: A feasibility study (MoTaStim –Foot)

Study Protocol

Version	Version 1.0
Date	8th January 2016
Sponsor	Keele University
Trial registration	[Trial registry name and identifier]
NRES #	[insert NRES number]

Authorisation: Chief Investigator

Name	Alison Aries
Role	Chief Investigator / Doctoral Fellowship Research Fellow
Signature	A.M. Aries
Date	8/1/16

Funded by NIHR

Authorisation: NCTU Director

Name Amswarr

Role CTU Director

Signature

Date 14/1/16.

Authorisation: Senior Operations Staff

Name Dr Erika Sims

Role Senior Clinical Trial Operations Manager

Signature

Date 14 Jan 2016.

Authorisation: Sponsor Representative

Name	Professor Simon Davies
Role	Clinical co-director for the Institute for Science and Technology in Medicine
Signature	
Date	8/1/16

Authorisation: Statistician

Name	Professor Julius Sim
Role	Director, NIHR Research Design Service, West Midlands (Keele Hub) Supervisor/statistician
Signature	
Date	8/1/16

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1 Administrative information

This document was constructed using the Norwich Clinical Trials Unit (NCTU) Protocol template Version 2.0. It describes the Sensory Stimulation of the Foot and Ankle Post-stroke Trial (MoTaStim-Foot), sponsored by Keele University and co-ordinated by NCTU.

It provides information about procedures for entering participants into the trial, and provides sufficient detail to enable: an understanding of the background, rationale, objectives, trial population, intervention, methods, statistical analyses, ethical considerations, dissemination plans and administration of the trial; replication of key aspects of trial methods and conduct; and appraisal of the trial's scientific and ethical rigour from the time of ethics approval through to dissemination of the results. The protocol should not be used as an aide-mémoire or guide for the treatment of other patients. Every care has been taken in drafting this protocol, but corrections or amendments may be necessary. These will be circulated to registered investigators in the trial. Sites entering participants for the first time should confirm they have the correct version through a member of the trial team at NCTU.

NCTU supports the commitment that its trials adhere to the SPIRIT guidelines. As such, the protocol template is based on an adaptation of the University College London CTU protocol template (2012) and the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 Statement for protocols of clinical trials (Chan et al 2013). The SPIRIT Statement Explanation and Elaboration document (Chan et al 2013) can be referred to, or a member of NCTU Protocol Review Committee can be contacted for further detail about specific items.

1.1 Compliance

The trial will be conducted in compliance with the approved protocol, the Declaration of Helsinki (2008), the principles of Good Clinical Practice (GCP) as laid down by the Commission Directive 2005/28/EC with implementation in national legislation in the UK by Statutory Instrument 2004/1031 and subsequent amendments, the Human Tissue (Quality and Safety for Human Application) Regulations 2007, the UK Data Protection Act, and the National Health Service (NHS) Research Governance Framework for Health and Social Care (RGF). Agreements that include detailed roles and responsibilities will be in place between participating sites and NCTU.

Participating sites will inform NCTU as soon as they are aware of a possible serious breach of compliance, so that NCTU can fulfil its requirement to report the breach if necessary within the timelines specified in the UK Clinical Trials Regulations (currently 7 days). For the purposes of this regulation a 'serious breach' is one that is likely to affect to a significant degree:

- The safety or physical or mental integrity of the subjects in the trial, or
- The scientific value of the trial.

1.2 Sponsor

Keele University is the trial sponsor and has delegated responsibility for the overall management of the Sensory Stimulation of the Foot and Ankle Post-stroke trial (MoTaStim-Foot) to the Chief Investigator and NCTU. Queries relating to sponsorship of this trial should be addressed to the Director, NCTU, or via the trial team.

1.3 Structured trial summary

Primary Registry and Trial Identifying Number	Name of primary registry, and the unique ID number assigned by the primary registry to this trial.
Date of Registration in Primary Registry	Date when trial was officially registered in the primary registry.
Secondary Identifying Numbers	Other identifiers besides the trial identifying number allocated by the primary registry, if any. These include: • The Universal Trial Number (UTN) • Identifiers assigned by the sponsor • Other trial registration numbers issued by other registries (both primary and partner registries in the WHO Registry Network, and other registries) • Identifiers issues by funding bodies, collaborative research groups, regulatory authorities, ethics committees, institutional review boards etc.
Source of Monetary or Material Support	National Institute for Health Research (NIHR) as part of a Clinical Academic Doctoral Fellowship - CDRF-2014-05-065
Sponsor	Keele University
Contact for Public Queries	ctu.enquiries@uea.ac.uk
Contacts for Scientific Queries	**Key Trial Contacts:** Mrs Alison Aries MSc MCSP (Chief Investigator / NIHR Doctoral Fellow/PhD student) School of Health and Rehabilitation, Mackay Building, Keele University, Keele, Staffordshire, ST5 5BG. Email: a.m.aries@keele.ac.uk Tel: 01782 734418 Dr Sue Hunter PhD BA(OU) GradDipPhys MCSP FHEA (Primary supervisor), Senior Lecturer, School of Health and Rehabilitation, Keele University Keele, Staffordshire, ST5 5BG. Email:s.m.hunter@keele.ac.uk Tel: 01782 733809
Public Title	Sensory stimulation of the foot and ankle early post-stroke: A feasibility study (MoTaStim-Foot)

Scientific Title	Sensory stimulation of the foot and ankle early post-stroke: A feasibility study (MoTaStim-Foot)
Countries of Recruitment	England
Health Condition(s) or Problem(s) Studied	Stroke
Intervention(s)	**Mobilization and Tactile Stimulation (MTS) Group:** Up to 60 minutes of MTS treatment to the lower limb plus standardized TSGT (30 minutes). 20 treatment sessions of MTS and TSGT will be given. **Textured Insole (TI) Group:** This group of participants will be encouraged to wear the TIs as much as possible, during their normal every day activities, and in addition they will be worn during 20 sessions of TSGT (30 minutes for each session). A daily diary will be kept to monitor duration of use.
Key Inclusion and Exclusion Criteria	**Inclusion criteria:** • Adult stroke survivors (aged 18 years or older), with anterior or posterior circulation stroke occurring 6-16 weeks earlier. • Ability to walk independently prior to stroke • Participants must also be able to follow simple commands using the non-paretic upper limb • Participants must be unable to step on and off a 7·5 cm high block more than 12 times in 15 seconds with either their paretic (affected) or non-paretic leg (Step test). **Exclusion criteria:** • Pre-existing conditions affecting sensation (feeling) of the foot and lower limb e.g. diabetic neuropathy, polyneuropathy, peripheral nerve lesion, previous stroke affecting sensation of the lower limb • Fixed contracture of the tendoAchillis • Pressure sores or ulcers on the foot or ankle (hemiparetic limb) • Deep vein thrombosis • Other conditions that affect the blood supply to/from the foot e.g. heart failure with peripheral oedema • Botulinum toxin injections to the lower limb in the previous six months • Pain sufficient to prevent delivery of treatments or outcomes. • Known HIV, Hepatitis non-A or related condition
Study Type	A randomized, single blinded feasibility trial is being undertaken as part of a PhD fellowship (overview of trial available in figure 1). A mixed-methods design will be undertaken, which will involve both quantitative

	(experimental) and qualitative (diaries and focus groups) methods. **Randomisation** Participants will be randomised to the interventions using 1:1 randomisation with stratification by left or right stroke. An independent web-based or telephone interactive voice response system randomisation service and electronic case record form will maintain concealment of the treatment allocation from investigators, research therapists and blinded assessors prior to randomisation of a participant (i.e. each participant allocation cannot be predicted from the allocation of the previous participant). Baseline data will be entered into the randomisation system and the system will randomize, sending an email confirmation of the allocation group for the participant. **Blinding** Outcome measurements that are subject to observer bias will be undertaken by assessors who are blinded to treatment group allocation. Participants will be asked not to inform assessors as to what treatment they are randomised to receive. **Purpose** To establish the feasibility of conducting a randomised trial comparing delivery of MTS plus TSGT, or wearing TIs plus TSGT. The results of this feasibility trial will be used to inform the design and delivery of a definitive trial. It is not the purpose of the feasibility study to demonstrate if the treatments are effective. The purpose is to provide data informing the main trial. For example, it will be possible to see if the way participants are recruited is effective, assess the willingness of participants to be randomized, assess how acceptable the treatments are, calculate how many participants drop out, and work out how many people would need to be recruited in a future larger trial. **Primary Research Aim:** 1. To explore the feasibility of delivering treatment designed to increase the feeling within the foot after stroke in a randomized trial. The treatments being evaluated are Mobilization and Tactile Stimulation (MTS) with TSGT versus wearing of TIs plus TSGT. **Research Objectives:**

	1. To find out if the treatments (MTS plus TSGT, and the wearing of TIs plus TSGT) are acceptable treatments for stroke survivors. 2. To find out the response to treatment (if any), in relation to the number of treatment sessions delivered. 3. To find out which measures will be most appropriate to measure outcomes of: sensorimotor impairment (feeling / sensation and movement), blood flow and lower limb function and balance. 4. To find out if daily diaries and focus groups are suitable ways to explore stroke survivors' experiences of receiving the treatments. 5. To find out if recruitment methods are effective, noting the number of people invited to participate, agreeing to consent and eligible to participate, as well as the number of people who drop out of the trial. The information will be used to inform a power calculation for a future study. 6. To generate information regarding the participants recruited i.e. population participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk.
Date of First Enrolment	It is anticipated that identification of participants will commence in March 2016 and the first participant will be recruited in April 2016.
Target Sample Size	34
Outcomes	As this is a feasibility trial one of the objectives is to identify which measure should be the primary outcome measure for future trials. The following clinical outcomes will therefore be evaluated as detailed below:
	Outcome: ***1. Characterization of clinical presentation of participants*** (to give an overview of the participants to assist with evaluation of the interventions) using the following tools: **(i) National Institutes of Health Stroke Scale (NIHSS)** - This includes assessment of the level of consciousness, vision, motor activity (face, arm and leg), coordination, sensation and speech. It is anticipated this will take a maximum of 15 minutes to complete. Timepoint: Baseline **(ii) Functional Ambulation category**, which assesses walking ability and categorizes according to basic motor skills necessary for functional walking. It is anticipated this will take a maximum of 2 minutes for the researcher to complete. It will not require additional

	time of the participant because the assessment can be made following the 5 metre walk test. Timepoints: Baseline, on completion of the twenty treatments and at one-month follow up. ***2. Sensorimotor impairment:*** The following measurements will be undertaken at baseline, after 5, 10, 15 and 20 treatments and one-month (+/-7 days) after last treatment (treatment number 20). **a) Pressure under the feet during stance phase of walking (measured with insoles).** This is important to measure because in order to walk there is a dependence upon the interaction between the feet and the environment. It is anticipated this will take a maximum of 10 minutes to complete. **b) Ankle range of motion (dorsiflexion and plantarflexion) during stance phase** This will be measured by an electrogoniometer (an electronic piece of equipment), in stance phase of walking. It is anticipated this will take a maximum of 10 minutes to complete. **c) Touch/pressure sensory thresholds (sole of foot) (the ability to feel at different points on the sole) of the foot** This will be measured using Semmes Weinstein Monofilaments. This involves touching the sole of the foot using a nylon filament which exerts a force when bowed into a C shape against the skin for 1 second. It is anticipated this will take a maximum of 5 minutes to complete. **d) Lower Extremity Motricity Index** This will measure motor impairment (strength) of hip flexors, knee extensors and ankle dorsiflexors (moving the foot upwards). This will be undertaken with the participant in sitting with the hip and knee at 90 degrees. It is anticipated this will take a maximum of 5 minutes to complete. Regular outcome measurements (a, b, c, and d) are being recorded to ascertain at what stage any changes are seen, to inform the dose (duration) of the intervention for the subsequent trial. ***2. Lower limb function and balance:*** Measures e) and f) will be collected at baseline, on completion of the twenty treatments and at one month follow up. **e) Walking speed 5 metre walk test** (self-selected walking speed), gives an indication of the overall walking ability of stroke survivors). To enable more

	detailed analysis the 5 metre walk test will be videoed. It is anticipated this will take a maximum of 10 minutes to complete. **f) Modified Rivermead Mobility Index** The test involves eight tasks including bed mobility, sitting and standing balance, transfers, walking and stairs. A rating is given relating to the amount of assistance the person requires. It is anticipated this will take a maximum of 17 minutes to complete. ***3. Lower leg blood flow:*** **gi) Peak systolic velocity (PSV) (cm/s) (an indicator of blood flow) and vessel diameter (mm)** of the posterior tibial and the dorsalis pedis artery, measured using a portable ultrasound machine (MyLabFive, Esoate). Left- and right-limb measures will be undertaken to determine if effects are local or systemic, possibly indicating altered sympathetic vasoconstrictor nerve activity. There will first be a period of 10 minutes rest, then the measurements will take approximately 15 minutes. Timepoints: Baseline, on completion of the twenty treatments and at one-month follow up. **gii) In order to ascertain the effects of one individual treatment (acute effects),** participants in the MTS group will have PSV and arterial diameter measured before and immediately after one of the first 10 MTS treatments. On this one occasion the participant will require an extended visit that will last between one and a half and two hours (MTS treatment 30-60 mins, blood flow studies 25 mins plus TSGT 30 mins). **h) Blood pressure, height and weight –** Resting blood pressure will be taken before each measurement of blood flow. Participant's height and weight will be measured at baseline to allow calculation of Body Mass Index (BMI). **Research Setting** Participants will be asked to attend an outpatient setting or a university rehabilitation research facility for baseline, post intervention assessment and one-month follow up, in order to ensure standardisation of the 5 metre walk test. All treatment and all other assessments undertaken after treatments 5, 10 and 15 will be undertaken in the setting of the participant, such as the in-patient setting or in the participant's home.

1.4 Roles and responsibilities

1.4.1 Protocol contributors

Name	Affiliation	Role
Alison Aries	Keele University NIHR	Chief Investigator/ Principal Investigator for Staffordshire and Stoke on Trent Partnership Trust (SSOTP) /PhD student (Doctoral Fellow) **Chief Investigator roles:** 1. Review all SAEs for seriousness, expectedness and causality in accordance with agreed process for the trial. 2. All other responsibilities as assigned by regulating bodies, the funder or the sponsor not otherwise delegated. In addition to the responsibilities set out above, responsibilities will be delegated by the CI to PIs, research therapists, blinded assessors, research technicians and others as appropriate and recorded on delegation logs. As this is a doctoral study the Chief Investigator is also the Clinical Trial Manager and therefore is also responsible for: 1. Preparing reports to Main REC, Sponsor, Funder and other such bodies 2. Providing strategic supervision and management of the project **Principal Investigator roles:** 1. Review, record and report all Adverse Events for seriousness and causality 2. All other responsibilities as listed on SSI form for the site which he or she has authorised.
Dr Sue Hunter	Keele University	Primary supervisor
Professor Val Pomeroy	University of East Anglia (UEA)	Supervisor
Professor Sue Read	Keele University	Supervisor and qualitative expert
Professor Julius Sim	Keele University	Supervisor and statistician
Dr Claire Stapleton	Keele University	Research therapist / sonographer

1.4.2 Role of trial sponsor and funders

Name	Affiliation	Role
Sponsor: Contact: Keele University, Directorate of Engagement and Partnerships, IC2, Keele University, Keele, Staffordshire, ST5 5BG. Email: e.skinner@keele.ac.uk Tel: 01782 733374	Keele University	Responsibility for the initiation, management and financing for the research, ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting.
Funder: Funding for this study has been approved as part of an NIHR Clinical Academic Doctoral Research Fellowship award (CDRF-2014-05-065)	NIHR	It is an expectation by the NIHR that this work will be published and disseminated appropriately and the NIHR will ensure this.

1.4.3 Trial Team

Name	Affiliation	Role and responsibilities
Alison Aries	Keele University	Chief Investigator (CI), Principal Investigator (PI) and Research Therapist (1) – roles to include Recruitment (once potential participants have been identified by research nurses / clinical team), consenting, screening, appropriate outcome measurements that do not require blinding e.g. (baseline measurements, objective measurements not subject to bias), interventions
Dr Sue Hunter	Keele University	Supervisor; Participation in trial team and trial management group (TMG) meetings.
Researcher Therapist (2) (0.8FTE)	Keele University	Recruitment (once potential participants have been identified by research nurses / clinical team), consenting, screening, appropriate outcome measurements that do not require blinding e.g. (baseline measurements, objective measurements not subject to bias), interventions
Blinded Assessor (0.19FTE)	Keele University	Clinical measurements at baseline, after 5, 10 and 15 interventions and outcome

		measurements (at completion of intervention and one month follow up)
Dr Claire Stapleton	Keele University	Research Therapist (3) - Sonographer
Dr Erika Sims	Norwich Clinical Trials Unit	Operational oversight for the set-up, conduct and delivery of the study.

1.4.4 Trial Management Group

Name	Affiliation	Role and responsibilities
Alison Aries	Keele University	CI, PI, Research Therapist;
Dr Sue Hunter	Keele University	Primary Supervisor
Professor Val Pomeroy	UEA	Supervisor
Professor Sue Read	Keele University	Supervisor
Professor Julius Sim	Keele University	Supervisor
Professor Christine Roffe	University Hospital of North Midlands (UHNM)	Consultant Stroke Physician
Carolyn Belford	Staffordshire and Stoke-on-Trent Partnership Trust (SSOTP)	Clinical Specialist Physiotherapist
Frances Davies	SSOTP	Research Delivery Unit Manager
Melvyn Jackson		Patient and Public Involvement (PPI) advisor
Alan Earp		PPI advisor
Dr Erika Sims	Norwich Clinical Trials Unit	Operational oversight for the set-up, conduct and delivery of the study.

1.4.5 Trial Steering Committee

Trial Steering Committee responsibility will be undertaken by the Trial Management Group

1.4.6 Data Monitoring Committee

Data monitoring responsibility will be undertaken by the Trial Management Group.

1.4.7 Other Trial Oversight Groups

Name	Affiliation	Role and responsibilities

2 Trial Diagram

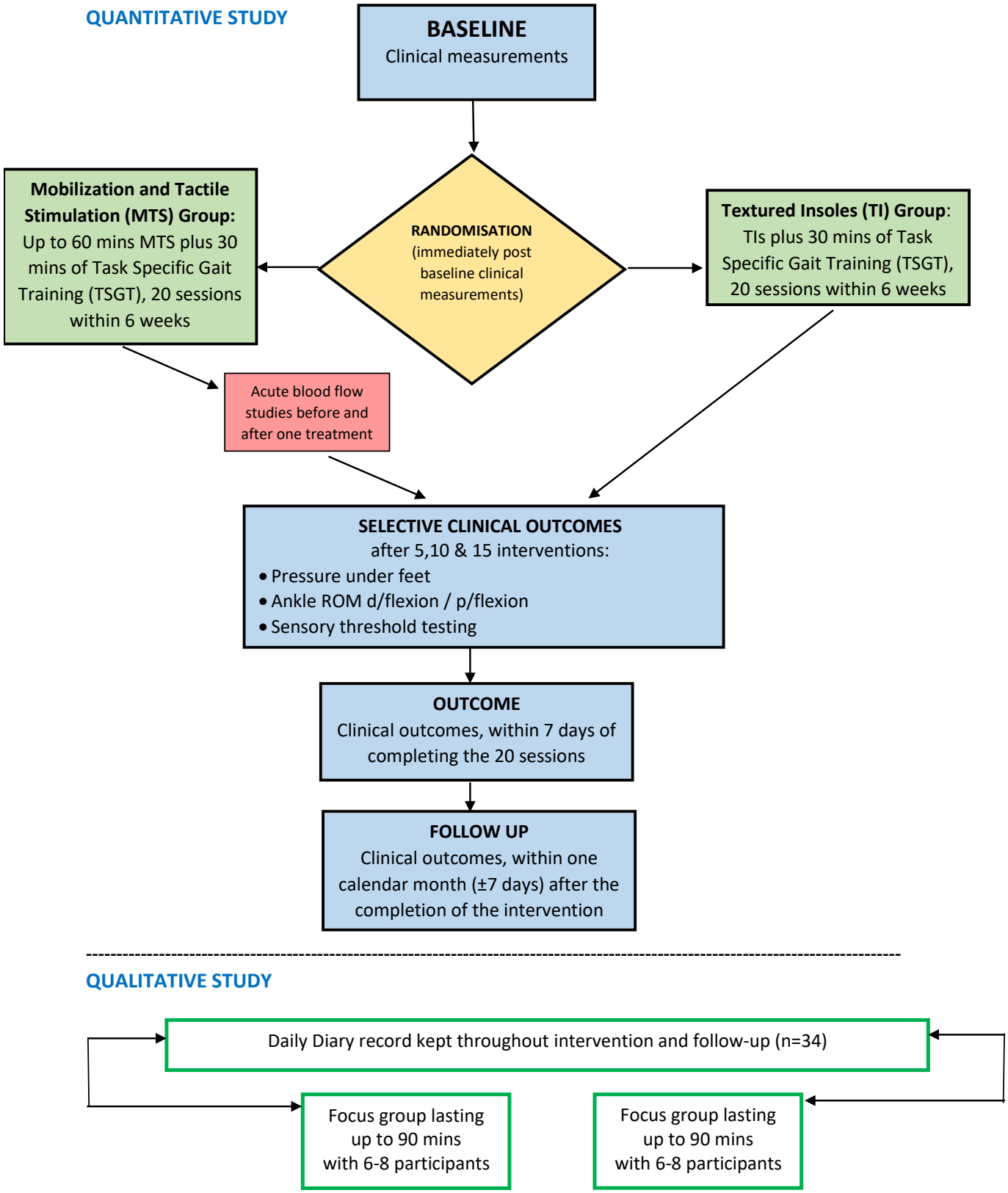

Figure 1: Overview: Sensory stimulation of the foot and ankle post stroke: A feasibility study (MoTaStim-Foot)

3 Abbreviations

AE	Adverse Event
ALARA	As Low As Reasonably Achievable
AR	Adverse Reaction
BMUS	British Medical Ultrasound Society
CI	Chief Investigator
CNS	Central Nervous System
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CTU	Clinical Trials Unit
DVT	Deep vein thrombosis
FAC	Functional Ambulation Category
GCP	Good Clinical Practice
MRC	Medical Research Council
MTS	Mobilization and Tactile Stimulation
NCTU	Norwich Clinical Trials Unit
NIHR	National Institute for Health Research
PI	Principal Investigator
PIS	Participant Information Sheet
PPI	Patient and Public Involvement
PSV	Peak systolic velocity
QA	Quality Assurance
QC	Quality Control
RCT	Randomized Controlled Trial
R&D	Research and Development
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SSOTP	Staffordshire and Stoke-on-Trent Partnership Trust

TI	Textured insole
TSGT	Task-specific gait training
TMF	Trial Master File
TMG	Trial Management Group
TMT	Trial Management Team
ToR	Terms of Reference
TSC	Trial Steering Committee
UEA	University of East Anglia
UHNM	University Hospitals of North Midlands
UK	United Kingdom

4 Glossary

Central Nervous System (CNS)	This is the part of the nervous system which consists of the brain and spinal cord.
Focus groups	Focus groups are a form of interview conducted with a few people who discuss topics, actively interacting with other group members and the moderator (Puchta and Potter 2004).
Mobilization and Tactile Stimulation (MTS):	A term given to a form of hands-on therapy treatment which is often delivered in conventional therapy, with an aim of mobilizing the area (e.g. hand or foot) and enhancing sensory input (feeling). It involves massage and tactile stimulation of the area and joint and soft tissue mobilisation techniques (passive movements, accessory movements, soft tissue stretching).
Sensory	Pertaining to systems which enable input to the central nervous system e.g. the ability to feel following tactile stimulation.
Task-specific Gait Training (TSGT)	A form of therapy which involves repetition of various activities e.g. sitting to standing, stepping etc. with an aim of improving the ability to walk.
Textured Insoles (TIs)	Insoles made of material with projections. The aim of these peaks is to stimulate the sole of the foot, increasing sensory input.

5 Introduction

5.1 Background and Rationale

Strokes are common. Indeed, every year 15 million people in the world have a stroke (Mackay and Mensah, 2004), and with an ageing population the financial burden of stroke is set to increase. This project is focused on a priority area for stroke survivors; namely, better treatments to enable them to recover the ability to balance and walk again. Although there is strong evidence that physical therapies do enhance recovery of balance and walking, many stroke survivors report that difficulty walking affects their quality of life (Algurén 2012). Neuroscience findings indicate that feedback to the brain via sensory processes is essential (Chersi et al. 2011, Laaksonen et al. 2012, Rossignol et al. 2006), and therefore information originating in the foot is important for balance and walking. Indeed, in clinical practice physiotherapists use an intervention called Mobilization and Tactile Stimulation (MTS) to enhance these sensory feedback processes. Yet there is a paucity of robust research to evidence this intervention. This project is an important step towards developing evidence based practice, in relation to treatment of the lower limb post-stroke.

Walking is a priority for many stroke survivors, confirmed by studies undertaken to define a national research agenda, which identified physical therapy to address balance and gait (walking) post-stroke within the top ten research priorities (James Lind Alliance, Pollock et al 2012). Often, challenging difficulties need to be overcome, and sometimes balance and walking are difficult because of: loss of control of movement (Zissimopoulos 2014); loss of feeling (sensation) (Feigenson 1977; which occurs in approximately 65% of people post stroke); problems with eyesight (Ali et al 2013); and/or challenges to understanding (Robinson et al 2011).

Loss of control of movement, for example difficulty controlling foot placement during walking (Zissimopoulos 2014), has an effect on functional ability, and it is clear that a loss of feeling also affects the capacity to undertake everyday activities (Patel et al 2000). The ability to move and feel are inextricably linked, with changing sensory input (feeling) altering the brain itself (Laarksonen 2012). Research findings indicate that the sensory input (feeling) from the sole (bottom) of the foot is important to achieve balance (Kavounoudias et al 1999, Maurer et al 2001, Meyer et al 2004, Horak et al 1990). Even a slight loss of this information from the sole of the foot can make it difficult to balance (Wang and Lin 2008). Some 83% of stroke survivors have difficulty balancing and therefore walking after stroke, especially if the sense of feeling or movement in the foot has altered. Increasing the ability to feel may, therefore, help a stroke survivor to balance and walk. However, despite the importance of sensory input being highlighted in the literature, therapy to increase the ability to feel is not always common in therapy treatment (Schabrun and Hillier 2009). There has been very little robust research looking at increasing sensory input (or feeling) after stroke (Carey et al 1993). The other important challenges of eyesight and understanding are also not to be forgotten, however, it is not the purpose of this feasibility study to address these issues.

Physical therapy involving joint and soft tissue mobilisation and stretching, manipulation and massage, to enhance the ability to feel with the arm and hand has been shown to improve function (Hunter and Crome 2002, Yekutiel and Guttman 1993), in both sub-acute (Hunter 2008) and chronic (Winter et al 2013) stroke survivors. MTS is a part of routine physical therapy used in clinical practice to prepare the foot and leg for standing and walking, but its effects have not yet been explored.

In clinical practice, physiotherapists use hands-on facilitation techniques to treat postural control and mobility problems (Tyson et al 2009), and this includes treatment such as muscle stretching, joint movement, and stimulation of the skin over the foot and ankle, with the aim of improving standing balance and walking after stroke. The limited number of studies that have investigated sensory stimulation to the lower limb include a pilot study (n=3) (Hillier and Dunsford 2006), and a randomized controlled pilot study (n=21) (Lynch et al 2007). It is not clear whether either of these studies included ‘hands on’ interventions such as MTS or not. These studies were not able to either support or negate the inclusion of routine sensory retraining to the lower limb in clinical practice. A further study investigated perceptual learning involving hardness

discrimination (n=28) (Morioka and Yagi 2003) and although postural sway was reduced, the findings cannot be generalized with such small samples. Although sensory stimulation is potentially key to influencing motor control and function it is not known if there are also other effects resulting from the MTS. Some of the techniques used are similar to massage techniques, which have been shown to provide several benefits to the body, such as increased blood flow, reduced muscle tension and neurological excitability (Weeraponng et al., 2005). A reduction in peripheral blood flow and arterial diameter is thought to be negatively associated with disease risk (Dinenno et al., 1999); however, it is not known whether treatments that mobilize and stimulate the foot may alter the blood flow to the limb post stroke, which could be beneficial for the stroke survivor.

The plantar (sole of the foot) mechanoreceptors are key, sending information to the central nervous system, and plantar stimulation has been shown to result in increased control of body sway (Watanabe and Okubo 1981). In view of the importance of cutaneous information from the sole of the foot to control balance (Kennedy and Inglis, 2002), other potential mechanisms of increasing plantar stimulation have been explored, and TIs have been shown to improve postural control in standing in healthy participants (Corbin et al 2007), and to improve walking patterns for people with multiple sclerosis (Dixon et al 2014). However, none of these specific or combined treatments have been evaluated robustly to determine their benefits for balance and walking recovery early after stroke. The use of TIs in the shoes of stroke survivors involves a hands-off (therapist independent) approach, which may potentially be a more economical option for achieving increased sensory stimulation to the foot and is therefore important to investigate.

Developing evidence and applying it to practice within stroke rehabilitation is difficult, due to a limited understanding and knowledge of therapy treatments (Langhorne et al 2011), which involve many different aspects (MRC 2008). There is strong evidence that task-specific gait (walking) practice can be used to improve walking after stroke (Foley et al 2013). However, for those stroke survivors who have a lot of muscle weakness and are therefore unable to do the task-specific training, other treatments are needed to prepare or enhance the sensorimotor system [the sensory 'feeling' system and the motor 'movement' systems] (Hunter et al, 2011), to help improve movement and function. The impact of the loss of feeling on movement and function, and what treatments are best to address the issue, have not been explored appropriately (Carey et al 1993). It is clear sensory rehabilitation requires further study (Magnusson et al 1994, Schabrun and Hillier 2009), and research involving the leg and foot with larger sample sizes is necessary (Lynch et al 2007, Hillier and Dunsford, 2006). It is also important to develop the scientific basis behind therapy treatments, for example establishing if changes to sensation, movement and blood flow are seen following MTS, and also the wearing of TIs.

This feasibility study involves a mixed-methods design and will be an important step in the research pathway, ensuring treatments are properly developed and procedures are tested in a rigorous manner, and participants' perceptions explored. It is necessary to see if it is possible to deliver the treatments (MTS or TIs followed by TSGT) and the outcome measurements before undertaking a larger study in the future. Both anterior and posterior circulation strokes (strokes involving blood vessels going to either the front or back of the brain) will be included in this feasibility study, because it is not yet known which stroke patients may respond to the treatments being investigated. Timing post stroke has been given careful consideration and participants will be included if they meet the other inclusion criteria, and have presented with a stroke 6-16 weeks (42-112 days) earlier. This time post stroke has been selected because starting rehabilitation early has been shown to be better for functional recovery, and the effects are maintained on long-term follow up at one year post stroke (Huang et al 2009). The most likely period for recovery of walking post stroke is between 4-7 weeks (Kollen et al 2006). In order to explore the effects of mobilization and tactile stimulation (MTS) / TIs – as opposed to natural, expected recovery – participants will be recruited at the end of this period associated with best recovery. The design of the research was chosen because it is vital that adequate time is spent developing standardized rehabilitation interventions, such as MTS, prior to undertaking a large randomized controlled trial looking at effectiveness; hence the decision to undertake a feasibility study.

5.1.1 Explanation for choice of comparators

Mobilization and tactile stimulation (MTS) is a treatment used in conventional physiotherapy practice to prepare or 'prime' the central nervous system (CNS), facilitating movement and function, by giving sensory input via the foot and ankle. TIs are a different way of delivering sensory information to the CNS, enabling 'augmentation' of sensory input to the CNS as a means of facilitating movement and function. It is important to explore in the future which sensory stimulation is more effective, hence this feasibility study to establish if it is possible to deliver these interventions in a research setting.

5.2 Objectives

Primary Research Aim:

To explore the feasibility of delivering treatment designed to increase the feeling within the foot after stroke in a randomized trial. The treatments being evaluated are Mobilization and Tactile Stimulation (MTS) with TSGT versus wearing of TIs plus TSGT.

Research Objectives:

1. To find out if the treatments (MTS plus TSGT, and the wearing of TIs plus TSGT) are acceptable treatments for stroke survivors.

2. To find out the response to treatment (if any), in relation to the number of treatment sessions delivered.

3. To find out which measures will be most appropriate to measure outcomes of: sensorimotor impairment (feeling / sensation and movement), blood flow, and lower limb function and balance.

4. To find out if daily diaries and focus groups are suitable ways to explore stroke survivors' experiences of receiving the treatments.

5. To find out if recruitment methods are effective, noting the number of people invited to participate, agreeing to consent and eligible to participate, as well as the number of people who drop out of the trial. The information will be used to inform a power calculation for a future study.

6. To generate information regarding the participants recruited i.e. population participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk.

5.3 Trial Design

A randomized, single blinded feasibility trial is being undertaken as part of an NIHR funded Clinical Doctoral Research Fellowship (overview of trial available in figure 1). A mixed-methods design will be adopted, which will involve both quantitative (experimental) and qualitative (focus groups) methods.

6 Methods

6.1 Site Selection

The trial sponsor has overall responsibility for site and investigator selection and has delegated this role to the Chief Investigator.

6.1.1 Study Setting

A case note review will be undertaken of stroke patients admitted to Staffordshire and Stoke on Trent Partnership Trust (SSOTP). Eligible participants will be identified and invited to participate. Participants may be inpatients or outpatients at the point of consent. For participants who are inpatients, consent, baseline measures, treatments and assessments will be completed within the hospital setting. Participants who are outpatients at the point of consent will be invited to attend either a hospital outpatient setting or university research facility for the baseline, post-intervention and one-month follow-up clinical measurements. The treatment sessions and interim outcome measurements (after 5, 10 and 15 treatment sessions) will take place in the

participant's own home. In the event that a participant enters the study as an inpatient and is then discharged during the study, provision will be made for the participant to continue to participate in the study by arranging for treatment sessions and assessments to be delivered at home, apart from the baseline, post-intervention and one-month follow-up clinical measurements, which will be undertaken in either a hospital out-patient setting or a university research facility.

6.1.2 Site/Investigator Eligibility Criteria

This is a single centre study. The Chief Investigator has written the NIHR funded Fellowship application and this protocol. It is not anticipated that additional investigators or sites will be recruited to the study.

6.1.2.1 Principal Investigator's (PI) Qualifications and Agreements

The Principal Investigator is the Chief Investigator and recipient of a NIHR Fellowship for this study. The PI will confirm qualifications, familiarity with the appropriate use of any assessment and treatment procedures and GCP training, to permit monitoring and audit as necessary at the site, and to maintain documented evidence of all staff at the site who have been delegated significant trial related duties.

6.1.2.2 Resourcing at site

The principal investigator will be able to demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period. An adequate number of qualified staff and facilities will be available for the foreseen duration of the trial to enable the trial to be conducted properly and safely.
A delegation of responsibilities log will be completed and staff contact details provided.

6.2 Site approval and activation

As this feasibility study is part of a doctoral training plan Alison Aries is the trial manager, CI and PI. The signed clinical trial agreement, or investigator agreement, approved delegation of responsibilities log and staff contact details will be checked by Dr Susan Hunter (Supervisor), and a written record of the plans for the site will be kept. The site will conduct the trial in compliance with the protocol as agreed by the Sponsor and, by the regulatory authority(ies) (as appropriate), and which was given favourable opinion by the Research Ethics Committee (REC). Alison Aries as the trial manager and PI will document and explain any deviation from the approved protocol, and report this to the Trial Management Group. A list of activated sites may be obtained from the Trial Manager.

6.3 Participants

6.3.1 Eligibility Criteria

Please see sections 6.3.1.2 and 6.3.1.3 and figures 2, 3 and 4 (appendices pages 59, 60 and 61)

6.3.1.1 Participant selection

There will be **NO EXCEPTIONS** (waivers) to eligibility requirements at the time of randomisation. Questions about eligibility criteria should be addressed PRIOR to attempting to randomize the participant.

The eligibility criteria for this trial have been carefully considered and are the standards used to ensure that only medically appropriate participants are entered, and this will be checked by reading the participant's medical notes / liaising with the clinical team, as appropriate. Participants not meeting the criteria should not be entered into the trial for their safety, and to ensure that the trial results can be appropriately used to inform future research and guide future treatment decisions for other people with similar diseases or conditions. It is therefore vital that exceptions are not made to these eligibility criteria.

Participants will be considered eligible for enrolment in this trial if they fulfil all the inclusion criteria and none of the exclusion criteria as defined below.

6.3.1.2 Participant Inclusion Criteria

Inclusion criteria:

- Able to provide written informed consent
- Adult stroke survivors (aged 18 years or older), with anterior or posterior circulation stroke, occurring 6-16 weeks (42-112 days) earlier.
- Ability to walk independently prior to stroke.
- Participants must also be able to follow simple commands and imitate actions, using the non-paretic upper limb (the arm that has not been affected by the stroke).
- Participants must be unable to step on and off a 7·5 cm high block more than 12 times in 15 seconds with either their paretic (affected) or non-paretic leg (Step test, Hill et al 1996).

6.3.1.3 Participant Exclusion Criteria

- Pre-existing conditions affecting sensation (feeling) of the foot and lower limb e.g. diabetic neuropathy, polyneuropathy (degeneration of the peripheral [not in the brain and spinal cord] nerves), peripheral nerve lesion [injury to a peripheral nerve], previous stroke affecting sensation of the lower limb.
- Fixed contracture of the tendoAchillis, assessed by being unable to achieve 90 degrees dorsiflexion at the ankle, either actively or passively with the knee extended.
- Pressure sores or ulcers on the foot or ankle (hemiparetic limb), due to the risk of infection.
- Deep vein thrombosis, because some of the MTS techniques would be contraindicated.
- Other conditions that affect the blood supply to/from the foot e.g. heart failure with peripheral oedema

- Botulinum toxin injections to the lower limb in the previous six months, because it may have an impact on the results
- Pain sufficient to prevent delivery of treatments or outcomes
- Known HIV, Hepatitis non-A or related condition

6.3.1.4 Eligibility Criteria for Individuals Performing the Interventions

The research therapists delivering the interventions will have sufficient neurological therapy expertise to deliver the interventions. Protocols are being developed in advance of the study and the research therapists will be trained to ensure delivery of standardized protocols for MTS, TIs and TSGT.

6.3.1.5 Co-enrolment Guidance

The issue of co-enrolment has been discussed with the Acute Research Team Sister at UHNM. She is responsible for the majority of the trials for stroke patients within the area. Details of this current study will be shared with the Principal Investigators responsible for other trials running, and discussed as applicable, and appropriate decisions made regarding any issues of co-enrolment. If a potential participant is already enrolled on a trial involving rehabilitation of the lower limb it may not be appropriate for them to be enrolled on this trial. The CI will discuss potential co-enrolment issues with the relevant PI where required, so an informed decision can be made. The burden on potential participants will also be considered. The CI will seek guidance from the TMG should co-enrolment issues arise. Due to the proposed timing of this trial major issues are not anticipated.

6.3.1.6 Retrospective case review

Potentially eligible participants will be referred by a member of the clinical team to the Chief Investigator or delegate, where appropriate. A retrospective case review of all participants will be conducted. The data will be collected using an anonymised form. The data captured will consist of: patient demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk. This will generate a reference population against which generalisability will be demonstrated for the randomised study population (feasibility objective number 6). Patients who meet inclusion criteria 2 and 3 and who do not obviously meet any exclusion criteria at pre-screening will be approached.

6.3.1.7 Screening Procedures and Baseline Investigations

Patients determined eligible to approach for the study, as established by the retrospective case review outlined above, will be provided with a participant information sheet. Written informed consent to enter and be randomized into the trial will be obtained from participants, after the explanation of the aims, methods, benefits and potential hazards of the trial and **BEFORE** any trial-specific procedures are performed. The only procedures that will be performed in advance of written informed consent being obtained are those that would be performed on all patients in the same situation

as a usual standard of care. Eligibility screening (figure 4, page 61) will take place after consent, conducted by a research therapist, and will include a test for fixed contracture of tendoAchillis, the step test and an ability to follow simple commands by imitating actions.

6.4 Interventions

Interventions:

The intervention phase will be 20 treatment sessions delivered within a 6-week period, after the completion of baseline measurements. Interventions will follow the agreed protocols, and research therapists will be appropriately trained to ensure they follow the protocol. If participants are receiving routine therapy, this will continue alongside the MTS / TIs research schedule, which will therefore be in addition to routine therapy. Fatigue will be accounted for as it would in usual therapy rehabilitation.

6.4.1 Arm A: Mobilization and Tactile Stimulation (MTS) Group:

Prior to each standardized TSGT session (30 minutes), each participant will receive 30-60 minutes of MTS treatment to the lower limb, to prepare the sensorimotor system. In total each participant will receive 20 sessions of MTS plus TSGT within a 6 week period. The MTS schedule has been developed and the treatment schedule will be submitted with the ethics application. The specific content of each treatment session will be individualised for each participant according to need e.g. to address a hypersensitive foot and to take into account tolerance, and will be recorded by ticking boxes on a treatment schedule (Hunter et al 2006). A research therapist will undertake the standardized MTS treatment. The schedule for the TSGT (for both groups) will also be available prior to commencement of the trial. A research therapist will deliver this intervention and will be appropriately trained so it can be ensured the same treatment is given to each group. A log will be kept regarding which research therapist delivers which session, and an exploratory analysis undertaken.

6.4.1.1 Products

Not applicable

6.4.1.2 Treatment Schedule

A standardized treatment schedule will be followed for both the MTS and TSGT.

6.4.1.3 Dispensing

Not applicable

6.4.1.4 Dose Modifications, Interruptions and Discontinuations

Not applicable, unless there is an adverse reaction – see section 6.4.6 for details

6.4.2 Arm B: Textured Insole (TI) Group

This group of participants will be encouraged to wear the TI on the hemiparetic side (and a smooth insole on the opposite side), as much as possible (to 'augment' the sensorimotor system), during the 4-6-week period of intervention, apart from when the outcomes are being assessed. In addition to wearing the TIs participants will also receive 20 sessions of TSGT (30 minutes for each session), during the 4-6-week intervention period. If help is required to put the TIs into shoes and put on footwear (and no family support is available), a research therapist will assist. The specific content of each treatment session will be documented and daily diaries will inform the researcher of the extent of wearing of the TIs. Outcome measurements will be undertaken without the participant wearing TIs, so that conditions are the same as for the MTS group.

6.4.2.1 Products

Smooth insoles and TIs will be used. The insole with the smooth surface will be of medium density EVA, 3-mm thickness, shore value A50, black, OG1304 manufactured by Algeos UK Ltd., Liverpool, UK. The TI has small, pyramidal peaks with centre-to-centre distances of approximately 2.5 mm Evalite Pyramid EVA, 3-mm thickness, shore value A50, black, OG1549 manufactured by Algeos UK Ltd. The insoles will be participant specific and cut to size so they fit in the participant's shoe.

6.4.2.2 Treatment Schedule

Participants will be encouraged to wear the TIs as much as possible and a standardized treatment schedule will be followed for the TSGT.

6.4.2.3 Dispensing

Not applicable

6.4.2.4 Dose Modifications, Interruptions and Discontinuations

Not applicable, unless there is an adverse reaction – see section 6.4.6 for details

6.4.3 Accountability

Not applicable

6.4.4 Compliance and Adherence

Although participants in the TI group will be encouraged to wear the TIs as often as possible, it will ultimately be the participants own choice how long they wear them for each day. Completion of a daily diary (by the participant), which will record the daily wearing duration, will be encouraged.

6.4.5 Concomitant Care

If participants are receiving routine therapy, this will continue alongside the MTS / TIs research schedule, which will therefore be in addition to routine therapy. Fatigue will be

accounted for as it would in usual therapy rehabilitation, for example by reducing the number of exercises prescribed, or the time of the intervention.

6.4.6 Overdose of Trial Intervention

There is a small possibility that either the MTS or TSGT could be associated with an overuse syndrome as expressed by a participant's experience of pain or fatigue.

a. Pain will be considered to be an adverse reaction if (i) a participant reports the onset or increase of paretic lower limb pain (verbally or behaviourally), (ii) the pain is sustained over four consecutive therapy sessions and (iii) if the research therapist and clinical team are unable to account for this in any other way than involvement in this trial. This will be addressed by the research therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session on which pain was apparent.

b. Fatigue will be considered to be an adverse reaction if (i) a participant demonstrates a decrease of two levels in the Lower Extremity Motricity Index score on four consecutive therapy sessions and (ii) the therapist and clinical team are unable to account for this in any other way than involvement in this trial. This will be addressed by the therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session in which fatigue was indicated.

Potential discomfort of wearing the TIs has been considered; however, work undertaken with people affected by multiple sclerosis has shown general acceptability of this intervention (Baron et al., 2014). Participants will be in control of how often, and for how long, they wear the TIs. If discomfort is felt the TIs can therefore be removed. It will be ensured that the participant is able to remove the TIs and if there is any doubt the research therapist will remove them at the end of the TSGT each time. Participants will be asked to record all experiences in their daily diaries as part of the feasibility trial, so any discomfort can be noted and the length of time participants wear the insoles can be monitored. Discomfort will be considered to be an adverse event if a participant is unable to wear the TIs for over four consecutive therapy sessions, due to discomfort, and the research therapist and clinical team are unable to account for this discomfort in any other way than involvement in this trial. This will be addressed by the research therapist advising the participant to reduce the time wearing the TIs or to stop wearing them altogether, either on a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session in which discomfort from insoles was reported.

6.4.7 Protocol Treatment Discontinuation

In consenting to the trial, participants are consenting to trial treatments, trial follow-up and data collection. However, an individual participant may stop treatment early or be stopped early for any of the following reasons:

- Unacceptable treatment response or adverse event
- Inter-current illness that prevents further treatment
- Any change in the participant's condition that in the clinician's opinion justifies the discontinuation of treatment
- Withdrawal of consent for treatment by the participant

As participation in the trial is entirely voluntary, the participant may choose to discontinue trial treatment at any time without penalty or loss of benefits to which they would otherwise be entitled. Although not obliged to give a reason for discontinuing their trial treatment, a reasonable effort should be made to establish this reason, whilst remaining fully respectful of the participant's rights.

Participants who discontinue protocol treatment, for any of the above reasons, should remain in the trial for the purpose of follow-up and data analysis.

6.5 Outcomes

The study outcomes include assessment of whether the way participants are recruited is effective, the number of people who consent to participate, the willingness of participants to be randomized, how acceptable the treatments are, how many participants drop out, and to work out how many people would need to be recruited in a future larger trial.

As this is a feasibility trial one of the objectives is to identify which measure should be the primary outcome measure for future trials.

The following outcomes will therefore be evaluated as detailed below:

Outcomes:
1. Characterization of clinical presentation of participants (to give an overview of the participants to assist with evaluation of the interventions) using the following measurement tools:

(i) National Institutes of Health Stroke Scale (NIHSS) - This includes assessment of the level of consciousness, vision, motor activity (face, arm and leg), coordination, sensation and speech. It is anticipated this will take a maximum of 15 minutes to complete. Timepoint: Baseline

(ii) Functional Ambulation category, which assesses walking ability and categorizes according to basic motor skills necessary for functional walking. It is anticipated this will

take a maximum of 2 minutes for the researcher to complete. It will not require additional time of the participant because the assessment can be made following the 5 metre walk test. It is anticipated that the step test will exclude people who would achieve a FAC level 6, requiring assessment on uneven surfaces and stairs.
Timepoints: Baseline, on completion of the twenty treatments and at one-month follow up.

2. Sensorimotor impairment:
The following outcome measurements will be undertaken at baseline, after 5, 10, 15 and 20 treatments and one-month (+/-7 days) after last treatment (treatment number 20).

a) Pressure under the feet during stance phase of walking (measured with insoles).
This is important to measure because in order to walk there is a dependence upon the interaction between the feet and the environment. It is anticipated this will take a maximum of 10 minutes to complete.

b) Ankle range of motion (dorsiflexion and plantarflexion) during stance phase
This will be measured by an electrogoniometer (an electronic piece of equipment), in stance phase of walking. It is anticipated this will take a maximum of 10 minutes to complete.

c) Touch/pressure sensory thresholds (sole of foot) (the ability to feel at different points on the sole) of the foot
This will be measured using Semmes Weinstein Monofilaments. This involves touching the sole of the foot using a monofilament nylon wire which exerts a force when bowed into a C shape against the skin for 1 second. It is anticipated this will take a maximum of 5 minutes to complete.

d) Lower Extremity Motricity Index
This will measure motor impairment (strength) of hip flexors, knee extensors and ankle dorsiflexors (moving the foot upwards). This will be undertaken with the participant in sitting with the hip and knee at 90 degrees. It is anticipated this will take a maximum of 5 minutes to complete.

Regular outcome measurements (a), b), c) and d)) are being recorded to ascertain at what stage any changes are seen, to inform the dose (duration) of the intervention for the subsequent trial.

3. Lower limb function and balance:
Measures e) and f) will be collected at baseline, on completion of the twenty treatments and at one month follow up.

e) Walking speed 5 metre walk test (self-selected walking speed), gives an indication of the overall walking ability of stroke survivors). To enable more detailed analysis, the

5 metre walk test will be videoed. It is anticipated this will take a maximum of 10 minutes to complete.

f) Modified Rivermead Mobility Index
The test involves eight tasks including bed mobility, sitting and standing balance, transfers, walking and stairs. A rating is given relating to the amount of assistance the person requires. It is anticipated this will take a maximum of 17 minutes to complete.

3. Measurements of blood flow:
gi) Peak systolic velocity (PSV) (cm/s) (an indicator of blood flow) and vessel diameter (mm) of the posterior tibial and the dorsalis pedis artery, measured using a portable ultrasound machine (MyLabFive, Esoate). Left- and right-limb measures will be undertaken to determine if effects are local or systemic, possibly indicating altered sympathetic vasoconstrictor nerve activity. There will first be a period of 10 minutes rest, then the measurements will take approximately 15 minutes.
Timepoints: Baseline, on completion of the twenty treatments and at one-month follow up.

gii) In order to ascertain the effects of one individual treatment (acute effects), participants in the MTS group will have PSV and arterial diameter measured before and immediately after one of the first 10 MTS treatments. On this one occasion the participant will require an extended visit that will last between one and a half and two hours (MTS treatment 30-60 mins, blood flow studies 25 mins plus TSGT 30 mins).

h) Blood pressure, height and weight – Resting blood pressure will be taken before each measurement of blood flow. Participant's height and weight will be measured at baseline to allow calculation of Body Mass Index (BMI).

Research Setting

Participants will be asked to attend an outpatient setting or a university rehabilitation research facility for baseline, post intervention assessment and one-month follow up, in order to ensure standardisation of the 5 metre walk test. All treatment and all other assessments undertaken after treatments 5, 10 and 15 will be undertaken in the setting of the participant, such as the in-patient setting or in the participant's home.

6.6 Participant Timeline

Table 1: Timeline for participants

STUDY PERIOD									
			**t_1 - t_4 *will be completed within 4-6 weeks*						
TIMEPOINT**	$-t_1$	0	t_1 *After 5 treatments*	t_2 *After 10 treatments*	t_3 *After 15 treatments*	t_4 *At end of 20 sessions of intervention (+/- 7 days)*	t_5 *Follow-up One-month after t4 (+/- 7 days)*	t_6 *Focus Group*	t_7 *Completion of trial*
ENROLMENT:									
Retrospective case review	X								
Informed consent		X							
Baseline measures		X							
Randomisation		X							
INTERVENTIONS:									
Intervention A: MTS +TSGT			◆———	———	———	———◆			
Intervention B: TIs +TSGT			◆———	———	———	———◆			
[Daily Diaries			◆———	———	———	———◆			
Focus groups								X	
ASSESSMENTS: (See table below for details)									
***Characterization of clinical presentation of participants*:**									
(i) National Institutes of Health Stroke Scale (NIHSS)		X							
(ii) Functional Ambulation category		X				X	X		
Measures of sensorimotor impairment:									

a) Pressure under the feet during stance phase of walking		X	X	X	X	X	X		
b) Ankle range of motion during stance phase		X	X	X	X	X	X		
c) Touch/pressure sensory thresholds of the foot		X	X	X	X	X	X		
d) Lower Extremity Motricity Index		X	X	X	X	X	X		
Measures of lower limb function and balance:									
e) Walking speed 5 metre walk test		X				X	X		
f) Modified Rivermead Mobility Index.		X				X	X		
Measurements of blood flow:									
gi) Peak systolic velocity (blood flow) (cm/s) and vessel diameter (mm) of posterior tibial artery and dorsalispedis artery		X				X	X		
gii) Acute blood flow studies before and after one MTS treatment			X*	X*					
h) Blood Pressure (prior to blood flow studies)		X				X	X		

***** Please note blood flow will be assessed before and after one MTS treatment at some stage within the first 10 treatments (during t1 or t2).

BOTH ARMS:

It is anticipated that the intervention therapy may not be given when: (1) the participant is otherwise unwell; (2) on the day of the baseline, outcome or follow up assessments; (3) the participant is out of the area due to holiday or other personal reasons; (4) there is a public holiday; or (5) during therapist sickness or annual leave, which cannot be covered by the 2nd research therapist. If a participant misses a planned treatment for any of these instances, it will be recorded.

If participants have been discharged from in-patient rehabilitation before the end of the 6-week intervention period, then they will either attend an out-patient setting or the research therapist will visit them in their 'home' to receive their allocated treatment. If it is most suitable for any participant to travel to an out-patient setting, then a pre-paid return taxi journey will be provided.

Protocols for MTS, TIs and TSGT are being developed in consultation with 12 experienced neurological therapists. The standardized protocols will be available, prior to commencement of the feasibility trial. Training in delivering the interventions will be provided before the trial begins. Fidelity to the protocol will be assessed through observation by an appropriately experienced member of the trial management team, at the beginning and at regular points throughout the trial, with little prior warning to the therapist.

Daily Diaries

Throughout the intervention period, participants will be asked to keep a daily diary (with appropriate prompts), helping the participants 'focus their thoughts' (Jacelon & Imperio 2005 p 993) on how their lower limb is ‘feeling’, or if there are any changes following intervention or outcome measurements.

Diaries have been suggested as a useful tool to reflect on issues that are of interest to the researcher, providing insight into the importance of events for participants (Jacelon & Imperio 2005). Diaries will either be written, or saved as a daily video or audio clip, according to participant preference. This will enable information relating to comfort of interventions, outcome measurements and TIs to be evaluated, and will also find out if participants have reported any changes to feeling within the foot and ankle or changes in daily activities during the six weeks.

Focus groups:

The sample will be drawn from the participants of the feasibility study. All participants from both arms of the trial will be invited to a focus group, on completion of the intervention and outcome measurements. Two focus groups, with ideally 6-8 participants, if feasible, (as suggested by Krueger and Casey (2000) as being an ideal size to promote discussion), will be conducted for each arm of the trial. Focus groups have been used as an appropriate method for exploring views on interventions and research (Tong et al 2007), providing a large quantity of rich data in a short period of time, allowing the researcher to find out 'what people really think and feel' (Krueger and Casey 2000 p7). Experience of taking part in the trial, and perceptions as to any changes following intervention will be explored. The focus groups are planned to last no longer than 90 minutes and a focus group schedule will be developed to facilitate the discussion (Bowling 2009).

Procedures:

The focus group will be held in a suitable quiet room at Keele University or local community venue (e.g. local church hall) and transport will be provided, or alternative travel costs reimbursed. A researcher will facilitate each group, which will be audiotaped; a Patient and Public Involvement (PPI) volunteer will assist at each group by taking field notes.

The following areas will be explored:

• The participants' individual responses to the MTS and insole protocols, including any changes noticed since the intervention e.g. changes in sensation (feeling), function and participation.

• Participants' experiences of being involved in the research project, to include their experiences of receiving the interventions and completing the outcome measures. This will be important to inform the subsequent trial.

6.6.1 Early Stopping of Follow-up

If participants choose to discontinue their trial treatment, they should continue to be followed up as closely as possible to the follow-up schedule defined in the protocol, providing they are willing. They should be encouraged and facilitated not to leave the whole trial, even though they no longer take the trial treatment. If, however, the participant expresses the view that he or she no longer wishes to be followed up either, this view must be respected and the participant withdrawn entirely from the trial. NCTU should be informed of the withdrawal in writing using the MoTaStim-Foot trial documentation. Data already collected will be kept and included in analyses.

Participants who stop the trial follow-up early will not be replaced.

6.6.2 Participant Transfers

As this is a feasibility study, with only one participating site, it will not be possible to follow up participants at a different centre if they move from the area. However due to the age of the potentially eligible population transfer away from the participating site is unlikely.

6.6.3 Loss to Follow-up

As follow-up will be at only one month it is not anticipated this will be a major issue. One of the purposes of the feasibility study is to monitor loss to follow-up. A decision will be made that a participant has been lost to follow-up if there have been three unsuccessful attempts to contact the participant (e.g. by telephone call or letter). However due to the age of the potentially eligible population transfer away from the participating site is unlikely.

6.6.4 Trial Closure

End of Trial

Participants are considered to have reached the end of the trial when the first of the following occurs: (1) completion of all data collection e.g. 1 month follow up outcome measurements, focus group; (2) withdrawal of consent; (3) SAE resulting in withdrawal of participant or death; (4) loss to follow-up. Loss to follow-up will be declared following three unsuccessful attempts (letter or telephone call) to contact the participant. If during therapy pain or fatigue (as defined above) or discomfort from insoles occurs, the MTS,

TSGT or TIs will be temporarily or permanently stopped depending on whether or not the symptoms dissipate.

After the one-month follow-up and the qualitative aspect of the study, for all 34 participants, any outstanding queries or adverse events will be resolved by the Chief Investigator on termination of the trial and correct storage of study documentation will be verified.

The end of the trial is defined as the collection of the last piece of data for the last participant; however, this will be followed by a further period of twelve months, during which the data will be analysed and prepared for dissemination.

6.7 Sample Size

A sample size of 30 has been suggested as the lower limit for working out how many participants will be required for future studies in terms of an estimate of the standard deviation of values on a continuous outcome measure (Browne 1995). Recruiting a sample of 34 participants will account for 10% drop out, and enable potentially equal numbers (n=17) in each arm of the trial. As the whole study needs to be completed within three years this sample size was deemed to be the largest feasible in the time frame.

6.8 Recruitment and Retention

6.8.1 Recruitment

Adult stroke survivors (n= 34) will be recruited from the North Staffordshire Stroke Service, identified by research nurses or the multidisciplinary teams caring for the stroke survivors. Stroke survivors (6-16 weeks or 42-112 days) expressing an interest in participating will be given a participant information sheet. The first seventeen right hemisphere and the first seventeen left hemisphere stroke survivors meeting the inclusion criteria and providing written informed consent will be recruited. It is anticipated that it will be necessary to recruit over a period of 18 months; recruitment levels will be monitored monthly.

6.8.2 Retention

As follow-up will be at only one month, following completion of the last interventional therapy, it is not anticipated this will be a major issue. One of the purposes of the feasibility study is to monitor loss to follow up.

6.9 Assignment of Intervention

6.9.1 Allocation

6.9.1.1 Sequence generation

The randomisation sequence will be generated before the trial commences and Professor Julius Sim, the statistician for the trial, will provide the randomisation order to Norwich CTU. Participants will be randomised to the interventions using 1:1 randomisation with stratification by left or right stroke. Stratified randomisation will ensure an equal number of right and left sided strokes in each treatment group.

6.9.1.2 Allocation concealment mechanism

An independent telephone interactive voice response system randomisation service and electronic case record form will maintain concealment of the treatment allocation from investigators, research therapists and blinded assessors prior to randomisation of a participant (i.e. each participant allocation cannot be predicted from the allocation of the previous participant). Baseline data will be entered into the randomisation system and the system will randomize, sending an email confirmation of the allocation group for the participant. Concealment of group allocation from the blinded assessor with continue throughout the trial process.

6.9.1.3 Allocation Implementation

Baseline data will be entered into the randomisation system and the system will randomize, sending an email confirmation of the allocation group for the participant.

6.9.2 Blinding

All outcome measurements in which observer bias could occur will be undertaken by assessors who are blinded to treatment group allocation. The touch/pressure sensory thresholds, Lower Extremity Motricity Index and Modified Rivermead Mobility Index will all be undertaken by a blinded assessor. However, a research therapist will undertake the five metre walk test, pressure under the feet and ankle range of movement assessments. As these are objective assessments the risk of bias is low. An experienced sonographer (not blinded to group allocation) will undertake the blood flow studies. As part of clinical decision making, in order to assess for possible fatigue, the research therapists will also measure the Lower Extremity Motricity Index, at each intervention; however, it will be the Lower Extremity Motricity Index measurement undertaken by the blinded assessor which will be formally analysed. Participants will be asked to refrain from telling the assessors which treatment they are receiving. To assess whether blinding of assessors was achieved, we will ask assessors, at the one-month follow-up point, to guess which group they think participants were assigned to. Agreement with actual allocation will be assessed with the kappa statistic.

6.9.3 Emergency Unblinding

Neither the participant nor the therapist is blinded therefore this is not relevant.

6.10 Data Collection, Management and Analysis

6.10.1 Data Collection Methods

The Chief Investigator will ensure that blinded assessors and research therapists undertaking any of the outcome measurements will be appropriately trained.

1. Characterization of clinical presentation of participants (to give an overview of the participants to assist with evaluation of the interventions):

(i) National Institutes of Health Stroke Scale (NIHSS) - reliability has been demonstrated by Goldstein and Samsa (1997).

(ii) Functional Ambulation category, which assesses walking ability and categorizes according to basic motor skills necessary for functional walking and has been found to be valid and responsive, with excellent reliability in stroke survivors (Mehrholz et al 2007).

2. Sensorimotor impairment:

a) Pressure under the feet during stance phase of walking (measured with insoles).

This is important to measure because in order to walk there is a dependence upon the interaction between the feet and the environment (Rasak et al 2012). The pressure measurements will be obtained by using a Tekscan F-Scan VersaTek clinical in-shoe pressure measurement kit system.

b) Ankle range of motion (dorsiflexion and plantarflexion) during stance phase

This will be measured by an electrogoniometer (an electrical piece of equipment, which has been shown to be valid and reliable (Bronner et al 2010), in stance phase of walking.

c) Touch/pressure sensory thresholds (sole of foot) (the ability to feel at different points on the sole) of the foot

This will be measured using Semmes Weinstein Monofilaments, which have been found to be reliable and responsive (Tracey et al 2012).

d) Lower Extremity Motricity Index

This will measure motor impairment (strength) of hip flexors, knee extensors and ankle dorsiflexors (moving the foot upwards). This will be undertaken with the participant in sitting with the hip and knee at 90 degrees. This was found to be a valid measure by Cameron and Bohannon (2000), which is reliable (Fayazi et al 2012).

3. Lower limb function and balance:

e) Walking speed 5 metre walk test (self-selected walking speed), gives an indication of the overall walking ability of stroke survivors (Olney et al 2006). A web-cam, attached to a computer will be used to video the 5 metre walk test enabling a more detailed analysis.

f) Modified Rivermead Mobility Index.

A valid, reliable, responsive measure of mobility in the early stages of stroke rehabilitation (Lennon and Johnson 2000).

4. Measurements of blood flow:

g) Peak systolic velocity (blood flow) (cm/s) and vessel diameter (mm) of posterior tibial artery and dorsalis pedis artery, measured using a portable ultrasound machine (MyLabFive, Esoate), following a 10 minute rest period, during which blood pressure will be taken. Posterior tibial artery reliability measures for vessel diameter at rest are good to excellent with intraclass correlation coefficient [ICC] of 0.95 (Sabatier et al., 2006).

h) Blood pressure, height and weight – Although not required as outcome measures, resting blood pressure will be taken before the measurements of blood flow. Participant's height and weight will be measured to allow calculation of Body Mass Index (BMI). Together with resting blood pressure these measures will provide some basic descriptive data related to the participants' health status.

Research therapists / blinded assessors who will be undertaking the above outcome measurements will be fully trained and procedures for each outcome measurement will be standardized.

Data collection

A Protocol, Standard Operating Procedures, Intervention protocols and Case Report Forms (CRFs) will be available at SSOTP. Data will be sent to the Norwich Clinical Trials Unit (CTU) for entry and quality control in a secure standardized manner.

Pre-study site visits

Before the study commences, SSOTP, as the recruiting site, will receive training visits, as required, by the Chief Investigator. These visits will ensure that the research team at each site (including principal investigators, co-investigators, research therapists and blinded assessors) fully understand the protocol, CRFs and the protocols for the study.

Monitoring site visits

A quality management and monitoring plan will be set up, which will detail the monitoring of activities to be undertaken, ensuring compliance with the protocol and that ethical and regulatory guidelines are met.

6.10.2 Non-Adherence and Non-Retention

All outcome data will be collected and file notes (identified by the participant's number) will be included as an explanation re non-adherence, as this is an important aspect of the feasibility trial. Analysis of file notes will be useful to ascertain links between non-adherence/dropout and specific patient characteristics in terms of age, sex, clinical severity, etc., further informing the future trial.

6.10.3 Data Management

The NHS Code of Confidentiality and Data Protection Act will be complied with. Specifically, we will keep data that could identify individuals separate from anonymous data and ensure that the linking information is accessed only by those who need to know. All data by which individuals may be identified will be kept in a lockable storage facility within the research offices or research laboratories. Any electronic data by which individuals can be identified will be placed in a password protected secure space on hard drives. Personal names and information will not be transferred via email.

Only members of the research team directly involved in the study will have access to identifiable data, and this will be only on a need-to-know basis. Use of personal addresses, postcodes, faxes, emails or telephone numbers will be restricted to the minimum number of people necessary to ensure the efficient and safe running of the trial. For example, telephone numbers will be used by members of the research team to organise appointments and addresses used to collect and return participants for appointments. Participant numbers will be utilised to anonymize data. Audio recording devices will be used for the planned focus groups. On transcription, pseudonyms will be used to maintain anonymity. Pseudonyms will be used in the interview transcripts and dissemination of findings. Faces will be blanked out on the 5 metre walk videos. The videos will be stored on a password protected computer. Transcriptions from the audio/visual recording devices will be anonymized, with pseudonyms used, prior to being stored on password protected computer or laptop. When the work is written up for publication all direct quotations will be anonymous and no individual will be identifiable.

Research therapists and administration staff will be appropriately trained in issues relating to confidentiality of personal data as part of their induction on commencement of their post. Only the minimal amount of information necessary to do the job will be disclosed and it will be ensured that all staff who have access to personal information, e.g. names and addresses, will respect that it is given to them in confidence.

Only anonymous data (by means of issuing each participant a unique trial number) will be shared with other organisations. The only identifiable data will be held on purpose built forms and stored in lockable cabinets in lockable rooms. Where it is necessary to share this information between organisations, for example when reporting a safety incident or complaint the paper form will be scanned in and saved in a password protected file (password will be emailed to the PI separately), then provided to the Principal Investigator who will, open the file, print it and destroy the electronic copy. The Trial Manager will then store the paper copy in a lockable cabinet in a lockable room.

All documentation including case report forms (CRFs), and clinical measurement forms will be photocopied and a copy stored safely in a locked cupboard prior to sending a copy to Norwich CTU.

At the end of the trial all data will be archived appropriately (see section 7.10 for details).

6.10.4 Statistical Methods

6.10.4.1 Statistical Analysis Plan

Statistical analysis (quantitative study)

As this is a feasibility study, no formal hypothesis tests will be undertaken. For statistical methods please see section 6.10.4.2.

Data collection and analysis for the qualitative study:

Daily diaries will be collected weekly from the participants. Data will be taken from the daily diaries kept by the participants; the data will then be coded and thematic analysis undertaken. Data from the focus groups will be analysed as the study progresses, with each focus group being transcribed and analysed prior to the next focus group, so that any emerging ideas can be included in subsequent discussions (Kisely and Kendall 2011). Discussion topics will be planned in advance and guided by the focus group schedule. Topics will relate to the interventions and participation within the study, as well as changes in functional ability. Individual responses relating to these topic areas will be facilitated. All the focus groups will be transcribed in full (funding has been incorporated into the project for this), and then analysed using a thematic content analysis approach, using NVivo to aid data management. The researcher and an independent reviewer will independently code the data in the transcripts, and identify themes. In addition to the themes decided in advance, others will be developed from analysing the data. Any differences of opinions will be highlighted and discussed, before agreement is reached and themes finalised. The final stage of analysis will involve both researchers collectively looking for conceptual relationships within and across the focus groups. Analysis of the field notes from the focus groups will provide additional insights and context behind the interactions of participants.

6.10.4.2 Statistical Methods – Outcomes

As this is a feasibility study, no formal hypothesis tests will be undertaken. Instead point estimates, with 95% confidence intervals, will be calculated for key outcome measures. The variance of scores for outcome measures will be calculated, providing information for the sample size calculation for the subsequent large trial. The distribution of outcome variables, and the extent of clustering of observations by therapist, will also be assessed, to further inform the sample size calculation and guide the choice of analysis in the main study. The number of eligible patients who are recruited, and the proportion of those recruited who are lost to follow up at one month, will also be calculated. Analysis will be conducted by the applicant, with guidance from the supervisory team. A single formal analysis will take place at the end of the study.

For those scaled outcomes that are recorded at each time point, a line graph of all individual participants' response trajectories will be constructed for each arm of the trial; this graph will also include a line representing the averaged response trajectory. The graph will be analysed visually to determine if there is a point at which the participants' responses tend to change direction upwards (indicating a response to treatment), as this information will provide information on the likely minimum length of treatment, or 'dosage', that is required to induce an improvement on the outcome concerned. Across these outcomes, the latest such change in trend will suggest the minimum length of treatment that should be utilized in the main trial.

Within the feasibility study, both research therapists will deliver either MTS or TSGT. A log will be kept detailing, for each participant, which therapist has delivered the treatment. An intra-cluster correlation coefficient will be calculated to assess the extent to which outcomes are correlated (clustered) within therapists. This information will be required as an adjustment factor in the sample size calculation for the subsequent main trial, in which it is likely that therapists will be specific to one or other arm of the trial.

In addition to quantifying variables such as walking speed for the 5 metre walk test, an observational analysis of the quality will be undertaken, as is common practice in therapy rehabilitation.

6.10.4.2.1 Economic evaluations

6.10.4.3 Additional Analyses - Subgroup

Not applicable, as this is a feasibility trial

6.10.4.4 Additional Analyses – Adjusted

6.10.4.5 Analysis Population and Missing Data

Not applicable, as this is a feasibility trial

6.11 Data Monitoring

6.11.1 Data Monitoring Committee

As this is a small feasibility study being undertaken as part of a doctoral fellowship a Data Monitoring Committee has not been deemed to be necessary. The trial will be overseen by the Trial Management Group.

6.11.2 Interim Analyses

No interim analysis is planned

6.11.3 Data Monitoring for Harm

Adverse events and any other unintended effects of trial interventions will be reported monthly to the Trial Management Group.

6.11.3.1 Safety reporting

Adverse events and serious adverse events related to stroke and the intervention will be recorded during the study. The participant's condition will be evaluated at each contact (treatment and assessment), in case the participant reports any of the stroke related expected adverse events.

Stroke-related expected adverse events:

- Death
- A fall requiring hospitalisation
- Further vascular events (including recurrent strokes, myocardial infarction, bowel ischemia)
- Cardiac, renal or liver problems
- Epileptic seizures
- Revascularisation
- Major bleed
- A fall
- Infections
- Mood disturbances
- Spasticity or contractures
- Deep vein thrombosis (DVT)

In addition to the above, potential Adverse Reactions of pain and fatigue are of clinical interest in informing the results of the trial. There is a small possibility that either the MTS or TSGT could be associated with an overuse syndrome as expressed by a participant's experience of pain or fatigue.

a. Pain will be considered to be an adverse reaction if: (i) a participant reports the onset or increase of paretic lower limb pain (verbally or behaviourally); (ii) the pain is sustained over four consecutive therapy sessions; and (iii) the research therapist and

clinical team are unable to account for this in any other way than involvement in this trial. This will be addressed by the research therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session after pain was first noted.

b. Fatigue will be considered to be an adverse reaction if: (i) a participant demonstrates a decrease of two levels in the Lower Extremity Motricity Index score on four consecutive therapy sessions; and (ii) the therapist and clinical team are unable to account for this in any other way than involvement in this trial. This will be addressed by the therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session, in which fatigue was indicated.

Potential discomfort of wearing the TIs has been considered; however, work undertaken with people affected by multiple sclerosis has shown general acceptability of this intervention. The participant will be in control of how often and for how long they wear the TIs. If discomfort is felt the TIs can be removed. It will be ensured that the participant is able to remove the TIs and if there is any doubt the research therapist will remove them at the end of the TSGT each time. Participants will be asked to record all experiences in their daily diaries as part of the feasibility trial, so any discomfort can be noted and the length of time participants wear the insoles can be monitored. Discomfort will be considered to be an adverse event if a participant is unable to wear the TIs for over four consecutive therapy sessions, due to discomfort, and the research therapist and clinical team are unable to account for this discomfort in any other way than involvement in this trial. This will be addressed by the research therapist advising the participant to reduce the time wearing the TIs or to stop wearing them altogether, either on a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session in which discomfort from insoles was reported.

Reporting of adverse events:
All adverse events, including those which are expected, will be recorded from date of randomisation to end of trial (see below). Adverse events will be reported to the Trial Management Group.

Safety reporting will conform to the requirements of the Safety and Progress Reports Table (non-CTIMPs) for UK health departments' RES version 2.1

Table 1: Adverse Event Definitions

Adverse Event (AE)	Any untoward medical occurrence in a patient or clinical trial participant administered a study intervention and which does not necessarily have a causal relationship with this intervention.
Adverse Reaction (AR)	Any untoward and unintended response to an investigational intervention.
Unexpected Adverse Reaction (UAR)	An adverse reaction, the nature or severity of which is not consistent with the expected complications of the intervention.
Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)	Any AE or AR that: • results in death • is life threatening* • requires hospitalisation or prolongation of existing hospitalisation** • results in persistent or significant disability or incapacity • consists of a congenital anomaly or birth defect • or is otherwise considered medically significant by the investigator***

* the term life threatening here refers to an event in which the patient is at risk of death at the time of the event; it does not refer to an event that might hypothetically cause death if it was more severe (e.g. a silent myocardial infarction)

** Hospitalisation is defined as an in-patient admission, regardless of length of stay, even if the hospitalisation is a precautionary measure for continued observation. Hospitalisation for pre-existing conditions (including elective procedures that have not worsened) do not constitute an SAE

*** Clinical judgement should be exercised in deciding whether an AE or AR is serious in other situations. Important AEs or ARs that may not be immediately life threatening or result in death or hospitalisation, but may seriously jeopardise the participant by requiring intervention to prevent one of the other outcomes listed in the table above (e.g. a secondary malignancy, an allergic bronchospasm requiring intensive emergency treatment, seizures or blood dyscrasias that do not require hospitalisation, or development of drug dependency) should also be considered serious.

Adverse events include:

- an exacerbation of a pre-existing illness
- an increase in the frequency or intensity of a pre-existing episodic event or condition

- a condition (regardless of whether PRESENT prior to the start of the trial) that is DETECTED after trial intervention. (This does not include pre-existing conditions recorded as such at baseline – as they are not detected after trial intervention)
- continuous persistent disease or a symptom present at baseline that worsens following administration of the trial treatment

Adverse events do NOT include:

- Medical or surgical procedures: the condition that leads to the procedure is the adverse event
- Pre-existing disease or a condition present before treatment that does not worsen
- Hospitalisation where no untoward or unintended response has occurred e.g. elective cosmetic surgery
- Overdose of medication without signs or symptoms

6.11.3.2 Other Notifiable Adverse Events

6.11.3.3 Procedures to follow in the event of female participants becoming pregnant

6.11.3.4 Investigator responsibilities relating to safety reporting

All non-serious AEs and ARs, whether expected or not, will be recorded on a case report form. SAEs and SARs will be notified to NCTU within 24 hours of the investigator being aware of the event.

6.11.3.4.1 Seriousness assessment

When an AE or AR occurs, the investigator responsible for the care of the participant must first assess whether or not the event is serious using the definition given in Table 1. If the event is classified as 'serious' then an SAE form must be completed and NCTU (or delegated body) notified within one working day.

6.11.3.4.2 Severity or grading of Adverse Events

Not applicable

6.11.3.4.3 Relatedness

The investigator must assess the causality of all serious events or reactions in relation to the trial therapy using the definitions in Table 2.

Table 2: Relatedness definitions

Relationship	Description	Event type
Unrelated	There is no evidence of any causal relationship	Unrelated SAE

Unlikely to be related	There is little evidence to suggest that there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial intervention). There is another reasonable explanation for the event (e.g. the participant's clinical condition or other concomitant treatment)	Unrelated SAE
Possibly related	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial intervention). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition or other concomitant treatment)	SAR
Probably related	There is evidence to suggest a causal relationship and the influence of other factors is unlikely	SAR
Definitely related	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.	SAR

If an SAE is considered to be related to trial treatment, and treatment is discontinued, interrupted or modified, refer to the relevant Interventions sections of the protocol.

6.11.3.4.4 Expectedness

Please see section 6.11.3.2 for possible adverse events which could be associated with this trial.

6.11.3.5 Notifications

6.11.3.5.1 Notifications by the Investigator to NCTU

NCTU will be notified of all SAEs within 1 working day of the investigator becoming aware of the event.

Investigators will notify NCTU of any SAEs and other Notifiable Adverse Events (NAEs) occurring from the time of randomisation until the one month follow up measurements.

The SAE form will be completed by the research therapist or the blinded assessor, in conjunction with the PI, dependent upon who becomes aware of the event occurring. In the absence of the responsible investigator, the SAE form will be completed and signed by a member of the site trial team and emailed as appropriate within the timeline. The responsible investigator will check the SAE form at the earliest opportunity, making any changes necessary, sign and then email to NCTU. Detailed written reports will be completed as appropriate. Systems will be in place at the site to enable the investigator to check the form for clinical accuracy as soon as possible.

The minimum criteria required for reporting an SAE are the trial number and date of birth, name of reporting investigator and sufficient information on the event to confirm seriousness. Any further information regarding the event that is unavailable at the time of the first report will be sent as soon as it becomes available.

The SAE form must be scanned and sent by email to the trial team at NCTU on

MoTaStim–Foot @uea.ac.uk

Participants will be followed up, until their final follow up measurement, one month after completion of the intervention. Follow-up SAE forms (clearly marked as follow-up) should be completed and emailed to NCTU as further information becomes available. Additional information and/or copies of test results etc may be provided separately. The participant must be identified by trial number, date of birth and initials only. The participant's name should not be used on any correspondence and should be blacked out and replaced with trial identifiers on any test results.

6.11.3.5.2 NCTU responsibilities

Chief Investigator (CI or a clinically qualified delegate) will review all SAE reports received. In the event of disagreement between the relatedness assessment given by the local investigator and the CI, both opinions and any justifications will be provided in subsequent reports.

The CI is undertaking the duties of trial sponsor and is responsible for the reporting of SARs to the REC as appropriate.

CI will keep investigators informed of any safety issues that arise during the course of the trial.

The CI, with the support of NCTU, will submit the Annual Safety Report to the REC.

6.11.4 Quality Assurance and Control

6.11.4.1 Risk Assessment

The Quality Assurance (QA) and Quality Control (QC) considerations for the “Sensory stimulation of the foot and ankle post-stroke” (MoTaStim-Foot) trial are based on the standard NCTU Quality Management Policy that includes a formal Risk Assessment, and that acknowledges the risks associated with the conduct of the trial and proposals of how to mitigate them through appropriate QA and QC processes. Risks are defined in terms of their impact on: the rights and safety of participants; project concept including trial design, reliability of results and institutional risk; project management; and other considerations.

QA is defined as all the planned and systematic actions established to ensure the trial is performed and data generated, documented and/or recorded and reported in compliance with the principles of GCP and applicable regulatory requirements. QC is defined as the operational techniques and activities performed within the QA system to verify that the requirements for quality of the trial related activities are fulfilled.

Risks and burdens:

The intensive nature of the interventions and potential for discomfort has been considered during the protocol development phase, with input from both stroke survivors and clinicians. The Mobilization and Tactile Stimulation and TSGT are part of routine, conventional daily stroke rehabilitation. Potential discomfort of wearing a TI has been considered; however, work undertaken with people affected by multiple sclerosis has shown general acceptability of this intervention. Participants will be asked to record all experiences in their daily diaries as part of the feasibility trial. There is a small risk that participating in extra therapy, either MTS or TSGT, might result in an overuse syndrome, which presents as pain in the leg / foot and /or fatigue. At the beginning of each therapy session, therefore, the research therapist will check for onset/increase of leg/foot pain and onset/increase of fatigue. An adverse event will be deemed to have occurred if onset/increase of pain or fatigue is recorded on four consecutive therapy treatments and the clinical team cannot account for this in any other way than involvement in the trial. Participants so affected will be withdrawn from treatment but will still be invited to attend the outcome and follow up assessment sessions.

In order to minimise bias in the measurement of blood flow characteristics (PSV and arterial diameter) participants will be requested, where possible, to adhere to the pre-test protocol stated below. Adherence to the protocol will be recorded. The pre-test protocol comprises of avoidance of caffeinated drinks, alcohol or smoking for 6 hours prior to data collection, no high fat meals or over-exertion from physical activity 2 hours prior to data collection. Any medications consumed in the preceding 4 hours prior to data collection will be monitored.

6.11.4.2 Central Monitoring at NCTU

NCTU will monitor site set up, delegation logs, GCP training and consent form completion. As this is a single centre study, data errors and missing key data points will be reviewed by the CI.

6.11.4.3 On-site Monitoring

The frequency, type and intensity of routine and triggered on-site monitoring will be detailed in the MoTaStim-Foot Quality Management and Monitoring Plan (QMMP). The QMMP will also detail the procedures for review and sign-off of monitoring reports.

6.11.4.3.1 Direct access to participant records

Participating investigators must agree to allow trial related monitoring, including audits, REC review and regulatory inspections, by providing access to source data and other trial related documentation as required. Participant consent for this must be obtained as part of the informed consent process for the trial.

6.11.4.4 Trial Oversight

Trial oversight is intended to preserve the integrity of the trial by independently verifying a variety of processes and prompting corrective action where necessary. The processes reviewed relate to participant enrolment, consent, eligibility, and allocation to trial groups; adherence to trial interventions and policies to protect participants, including reporting of harms; completeness, accuracy and timeliness of data collection. These processes will verify adherence to applicable policies detailed in the Compliance section of the protocol. Independent trial oversight complies with the NCTU trial oversight policy.

Trial oversight will occur as described in the MoTaStim-Foot Quality Management and Monitoring Plan.

6.11.4.4.1 Trial Management Team

The Trial Management Team (TMT) will be set up to assist with developing the design, co-ordination and day to day operational issues in the management of the trial, including budget management. The membership, frequency of meetings, activity (including trial conduct and data review) and authority will be agreed with NCTU and Chief Investigator.

6.11.4.4.2 Trial Management Group

A Trial Management Group (TMG) will be set up to assist with developing the design, co-ordination and strategic management of the trial. The membership, frequency of meetings, activity (including trial conduct and data review) and authority will be covered in the TMG terms of reference.

6.11.4.4.3 Independent Trial Steering Committee

This is a feasibility study so an independent trial steering committee is not required.

6.11.4.4.4 Independent Data Monitoring Committee

As this is a feasibility study there will not be a formal independent Data Monitoring Committee; however, a copy of all data will be sent back to Norwich CTU for checking.

6.11.4.4.5 Trial Sponsor

The role of the sponsor is to take on responsibility for securing the arrangements to initiate, manage and finance the trial. Keele University is the trial sponsor and has delegated the management of the trial to the Chief Investigator. Queries relating to sponsorship of this trial should be addressed to the Chief Investigator.

7 Ethics and Dissemination

7.1 Research Ethics Approval

Before initiation of the trial at any clinical site, the protocol, all informed consent forms and any material to be given to the prospective participant will be submitted to the relevant REC for approval. Any subsequent amendments to these documents will be submitted for further approval. Before initiation of the trial at each additional clinical site, the same/amended documents will be submitted for local Research and Development (R&D) approval.

The rights of the participant to refuse to participate in the trial without giving a reason must be respected. After the participant has entered the trial, the clinician remains free to give alternative treatment to that specified in the protocol, at any stage, if s/he feels it to be in the best interest of the participant. The reasons for doing so must be recorded. After randomisation the participant must remain within the trial for the purpose of follow up and data analysis according to the treatment option to which they have been allocated. However, the participant remains free to change their mind at any time about the protocol treatment and follow-up without giving a reason and without prejudicing their further treatment.

7.2 Competent Authority Approvals

This is not a Clinical Trial of an Investigational Medicinal Product as defined by the EU Directive 2001/20/EC. Therefore, a clinical trial authorisation is not required in the UK.

The progress of the trial, safety issues and reports, will be reported to the Competent Authority, regulatory agency or equivalent in accordance with relevant national and local requirements and practices, where applicable.

7.3 Other Approvals

The protocol will be submitted by those delegated to do so to the relevant R&D department of each participating site or to other local departments for approval as required in each country. A copy of the local R&D approval (or other relevant approval as above) and of the Participant Information Sheet (PIS) and consent form on local headed paper must be forwarded to the co-ordinating centre before participants are randomized to the trial.

The protocol has received formal approval and methodological, statistical, clinical and operational input from the NCTU Protocol Review Committee.

7.4 Protocol Amendments

The protocol, informed consent form and participant information sheet will be submitted to an appropriate Research Ethics Committee (REC) via an IRAS application and to SSOTP R&D for written approval. The CI will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

7.5 Consent or Assent

This feasibility trial has been designed to avoid conflicts of interest so all of the recruitment process and research activity will be undertaken by either a member of the research team or a research nurse/therapist. Members of the research team or research nurses/therapists will provide the potential participants with information on the trial, and take informed consent where appropriate and in keeping with the principles of GCP. All members of the research team will have honorary contracts/letters of access, research passports within the NHS within which the research is conducted. All members of the research team will have completed GCP training and will be aware of how potential conflicts of interest could arise and the need to avoid these.

Clinically trained members of the research team will also be registered with the appropriate section of the Health and Care Professions Council or other professional regulatory organisation as appropriate. Therefore, the clinically trained members of the research team will be subject to the same professional conduct regulations as the clinical team. Routine and research treatment will be kept distinct.

PROCESS (This will take place either in the potential participant’s clinical setting within an NHS organisation or at their place of residence, as appropriate.)

1. A member of the clinical team or a research nurse will screen potential participants in keeping with GCP and data protection act standards.

2. A clinical team member or research nurse will approach potential participants to establish whether they would like to find out more about the trial. Verbal consent will be sought for a member of the research team to look at their medical notes and Stage 1 of the screening process (case note review) will occur to determine whether the potential participant is potentially eligible for the trial (i.e. to check: [1] age, [2] time since stroke, [3] type of stroke and [4] previous ability to walk independently).

3. Interested potential participants will be approached by a member of the research team or a research nurse/therapist who will: introduce him/herself and discuss the trial; explain the purposes of the trial; clearly delineate what is research and what is clinical practice; explain potential benefits and risks and go through the Participant Information Sheet (PIS). PIS refers to the summary and full participant information sheets, which will BOTH be discussed with every participant. Any questions the potential participant may have will be answered. The potential participant will then be left with a PIS to read and consider further. A record will be kept of the contact and leaving of the PIS, and members of the clinical team will also be informed either verbally or in writing.

A member of the research team or research nurse/therapist will return (after the potential participant has been given as much time as they need), establish if the participant wishes to take part in the trial, answer any questions about the trial and participation, and take consent if appropriate. This contact and the result will be recorded and also communicated either verbally or in writing (in the participant's medical notes) to members of the clinical team. Potential participants will also be encouraged to discuss their possible involvement in the trial with other people such as friends and relatives. If any potential participant wants the researcher to also talk to somebody who is significant to them then the researcher will do so. However, it must be ensured that informed consent is freely given (see decision making capacity section below).

4. This process may need to be repeated if the potential participant requests more time to consider whether or not to become involved.

Because of (i) the inclusion / exclusion criteria necessary for this trial, and (ii) the wish not to create conflicts of interest or create extra work for the clinical team, further eligibility screening (Stage 2) of potential participants is required after participants have given consent. Therefore, the participants will be informed that if they provide consent, there will be a few measures undertaken to check they meet all the inclusion / exclusion criteria for the trial. These measures are not a part of routine clinical practice. The need for informed consent prior to this additional screening will be explained to the potential participant.

Stage 2: After participants have been given as much time as they need, and then consented to take part in the trial, if they wish, the researcher will reiterate that inclusion

in the trial is dependent on the potential participant's performance on a couple of short assessments, and explain what these assessments are: [i] Assessment for fixed flexion contracture of the tendo Achillis; [ii] Step test; and [iii] ability to follow simple commands by imitating actions.

Should a participant not meet the eligibility (inclusion and exclusion) criteria, but indicate continuing interest, then he or she will be followed up no more than three times a week (frequency will depend on speed of recovery) until he or she either (i) withdraws consent, (ii) meets all eligibility criteria, or (iii) reaches the maximum time since stroke for recruitment into the trial.

At all times during the consent process it will be made explicit that the participant is free to refuse to participate in all or any aspect of the trial, at any time and for any reason, without incurring any penalty or affecting their treatment.

Consent will only be taken by researchers or research nurses/therapists who have completed GCP training and have been trained in enhanced communication strategies*, and have a working knowledge of the Mental Capacity Act (2005) and the important aspects of consent, which include: (i) understanding the purpose and nature of the research; (ii) understanding what the research involves, its benefits (or lack of benefits), risks and burdens; (iii) understanding the alternatives to taking part; (iv) able to retain the information long enough to make an effective decision; (v) able to make a free choice; and (vi) capable of making this particular decision at the time it needs to be made.

Some stroke survivors experience difficulty making decisions. Either (or both) language skills or cognition can be impaired (e.g. attention, memory) which can affect the ability to understand information explained to them. They may not be able to understand their situation or the consequences of their stroke. They also may not understand about the risks or benefits of taking part in the trial and therefore they may not be able to make the decision about whether they should participate in the trial or not.

Before approaching a potential participant, the researcher or research nurse/therapist will discuss decision making capacity of individuals with the clinical team. If the clinical team believe that communication impairment is too great to allow an individual to give informed consent, then the potential participant will not be approached. If the clinical team conclusion is that informed consent is possible, albeit with the use of enhanced communication strategies, then the researcher will approach the potential participant and adapt their communication strategies, as required, in relation to the provision of information relating to the trial.

It will be ensured that all potential participants, whether they have a communication impairment or not, are given sufficient time to assimilate information, understand information and ask questions. It will be ensured that the participant understands the information about the trial and potential consequences of being involved in a trial before asking a potential participant to provide written informed consent.

* Various communication strategies will be employed including: verbal, hand gestures, demonstrations, and diagrammatic presentation of information and checking retention and comprehension by asking closed questions, selection of written words or pictures and confirmatory checks such as repeating and rewording verbal communication. These strategies have proved to be useful in other trials even when potential participants do not have a communication impairment.

Simple screening procedures will be used to make sure the potential participants can follow simple commands and undertake a task involving imitating actions. Some participants may have dominant arm weakness and difficulty signing the form, or speech problems. If this is the case an independent witness will be used to sign the consent form, if required, on behalf of the participant. This may be a family member or one of the clinical team working with the patient, but not a member of the trial team. Consent and the means by which consent occurs (i.e. if there is an independent witness) will be documented in the participant's medical notes. Throughout the consent and trial processes it will be made clear to participants that they will be free to withdraw from the study at any stage.

A copy of the approved consent form is available from the NCTU trial team.

7.5.1 Consent or Assent in Ancillary Studies

Not applicable

7.6 Confidentiality

Access to medical records by those outside the direct healthcare team will only take place after consent is obtained, or by research nurses/therapists, where appropriate and local R&D governance deems this acceptable.

Only anonymous data (by means of issuing each participant a unique trial number) will be shared with other organisations. The only identifiable data will be held on purpose built forms and stored in lockable cabinets in lockable rooms. Where it is necessary to share this information between organisations, for example when reporting a safety incident or complaint the paper form will be scanned in and saved in a password protected file (password will be emailed to the PI separately), then provided to the Principal Investigator who will, open the file, print it and destroy the electronic copy. The Trial Manager will then store the paper copy in a lockable cabinet in a lockable room.

Data will be transferred from one secure destination to another secure destination in a secure manner.

Use of personal addresses, postcodes, faxes, emails or telephone numbers will be restricted to the minimum number of people necessary to ensure the efficient and safe running of the trial. For example, telephone numbers will be used by members of the research team to organise appointments and addresses used to collect and return participants for appointments or for the research therapist to visit the participant's residence.

All electronic data will have access controls restricting the data on a need only basis. All data stored on university desktop and laptop computers will be password protected.

Audio recording devices will be used for the planned focus groups. On transcription, pseudonyms will be used to maintain anonymity. When the work is written up for publication all direct quotations will be anonymous.

Time to walk 5 metres will be assessed, and in addition a video recording will provide an opportunity for motion analysis, assessing the quality of the walking (gait) pattern. Use of videos to analyse gait is commonly used within therapy rehabilitation. An attempt will be made at blinding by blanking out the faces.

7.7 Declaration of Interests

The investigators named on the protocol have no financial or other competing interests that impact on their responsibilities towards the scientific value or potential publishing activities associated with the trial.

7.8 Indemnity

Keele University holds insurance to cover participants for injury caused by their participation in the clinical trial. Participants may be able to claim compensation if they can prove that Keele has been negligent. However, as this clinical trial is being carried out in a hospital, the hospital continues to have a duty of care to the participant in the clinical trial. For any time that participants are asked to attend the Keele University campus, this will be covered by the University's indemnity. Keele University and UEA do not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or not.

Participants who sustain injury and wish to make a claim for compensation should do so in writing in the first instance to the Chief Investigator, who will pass the claim to Keele University's insurers, via the Sponsor's office.

7.9 Finance

The MoTaStim-Foot trial is fully funded by the NIHR (CDRF-2014-05-065)

7.10 Archiving

The investigators agree to archive and/or arrange for secure storage of MoTaStim-Foot trial materials and records for a minimum of 5 years after the close of the trial unless otherwise advised by the Sponsor.
On completion of the trial all data will be stored in accordance with the Keele University guidelines for storage of data, (for 5 years from completion of the PhD) and the standard procedure guidelines for clinical trials units for any information stored within the CTU in Norwich. Standard operating procedures will be followed. Data will be held in a locked facility with access limited to appropriate staff e.g. Chief Investigator, supervisors and administration staff.

7.11 Access to Data

Requests for access to trial data will be considered, and approved in writing where appropriate, after formal application to the Chief Investigator in consultation with NCTU.

7.12 Ancillary and Post-trial Care

Not applicable

7.13 Publication Policy

7.13.1 Trial Results

Wide dissemination within two years of the completion of the trial, utilising a variety of arenas from professional forums to general public resources is anticipated, including journal articles and conference presentations.

7.13.2 Authorship

Authorship will in line with the International Committee of Medical Journal Editors guidelines.

7.13.3 Reproducible Research

Not applicable, as this is a feasibility study.

8 Ancillary Studies

9 Protocol Amendments

This is the version 1.0 of the protocol. No prior versions of the protocol exist. [A brief summary of areas of the protocol that have undergone major amendment along with details of the ethics approval dates. Full details of old and new wording should be kept according to the NCTU procedures for tracking amendments.]

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11 Appendices

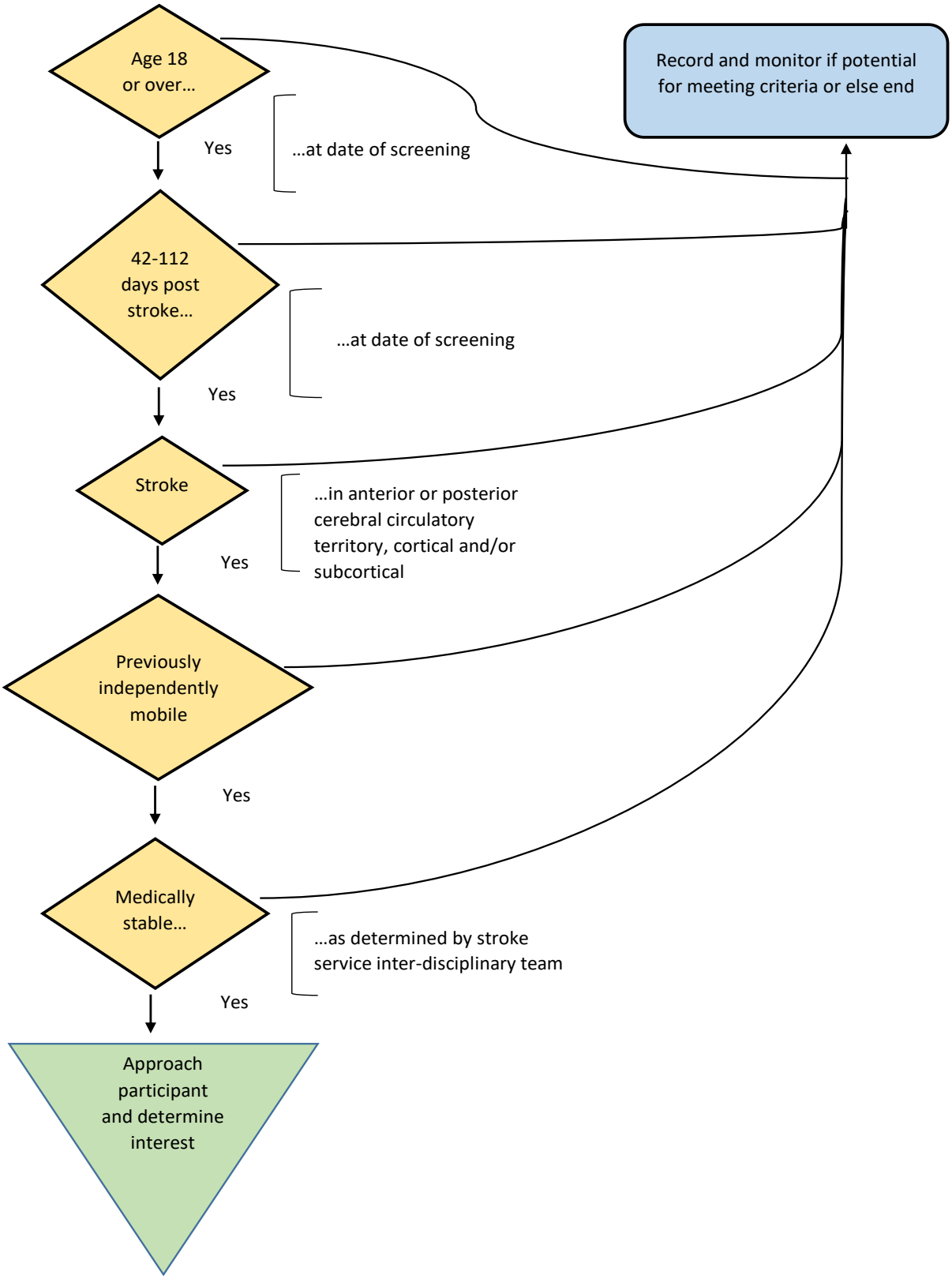

Figure 2: Initial screening (case note review): Sensory stimulation of the foot and ankle post stroke: A feasibility study (MoTaStim-Foot)

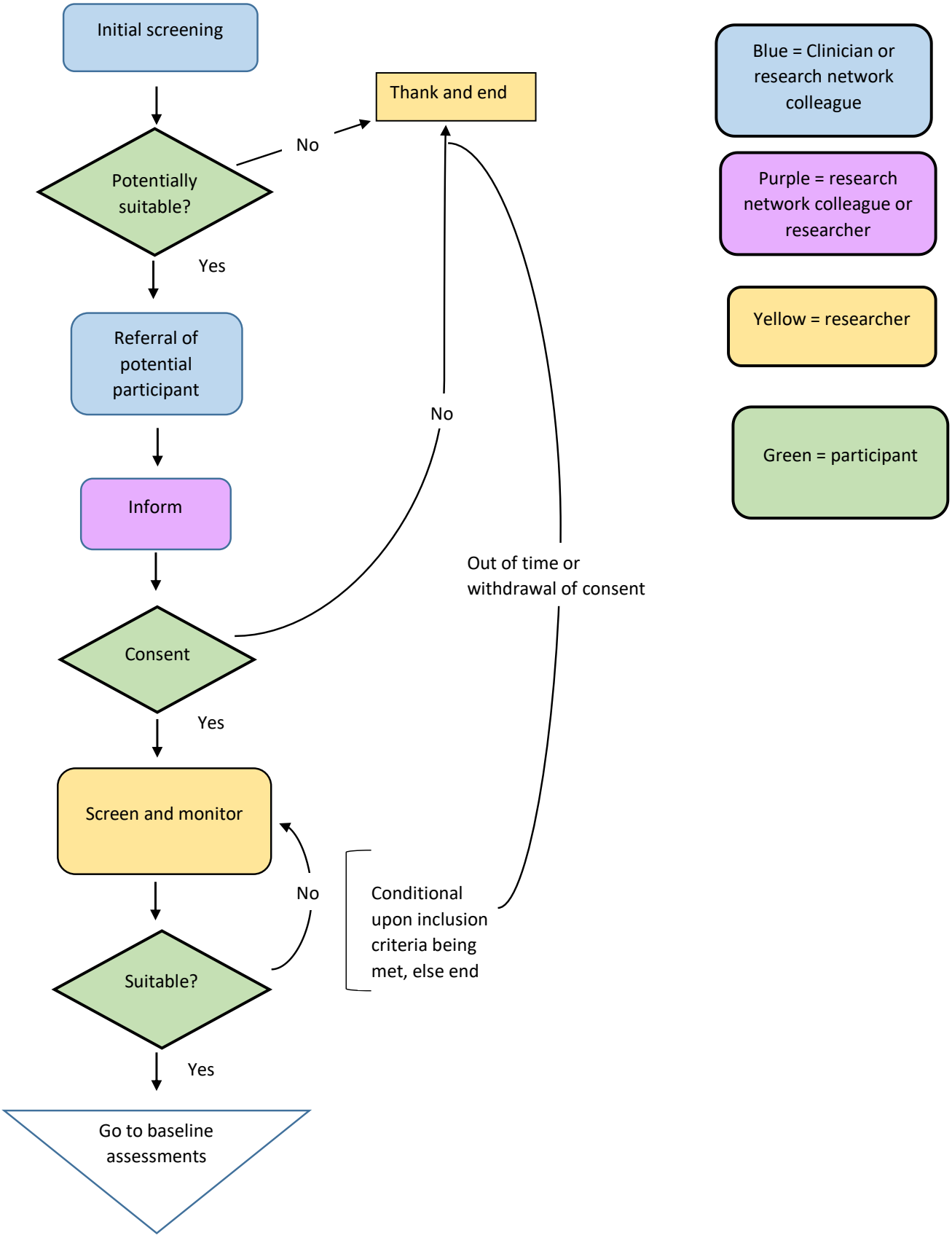

Figure 3: Participant eligibility pathway: Sensory stimulation of the foot and ankle post stroke: A feasibility study (MoTaStim-Foot)

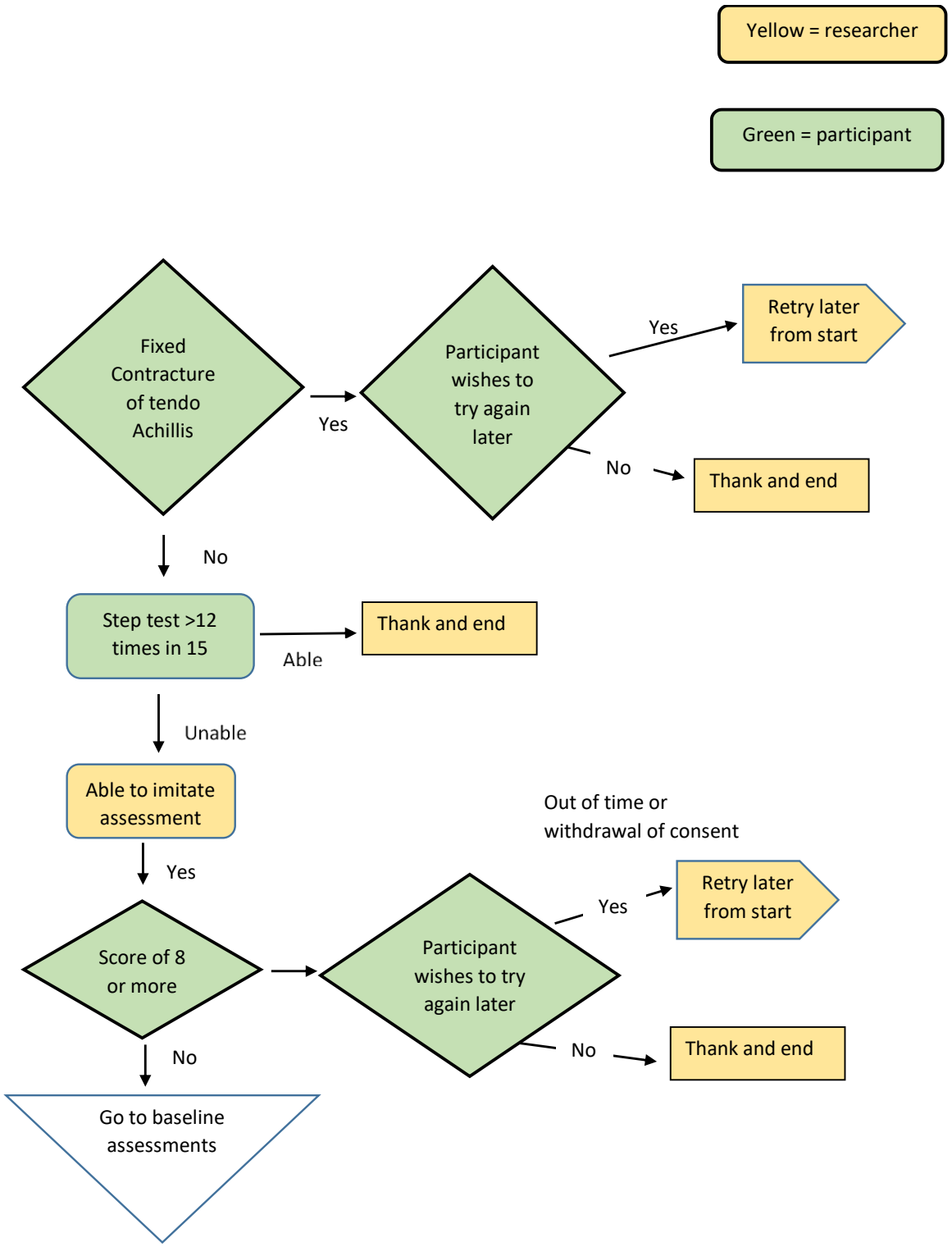

Figure 4: Eligibility Screening: Sensory stimulation of the foot and ankle post stroke: A feasibility study (MoTaStim-Foot)

Appendix 26 Therapy treatment record

Lower LimbTherapy Treatment Record for Patients in MoTaStim-Foot Trial
(instructions for completion are on the back)

Date ..... **Patient ID .....** **Therapist ID .....**

No. Physiotherapists used .....No. Rehab Assistants used .....Estimated duration of session .....

Aims

1. To reduce pain ☐
2. To improve sensory awareness ☐
3. To improve muscle activity/function ☐
4. To improve postural control ☐
5. To improve gross mobility ☐
6. To improve endurance ☐

Gross position of patient during activities used – what about kneeling postures?

1. Supine lying ☐
2. Crook lying ☐
3. Paretic side lying ☐
4. Non-paretic side lying ☐
5. Sitting – 90° ☐
6. Sitting – perch ☐
7. 4 pt kneeling ☐
8. 2 pt kneeling ☐
9. ½ kneeling ☐
10. Standing ☐
11. Walking ☐
12. Other ☐

Equipment used

1. High hold/surface ☐
2. Low hold/surface ☐
3. Hip high hold/surface ☐
4. Perching stool ☐
5. Rolled up towel ☐
6. Gym ball ☐
7. Walking aid ☐
8. Tilt table ☐
9. Standing frame ☐
10. Other ☐

(continued)

Adapted from V.M. Pomeroy et al (2005)

Specific therapy interventions

1. **Soft tissue mobilisation**
   - 1.1 Specific soft tissue mobilisation ☐
   - 1.2 Passive movement ☐
   - 1.3 Muscle stretching ☐
2. **Facilitation of activity in specific muscles**
   - 2.1 Imagery of specific muscle activity ☐
   - 2.2 Specific muscle activation ☐
   - 2.3 Activation of muscle activity during function ☐
3. **Facilitation of isolated (selective) joint movement**
   - 3.1 Imagery specific joint movement ☐
   - 3.2 Active assisted isolated joint movement ☐
   - 3.3 Facilitate specific joint movement during function ☐
4. **Facilitation of coordinated (combined) movement**
   - 4.1. Imagery of coordinated patterns of movement ☐
   - 4.2 Active assisted coordinated patterns of movement ☐
   - 4.3 Facilitate coordinated movement during function ☐
   - 4.4 Facilitate leg/foot activity from another body part ☐
5. **Resistive exercise**
   - 5.1 Resistance from therapist ☐
   - 5.2 Resistance from patient's bodyweight ☐
   - 5.3 Resistance from equipment ☐
6. **Specific sensory (tactile & proprioceptive) input**
   - 6.1 "Hands-on" techniques ☐
   - 6.2 Provision of environmental surface ☐
7. **Splinting techniques**
   - 7.1 Strapping ☐
   - 7.2 Splinting ☐
8. **Function – in lying towards sitting**
   - 8.1 Therapy "hands-on" techniques to r e -ed posture ☐
   - 8.2 Re-ed of funct act through specific mvmnt patterns ☐
   - 8.3 Rolling – functional activity training ☐
   - 8.4. Bridging – functional activity training ☐
   - 8.5 Lying to sitting – functional activity training ☐
   - 8.6 Sitting to lying – functional activity training ☐
   - 8.7 Static sitting balance training ☐
9. **Function – in sitting towards standing**
   - 9.1 Therapy "hands-on" techniques to r e -ed posture ☐
   - 9.2 Re-ed of funct act through specific mvmnt patterns ☐
   - 9.3 Dynamic sitting balance training ☐
   - 9.4 Transfers training ☐
   - 9.5 Sit to standing – functional activity training ☐
   - 9.6 Stand to sit – functional activity training ☐
10. **Function – in standing towards walking**
    - 10.1 Therapy "hands-on" techniques to r e -ed posture ☐
    - 10.2 Re-ed of funct act through specific mvmnt patterns ☐
    - 10.3 Static standing balance training ☐
    - 10.4 Dynamic standing balance training ☐
    - 10.5 One leg stands activities – functional training ☐
11. **Function – walking and onward**
    - 11.1 Therapy "hands-on" techniques to r e -ed posture ☐
    - 11.2 Re-ed of funct act through specific mvmnt patterns ☐
    - 11.3 Overground indoor walking training ☐
    - 11.4 Overground outdoor walking training ☐
    - 11.5 Treadmill walking/bicycle training ☐
    - 11.6 Obstacle negotiation training ☐
    - 11.7 Ascending/descending stair training ☐

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Appendix 27 Participant information sheets (full and summary)

Study Title: Sensory stimulation of the foot and ankle early post stroke:

a feasibility study (MoTaStim-Foot)

Participant Information Sheet

This document is associated with the study protocol version 4.0, dated 23/10/16.

An invitation to you

We invite you to take part in our research study. Before you decide, **we would like you to understand why the research is being done** and **what it would involve for you**. One of our team will go through the information sheet with you and answer any questions you have. This is likely to take approximately 30 minutes.

Please talk to others about the study if you wish.

Part 1 of this information sheet tells you the purpose of this study and what will happen if you take part.

Part 2 of the information sheet gives you more detailed information about the conduct of the study.

Please ask if there is anything that is not clear**. Page 17** has the names and contact details of **people who can help**.

What is the purpose of this study?

Many **people who have had a stroke may experience** difficulty **balancing and walking**. Therapists (Physiotherapists and Occupational Therapists) use many different techniques to try and improve balance and walking after stroke, to help people return to their usual daily activities, for example walking around the house and up and downstairs.

One technique used by therapists when treating people with stroke is **'task specific walking training'.** This involves the person repeating various tasks such as sit-to-stand, stepping onto and off a low step and walking training. This 'task specific walking training' may work better if people are given a therapy beforehand to prepare (stimulate) the nerves in their feet and ankles. The nerves can be stimulated in different ways.

This is a **feasibility study**, a piece of research which is being done before a larger study in order to answer the question "Can this study be done?" We are checking that it is possible to deliver the treatments (the nerve stimulation techniques) and to undertake the necessary measurements prior to doing the large study.
In the future a large study is needed to find out whether stimulating the nerves in the foot and ankle helps people to recover their balance and

walking more quickly, and to find out which nerve stimulation technique works best.

Why have I been invited to take part in the study?

We are looking for people **who have been, or are a patient of the Staffordshire and Stoke-on-Trent Partnership NHS Trust Stroke Services** and who have recently had a stroke and may benefit from therapy to help improve their balance and walking.

You are the sort of person we are looking for. For example, you

- Are aged over 18 years;
- Have had a stroke between 6 and 16 weeks ago (42 and 112 days);
- Have some loss of control of your legs after your stroke;
- Are able to use your stronger arm to imitate the action of another person;
- Were able to walk without help before your stroke.

Do I have to take part?

We will explain the study by going through this information sheet with you. **It is then your decision whether or not you wish to participate**. If you agree to take part, we will then **ask you to sign a consent form.** You are free to **withdraw from the study at any time, without giving a reason.** This would **not affect** the standard of **the care you receive.**

If you are **unable to write or hold a pen** (either **due to the effects of your stroke** or for **another reason**), you can **choose** an **independent person** to sign the consent form, or if you prefer, an independent person will be **found for you, to write on the consent form**. The independent person may be a **member of your medical team**, **a family member** or **friend**. This independent person **cannot decide for you** if you should take part and **you will not be asked or made to do anything you do not want to do**.

What will happen to me if I take part?

If you decide to take part, you will be one of **34 participants** in this research and we will work with you and your medical team to try to make sure that your taking part in the
research suits everyone. We will tell your medical team that you have agreed to take part in this study.

In addition to the routine therapy you may be receiving from your rehabilitation team, you will receive **extra therapy for up to 5 days a week for up to 6 weeks, until you have received 20 treatments**.

Sometimes **we do not know** which way of treating patients is best. To find out, we need to **compare different treatments.** To try to **make sure both groups are the same** to start with, **each participant will be put into a group by chance (randomly) using a computer programme. Therefore, you cannot choose which research therapy (Therapy 1 and Therapy 2) you are given.**

What is the extra therapy?

Therapy 1) **Mobilization and Tactile Stimulation (MTS)** is a form of therapy treatment. It involves handling the foot and ankle, mobilizing and stretching the joints and tissues, preparing the foot for placement on the floor and for functional activities such as sitting to standing, balancing and walking.

MTS patients will receive therapy lasting between 30 minutes and one hour, followed by up to 30 minutes of task specific walking training, **as appropriate for you**. You will receive up to 20 sessions of this treatment.

Therapy 2) **Textured insoles are insoles** which can be inserted in your own shoes and can be moved from shoe to shoe. They have a textured surface, meaning they are covered in bumps. These bumps stimulate the nerves in the sole of the foot. Patients in this group will have a textured insole inserted in the shoe, on the side affected by the stroke, and a smooth insole in the other side, to be worn for as much of the day as possible **(as appropriate for you)**, and during your 30 minutes of task specific walking training. You will receive up to 20 sessions of this task specific walking training.

As is usual practice following a stroke, both groups will also be given **task specific walking training.**

What is task specific walking training?

Task specific walking training is a part of routine therapy practice following a stroke. It involves practising activities such as sitting to standing, standing balance, stepping and walking. 30 minutes of task specific walking training will be given after the MTS treatment or whilst wearing the textured insoles.

What else will I have to do?

- Aside from the additional therapy provided, you will also have **assessments, where we will measure your strength, movement, feeling and blood flow in your lower leg.** The first will take place soon after you agree to take part in the research. Blood flow studies may also be done to assess the immediate effects of MTS treatment on blood flow, before and after a single MTS treatment (if you are allocated to this group). Measures will take place after 5 treatments, 10 treatments and then 15 treatments, with the sixth assessment after all 20 treatments have been delivered and the last assessment one month later, to check if any changes are maintained. **The measurement of blood flow will only be performed if our specialist research therapist and equipment are available. You will be advised if blood flow measures are to be included when you discuss your participation with a member of the research team.**

- All treatment sessions and assessments will either take place in your home, at the Haywood Hospital, Staffordshire and Stoke-on-Trent Partnership NHS Trust, Stoke on Trent or at Keele University rehabilitation research facility.
- During your 20 sessions of treatment you, or someone on your behalf, will be encouraged to complete a simple daily diary, with tick boxes relating to how your affected leg is feeling, or if there are any changes following the treatment or measurements
- After you have finished the 20 sessions you will be invited to attend a focus group with approximately 6-8 other people who have received the same treatment as you (either MTS **OR** textured insoles), this may be several months later. Focus groups are a form of interview where a few people discuss topics with other group members and the researcher and the discussion will be recorded. The purpose of the focus groups is to find out what you thought of the treatments, how your foot feels and whether it has made any difference in your daily activities.

How long does the research last?

The treatment and assessment phase of the research will last for up to 3 months. However, you will only **receive the extra therapy within the first 6 weeks of involvement with the study**. This duration of treatment has been shown to be long enough to assess whether the treatment has any effect. You will also be invited back to take part in a focus group, which will take place within the following twelve months.

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This Diagram is an overview of what taking part in the research would involve:

Assessment 1 Baseline assessment	Assessment 2 After 5 treatments +/-3 days	Assessment 3 After 10 treatments +/-3 days	Assessment 4 After 15 treatments +/-3 days	Assessment 5 After all 20 treatments	Assessment one month later	Focus Group
Walk test, measuring pressure under foot and ankle movement	Receive extra therapy for up to 1½ hours a day - 20					
Test to see how much you can feel with your foot	Test to see how much you can feel with your foot	Test to see how much you can feel with your foot	Test to see how much you can feel with your foot	Walk test, measuring pressure under foot and ankle movement	Walk test, measuring pressure under foot and ankle movement	
A test to assess strength of your leg	A test to assess strength of your leg	A test to assess strength of your leg	A test to assess strength of your leg	Test to see how much you can feel with your foot	Test to see how much you can feel with your foot	
Tests to assess you after your stroke, including your functional activities				A test to assess strength of your leg	A test to assess strength of your leg	
Randomly allocated to receive one of the extra therapies						

[2]Please note the blood flow studies will only be undertaken if the specialist research therapist and equipment are available

What do the assessments involve?

Each assessment uses a number of tests of: **how well you are able to use your weaker leg; how well you feel with your foot;** and **what impact the stroke has had on you**. The assessments will take place soon after agreeing to take part in the research, regularly during your treatment and one month after finishing the treatment. The initial assessments at the start of the study, on completion of the treatments and at one month after completion of the treatments, will last approximately 1 hour and 30 minutes. The regular assessments throughout your treatment (assessments 3, 4 and 5) will only take approximately 20-30 minutes.

The researcher doing some of the assessments, once you have finished your additional therapy, will **not know which group you are** in and cannot influence the findings. This is called "**blinding"**. Please do not tell the assessor which group you are in.

In **more detail** the assessments are:

- **Pressure under the feet.**
  For these assessments you will be asked to put a pressure measuring device in your shoe, which is connected to a computer. You will be asked to walk, providing you are able to walk. This will take approximately 10 minutes.

- **Ankle range of movement**

  You will be asked to walk and the movement in the ankle affected by your stroke will be measured. This will take approximately 10 minutes.

- **Sensory testing**

  The foot affected by your stroke will be tested to see whether and how much you can feel, and compared to the other side. It involves touching the sole of your feet. This will take approximately 5 minutes.

- **Lower Extremity Motricity Index** (a quick test of your leg strength in sitting)

  This will measure the strength of your hips, knees and ankles. This will take approximately 5 minutes.

- **5 metre walk test**

  If you are able to walk, you will be asked to walk 5 metres (m) as quickly as you feel able. If you are unable to walk you will not be expected to undertake this assessment. A video recording will be made of your 5m walk. This will take approximately 10 minutes.

- **Blood flow studies**

The flow of blood in your legs may be assessed at the beginning of the study, after all 20 interventions and at one month follow up taking approximately 25 minutes to complete. If you are in the MTS therapy group, this may also be done before and after one of your first ten

treatments (to assess the immediate effects of the treatment). Firstly, your resting blood pressure will be taken (and your height and weight, if not available in your medical notes). An ultrasound machine will be used on the surface of your skin. It is important to examine your blood flow at approximately the same time each day, on each occasion. A record of your age, height, weight and resting blood pressure will be required for this assessment. If having blood flow studies you will also be asked to:

- Not drink caffeinated drinks e.g. coffee, tea and coke, and also alcohol or smoking for 6 hours prior to assessment
- Not take medications (if feasible and safe) for 4 hours prior to assessment
- Avoid physical activity for 2 hours prior to assessment
- Avoid high fat meals 2 hours prior to assessment

- **Modified Rivermead Mobility Index**

  This is a specific test which looks at what you are able to do. It will assess your ability to do some functional activities e.g. rolling over in bed, sitting, and standing. This will take approximately 17 minutes.

- **Functional Ambulation Category**

  This will assess your walking ability and how much help you require. It will be undertaken by the researcher – you will not have to do anything. The researcher will just assess your ability to walk following the 5m test. This will not take any extra time for you, it will just take the researcher 2 minutes to complete.

- **National Institutes of Health Stroke Scale**
  This is an assessment of how your stroke has affected you and will only be completed once, at the beginning of the study. This will take approximately 15 minutes.

Focus Groups

Within twelve months of you completing your 20 sessions of treatment you will be invited to attend a focus group (lasting no longer than 1½ hours). You will be given the opportunity to tell us about your experiences (physical and emotional) as a participant in the study. The focus group will be audio taped.

Expenses and payments

We cannot pay you to take part in the research but **will arrange and pay for any taxi journeys** you may need, to take you to and from the assessments, or to go for extra therapy. It will not cost you money to take part in the research.

Will I stop getting any treatment?

If you take part in the research, **you will still receive all the treatment that you would receive if you did not take part**.

What are the possible disadvantages and risk of taking part?

There is a **small risk** that you may experience some discomfort caused by working muscles or mobilization techniques during the extra therapy,

or from pressure from the textured insoles. If you tell us you are in discomfort we can stop the extra therapy that day. You will be able to choose how long to wear the textured insoles for, so if they are uncomfortable you can just take them out of your shoes.

Blood flow will be assessed by applying a gel to the skin of your leg / foot and using an ultrasound machine to measure the flow of blood in your vessels. There is, to date, no evidence that diagnostic ultrasound has produced any harm to humans and it is commonly used in pregnant women.

Before all of the **assessments** we will **ask you questions to ensure it is safe for you to continue.** If we think that it is not safe for you to proceed then you will not have that particular assessment.

We will make every effort to minimise any risk to you as we follow a range of safety standards and best practice policies.

What are the possible benefits of taking part in the study?

All participants will undergo a **comprehensive assessment and** will receive extra therapy. However, we do not know if this will lead to health benefits. The information we get from the study may help improve the treatment for other people in the future who have survived a stroke.

What happens when the study stops?

When the study stops, you **will return to the usual care** provided by the local stroke team. Whether or not you take part in this research will make no difference to either the type or amount of therapy you may receive from the clinical team

What if there is a problem?

Any **complaint** about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information on this is given in part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1.

If the information in Part 1 interests you and you are considering taking part, please read the information in Part 2 before making any decision.

Part 2

What happens if new information becomes available?

Very few studies have been done about Mobilization and Tactile Stimulation (MTS) or the use of textured insoles after stroke. But, sometimes we get new information. If this happens, your researcher will tell you and discuss whether you should continue in the study. If you decide not to carry on, your usual routine care would still continue. If you decide to continue with the study, we may record the fact that we discussed the new information with you.

What happens if I do not want to carry on in the study?

You may withdraw at any time without giving a reason.
Withdrawing from the study will not affect your treatment now or at any time in the future by any healthcare team. If you withdraw from the study, any information already collected may still be used.

What if there is a problem?

If you have a **concern** about this study, you should ask to speak to your researcher who will answer any questions or find someone who can. Your researcher's contact details can be found on page 18.

If you remain unhappy or wish to complain formally, you can do this through the **NHS Complaints Procedure**. Details can be obtained from: http://www.nhs.uk/choiceintheNHS/Rightsandpledges/complaints/Pages/NHScomplaints.aspx. Alternatively, you could call the Stoke-on-Trent,

North Staffordshire and South Staffordshire Team Patient Advice and Liaison Services (PALS) on 0800 783 2865.

What if I am harmed?

If something does go wrong and you are harmed during the research study there are **no special compensation arrangements**.

If you are harmed due to someone's negligence, then you may have grounds for legal action for compensation against this, but you may have to pay your own legal costs.

Will anyone else know that I am in this study?

We will inform your medical team that you are taking part in the study.

If we are concerned at any time about your health during your participation in this study **we will report this to someone** in your medical team.

We will not inform your GP directly that you are taking part in this study, however, if there are any concerns about your health we will report this issue, with your permission to your consultant, your GP, or one of the clinicians involved in your care.

Who is organising the research?

This research is funded by the National Institute for Health Research (NIHR) as part of a Clinical Academic Doctoral Programme. The clinical centre is Staffordshire and Stoke-on-Trent Partnership Trust. The

Research Team at Keele University, with support from Norwich Clinical Trials Unit are responsible for **organising** and **running** the study, led by **Alison Aries, supervised by Dr Susan Hunter, both from the School of Health and Rehabilitation, Keele University.**

Will my taking part in the study be kept confidential?

The research team will be able to access information about you that is relevant to the study, from your medical notes. **All information which is collected about you** during the course of the research will be **kept strictly confidential**, and except for the consent form **information about you will have your name removed,** so that you cannot be recognised. Your face will be blanked out if video recordings are used in the presentation of the research findings, to try to ensure anonymity. Pseudonyms (false names) will be used when reporting findings from the focus groups.

The data will only **be accessed by authorised persons** within the **Research Team**, **Research and Development Office of the NHS Trusts and trial Sponsor representatives,** who ensure the quality of the research carried out. Information may include details such as your **date of birth** and the **date and diagnosis of your stroke.** Personal information such as your **address** will be required to allow us to send you information about the results when the study is finished and visit you at home during the research, if this is appropriate. **This information along with your NHS number may be collected from your medical notes.**

You will be given a **study number** for the purpose of **collecting and analysing data**. This means you will remain anonymous.

How will my information be stored?

Data will be **stored securely** in **research office**s at Keele University and Norwich Clinical Trials Unit during the study and for **1 year** after the study. On completion of the study all data will be stored in accordance with the Keele University guidelines for storage of data, (for 5 years from completion of the feasibility study). All procedures for **handling, processing, storage** and **destruction of data** are compliant with the Data Protection Act 1998. All **computer files** will either be stored in a **secure user authenticated area or encrypted** to protect them from unauthorised access**. All the computer files will be anonymous.**

What will happen to the results of the research study?

The results of the study will be **analysed** and used to inform the design of a future, larger study about MTS and textured insoles.

The results will be **published in academic journals** and shared with colleagues at conferences but **individual participants will not be identifiable**. In some cases, information e.g. from the daily diaries may be presented in an anonymised case study format to show the participant's journey through the trial. If this is the case for you the researcher will discuss this with you and offer you the opportunity to read the information and verify that you think it is accurate. Participants can be sent a report of

the study when it has been completed. Please contact the researcher Alison Aries to request this.

Who has reviewed the study?

The study has been reviewed by the **National Institute for Health Research.**

The study will be monitored by a Trial Management Group who will put your safety above everything else.

Further Information and Contact Details

Alison Aries

Chief Investigator / Research Therapist

a.m.aries@keele.ac.uk

OR

Dr Susan Hunter, Supervisor

s.m.hunter@keele.ac.uk

All of the research therapists can be contacted by post:

School of Health and Rehabilitation, Keele University, Keele, Staffordshire, ST5 5BG.

Independent Contact Details:

If you wish to discuss this study with **someone who is not involved** in the research then you can contact the Stoke-on-Trent, North Staffordshire and South Staffordshire Team Patient Advice and Liaison Services (PALS) on0800 783 2865.

Thank you for taking the time to read this information. If you choose to participate, you will keep a copy of this participant information sheet and the completed consent form.

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Sensory stimulation of the foot and ankle early post stroke: a feasibility study (MoTaStim-Foot)

Participant Information Sheet – SUMMARY SHEET

This document is associated with the study protocol version 4.0 dated 23/10/2016 and the full participant information sheet (Version 1.4).

What is the purpose of this study?

Many **people who have had a stroke may experience** difficulty **balancing and walking**. This is a feasibility study, which is being done before doing a larger study. The study will look at stimulation of the foot (by a therapist massaging and stretching, a treatment called **Mobilization and Tactile Stimulation** [Therapy 1], or wearing a **textured insole**, which is covered in small bumps [Therapy 2]).

In total 34 people will take part in this trial. We are offering you a chance to be included. In addition to your routine therapy you would receive one of the above therapies plus **'task specific walking training'** (20 sessions in total over 4-6 weeks). You will be asked to keep a short, simple diary of your experiences and how your leg feels and invited to a meeting (focus group) afterwards. There will also be **assessments,** to measure the **strength, movement, feeling** in your lower leg. Blood flow measures may also be taken along with your blood pressure, height and weight. You would be involved for a maximum of four months.

Why have I been invited to take part in the study?

We are inviting you to take part because we are looking for people who have recently had a stroke. We want to find out if therapy can change balance and walking.

Do I have to take part?

We will explain the study to you, going through the full information sheet, which will take approximately 30 minutes. **It is then your decision whether you wish to participate** in this study. If you agree to take part, we will then **ask you to sign a consent form.** You are free to **withdraw from the study at any time, without giving a reason.** This would **not affect** the standard of **the care you receive.**

Further Information and Contact Details

Alison Aries
Chief Investigator / Research Therapist
a.m.aries@keele.ac.uk **OR**
Dr Susan Hunter, Supervisor s.m.hunter@keele.ac.uk

All of the research therapists can be contacted by post:

School of Health and Rehabilitation, Keele University, Keele, Staffordshire, ST5 5BG.

Independent Contact Details:

If you wish to discuss this study with **someone who is not involved** in the research then you can contact the Stoke-on-Trent, North Staffordshire and South Staffordshire Team Patient Advice and Liaison Services (PALS) on 0800 783 2865.

Thank you for taking the time to read this summary information sheet.

Appendix 28 Emails relating to the summary and full participant information sheets

Date: Fri, 7 Aug 2015 21:30:30 +0100
Subject: Re: Participant Information Sheet (PIS)
From: a.m.aries@keele.ac.uk
To
CC: a.m.aries@keele.ac.uk

Dear Alan
Thank you - that is absolutely perfect feedback but it is an expectation that everything is explained fully to the participant so they can make an informed choice as to whether they wish to take part or not. I probably do not have a lot of choice about that - sorry!
Many thanks once again.
Ali

Alison Aries MSc MCSP
National Institute for Health (NIHR) Research Fellow
School of Health and Rehabilitation
Keele University
Staffordshire
ST5 5BG
01782 734418

On 7 August 2015 at 20:24, alan > wrote:
hello Alison, thank you for you e mail and the information sheets,which I am having a look through, and will get back to you asap, while I am on though, may I ask you a question regarding the info sheets, there are 20 sheets in total and as you say will take approx. 30 mins to explain to participants, do you think it is a lot for a person who has had a stroke maybe 6 or so months previous to take in, please do not think I am being too forward in thinking this but I know from past experience the situation a stroke survivor is in for a long time, and obviously you and mel know far far better than I do, please correct me if you think I am being too much,and please excuse if I am speaking out of turn, meanwhile I will continue to read the sheets, our best wishes as always

---

Date: Wed, 5 Aug 2015 23:03:23 +0100
Subject: Participant Information Sheet (PIS)
From: a.m.aries@keele.ac.uk
To:
CC: a.m.aries@keele.ac.uk

Dear
I have made a few changes to the participant information sheet (easy to see because they are all in red!).
The reason for the changes are:
1)Some of the wording was too similar / identical to another study which I based the PIS on.
2) We will also be looking at blood flow so I have added some information about this too.
I would be grateful if you have the time to look at it and let me know if you think it is OK or not.
Many thanks
Ali

Re: Summary participant information sheet.

01/12/2015

Dear Alison

My apologies for the delay in replying to your e-mails but unfortunately it is just over a week since my last discharge from hospital. I have, however, found time to read both PIS docs. I found them both to be excellent pieces of work & totally fit for purpose. My congratulations on a job well done!!!!

From: Alison Aries <a.m.aries@keele.ac.uk>
To: >
Cc: Alison Aries <a.m.aries@keele.ac.uk>
Sent: Thursday, 26 November 2015, 14:25
Subject: Summary participant information sheet.

Dear

Please find attached a summary participant information sheet (PIS). In view of the length of the other PIS I felt it may be useful to have an introductory sheet. It would have to be used **in addition** to the other PIS (because of the required information). I would be very interested in hearing your opinions on this summary sheet too. It is literally one sheet (front and back). Please let me know if you require a hard copy of this.

Many thanks in anticipation.

Best wishes

Alison

Appendix 29

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CONSENT FORM

Study Title: Mobilization and sensory stimulation of the foot and ankle post stroke: a feasibility study

Name of researcher: _____

Name of participant: _____

NB If the potential participant is unable to write, please find an independent witness who may complete this form as verbal consent is given by the potential participant. The independent witness should read each of the five items to the potential participant and if the participant agrees, the independent witness should initial each of the boxes with his/her own initials.

The purpose of the independent witness is to physically complete this consent form on the instruction of the participant in the instance that the participant cannot do so for himself or herself due to physical inability to hold and or use a pen, or in the instance in which attempting to do so would or appears to cause distress to the participant. The independent witness cannot provide consent on behalf of a participant.

An independent witness must:

- *Not be a part of the research team*
- *Not be managed by a member of the research team*

One original copy of this form should be completed. The original should be stored in the investigator site file. Two photocopies should be made of the original, one copy for the participant and one copy to be placed in the participant's medical notes.

Funded by NIHR

This document should be used together with the Participant Information Sheet Version 1.4 dated 23/10/16

	Please **initial** each box below
1. I confirm that **I have read and understood the Participant Information Sheet dated 23/10/16 (Version 1.4)** for the above study. I have had the opportunity to consider the information and ask questions, and have had these answered satisfactorily.	
2. I understand that **my participation is voluntary** and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3. I understand that relevant sections of **my medical notes and data collected during the study may be looked at** by individuals for the research team, from regulatory authorities, Norwich Clinical Trials Unit or from the NHS Trust to allow trial related monitoring, including audits, REC review and regulatory inspections, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	
5. I consent to the focus groups being audio-taped.	
6. If I choose to record daily diary information by audio clip, I give permission for the transcribed information to be used to support other research in the future, and that it may be shared anonymously with other researchers	
7. I consent for my walking to be videoed.	
8. I agree that **my consultant, nurses and therapists** in the clinical team can be **informed of my participation** in the study. I agree for them to be **told of any concerns** the research team may **have about my health** during the study.	
9. I agree to keep the issues discussed within the focus group confidential, in particular to avoid identifying any of the participants involved. I understand that all data collected about me during this study will be **anonymised** before it is submitted for publication.	
10. I agree to the use of any quotes.	
11. **I agree to take part** in the above study	

Please ask either the participant or, if appropriate, the independent witness to sign, print their name and date this form in long format below. Please then countersign, print and date in long format in the spaces below.

Signed (participant): _____

Print name (participant): _____

Date: (DD-MM-YYYY) _ _. _ _ . _ _ _ _

or

Signed (independent witness):

_____

Print name (independent witness):

_____

Date: (DD-MM-YYYY) _ _. _ _ . _ _ _ _

And

Signed (researcher): _____

Print name (researcher): _____

Date: (DD-MM-YYYY) _ _. _ _ . _ _ _ _

Appendix 30 National Institutes for Health Stroke Scale (NIHSS)

N I H
STROKE
SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

Time: ___ ___:___ ___ [ ]am [ ]pm

Person Administering Scale _____

Administer stroke scale items in the order listed. Record performance in each category after each subscale exam. Do not go back and change scores. Follow directions provided for each exam technique. Scores should reflect what the patient does, not what the clinician thinks the patient can do. The clinician should record answers while administering the exam and work quickly. Except where indicated, the patient should not be coached (i.e., repeated requests to patient to make a special effort).

Instructions	Scale Definition	Score
1a. Level of Consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = **Alert**; keenly responsive. 1 = **Not alert**; but arousable by minor stimulation to obey, answer, or respond. 2 = **Not alert**; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.	_____
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0 = **Answers** both questions correctly. 1 = **Answers** one question correctly. 2 = **Answers** neither question correctly.	_____
1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.	0 = **Performs** both tasks correctly. 1 = **Performs** one task correctly. 2 = **Performs** neither task correctly.	_____
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 = **Normal.** 1 = **Partial gaze palsy**; gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = **Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.	0 = **No visual loss.** 1 = **Partial hemianopia.** 2 = **Complete hemianopia.** 3 = **Bilateral hemianopia** (blind including cortical blindness).	_____
4. Facial Palsy: Ask – or use pantomime to encourage – the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barriers obscure the face, these should be removed to the extent possible.	0 = **Normal** symmetrical movements. 1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling). 2 = **Partial paralysis** (total or near-total paralysis of lower face). 3 = **Complete paralysis** of one or both sides (absence of facial movement in the upper and lower face).	_____
5. Motor Arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** limb holds 90 (or 45) degrees for full 10 seconds. 1 = **Drift;** limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = **Some effort against gravity;** limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = **No effort against gravity;** limb falls. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **5a. Left Arm** **5b. Right Arm**	_____ _____
6. Motor Leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** leg holds 30-degree position for full 5 seconds. 1 = **Drift;** leg falls by the end of the 5-second period but does not hit bed. 2 = **Some effort against gravity;** leg falls to bed by 5 seconds, but has some effort against gravity. 3 = **No effort against gravity;** leg falls to bed immediately. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **6a. Left Leg** **6b. Right Leg**	_____

Rev 10/1/2003

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.	0 = **Absent.** 1 = **Present in one limb.** 2 = **Present in two limbs.** UN = **Amputation** or joint fusion, explain: _____	_____
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.	0 = **Normal**; no sensory loss. 1 = **Mild-to-moderate sensory loss**; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = **Severe to total sensory loss**; patient is not aware of being touched in the face, arm, and leg.	_____
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 = **No aphasia**; normal. 1 = **Mild-to-moderate aphasia**; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = **Severe aphasia**; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = **Mute, global aphasia**; no usable speech or auditory comprehension.	_____
10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested.	0 = **Normal.** 1 = **Mild-to-moderate dysarthria**; patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = **Severe dysarthria**; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. UN = **Intubated** or other physical barrier, explain:_____	_____

Rev 10/1/2003

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

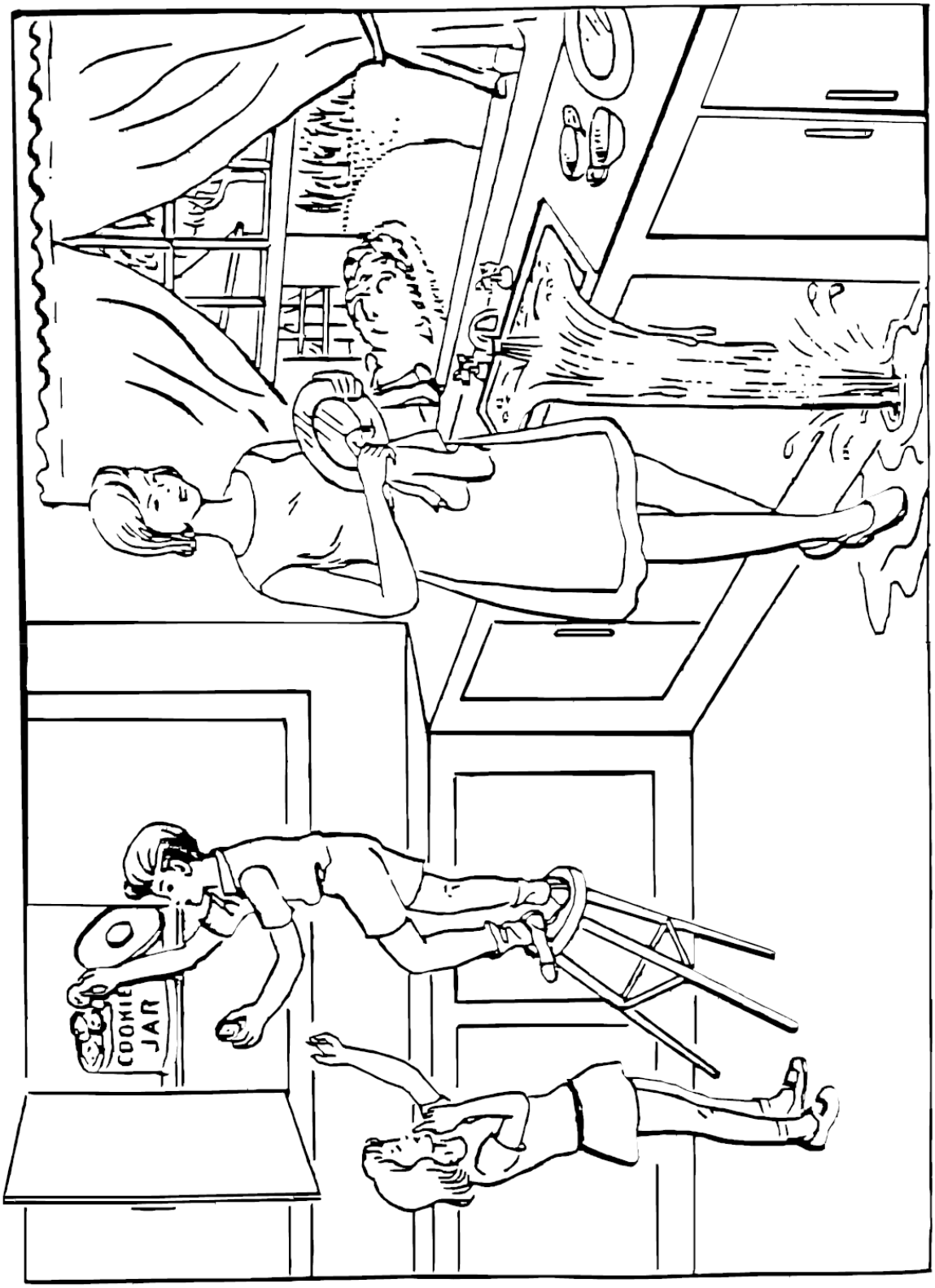
Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	0 = **No abnormality.** 1 = **Visual, tactile, auditory, spatial, or personal inattention** or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = **Profound hemi-inattention or extinction to more than one modality**; does not recognize own hand or orients to only one side of space.	_____

_____

_____


COOKIE
JAR

You know how.

Down to earth.

I got home from work.

Near the table in the dining room.

They heard him speak on the radio last night.

MAMA

TIP – TOP

FIFTY – FIFTY

THANKS

HUCKLEBERRY

BASEBALL PLAYER

Appendix 31 Functional Ambulation Classification (FAC)

Massachusetts General Hospital
Functional Ambulation Classification

General Information:

- Categorizes patients according to basic motor skills necessary for functional ambulation
- Does not assess endurance

Instructions:

- Use the definitions below to classify the patient to a category
- Patients should be rated at their most independent level (supervision or physical assistance required to ambulate)
    - As an example, the patient is able to ambulate independently with a walker on level surfaces but requires can ambulate with crutches with supervision, the patient should receive the rating of "5" (ambulator—independent, level surfaces only).
- Only rate patients on the ability to ambulate.
- The ability to rise from sitting to standing should not be included

Definitions:

- Ambulation: Individual is able to walk at least 10 feet outside the parallel bars with supervision or physical assistance from only one person. Mechanical assistance from any device or ambulation aid (except parallel bars) may be used.
    - Level surface: Tile, rugs, pavement
    - Non-level surface: Grass, gravel, dirt, snow, ice
    - Stairs: Up and down at least seven steps with rail
    - Incline: Up and down 5-ft (1.52-m) incline of 30 degrees or greater

- Supervision: the patient is able to ambulate without manual contact from another person but requires stand-by guarding of one person for safety. This may be the result of poor judgment, questionable cardiac status, or verbal cues required to complete the task.

- Physical assistance level –I: manual contact is required from one person during ambulation to prevent falling. Manual contact may be continuous or intermittent light touch to assist balance or coordination.

- Physical assistance Level –II: manual contact of one person is required during ambulation to prevent falling. Manual contact may be continuous and necessary to support body weight and/or to maintain balance or assist coordination.

Downloaded from www.rehabmeasures.org

- Independent: ambulation is independent and without supervision or physical assistance from another person. The patient may utilize assistive devices (except parallel bars), orthoses, and prostheses.

Categories (Holden et al, 1994):

FAC Level	Ambulation Description	Definition
1	Nonfunctional	• Unable to ambulate • Ambulates only in parallel bars • Requires supervision or physical assistance from > 1 person
2	Dependent, Level II	• Requires manual contact of one person during ambulation on level surfaces • Manual contact is continuous and necessary to support body weight and/or to maintain balance or assist coordination
3	Dependent, Level I	• Requires manual contact of one person during ambulation on level surfaces • Manual contact is continuous or intermittent light touch to assist balance or coordination
4	Dependent, Supervision	• Ambulation occurs on level surfaces without manual contact of another person • Requires stand-by guarding of one person because of poor judgment, questionable cardiac status, or the need for verbal cuing to complete the task
5	Independent, Level Surfaces Only	• Ambulate is independent on level surfaces • Requires supervision/physical assistance to negotiate stairs, inclines, or unlevel surfaces.
6	Independent, Level and Non-Level Surfaces	• Ambulation is independent on unlevel and level surfaces, stairs, and inclines.

Reference: (Holden, Gill et al. 1984)

Holden, M. K., Gill K.M., et al. (1984). "Clinical gait assessment in the neurologically impaired. Reliability and meaningfulness." Phys Ther **64**(1): 35-40.

Downloaded from www.rehabmeasures.org
Test instructions provided courtesy of Maureen Holden PT, PhD

Appendix 32 TI daily diary

Week Commencing: _ _ _ _ . _ _ _ _ (DD-MM-YYYY)
Screening Number: _____

Site Code: _____
Participant number: _____

Staffordshire and Stoke on Trent Partnership NHS Trust

DAILY DIARY

Study Title: Sensory stimulation of the foot and ankle early post stroke: a feasibility study (MoTaStim –Foot)

Name of researcher: _____ Name of participant: _____

WEEK BEGINNING:	Sun	Mon	Tue	Wed	Thur	Fri	Sat
1. The Feeling within your foot: (Please tick any that apply to you)							
1a)Today my foot feels cold							
1b)Today my foot feels warm							
1c) Today my foot felt sensitive							
1d) Today my foot did not feel sensitive							
1e) There is no change in my foot at all →							
1f) Today I am unable to feel as much in my foot ↓							
1g) Today I can feel my foot more ↑							
2. Wearing the textured insoles (TIs)							
2a) Today I have not worn my TIs							
2a) Today I have worn my TIs for less than one hour							
2b) Today I have worn my TIs for between 2-4 hours							
2c) Today I have worn my TIs for more than 5 hours							

Week Commencing: _ _ _ _ - _ _ _ _ (DD-MM-YYYY)
Screening Number: _____

Site Code: _____
Participant number: _____

3. About your treatments: (Please tick any that apply to you)	Sun	Mon	Tue	Wed	Thur	Fri	Sat
3a) Today wearing my TIs was uncomfortable							
3b) Today wearing my TIs was **NOT** uncomfortable							
3c) Today the task specific walking training was uncomfortable							
3d) Today the task specific walking training was **NOT** uncomfortable							
3e) Today the outcome measurements were uncomfortable							
3f) Today the outcome measurements were **NOT** uncomfortable							
Additional comments:							

Appendix 33 MTS daily diary

Week commencing: _ _ _ _ . _ _ _ _ (DD-MM-YYYY)
Screening Number: _____

Site Code: _____
Participant Number: _____

Staffordshire and Stoke on Trent Partnership NHS Trust

DAILY DIARY

Study Title: Mobilization and sensory stimulation of the foot and ankle post stroke: a feasibility study

Name of researcher: _____ Name of participant: _____

WEEK BEGINNING: (Please tick any that apply to you)	Sun	Mon	Tue	Wed	Thur	Fri	Sat
1. **The Feeling within your foot:**							
1a)Today my foot feels cold							
1b)Today my foot feels warm							
1c) Today my foot felt sensitive							
1d) Today my foot did not feel sensitive							
1e) There is no change in my foot at all →							
1f) Today I am unable to feel as much in my foot ↓							
1g) Today I can feel my foot more ↑							

Week commencing: _ _ _ _ . _ _ _ _ (DD-MM-YYYY)
Screening Number: _____

Site Code: _____
Participant Number: _____

2. About your treatments: (Please tick any that apply to you)	Sun	Mon	Tue	Wed	Thur	Fri	Sat
2a) Today the mobilization and tactile stimulation (MTS) was uncomfortable							
2b) The discomfort lasted for a long time e.g. several hours							
2c) The discomfort did not last long e.g. less than one hour							
2d) Today the mobilization and tactile stimulation (MTS) was **NOT** uncomfortable							
2e) Today the task specific walking training was uncomfortable							
2d) Today the task specific walking training was **NOT** uncomfortable							
2e) Today the outcome measurements were uncomfortable							
2f) Today the outcome measurements were **NOT** uncomfortable							
Additional comments:							

Appendix 34 SWMs protocol for testing

Protocol for the Semmes Weinstein Monofilament (SWM) testing

The Semmes Weinstein Monofilament (SWM) testing allows for the assessment of light touch sensation. The calibrated 20-piece SWM kit (Patterson Medical) should be used. Four points of the plantar surface of the foot should be tested:

1. Under the heel, in the midline of the foot, 1 cm forwards of the back of the heel.
2. Under the pad of the hallux
3. Under the 1st Metatarsal joint
4. Under the 5th metatarsal head

Commence by explaining the testing procedure to the participant and letting them feel the 2.83 SWM, on the hand (thenar eminence), of the side which is **less affected** by their stroke.

Then proceed to test each point in turn using the following procedure:
When applying the stimulation, you should take 1.5 seconds to apply the SWM, leave it in touch with the skin for 1.5 seconds and then remove for 1.5 seconds (one touch – do not repeat). The instruction to the participant is 'tell me when you can feel something'. NB Filaments must be applied at a 90-degree angle to the skin which is being tested. [13]

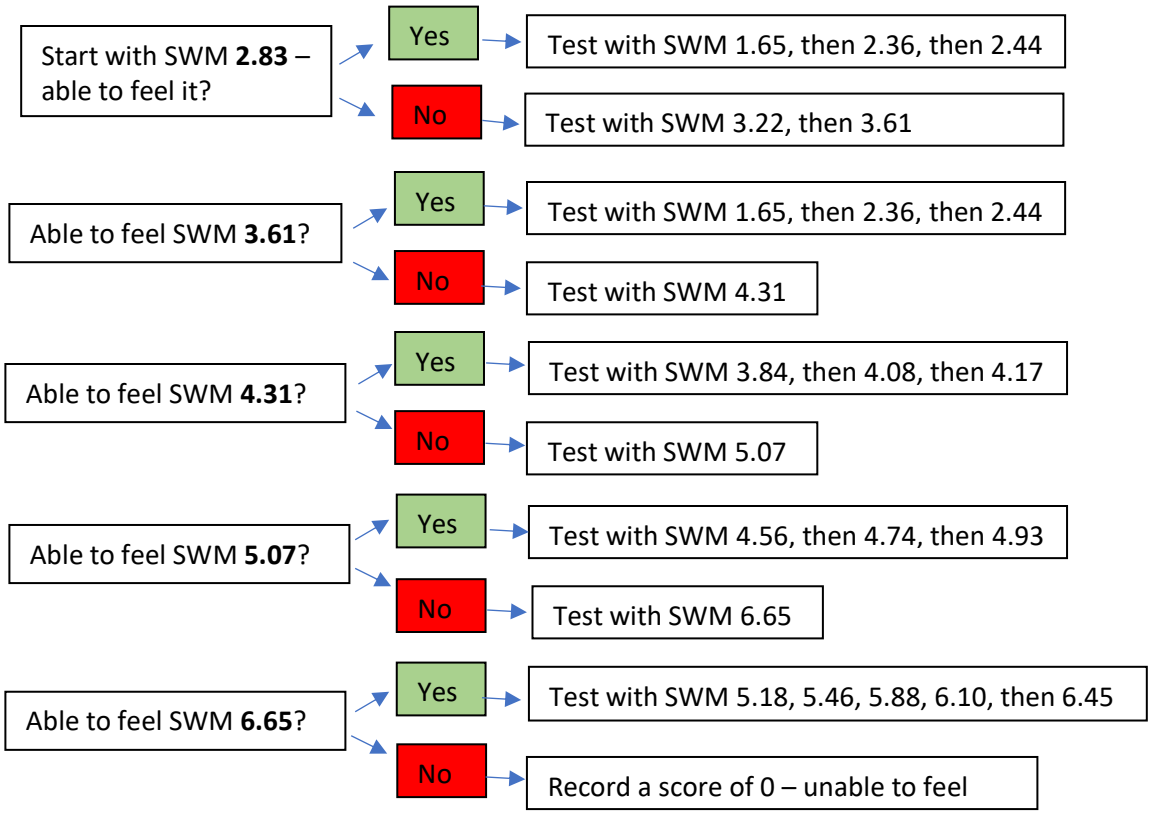
Touch-Test Sensory Evaluator

	SWM Code	Target Force (grams)	Threshold
1	1.65	0.008	**Normal plantar threshold**
2	2.36	0.02	
3	2.44	0.04	
4	2.83	0.07	
5	3.22	0.16	
6	3.61	0.4	
7	3.84	0.6	**Diminished light touch**
8	4.08	1	
9	4.17	1.4	
10	4.31	2	
11	4.56	4	
12	4.74	6	

[13] Adapted from 2000 North Coast Medical Inc. Morgan Hill

13	4.93	8	**Diminished protective sensation**
14	5.07	10	**Loss of protective sensation**
15	5.18	15	
16	5.46	26	
17	5.88	60	
18	6.10	100	
19	6.45	180	
20	6.65	300	**Deep pressure sensation**

Commencing at SWM 2.83 (which is in the middle of the normal threshold for plantar threshold normative touch-pressure data). Please follow the flow chart below:



The decision to apply a thinner or thicker diameter SWM is determined by the subject's positive or negative detection of the stimulus. A positive detection is observed when

subjects indicate verbally that they feel the stimulus within 1 second of the stimulus being removed, by saying “yes.” If subjects do not indicate they feel the stimulus or have a delayed response (saying “yes” greater than 1 second following removal of the stimulus), it should be considered a negative detection. A positive detection should lead to a thinner diameter being tested. A negative detection (i.e., no verbal response) should lead to a thicker diameter SWM being tested. Time between stimuli should be varied so the subject does not preempt the application pattern.
The SWM perceived most consistently should be recorded as the sensation threshold. Thicker diameter SWMs involve a greater force and are associated with decreased light touch sensitivity.

NB For baseline and end of intervention both sides should be assessed with the SWMs, however, for all other assessments just the affected foot should be assessed.

Appendix 35 LEMI protocol

Lower Extremity Motricity Index (LEMI) Protocol

Motricity Index (MI)

The LEMI is a valid and reliable measure used to determine the strength of the paretic limb (leg). Scores range from 0 (no activity) to 33 (maximum muscle force) for each dimension.

The procedure described by Fayazi (2011) should be followed:

Participants should sit in a chair with a back support.

Dorsiflexion: should be assessed from a position of relaxed plantar flexion. The assessor should place a hand on the forefoot. The participant should be asked to dorsiflex the foot (as if standing on your heels'), and the assessor should resist the contraction of tibialis anterior and palpate for muscle activity.

Knee extension: should be tested from a position where the knee is bent at 90° flexion with the foot unsupported (if possible). The assessor should ask the participant to extend the knee. During this movement the assessor should monitor the contraction of the quadriceps with the other hand. The score should be recorded (see below).

Hip flexion: should be tested with the hip joint with a 90 ° bent. Instruction to the participant is 'to bring the knee towards the chin, assessor should monitor the contraction of hip flexors (iliopsoas) by placing a hand on the anterior of the distal of thigh. The assessor should then resist the movement. The quality of muscle contraction score should be recorded in accordance with the quality of the contraction (see below). The assessor should be aware of any trick movements e.g leaning backwards during the movement. This should be monitored by placing one hand on the participant's back.

Finally, all three scores should be added together and the Motricity Index for the lower extremity should be calculated.

Tests for Each Leg:

(1) ankle dorsiflexion with foot in a plantar flexed position

- 14 points are given if there is less than a full range of dorsiflexion

(2) knee extension with the foot unsupported and the knee at 90°

- 14 points are given for less than 50% of full extension (i.e. 45 degrees only)
- 19 points are given for full extension yet it can be easily pushed down

(3) hip flexion with the hip bent at 90° moving the knee towards the chin

- 14 points are given if there is less than a full range of possible passive flexion, check ROM
- 19 points are given if the hip is fully flexed yet it can be easily pushed down

MRC Grade	MRC Score	Points for Tests
no movement	0	0
palpable flicker but no movement	1	9
movement but not against gravity	2	14
movement against gravity	3	19
movement against resistance	4	25
Normal	5	33

NB Only give a score of 33 for normal if both legs are the same i.e. the resistance applied when testing is equal.

Total score for each leg should be recorded. i.e. all three scores should be added up +1 point

Minimum score: 0

Maximum score: 100

References:

Wade D*. Measurement in Neurological Rehabilitation* 1992 Oxford University Press, New York.

Fayazi M, Dehkordi S N, Dadgoo M, Salehi M 2012 Test-retest reliability of Motricity Index
strength assessments for lower extremity in post stroke hemiparesis. *Medical Journal of Islamic*
Republic of Iran, Vol. 26, No. 1, Feb. 2012, pp. 27-30

Appendix 36 modified Rivermead Mobility Index

Guidelines for the Modified Rivermead Mobility Index

PREPARATION

- The assessor needs a stopwatch, a tape measure, a chair and access to a bed and a flight of stairs. The patient should be wearing his/her normal clothes and footwear.

GENERAL OBSERVATIONS

- It is essential that the patient perform each item as independently as possible. The assessor should only assist the patient if safety is at risk.

  The assessor should not facilitate the patient's performance to improve the quality of the movement.

- It is preferable to score the patient's performance at the beginning of a therapy session to minimize any potential carryover effects of the therapy session.
- The assessor should always carry out the test in the same way for example by the patient's bedside or in the gym using a plinth and using the same chair. The height of the bed or plinth should be adjusted to 45 cm. If this is not possible note down the height of the bed and the chair used for re-testing purposes at a later date.
- The instruction is verbal supplemented by demonstration where necessary.
- The patient is instructed to start performing each item towards the unaffected side. If you wish to score appropriate activities bilaterally, please start with the unaffected side first. You will need to prepare a separate column for each side, please add up the score independently for each side.
- If the overall score is to be used as a basis of comparison between patients, there needs to be a difference of more than 4.5 points in the overall score to detect actual changes in the patient's level of mobility.

SCORING OF ITEMS

(1) If the patient turns over in bed by pulling himself/herself over with his/her unaffected arm, this counts as using an aid. The patient should be asked to roll onto his unaffected side first. Both sides can be tested if appropriate.

(2) The patient should be asked to sit up while lying on his/her unaffected side first. Pulling himself/herself up on the edge of the bed with the unaffected arm counts as using an aid.

(3) The use of the hands to hold on constitutes an aid.

(4) The use of the hands to push up into standing constitutes an aid.

(5) The patient should start the transfer towards the unaffected side.

(6) Using a railing constitutes using an aid.

(7) Supervision or verbal instruction excludes any physical contact

Reference: Lennon, S, Johnson, L 2000 The **Modified Rivermead Mobility Index: validity** and **reliability.** *Disability & Rehabilitation* 12/15/2000, Vol. 22 Issue 18, p833 7p

The Modified Rivermead Mobility Index

Patient's name : **Test date :**

Assessor's name : **Test location :**

Scoring: 0 unable to perform
1 assistance of 2 people
2 assistance of 1 person
3 requires supervision or verbal instruction
4 requires an aid or an appliance
5 independent Item

	ITEM	Score
1	Turning over: Please turn over from your back to your ..... side.	
2	Lying to sitting: Please sit up on the side of the bed.	
3	Sitting balance: Please sit on the edge of the bed	
4	Sitting to standing: Please stand up from your chair	
5	Standing: Please remain standing (The assessor times the patient for 10 seconds)	
6	Transfers: Please go from your bed to the chair and back again (The assessor places the chair on the patient's unaffected side)	
7	Walking indoors: Please walk for 10 meters in your usual way	
8	Stairs: Please climb up and down this flight of stairs in your usual way	

Reference: Lennon, S, Johnson, L 2000 The **Modified Rivermead Mobility Index: validity** and **reliability.** *Disability & Rehabilitation* 12/15/2000, Vol. 22 Issue 18, p833 7p

Appendix 37 Letter of invitation to the focus group

Study Title: Sensory stimulation of the foot and ankle early post stroke: a feasibility study (MoTaStim-Foot)

(Date)

Dear ……

Following our telephone conversation, I am writing to formally invite you to attend the focus group for the MoTaStim-Foot trial, which is being held on **????????**

Venue: Wolstanton Methodist Church, Grosvenor Place, Wolstanton, Newcastle-under-Lyme, ST5 0HE. There is plenty of free parking in the church car-park.

Time: Please try to arrive by 11am. The focus group will commence at 11.30am and will last for up to a maximum of 90 minutes.

Refreshments:

Refreshments (tea and coffee) will be available on arrival, and a light lunch will be provided after the focus group.

Travel arrangements / costs: We can book a taxi for you if required, or you can be reimbursed for your own travel costs. If you would like to claim your travel costs you will need to complete a form on the day please, and you will then be reimbursed from Keele University via your bank account.

If you have any queries regarding any aspects related to the focus group please phone Alison Aries (Chief Investigator) on ?????????????.

We look forward to seeing you on **????????.**

Thank you once again for your participation in this research trial.

Best wishes

Alison Aries

(Chief Investigator for MoTaStim-Foot trial)

Appendix 38 MTS focus group schedule

Title: **Sensory stimulation of the foot and ankle early post stroke: a feasibility study (MoTaStim –Foot)**

Date:

Nature of Group: Mobilization and Tactile Stimulation (MTS) Group

Name of Facilitator: Alison Aries

Name of Note taker:

Introduction to the process

Thank the participants for agreeing to attend a focus group discussion regarding their participation in the study Mobilization and sensory stimulation of the foot and ankle post stroke: a feasibility study (MoTaStim-Foot). Provide the participant with a copy of the consent form which has previously been completed. Answer any questions that may arise as comprehensively as possible. Emphasise to the participant that:

1. The Focus Group interview will take no longer than one and a half hours.

2. To accurately capture what is being said the interview will be audiotaped

3. All information that is collected about the participant during the course of the study will be kept strictly confidential. Everyone needs to respect this please.

4. Any participants will remain anonymous in any dissemination work undertaken external or internal to the University

5. In addition to consenting to be interviewed, the participant will also have given consent for direct quotations from the interview to be used in the write up of the evaluation. Please note that should you choose to withdraw at any point in time any information already collected will be used.

6. Any quotations that are used will be completely anonymous

7. The information provided by the participant will be used to inform a future study looking at Mobilization and Tactile Stimulation to the foot post stroke and in dissemination activities (conference presentations/ paper etc).

Ensure that the above points have been fully considered by the participant. Ask if they have any questions and then

Introduce the team:

When verbal consent on the day has been obtained, ask the participants if it is OK to turn on the tape recorder and conduct the interview. Remind people that there is no

right or wrong answer and they should just give their honest opinion. Switch on the audiotape.

Focus Group Schedule

The following topic areas will be explored and similar questions to those below will be asked:

A. **About the interventions –** Remind participants that they had two different types of intervention at each treatment session – Mobilization and Tactile Stimulation and TaskSpecific Walking Training.

1.0 Mobilization and Tactile Stimulation (MTS) - I want to find out more about how the MTS felt

1.0 Can you tell me how you found the Mobilization and Tactile Stimulation (MTS)?

More specifically:

I want to find out more about how the treatment felt

1.1 If you were describing the MTS treatment to someone else – from your experience what would you say?
1.2 Was it comfortable or uncomfortable? – What did you do if it became uncomfortable?
1.3 How long did any discomfort last?
1.4 Have you any other comments to make about the treatment?

2.0 Task Specific Gait Training: I want to find out more about how the Task Specific Walking Training felt.

2.1 If you were describing the Task Specific Walking Training treatment to someone else – from your experience what would you say?
2.2 Was it comfortable or uncomfortable? – What did you do if it became uncomfortable?
2.3 How long did any discomfort last?
2.4 Have you any other comments to make about the treatment?

3.0 How was it for you when you had your treatments?

3.1 Treatment took place regularly – can you tell us how it felt to have people coming to you that regularly?
3.2 How easy was it to access your treatment?...or did you have your treatment at home?
3.3 Did you feel comfortable with the situation?
3.4 How did you feel when the treatments finished?

B. About the outcome measurements:

4.0 Can you say a little about the outcome measures?

4.1 Were the outcome measures uncomfortable or difficult?

4.2 Was there anything in particular about a specific outcome measure and why?

When you went for the outcome measures, can you say what was it like?

4.3 Was it easy to find?

4.4 Did you have to travel far?

4.5 Did you feel comfortable?

C. About the daily diaries:

5.0 Can you say a little about using the daily diaries?

5.1 How did you find filling in the daily diaries?

5.2 Can you say how easy or difficult you found them to complete?

5.3 Did you develop any particular patterns for filling them in?

5.4 Did you personally get anything from filling in the diaries?

5.5 Can you make any suggestions for changing the diaries in any way?

D. About any changes the participants may have perceived:

6.0 Have you noticed any changes?

6.1 Have you noticed any differences in your foot at all?

6.2 Can you say if your ability to walk / function has changed in any way?

6.3 Can you say if your confidence whilst walking changed at all?

6.4 Has the treatment made any difference to your lives?

6.5 What impact has it had on you....and your family?

6.6 Have we helped you achieve your goals for the future?

Please can you describe your experience on the trial in one word or one sentence?

Is there anything else you would like to tell me about your experiences of MTS and task specific gait training?

Thank you for your time today.

Debriefing session - Check if there is anything else which should be added.

Appendix 39 TI focus group schedule

Title: **Sensory stimulation of the foot and ankle early post stroke: a feasibility study (MoTaStim –Foot)**

Date:

Nature of Group: Textured Insoles Group

Name of Facilitator: Alison Aries

Name of Note taker:

Introduction to the process

Thank the participants for agreeing to attend a focus group discussion regarding their participation in the study Mobilization and sensory stimulation of the foot and ankle post stroke: a feasibility study (MoTaStim-Foot). Provide the participant with a copy of the consent form which has previously been completed. Answer any questions that may arise as comprehensively as possible. Emphasise to the participant that:

1. The Focus Group interview will take no longer than one and a half hours.

2. To accurately capture what is being said the interview will be audiotaped

3. All information that is collected about the participant during the course of the study will be kept strictly confidential. Everyone needs to respect this please.

4. Any participants will remain anonymous in any dissemination work undertaken external or internal to the University

5. In addition to consenting to be interviewed, the participant will also have given consent for direct quotations from the interview to be used in the write up of the evaluation. Please note that should you choose to withdraw at any point in time any information already collected will be used.

6. Any quotations that are used will be completely anonymous

7. The information provided by the participant will be used to inform a future study looking at Mobilization and Tactile Stimulation to the foot post stroke and in dissemination activities (conference presentations/ paper etc).

Ensure that the above points have been fully considered by the participant. Ask if they have any questions.

Introduce the team:

When verbal consent on the day has been obtained, ask the participants if it is OK to turn on the tape recorder and conduct the interview. Remind people that there is no right or wrong answer and they should just give their honest opinion. Switch on the audiotape.

Focus Group Schedule

The following topic areas will be explored and similar questions to those below will be asked:

A. About the interventions – Remind participants that they had two different types of intervention at each treatment session – Wearing textured Insoles and Task Specific Walking Training.

1.0 Textured Insoles - I want to find out more about what it was like to wear the textured insoles

1.1 Can you tell me how the textured insoles felt to wear?

More specifically:

I want to find out more about how the treatment felt

1.2 If you were describing what it was like to wear textured insoles to someone else – from your experience what would you say?
1.3 Was it comfortable or uncomfortable? – What did you do if they became uncomfortable?
1.4 How long did any discomfort last?
1.5 What could you say about the time given for you wearing the textured insoles?
1.6 Was the time too long / too short or, just right?
1.7 How might you describe the ease of wearing the textured insoles?
1.8 Were they easy to put in your footwear?
1.9 Have you any other comments to make about wearing textured insoles?

2.0 Task Specific Gait Training: I want to find out more about how the Task Specific Walking Training felt.

2.1 If you were describing the Task Specific Walking Training treatment to someone else – from your experience what would you say?
2.2 Was it comfortable or uncomfortable? – What did you do if it became uncomfortable?
2.3 How long did any discomfort last?
2.4 Have you any other comments to make about the treatment?

3.0 How was it for you when you had your treatments?

3.2 Treatment took place regularly – can you tell us how it felt to have people coming to you that regularly?
3.3 How easy was it to access your treatment?....or did you have your treatment at home?
3.4 Did you feel comfortable with the situation?
3.5 How did you feel when the treatments finished?

B. About the outcome measurements:

4.0 Can you say a little about the outcome measures?

4.1 Were the outcome measures uncomfortable or difficult?

4.2 Was there anything in particular about a specific outcome measure and why?

When you went for the outcome measures, can you say what was it like?

4.3 Was it easy to find?

4.4 Did you have to travel far?

4.5 Did you feel comfortable?

C. About the daily diaries:

5.0 Can you say a little about using the daily diaries?

5.1 How did you find filling in the daily diaries?

5.2 Can you say how easy or difficult you found them to complete?

5.3 Did you develop any particular patterns for filling them in?

5.4 Did you personally get anything from filling in the diaries?

5.5 Can you make any suggestions for changing the diaries in any way?

D. About any changes the participants may have perceived:

6.0 Have you noticed any changes?

6.1 Have you noticed any differences in your foot at all?

6.2 Can you say if your ability to walk / function has changed in any way?

6.3 Can you say if your confidence whilst walking changed at all?

6.4 Has the treatment made any difference to your lives?

6.5 What impact has it had on you?....and your family?

6.6 Have we helped you achieve your goals for the future?

Please can you describe your experience on the trial in one word or one sentence?

Is there anything else you would like to tell me about your experiences of TIs and task-specific gait training?

Thank you for your time today.

Debriefing session - Check if there is anything else that should be added.

Appendix 40 Researcher's assumptions

Researcher's (AA's) assumptions prior to undertaking MoTaStim-Foot:

- Participants will notice a change in feeling within the foot and ankle in the MTS group
- Participants will notice a change in movement within the foot and ankle in the MTS group
- Participants will feel the benefit of the extra treatments in both groups because it is known that TSGT will improve function
- Function and ability to undertake ADL will improve for all participants
- Participants might find it uncomfortable to wear the TIs
- AA has concerns about the possibility of TIs rubbing the sole of the foot
- AA has no idea whether participants will be able to feel the TIs or whether wearing them will make a difference to the feeling of the plantar surface of the foot.
- Participants may not be very compliant with wearing the TIs
- Although participants will value the extra treatment received almost daily treatment may be too much for them
- The TSGT will push the participants hard and this may be too much for some participants
- AA is concerned that the battery of outcome measures will take too long, and participants may not cope with them.

Appendix 41 Report on observations of research therapists

MoTaSTim-Foot Trial – observation of research therapists delivering MTS and TSGT

As an independent assessor of practice, I carried out observation visits with four research therapists, and observed treatment with five participants, between February and October 2017.

Visit 1 – 24th February 2017

Participant 017

All treatment was delivered in accordance with the protocols. TSGT was delivered in the downstairs living area, and relevant equipment was used – e.g. football, balance cushion. After the visit, we had some discussion around the content of the TSGT schedule and checked under which sections the treatments / interventions would be recorded.

Visit 2 – 12th July 2017

Participant 026

All treatment was delivered in accordance with the protocols. MTS was delivered with the pt in supine lying on the bed, with his wife present. TSGT was delivered downstairs in the living room using relevant equipment e.g. football, balance cushion.

Visit 3 – 12th July 2017

Participant 030

All treatment was delivered in accordance with the protocols. MTS was delivered with the pt in supine lying on the sofa. TSGT was delivered in a downstairs area and consisted of specific components of walking and balance activities.

Visit 4 – 11th August 2017

Participant 033

All treatment was delivered in accordance with the protocols. MTS was delivered with the pt sitting in an armchair. TSGT was delivered both indoors and outdoors, culminating in walking across the grass.

Visit 5 – 19th October 2017

Participant 035

All treatment was delivered in accordance with the protocols. MTS was delivered with the pt sitting over the side of the bed. TSGT was delivered indoors, using relevant equipment e.g. football, and included muscle strengthening activities e.g. repeated sit→stand.

In summary, I was happy that all treatments were delivered in accordance with the protocols and could be recorded on the treatment schedules. There was no treatment delivered that did not feature in the schedules (MTS or TSGT). I did note a difference in delivery between the therapists, which I attribute to their differences in experience of treating stroke survivors in general. However, this is representative of the differences likely to be seen in clinical practice amongst and across different NHS Grades and according to individual skills and expertise. All treatments were delivered safely and competently.

SMH

Reflections:

Two Research Therapists were particularly skilled in neurological rehabilitation and this was evident from the confidence and expertise in handling with which they provided both MTS and TSGT. TSGT activities were progressed quickly and appropriately, and the pt's ability was challenged to a high level. Whilst the activities were clearly difficult, they were managed by the pt, who was not at risk of any adverse event e.g. fall at any time. Indeed, pts appeared to fully appreciate the benefit of the challenges they were given during the TSGT.

The Research Therapist who was least skilled in neurological rehabilitation had less confidence and skill in the handling used to deliver MTS which was more focussed on massage and pressure stimulation than on specific mobilisation of soft tissues. TSGT was challenging but the participant was very chatty, which detracted from the intensity of the therapy at times.

One other Research Therapist was very careful to ensure that the MTS treatment followed the protocol, and this was delivered carefully but perhaps not with the same depth of soft tissue mobilisation as that seen by the more skilled and experienced neurological therapists. TSGT was less challenging than I had seen with other pts, but the importance of participant safety was a key focus throughout.

Appendix 42 Statistical Analysis plan for MoTaStim-Foot

Sensory stimulation of the foot and ankle early post-stroke: A feasibility study (MoTaStim – Foot): statistical analysis plan

Sponsor: Keele University

Trial registration: ISRCTN registry 13676183

Central Portfolio Management System ID 30449

NRES: IRAS No: 171968 / REC Ref 16/WM/0080

Study team:

Alison Aries (Chief Investigator/Research Therapist/PhD Student)

Dr Susan Hunter (Blinded Assessor/Lead Supervisor)

Professor Valerie Pomeroy (Supervisor)

Professor Julius Sim (Statistician/Supervisor)

Authors of the SAP:

Statistician: PROFESSOR JULIUS SIM

Lead Supervisor: Dr SUSAN HUNTER

Chief Investigator: ALISON ARIES

Declaration regarding undertaking of the analysis

Alison Aries (Chief Investigator and PhD student) will be undertaking data cleaning and analysis of the study data under the guidance and supervision of Professor Julius Sim (statistician/supervisor/advisor) and Dr Susan Hunter (Lead Supervisor).

With reference to Protocol version: v 4.0 – dated 23rd October 2016

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1. Abbreviations (list)

AE	Adverse event
AR	Adverse reaction
CI	Chief Investigator
CNS	Central Nervous System
CONSORT	Consolidated Standards of Reporting Trials
CTU	Clinical Trials Unit
DVT	Deep vein thrombosis
FAC	Functional Ambulation Category
MRC	Medical Research Council
MTS	Mobilization and tactile stimulation
NCTU	Norwich Clinical Trials Unit
NIHR	National Institute for Health Research
RCT	Randomized controlled trial
REC	Research Ethics Committee
SAP	Statistical analysis plan
SSOTP	Staffordshire and Stoke-on-Trent Partnership Trust
TI	Textured insole
TSGT	Task-specific gait training
UK	United Kingdom

2. Glossary of terms

Mobilization and tactile stimulation (MTS):	A term given to a form of hands-on therapy treatment which is often delivered in conventional therapy, with an aim of mobilizing the area (e.g. hand or foot) and enhancing sensory input (feeling). It involves massage and tactile stimulation of the area and joint and soft tissue mobilisation techniques (passive movements, accessory movements, soft tissue stretching).
Task-specific gait training (TSGT)	A form of therapy which involves repetition of various activities e.g. sitting to standing, stepping etc. with an aim of improving the ability to walk.
Textured insoles (TIs)	Insoles made of material with projections. The aim of these peaks is to stimulate the sole of the foot, increasing sensory input.

3. Background and Aims

Strokes are common. Indeed, every year 15 million people in the world have a stroke (Mackay and Mensah, 2004). Neuroscience findings indicate that feedback to the brain via sensory processes is essential for motor function (Chersi et al. 2011, Laaksonen et al. 2012, Rossignol et al. 2006), and therefore information originating in the foot is important for balance and walking

Mobilization and tactile stimulation (MTS) is a treatment used in conventional physiotherapy practice to prepare or 'prime' the central nervous system (CNS), facilitating movement and function, by giving sensory input via the foot and ankle. MTS is a part of routine physical therapy used in clinical practice to prepare the foot and leg for standing and walking, but its effects have not yet been explored.

The plantar (sole of the foot) mechanoreceptors are key, sending information to the CNS, and plantar stimulation has been shown to result in increased control of body sway (Watanabe and Okubo 1981). In view of the importance of cutaneous information from the sole of the foot to control balance (Kennedy and Inglis, 2002), other potential mechanisms of increasing plantar stimulation have been explored, and texture insoles (TIs) have been shown to improve postural control in standing in healthy participants (Corbin et al 2007), and to improve walking patterns for people with multiple sclerosis (Dixon et al 2014). However, none of these specific or combined treatments have been evaluated robustly to determine their benefits for balance and walking recovery early after stroke. The use of TIs in the shoes of stroke survivors involves a hands-off (therapist independent) approach, which may potentially be a more economical option for achieving increased sensory stimulation to the foot and is therefore important to investigate. TIs are a different way of delivering sensory information to the CNS, enabling 'augmentation' of sensory input to the CNS as a means of facilitating movement and function. It is important to explore in the future which sensory stimulation is more effective, hence this feasibility study to establish if it is possible to deliver these interventions in a research setting.

This feasibility study involves a mixed-methods design and will be an important step in the research pathway, ensuring treatments are properly developed and procedures are tested in a rigorous manner, and participants' perceptions explored. It is necessary to see if it is possible to deliver the treatments (MTS or TIs followed by TSGT) and the outcome measurements before undertaking a larger study in the future.

Primary Research Aim:

To explore the feasibility of delivering treatment designed to increase the feeling within the foot after stroke in a randomized trial. The treatments being evaluated are MTS with TSGT versus wearing of TIs plus TSGT.

Research Objectives:

1. To find out if the treatments (MTS plus TSGT, and the wearing of TIs plus TSGT) are acceptable treatments for stroke survivors.

2. To explore the response to treatment (if any), in relation to the number of treatment sessions delivered.

3. To find out which measures will be most appropriate to measure outcomes of: sensorimotor impairment (feeling/sensation and movement), and lower-limb function and balance.

4. To find out if daily diaries and focus groups are suitable ways to explore stroke survivors' experiences of receiving the treatments.

5. To find out if recruitment methods are effective, noting the numbers of people invited to participate, eligible to participate, and agreeing to consent as well as the number of people who drop out of the trial. The information will be used to inform a power calculation for a future study.

6. To gather data on outcome measures, and their completion, that will inform a sample size calculation for a subsequent main trial.

4. Design

This is a single-site, randomized, single-blinded feasibility trial, being undertaken as part of an NIHR funded Clinical Doctoral Research Fellowship (CONSORT diagram, figure 1 and overview of trial, figure 2). A mixed-methods design will be adopted, which will involve both quantitative (experimental) and qualitative (focus groups) methods.
The randomisation sequence was generated before the trial commenced and Professor Julius Sim, the statistician for the trial, provided the randomisation order to Norwich CTU. Participants are randomised to the interventions using 1:1 randomisation, with stratification by left or right stroke to ensure an equal number of right- and left-sided strokes in each treatment group.

Allocation concealment mechanism

An independent telephone interactive voice response system and computer system randomisation service and electronic case record form maintained concealment of the treatment allocation from investigators, research therapists and blinded assessors prior to randomisation of a participant (i.e. each participant's allocation could not be predicted from the allocation of the previous participant).

Allocation Implementation

Baseline data was entered into the randomisation system and the system randomized, sending an email confirmation of the allocation group for the participant. Concealment of group allocation from the blinded assessor continued throughout the trial process.

Blinding

All outcome measurements in which observer bias could occur will be undertaken by assessors who are blinded to treatment group allocation. The touch/pressure sensory thresholds, Lower Extremity Motricity Index and modified Rivermead Mobility Index will all be undertaken by a blinded assessor. However, a research therapist will undertake the five-metre walk test, pressure under the feet and ankle range of movement assessments. As these are objective assessments, the risk of bias is low. As part of clinical decision making, to assess for possible fatigue, the research therapists will also measure the Lower Extremity Motricity Index, at each intervention; however, it will be the Lower Extremity Motricity Index measurement undertaken by the blinded assessor that will be formally analysed. Participants will be asked to refrain from telling the assessors which treatment they are receiving. To assess whether blinding of assessors was achieved, we will ask assessors, at the one-month follow-up point, to guess which group they think participants were assigned to. Agreement with actual allocation will be assessed.

5. Study and population

Study setting:

Participants will be stroke patients admitted to Staffordshire and Stoke-on-Trent Partnership Trust (SSOTP), both inpatients and outpatients.

Inclusion criteria:

- Able to provide written informed consent
- Adult stroke survivors (aged 18 years or older), with anterior or posterior circulation stroke, occurring 6–16 weeks (42–112 days) earlier.
- Ability to walk independently prior to stroke.
- Participants must also be able to follow simple commands and imitate actions, using the non-paretic upper limb (the arm that has not been affected by the stroke).
- Participants must be unable to step on and off a 7·5 cm high block more than 12 times in 15 seconds with either their paretic (affected) or non-paretic leg (Step test: Hill et al., 1996).

Exclusion criteria:

- Pre-existing conditions affecting sensation of the foot and lower limb e.g. diabetic neuropathy, polyneuropathy (degeneration of the peripheral [not in the brain and

spinal cord] nerves), peripheral nerve lesion [injury to a peripheral nerve], previous stroke affecting sensation of the lower limb.

- Fixed contracture of the tendo Achilles, assessed by being unable to achieve 90 degrees dorsiflexion at the ankle, either actively or passively with the knee extended.
- Pressure sores or ulcers on the foot or ankle (hemiparetic limb), due to the risk of infection.
- Deep vein thrombosis, because some of the MTS techniques would be contraindicated.
- Other conditions that affect the blood supply to/from the foot, e.g. heart failure with peripheral oedema
- Botulinum toxin injections to the lower limb in the previous six months, because these might have an impact on the results
- Pain sufficient to prevent delivery of treatments or outcomes
- Known HIV, hepatitis non-A or related condition
- The participant's home address is outside of a feasible recruitment zone (for example ST10 or ST13).

Monitoring of recruitment:

The number of potential participants approached will be recorded and a note taken, as appropriate, of why people were excluded at first screening, with reasons documented. The number of potential participants excluded on post consent screening will also be noted.

A record will be kept of all participants required to withdraw from the study, with reasons noted. Any participant found to be ineligible after randomisation will be noted and reasons explored.

Monitoring non-compliance to protocol:

Conduction of the trial is in compliance with the approved protocol, the Declaration of Helsinki (2008), the principles of Good Clinical Practice (GCP) as laid down by the Commission Directive 2005/28/EC with implementation in national legislation in the UK by Statutory Instrument 2004/1031 and subsequent amendments, the Human Tissue (Quality and Safety for Human Application) Regulations 2007, the UK Data Protection Act, and the National Health Service (NHS) Research Governance Framework for Health and Social Care (RGF). A record of any non-conformances to protocol will be maintained and these will be summarised by type and treatment group.

Serious breaches:

Should a serious breach occur it will be recorded and notified within the necessary timelines specified in the UK Clinical Trials Regulations (currently 7 days).

Serious adverse events:

All serious adverse events will be recorded and notified to the Sponsor within the necessary 24-hour time period.

Adverse events:

A record will be kept of the number of adverse events and the reason for these adverse events.

Adverse reactions:

All adverse reactions will be documented and monitored.

In relation to adverse reactions related to overdose of intervention:

There is a small possibility that either the MTS or TSGT could be associated with an overuse syndrome as expressed by a participant's experience of pain or fatigue.
a. Pain will be considered to be an adverse reaction if (i) a participant reports the onset or increase of paretic lower-limb pain (verbally or behaviourally), (ii) the pain is sustained over four consecutive therapy sessions and (iii) if the research therapist and clinical team are unable to account for this in any other way than involvement in this trial. This will be addressed by the research therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session on which pain was apparent.

b. Fatigue will be considered to be an adverse reaction if (i) a participant demonstrates a decrease of two levels in the Lower Extremity Motricity Index score on four consecutive therapy sessions and (ii) the therapist and clinical team are unable to account for this in any other way than involvement in this trial. This will be addressed by the therapist adjusting the therapy as appropriate or, if indicated, stopping the extra therapy on either a permanent or temporary basis. The date of adverse reaction will be the date of the fourth consecutive therapy session in which fatigue was indicated.

6. Outcomes

Statistical analysis

As this is a feasibility study, no formal hypothesis tests will be undertaken. All data analysis will take place after data lock down

Statistical Methods – Outcomes

Point estimates, with 95% two-sided confidence intervals, will be calculated for key variables. For proportions, the Wilson interval will be used in view of the small sample size, as recommended by Brown et al (2001). The variance of scores for outcome measures will be calculated, providing information for the sample size calculation for the subsequent large trial. Outcome measures resulting in numerical data will be presented as mean and standard deviation, unless the data are skewed, in which case

the median and interquartile range will be reported. Ordinal data will be presented as medians and interquartile ranges. The NIHSS will be treated as ordinal data as recommended by Harrison et al (2013). The distribution of outcome variables will also be assessed, to evaluate the suitability for a main trial, to further inform the sample size calculation, and to guide the choice of analysis in the main study. Additionally, 95% confidence intervals will be calculated for within-group effects on the outcome variables, so as to indicate a range of plausible effects of the study interventions in a main trial.

The number of eligible patients who are recruited, and the proportion of those recruited who are lost to follow-up at one month, will also be calculated. In accordance with the CONSORT (2010) guidelines, baseline demographics and characteristics of the two groups will be transparent. Analysis will be conducted by the applicant, with guidance from the supervisory team. A single formal analysis will take place at the end of the study.

For those scaled outcomes that are recorded at each time point, a line graph of all individual participants' response trajectories will be constructed for each arm of the trial; this graph will also include a line representing the averaged response trajectory. The graph will be analysed visually to determine if there is a point at which the participants' responses tend to change direction upwards (indicating a response to treatment), as this information will provide information on the likely minimum length of treatment, or 'dosage', that is required to induce an improvement on the outcome concerned. Across these outcomes, the latest such change in trend will suggest the minimum length of treatment that should be utilized in the main trial.

Within the feasibility study, both research therapists will deliver either MTS or TSGT. A log will be kept detailing, for each participant, which therapist has delivered the treatment.

1. Characterization of clinical presentation of participants (to give an overview of the participants to assist with evaluation of the interventions) using the following tools:

(i) National Institutes of Health Stroke Scale (NIHSS) - This includes assessment of the level of consciousness, vision, motor activity (face, arm and leg), coordination, sensation and speech. This assessment is only occurring at baseline. This assessment indicating the level of disability will be summarised according to intervention group.

(ii) Functional Ambulation category, which assesses walking ability and categorizes according to basic motor skills necessary for functional walking. Point estimates, interquartile ranges, and the variance of scores will be calculated. The time-points for this assessment are baseline, end of intervention and one-month follow-up.

2. Sensorimotor impairment:

a) Pressure under the feet during stance phase of walking (measured with insoles).

The force time integral and centre of force velocity (COF) will be calculated for each participant. Centre of force trajectory will be analysed visually. Point estimates, with 95% confidence intervals, will be calculated as well as the variance of scores. The time-points for this assessment are baseline, end of intervention and one-month follow-up. Pressure will be measured in KiloPascals (kPa) and COF velocity in cm/second.

b) Ankle range of motion (dorsiflexion, plantarflexion, inversion, eversion) during stance phase

This will be measured by an electrogoniometer, in stance phase of walking. Maximum and minimum angles of dorsiflexion and inversion will be calculated. Point estimates, with 95% confidence intervals or interquartile ranges (as appropriate), will be calculated and the variance of scores calculated. The time-points for this assessment are baseline, end of intervention and one-month follow-up. Range will be measured in degrees of movement.

c) Touch/pressure sensory thresholds on the sole of foot (to determine the ability to feel at different points)

This is measured using Semmes Weinstein Monofilaments and reported on a scale of 1-20, correlating with the force measured in mg. The median value and interquartile ranges for the point of sensory detection for each of the four areas on the foot (heel, under pad of hallux, under 1st metatarsal and under 5th metatarsal) will be calculated, and the variance of scores will be established. The time-points for this assessment are baseline, after five interventions, after 10 interventions, after 15 interventions, end of intervention and one-month follow-up.

d) Lower Extremity Motricity Index (LEMI)

Mean strength of hip flexors, knee extensors and ankle dorsiflexors and total LEMI score will be calculated. Point estimates, with 95% confidence intervals, will be calculated and the variance of scores noted if data is normally distributed. Alternatively, median and interquartile ranges will be calculated. The time-points for this assessment are baseline, after five interventions, after 10 interventions, after 15 interventions, end of intervention and one-month follow-up.

Regular outcome measurements (c and d) are being recorded to ascertain at what stage any changes are seen, to inform the dose (duration) of the intervention for the subsequent trial.

For c) and d) a line graph of all individual participants' response trajectories will be constructed for each arm of the trial; this graph will also include a line representing the averaged response trajectory. The graph will be analysed visually to determine if there is a point at which the participants' responses tend to change direction upwards (indicating a response to treatment), as this information will provide information on the likely minimum length of treatment, or 'dosage', that is required to induce an improvement on the outcome concerned. Across these outcomes, the latest such change in trend will suggest the minimum length of treatment that should be utilized in the main trial.

3. Lower limb function and balance:

Measures e) and f) will be collected at baseline, on completion of the twenty treatments and at one-month follow-up.

e) Walking speed 5-metre walk test (self-selected walking speed), gives an indication of the overall walking ability of stroke survivors (measured in metres per second). Point estimates, with 95% confidence intervals or median and interquartile ranges (as appropriate), will be calculated and the variance of scores noted.

To enable more detailed analysis, the 5-metre walk test is videoed. In addition to quantifying variables such as walking speed for the 5-metre walk test, an observational analysis of the quality will be undertaken, as is common practice in therapy rehabilitation. The time-points for this assessment are baseline, end of intervention and one-month follow-up.

f) Modified Rivermead Mobility Index

The test involves eight tasks including bed mobility, sitting and standing balance, transfers, walking and stairs. A rating is given relating to the amount of assistance the person requires.

Point estimates, with 95% confidence intervals, will be calculated for the both the affected and unaffected side results, and the variance of scores noted. The time-points for this assessment are baseline, end of intervention and one-month follow-up.

7. Sample size

One of the aims of the study is to be able to undertake a sample size calculation prior to a follow up study. A sample size of 30 has been suggested as the lower limit for working out how many participants will be required for future studies in terms of an estimate of the standard deviation of values on a continuous outcome measure (Browne 1995). Recruiting a sample of 34 participants will account for 10% attrition, and enable potentially equal numbers (n=17) in each arm of the trial. As the whole

study needs to be completed within three years this sample size was deemed to be the largest feasible in the time frame.

8. Participant (baseline) characteristics

Baseline characteristics will include age, gender, ability to walk independently prior to the stroke, level of stroke severity (NIHSS), as well as the outcome measures: touch/pressure sensory threshold measured with Semmes Weinstein monofilaments; Lower Extremity Motricity Index; five-metre walk test; force time integral (force through foot and time spent on the foot) and centre of force velocity from the pressure insoles; ankle range of movement; modified Rivermead Mobility Index; and Functional Ambulation category. Information will be generated regarding the participants recruited; i.e. population participant demographics, clinical characteristics, including time since stroke, type of stroke and previous impairment affecting the ability to walk, and these will be summarised according to intervention group. Count variables will be presented as frequencies and proportions, ordinal variables as medians and interquartile ranges, and numerical variables as means and standard deviations (or medians and interquartile ranges if skewed).

9. Health Economics

N/A for this feasibility study.

10. References

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11. Tables/Figures

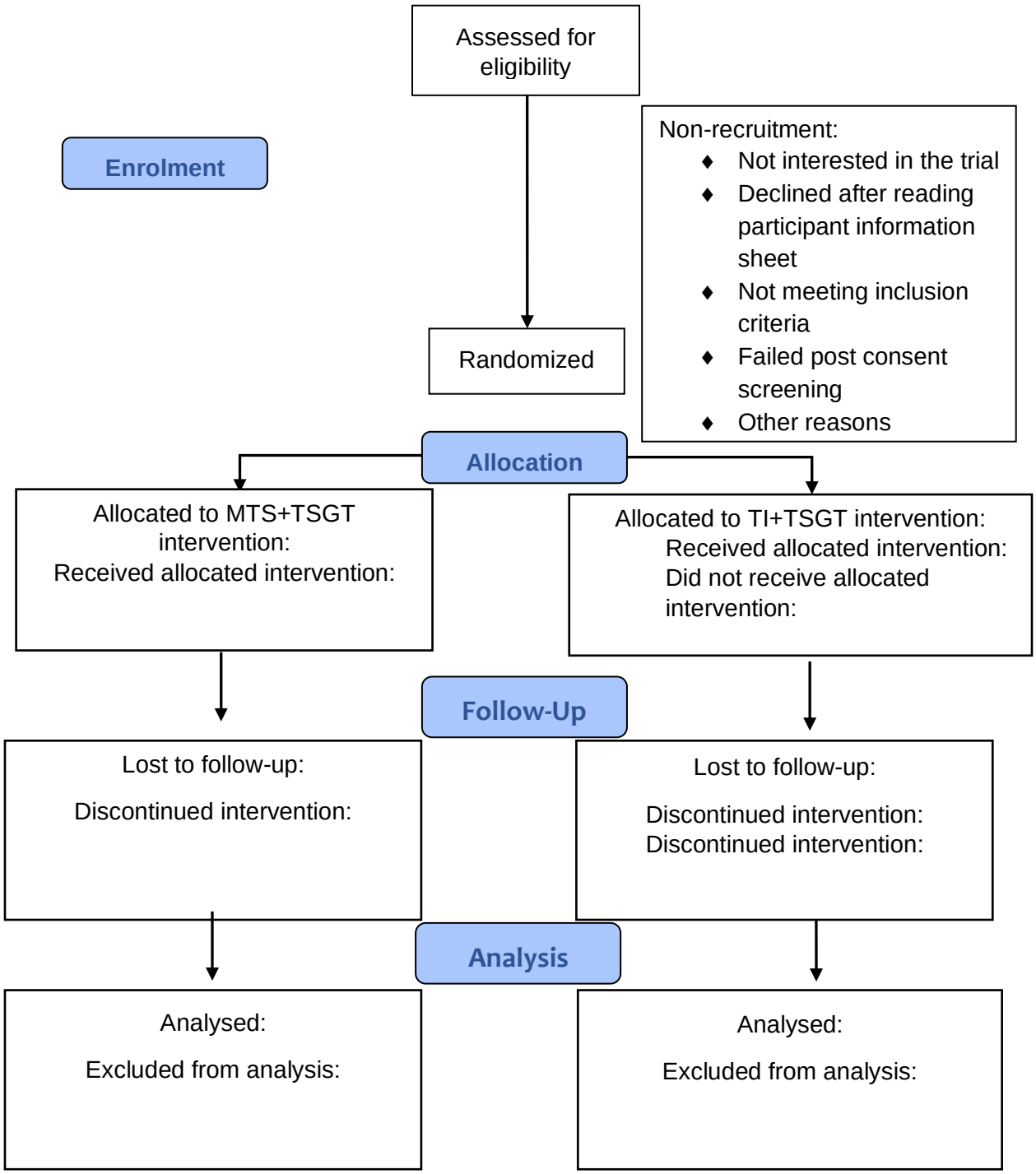


Figure 1: CONSORT 2010 Flow Diagram

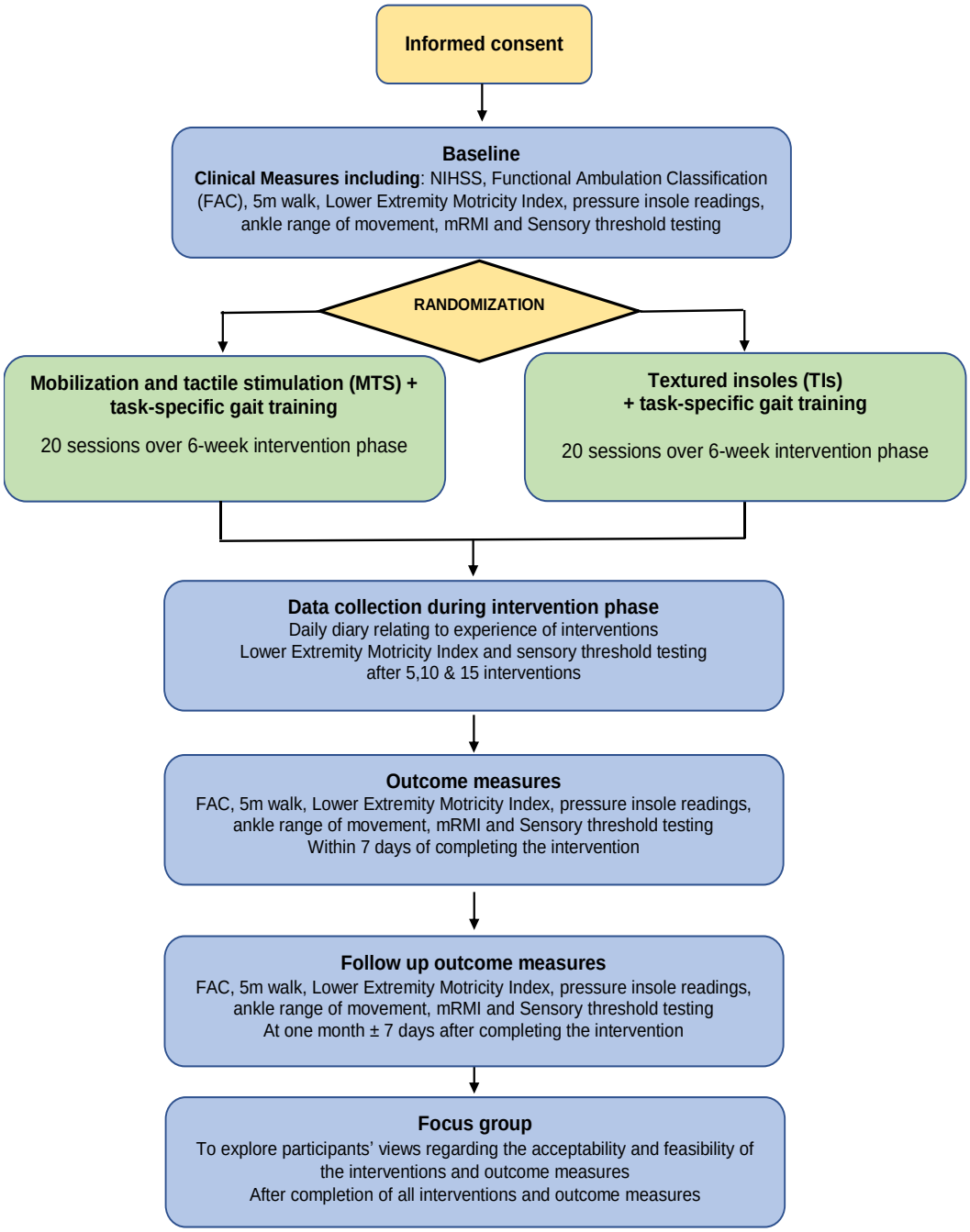


Figure 2: Overview: Sensory stimulation of the foot and ankle post stroke: A feasibility study (MoTaStim-Foot)

Appendix 43 A priori topics and initial themes identified from the FGs

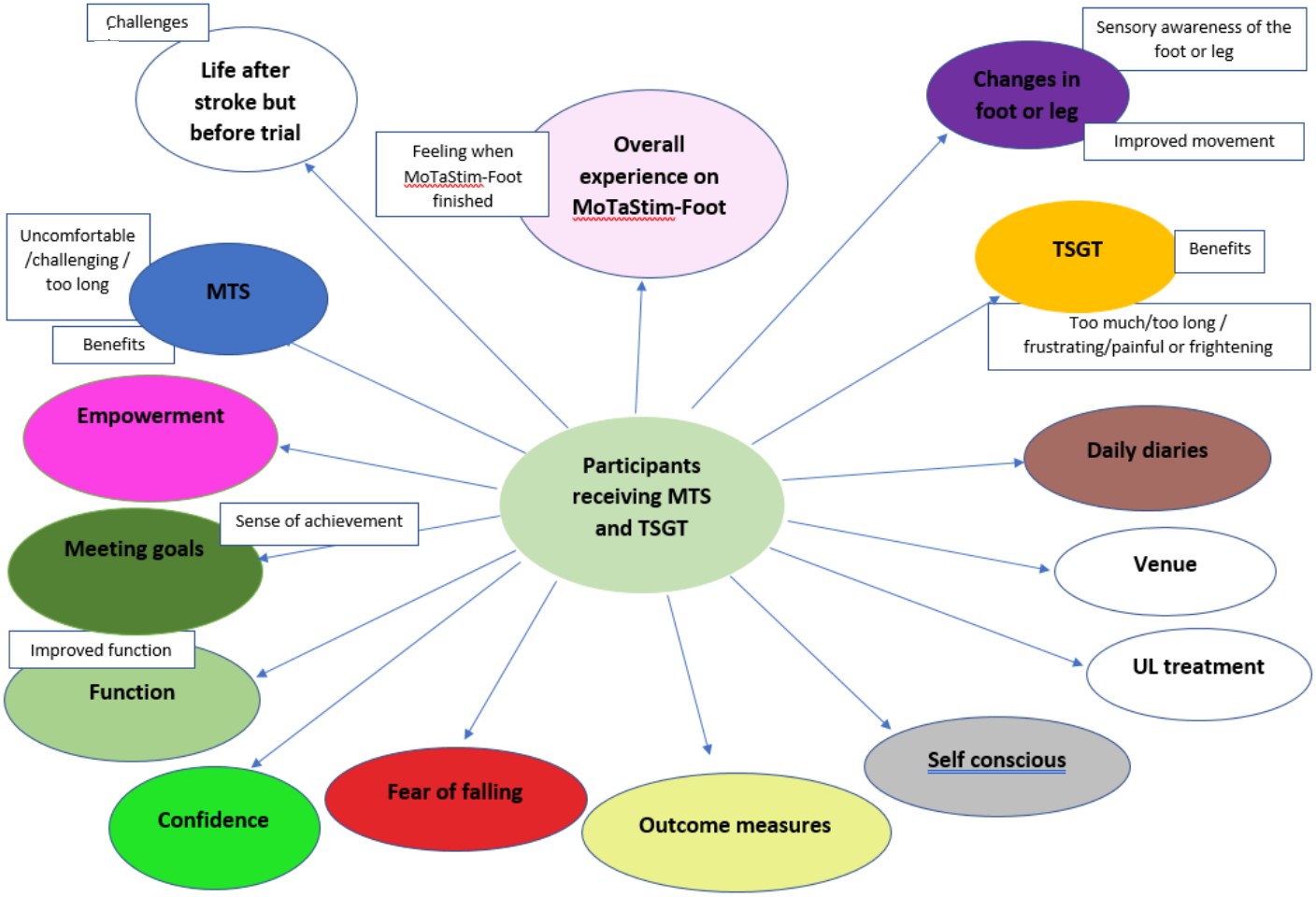
A priori topics	Themes (FGs)	FG 1	FG 2	FG 3	FG 4
MTS	Uncomfortable/challenging / too long (1,3) Benefits (1,3) Foot feeling different (3) Info re MTS being given by a carer (3)	✓		✓	
Wearing TIs	Comfort (2,4) Benefits (2,4) TIs were helpful (2) Increased stability of the foot (2) Length of time wearing TIs (4) General information relating to wearing TIs (4) Difficulties (4) General concerns/perceptions (4) Uncomfortable (4)		✓		✓
TSGT	Benefits (1,2,3,4) Too much/too long/frustrating/ painful or frightening (1,3) Difficult/challenging (2,4) Comfort (2,4) Convenience (2,4) General comments (2,4)	✓	✓	✓	✓
Outcome measures		✓	✓	✓	✓
Venue		✓		✓	
Daily diaries		✓	✓	✓	✓
Changes in the foot or leg	Sensory awareness of the foot or leg (1,2) Change in movement (1,2,3) Change in temperature of the foot (2) Change of feeling (1,2) Increased stability of the foot (2)	✓	✓	✓	✓
Overall experience	Feeling when MoTaStim-Foot finished (1,3)	✓	✓	✓	✓

on MoTaStim - Foot	Re daily/regular interventions (2,3) Impact (2) Impact on family (2) Venue (2,3) Length of sessions (2) Number of sessions (2)				
Life after MoTaStim-Foot			✓	✓	

Themes identified on analysis	Sub-themes	FG 1	FG 2	FG 3	FG 4
Life after stroke but before MoTaStim-Foot	Challenges (1)	✓	✓	✓	
Confidence		✓	✓	✓	✓
Function	Improved function (1) Difficulties undertaking functional activities (2)	✓	✓	✓	
Meeting / achieving goals		✓			✓
Feeling of control or autonomy or achievement			✓		
Sense of achievement/goals achieved				✓	
Empowerment		✓			
Self-conscious		✓			
Fear of falling		✓	✓	✓	✓
Upper limb treatment		✓		✓	
Impact				✓	

Appendix 44 One sheet of paper analysis of focus groups examples-

One sheet of paper analysis for FG 1 – MTS (Analysis 1- uploaded to NVivo 20-1-18) – without quotes



One sheet of paper analysis for FG 1 – MTS (Analysis 1- uploaded to NVivo 20-1-18) – with quotes

Life after stroke

- Challenges
  - L290_E: Many people are interfering with your life
- L433-434_G: Well, when I was in the hospital lying in the bed and I thought, now I've come by yours, am I going to walk again? Now I know I will walk again.
- L966-969_J: I think when I had the stroke, I thought that was the finish
- L891-893_E: I stress to the positivity I've got of life. I just thought when I woke and I realised that the stroke…was…my illness and I thought that, er, there would be nothing…in life.

Overall experience on MoTaStim-Foot

- L461-463_E: For me it come for me as made me realise I'd got the left side of my body!
  L462_S: Yeah it was there and it was working
  E: Yeah that's what it's done for me, very nice, thanks!
- L67-70_E: over the duration of when the massage started I lost this feeling that the leg was broken ….. I must say things have turned out well for me because I can feel my left leg... L73-74_E: I think it is my brain realising that it's got a left side to the body and I think the treatment has brought that on
- 23_E: Can I just say, Alison, that I feel a ed person to have (*been part of the and)* what you have done…it's brilliant!
- L368-370_S: It was all hard work but good, it was hard work though and, er, they (ESD) gave me some treatment on my arm, my fingers, my movement that then there was the leg, so it was like it was good all round rehabilitation
- Feeling when MoTaStim-Foot finished

Changes in foot or leg

- L695-696_E: I've got the same…feeling, I can tell you what I'm walking on, with the feel, with the touch.
- L37_G: It was like…knowing I've got two legs instead of one.
- Sensory awareness of the foot or leg
- Improved movement
- L_698-700_ E: it had changed earlier through what you were doing to me, it changed because of the different feelings of that foot.
- L708-709_G: But I think my left leg now, foot, is as strong as my right one; there's not much difference in them.
- L668_G: I think I've got more movement in my foot.
- L116_S: it *(his leg)* was more practically useful

MTS

- L66_E: when the massage was done it was painful for me to
- Uncomfortable /challenging / too long
- L3319_G: It was a pity it had to come to an end
- L285_S: I felt it was a bit stress…stressful, a bit 'oh no, she's coming again'
- L90-91_E: the massage to the left side, its put everything in context.
- Benefits
- L305-307_E: the reward of doing the trial was that I could gain the mobility and as a human being to go and get access for cleaning hygiene and of course toilets

TSGT

- L193 - 194_GS: Well I feel if it wasn't for that treatment I wouldn't be walking now. L269_G: Great! I thought 'I'm going to get back on my feet again now'.
- Benefits
- Too much/too long / frustrating/painful or frightening

Empowerment

- L168_S: I am walking about point 88 miles a day
- L125-127_E: The treatment's given me the ability to walk with my partner. To get myself from A to B which is great, er…to do physical things that you expect your body to do, er, Yeah…I got that chance to achieve those goals

Participants receiving MTS and TSGT

- L761_G: Well every session I had I felt better after it.
- L272-273_S: Yeah it made me feel good as well that I could be back on my feet and using not using any sticks.
- L914_S: What I've achieved on the trial. Massive achievement.
- *L945-957 Comments re trial:* G: Brilliant! , F: I loved it, E: Yeah. I feel honoured that I've had that coaching by you guys S: Success, successful. Successful.
- L310-315_E: It made a big difference in my life for me and my partner because it meant I'd, well it meant to me, because I didn't like the idea of going in a wheelchair to the…town centre and to the…shopping facilities, with the wheel, sitting in a wheelchair and [*****] pushing me around I didn't enjoy that. The ability I'd got was that I could walk side by side with my partner to the shops and I enjoyed that part of life

Daily diaries

Venue

UL treatment

Meeting goals

- Sense of achievement
- L748-751_G: I feel different. I was out in the garden yesterday potting up and doing two hanging baskets.
- L819-822_E: I go out … my partner … while she's nattering to somebody I'll just walk away
- L757-758_S: I forgot my foot was bad, completely forgot and we remembered afterwards that it was my foot but…. it did do the thing what I expected a normal leg to do for me.

Function

- Improved function
- L779-781_G: Well its improved I think...I feel as though I want to walk **more** now. I want to get up and walk **now.**
- L272-273_S: Yeah it made me feel good as well that I could be back on my feet and using not using any sticks.

Confidence

- L228-229_GS: I'd like to say that the confidence you've given me in walking that helped me a lot
- L817_E: My confidence, yep, confidence has grown
- L787_G: Mine went as soon as **you** dropped off, my confidence dropped
- L242-244_J: Without you, I mean, er, I probably wouldn't have been walking properly I think. I feel I get up in the morning sometimes and I feel like I can run. Honestly, I feel like I can run again

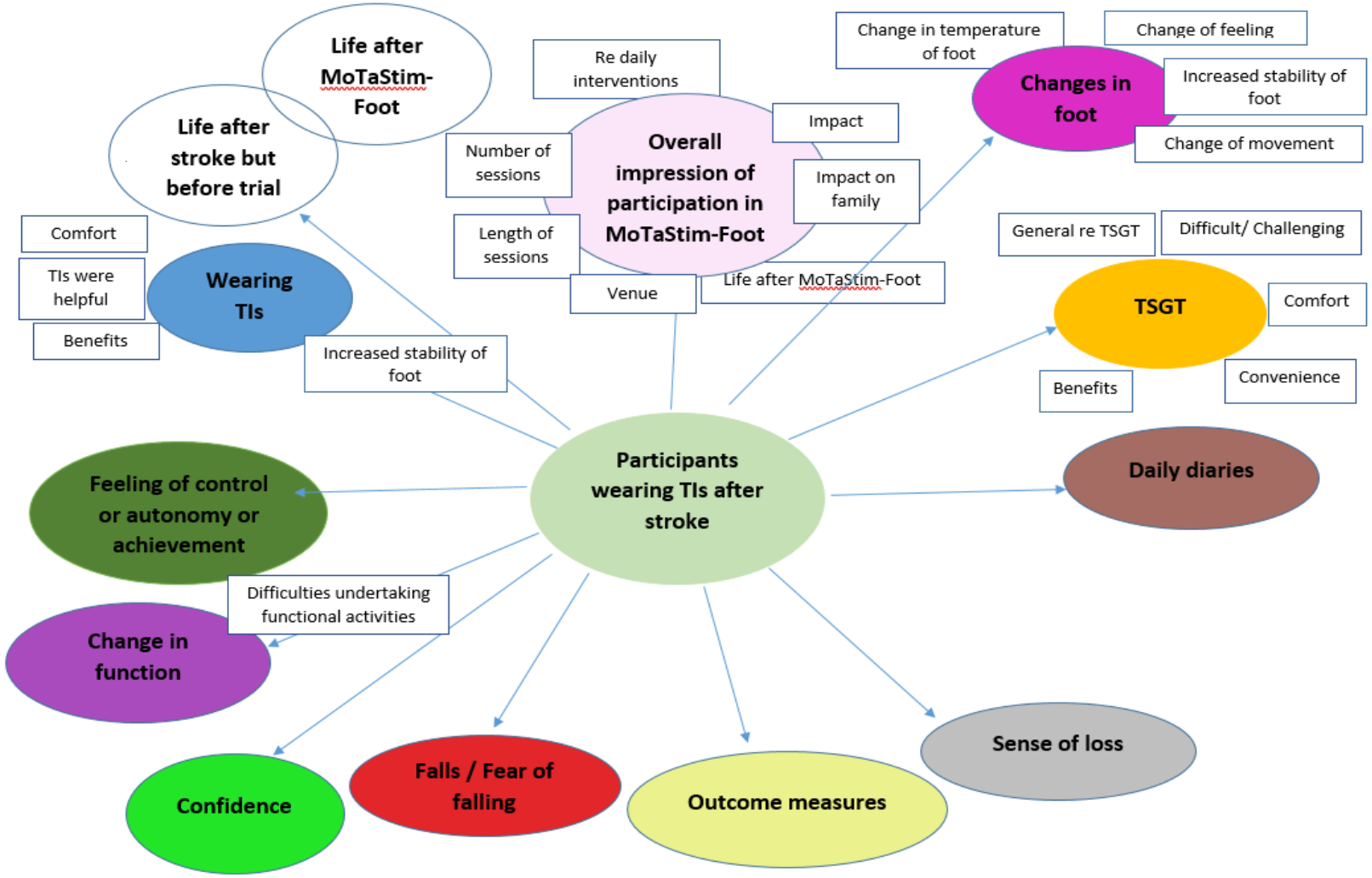
Fear of falling

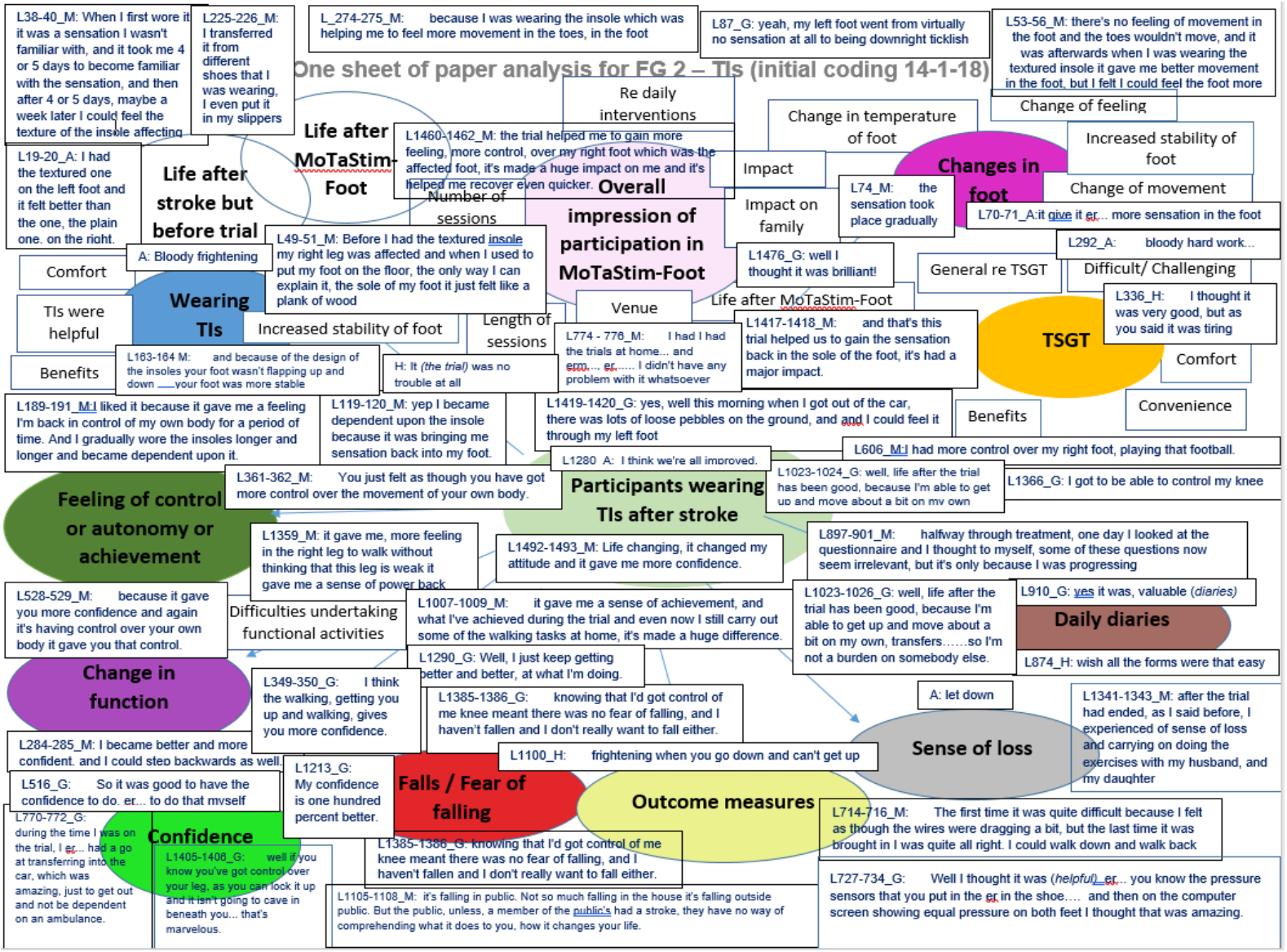
Outcome measures

Self conscious

- L845-851_S: this treatment has given me the ability to go out and to be walk into a store and, er, it's been great from that, it's been great; but the…but the **ability** it's given me, then, to see is actually worse!…It's worse in a different way. … you find that you're *[sigh]* struggling.
- L854-856_S: …it's the stroke…from the stroke, that three months of your treatment has been no doubt better because it's, you've gotta get out, you've gotta face the world and you just have to take, take it.

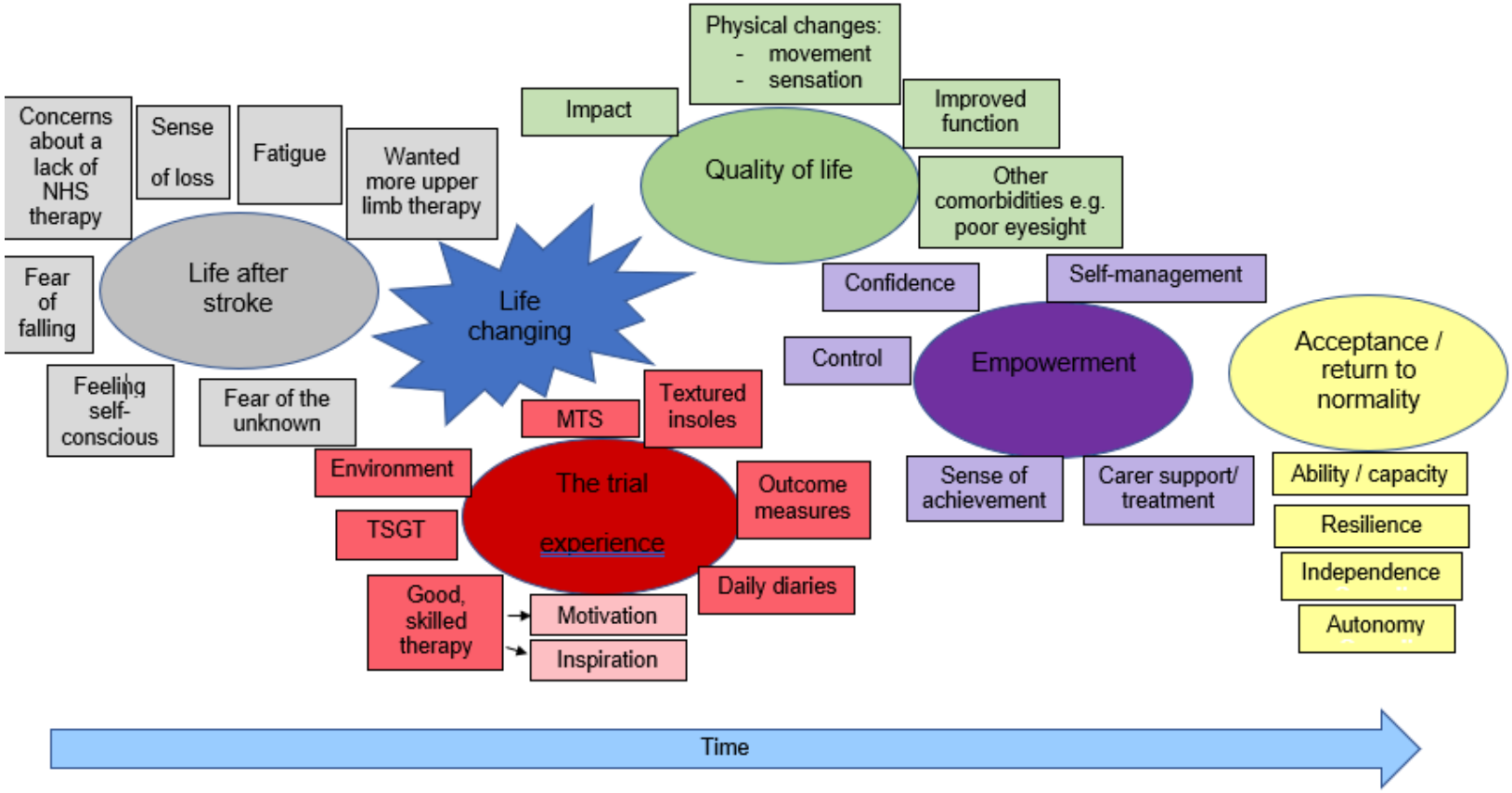
One sheet of paper analysis for FG 2 – TIs (initial coding 11-1-18) – without quotes



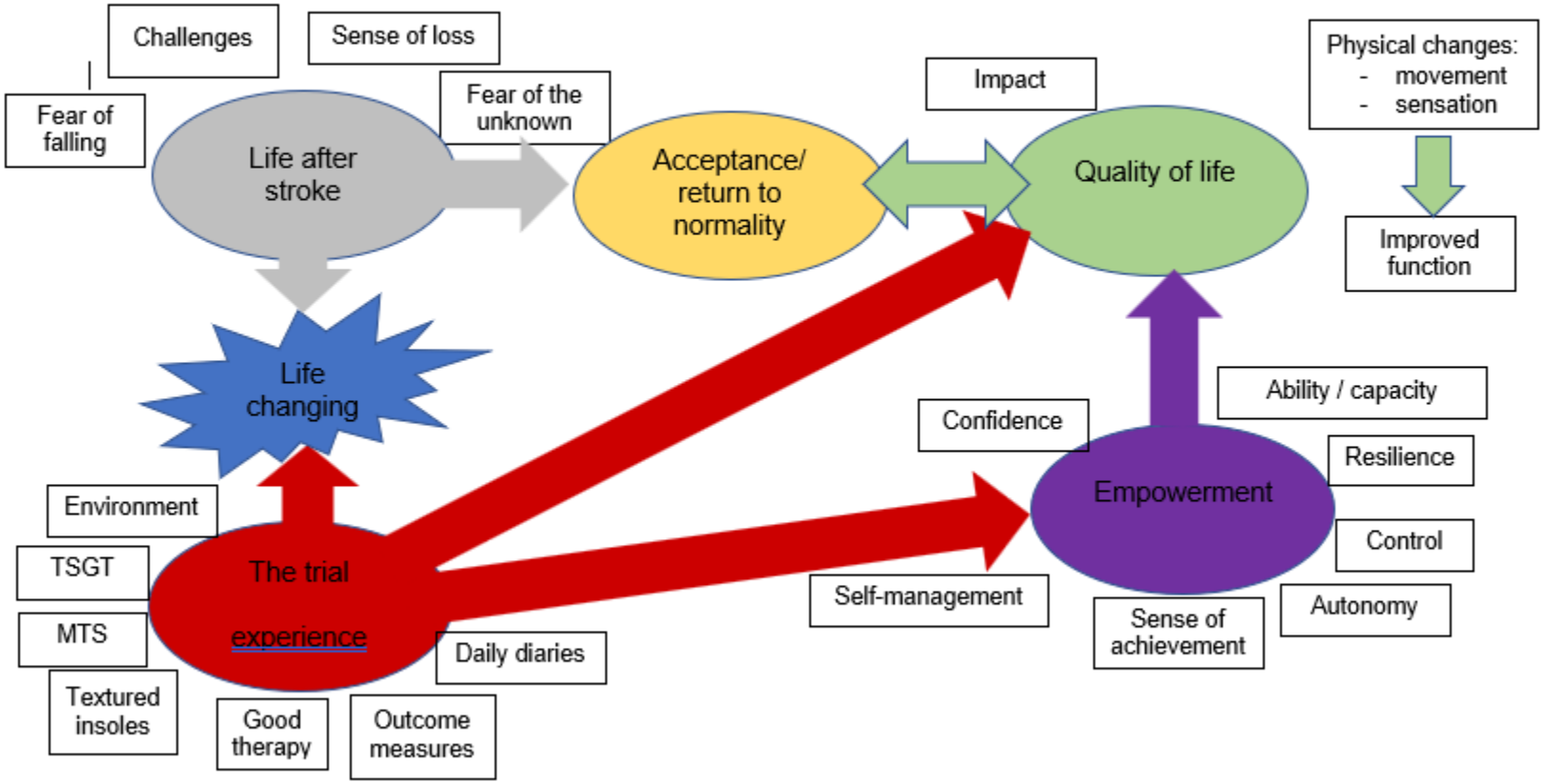

One sheet of paper analysis for FG 2 – TIs (initial coding 14-1-18)
L38-40_M: When I first wore it it was a sensation I wasn't familiar with, and it took me 4 or 5 days to become familiar with the sensation, and then after 4 or 5 days, maybe a week later I could feel the texture of the insole affecting
L225-226_M: I transferred it from different shoes that I was wearing, I even put it in my slippers
L_274-275_M: because I was wearing the insole which was helping me to feel more movement in the toes, in the foot
L87_G: yeah, my left foot went from virtually no sensation at all to being downright ticklish
L53-56_M: there's no feeling of movement in the foot and the toes wouldn't move, and it was afterwards when I was wearing the textured insole it gave me better movement in the foot, but I felt I could feel the foot more
Change of feeling
Re daily interventions
Change in temperature of foot
Increased stability of foot
Life after MoTaStim-Foot
L1460-1462_M: the trial helped me to gain more feeling, more control, over my right foot which was the affected foot, it's made a huge impact on me and it's helped me recover even quicker.
Overall impression of participation in MoTaStim-Foot
Impact
Changes in foot
Change of movement
L19-20_A: I had the textured one on the left foot and it felt better than the one, the plain one, on the right.
Life after stroke but before trial
Number of sessions
Impact on family
L74_M: the sensation took place gradually
L70-71_A:it give it er... more sensation in the foot
L292_A: bloody hard work...
A: Bloody frightening
L49-51_M: Before I had the textured insole my right leg was affected and when I used to put my foot on the floor, the only way I can explain it, the sole of my foot it just felt like a plank of wood
L1476_G: well I thought it was brilliant!
Comfort
General re TSGT
Difficult/ Challenging
Wearing TIs
Venue
Life after MoTaStim-Foot
L336_H: I thought it was very good, but as you said it was tiring
TIs were helpful
Increased stability of foot
Length of sessions
L1417-1418_M: and that's this trial helped us to gain the sensation back in the sole of the foot, it's had a major impact.
TSGT
L774 - 776_M: I had I had the trials at home... and erm..., er,..... I didn't have any problem with it whatsoever
L163-164 M: and because of the design of the insoles your foot wasn't flapping up and down ___your foot was more stable
H: It (the trial) was no trouble at all
Comfort
Benefits
L189-191_M:I liked it because it gave me a feeling I'm back in control of my own body for a period of time. And I gradually wore the insoles longer and longer and became dependent upon it.
L119-120_M: yep I became dependent upon the insole because it was bringing me sensation back into my foot.
L1419-1420_G: yes, well this morning when I got out of the car, there was lots of loose pebbles on the ground, and and I could feel it through my left foot
Benefits
Convenience
L606_M:I had more control over my right foot, playing that football.
L1280 A: I think we're all improved.
L361-362_M: You just felt as though you have got more control over the movement of your own body.
Participants wearing TIs after stroke
L1023-1024_G: well, life after the trial has been good, because I'm able to get up and move about a bit on my own
L1366_G: I got to be able to control my knee
Feeling of control or autonomy or achievement
L1359_M: it gave me, more feeling in the right leg to walk without thinking that this leg is weak it gave me a sense of power back
L1492-1493_M: Life changing, it changed my attitude and it gave me more confidence.
L897-901_M: halfway through treatment, one day I looked at the questionnaire and I thought to myself, some of these questions now seem irrelevant, but it's only because I was progressing
L528-529_M: because it gave you more confidence and again it's having control over your own body it gave you that control.
Difficulties undertaking functional activities
L1007-1009_M: it gave me a sense of achievement, and what I've achieved during the trial and even now I still carry out some of the walking tasks at home, it's made a huge difference.
L1023-1026_G: well, life after the trial has been good, because I'm able to get up and move about a bit on my own, transfers.....so I'm not a burden on somebody else.
L910_G: yes it was, valuable (diaries)
Daily diaries
L874_H: wish all the forms were that easy
Change in function
L1290_G: Well, I just keep getting better and better, at what I'm doing.
L349-350_G: I think the walking, getting you up and walking, gives you more confidence.
L1385-1386_G: knowing that I'd got control of me knee meant there was no fear of falling, and I haven't fallen and I don't really want to fall either.
A: let down
L1341-1343_M: after the trial had ended, as I said before, I experienced of sense of loss and carrying on doing the exercises with my husband, and my daughter
L284-285_M: I became better and more confident, and I could step backwards as well.
L1100_H: frightening when you go down and can't get up
Sense of loss
L516_G: So it was good to have the confidence to do, er... to do that myself
L1213_G: My confidence is one hundred percent better.
Falls / Fear of falling
Outcome measures
L714-716_M: The first time it was quite difficult because I felt as though the wires were dragging a bit, but the last time it was brought in I was quite all right. I could walk down and walk back
L770-772_G: during the time I was on the trial, I er... had a go at transferring into the car, which was amazing, just to get out and not be dependent on an ambulance.
Confidence
L1405-1406_G: well if you know you've got control over your leg, as you can lock it up and it isn't going to cave in beneath you... that's marvelous.
L1385-1386_G: knowing that I'd got control of me knee meant there was no fear of falling, and I haven't fallen and I don't really want to fall either.
L1105-1108_M: it's falling in public. Not so much falling in the house it's falling outside public. But the public, unless, a member of the public's had a stroke, they have no way of comprehending what it does to you, how it changes your life.
L727-734_G: Well I thought it was (helpful) er... you know the pressure sensors that you put in the er in the shoe.... and then on the computer screen showing equal pressure on both feet I thought that was amazing.

Appendix 45 Audit trail – how the themes were developed

Overall themes for all focus groups following discussions with SR, SH and PB 20/3/18



FG 1 & 2 – Further analysis by AA following discussions with SR and SH 5/4/17



Appendix 46 Fatigue and pain monitoring form

MoTaStim-Foot Study Protocol version 4.0 23-10-16 FORM P Pain and Fatigue Page 2

Site Number Screening Number Participant Number (ID) Date of Visits:

01 / 02 03 D D M M Y Y Y Y TO D D M M Y Y Y Y 04

	Date of Intervention (ddmmyyyy)	Pain B = Behavioural V = Verbal	Adverse Event Yes/No	Adverse Event Reference (to be completed if reported as adverse event)	Fatigue (Motricity Index Lower Limb Score) Ankle / Knee / Hip	Adverse Event Yes/No	Adverse Event Reference (to be completed if	Research Therapist Initials
16.	d d m m y y y y 05	Yes (B) 1 Yes (V) 2 No 3 06	Yes 1 No 2 07	/ A E 08	TOTAL 09	Yes 1 No 2 10	/ A E 11	12
17.	d d m m y y y y 13	Yes (B) 1 Yes (V) 2 No 3 14	Yes 1 No 2 15	/ A E 16	TOTAL 17	Yes 1 No 2 18	/ A E 19	20
18.	d d m m y y y y 21	Yes (B) 1 Yes (V) 2 No 3 22	Yes 1 No 2 23	/ A E 24	TOTAL 25	Yes 1 No 2 26	/ A E 27	28
19.	d d m m y y y y 29	Yes (B) 1 Yes (V) 2 No 3 30	Yes 1 No 2 31	/ A E 32	TOTAL 33	Yes 1 No 2 34	/ A E 35	36
20.	d d m m y y y y 37	Yes (B) 1 Yes (V) 2 No 3 38	Yes 1 No 2 39	/ A E 40	TOTAL 41	Yes 1 No 2 42	/ A E 43	44
21.	d d m m y y y y 45	Yes (B) 1 Yes (V) 2 No 3 46	Yes 1 No 2 47	/ A E 48	TOTAL 49	Yes 1 No 2 50	/ A E 51	52
22.	d d m m y y y y 53	Yes (B) 1 Yes (V) 2 No 3 54	Yes 1 No 2 55	/ A E 56	TOTAL 57	Yes 1 No 2 58	/ A E 59	60
23.	d d m m y y y y 61	Yes (B) 1 Yes (V) 2 No 3 62	Yes 1 No 2 63	/ A E 64	TOTAL 65	Yes 1 No 2 66	/ A E 67	68
24.	d d m m y y y y 69	Yes (B) 1 Yes (V) 2 No 3 70	Yes 1 No 2 71	/ A E 72	TOTAL 73	Yes 1 No 2 74	/ A E 75	76
25.	d d m m y y y y 77	Yes (B) 1 Yes (V) 2 No 3 78	Yes 1 No 2 79	/ A E 80	TOTAL 81	Yes 1 No 2 82	/ A E 83	84
26.	d d m m y y y y 85	Yes (B) 1 Yes (V) 2 No 3 86	Yes 1 No 2 87	/ A E 88	TOTAL 89	Yes 1 No 2 90	/ A E 91	92
27.	d d m m y y y y 93	Yes (B) 1 Yes (V) 2 No 3 94	Yes 1 No 2 95	/ A E 96	TOTAL 97	Yes 1 No 2 98	/ A E 99	100
28.	d d m m y y y y 101	Yes (B) 1 Yes (V) 2 No 3 102	Yes 1 No 2 103	/ A E 104	TOTAL 105	Yes 1 No 2 106	/ A E 107	108
29.	d d m m y y y y 109	Yes (B) 1 Yes (V) 2 No 3 110	Yes 1 No 2 111	/ A E 112	TOTAL 113	Yes 1 No 2 114	/ A E 115	116
30.	d d m m y y y y 117	Yes (B) 1 Yes (V) 2 No 3 118	Yes 1 No 2 119	/ A E 120	TOTAL 121	Yes 1 No 2 122	/ A E 123	124

Adapted from the template by Robertson Centre for Biostatistics, University of Glasgow

Version 1.3 15/11/16

Appendix 47 Trial management group terms of reference

Document Title:	**MoTaStim-Foot** **Trial Management Group (TMG) Terms of Reference**
Document Type:	**Terms of Reference (ToR)**
Version Number:	**1.0**
Date of Final Release:	**5th May 2016**
Review Date: 1 year from initial release and 2 years thereafter	
(If applicable) Version of ToR being superseded:	

Author	Title	Signature	Date
Alison Aries	Chief Investigator		
Reviewer	**Title**	**Signature**	**Date**
Dr Sue Hunter	Supervisor		

Details of NCTU Trial Management Group (TMG)	
Introduction	
Name of trial	MoTaStim-Foot – Sensory training for the foot and ankle early post stroke: A feasibility study.
Name of Trial Management Group (TMG)	MoTaStim-Foot TMG
Sponsors Name & ID	Keele University / 2013-338.
	The purpose of this document is to describe the membership, terms of reference, roles, responsibilities, authority, decision-making and relationships of the TMG for the MoTaStim-Foot trial, including the timing of meetings, methods of providing information to and from the TMG, frequency and format of meetings and relationships with other trial committees.
Facilitation	The Chief Investigator (Alison Aries) will act as Facilitator for the TMG. The Facilitator will be responsible for the organisation of meetings and should be copied into all communications with the TMG and other bodies and between the TMG members.
Roles and Responsibilities	
A broad statement of the aims of the TMG	The TMG is led by the Chief Investigator (CI) who is responsible for leading the activities associated with trial management.
Specific roles of TMG	• provide expert input into the development of trial specific

Details of NCTU Trial Management Group (TMG)	
	documents and procedures necessary to run the trial • monitor patient safety in order to protect the rights, safety and wellbeing of patients • monitor recruitment rates and develop strategies to deal with any recruitment problems • review regular reports of the trial from the Chief Investigator (Alison Aries) and Norwich CTU • be aware of and provide to other TMG members any accumulating external evidence relevant to the intervention or treatment of patients • monitor completion rates of CRFs and assist the trial team to encourage satisfactory completion in the future • monitor follow-up rates and develop strategies to deal with problems • review reports of quality management and monitoring activities from the trial team and advise on and help to promote strategies to maintain the collection of high quality data • advise on any amendments to the protocol, where appropriate • provide input into any issues with patient recruitment and sample collection for mechanistic sub studies • propose any changes to the design of the trial, including additional sub studies • provide input into the timely reporting of trial results

Details of NCTU Trial Management Group (TMG)	
	• develop the publication strategy for the main trial and any secondary publications • provide input into the main trial manuscript and secondary publications where appropriate • provide input into any abstracts and presentations of any results *during* the running of the trial • review external or early internal requests for release of data or subsets of data or samples including clinical data and stored biological samples
Before or early in the trial	
Protocol Input	All TMG members will be given a copy of the protocol for MoTaStim-Foot, which has been developed in collaboration with Norwich CTU and PPI advisors.

Details of NCTU Trial Management Group (TMG)	
Composition	
Membership	The TMG membership includes: Alison Aries (Chief Investigator/ Principal Investigator / Research Fellow) Dr Sue Hunter (Primary Supervisor, Keele University) Prof Valerie Pomeroy (Supervisor, UEA) Prof Sue Read (Supervisor, Keele University) Prof Julius Sim (Supervisor, Keele University) Patient and Public Involvement (PPI) advisor Carolyn Belford, Clinical Specialist (Band 8) Physiotherapist from the recruiting centre (SSOTP). Frances Davies (Research Delivery Unit Manager) Prof Christine Roffe (Consultant Stroke Physician, UHNM) Dr Erika Sims (Senior Clinical Trials Operations Manager Norwich Clinical Trials Unit (CTU))
Responsibilities of the NCTU Trial Team	The Chief Investigator will produce a short report on the trial before each meeting of the TMG.
Relationships	
Relationships with Chief Investigators, other trial committees (e.g. TSC and DMC),	The responsibilities of each trial committee are detailed in the protocol and in the respective Terms of Reference. The

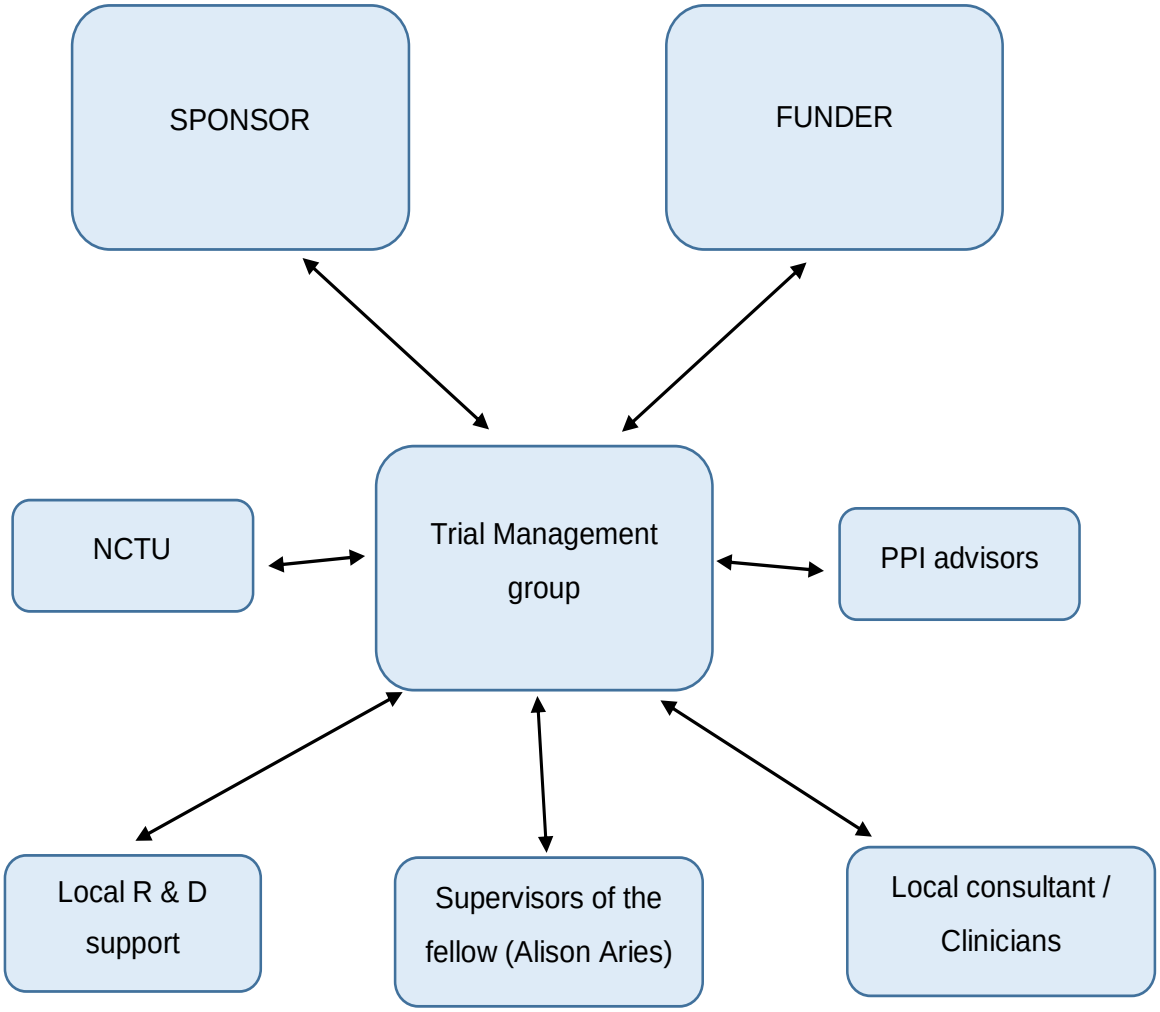
Details of NCTU Trial Management Group (TMG)	
Sponsor/Funder and regulatory bodies	relationships between these groups are summarised in figure 1.
Payments to TMG members	Reasonable travel costs (where necessary) and other expenses will be reimbursed. No other payments or rewards will be given to professional members.
The need for TMG members to disclose information about any real or potential competing interests	Any competing interests, either real or potential, should be disclosed. These are not restricted to financial matters – involvement in other trials or intellectual investment could be relevant. Although members may well be able to act objectively despite such connections, complete disclosure enhances credibility (Annexe 1) TMG members should not use any trial data to inform trading of products related to the trial e.g. textured insoles, and careful consideration should be given to trading in stock of companies with competing products. Changes in declarations of real or potential competing interests should be minuted at the start of each meeting.
Organisation of meetings	
Expected frequency of TMG meetings	The TMG will plan to meet 4 monthly. At the request of the TMG interim meetings, in person or by teleconference, will be organised. Trial issues may need to be dealt with between meetings, by phone or by email. TMG members should be prepared for such instances.

Details of NCTU Trial Management Group (TMG)	
Attendance of TMG members at meetings	Effort will be made for all members to attend. The Facilitator will work for a date that enables this. Members who cannot attend in person should be encouraged to participate by teleconference. If, at short notice, any TMG members cannot attend then the TMG may still meet if at least two independent members, including the Chair – Alison Aries, (unless otherwise agreed), will be present as well as a representative of the trial team. If the TMG is considering a major action after such a meeting the TMG Chair should communicate with the absent members, including the CI, as soon after the meeting as possible to check that they agree. If they do not, a further teleconference should be arranged with the full TMG. Similarly, if the Chair is unavoidably absent and there are difficult issues or disagreements raised at the meeting, these issues should be dealt with by telephone discussion, or email, through the Chair, as soon after the meeting as possible and, if necessary, a teleconference arranged with the full TMG.
How TMG meetings will be organised, especially regarding open and closed sessions, including who will be present in each session	Presence will be usually limited to the TMG members, observers from the Sponsor/Funder, trials unit and the Facilitator. Other attendees may be invited for all or part of the meeting as required.
Can TMG members who cannot attend the meeting input?	If the report is circulated before the meeting, TMG members who will not be able to attend the meeting may pass comments to the TMG Chair/Facilitator or MoTaStim-Foot trial team for consideration during the discussions.

Details of NCTU Trial Management Group (TMG)	
What happens to members who do not attend meetings?	If a member does not attend a meeting or provide comments when requested between meetings, it should be ensured, where possible, that the member is available for the next meeting. If a member does not attend the next meeting or provide comments when next requested, they should be asked if they wish to remain part of the TMG. If a member does not attend a third meeting, strong consideration should be given to replacing that member.
Trial documentation and procedures to ensure confidentiality and proper communication	
Intended content of material to be considered during meetings	A short report will be prepared by the Chief Investigator following a standard template. This will report on accrual and any matters affecting the trial. Additionally, the material may include draft publications. No trial outcome measure data will be presented by arm. Where relevant, accrual, compliance with follow-up and adherence to treatment may be presented.
Responsibility for identifying and circulating external evidence (e.g. from other trials/ systematic reviews)	Identification and circulation of external evidence (e.g. from other trials/ systematic reviews) is a responsibility of the TMG.

Details of NCTU Trial Management Group (TMG)	
What will happen to the papers after the meeting	TMG members should delete, destroy or store securely copies of the reports to and from the TMG, agenda and minutes, as well as copies of communications between meetings. All documentation should be considered confidential. The Chief Investigator/Facilitator (Alison Aries) will keep a central record of all minutes, reports and correspondence by the TMG.

FIGURE 1: RELATIONSHIPS WITHIN THE MoTaStim-Foot TRIAL



Abbreviations:

NCTU= Norwich Clinical Trials Unit

PPI – Patient and Public Involvement

R & D = Research and development

Main point of contact is Alison Aries the Fellow / Chief Investigator / Facilitator via email: a.m.aries@keele.ac.uk

ANNEXE 1: AGREEMENT AND POTENTIAL COMPETING INTERESTS FORM FOR MEMBERS

MoTaStim-Foot: Agreement to join the Trial Management Group and disclosure of potential competing interests

Please complete the following document and return to the Facilitator.

(Please initial box to agree)

	I have read and understood the TMG Terms of Reference version 1.0 6/4/16
	I agree to join the TMG for this trial
	I agree to treat all sensitive trial data and discussions confidentially

The avoidance of any perception members of a TMG may be biased in some fashion is important for the credibility of the decisions made by the TMG and for the integrity of the trial.

Potential competing interests should be disclosed via Alison Aries (Chief Investigator for MoTaStim-Foot trial). In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) TMG member should remove the conflict or stop participating in the TMG. The table below lists potential competing interests.

Potential Competing Interests for TMG Members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Career tied up in a product or technique assessed by trial
- Intellectual conflict e.g. strong prior belief in the trial's experimental arm
- Involvement in regulatory issues relevant to the trial procedures
- Investment (financial or intellectual) or career tied up in competing products
-

(Please tick as appropriate)

	No, I have no potential competing interests to declare
	Yes, I have potential competing interests to declare (please detail below)

Please provide details of any potential competing interests:

_____

_____

_____

Name: _____

Signed: _____ Date: _____

Appendix 48 Adverse events

List of adverse events

Pain ? Flare up of Polymyalgia Rheumatica

Falls x 16

Back pain x2

Painful heel (ipsilesional side)

Viral infection

Atrial fibrillation

Pain back of heel (pressure sores)

Scratch on dorsum of foot

Tired with swollen painful feet

UTI

Pain hip and knee

Slip off bed – laceration of shin

Serious adverse events x3

Fall – hip pain no bony injury

Chest infection admitted to hospital overnight

Further stroke

Appendix 49 Email from participant one re inclusion of people with a posterior circulation stroke

23/11/2015

to me, Sue

Hi Ladies

I hope you are both well and not working too hard!!!

1) The main difference between anterior and posterior strokes for me would be the ataxia that some posterior stroke patients suffer from. The severity of the ataxia certainly does vary an great deal from patient to patient with some being affected a great deal and some not at all. there's also the visual problems that some posterior stroke patients suffer from.

2) I would definitley use MTS and foot prep in these groups of patients as I think it is important that the patients have a stable base to mobilise on when they are unsteady. In the early days it is successful as it can stimulate and strenghten otherwise weak feet and improve activation of dorsiflexion.

I have used MTS in more chronic patients too as I find that ataxic patients can end up with tight, inflexible feet as they adopt and 'fix'. So MTS has been useful too. I learnt this from a training day we had at the haywood years ago with an ex Bobath tutor on the best way to treat ataxic patients. I used it ever since.

Hope that helps and makes sense!!

Clare