The evaluation of and comparative evidence for two types of interventional devices for foot-drop of central neurological origin.

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I would also to thank all the collaborators involved in the presented publications, both researchers and participants. Their enthusiasm and commitment has inspired me.

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Abbreviations

AFO	Ankle Foot Orthosis
ARIMA	Autoregressive Integrated Moving Average
AT	Assistive Technology
BFS	Body Functions and Structures
BI	Brain Injury
CAST	Calibration Anatomical System Technique
CE	Conformité Européenne
CNO	Central Neurological Origin
CP	Cerebral Palsy
CQ	Capacity Qualifiers
DF	Dorsiflexion
DMO	Dynamic Movement Orthoses
EMG	Electromyography
FAC	Functional Ambulation Categories
FDS	Foot Drop Stimulation
FES	Functional Electrical Stimulation
FHEQ	Framework for Higher Education Qualifications
HTD480	Health Technology Devices (project 480)
IC	Initial Contact
ICF	International Classification of Functioning, disability and health
ISPGR	International Society of Posture and Gait Research
ITSA	Interrupted Time-Series Analysis
MAS	Modified Ashworth Scale
MCID	Minimal Clinically Important Difference
mEFAP	modified Emory Functional Ambulation Profile
MRC	Medical Research Council
MS	Multiple Sclerosis

NHS	National Health Service
NHSQIS	NHS Quality Improvement Scotland
NICE	National Institute for health and Care Excellence
NIHR	National Institute for Health Research
PCI	Physiological Cost Index
PF	Plantarflexion
PhD	Doctor of Philosophy
PQ	Performance Qualifiers
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PROSPERO	International prospective register of systematic reviews
QAA	Quality Assurance Agency
QUEST 2.0	Quebec User Evaluation of Satisfaction with Technology 2.0
QoL	Quality of Life
RCT	Randomised Controlled Trial
ROM	Range Of Movement
SCED	Single Case Experimental Design
SCI	Spinal Cord Injury
SD	Standard Deviation
SIGN	Scottish Intercollegiate Guidelines Network
SIS	Stroke Impact Scale
THBI	Total Heart Beat Index
Tib Ant	Tibialis Anterior
TUG	Timed Up and Go
UK	United Kingdom
UKIFESS	UK and Ireland chapter of the International FES Society
UMNS	Upper Motor Neuron Syndrome
WHO	World Health Organisation

Declaration

I, **Sarah Prenton**, hereby declare that this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis. With regards primary research, I have maintained confidentiality of participants throughout the research.

This thesis has been completed under the guidance of supervisors at the University of Salford (School of Health Sciences) for the award of Doctor of Philosophy (PhD) by Published Works and adheres to University of Salford's Code of Practice for the Conduct of Postgraduate Research Degree Programmes 2016/17 (University of Salford, 2016)

Signature _____ **Date**_____

A brief overview of the contribution to each article by the PhD candidate is as follows[1]:

Article	Contribution by S. Prenton (PhD candidate)
1 Williamson et al. (2015)	• Involved in lay-advisory group: suggested and led sessions related to the design of two clinical studies and also involved in other sessions about device development • Provided manuscript feedback
2 Prenton, Kenney, Cooper, and Major (2014)	• Made methodological decisions • Gained ethical approval • Recruited participants • Collected data • Completed data analysis • Wrote manuscript and managed re-writes based on co-author feedback • Chose Journal(s) and managed re-writes based on reviewer and co-author feedback
3 Prenton, Kenney, Stapleton, et al. (2014)	• Conceptualised study • Involved in device development • Designed study • Gained ethical (University & IRAS) and R&D approval • Recruited participants • Collected data • Completed data analysis • Wrote manuscript and managed re-writes based on co-author feedback • Chose Journal(s) and managed re-writes based on reviewer and co-author feedback
4 Kenney et al. (2016)	• Discussed clinical evaluation and discussion sections of manuscript • Provided manuscript feedback
5 Prenton, Hollands, and Kenney (2016) & 6 Prenton, Hollands, Kenney and Onmanee (2018)	• Conceptualised reviews and chose focus • Developed protocol including all methodological choices, with feedback from co-authors • Submitted protocol to PROSPERO and managed updates • Completed phase 1 (screening of titles and abstracts) • Completed phase 2 (screening of full articles) alongside co-author (K. Hollands Article 5 and P. Onmanee Article 6) • Completed quality assessment alongside co-author (as previous point) • Did all meta-analyses and narrative syntheses • Wrote manuscript and managed re-writes based on co-author feedback • Chose Journal(s) and managed re-writes based on reviewer and co-author feedback

Table 1: Overview of candidate's contribution to each article presented in the thesis

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[1] A list of the collaborators for the articles that constitute the body of work presented in this thesis and a summary of what they contributed is presented in Appendix 1

Substantiation of candidate's contribution

The contribution of the PhD candidate has been recognised by Professor Laurence Kenney for all the articles included in this PhD by Published Works thesis as he has been a co (or lead)-author on them all.

I hereby declare that the following statements have been satisfied in accordance with the University of Salford's Code of Practice for the Conduct of Postgraduate Research Degree Programmes 2016/17 (University of Salford, 2016).

- The contribution of the PhD candidate in the above table is accurate
- No eligible co-author has been denied authorship
- No ineligible co-author has been included on any article
- Where appropriate acknowledgements have been made to contributors who did not satisfy enough criteria to be considered as a co-author

Signed   **Date**_____

Professor Laurence Kenney

THESIS ABSTRACT

Introduction

This thesis focusses on ankle foot orthoses (AFO) and functional electrical stimulation (FES) for the correction of foot-drop. It consists of two parts linked through identification of three gaps in the knowledge base: 1) limitations in device design, 2) limitations in device evaluation and 3) a lack of clear clinical guidance surrounding which of the two devices to use.

Methods and Results

PART 1 reports on the design and evaluation of an AFO alternative (dorsiflex sock) and an alternative to conventional FES systems (ShefStim®). Article 1 reports the evaluation of the researcher/user co-design approach used in the development of both devices, finding that lay-advisory involvement guided aspects such as where to locate the stimulator and informed the revision of the evaluation studies. Article 2 used a single case experimental design with 2 stroke participants to preliminarily explore the efficacy and user views of the dorsiflex sock. It found no clear evidence to demonstrate that the dorsiflex sock with its current design was effective, despite user views to the contrary.

Article 3 reported on the feasibility of ShefStim®. Seven current foot-drop FES users used ShefStim® unsupervised for two weeks at home, alongside gait laboratory testing of foot-clearance and kinematics at initial contact. Number of heel rises in day-day use was logged, as well as user satisfaction, donning/setup times and diary data. This data demonstrated that ShefStim® could be used in the community. Lab-based testing suggested that ShefStim® was comparable to conventional FES systems with regards kinematics at initial contact and foot-clearance. User satisfaction was comparable for both devices. However, further product refinement around setup and the electrode array-skin interface is necessary to make ShefStim® commercially viable. Article 4 reports on the design, development and evaluation of ShefStim®.

PART 2 comprises two meta-analyses focussing on orthotic (Article 5) and therapeutic (Article 6) effects. Article 5 revealed statistically comparable positive orthotic effects on walking speed, exercise capacity and the stroke impact scale. Article 6 found comparable therapeutic speed increases, but both reviews highlighted the lack of high quality evidence

on use of each device outside of the laboratory. It was not possible draw any conclusions about the mechanisms-of-action underlying these findings.

Conclusion and future study

The dorsiflex sock and ShefStim® are both feasible devices and the novel approaches taken to their evaluation merit wider use in the field. Further work is necessary to improve the design of both devices before definitive clinical trials are carried out.

Despite AFO and FES showing similar levels of efficacy there is very little published work on the real world evaluation of either type of device or foot-drop specific mechanistic evaluations that might help to guide clinical choice. Therefore, this thesis highlights the need for further comparative randomised controlled trials, focussing on biomechanical and real world measures, informed by potential end-users.

CHAPTER 1: CONTEXTUAL BACKGROUND

1.1 Walking

Independent walking is a primary goal for most people with disorders of central neurological origin (CNO) such as cerebrovascular accident/stroke, cerebral palsy (CP), multiple sclerosis (MS) or other brain injury (BI) or spinal cord injury (SCI) (de Wit, Buurke, Nijlant, IJzerman, & Hermens, 2004; Dobkin, 2005; Intercollegiate Stroke Working Party, 2016) as well as their families and health professionals (Condie, Campbell, & Martina, 2004). Functional walking has been characterised by five key features (Baker, 2013). Crucially these include the ability to clear the foot sufficiently during swing and having a smooth transition from swing to stance. These abilities are frequently disrupted by what is known as foot-drop/ drop foot/ equinus/ equinovarus.

1.2 Foot-drop

Although the literature on prevalence of foot-drop is both old and reports on limited numbers of participants, foot-drop is estimated to be present in around 20% of the most prevalent of the CNO disorders population, stroke (Verdié et al., 2004; Wade, Wood, Heller, Maggs, & Langton Hewer, 1987). Prevalence data is not published for other CNO disorders but, based on the stroke numbers alone, there are approximately 240,000 people in the United Kingdom (UK) who may have foot-drop (Stroke Association, 2016).

Foot-drop gait is characterised by a lack of ankle dorsiflexion (DF) (Dunning, O'Dell, Kluding, & McBride, 2015) often accompanied by a lack of eversion. This is a result of what is referred to as the upper motor neuron syndrome (UMNS) (Carr & Shepherd, 2010; Sheean & McGuire, 2009) where negative features such as weakness/ paralysis sit alongside positive features such as spasticity. These, in combination with imposed immobility and disuse, leads over time to secondary musculoskeletal issues such as increased muscle stiffness, often termed adaptive features (Carr & Shepherd, 2010).

In the case of foot-drop the UMNS causes an imbalance between the activity in muscles of the anterior compartment of the lower leg (Figure 1: left) and triceps surae complex posteriorly (Carr & Shepherd, 2010) (Figure 1: middle and right).
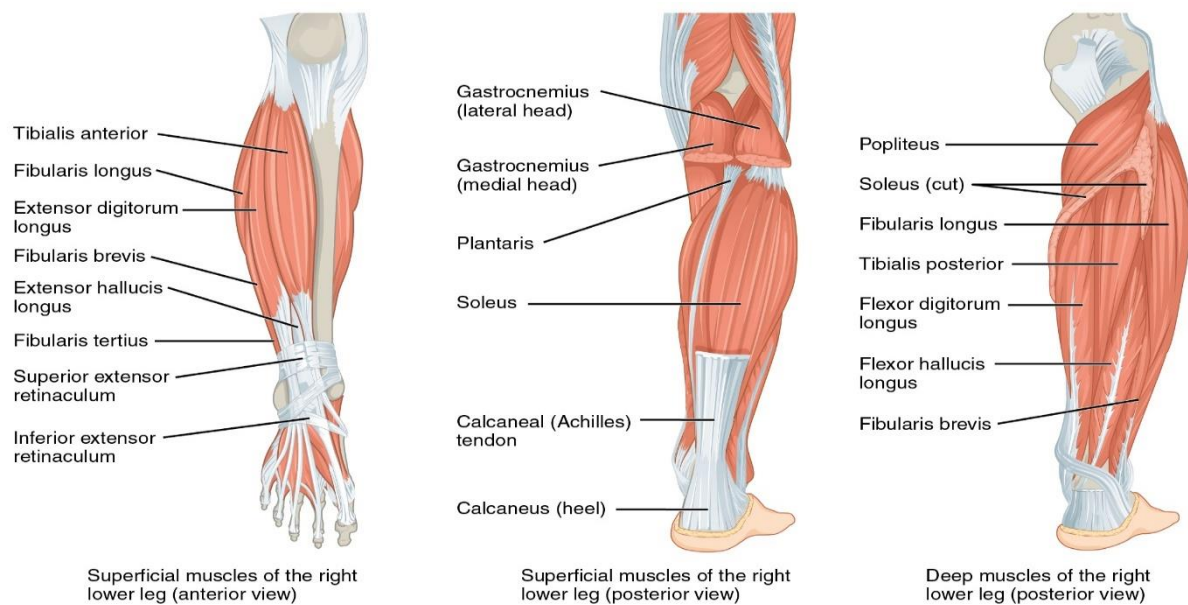
Tibialis anterior

Fibularis longus

Extensor digitorum longus

Fibularis brevis

Extensor hallucis longus

Fibularis tertius

Superior extensor retinaculum

Inferior extensor retinaculum

Gastrocnemius (lateral head)

Gastrocnemius (medial head)

Plantaris

Soleus

Calcaneal (Achilles) tendon

Calcaneus (heel)

Popliteus

Soleus (cut)

Fibularis longus

Tibialis posterior

Flexor digitorum longus

Flexor hallucis longus

Fibularis brevis

Superficial muscles of the right lower leg (anterior view)

Superficial muscles of the right lower leg (posterior view)

Deep muscles of the right lower leg (posterior view)

Figure 1: Muscles of the Lower Leg by OpenStax licensed under CC BY 4.0.

Foot-drop affects both the stance and swing periods of the gait cycle but fundamentally it makes the ability to clear the foot during swing more challenging, which increases the risk of tripping (Blaya & Herr, 2004). It also inhibits the ability to make initial contact (IC) with the heel at the start of stance (Leung & Moseley, 2003) making this transition less stable and smooth, which also reduces stability. These two factors can restrict the person's motivation, confidence and ability to walk in their own environment.

Given its prevalence and impact, the foot-drop impairment is of clinical importance and any intervention that can address it warrants investigation. The most commonly used interventions to address foot-drop are physiotherapy, botulinum toxin, surgery, orthotics and functional electrical stimulation (FES). This thesis focuses on the two most common devices to correct foot-drop; orthotics and FES.

1.3 Ankle Foot Orthoses

Orthotics, most commonly ankle-foot orthoses (AFO), are the most frequently used device for foot-drop (Bosch, Harris & Wing, 2014). AFOs are externally applied devices that add stiffness to the ankle joint complex thereby controlling its motion and alignment (National Health Service (NHS) Quality Improvement (NHSQIS) Scotland, 2009). The mechanical properties of an AFO, notably stiffness (Bregman et al., 2010; Bregman et al., 2011), can be

manipulated through the geometry of the device and choice of materials during the design stage to achieve the desired outcome. There are a range of AFO designs (NHSIQ, 2009). Posterior leaf spring and hinged AFOs address foot-drop caused by anterior compartment musculature weakness but may not address any associated medio-lateral instability or over activity in the triceps surae complex (NHSIQ, 2009). Unlike posterior leaf spring AFOs, hinged AFOs allow tibial progression through stance supporting a more typical gait pattern. However, a hinged AFO cannot be used if there is inadequate length in gastrocnemius, as this will limit knee extension (NHSIQ, 2009). Solid AFOs, and ground reaction AFOs (derivatives of solid AFOs), provide medio-lateral stability and are indicated when foot-drop is caused by over activation of the triceps surae complex, as opposed to DF weakness. Ground reaction AFOs can also alter knee moments during gait, which may be beneficial in certain cases. The choice of which to use and how to customise the AFO to the individual user should be made by an orthotist (NHSIQ, 2009) following a detailed assessment, with the aim to provide external plantigrade support to help with foot clearance and stability during stance (Mulroy, Eberly, Gronely, Weiss, & Newsam, 2010) by altering the biomechanics of the whole lower limb. AFOs have been shown to statistically increase DF at IC as well as increasing peak DF during early stance, toe off and swing (Tyson, Sadeghi-Demneh, & Nester, 2013); although it should be noted that peak DF through swing does not accurately capture either toe or foot clearance. Wearing an AFO during walking influences not only the ankle but also the more proximal joints in the lower extremity (Karandikar & Vargas, 2011). With regards the knee AFOs have been shown to increase flexion at IC, increase peak flexion during the loading response of the stance phase and improve peak extension in stance phase (Tyson et al., 2013). No statistically significant kinematic effects have been observed at the hip. AFOs have also been shown to facilitate weight bearing over the paretic leg during stance (Tyson et al., 2013).

It is also accepted that reducing or eliminating the foot-drop impairment by wearing an AFO then allows for an increase in repetitive task-specific activity, walking, which is accepted as causing functional improvement (Langhorne, Coupar, & Pollock, 2009; National Institute of health and Care Excellence (NICE), 2014; Intercollegiate Stroke Working Party, 2016). The link between repetitive task-specific activity and functional improvement assumes neuromuscular plasticity, in which cells are able to phenotypically change in response to

changes in their state or environment (Brown & Hardman, 1987, as cited in Laidler, 1994). This process is experience-dependent (Kleim, 2011; Kleim & Jones, 2008) thus increased repetition of a specific functional task such as walking firstly results in short-term increased excitation of the nervous system, specifically the motor cortices and corticospinal tract (Thompson & Stein, 2004), and through longer-term repetition can result in genetic, synaptic, neuronal, spinal, cortical, muscular and skeletal structural changes. Any intervention that induces such changes is said to be working therapeutically (Dunning et al., 2013).

Until the 1960s callipers made from metal and leather (Figure 2) were the only widely used orthotic intervention for foot-drop (Condie, 2008).

Figure 2: A Victorian child's shoe and leg calliper in leather and steel by The Wellcome Collection is licensed under CC BY 4.0

In the late 1960s, with the advent of thermoplastics (Condie, 2008) and complaints about issues such as appearance, weight and shoe choice difficulties (Ofir & Sell, 1980) there was a move away from metal and leather versions to plastic alternatives; which are largely still used today.

AFO users report a number of benefits from using their device including ease of walking, increased independence, greater stability and increased confidence (Bulley et al., 2014; Leung & Moseley, 2003; Tyson & Thornton, 2001), but there are recognised limitations of AFOs reported by users. Some of these limitations relate to usability, which is defined by International Standards Organisation 9241 as the "extent to which a product can be used by

specified users to achieve specified goals with effectiveness, efficiency and satisfaction"
(Arthanat, Bauer, Lenker, Nochajski, & Wu, 2007; Choi & Sprigle, 2011). The commonly cited
usability limitations for AFO devices vary (Holtkamp, Wouters, van Hoof, van Zaalen, &
Verkerk, 2015) but have been broadly categorised as:

1. <u>Health</u> which includes pain, chafing and skin damage
2. <u>Product</u> such as dimensions, weight, size, adjustability
3. <u>User practice</u> relating to aspects such as cosmesis, effectiveness and ease of use
4. <u>Functionality</u> which includes hygiene, handling and freedom of movement (Holtkamp et al., 2015)

These issues can result in dissatisfaction (Holtkamp et al., 2015) which has qualitatively been
reported as potentially leading to reduced compliance (Bulley et al., 2014; Bulley, Shiels,
Wilkie, & Salisbury, 2011; Holtkamp et al., 2015; Vinci & Gargiulo, 2008). Whether reduced
compliance actually occurs has not been objectively evaluated, to the candidate's
knowledge but Holtkamp et al. (2015) reported that approximately 6.7% of 211 people who
had an AFO prescribed to them, self-reported not using their AFO at all.

The other commonly cited AFO limitation relates to the restriction to the available range of
ankle movement (Hesse, Werner, Matthias, Stephen, & Berteanu, 1999; Leung & Moseley,
2003). Mechanical requirements from an AFO vary over the gait cycle and hence passive
devices, whose properties are fixed, are inherently limited (Blaya & Herr, 2004). The passive
control exerted by the AFO will result in a limitation of further range of movement (ROM)
into plantarflexion (PF) and, with the exception of some hinged AFOs, further DF. This
means that a conventional AFO will always tend to bring the foot back to its neutral
orientation and hence may take over from the DF muscles during swing and early stance
phase; as well as opposing PF muscles used in push-off at the end of stance. This has been
assumed to result in disuse effects leading to a worsening in the existing loss of volitional
muscle activity which also leads to negative central neuroplasticity (Geboers, Drost, Spaans,
Kuipers, & Seelen, 2002). These effects may partly explain users' reports that gait feels
"non-normal" and that there is a sense of reliance on the device (Bulley et al., 2014).
Objectively there is mixed evidence to support these claims with some studies showing an
immediate reduction in Tibialis Anterior (Tib Ant), a key ankle dorsiflexor, muscle activity
(Crabtree & Higginson, 2009; Hesse et al., 1999; Lairamore, Garrison, Bandy, & Zabel, 2011;

Lam, Leong, Li, Hu, & Lu, 2005; Romkes, Hell, & Brunner, 2006). However no further reduction has been found following continued use (Geboers et al., 2002) and a meta-analysis in this field was unable to draw inferences regarding the overall effect on muscle activity due to an inability to pool suitable studies (Tyson et al., 2013).

Whether the assumption that the mechanism-of-action is simply immediately orthotic and/or that long-term use results in negative neuromuscular effects has influenced the focus for research in this field is unclear. However, it is clear that research has almost solely focussed on studying the effects of AFOs whilst they are worn; most commonly on a single day (Tyson & Kent, 2013; Tyson et al., 2013). These primary studies have informed a number of CNO disorder specific guidelines that recommend AFOs as an appropriate interventional device for foot-drop management (NICE, 2013; NICE, 2012; NICE., 2014; Intercollegiate Stroke Working Party, 2016; Scottish Intercollegiate Guidelines Network (SIGN), 2010) reporting AFO efficacy in increasing walking speed, reducing energy expenditure, improving spatial gait features (step/ stride length/ symmetry), increasing cadence, improving functional mobility (Modified Emory Functional Ambulation Profile (mEFAP) and Functional Ambulation Categories (FAC)) and normalising foot positioning at IC and toe-off. Although these are measures appropriate for evaluating effects on walking (Mudge & Stott, 2007) what they do not directly capture are the effects of the AFO on the foot-drop impairment during swing, where arguably the greatest impact of the impairment on the gait cycle is seen, nor do they explore the claim about the effect on volitional muscle activity. The single day crossover design primarily used by these studies preclude evaluation of whether AFOs are actually used following prescription, and/or how much walking a person does (rather than reports doing) outside of the lab. There has also been no evaluation in these studies of whether those provided with an AFO are satisfied with the usability of their device once it is taken home. As such the specific impact of AFOs on the foot-drop impairment and the AFO user is unanswered by current guidelines; which limits discerning prescription.

Alongside primary studies one systematic review was used to inform current AFO guidelines (Tyson & Kent, 2013) but in total four systematic reviews have explored the effects of AFO for foot-drop, caused by stroke (Dunning et al., 2015; Ferreira et al., 2013; Tyson & Kent, 2013; Tyson et al., 2013). Two of these performed meta-analyses (Tyson & Kent, 2013; Tyson et al., 2013). Statistically and narratively these reviews collectively reported that as

soon as AFOs are worn there are observed increases in walking speed (although it does not meet the minimal clinically important difference (MCID) (>0.1 metres per second) (O'Dell et al., 2014)), increased step and stride length, improved functional ambulation, better balance (as determined by postural sway and weight transference), reduced energy cost and improvements in DF at necessary points of the gait cycle and knee range of movement.

Somewhat surprisingly, given the uncertain effects on long-term changes to the neuromuscular system, Dunning et al's (2015) narrative synthesis (Grant & Booth, 2009) also reported that AFOs have a positive long-term effects on walking speed, timed up and go (TUG), mEFAP, balance, functional exercise capacity (six minute walk test) and Quality of Life (QoL) both with and notably without wearing the AFO following a period of use. The reasons why a therapeutic effect was observed was not discussed by the authors, although they did note that the studies were likely underpowered, so the results should be viewed cautiously.

With the exception of Dunning et al. (2015) the other three systematic reviews were primarily based on non-Randomised Controlled Trials (RCT). Tyson and colleagues (Tyson & Kent, 2013; Tyson et al., 2013) reported that RCTs were included but their findings were based on single group crossover studies, limiting the strength of their conclusions (Oxford centre for evidence-based medicine, 2009). Dunning et al. (2015) findings, while RCT based, are inconclusive due to methodological flaws in the review. Primarily these flaws related to the broadness of the comparisons made, which attempted to synthesise different interventions, using different evaluation measures whilst exploring different device effects; this prohibited meta-analysis.

Therefore, whilst these reviews are able to suggest that AFOs impact on a wide range of evaluation measures both immediately, following a period of use and without them being worn they are unable to advance current clinical guidelines. This is because their findings are inconclusive and they do not further comment on AFO mechanisms-of-action or if/how AFOs are used outside of a laboratory setting.

1.4 Functional Electrical Stimulation

The alternative interventional device for foot-drop is FES. FES has been defined as:

> "the long-term or permanent use of an electrical stimulus to initiate and maintain a physiological response to supplement or replace an impaired or lost function. Although with the passage of time it may help in recovery that is not its objective (National Research Council, 1973, p. 78)"

In the case of foot-drop FES this, usually, supplements or replaces impaired function of the musculature innervated by the common peroneal nerve. Stimulation is typically applied near to where it bifurcates into its deep and superficial branches (Stewart, 2008) with the aim of eliciting DF with appropriate levels of eversion so the foot clears the floor during swing. This stimulation is introduced and reduced gradually, referred to as rising and falling ramps, to limit eliciting spasticity (Singer, 1987) and mimic the eccentric control of the DF muscles during early stance; aiding a smoother transition from swing to stance. Although there is limited evidence of the effects on gait, when worn as an orthotic FES has been shown to positively influence the kinematics of the ankle; increasing DF at IC (Heller et al., 2013; van der Linden, Hooper, Cowan, & Weller, 2014) during swing (Heller et al., 2013; van der Linden et al., 2014; Voigt & Sinkjaer, 2000) and at toe off (Voigt & Sinkjaer, 2000). However no other consistent effect on joint angles has been found (Voigt & Sinkjaer, 2000). Power generation during stance at the ankle, knee and hip has also been shown to significantly increase with FES (Voigt & Sinkjaer, 2000). As with AFOs regardless of mechanism the remediation of the foot-drop impairment allows the potential for increased task-specific repetitive activity (Langhorne et al., 2009). However in contrast to the literature on AFOs, in addition to this mechanism-of-action, some effects of having used FES have been observed after it was removed (Liberson, Holmquest, Scot, & Dow, 1961). This observation was referred to as carryover and assumed to be transient (Liberson et al., 1961; Moe & Post, 1962). Subsequently it has been recognised that the transient carryover effect is the impact of increased cortical excitation (Thompson & Stein, 2004) but that long-lasting therapeutic benefit can also occur as a result of FES use which is hypothesised to occur due to structural plasticity at spinal, cortical and muscular levels. This is turn is thought to result in positive effects on volitional muscle activity. The hypothesised mechanisms are:

- Spinal: A single pulse of electrical stimulation applied to a motor axon between the muscle and the anterior horn cell produces a pair of action potentials, one travelling orthodromically (to the muscle), to produce the desired movement, the other antidromically (to the spinal cord/ anterior horn cell) (Crago & Makowski, 2012). This, if combined with volitional effort (descending tract action potential), has been hypothesised to strengthen the modifiable Hebbian synapses within the spinal cord (Rushton, 2003). .

- Cortical: FES stimulates sensory as well as motor neurons (Quandt & Hummel, 2014) resulting in increased potential for sensori-motor integration which will be processed centrally and has been shown to cause plastic changes (Everaert, Thompson, Chong, & Stein, 2010).

- Muscular: Peripheral stimulation causes increased oxidative capacity, increases micro-capillaries and changes muscle fibre type (Kluding et al., 2013).

These possible positive mechanisms-of-action have led researchers to consider whether FES devices could also be used as a short-term interventional device to positively influence UMNS features such as weakness and spasticity (Burridge, Taylor, Hagan, Wood, & Swain, 1996; Glanz, Klawansky, Stason, Berkey, & Chalmers, 1996; Glinsky, Harvey, & Van Es, 2007; Sabut, Sikdar, Kumar, & Mahadevappa, 2011) and functional outcomes such as walking speed and functional exercise capacity (Dunning et al., 2015; Robbins, Houghton, Woodbury, & Brown, 2006).

This consideration has led to the recognition of a number of possible device effects (Figure 3). In recent AFO-FES comparison studies testing for some of these effects has also been investigated.
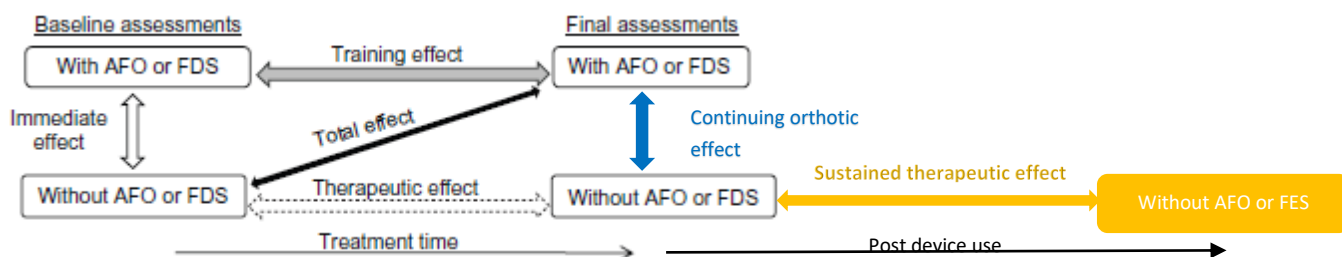

Figure 3: Possible device effects (FDS=Foot Drop Stimulation). Adapted from Dunning et al. (2013) with continuing orthotic effect (Miller et al., 2017; Street, Taylor, & Swain, 2014) and

sustained therapeutic effect (new term proposed by Prenton, Hollands, Kenney & Onmannee, 2018) added.

These device effects can be summarised as follows:

1. Immediate (orthotic) effects: evaluations conducted before the device is provided and compared the evaluations conducted immediately after it has been provided, whilst the device is being worn (Dunning et al., 2013). Both evaluations are carried out on a single day.

2. Continuing/Ongoing orthotic effects: evaluations conducted with and without device being worn at a given time point following a period of use (Miller et al., 2017). Both evaluations are carried out on a single day.

3. Combined/ Total orthotic effects: evaluations conducted before the device is provided and compared to evaluations with the device being worn at a given time point following a period of use (Everaert et al., 2013)

4. Training effects: evaluations conducted with the device being worn as soon as it has been provided and compared to evaluations again with the device being worn at a given time point following a period of use (Dunning et al., 2013)

5. Therapeutic effects: evaluations conducted before the device is provided and compared to evaluations without the device being worn immediately following a period of use (Dunning et al., 2013)

6. Sustained therapeutic effects: evaluations conducted before the device is provided and compared to evaluations without the device being worn at a given time point after the device is no longer used. These effects have been first described by the candidate in Article 6 of this thesis (Prenton et al, 2018).

The first record of "Functional Electrotherapy" was published by Liberson et al. (1961) and the first commercially available system was the Ljubljana functional electrical peroneal brace (Figure 4) in the early 1970s (Condie, 2008; National Research Council, 1973).

Figure 4: Ljubljana Functional Electrical Peroneal Brace. From (National Research Council, 1973)

The first partially implantable version was reported in 1975 (Waters, McNeal, & Perry, 1975). The change from stance to swing (and swing to stance) was detected by a heel (tape) switch which allowed activation (and deactivation) of the stimulation (National Research Council, 1973). Since that time this approach has not changed significantly with most systems still using a form of footswitch; although other gait event detection options are now available (Melo, Silva, Martins, & Newman, 2015). Appropriately trained clinicians currently have access to surface foot-drop FES systems from five manufacturers: Odstock Medical Ltd[TM]; Bioness[TM]; Innovative Neurotronics[TM]; Ottobock[TM] and Shenzen XFT Electronics Co., Ltd[TM]. Previously two partially implantable FES devices were on the market, Odstock Medical Ltd[TM] (STIMuSTEP®) and Ottobock[TM] (Actigait®), but these are no longer commercially available.

As with wearers of AFOs, FES users report that the positive effects such as reduced trips and falls, increased participation and capacity to walk longer distances outweigh any negatives (Bulley et al., 2014) but FES users also report usability issues (Bulley et al., 2014). These include discomfort caused by stimulation, skin irritation, the bulk of FES devices, the reliance on footwear (if using a footswitch), and problems with trailing wires sometimes used to connect the individual components (Bulley et al., 2014; Bulley et al., 2011). The most common complaint amongst users, cited by 44% (Taylor, Burridge, et al., 1999a), relates to difficulty in electrode placement. As previously stated stimulation, via the active electrode

(cathode), should typically be placed over where the common peroneal bifurcates into deep and superficial branches (Stewart, 2008). The more posterior nerve (the superficial peroneal nerve) innervates the peronei muscles which evert and PF the foot whereas the more anterior deep peroneal nerve innervates the Tib Ant, as well as the toe extensors, which DF and invert the foot. In order to get an acceptable foot response, it is therefore important that each individual user knows how to place electrodes correctly and to recognise what is an acceptable foot response. Odstock Medical Ltd[TM], the largest UK FES manufacturer, have developed an instruction sheet detailing how to accurately place both electrodes (Appendix 2). As can be seen this is not always easy to achieve especially given the variation in individual anatomy and clinical presentation; which can also vary day-to-day. It relies on the user to have sufficient dexterity and cognition to achieve satisfactory placement, both of which can be impaired by CNO disorders. This coupled with inaccuracies in user perception of when they have achieved a satisfactory foot response, which is influenced both by electrode placement and amplitude of stimulation, results in setup being a significant usability issue with FES devices (Heller et al., 2013; Prenton, Kenney, Stapleton, et al., 2014). Despite the comprehensive education and support provided by many of the manufacturers, which may address these issues for a large percentage of the population, this can also undermine the efficacy of the device (Figure 5). These factors extend setup time, can present a barrier to clinical prescription (Roche & Coote, 2007) and can result in dissatisfaction. As with AFOs, whether these factors reduce daily compliance is unknown, to the candidate's knowledge, but again as with AFOs self-reported discontinuation of use is low at approximately 10% each year (Taylor, Humphreys & Swain, 2013). In Taylor et al's (2013) study only 1 directly reported electrode placement difficulties for why they discontinued with FES use, but 1 other reported finding it too much bother, another 4 found FES difficult to use and a final 5 found insufficient benefit from use (Taylor et al., 2013). These latter reasons were not expanded upon but it is possible that they may be, in part, related to electrode placement issues. It is worth noting that the 2013 paper reported data from the UK National Clinical FES Centre. It is possible that other centres in different regions/countries offer different levels of user training and support, which may in turn result in different levels of compliance.
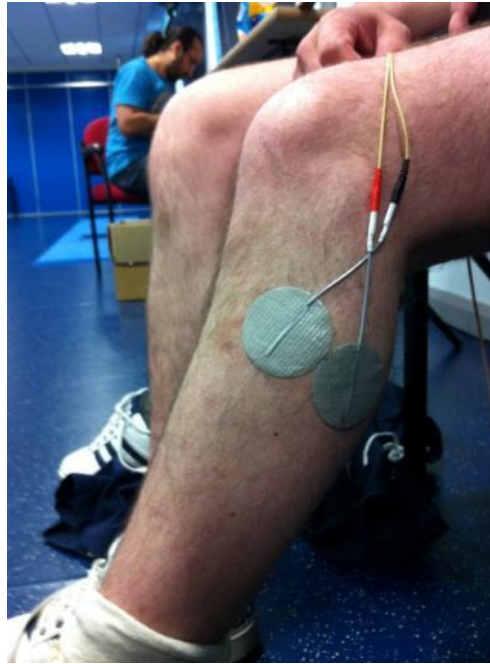
Figure 5: Example of inappropriate electrode placement in a participant from Prenton, Kenney, Stapleton, et al. (2014)

Manufacturers have sought to address the electrode placement issues by developing versions with leg-cuffs to house the electrodes, the location of which the clinician sets when prescribing. However, these do not allow for easy adjustment of electrode location to address individual or day-to-day variations nor can they address the issue of stimulation amplitude selection during setup. Partially implanted devices address some of these issues but at a greater cost and risk; hence the withdrawal of them from the market.

There is a UK-wide guideline that specifically endorses FES (NICE, 2009) as an appropriate interventional device for foot-drop for all CNO disorders despite all-but-one included study (Taylor, Burridge, et al., 1999b) solely studying stroke. This guideline used a variety of primary and secondary sources to recommend that FES has positive effects on speed, energy cost (Physiological Cost Index (PCI)), exercise capacity, the ordinal gait scale by Tinetti, "functional milestones", activity monitoring and the Fugl-Meyer assessment of motor recovery. This guideline is used as the basis for a National Stroke Guideline (Intercollegiate Stroke Working Party, 2016). As with AFO guidelines although these recommendations are based on evidence of effects the measures of evaluation are unable to determine how FES impacts the foot-drop impairment as there are no direct measures of if/how they affect the foot clearing the floor during swing, or from swing to stance, or what

effect there is on volitional muscle activity. Activity monitoring, which has been used by a small number of studies (Kluding et al., 2013; Kottink et al., 2007; Sheffler et al., 2015; Van Swigchem, Vloothuis, Den Boer, Weerdesteyn, & Geurts, 2010) might be assumed to capture task-specific repetitive activity but whilst the types of monitor used can distinguish between time spent in sitting/lying, standing and stepping (Godfrey, Culhane, & Lyons, 2007) and/or the number of steps taken they cannot not distinguish between walking when the FES device is being worn and when it is not. Thus they cannot accurately capture this potential mechanism-of-action and as with AFOs, although shown to be effective, these studies are unable to report on whether individuals provided with an FES are satisfied with the usability of their device. One other guideline exists that mentions FES for the treatment of foot-drop caused by stroke (Scottish Intercollegiate Guidelines Network (SIGN), 2010). This guideline recommends FES use where the aim of treatment is the immediate improvement in walking speed and/or efficiency (PCI).

Although a number of systematic reviews of FES include some foot-drop primary studies and meta-analysis (Glanz et al., 1996; Howlett, Lannin, Ada, & McKinstry, 2015; Pereira, Mehta, McIntyre, Lobo, & Teasell, 2012; Robbins et al., 2006), to the candidate's knowledge, only four have been foot-drop specific (Dunning et al., 2015; Kottink et al., 2004; Miller et al., 2017; Roche, o'Laighin, & Coote, 2009); three focus on stroke (Dunning et al., 2015; Roche et al., 2009) the other on MS (Miller et al., 2017). Of these only two were specific enough to afford meta-analysis (Kottink et al., 2004; Miller et al., 2017). All four of these reviews reported that FES has positive orthotic effects on walking speed and for those that meta-analysed the improvement was found to be both statistically significant and, in contrast to AFOs, exceeding the MCID (O'Dell et al., 2014). Energy expenditure was reported to be reduced (Dunning et al., 2015; Kottink et al., 2004; Roche et al., 2009) and balance, TUG and functional exercise capacity improved with the use of an FES device (Dunning et al., 2015). However this was based on narrative synthesis only (Grant & Booth, 2009). Therapeutically Dunning et al. (2015) narratively reported that FES improves TUG, mEFAP, functional exercise capacity, balance and reduces energy expenditure (Dunning et al., 2015). Conversely Roche et al. (2009) found inconclusive evidence for any therapeutic effects and the meta-analysis by Miller et al. (2017) did not find a statistically significant therapeutic improvement in walking speed. Dunning et al. (2015) also reported that FES improved the

QoL for users. As with AFO systematic reviews here again it can be seen that whilst these reviews highlight positive effects of FES devices on appropriate walking measures they do not further our understanding of the mechanisms-of-action or whether provision leads to actual use outside of a laboratory, related to how usable the devices are.

Additionally, with the exception of Dunning et al. (2015), and in keeping with the AFO literature these reviews were primarily based on non-RCT studies which limits the strength of their conclusions; and again Dunning et al. (2015) results are based on a focus that was too broad as to afford a statistical analysis. Therefore, similarly to AFO reviews whilst synthesised evidence exists it is not robust nor able to further develop our understanding of how FES works so cannot enhance current clinical guidance.

1.5 Comparative Study

Confusingly for clinicians both AFOs and FES for foot-drop are recommended to manage foot-drop but due to the way in which the devices' efficacy have been evaluated the associated current guidelines cannot advise which is overall better/more effective; nor do they report on how the devices work, knowledge of which could help clinicians match a device to a person (Tyson et al., 2013).

A body of evidence does exist which compares the two devices. These are either studies in which a single group of AFO users are then prescribed an FES device (Ring, Treger, Greundlinger, & Hausdorff, 2009; Schiemanck et al., 2015) those where the devices are randomly assigned test conditions on the same participant on a single day, to evaluate immediate orthotic effects only (Sheffler, Hennessey, Knutson, & Chae, 2009; Sheffler, Hennessey, Naples, & Chae, 2006), or are RCTs (Bethoux et al., 2014; Everaert et al., 2013; Sheffler et al., 2013).

To date only one systematic review (Dunning et al., 2015) has had the potential to further clinical guidance as it synthesised comparative evidence focussing on RCTs alone (Howick et al., 2011). This review found between device comparability in terms of improvements in walking speed, TUG, mEFAP, Berg balance scale, functional exercise capacity, QoL and the lower limb Fugl-Meyer. But as previously stated, this review had too broad a focus, which

prohibited the meta-analysis expected when this level of evidence is synthesised. Emphasis was placed on which device participants would choose, with FES preferred, but this was only based on two studies (Everaert et al., 2013; Kluding et al., 2013) using unvalidated questionnaires. FES was also reported as being superior in reducing energy expenditure (PCI) but again this was only based on two studies (Burridge, Taylor, Hagan, Wood, & Swain, 1997; Johnson, Burridge, Strike, Wood, & Swain, 2004) both of which did not compare FES to AFO.

This review was the first to synthesise RCT level evidence and so was able to suggest for the first time that there is equal observed improvement in a variety of device effects, against many evaluation measures for both devices, but that despite this users prefer FES and require less energy to walk when it is worn. However, the conclusions are undermined by these flaws. Therefore, there is currently no robust comparative evidence to guide clinical prescription or enhance current guidelines.

1.6 Gaps in the Evidence Base

Based on this exploration of the knowledge base three clear gaps for the two foot-drop interventional Assistive Technology (AT) devices were identified. Firstly, limitations with device design. Advances in the materials used in AFO manufacturing and the technology around stimulator and electrode design afforded opportunities to address these limitations.

The second issue is that although both devices have been shown to positively improve certain evaluation measures the measures chosen do not directly evaluate: the fundamental effects of the devices on the walking deficits caused by the foot-drop impairment; if the devices are usable and whether/how device prescription translates into actual increased levels of walking (with the device) in the user's own environment.

The third issue is that whilst clinical guidelines individually endorse both devices this guidance is based on sub-optimal sources with limitations in regards to how they have been evaluated. It is acknowledged that there are different types of AFO and FES systems. It is therefore likely to be the case that a particular device may be better suited to a certain type of user than another. However, in practice clinicians have limited time and cannot explore

all possible options for a given patient. Therefore, guidelines as to the relative merits of AFOs compared to FES would help guide the prescription process. The only RCT comparative systematic review in the field (Dunning et al., 2015) does not report a statistical synthesis of the evidence and reported on similar evaluation measures to those used in the associated guidelines, so offers no further guidance in this regard.

1.7 Body of Work Synopsis

Prior to commencing the PhD an externally funded project had started to develop alternatives to recognised AFOs and FES to address some of the usability limitations that impact provision and compliance (Health Technology Devices (HTD) 480) including appearance, comfort and ROM restriction for AFOs and setup issues for FES. This group comprising engineers, an orthotist, nurses and (latterly) the PhD candidate (physiotherapist) recognised that user-involvement to design decisions would be a sensible approach. The description and evaluation of the co-design (lay advisors and researchers) process followed is provided in the first article. This article contributes to the rather limited evidence base concerning how to use such a group and the impact of their involvement on product and study design.

The second article in the body of the work presented in this thesis explored the feasibility, preliminary efficacy and user views of an elasticated orthotic sock (DMO dorsiflex sock®) as alternative to an AFO designed to addressed some of the cited usability and ROM limitations. Unlike other work in the field it used an A-B single case experimental design (SCED) methodology (Ottenbacher, 1986) with two stroke participants. Measures of gait symmetry, energy expenditure, walking speed, functional exercise capacity and FAC were utilised to preliminarily evaluate the efficacy of the device. A diary and a questionnaire (Tyson & Thornton, 2001) were also used to gather user views. The measures used spanned the three World health Organisation (WHO) International Classification of Functioning, disability and health (ICF) domains (WHO, 2001) and included a battery of measures that were clearly justified and, in some cases, novel (gait symmetry and the total heart beat index (THBI) as a measure of energy expenditure). This study was the first publication to look at this alternative to conventional AFO devices, with this population, in this way.

The third article is based on work that explored the feasibility (Arain, Campbell, Cooper, & Lancaster, 2010) and usability of an array-based FES device that used an automated setup process (ShefStim®). This device was the first to automate the setup process to address the cited electrode placement issues. An earlier prototype of the device had been shown to be effective in a laboratory based study (Heller et al., 2013). However, the Conformité Européenne (CE) approved device (ShefStim®) had not been previously studied. The study used a single-group of current FES users (Prenton, Kenney, Stapleton, et al., 2014). Careful consideration was given to the choice of evaluation measures used, in comparison to the participants own FES devices and no FES. Measures were chosen to: explore whether ShefStim® could be feasibly used outside of a laboratory; capture usability; directly capture the effects of ShefStim® on the foot-drop impairment to preliminarily explore the mechanisms-of-action and start to evaluate the impact on function. Three of these methods in this field were previously unused (Usage, foot clearance and a user satisfaction questionnaire (Demers, Monette, Lapierre, Arnold, & Wolfson, 2002)), indeed the foot clearance method was specifically adapted for this study. Other, more widely used measures (diary, kinematics at initial contact and walking speed) were also used. This was the first publication reporting on the real world evaluation of any FES system for foot-drop with automated setup.

The fourth article reports on the design work leading to the development of ShefStim® (Kenney et al., 2016). The article cites and discusses the earlier ShefStim® article (Article 3), placing it in the context of the preceding design work.

A phase III trial of ShefStim® (Medical Research Council, 2000) would have been a sensible next step following the demonstration of device and evaluation measure feasibility as well as a suggestion of worthy effect sizes (Article 3). However, it proved impossible to identify the commercial partnership needed to make the necessary product design changes and produce a larger number of stimulators needed for such a study.

Through the empirical studies (Articles 2 and 3) it had become clear to the PhD candidate that:

a) Some of the measures chosen for the two HTD480 empirical studies were not typically used in either the AFO or FES fields of research. The first use of *foot-*

clearance as an outcome measure represents a clear advance for the field, which has previously relied on DF/PF trajectories, or *toe*-clearance to characterise how well the device achieves one of the key functions (ground clearance). Further, the measures capturing use within the user's own environment (logged usage, diary, donning/ setup times) and user satisfaction (face-to-face questionnaire, Quebec User Evaluation of Satisfaction with assistive Technology (QUEST) 2.0) also provided a novel perspective on these types of device.

a) That the AFO and FES fields of research had been largely mutually exclusive until around the start of the PhD.

b) Clinical guidance did not extend to which of the two AT interventional devices for foot-drop was better overall or how they worked.

c) A number of RCTs comparing AFOs and FES had been conducted at the start of the PhD.

As a result, the last two articles presented in the PhD (Articles 5 and 6) are two systematic reviews of RCTs, including meta-analysis, directly comparing the effects of AFO and FES on walking behaviours.

The first systematic review (Article 5) focussed on their orthotic effectiveness following a period of use (Bosch, Harris & Wing, 2014). This review provided the first gold standard comparison (Howick et al., 2011) of the devices. It also drew attention to gaps in the knowledge base with particular reference to the comparison of the mechanisms-of-action.

As rehabilitation aims to promote motor recovery (Langhorne et al., 2009; Levin, Kleim, & Wolf, 2009) the second systematic review (Article 6) compared the therapeutic effects of the devices. This was the first systematic review with meta-analysis in the area. Again it highlighted gaps in our understanding of the mechanisms-of-action and also the impact of the devices on the users' participation in walking in their own environment.

Although all the articles presented in this thesis sit within the realm of the two devices for foot-drop focussing on the three identified gaps in the evidence base there was a natural split in the focus. **PART 1** focussed on evaluation of two new device designs aimed at addressing their cited limitations (Articles 1-4) and **PART 2** compared the RCT evidence for AFOs and FES (Articles 5 & 6).

CHAPTER 2: PUBLICATIONS, including CRITICAL APPRAISAL

PART 1

2.1 Article 1

Williamson, T., Kenney, L., Barker, A. T., Cooper, G., Good, T., Healey, J., Heller, B., Howard, D., Matthews, M., Prenton, S., Ryan, J., Smith, C. (2015). Enhancing public involvement in assistive technology design research. *Disability and Rehabilitation: Assistive Technology, 10*(3), 258-265. doi: 10.3109/17483107.2014.908247

2.1.1 Article 1 summary and publication

This study sought to address the first identified gap in the evidence base by describing and evaluating the user involvement in the development of two new foot-drop devices.

Users have reported limitations in foot-drop devices (Bulley et al., 2014; Bulley et al., 2011; Holtkamp et al., 2015; Taylor, Burridge, et al., 1999a) and the project team recognised that in order to match a new product with potential end users the device design development process would benefit from user involvement. This first article was based on a case study evaluation of the lay-advisory group that co-designed the new AFO and FES devices as part of the HTD480 project, alongside the device development/researcher team. The lay-advisory group comprised 10 individuals; five were current FES users and one was a past user of FES. By the end of the project there were six group members remaining. They met nine times over the course of the project (HTD480) and discussed the design of the devices and the design and evaluation measures of the two associated clinical studies. Each meeting had clear objectives set by the research team and were recorded for accurate documentation and interpretation.

The evaluation involved interviewing both the researchers and lay-advisory group members at the beginning and end of the project; the lay-advisory group members were also interviewed at the mid-point. An *a priori* framework was developed to analyse the transcripts on these interviews.

The evaluation highlighted that for lay-advisors benefits included increased confidence and feeling valued. They found the meetings to be well organised and the research to be engaging. The main issue raised related to parking challenges.

The results of the researcher group interviews highlighted a change in attitude from one of thinking the lay-advisors had little to offer to a realisation that lay-advisor contributions were invaluable with regards to product and clinical study development.

The conclusions drawn related to how this article provides a model for public involvement that should help other AT researchers.

RESEARCH PAPER

Enhancing public involvement in assistive technology design research

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Abstract

Purpose: To appraise the application of accepted good practice guidance on public involvement in assistive technology research and to identify its impact on the research team, the public, device and trial design. *Methods*: Critical reflection and within-project evaluation were undertaken in a case study of the development of a functional electrical stimulation device. Individual and group interviews were undertaken with lay members of a 10 strong study user advisory group and also research team members. *Results*: Public involvement was seen positively by research team members, who reported a positive impact on device and study designs. The public identified positive impact on confidence, skills, self-esteem, enjoyment, contribution to improving the care of others and opportunities for further involvement in research. A negative impact concerned the challenge of engaging the public in dissemination after the study end. *Conclusions*: The public were able to impact significantly on the design of an assistive technology device which was made more fit for purpose. Research team attitudes to public involvement were more positive after having witnessed its potential first hand. Within-project evaluation underpins this case study which presents a much needed detailed account of public involvement in assistive technology design research to add to the existing weak evidence base.

➤ **Implications for Rehabilitation**

- The evidence base for impact of public involvement in rehabilitation technology design is in need of development.
- Public involvement in co-design of rehabilitation devices can lead to technologies that are fit for purpose.
- Rehabilitation researchers need to consider the merits of active public involvement in research.

Background

Assistive technology has been defined as ''any device or system that allows an individual to perform a task that they would otherwise be unable to do, or increases the ease and safety with which the task can be performed'' [1]. Although there is a vast range of ATs on the market, widespread concern exists around their under-utilisation which may take many forms, including the device being returned to the provider, or at worst left unused in the person's home. It has been estimated that a third of ATs are

abandoned after initial use [2]. The financial cost of under, or unused AT could be considerable and the associated personal costs could also be substantial in terms of quality of life, social stigma, isolation and loneliness.

A survey of 227 adults with disabilities, found mobility aids to be the most commonly abandoned device type [3]. In another paper reasons for abandoning of prosthetic devices include lack of identified need by the intended user and uncomfortable designs [4]. Seamless integration of user capabilities and AT has been advocated which can be enhanced by improved user-technology physical interface (the way a person interacts with the physical aspects of a technology) [5]. These authors go on to suggest that user involvement can help create a better match between what users want and need, and available technologies [5] which in turn could lead to optimised use of AT [2]. Some users of AT have not felt that the motivations of designers have been aligned with their

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own when developing AT [6]. Yet, people have been expected to embrace the resultant AT products designed *for* and not *with* them, even when unfit for purpose or aesthetically displeasing [7].

An increasingly recognised solution to these issues is that of ''co-design'' in its many guises. Co-design [8] is an approach by which AT can be developed with input by end-users and other stakeholders. It is underpinned by the assumption that those for whom the AT is designed, have a moral right to be engaged in the design process. End-users typically include patients, informal (unpaid) carers and health professionals who may assess for, prescribe and fit AT products. Throughout this article the terms ''user involvement'' and ''public involvement'' are used interchangeably and in this context mean involvement of people in any stage/s of the research process [9]. Increasingly researchers and others engaged in participatory co-design and AT development no longer see the public as merely ''end-users'', preferring to actively seek user views throughout the AT development process and not just at its end for testing purposes.

While public involvement in AT design research is increasingly the norm, it is little evaluated. In the absence of a substantive and specific body of public involvement evidence within the AT field, the evidence base for public involvement in general health related research can be drawn on [10]. However, while elements of this work may be directly and successfully transferable, the AT design field would likely benefit from its own evidence base for what works, and why in user involvement [11]. This article reports on one such contribution to the AT evidence base, derived from a within-project evaluation of user involvement during research to design a device to assist people to walk following stroke. Presented as a case study [12], it appraises the application of accepted good practice guidance on public involvement in research and identifies new insights into what works with regard to public involvement in AT design.

Context

The National Institute for Health Research (NIHR) funded study ''*Dynamic orthosis with virtual electrodes for the lower limb*'' ran from July 2008 to September 2011 and sought to develop a novel device to assist people with a condition known as ''foot drop'' which is common after a stroke. Foot drop is characterised by an inability to adequately lift the foot during the swing phase of walking, and is typically associated with a slow, tiring and unstable walking pattern. One AT device which is now commonly used for the correction of foot drop is the functional electrical stimulation (FES) which uses externally generated electrical pulses to generate functionally useful movements in weak or paralysed muscles [13]. To correct drop foot, stimulation is applied to the common peroneal nerve during the swing phase of walking, thereby lifting the foot. This has been shown to have the effect of making walking faster, less tiring and more stable [14]. Stimulation systems that were available prior to the study required the user, each time the system was donned, to carefully apply a pair of self-adhesive electrodes, typically one near to the fibula head (just below the knee) and one over the muscle at the front of the lower leg (tibialis anterior). Small errors in placement of electrodes could lead to significant differences in the response of the foot to stimulation and, in extreme cases, exacerbate the effects of the foot drop. Some users found this sensitivity to electrode placement to be a major problem, leading to long setup times and in some cases, abandonment of the technology [15]. In the ''*Dynamic orthosis with virtual electrodes for the lower limb*'' study, the aim was to produce a drop foot stimulator system in which the set up of the stimulator was automated while exploring potential for integrating the new stimulator in a passive device to help lift the foot (an orthotic sock).

The research team comprised an industry partner, two North of England Universities and an NHS Foundation Trust. Team members came from a range of backgrounds, including electronic engineering, mechanical engineering, biomedical engineering, patient and public involvement, physiotherapy and orthotics. The value of public involvement was stressed by the funder early on and a model for engaging the public was developed and implemented. Our approach to public involvement included a built-in evaluation which has provided opportunity to gain rich contextual data necessary when developing a case study such as this.

Methods

The case

We adopted a case study approach, involving an in-depth analysis of a single bounded programme of work [16]. Case studies are particularly appropriate when contextual conditions are pertinent to the phenomenon being studied and the case being investigated is unique [12]. The main criticism of the case study concerns generalisability of findings, yet it is valid theoretical generalisation, as opposed to statistical generalisation, that is being sought [17]. Our approach taken to public involvement in this assistive technology design study has been extensively planned, delivered, explored and recorded. It is this attention to detail which provides the necessary novelty and uniqueness to justify its presentation as a single exploratory case study [18]. Next the case is detailed so that others may consider its relevance and utility to their own public involvement practice.

The public involvement model: lay advisory group

The approach to public involvement was informed by previous studies undertaken by research team members who had worked extensively with, and developed members of the public to be involved in, ageing research [19–21]. The model also drew on good practice guidance by INVOLVE [9]. Many of these well-established principles of general involvement in research were considered by the team to be directly applicable to AT research and AT co-design. Our FES study provided an arena to apply and test these good practice principles within an evaluation framework to see which of them worked and why.

Ethical approval for the evaluation was received from the Salford University Research Governance and Ethics Committee.

Ten lay advisers were identified through research team members' personal networks, clinical contacts and the NIHR funded Greater Manchester Stroke Research Network. An information sheet describing the nature of the role of an adviser was distributed and followed-up by a telephone discussion by the FES study's involvement lead (T.W.).

Advisers were:
- current or previous users of an FES device
- and/or who knew others who had used FES e.g. someone they cared for
- and/or who were actively involved in community stroke groups where they had contact with FES users

As the study was not developing an entirely new technology, it was valuable to uncover user and carer views of the existing FES systems, as well as the views of those who had discontinued FES use. Advisers were aged between 40 and 75 years of age (6 females and 4 males). Six had direct personal experience of using FES with five of these being current users with mixed levels of success.

At the study outset, research team members attended a public involvement workshop specifically for them, led by the public

involvement lead, to prepare them for working closely with the public as advisers.

Lay advisory group processes

Lay Advisory Group meetings were held on the Salford University campus and venues were arranged with accessibility in mind e.g. reasonable distance from accessible parking spaces, lifts and toilets, plus good acoustic and visual resources, and suitable seating with room to manoeuvre wheelchairs and walking sticks.

At the initial meeting, the public involvement lead first described health research principles and processes and the study itself. She then gathered advisers' hopes and expectations of involvement, their support needs (e.g. transport and dietary), past and present experiences of FES, and preferred ways of working and learning. As the emphasis was on relationship building, only two members of the research team were introduced to advisers in the morning, with other team members joining the group at lunchtime. Informal research team biographies including photographs had been sent out with the meeting papers prior to the day. Advisers were then invited to develop their own biographies to help them get to know each other, which most of them did.

From this meeting on, all papers (agenda, notes of previous meetings, location map, etc.) were sent out to advisers at least one week in advance of the meetings in a format (email or paper copy) of their choosing. These always contained a reminder of the venue location and clear directions to the building and meeting room itself. All meeting papers were emailed or printed in minimum size 14 Arial font using suitable colours to be visually accessible, written in plain language, and with technical terms explained and abbreviations avoided. Advisers then had adequate opportunity prior to each meeting to speak with the public involvement lead to go through the meeting agenda and clarify any concerns or issues they had.

Advisers were met on arrival (sometimes in the car park) and assisted to their means of transport home following each meeting. Transport sometimes included supply of door to door taxis, so that people more affected by a disability were enabled to participate. Temporary rescue seating was placed between the building entrance and meeting room and extra signage was displayed to minimise any stress in locating the meeting room.

Although advisory meetings were planned to be held regularly throughout the study, in practice their frequency changed over time. At the start of the study, when key design decisions were being taken (such as where the stimulator unit should be worn), there were frequent meetings. During the middle part of the project, when the designers were working on detailed implementation of the design specification, there were fewer advisory meetings. During long gaps between meetings, email updates were sent by the involvement lead to advisers to keep them informed of progress and to avoid feelings of being neglected.

The total funding awarded for the public involvement work package was £8000. As is good practice, a payment of £50 was made to each lay adviser at every meeting as a reward for their contribution. Arrangements had been made with University Finance Department colleagues to make payments in cash on the day of the meeting to avoid advisers being out of pocket and to prevent then having to complete onerous forms to claim tax back (those beyond retirement age). It was made clear verbally and in writing that advisers were responsible for checking out their personal situation (income tax, state benefits) in relation to these payments. Issues around payments are very complex and the receipt or refusal of payment by a member of the public can have far reaching negative effects [22].

Communication and facilitation style were thought to be critical in supporting the co-design process. Early meetings created a friendly and informal environment despite there being lots of activities to be covered during the available time. We attempted to anticipate, elicit and respond to needs by, for example pacing the introduction of new ideas and concepts. There was considerable potential for this study to involve a lot of technical discussions although at the time these were seemingly executed well. All new terms were explained and abbreviations avoided. Reassurances were given that there were no ''wrong answers'' or ''stupid questions'' and that each adviser's input could help the team to design a device that would meet the needs of people like them. Feeding back to the advisers when their suggestions/comments had been helpful was also considered useful in building their confidence as well as simply letting them know when and how they were making a difference and fulfilling their role.

To accurately record design discussions and decisions, photographs of white board notes were taken and meetings were either audio recorded or video recorded with written consent for these to also be used for dissemination from the study. Detailed meeting notes captured design decisions and were verified with advisers. Several research team members were present at every meeting which not only demonstrated the value placed on the ideas and suggestions of the advisers, but also provided a direct channel of communication of meaning. In this way, it was possible to note which advisers had made which suggestions and how the research team had responded.

The meetings were facilitated in an informal manner by the involvement lead around clear objectives that had been agreed beforehand with the study Primary Investigator. Informality did not translate into unfocused meetings with unclear outcomes; it merely allowed flexibility in the meeting timings and scope for the advisers to influence the agenda to meet their own needs and not just those of the facilitator. Meeting content included the core activities shown in Table 1.

An explanation was given to advisers about intellectual property issues and the need for confidentiality concerning the device and associated technology being developed. A project confidentiality agreement was duly signed by each adviser. This was a standardised, badly worded document and difficult to understand as written in legal jargon which needed some explanation.

Steps were taken to manage risk of harm to the advisers, even though they were not research participants/subjects. The involvement lead ensured that advisers did not exceed their role boundaries, e.g. they did not have a free rein to formally test sample products or prototypes but did examine and comment on these during meetings. On one occasion, advisers asked if they could be considered as potential participants in the pilot clinical trial which commenced late in the study, and this was permitted by the University's Research Governance and Ethics Committee. Second, as an adjunct to the main device being developed, an elasticated orthotic sock was being developed and some advisers wanted to be measured for these and to take them home to wear prior to commenting on such things as their comfort, warmth, and moisture management properties etc. Again, the University Research Governance and Ethics Committee was approached and this activity was allowed so long as the manufacturer's product leaflet was given with the sock (as it was already a commercially available product).

The Lay Advisory Group went on to meet nine times during the study lifetime with each meeting lasting approximately 4 h including a refreshment break, comfort break and a 40-min lunch break.

Table 1. Core meeting activities.

- Orientation to the project and each other
- Development of biographies
- Discussion of user adviser roles, training and support needs
- Discussion of dissemination of study findings – introduced in the first User Advisory Group meeting
- Written informed consent for user advisers to be photographed and video recorded
- Confidentiality agreements (concerning non-disclosure of device design information)
- Commenting on various aspects of device design – discussion of concepts and design ideas as well as commenting on mock-ups of devices (non-functioning dummy versions) and working prototypes
- Commenting on pilot clinical trial design
- Agreeing an approach to within-project evaluation
- Taking part in within-project evaluation discussions
- Planning for co-presentation at INVOLVE conference 2010
- Completion of question sheets concerning user views of device prototypes
- Study update presentations
- Discussion of end of project planning – user adviser's debrief, withdrawal and celebration
- Commenting on the text drafted for the user involvement section of the final report to the study funder – this was approved
- Discussion of user adviser's preferences for involvement in writing this involvement report – co-writing was declined, commenting on a draft was preferred

Evaluating public involvement

The main driver for undertaking a within-project evaluation of the public involvement aspects was to identify areas for improvement or reinforcement within our own study. Additionally we wanted to develop evidence in support of impact of involvement and stakeholders' experiences of involvement that could be useful to others and especially AT researchers.

Within-project evaluation approach

Through discussion with lay advisers and research team members, it was agreed to undertake audio-taped interviews with these two groups early on in the study, at mid-point and at its end. Schedules of interview questions were developed collaboratively for advisers and research team members (see Table 2). Questions were included that were expected to elicit insights to meet the known gaps in the evidence base about public involvement. Advisers and research team members indicated a preference for the public involvement lead to undertake the interviews. In reality, it was only possible to interview research team members twice due to a delay in carrying out the first group interview with them in Year 1 of the study. Two advisers left the study early on and so eight participated in initial group interviews while six were interviewed at study end following further attrition of two advisers. Reasons for attrition included re-location and worsening health. At midpoint, two study advisers were unable to take part in a group interview and so separate individual audio-recorded discussions were undertaken by telephone with them. Interviews were transcribed by secretariat yet read through several times by the interviewer prior to analysing. From the interview schedules, an *a priori* analysis framework was devised. Text within the transcripts was examined with the analysis framework in mind. Analysis also allowed for inductive insights to be gained as chunks of data were coded and themed into categories [23]. Verification of interpretation was done with another research team member experienced in qualitative research. A study timeline is presented in Table 3.

In the next section, findings are presented and illuminated with a selection of direct quotes from the interviews. Quotes were

Table 2. Combined researcher and lay adviser interview guide.

1. Have you been involved in any other projects with a user involvement element? If so please describe (R, LA)
2. Tell me about your <u>initial</u> expectations of involvement in the project
    - at a personal level e.g. confidence, opportunities, fears, apprehensions (R, LA)
    - from a research topic point of view e.g. to improve practice, help develop a useful product, add value to the project (R, LA)
    - concerning the design itself e.g. expect to be listened to, useful experiences to share (LA)
    - in relation to members of the Lay Advisory Group or Research Team e.g. social contacts, working with experts, relationships with advisers and Research Team members, inter-disciplinarity (R, LA)
3. Tell me about your <u>current</u> experiences of involvement in the project and whether your initial expectations have been met
    - at a personal level e.g. confidence, opportunities, fears, apprehensions (R, LA)
    - from a research topic point of view e.g. to improve practice, help develop a useful product (R, LA)
    - concerning the design itself e.g. being listened to, useful experiences to share (LA)
    - in relation to members of the Lay Advisory Group or Research Team e.g. social contacts, working with experts, relationships with advisers and Research Team members, inter-disciplinarity (R, LA)
4. Overall, how well were you prepared and supported for involvement in the project?
    Specifically,
    a) Did you find the biographies helpful? Did they influence how you view other members? (R, LA)
    b) Were the initial invite papers adequate (invite letter, adviser information sheet)? (LA)
    c) Are meeting papers adequate (agenda, notes)? (R, LA)
    d) Are the meeting environments and facilities suitable? (R, LA)
    e) Do you feel your personal needs were met sufficiently for you to attend and take part? (R, LA)
    f) What helped you to settle into your role? (R, LA)
5. How could any of the above preparation and support mechanisms be improved? (R, LA)
6. Have any of your previous conceptions/mis-conceptions of user involvement altered during this project? (R)
7. Has the approach of having a mixed group of advisers (current, past and non-FES users) made a difference to the project? (R, LA)
8. Can you give any examples where the public involvement has made a difference to the study e.g. on the design processes/decisions? e.g. tangible impacts and less obvious ones, confidence in process (R, LA)
9. Can you give any examples where public involvement (ideas, suggestions, views) have not made a difference in relation to design decisions? (R, LA)
10. What difference do you think it would have made if there had been no user involvement in this project? (R)
11. What are your expectations about the remainder of the project? e.g. your learning needs, commitment, impact on the project? (LA); further impact of public involvement (R)

R = Researcher LA = Lay Adviser.

selected that best illustrate the point being made rather than selecting the most sensational findings, and the perspectives of a broad range of individuals have been represented.

Findings

Impact on lay advisers

From the outset of involvement, the advisers were relatively relaxed and said they expected smoothly facilitated involvement in co-design of the FES device. There was a consensus among the group that this was achieved and they believed that the model of involvement we adopted was exemplary. The only reported difficulty related to University parking.

Table 3. Public involvement timeline.

Activity\Months	1–3	4–6	7–9	10–12	13–15	16–18	19–21	22–24	25–27	28–30	31–33	34–36	37–39
Adviser recruitment	*												
Adviser preparation	*												
Researcher preparation	*												
No. of Advisory Group meetings	2	2		1		1			1		1		1
Adviser interviews			*						*		*		*
Researcher interviews			*										*
Analysis				*	*					*	*	*	*
Summative findings													*
End of study celebration													*

Key: * = activity took place.

Approaches taken to orientate and support advisers were well received and advisers said that they could not have been improved upon. Meeting papers were considered accessible, sufficiently detailed and distributed in a timely manner. Advisers particularly liked the plain language biographies of research team members being sent out prior to meeting them. As these contained photographs also, they were said to have been a useful tool to have at meetings to see who was who and their backgrounds. This is illustrated by one adviser who unavoidably began his adviser role from the second Advisory Group meeting, which could have presented him with a problem:

"I think it was good. I think, you know, the initial listing (biographies) and backgrounds to the people who were involved was very good because, you know, you walk into the first meeting and you start to know people straight away."

Steps taken to make the meetings accessible such as signage were greatly welcomed. Small details such as identifying adviser's individual food and drink preferences and not just basic dietary requirements were appreciated, as well as our practice of making refreshments available on arrival and providing a good quality lunch. Personal needs were met such an electric fan and iced water for an adviser experiencing hot flushes. Lay advisers particularly appreciated these efforts to "go the extra mile" as it made them feel valued.

There were no expressions of apprehension about involvement in the study with one exception:

"I had never been involved in a study like this. I felt quite intimidated. I thought it was going to be all professor and boffin types . . . And that it would all be very wordy and it would be frightening. And I did not think I was actually going to be bright enough to give anything to the study actually. But actually after the very first meeting I realised how very down to earth you all were . . . ''

All advisers felt that they contributed meaningfully and were listened to by the research team. The research team were considered to use plain language most of the time and to explain technical terms as they went along. A particular preference of advisers was to view, handle and critique "mock ups" of the FES device as its design evolved. There was a distinct preference for various concepts being explained to the advisers side by side so that they could compare and contrast them and comment on the possible solutions, which provided valuable feedback for the design team.

Several advisers said how much they valued the social side of the study in terms of positive relationships being built with each other and the relaxed friendly style of the research team. Advisers felt that their views were listened to and not disregarded out of hand. One adviser felt sufficiently comfortable to ask the involvement lead for help in applying for funding for her local stroke club. Guidance was given and following a later application funding was awarded. Therefore skills and knowledge transfer was not simply as a result of the training given to advisers on appointment (which covered public involvement and research and evaluation principles).

Advisers concurred that they enjoyed the meetings and the mental stimulation they provided. Several reported growing their confidence levels. One adviser explained that involvement had made her feel like she was a valuable contributor to society again, which is something she had not felt since having her stroke:

Adviser: "Yes. I mean, what I love is going to the university and pretending to be a human being again . . . Yes, and to feel that life is a bit more normal, you know, nearer to what I used to do . . . rather than lying on your back and dribbling."
Facilitator: "Okay. So having a useful role then in society, as it were. Those are my words I know, but is that the kind of thing that you mean?"
Adviser: "Yes, that's exactly it because that's what you miss a lot, you know, when you've done my sort of job, then suddenly you're nothing."

This same adviser successfully drew on her experiences of involvement in this study while at an interview for another involvement activity in which she is required to undertake lay reviews of research applications. Several advisers reported getting involved in other research studies as advisers or participants as a result of being involved in this study. Some but not all of these contacts were made through the study's research team members. Therefore the impact of involvement went beyond the confines and lifetime of this study.

Impact on research team members

At the study outset, several members of the research team were not convinced that public involvement could add that much to the study:

"I thought if we did our job well we ought to be able to predict what the users would want anyway. I think I felt that we could have worked it out without a user group. You'll be pleased to hear that with hindsight I think we were in fact wrong with such an arrogant position (laughter). I didn't think there would be significant added value because I thought we ought to be able to answer the questions before we started."

Research team members were somewhat surprised by the impact advisers had:

"I personally wasn't convinced they'd make a difference to the design. The design really was fairly constrained. Apart from

choosing between different options, I didn't think they'd make a lot of difference. But I've been pleasantly surprised that they have raised the very issues that we wouldn't have anticipated and their input has been very useful beyond just choosing between different designs, in refining each of those designs and suggesting other options.''

Aspects of the FES study that were observed and reported by research team members to have been directly influenced through discussions with advisers are summarised below:

- Technical input regarding equipment, e.g. footswitch samples
- Design and location of the FES body worn device stimulator box
- Feedback on foot-mounted sensor design
- Involvement in gait laboratory study design, e.g. what to measure
- Design of a clinical trial (feasibility study)

Advisers either advised on design, such as whether to have visual or audible error alarms, buttons or knobs on the FES control box and so on, or challenged the research team's thinking. Overall, the device ended up more likely to have utility once the research team developed a greater understanding about FES use in day-to-day situations. For example, one adviser pointed out his susceptibility to sore skin and use of topical ointments to manage this, which had implications for electrode design which required good skin contact. Data went on to be gathered about such issues.

While not initially viewed by the research team as an involvement opportunity, advisers evidently impacted positively on design of the FES study's small clinical trial. They challenged the research team's initial trial design and suggested alternatives which were responded to positively by the research team. The original trial design lasted 18 weeks, with participants being assessed weekly using a number of measures, including walking speed, and energy consumption during gait. The advisers strongly suggested that the overall duration of the study was too long and hence the duration was significantly reduced. Advisers also proposed reducing the frequency of measurement sessions and in the final design, gait was evaluated on a bi-weekly basis, rather than weekly.

Researchers believed this consultation contributed to the successful recruitment and retention of trial participants for whom the original trial design may have been off putting. One research team member stated:

''The user involvement has certainly helped with the configuration of the stimulator and had some impact on the clinical trial design ... Without their input the design configuration may have been different and we would have had less confidence going into the trial.''

Another reported example of impact is where advisers contributed to a discussion about features in the environment that can make walking for non-FES users difficult. Emphasis by the research team was on what they referred to as ''tripables'', that is objects that people could trip over, or that cause unsteadiness, such as pebbles, kerbs, or pavement unevenness. Adviser's held different, but related concerns including stability and balance, and their ability to dodge oncoming pedestrians when wearing an FES device. The Gait Laboratory work plans were subsequently reviewed.

The advisers reportedly contributed to increased understanding by the research team about what works in public involvement in research and co-design through experiential learning during the study. Other learning points pertained to ethical issues. Through challenging the research team's usual practice and asking to be involved themselves in for example, the clinical trial and orthotic sock appraisal, new insights were gained following debate about these requests with the University's Research Governance and Ethical Committee Chair. So long as risk was suitably managed, it was concluded that in this case, advisers were no less eligible to take part in the clinical trial than anyone else who fitted the trial's inclusion criteria. Trying out a bespoke orthotic sock from a wearability point of view was also acceptable so long as the wearer was fully informed about the product.

University of Salford financial processes were influenced directly by the advisers as payment systems were prompted to adapt to be more responsive to their needs. Reimbursement of travel expenses and payment in cash on the day became the new benchmark which prompted enhanced public involvement in other colleague's studies. Specifically, this led to development of improved payment guidance for the University's College of Health and Social Care.

Overall, the feedback from the evaluation coupled with personal learning from facilitating the public involvement in the FES study, continues to be drawn on heavily by the research team member acting as public involvement lead. She went on to develop a ''How to'' guide for public involvement in research generally for the NIHR [24]. Furthermore she accepted an offer of a second term of appointment as an INVOLVE member (Department of Health advisory group on public involvement in NHS, public health and social care research) and role within the NIHR Research Design Service North West as a patient and public involvement adviser. This positive impact of public involvement on a researcher's career has been acknowledged in a community study around asthma [25]. One negative effect that has not been identified anywhere else in the literature to date, concerns a sense of guilt when high standards of involvement were not achieved. In this case, this was because a report on the public involvement aspects was finalised much later than intended and the opportunity for meaningful involvement of the disbanded Advisory Group members, while their recollections were fresh in their minds, was no longer possible.

Discussion and concluding remarks

There is good evidence that the study's involvement approach had a significant positive impact on the study processes and outcomes. This conclusion is based on consideration of insights from the within-project evaluation along with personal critical reflection on the study and Advisory Group conduct by the public involvement lead. While not involved in the design of the original FES study funding application, the advisers were able to meaningfully contribute to FES device design and shape the clinical trial of the prototype FES device resulting from the study. As proposed by INVOLVE [9], if the public involvement field is to improve, it is better to build involvement in later rather than avoid it altogether in studies where researchers have not considered or implemented involvement at an early stage. This case study is therefore an example to others of how late involvement can still be meaningful and have valuable results, if managed appropriately.

Careful planning and preparation of study advisers and research team members has evidently paid off in terms of optimising working relationships, leading to enjoyable and productive discussions that were widely believed by those researchers and advisers to have resulted in better FES device design. This reflects the view of other researchers who have identified the main success factors for involvement as being adequate training and long-term involvement [10]. Evidence of the specific contributions of the advisers has been gathered as opposed to general claims of a positive impact being made with little substantiation. All too often glossy claims of a positive

impact of involvement are made in reports of public involvement and less evident are the realities of the challenges and negative effects of involving the public in research [10].

The co-design of the world's first wearable array-based (self-tuning) FES device [26,27] was enhanced through active public involvement in research. This has been achieved by developing and sustaining a group of lay advisers who were flexible and came together to meet at times to suit the needs of the design team and embraced the often hard to predict demands of the design process. Advisers reported the well documented impacts of gained confidence [28], self-esteem [29], enjoyment [30], research skills [10] and further involvement in research [32].

The FES device developed was an enhancement of previously available technology and the views of a range of advisers (existing and past FES users) were demonstrably useful. Pre-existing knowledge and experience of using FES devices among some of the advisers proved helpful in identifying previous problems with FES device design and use. Similarly input by other advisers without such experience was also useful as they did not frame their thinking around past experience and so were unconstrained in their expressions about what an ideal FES device would comprise.

As occurred in other research studies, research team members benefitted from a better understanding of the user perspective [32], better informed prototypes, and prompt feedback on device design. They also enjoyed and looked forward to the Advisory Group meetings as has been experienced by researchers in studies in the mental health field [28]. The clinical trial that advisers shaped went on to be successful. Improvement in the design of clinical trials is a previously recognised impact of involvement [33]. As in other studies [34], advisers were able to make recruitment approaches more sensitive to the needs of potential recruits which was made possible by their early involvement in its design. Furthermore, advisers were able to challenge the perceived ethical constraints that might otherwise have prevented their own involvement in the clinical trial and orthotic sock testing. Other researchers have also experienced this impact of the public on developing ethically acceptable research [31].

Once aspect of involvement that the advisers did not greatly embrace was assistance with dissemination or report writing. This was their preference (although one did contribute to development of a conference paper) yet there were also challenges around time and other resources to do this after study end. It was agreed that advisers would comment on the involvement report once drafted. While involvement in dissemination is encouraged in the involvement field, in reality it rarely happens [35].

While the facilitation of involvement and the approach taken by the research team was conducive to effective co-design, the attributes of the advisers themselves will likely have played a part. This is more difficult to evidence yet it is acknowledged that a different group of advisers may not have realised the same successes under the same conditions. The contribution of the advisers in this study was outstanding. Careful recruitment is advised when seeking members of the public to be involved in research to ensure they have qualities, skills or experiences to draw on that are needed by the research team. Some skills and knowledge can be developed within individuals but realistically there is not always the time to do this in a time-limited study. Some studies simply do not lend themselves as well to public involvement as others, and may not suit an advisory group approach such as the one described here.

Critical to success was the adequately resourced model of involvement that permitted travel and subsistence to be met, with adequate funding for the public involvement activities and the dedicated input of the involvement lead. All too often, coordination of public involvement can fall to the most junior member of

a team or to one with little actual involvement experience. The insights presented here go some way to illuminate the considerations that other research teams should be aware of.

This case study has set out one model of public involvement and other approaches may have been as effective, e.g. a series of one-off consultations. A considerable amount of detail has been presented to illuminate the ''how'' as well as the ''what'' of involvement. The insights gained from this within-project evaluation have utility to other AT researchers seeking to develop a product that is ''fit for purpose'', as well as have potential to enhance the design of their overall studies.

Acknowledgements

Declaration of interest

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2.1.2 Candidate involvement[2]

The candidate was not involved in the development of the National Institute for Health Research (NIHR) bid for the Health Technology Device (HTD480) project that proposed the use of a lay-advisory group. The candidate's clinical experience led her to raise some issues with the proposed single clinical study which expected the participants to attend weekly data collection appointments over 18 weeks using a single case experimental design (SCED). The proposed weekly evaluation measures were walking speed; the six-minute walk test, falls diary, PCI, the modified Ashworth scale of spasticity (MAS) and activity monitoring; accompanied by "gait lab measurements". The candidate's questioning of the appropriateness of this approach had a key influence on what the lay-advisory group would input to with the candidate introducing and leading discussions pertaining to the attendance schedule and battery of measures. This resulted in changes being made to the subsequent studies (Articles 2 and 3). This is detailed within Article 1 and critically discussed in section 3.1.3. The candidate was present at most of the lay-advisory group meetings and was involved in the researcher group interviews. Additionally, she contributed to manuscript review and feedback. This work was also presented at the INVOLVE conference in 2013 by the lead author, Tracey Williamson, and some members of the lay-advisory group (Appendix 3a).

2.1.3 Critical Appraisal

User centred, inclusive or participatory design has been recognised as necessary if AT is to align with the needs and expectations of the user thereby avoiding inappropriately designed products (Wilkinson & De Angeli, 2014). The user-centred design approach has been applied to, amongst other products, the development of mobility aids, (Wilkinson & De Angeli, 2014) wheelchairs (Sharma et al., 2008; Wilkinson & De Angeli, 2014) and environmental control switches (Dorrington, Wilkinson, Tasker, & Walters, 2016) but in the field of AT interventional devices for CNO foot-drop, despite user desire to be involved (Holtkamp et al., 2015) and devices not always meeting user needs/expectations (Holtkamp et al., 2015; Taylor, Burridge, et al., 1999a), if this approach has been used before it had not been published prior to the article. Purposive questionnaires have been used as post-market

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[2] A summary of the candidate's involvement in each article is presented in Table 1 on page 5

surveillance (Taylor, Burridge, et al., 1999a; Taylor, Burridge, Dunkerley, Lamb, et al., 1999). Where this publication differs from other user-led non foot-drop design reports is that the process of the public involvement was evaluated and that the lay-advisory group, at the candidate's suggestion, was able to contribute to the methodological decisions made for the associated empirical studies of the two new devices, as well as the design of the products themselves.

The purposeful sample used to recruit the lay-advisory group was appropriate for the case-study design (Marshall, 1996). The reported prevalence figures of foot-drop resulting from stroke (Verdié et al., 2004; Wade et al., 1987) suggested large numbers of potential participants from which to recruit to the empirical studies. It was only when the larger FES device study (Articles 3 & 4) was started that this was found not to be realistic. The reasons for this appeared to relate to a potential overestimation of foot-drop prevalence, certainly with regards foot-drop presenting in the absence of other significant impairments which excluded potential participants. This was coupled with local clinicians not engaging with recruitment citing time pressures and a lack of value placed on AT interventional devices in the context of physiotherapy. In line with the challenge of recruiting from the stroke diagnosis alone the candidate adjusted the recruitment strategy for the FES device evaluation study to include all CNO diagnoses. The impact of Article 1 basing all its results on stroke participants alone is unknown. The other potentially limiting factor in this regard is that only FES users were described in the article. As such despite some members trialling the new AFO device and commenting on its design it is unknown whether any of the lay-advisory group had any previous experience of using an AFO or the impact of this. The study was also limited by a lack of discussion as to why there was a high participant attrition (40%) but there was sufficient data to meet the study aims.

As the basis for the HTD480 project was to address cited limitations emphasis was placed on the extent and impact of the electrode placement issue. This resulted in the lead author over interpreting one piece of evidence (Taylor et al., 1999) by stating that some users found electrode placement issues to be a major problem, leading to long setup times and device abandonment. The Taylor et al (1999) study reported that 45% of past users cited electrode positioning problems as being either the primary (11%) or one of several (34%) reasons for discontinuing use. However, the paper did not link electrode positioning

problems to setup time. The paper was based on postal questionnaires with a return rate of 64% for current users and 43% for past users (Taylor et al, 1999).

Overall the case study design and how it was evaluated was appropriate and reproducible. The utilisation of the lay-advisory group to guide how the two new devices were evaluated in terms of discussion around study design and measures used was conceptualised and led by the candidate which aligned closely with the Medical Research Council (MRC) guidance in the evaluation of complex interventions of a phase I study (Medical Research Council, 2000). The feedback provided by the lay-advisory group about these methodological aspects were pivotal in highlighting the need to study the feasibility of the SCED proposed in the HTD480 project alongside the first, AFO, device (Article 2) as well as guiding the choice of evaluation measures which then led to the change in study design used to evaluate the new FES device (Article 3 & 4).

2.2 Article 2

Prenton, S., Kenney, L.P., Cooper, G. Major, M.J. (2014). A sock for foot-drop: A preliminary study on two chronic stroke patients. *Prosthetics & Orthotics International*. 38(5), 425-430. doi: 10.1177/0309364613505107

2.2.1 Article 2 Summary & Publication

This study was designed to fill the first two gaps identified in the evidence base. Firstly, it described an alternative to a conventional AFO device, designed to address cited limitations, and secondly aimed to evaluate the device using foot-drop specific and person-centred measures.

The limitations cited for conventional AFOs relate to usability (Holtkamp et al., 2015) and potentially reduced volitional muscle activity (Crabtree & Higginson, 2009; Hesse et al., 1999; Lairamore et al., 2011; Lam et al., 2005; Romkes et al., 2006) precipitated by ROM restrictions, both of which could result in user dissatisfaction. One solution to these limitations was an AFO constructed from a Lycra® like material (now marketed as the Dynamic Movement Orthoses (DMO) dorsiflex sock® by DMOrthotics™). This article reports on an evaluation of this elasticated orthotic device to establish its feasibility, gather user views, preliminarily evaluate its efficacy and evaluate the, revised, SCED design and choice

of measures that resulted from candidate direction and lay-advisory group involvement in the HTD480 project (Article 1). "The DMO Dorsiflex sock is designed to lift the foot up during walking and running (active dorsiflexion). This sock will improve incorrect walking patterns and provide additional uplift for patients with reduced strength" (DMOrthotics, n.d.). The principle suggested to achieve this is to introduce a net dorsiflexion moment through elastic panels that are stiffer on the dorsum of the foot/ankle as well as increasing proprioception (Gracies et al., 2000; Prenton, Kenney, Cooper, et al., 2014). This, is hoped, will remedy the foot-drop impairment, whilst at the same time the device addresses the usability limitations of appearance, poor comfort, restricted movement, and the associated, but largely unsubstantiated, claims of reduced volitional DF muscle activity, cited within the literature (Crabtree & Higginson, 2009; Hesse et al., 1999; Lairamore et al., 2011; Lam et al., 2005; Romkes et al., 2006). The manufacturer had been relying on an unpublished small (n=6) before-after study which focussed on sock use with children who had cerebral palsy which was published on their website (DMOrthotics, n.d.) but no evaluations on other pathologies had been undertaken. To explore the proof-of-concept of the DMO dorsiflex sock® the study undertaken by the candidate recruited two stroke participants as this was the most prevalent CNO diagnosis that had not been studied using such a device and there were potentially large numbers of potential participants from which to recruit.

An A-B SCED (Ottenbacher, 1986) was used. In this design there is an A-phase when each participant is repeatedly evaluated without the intervention over a series of days/weeks followed by the B-phase whether the same number of observations are conducted over the same length of time but with the intervention being used. Each phase in the study undertaken by the candidate was four weeks with bi-weekly observations of the evaluation measures resulting in 16 data points, eight in each phase. The choice of this number of data points was guided by SCED literature (Ottenbacher, 1986).

The second identified gap in the evidence base was considered in the context of their suitability and feasibility within the SCED with the original battery of measures in the HTD480 proposal first reviewed. The work by Brehm, Bus, Harlaar, and Nollet (2011) and Harlaar et al. (2010) as well as the WHO's ICF (WHO, 2001) were also influential in guiding choices. These sources indicated that measures of body functions and structures (BFS) (WHO, 2001) were necessary if the mechanisms-of-action were to be determined as well as

measures that capture the functional effects of the device (Harlaar et al., 2010). Mechanisms-of-action measures were needed to build evidence to determine if/how the device works and whether the changes to the materials used to construct the DMO dorsiflex sock® preserved known mechanisms of AFOs on the fundamental effects on walking deficits caused by the foot-drop impairment. Functional measures were necessary to evaluate whether any mechanistic effects translated into meaningful outcomes for the user (Brehm et al., 2011). Functional measures were further sub-divided into capacity qualifiers (CQ) and performance qualifiers (PQ)(Brehm et al., 2011). The lower limb orthotic candidate core set developed by Brehm et al. (2011) was used alongside evaluation measure literature, the candidate's clinical knowledge, lay-advisory group discussions and expertise within the research team to choose a justifiable battery of measures. Although the original set of measures in the HTD480 proposal covered the three ICF domains some of them were not deemed to be foot-drop specific or person-centred. As a result, some of the originally proposed, and commonly utilised, CQ measures were used (walking speed and six minute walk test), as was a variation of the user-perception measure (falls diary), but the BFS (PCI, MAS, "gait laboratory measurements") and PQ measures (activity monitoring) were substituted for alternatives, following discussion with the lay-advisory group (Article 1). As recognised as part of the first identified gap in the evidence base participant views were also sought about the device and the study design. The success of the chosen evaluation measures is discussed in the critical appraisal of this article (2.2.3).

Similarly, well-considered measures were lacking in previous foot-drop device evaluation literature. For example the proposed BFS measure that evaluates energy expenditure, PCI, tends to be collected over short distances (Burridge et al., 1997) this, coupled with the population being frequently physically unfit, means the steady heart rate needed to establish physiological cost is less likely to be achieved with the measurement protocols used. This invalidates such a measure (Danielsson, Willen, & Sunnerhagen, 2007). Similarly the MAS displays poor validity and reliability (Fleuren et al., 2010). Moreover, the candidate recognised that these commonly used measures, while allowing for study comparison, did not advance an understanding of whether there was any effect on the fundamental walking deficits caused by the foot-drop impairment nor whether there were discernible effects on user important outcomes. On reflection, activity monitoring would have added to the data

collected, albeit that it would not have indicated whether or not wearing the device was instrumental in any observed changes. It was discounted at the time due to concerns about whether participants' had sufficient dexterity to use the monitors as well as concerns that the introduction of another device would overcomplicate the use of the sock.

Electromyography would have also been an insightful addition to the battery of measures. This was not included due to a lack of knowledge on the candidate's part at the time of how AFOs might influence volitional muscle activity.

As a result the measures used to evaluate the device's feasibility and efficacy were (Table 2):

Evaluation measure	Visit Number															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Measures of body function and structure																
Trunk tri-axial accelerometry detecting vertical accelerations (step & stride regularity and step symmetry)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Total Heart Beat Index (THBI) (energy expenditure)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Measures of functional capacity																
Average self-selected gait speed over six metres	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Six minute walk test (functional exercise capacity)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Measures of functional performance																
Functional Ambulation Categories (FAC)	✓															✓
Measures of user perception																
User opinion questionnaire (Tyson & Thornton, 2001)																✓
Diary recording donning/doffing time & any issues with use (1 day a week)									✓		✓		✓		✓	
End-of-study questions																✓

Table 2: Evaluation measures used in Article 2. A-Phase

As stated in Chapter 1 the foot-drop impairment results in a slower speed and reduced endurance in walking. As such the evaluation of these frequently used aspects (Mudge & Stott, 2007) were deemed appropriate to evaluate. FAC is also frequently used (Mudge & Stott, 2007) and was chosen as the PQ alternative because it establishes a meaningful measure of mobility and was easy to administer (Williams, 2011). In contrast to the commonly used functional measures consideration of the most appropriate measures to use resulted in the chosen BFS substitute measures (THBI, trunk accelerometry) being novel in the field of research. Although the PCI has been criticised it was acknowledged that one potential mechanism-of-action of AFO, and the DMO dorsiflex sock® as a new iteration of this device, might be a reduction in the physical energy expenditure. The THBI (Hood, Granat, Maxwell, & Hasler, 2002) was chosen as a PCI alternative that was feasible within a SCED. An alternative measure for altered tone was not sought as the inclusion criteria required passive plantigrade to be achievable, thereby discounting potential participants with significant spasticity. The "gait laboratory measurements", such as the kinematic and/or kinetic features of gait, proposed in the HTD480 project are frequently used measures within the BFS domain (Mudge & Stott, 2007) that can evaluate the mechanism-of-action of a device on the transition from swing to stance, a key foot-drop walking deficit. However, gait laboratory based measures were logistically impossible to collect over the SCED bi-weekly, eight-week data collection schedule due to the lack of sufficient access to the University of Salford's gait laboratories and the associated time commitment needed to analyse the resulting data. Therefore, alternative, more practical, measures were sought. Gait variability using a tri-axial lumbar accelerometer which used inertial sensors to detect vertical accelerations (Moe-Nilssen, Aaslund, Hodt-Billington, & Helbostad, 2010) was chosen. These determined step and stride regularity and symmetry as a function of these (Hodt-Billington, Helbostad, & Moe-Nilssen, 2008) without the need for a gait laboratory. The chosen user-perception measures, which considered the feasibility of the device, were a generic diary which was collected weekly during the B-phase to log donning/doffing times, use and any issues/effects experienced. This was used alongside the AFO questionnaire developed by Tyson and Thornton (2001) and end-of-study questions that collected

information pertaining to the participant's views on the study design and chosen evaluation measures.

Data analysis of objective measures was based on visual inspection of graphical representation and use of the 2-Standard Deviation (SD) method (Ottenbacher, 1986). This method calculates the mean of the A-phase and plots a 2SD band either side of this. This is extrapolated across the B-phase and, in the absence of autocorrelation, if two consecutive points sit outside of that band in the B-phase the result is said to be significant. Measures of user perception (Questionnaire, diary and end of study questions) were narratively reported.

The study was able to report that the included participants found the DMO dorsiflex sock® feasible to use; this was the first time this had been shown for this population. It also highlighted that users perceived it to improve their walking. The study showed that the chosen and justified range of evaluation measures was feasible within the previously unused study design (SCED). Preliminary evaluation of these measures, that spanned BFS, CQ and PQ domains suggested that, in contrast to user-perception, objectively there were no clear effects. These findings concluded that the DMO dorsiflex sock® should be viewed with caution as an alternative to AFOs.

Finally, it also helped to highlight, alongside the lay-advisory group, potential limitations with the methodologies chosen. Namely the challenges of recruiting a larger group of participants who could commit to attending the intensive evaluation schedule and the logistical challenges of timetabling all the necessary data collection appointments for that larger sample size. It also showed that, although clearly justified and appropriate within the SCED, a different study design might allow the evaluation of effects on measures that could more specifically capture the fundamental effects on walking deficits caused by the foot-drop impairment. Thus this study influenced the methods used in the subsequent study (Articles 3 & 4).

A sock for foot-drop: A preliminary study on two chronic stroke patients

Sarah Prenton[1], Laurence PJ Kenney[1], Glen Cooper[2] and Matthew J Major[3]

Abstract

Background: Foot-drop is a common motor impairment of chronic stroke patients, which may be addressed with an ankle foot orthosis. Although there is reasonable evidence of effectiveness for ankle foot orthoses, user compliance is sometimes poor. This study investigated a new alternative to the ankle foot orthosis, the dorsiflex sock.
Case description and methods: The dorsiflex sock was evaluated using an A-B single case experimental design. Two community-dwelling, chronic stroke patients with foot-drop participated in this study. Measures were selected to span the International Classification of Function, Disability and Health domains and user views on the dorsiflex sock were also collected.
Findings and outcomes: The dorsiflex sock was not effective in improving participants' walking symmetry, speed or energy expenditure. Participant I showed improvement in the distance he could walk in 6 min when using the dorsiflex sock, but this was in keeping with a general improvement trend over the course of this study. However, both participants viewed the dorsiflex sock positively and reported a positive effect on their walking.
Conclusion: Despite positive user perceptions, the study found no clear evidence that dorsiflex sock is effective in improving foot-drop.

Clinical relevance

Although the dorsiflex sock offers an attractive alternative to an ankle foot orthosis, the case studies found no clear evidence of its efficacy. Clinicians should view this device with caution until further research becomes available.

Background

Foot-drop is a common motor impairment seen among chronic stroke patients, characterised by a lack of active dorsiflexion.[1] Plastic, metal or composite-based ankle foot orthoses (AFOs) are commonly used to manage foot-drop, as recommended by the Royal College of Physicians.[2] Despite this recommendation, issues around comfort, usability and their restrictive nature during walking can limit their use.[3] Orthoses based on Lycra® or other similar materials (fabric orthoses) are being used clinically and may address these issues. However, despite positive results with similar products, primarily in a paediatric population,[4–6] there are no reports on the efficacy of the application designed to correct foot-drop in an adult population with stroke. The principle behind the foot-drop application is to introduce a net dorsiflexion moment through elastic panels that are stiffer on the dorsal than the plantar aspect of a custom-fitted Lycra® sock.

In addition, there is a suggested benefit from increased proprioception due to the tight-fitting nature of the garment.[7] We, therefore, aimed to investigate the effects of the dorsiflex sock (DS) in addressing foot-drop (DMOrthotics, Redruth, Cornwall, UK, http://www.dmorthotics.com/products/dynamic-lycra-orthotics.php) (Figure 1) by

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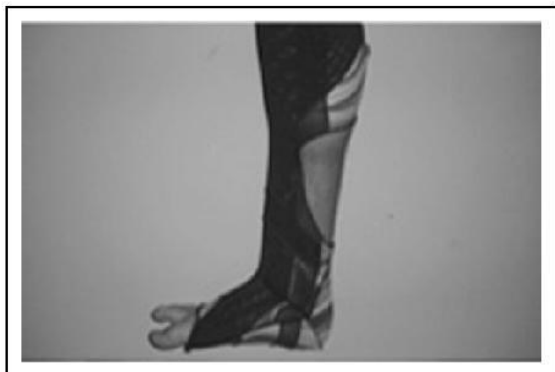Email: S.Prenton@salford.ac.uk

Figure 1. Dorsiflex sock.

Table 1. Inclusion/exclusion criteria.

Inclusion	Exclusion
Primary stroke resulting in hemiplegia, with unilateral foot-drop (defined as inability to actively dorsiflex the foot), more than 6 months ago	Another neurological/concurrent diagnosis impacting gait
Not currently receiving any other form of therapy	Inability to give consent
Passive plantargrade achievable	Other modality for foot-drop correction
Able to walk without physical assistance	Unable to attend over 8 consecutive weeks (twice weekly)

1. Collecting initial data on the efficacy of the DS on step symmetry, energy expenditure, speed, exercise capacity and walking ability;
2. Investigating users' perception of the DS.

Case description and methods

Following ethical approval from University of Salford (REP 09/030), participants were recruited through the Manchester stroke club network. Participant information sheets were given to local stroke club network co-ordinators and distributed at meetings and electronically. Potential participants contacted the chief investigator and were screened against inclusion and exclusion criteria (Table 1).

The majority of the screened volunteers were already using modalities for their foot-drop and hence were ineligible (see Table 1). A convenience sample of two who met the criteria, and were willing to complete the study protocol, were recruited to participate in this study.

Participants

Participant 1 was an unemployed 56-year-old gentleman with right hemiplegia. He could walk indoors with no walking aid, but used a four-point stick at night for safety. Outdoors he was independent with a stick over short distances, although he lacked the confidence to do this, depending on the conditions. He lived alone and was receiving no other therapy. His foot-drop was primarily due to weakness in his dorsiflexors. He had no cognitive deficit but did have expressive dysphasia.

Participant 2 was an unemployed 48-year-old gentleman with right hemiplegia. He was independently mobile both inside and out with a stick. He had been given a functional electrical stimulator but did not use it due to difficulties in donning. He lived with his partner and was receiving no other therapy. His foot-drop was primarily due to increased tone in his plantarflexors. He had no cognitive or communication deficits. Written informed consent for participation and publication was collected for both participants.

Design

An A-B single case experimental design (SCED)[8] was used. Both phases (A and B) spanned 4 weeks, with participants visiting the University of Salford for testing twice weekly (V1–V16). This produced eight baseline (A) and eight intervention (B) data points, over a total of 8 weeks (Figure 2). Testing was on the same days each week and approximately the same time, no food or caffeine was allowed 1 h prior to testing, and participants rested for 2 min prior to testing to allow heart rate to settle. Participants wore the same shoes at every visit.

At V1, participants were measured for a custom DS, according to manufacturer guidelines, and the measurements were sent to the manufacturer. The DS was provided at the end of V8, then donning/doffing and care guidelines were explained, according to the manufacturer's instructions. The participants were encouraged to take their DS home and use it between subsequent visits.

Outcome measures

According to the World Health Organization International Classification of Functioning, Disability and Health (ICF) model, measuring human function can be categorised as measures of 'body functions and structures' (BFS) and/or 'activities and participation'. 'Activities and participation' can be further categorised into measurements within a standardised environment (capacity qualifiers (CQ)) and a person's own environment (performance qualifiers (PQ)).[9] Outcome measurements that assess specific domains of these three ICF components (BFS, capacity qualifiers and PQ) were chosen from the relevant lower limb orthotic evaluation core set, developed by Brehm et al.[10]

BFS

Gait pattern. At each visit (V1–V16), participants first performed three self-paced 6-m walks (with 1.5 m at either
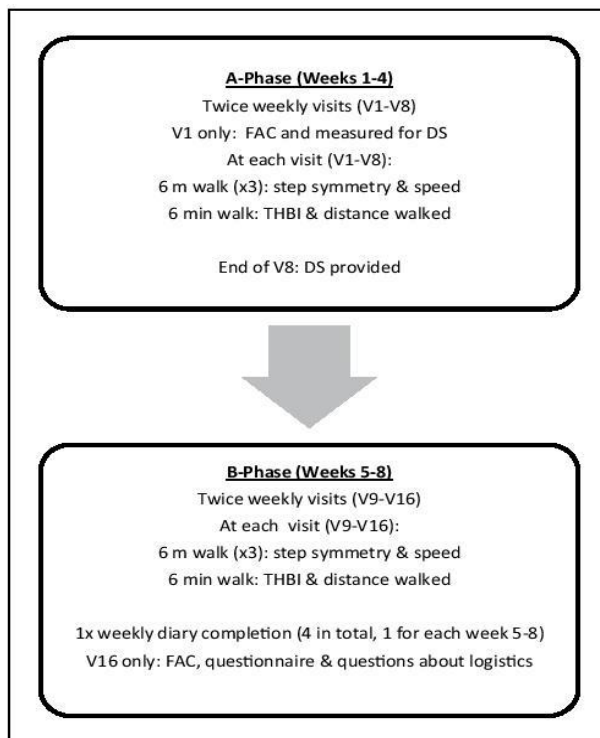
Figure 2. Protocol: all measures in A phase were taken without the DS; all measures in B phase were taken with the participant wearing the DS.
DS: dorsiflex sock.

end[11]). Mean values for step and stride regularity were calculated from vertical accelerations taken using a tri-axial lumbar-located accelerometer (Biometrics Ltd., Cwmfelinfach, Gwent, UK).[11] Step symmetry was then determined as a function of these.[11]

Energy expenditure. Heart rate was monitored while the participants then walked for 6 min over a pre-defined course to calculate the total heart beat index (THBI).[12] This is a measure of energy expenditure which is reliable in non-steady-state conditions and is comparable to more established measures.[12]

CQ

Gait speed. Mean values over the three 6-m walks[13] were calculated using a stopwatch.

6-min walk distance. The distance walked during 6 min (6-min walk distance, 6MWD) was recorded. This is a recognised measure of sub-maximal functional exercise capacity.[14]

PQ

Walking ability. Functional ambulation categories (FAC) distinguish walking ability by the amount of physical assistance required ranging from '0' (non-functional, ambulatory) to '5' (independent, ambulatory).[15] These were recorded at V1 and V16.

User perception. Participants completed the validated user opinion orthotic questionnaire by Tyson and Thornton[16] at the end of V16. Diaries which recorded donning/doffing times, time worn and any effects/issues participants encountered were completed once a week in the intervention (B) phase on a day the participants were not at the university.[4] On V16, participants were asked specific questions on the logistical feasibility of the design and whether they would continue to use the DS. Although these measures are not within the core set of measures proposed by Brehm et al.,[10] inclusion was justified in this first study of a new product. Figure 2 summarises when measures were collected.

Data analysis

Graphical interpretation and visual inspection was performed on all BFS and CQ data.[17] The autocorrelation coefficient, 'the extent to which scores at one point in a series are predictive of scores at other points in the same series' (p. 652),[18] was calculated for the baseline (A) data points using the method described by Bengali and Ottenbacher.[18] In the absence of significant autocorrelation ($p \leq 0.05$), which would bias any calculations based on averages, the quasi-experimental 2-standard deviation (SD) method was applied.[19] This involves calculating a 2-SD 'band' based on baseline (A) data points which is then projected onto the intervention (B) phase. If two successive intervention (B) phase data points sit outside of the band, it is said to show a significant ($p < 0.05$) improvement.[19] PQ measures were recorded and summarised.

Findings and outcomes

BFS and CQ measures

Visual inspection of THBI, walking speed and 6MWD (Figures 3 and 4) showed an improvement trend for Participant 1 over the course of testing (V1–V16). Conversely, step symmetry demonstrated a declining trend for Participant 1. Neither of these trends appeared to be affected in any way by the introduction of the DS (Figures 3 and 4). Significant baseline autocorrelation,[18] even with first difference transformation,[19] was found in all measures apart from 6MWD. Participant 1's improvement in this measure was classed as significant ($p < 0.05$) using the 2-SD method.[17] Participant 2 showed no change in any measure (Figures 3 and 4).

PQ measures

Walking ability. According to the descriptions by Mehrholz et al.[15] at V1, the FAC for Participant 1 was 4 (ambulatory,
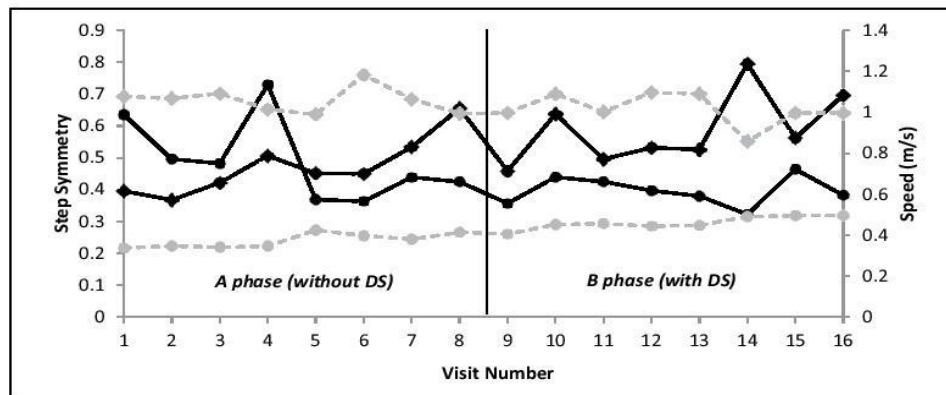
Figure 3. Average step symmetry and walking speed, both measured over three self-paced 6-m walk tests. Symmetry is depicted with a solid black line and speed with a dashed grey line. Participant 1 is represented by a circle and Participant 2 by a diamond. The 2-SD bands are not depicted to aid visual inspection and two data sets are shown to minimise the number of figures used.
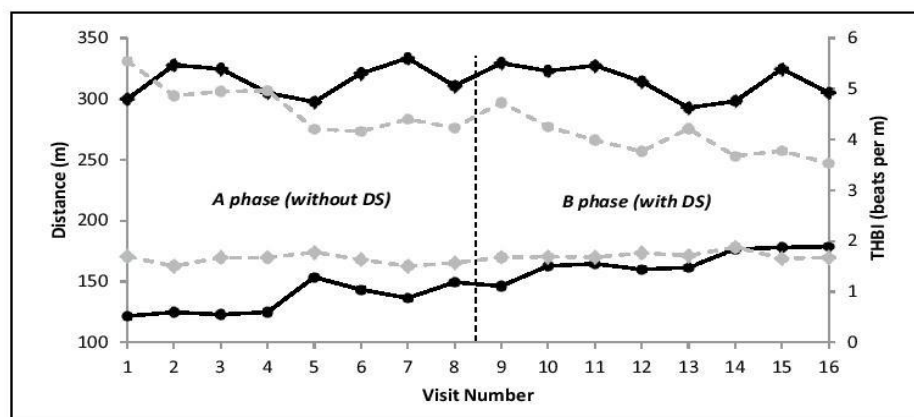SD: standard deviation.

Figure 4. Both THBI and 6MWD were measured over a 6-min walk test. Distance is depicted with a black solid line and energy expenditure with a grey dashed line. Participant 1 is represented by a circle and Participant 2 by a diamond. The 2-SD bands are not depicted to aid visual inspection and two data sets are shown to minimise the number of figures used.
THBI: total heart beat index; 6MWD: 6-min walk distance; SD: standard deviation.

independent, level surface only), and for Participant 2 was 5 (ambulatory, independent). These scores were unchanged at V16.

User perception. With regard to the questionnaire,[16] Participant 1 reported the DS resulting in 'little' or 'much' improvement in all the areas of gait asked about. Overall, he reported his walking being 'much better'.[16] The only impact Participant 2 reported was 'a little improvement' in the ability to lift his toes, but overall he felt his walking was 'better'.[16] Both felt the DS was 'easy' to don/doff, 'comfortable' and were 'not concerned' by its appearance.[16]

Diary entries showed that donning/doffing was consistently independent for both participants and times remained

consistent throughout (Participant 1 reporting 2–3 min to don/doff; Participant 2 reporting 10–15 s to don and 5–10 s to doff). This was not consistent with what was observed, with both underestimating how long it took. Participants wore the DS all day after their first week, where the manufacturer recommended a gradual increase in use. Regarding the effects of the device, Participant 1 consistently wrote that his affected leg felt 'very very limp' without the DS on and he wrote he felt 'better with it on'. Participant 2 had less to report, but noted that with the DS, 'his toes were not catching when walking'.

Questioning around the logistics of the study design indicated that for Participant 1, two visits per week were all they could manage, but that he enjoyed his involvement as

'it got him out of the house', whereas Participant 2 could have come more frequently. Both stated they would carry on using the DS.

This study set out to preliminarily investigate the efficacy and users' perceptions of the DS. The single quasi-statistical change in the 6MWD seen for Participant 1 cannot be confidently attributed to the effects of the DS. There was no change in any other BFS or CQ measures, and the change in the 6MWD is confounded by the continually improving trend observed for Participant 1 (Figures 3 and 4).[20] When taken together, this suggests it is more likely that the observed change was due to the repeated bouts of exercise during the walking tests at V1–V16, rather than the wearing of the DS. The DS had no impact on any measured aspect of Participant 2's walking.

In terms of PQ measures, walking ability (FAC) was not affected by the DS. In contrast to the objective findings both participants' perceptions of the impact of the DS on their gait were positive. This could be due to the inclusion/ exclusion criteria (Table 1), which notably required repeated dedicated testing over 8 weeks during the day and the absence of other foot-drop modalities (Table 1). This restricted eligibility to those without daytime commitments and who were not having health-care input. The combination of these factors may well have resulted in a self-referred convenience sample whose views were positively influenced by the fact that their foot-drop was being addressed.

The A-B design is the basic SCED and has well-established limitations.[8,17] As the DS could have a carryover effect, recruitment numbers were unknown (and were ultimately small), and compliance could not be predicted, alternatives such as A-B-A or multiple baseline design[8,21] were not deemed appropriate. In addition, the participants were rather homogenous being male, right-sided hemiplegic and functioning at a relatively high level which limits the generalisability of the findings.

However, the design and measures chosen aimed to capture the breadth of impact of the DS and are indicative of measures used in studies that informed the Royal College of Physicians guidelines.[2] In contrast to our findings, thermoplastic AFOs have been reported to have a significant impact on a range of measures including speed, symmetry, exercise capacity and walking performance.[2,3,22]

Conclusion

Despite positive views of the DS from both participants, and the recognised limitations, this preliminary study found no clear evidence to demonstrate that the DS, with its current design, was effective in improving walking for two community-dwelling, chronic stroke patients with foot-drop. It should be viewed with caution as an alternative to AFOs, until further research becomes available. To strengthen the external validity of these findings further research should include a greater variety of participants in terms of side of hemiplegia, age, gender and FAC to represent the heterogeneous stroke population. Comparison to an AFO, or placebo, using either a SCED or a group design would strengthen internal validity. Measures should continue to refer to Brehm et al.[10] core set recommendations; however, BFS might be best served by using three-dimensional (3D) gait analysis, which would record the effect of the DS on kinematics, including toe clearance, a measure of trip risk, during swing.[23]

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2.2.2 Candidate involvement[3]

The candidate was the driving force behind this study and its publication. The original HTD480 project had suggested the use of A-B SCED with weekly measures for the final work package (single evaluation study of both devices). The candidate questioned the appropriateness of this based on clinical knowledge of potential participant availability over extended periods and lay-advisor feedback. This was therefore refined by the candidate, with input from the lay-advisory group and extensive reading around this methodology for this initial study, as a pilot study to evaluate the proof-of-concept of the sock and to inform the final larger planned study. All measures were chosen and the majority of the data collection was done by the candidate. The manuscript write up, the journal chosen and the submission/ manuscript changes was led by the candidate.

2.2.3 Critical appraisal

Single case studies and case series had been used in the evaluation of FES devices (Burridge et al., 2007; Daly et al., 2001; Taylor, Burridge, et al., 1999b) before but this publication was the first within the AFO/FES field of research to use SCED. SCED is a clinically relevant alternative to experimental design (Barlow, Nock, & Hersen, 2009) that seeks to address some of the limitations with traditional group design. Of note group design relies on large representative randomised samples in order to address threats of internal and external validity. This is not always possible, especially within a heterogeneous population such as stroke (Todman & Dugard, 2010). Traditional group design also aims to statistically prove or disprove a hypothesis, based on group averages. This can be difficult to clinically apply to individual patients especially if they differ from those included. SCED addresses this by allowing focus on individual results (Barlow et al., 2009). Pragmatically the SCED approach allowed for a preliminary study of the DMO dorsiflex sock® without the need for extensive recruitment.

This proof-of-concept study met its aims by showing that the device could be successfully implemented and credibly evaluated. As such it was able to comment on the appropriateness of further direct replication studies (Byiers, Reichle, & Symons, 2012) or a

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[3] A summary of the candidate's involvement in each article is presented in Table 1 on page 5

more traditional phase II/III trial (Medical Research Council, 2000) and indicate how this might be undertaken.

With regards the SCED, the number of data points used in each of the two phases (eight per phase, 16 in total) was supported by SCED literature (Johnston & Smith, 2010) and the decision to make the visits twice weekly was made with lay-advisory group involvement to reduce the time commitment to the participants. Both participants attended all the sessions and 100% of the planned data was collected at each session. However, the design highlighted the logistical difficulties this schedule might pose with larger participant numbers. Alternative SCED were considered and discounted. Withdrawal (A-B-A) and alternating designs (A-B-A-B) assume there are no lasting carryover effects (Barlow et al., 2009; Todman & Dugard, 2010), and whether these occur with this device was unknown. The feasibility of recruitment and participant compliance with the SCED design was also unknown which discounted the use of the multiple baseline design (Todman & Dugard, 2010).

As described, the measures used to evaluate the feasibility and efficacy of the DMO dorsiflex sock® were chosen following detailed consideration of relevant literature, consideration of the possible mechanisms-of-action and functional effects of the device, the practicalities of undertaking repeated measurements within an A-B SCED, how to explore device feasibility as well as candidate clinical experience and discussion with co-researchers and the lay-advisory group. The candidate did not constrain the choices with a desire to ensure they were comparable to other studies in the field resulting in a novel combination of measures that, importantly, were shown to be feasible. This innovative approach, coupled with the previously unused SCED, sets it apart from other work in the field. As indicated in the article this originality did mean that results were harder to compare to others but do advance the field by suggesting a different approach to study design and measure selection. With hindsight it became evident that the THBI & gait symmetry measures, whilst being easy to implement and capturing gait features in the BFS domain that could potentially indicate mechanisms-of-action, were not sufficiently foot-drop impairment specific. This allowed reconsideration of the evaluation measures used in the subsequent, larger, study and how that study was best designed to utilise those measures (reported in Articles 3 & 4). The chosen CQ measures (walking speed and six-minute walk

test) in conjunction with the SCED may have had a confounding effect of the results, particularly in the more impaired and probably least fit participant, participant 1. In this participant it was not possible to clearly distinguish the exercise/practice effects of participating in the protocol (twice weekly data collection visits each involving a six-minute walk and three nine metre walks) from any benefits of wearing the DMO dorsiflex sock®. This finding again allowed for re-consideration of how best to design the subsequent final study of the FES device (Article 3 & 4).

The user-perception measures (diary, questionnaire, end-of-study questions) contributed to the demonstration of device feasibility. However, they also highlighted the tendency for the participants in this study to underestimate donning/doffing time, as what was observed when participants were in being evaluated did not appear to reflect the times reported in the diaries. These measures also suggested that subjective user-perception of improvement did not match with objective data. This again helped to inform evaluation measure choices for the subsequent study (Articles 3 & 4) as it highlighted that evaluative measures such as these introduced social desirability bias (Grimm, 2010).

Visual inspection of graphically represented data is the most commonly used method to analyse SCED data, with debate as to the appropriateness of applying statistical testing to SCED, given its focus on the individual (Ottenbacher, 1986). However, to justify further, larger scale, study effect sizes need to be explored. The use of traditional parametric tests; randomization tests, autoregressive integrated moving average (ARIMA), interrupted time-series analysis (ITSA), Revusky's Rn, split middle/ celebration line technique, double boot-strap, the 2-SD band method (Barlow et al., 2009) C statistic (Ottenbacher, 1986) and running median (Zhan & Ottenbacher, 2001) were researched. Traditional parametric tests are not appropriate for SCED as they violate the required assumptions (Barlow et al., 2009). Some of the SCED specific tests required too many data points (running median, ARIMA & ITSA), others required other SCED designs and randomization of when intervention is introduced (randomization; Revusky's); the data showed an improving baseline for one participant in some of the outcome measurements which discounted the split-middle/celeration technique and C statistic and the candidate could not find sufficient information about the double-boot strap method. The semi-statistical 2-SD band method was decided upon by the candidate to be the only appropriate approach (Ottenbacher,

1986) alongside the visual inspection of graphically represented data. A lag-1 autocorrelation coefficient (r_k) for the baseline was calculated (Bengali & Ottenbacher, 1998) and the significance of serial dependency was calculated using Bartlett's method (Bloom, Fischer, & Orme, 2003). Whilst more rigorous statistical methods could have provided greater strength of inference (Johnston & Smith, 2010) ultimately the design met the aims of the study of evaluating the feasibility of the DMO dorsiflex sock®, gathering user views, preliminarily evaluating the efficacy of the device and evaluating the credibility of the methods chosen.

The two participants that were recruited, through local stroke groups, were both male with right sided hemiplegia of a similar age and ambulatory class (as determined by the FAC (Mehrholz, Wagner, Rutte, Meissner, & Pohl, 2007)) and neither were employed. This homogeneity could be seen as a threat to the external validity of the results. Conversely some would argue that the homogeneity could highlight direct replicability which strengthens the reliability of SCED findings to that specific part of the population (Barlow et al., 2009).

With regards the device itself the mechanical properties were not reported nor was this reported in the article. This is now recognised as a limitation of all AFO evaluation studies (Bregman et al., 2010; Ridgewell, Dobson, Bach, & Baker, 2010) but was not considered at the time. However, given the nature of the elasticated materials used it is unlikely to be possible to report the mechanical properties of the sock in comparable way to conventional AFOs, which raises challenges for future studies.

It is acknowledged that the conclusion drawn by this article that the DMO dorsiflex sock® should be cautiously viewed as an alternative to a conventional AFO is undermined by the limitations discussed above and therefore further study is necessary to substantiate the findings. However overall this study was able to demonstrate that a commercially available elasticated orthotic (DMO dorsiflex sock®) suggested as an alternative to conventional AFOs, to address their commonly reported limitations, could be feasibly used by stroke participants. However, that by addressing those limitations efficacy would be appear to be undermined; as shown by the negligible effect sizes on walking measures across the ICF domains. Moreover, this study has the potential to indirectly impact future clinical guidelines as it contributed an evaluation of a foot-drop device using a novel study design

(SCED) and a justified approach to the measure choice, thereby informing future study design in this area. This study incorporated user/participant feedback to inform the design and evaluation of the device, from the lay-advisory group and participant perspective. The users' feedback, as well as the consideration of the appropriateness the evaluation methods used within the SCED, in particular those that might specifically evaluate the fundamental mechanistic effects on walking were pivotal to how the next study was approached with regards design and measures chosen.

2.3 Article 3

Prenton, S., Kenney, L.P, Stapleton, C., Cooper, G., Reeves, M.L., Heller, B.W., Sobuh, M., Barker, A.T., Healey, J., Good, T.R., Thies, S.B., Howard, D., Williamson, T. (2014). A feasibility study of a take-home array-based functional electrical stimulation system with automated setup for current functional electrical stimulation users with foot-drop. *Archives of Physical Medicine & Rehabilitation, 95*(10), 1870-1877. doi: 10.1177/0309364613505107

2.3.1 Article summary & Publication

As with Article 2 this study sought to address both the first identified gap in the evidence base by looking at the feasibility of an alternative version of a conventional FES foot-drop device, designed to address cited limitations (electrode placement difficulties). It focussed on using foot-drop specific and user-important evaluation measures so as to address the second identified gap around limitations in device evaluation.

The preliminary findings from Article 2 that it was feasible to collect and measure a range of evaluation measures supported by the literature as being necessary to capture effects but that the DMO dorsiflex sock® may not show effect sizes worthy of further definitive evaluation of efficacy meant that further study into this device was not deemed appropriate. The next, and final study, to come from the HTD480 project therefore investigated the FES device designed to address the setup limitation of conventional devices, called ShefStim®. The ShefStim® replaces the active electrode (cathode) with an 8x8 array of 64 channels (Figure 6).
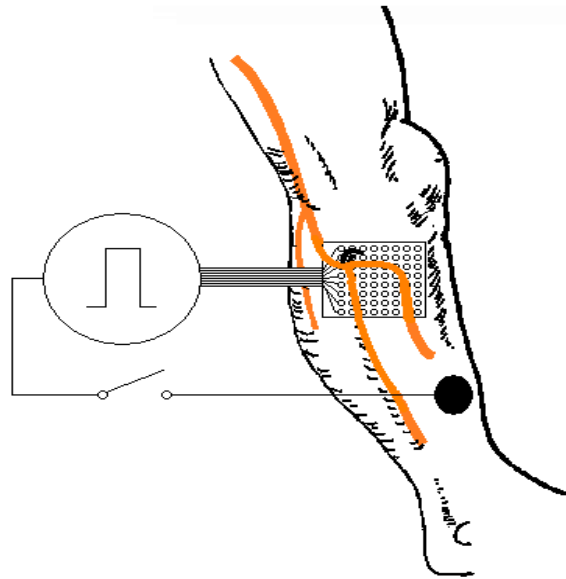
Figure 6: ShefStim® device showing the electrode array replacing the traditional cathode over the common peroneal bifurcation point. The conventional anode is shown in black. From Heller et al. (2013)

Setup is automated, using a search algorithm to create 4x4 "virtual electrode" from that array. A phased approach which first detects the motor threshold required, then which virtual electrodes produce an acceptable foot response and finally ranks which of those is the most appropriate, based on a three-part cost function is used (Heller et al., 2013). This automation removes the reliance on the user to identify and perceive the correct, active, electrode position. The proof-of-concept laboratory based study of a ShefStim® prototype demonstrated that this prototype produced foot responses which were comparable to those produced by a clinician setup of a conventional FES system (Heller et al., 2013). The study was conducted with technical support on hand and with some of the setup process running on a computer. The product had been further developed, with consultation and input from the lay-advisory group, into the CE marked ShefStim® device. The next logical step was therefore to see if people could use this fully self-contained system in a real world environment.

This study sought to evaluate the feasibility of using ShefStim® within a real world environment as well as to collect preliminary data regarding its usability (effectiveness, efficiency and satisfaction) (Arthanat et al., 2007; Choi & Sprigle, 2011)). Ten participants were recruited but three withdrew before it started resulting in a single group of seven

current FES users being studied. Participants were first evaluated with and without their own FES device being worn. They were then provided with a ShefStim® device, which they were shown how to use and then took home to use for two weeks. After which they were evaluated while ShefStim® was worn.

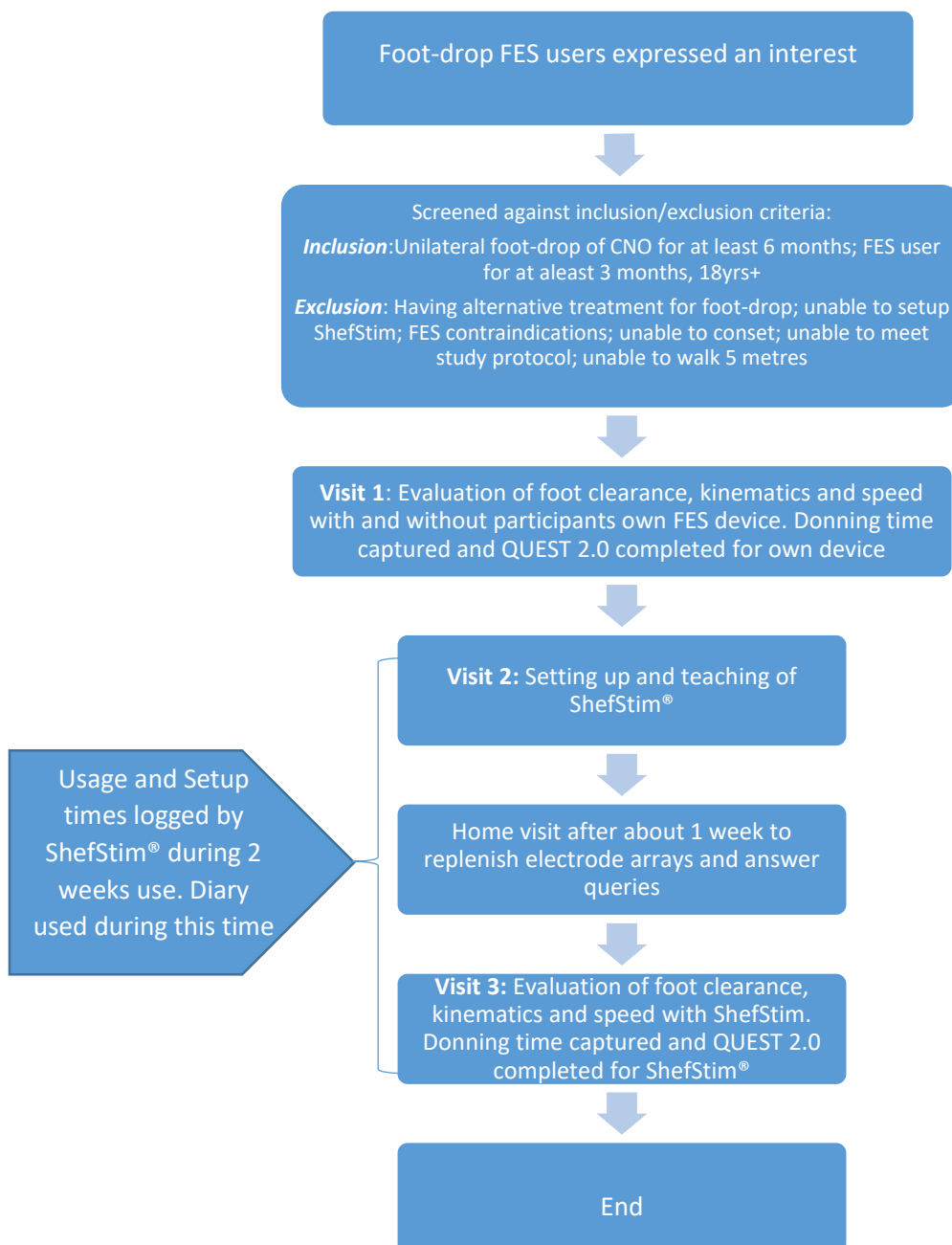The participant journey is detailed in Figure 7.

Figure 7: Participant journey through ShefStim® study (Article 3).

The evaluation measures used were:

- Monitored ShefStim® Usage. The device logged the number of heel lifts as an approximation of the number of steps taken. This measure evaluated whether ShefStim® could be feasibly used and how much task-specific repetitive activity was engaged with.

- Timed donning/automated setup for own FES device and ShefStim®. Whole system donning time was surreptitiously done when participants came for gait laboratory visits and the ShefStim® devices also recorded the time for each automated setup. The cited setup issues (Heller et al., 2013; Taylor, Burridge, Dunkerley, Lamb, et al., 1999) extend the time of setup. The automation process employed by the ShefStim® was designed to reduce this and so whether this occurred was a necessary evaluation measure. This measure also explored the feasibility of ShefStim® use

- Diary for the two weeks of use for the participants to record any external or setup issues they experienced, either completed by the participant or a carer. The diary again explored whether ShefStim® could be feasibly used outside of a laboratory environment in real time.

- Foot clearance during swing based on the work by Sibylle Thies and colleagues (Thies, Jones, Kenney, Howard, & Baker, 2011; Thies, Kenney, et al. (2011)) to directly evaluate any effects on the foot-drop impairment. Figure 8 shows how these were setup prior to the arrival of the participant using a static capture. These were then removed and re-created virtually after data collection (Thies, Jones, et al., 2011; Thies, Kenney, et al., 2011). Ultimately only virtual markers P1, 2 and 4 (Figure 8) were investigated given that these most directly reflected the mechanical manifestation of the foot-drop impairment. The novel aspect in this study was that the positions of these virtual markers were analysed when they passed the contralateral medial malleolus.

Figure 8: Sole marker setup to evaluate foot clearance. From Thies, Jones et al., (2011); Thies, Kenney, et al., (2011)

- 3D kinematic gait analysis: sagittal and frontal plane ankle angles at initial contact (IC), to directly evaluate the effect on foot positioning from swing to stance, using the shank Calibration Anatomical System Technique (CAST) marker setup (Cappozzo, Catani, Della Croce, & Laeardini, 1995; Levine, Richards, & Whittle, 2012) alongside a shod foot model as seen in Figure 9 (Pratt, Reeves, van der Meulen, Heller, & Good, 2012). Walking speed was also captured from an additional lumbar marker.
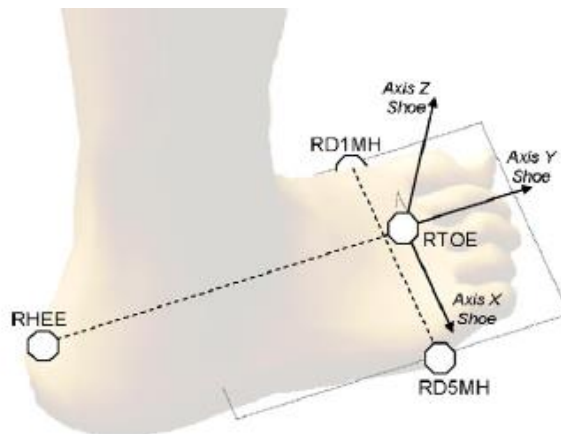

Figure 9: Shod foot model. From Pratt et al. (2012)

- User satisfaction with own FES device and ShefStim®: The device sub-scale of the Quebec User Evaluation of Satisfaction with assistive Technology 2.0 (QUEST 2.0)

(Appendix 4) (Demers et al., 2002); which had not been considered by previous work in the field.

Usage results showed that Shefstim® could be used unsupervised by all participants outside of a laboratory setting. The efficiency element of usability (Arthanat et al., 2007; Choi & Sprigle, 2011), as captured by donning/setup times, showed that although automated, and therefore not requiring effort or relying on perception on the part of the user, it took longer than expected. This was further noted as a problem by users in diary entries. As a feasibility study (Arain et al., 2010) the total setup time and diary results, alongside other reported setup and external issues, were useful for the further product refinement suggestions noted in the article (for example: user training material, voice commands, device charging). Not noted by users but recognised by researchers were the issues with the electrode-skin interface. The hydrogel used lost resistivity over time due to sweat ingress which could have led to transverse currents (Cooper et al., 2011). To combat this problem arrays had changed daily. This was neither clinically or commercially viable. Despite these reported issues participants were, overall, equally satisfied with both devices, as determined by the QUEST 2.0; this was encouraging given the limited period of time it was used and its precommerical nature.

Inferential statistics were not used but descriptive statistics indicated that the mechanisms-of-action employed by conventional and ShefStim FES devices were comparable; with a suggestion of a better foot clearance during swing, as highlighted by the novel use of foot clearance as a foot-drop specific measure, and foot orientation correction at IC with ShefStim®, as indicated by ankle kinematics. The ShefStim device also had comparable effects on walking speed to conventional FES devices. These results indicated that the device, once the hydrogel issue had been solved, warranted a definitive efficacy trial, which would be required as an evidence base for prescription.

Thus the study was able to conclude that the ShefStim was a feasible device that warranted further development work, followed by a definitive efficacy trial. It was able to achieve this due to the justified, and often novel use of the, battery of measures chosen.

ORIGINAL ARTICLE

Feasibility Study of a Take-Home Array-Based Functional Electrical Stimulation System With Automated Setup for Current Functional Electrical Stimulation Users With Foot-Drop

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Abstract

Objective: To investigate the feasibility of unsupervised community use of an array-based automated setup functional electrical stimulator for current foot-drop functional electrical stimulation (FES) users.

Design: Feasibility study.

Setting: Gait laboratory and community use.

Participants: Participants (N=7) with diagnosis of unilateral foot-drop of central neurologic origin (>6mo) who were regular users of a foot-drop FES system (>3mo).

Intervention: Array-based automated setup FES system for foot-drop (ShefStim).

Main Outcome Measures: Logged usage, logged automated setup times for the array-based automated setup FES system and diary recording of problems experienced, all collected in the community environment. Walking speed, ankle angles at initial contact, foot clearance during swing, and the Quebec User Evaluation of Satisfaction with Assistive Technology version 2.0 (QUEST version 2.0) questionnaire, all collected in the gait laboratory.

Results: All participants were able to use the array-based automated setup FES system. Total setup time took longer than participants' own FES systems, and automated setup time was longer than in a previous study of a similar system. Some problems were experienced, but overall, participants were as satisfied with this system as their own FES system. The increase in walking speed (N=7) relative to no stimulation was comparable between both systems, and appropriate ankle angles at initial contact (N=7) and foot clearance during swing (n=5) were greater with the array-based automated setup FES system.

Conclusions: This study demonstrates that an array-based automated setup FES system for foot-drop can be successfully used unsupervised. Despite setup's taking longer and some problems, users are satisfied with the system and it would appear as effective, if not better, at addressing the foot-drop impairment. Further product development of this unique system, followed by a larger-scale and longer-term study, is required before firm conclusions about its efficacy can be reached.

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The efficacy and safety of functional electrical stimulation (FES) as a treatment for foot-drop of central neurologic origin is well established[1]; however, usability issues have been noted.[2,3] In fact, a survey of new and established users of the Odstock drop foot stimulator found that 44% of users reported difficulties in locating

the correct electrode position,[3] and this finding is of particular relevance to this study. Traditional single-channel surface foot-drop FES systems deliver current via a pair of electrodes, accurate placement of which is crucial to the correct functioning of the system. The optimal site for stimulation may vary from day to day and even throughout a day, which further complicates the setup process.[3] Interestingly, despite wide recognition of this issue,[4] only 1 study specifically reported on the impact of user-defined electrode placement on functional outcomes.[5] The study found a poorer foot response when participants located electrodes themselves compared with clinician setup.

In response to this issue, new designs of FES systems have been produced. These include electrodes integrated into cuffs[6,7] and implantable systems.[4,8] Most recently, Heller et al[5] reported on an array-based FES stimulator for foot-drop. The system uses the principle of a virtual electrode. Stimulation is delivered via a 4×4 cluster of small electrodes, chosen from within an 8×8 array. The choice of which virtual electrode to use and at what level to stimulate is determined automatically during setup by an algorithm, which uses the foot response to stimulation as its input. This approach fully automates the setup process (both location and amplitude of stimulation), potentially reducing setup difficulty. Heller's study found that automated setup was comparably effective and quicker than user setup of conventional FES. The system, originally studied by Heller, has been further developed, named ShefStim, and has met appropriate European Union health, safety, and environmental protection legislation (Conformite Europeene marking). To our knowledge, this article is the first feasibility[9] study of this system, which combines a period of unsupervised use in conjunction with gait evaluation at the start and end of the study period. The primary aim of this study was to investigate whether this array-based automated setup FES system could be used unsupervised by foot-drop FES users within the community environment. In addition, a number of other subaims were addressed. These were as follows: (1) to investigate the community-usage patterns and user satisfaction with the system; (2) to investigate the total setup time and automated setup time for the system compared with the participant's current FES system; and (3) to investigate the effects of the system on walking speed, ankle angles (at initial contact), and foot clearance during swing compared with the participants' current FES system.

Methods

ShefStim system

A detailed description of the operating principles of the stimulator and changes in order to achieve Conformité Européenne marking are given in Heller.[5] The same fixed parameters (monophasic waveform, charge balanced, 40Hz, 160µs) were used, but the system used in Heller's study restrained the leg in a support during the automated setup process. This was deemed impractical for a take-home device; therefore, users were instead requested to

extend their leg and rest their heel on the floor during home automated setup.

Figure 1 shows the ShefStim, which consists of a leg-worn stimulator (part a) housed in a modified knee sleeve[a] (part b) and a flexible printed circuit board array of 64 electrodes (cathode electrodes) (part c) covered with a thin layer of high resistivity hydrogel.[10-12] Sweat ingress changes the conductive properties of the hydrogel sheet; therefore, a replacement array fitted with a new sheet of hydrogel is used each day.[12] Figure 1 also shows the conventional footswitch, conventional anode (5×5 PALS platinum neurostimulation electrode[b]) (part d), and a foot sensor and remote control device housed in a bespoke foot pod[c] (part e). The foot sensor and remote control device detect foot orientation, provide voice commands during automated setup, and act as a handheld remote unit postautomated setup, allowing the user to pause and change intensity as required.

Donning the system

To don the ShefStim the following steps are required: (1) the footswitch (see fig 1 part f) is placed under the heel with the connecting cable extending from the shoe; (2) the knee sleeve is donned aligning the stimulator pocket with the long axis of the tibia; (3) the stimulator is placed in the knee sleeve's stimulator pocket; (4) the foot pod containing the foot sensor and remote control device is positioned over the shoe, which is located approximately central over the dorsum of the foot and attached with Velcro[d]; (5) the electrode array placement, the center of the third row of electrodes down from the top of the array, is aligned with the head of the fibula and the inner edge parallel to the tibia; (6) the electrical connector for the array (see fig 1 part g) is inserted into the array socket on the side of the stimulator, and the array is secured with a Velcro strap; (7) the self-adhesive anode is positioned over the tibialis anterior; and (8) the footswitch connector (see fig 1 part h) is inserted in the stimulator. The automated setup is then started.

Automated setup

For a more detailed description of the automated setup algorithm, refer to the study by Heller.[5] The only difference between the algorithm used in the Heller study[5] and the ShefStim algorithm relates to the cost function used in stage 3 of the setup process. The cost function enables many factors that are not directly comparable (eg, angle of dorsiflexion [DF], stimulation current) to be combined into 1 optimization routine. In this case, for example, the angle of the DF and stimulation current are related, and the benefits of increasing DF have to be balanced against the potential disadvantages of excessively increasing current. Each cost function attributes a cost score (the lower the cost the better), and the optimization routine is used to find a minimum cost solution. Compared with the cost function described in the Heller study, the function used in the ShefStim reduced the degree of eversion associated with zero cost from 10° to 5°. This change was implemented after observation of excessive (>10°) eversion in 19% of the Heller study participants.

Participants

Ethical approval was granted from the University of Salford (REP10/113) and the integrated research application system (10/H1003/107) for 10 participants. Existing foot-drop FES users within the northwest region of England were given information by

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List of abbreviations:

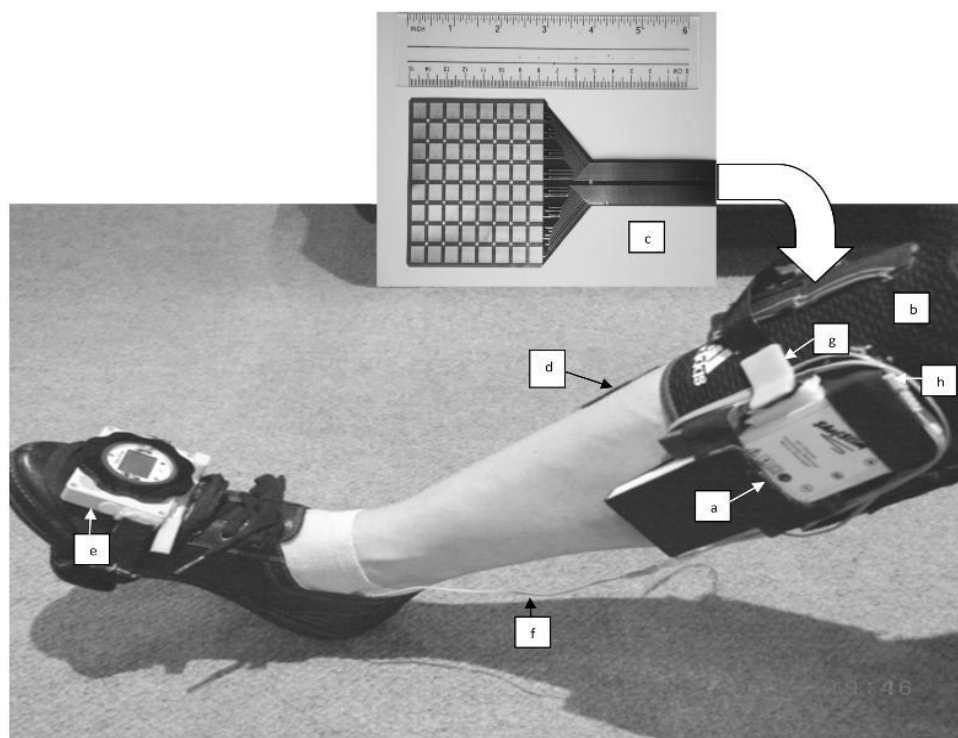|	
DF	dorsiflexion
FES	functional electrical stimulation
QUEST	Quebec User Evaluation of Satisfaction with Assistive Technology

Fig 1 ShefStim system (medial view of leg during automated setup). The parts are: a, ShefStim stimulator; b, modified knee sleeve; c, flexible printed circuit board array of 64 electrodes (cathode electrodes); d, conventional anode; e, foot sensor and remote control device housed in a bespoke foot-pod; f, conventional footswitch; g, electrical connector for the array; h, footswitch connector.

clinicians. Interested participants contacted the chief investigator. Inclusion and exclusion criteria are shown in appendix 1.

Protocol

During visit 1, participants attended the University of Salford Gait Laboratory and were provided with standard shoes[e,f] (depending on sex) for all conditions to avoid the potential impact of different footwear on foot clearance.[13] Participants walked approximately 5m along the gait laboratory up to 5 times at a self-selected speed; this was initially done with no stimulation and then with the participant's own FES system (self-setup). After visit 1, the knee sleeve, stimulator, and electrode arrays were prepared for that individual. The participants returned for visit 2 to complete the fitting, configure the rising/falling ramps and extension, adjust automated setup settings if required (to ensure appropriate virtual electrode selection), and teach the participant how to use the ShefStim. After 2 weeks of unsupervised use of the ShefStim at home (with a home visit after approximately 1wk to replenish arrays and answer any queries), participants returned to the gait laboratory (visit 3), which duplicated visit 1 except the ShefStim was used rather than the participant's own FES system.

Measures

Estimate of usage (between visits 2 and 3)

Usage data have been collected in previous foot-drop FES studies.[14-17] The ShefStim logs the number of heel lifts per day, which can be used as an estimate of usage.

Total setup (visits 1 and 3) and automated setup time (between visits 2 and 3)

With 1 notable exception,[5] setup time has been largely neglected in previous foot-drop FES research. Total setup time, defined as the time from first donning the equipment to being satisfied with the outcome and walking away (including automated setup time for the ShefStim), was recorded for participants' own FES (visit 1) and the ShefStim (visit 3). Average automated setup time (time for automated setup to complete) was logged by the ShefStim.

Diary recording problems during community use (between visits 2 and 3)

Problems encountered were recorded in a paper diary by each participant. User-reported problems have been collected previously[15] but never during the period of use. Recorded problems were collated and grouped into 2 categories[18]: external and setup. External were classed as being independent of the stimulator design and referred to the housing of ShefStim (knee sleeve), issues with the standard wired footswitch, or issues with charging. Setup was defined as any problem related to setup or satisfaction with the foot response.

User satisfaction (visits 1 and 3)

User satisfaction has previously been captured using purposive questionnaires.[3,15,17] Given the risk of bias and lack of validation, we sought an alternative. The Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST) (version 2.0)[19] is a validated user satisfaction measure. Participants rated their satisfaction against 8 single item criteria (dimensions, weight, ease of adjustment, safety and security, durability, ease of use, comfort,

Table 1 Participant demographics

Participant	Age (y) at Time of Recruitment	Sex	Diagnosis	Side Affected	Assistive Device Used	Participant's Current FES System Details
1	58	M	CVA	Right	SPWS	ODFS III (Odstock Medical, Salisbury, UK)
2	69	M	CVA	Left	SPWS	ODFS Pace (Odstock Medical, Salisbury, UK)
3	58	F	MS	Right	SPWS	WalkAide (Innovative Neurotronics, Austin, TX)
4	41	M	TBI	Left	None	ODFS Pace (Odstock Medical, Salisbury, UK)
5	79	M	CVA	Right	QBWS	ODFS III (Odstock Medical, Salisbury, UK)
6	63	M	CVA	Right	SPWS	ODFS Pace (Odstock Medical, Salisbury, UK)
7	49	F	MS	Right	SPWS	ODFS Pace (Odstock Medical, Salisbury, UK)
8	62	M	CVA	Left	None	ODFS Pace (Odstock Medical, Salisbury, UK)
9	51	M	MS	Right	None	ODFS Pace (Odstock Medical, Salisbury, UK)
10	26	M	CVA	Left	None	ODFS Pace (Odstock Medical, Salisbury, UK)

Abbreviations: CVA, cerebrovascular accident/stroke; F, female; M, male; MS, multiple sclerosis; QBWS, quad base walking stick; SPWS, single point walking stick; TBI, traumatic brain injury.

effectiveness) using a 5-point Likert scale (where 1 is not satisfied at all and 5 is very satisfied; maximum score, 40) for their own FES system and the ShefStim. In addition, participants ranked their top 3 priorities from the 8 criteria.

Speed and ankle angles at initial contact (visits 1 and 3)

Increased walking speed indicates an improvement in overall walking performance[20] and is frequently used in FES research.[21,22] Measuring walking speed over 5m from a static starting position is a validated measure with neurologic populations[23] and was calculated by averaging the velocity of a recorded waist marker (L3 vertebra) over the measurement space.[13]

Foot-drop leads to abnormal joint alignment during stance,[24] with a tendency for plantarflexion and inversion,[20] which can reduce ankle stability. Sagittal and frontal plane ankle angles were captured at initial contact to measure this. The calibrated anatomic system technique[25,26] was used for shank marker placement. Foot marker placement was based on the shod foot model by Pratt et al.[27]

Data for both speed and ankle angles were captured at 100Hz using a 16-camera three-dimensional motion analysis system.[g] A fourth-order low-pass Butterworth filter was used with a 6Hz cutoff frequency. Ankle angles at initial contact were analyzed using Visual3D.[h]

Foot clearance during swing (visits 1 and 3)

Foot-drop is associated with an increased risk of tripping and falling and is caused by a lack of foot clearance during the swing phase.[28] Foot clearance was obtained for 7 different points on the shoe sole as described in Thies et al.[13] Only 3 of the 7 markers from the Thies study[13] (distal toe, medial forefoot, lateral forefoot) were investigated because these were deemed most relevant. Healthy gait consistently has a minimum clearance value during swing.[13,29] Hemiplegic gait, however, has an altered clearance trajectory and does not always produce a minimum value during swing; therefore, an alternative and consistently definable point along the trajectory was chosen. Specifically, in this study, it was calculated at the moment in time when the reference point on the shoe sole passed the contralateral medial malleolus. Data were processed using MATLAB[i] software.[13]

Data analysis

As a feasibility study,[9,30] statistical analysis was limited to graphical representation of data and descriptive methods. Ratio data (automated setup log data, speed, ankle angles at initial contact) were analyzed using mean ± SD. Median and interquartile range were used for skewed data (usage, foot clearance[31]), median and range was used for total setup time, and median was used for ordinal data (QUEST version 2.0[32]).

Results

Table 1 provides participant characteristics. Prior to data collection, 3 participants were withdrawn from the study.[5,6,10] The withdrawal of participants 1 and 10 was because of unrelated medical issues. Subject 6 was withdrawn because it became clear postrecruitment that he was not a regular user of FES for foot-drop. He had discontinued use after ankle instability problems and a number of falls. The average age of the remaining participants was 58±12.9 years, which is comparable with other foot-drop FES studies.[5,20,33] Of the 5 men and 2 women, 4 had nonprogressive and 3 had progressive neurologic disorders, which is representative of the FES user population.[16,34] The FES systems used by participants varied, but all use a single cathode and single anode and were classed as conventional.

Estimate of usage

All participants used the ShefStim (fig 2) with an average of 1314 heel lifts (steps) per day. There was variability in the number of heel lifts from day to day for each participant (eg, participant 8) and between participants (participants 5 and 7 vs participant 3). The number of days participants used the ShefStim within the 2-week period also varied, with participants 7 (6 of 15d) and 9 (4 of 15d) using it far less than participants 5 (14 of 15d) or 2 (13 of 15d) (see fig 2).

Total setup and automated setup time

Total setup time for the ShefStim took an average of exactly 14 minutes (range, 12min 24s to 37min 30s) compared with 3 minutes 20 seconds (range, 40s to 8min) for their own FES. The average automated setup time was 9 minutes (range, 7min 34s to 10min 20s).

Diary recording problems during community use

Of the recorded problems, 64% (48 problems) were related to setup with poor voice command clarity from the foot sensor and remote control device (eg, for participant 2 on day 3: "remote voice garbled"), frequent pausing during automated setup, and/or unacceptable automated setup (eg, for participant 5 on day 9:

	Participant						
Day of Use	2	3	4	5	7	8	9
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							
Total	18841	19879	15016	5844	2058	10992	2209
Median	1336	2039	1557	389	389.5	1314	276.5
Range	0-3077	0-2879	0-2628	0-558	0-619	0-3247	0-1593
IQR	526	693.75	618.75	161.5	277.5	940	582.75

Fig 2 Logged heel lifts (N=7). Blank cells refer to 0 heel lifts. The length of the bar represents the number of heel lifts. The median number overall of steps per day was 1314. Abbreviation: IQR, interquartile range.

"pausing, why?"; for participant 2 on day 2: "2 times setups as chaplin walk"). Of the problems, 36% (27 problems) were related to external issues (eg, for participant 8 on day 6: "despite charging overnight controller battery was flat"). The overall number of reported problems diminished toward the end of the testing period (fig 3).

User satisfaction

Overall, on average, participants were as satisfied with the Shef-Stim as with their own FES system (fig 4). They were more satisfied with their own FES in terms of ease of use, which was the criterion most frequently prioritized on QUEST, and safety and security. The ShefStim outscored participants' own FES system with regards to effectiveness, the second most frequently cited priority, and ease of adjustment. On the remaining 4 criteria the systems scored equally.

Speed

Both FES systems produced the same increase in walking speed (.06m/s) compared with no stimulation (table 2).

Ankle angles at initial contact

With no stimulation, plantarflexion with inversion was seen (see table 2). Both the ShefStim and conventional systems corrected this; however, the ShefStim achieved this to a greater extent (see table 2).
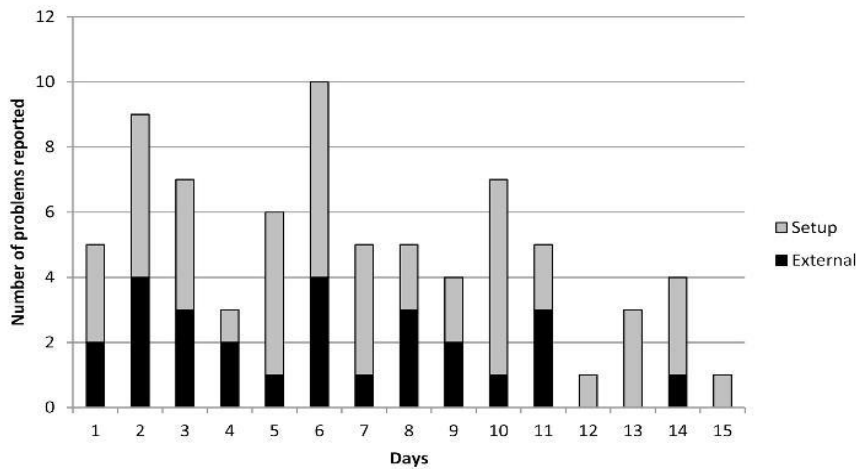

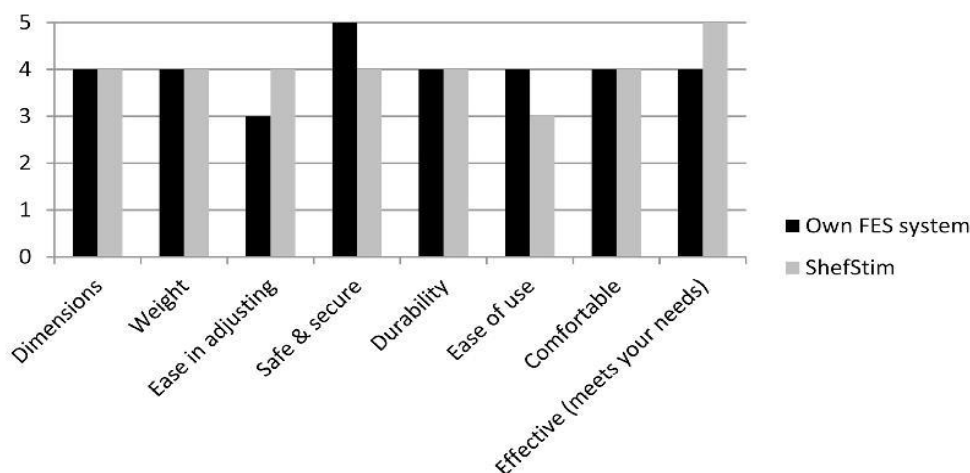**Fig 3** Recorded problems over 2-week unsupervised community use (N=7).

Fig 4 Median QUEST version 2.0 results (N=7). Both systems scored a total of 32 out of 40.

Foot clearance during swing

This outcome could not be determined for participants 5 and 7, who exhibited both short step lengths and a significant degree of external rotation of the leg during swing. Therefore, none of the reference points passed the contralateral malleolus during swing as was required by the algorithm. The distal toe marker showed the smallest overall clearance values, and the clearance was greatest with the ShefStim (see table 2). Table 2 shows that without FES, the median value of the medial marker was higher than the lateral marker; with the participant's own FES, they were approximately equal. With the ShefStim, the lateral marker was higher than the medial marker. This foot pose at midswing was consistent with the ankle angles at initial contact.

Discussion

This study sought to investigate the feasibility of unsupervised use of the ShefStim by FES users within the community. Usage results show that the ShefStim is a usable device because without exception, albeit with variation, all participants used the ShefStim.

Previous studies have reported a number of different measures of usage.[4,6,14,15,17] Only our results for steps (heel lifts) per day could be compared with previous larger studies,[6,15,17] with our participants generally walking less. For example, the participants in the study by Stein et al[6] took 1842±198 steps per day when first

starting to use the WalkAide system, whereas participants in the van Swigchem et al study[17] took 5733±2516 steps per day. The participants in the van Swigchem study[17] were encouraged to wear the NESS L300 for the entire day, whereas participants in our study and the Stein study were not guided in this way. Further, our participants reported a number of problems associated with the precommercial nature of the ShefStim system, which may have impacted on use on certain days (see fig 3). Further studies should continue to report detailed FES usage to allow further exploration of the population and allow comparison between systems and/or baseline.

Results did not fully meet the prediction made by Heller[5] that the ShefStim would result in shorter total setup times. There are a number of possible reasons for this. First, Heller used self-report to assess setup time with participants' own FES systems, finding an average of 11 minutes. In our study, participants were timed during setup in the laboratory and took an average of 3 minutes to set up their own FES systems. In the Heller study, participants placed their affected leg in a rigid brace, thereby removing the possibility of significant leg movement. In our study, the participant's leg was not constrained during setup, and leg movement detected during the automated setup process led to pauses, which lengthened the process, a problem recorded by participants. Further, our ShefStim users relied on audio feedback from the foot sensor and remote control device, which participants reported was sometimes difficult to hear. Participants also sometimes reached the end of setup and decided that the automatically chosen site

Table 2 Average speed, ankle angles at initial contact, and foot clearance during swing

Outcome	No FES	Participant's Current FES System	ShefStim
Speed (m/s)	0.72±0.52	0.78±0.51	0.78 (0.53)[*]
DF (deg)	−3.95±5.89	1.96±5.73	4.22 (4.64)[†]
Inversion (deg)	9.24±6.12	1.65±10.21	−1.56 (7.73)[‡]
Foot clearance: distal toe (cm)	1.08±0.62	1.58±0.47	1.82 (0.89)[†]
Foot clearance: medial (cm)	2.71±1.06	2.50±1.12	2.32 (0.83)[‡]
Foot clearance: lateral (cm)	1.19±0.99	2.38±0.88	2.97 (1.82)[†]

NOTE. Values are mean ± SD (speed, DF + inversion) or median ± interquartile range (foot clearance).
* Equal to the participant's own FES system.
† Greater than the participant's own FES system.
‡ Less than the participant's own FES system.

was not acceptable and then ran the entire automated setup again. Although a skip-site function was available[5] to address this issue (alternative sites identified as suitable to be selected manually), participants did not use it; therefore, further refinement of user training material and/or the user interface is warranted.

The finding that participants were as overall satisfied with the ShefStim as with their own FES systems is encouraging because unlike conventional foot-drop FES systems, the ShefStim has not been subject to significant product design. The fact that problems diminished and ease of use was rated lower than participants own FES systems, however, suggests that 2 weeks was insufficient for participants to fully familiarize themselves with the ShefStim. Alternatively, it might be caused by the cited problems with the ShefStim itself. Our results cannot be compared with other studies because QUEST version 2.0 has not been used before in this field of research. Future studies should allow longer unsupervised periods of use and should use a validated measure (eg, QUEST version 2.0).

Speed increase for both the ShefStim and conventional FES systems compared with no FES system was in keeping with previous studies[20] and classed as clinically meaningful.[35] In the Heller study,[5] in which subjects did not have time to accommodate to the automated setup, speed increase (relative to no FES) when using the automated setup system was less than with their own system (.04m/s vs .11m/s). In both studies, foot response with automated setup was improved compared with participants' setup of their own stimulators. Although there is a risk of over-interpretation of the results, our findings may suggest that once users become accustomed to a new FES system, their walking speed is relatively insensitive to small differences in foot response. These findings are supported by the foot clearance results and indicate that the underlying operating principle of an array-based FES system with automated setup may be more effective at addressing foot-drop than conventional FES systems by reducing human error/influence over electrode placement. However, larger-scale studies are required to fully substantiate these initial findings.

Study limitations

This was a feasibility study with a small sample size and self-referred participants and was not randomized.[9,30] Although the results are encouraging, they should be viewed with caution. The outcome measures selected seem appropriate, but many have been largely unused in previous research in this field, making comparison with previous studies challenging.

Further development of the electrode skin interface is required[12] to negate the need for daily array replacement and improve future commercial viability. Further iterations of the ShefStim need to also consider addressing the cited setup and external problems (eg, voice command clarity), impact of pausing on automated setup time, user training, and charging to facilitate further study and widespread implementation.

Conclusions

To our knowledge, this is the first study of the ShefStim and one of very few studies investigating foot-drop FES systems both within the laboratory and during unsupervised use.[36,37] Ultimately, this study demonstrates that an array-based automated setup FES system (ShefStim) for foot-drop can be successfully used unsupervised. Despite longer and more problematic setup in the population studied, users were satisfied with it, and it would appear to have comparable if not better effects on gait than conventional foot-drop FES systems.

Further product development and a larger-scale, longer-term study is required before firm conclusions about the efficacy and effectiveness of the ShefStim compared with conventional FES can be reached.

Suppliers

a. Adidas AG, World of Sport, Adi-Dassler-Strabe 1, 91074, Herzogenaurach, Germany.
b. Axelgaard Manufacturing, 520 Industrial Way, Fallbrook, CA 92028.
c. Apple Distribution International, Hollyhill Industrial Estate, Hollyhill, Cork, Republic of Ireland.
d. Velcro, 1 Aston Way, Middlewich Industrial Estate, Middlewich, Cheshire, CW10 OHS, UK.
e. Hotter Comfort Concept Shoes Peel Rd, Skelmersdale, Lancashire WN8 9PT, UK.
f. Clarks International Registered Office, 40 High St, Somerset, BA16 OEQ, UK.
g. Qualisys, Packhusgatan 6, 411 13 Göteborg, Sweden.
h. C-Motion, 20030 Century Blvd, Germantown, MD 20874.
i. Mathworks, Matrix House, 10 Cowley Park, Cambridge CB4 0HH, UK.

Keywords

Electric stimulation therapy; Gait disorders, neurologic; Hemiplegia; Peroneal nerve; Rehabilitation

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Appendix 1 Inclusion and exclusion criteria

Inclusion	Exclusion
• Unilateral foot drop caused by disorder of central neurologic origin diagnosed at least 6mo prior to the study • Regular user of a foot drop FES system for at least 3mo • ≥18y of age	• Using alternative method to treat foot drop (orthosis, physiotherapy, botulinum toxin) • Unable to set up ShefStim, even with assistance • Contraindications to FES use • Unable to consent (Mini-Mental State Examination score <25) • Unable to meet protocol/timetable of study • Unable to walk 5m without physical assistance

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2.3.2 Candidate involvement[4]

This study was originally proposed to be an A-B SCED using stroke participants (with walking speed, six-minute walk test, PCI, MAS, falls diary and activity monitoring used as evaluation measures). Article 2 highlighted that the logistics of running the study in this way were prohibitive both in terms of number of available potential participants and the practical logistics of repeated measure design if gait laboratory based measures were to be used.

On the basis of experience and results from the first two studies the candidate redesigned this third study as a pre/post single group design focussing on device feasibility, device usability and measures that could specifically evaluate the fundamental effects on the foot-drop impairment with recruitment encompassing any CNO pathology that had resulted in unilateral foot-drop. In accordance with the MRC guidance in the evaluation of complex interventions (Medical Research Council, 2000) the array FES device had passed through the pre-clinical (Kenney et al., 2015) and phase I/modelling phases (where components had been tested to develop an understanding of each and how they interrelate (Cooper et al., 2011; Heller et al., 2013; Pratt et al., 2012; Sha, Kenney, Heller, Barker, Howard, & Moatamedi, 2008; Sha, Kenney, Heller, Barker, Howard, & Wang, 2008; Williamson et al., 2015). This study was a phase II trial (Medical Research Council, 2000) which sought to look at the feasibility of use outside of a laboratory and methods such as recruitment estimates, appropriateness of outcome measures to evaluate usability and an appropriate control group (Medical Research Council, 2000). Three visits over three to four weeks placed less burden on participants and, alongside the widened diagnoses, was hoped to improve recruitment and minimise attrition.

The candidate initiated all procedures with regards NHS and University ethics, research and development liaison at various hospital trusts, recruitment, data collection, analysis and write up. The candidate also inputted into some aspects of design for example the suggestion to use an IPod holder as the foot pod (which housed the foot sensor and remote control device). The candidate took maternity leave during part of the study data collection period. On her return, part of this work was presented at the UK and Ireland FES symposium (UKIFESS) in Southampton that took place in 2013 (Appendix 3b).

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[4] A summary of the candidate's involvement in each article is presented in Table 1 on page 5

2.3.3 Critical appraisal

This small-scale feasibility (Medical Research Council, 2006) study was the first publication that showed that an array-based FES with automated setup can be used unsupervised in a "real" environment; as such it has ecological validity.

The length of study and the sample size were chosen based on pragmatic and budgetary constraints. Due to unforeseen technical challenges the HTD480 project ran significantly behind schedule restricting the available time, within the budget, to complete the evaluation of the system (final work package). Two weeks is a relatively short time to have studied the device however it was in keeping with acclimation periods in other studies (van Swigchem et al., 2011). The recruitment of current FES users also meant that the participants were not having to acclimatise to FES itself. The number of available ShefStim® units and array electrodes also influenced the study design. Without these externally imposed restrictions a longer study period and alternative study designs might have been considered. However, the equal improvements seen between the two FES devices suggested that two weeks was sufficient to meet the study aims of preliminarily investigating usage, satisfaction, setup times and effects. Two weeks was also sufficient to provide confident proof-of-concept results demonstrating that the ShefStim® device had effects on intended evaluation measures

The candidate is confident in the choice of evaluation measures. Unlike the activity monitoring used in some studies (Kluding et al., 2013; Kottink et al., 2007; Van Swigchem et al., 2010) actual device usage indicates how many steps were taken whilst the device is worn. It cannot be constrained to one ICF domain as it shows actual participation in walking while simultaneously showing a potential mechanism-of-action (remediation of foot-drop leading to greater task-specific activity). Without the candidate's consideration of the foot-drop impairment and the concept of usability this measure might not have been chosen.

It was recognised by the candidate that unless device usage was evaluated it would not be possible to quantify the dosage of either intervention a participant receives making understanding of mechanisms-of-action very difficult. Despite the clear potential to accurately track FES device usage this study was one of the first (Stein et al., 2010; Stein et al., 2006) to use the feature of some FES devices to collect steps taken and the first to report

individual participant's results as well as group averages and to the candidate's knowledge usage data has never been reported for AFOs. Reporting on the individual meant that the usage results were not only able to demonstrate ShefStim® proof-of-concept, as a feasible device within a home environment, but also highlighted that although task specific activity was engaged in by all participants there was large variation amongst the participants both in terms of the frequency and intensity of use. This resulted in very different "dosages" of ShefStim® FES stimulation for each person over the two-week period of use. The lack or sporadic use by some participants was discussed within the article as potentially being due to issues with ShefStim® use which were captured due to the decision to capture usability measures of efficiency and satisfaction. If device usage were to be used on a wider scale it is conceivable that observed results might differentiate between different patterns of use which could be correlated to user characteristics and user reported issues. This might ultimately help with more discerning prescription and/or product refinement. Further, combining such data with long-term generic activity monitoring would tell us the total activity levels, the types of activities engaged with (both captured by the generic activity monitor) and the amount of time a person chooses the device to walk compared to the time they choose to walk unassisted, calculated by subtracting the device usage data from the total activity level (activity monitor). More unassisted activity would indicate either less reliant on the device/improvement or a device usability issue. For FES this data could be viewed alongside the recorded setup parameters for FES providing a more accurate dosage estimation. This point was not discussed in the article as it detracted for the key take home messages plus it was not directly linked to the results found.

Objectively timing donning and setup was evaluating a driving principle of ShefStim® namely that automated setup is easier for the user as it removes the requirement for electrode placement and determination of appropriate stimulation intensity. The ShefStim® prototype had found setup up time was less with the device compared to the participants own FES device; but this was compared to user self-reported times (Heller et al., 2013), a measure that the candidate had found to show poor accuracy in the DMO dorsiflex sock® study (Article 2). Therefore, neither traditional FES systems nor the ShefStim had not been subjected to objective scrutiny of setup times. Surreptitiously evaluating whole system donning time brought to light that some FES users of more than three months were

unaware of how to correctly don their system. Whether previous FES studies have relied on clinicians to don systems is largely unreported (Salisbury, Shiels, Todd, & Dennis, 2013) but there is a suggestion that this is the case. FES efficacy has been shown to vary depending on whether a trained clinician or the user setups up the system, with user setup being less efficacious (Heller et al., 2013). If the majority of current FES evidence is reporting results from clinician setup it could be overestimating FES effects. Logged automated setup times showed that, although user effort was not required, setup took considerably longer than expected. Recognition of this within the article allowed possible reasons for this to be explored which was helped by the use of the collected diary data to identify where product refinement was necessary.

The chosen efficacy measures had face validity (Bloom et al., 2003) in relation to the fundamental deficits caused by foot-drop; namely trip risk caused by impaired foot clearance during swing (Begg, Best, Dell'Oro, & Taylor, 2007; Thies, Jones, et al., 2011) and poor foot orientation at initial contact which may also increase the risk of falls. DF at IC has been a key focus within some FES literature (Heller et al., 2013; Kottink, Tenniglo, de, Hermens, & Buurke, 2012; Meilahn, 2013; Voigt & Sinkjaer, 2000) but *foot*-clearance, which is arguably the primary purpose of a foot-drop device, had not been evaluated previously, although *toe* clearance was first reported by Kim, Eng, and Whittaker (2004). The difference between Kim et al's (2004) evaluation of *toe*-clearance and our approach is that Kim et al measured only the minimal clearance of the fifth metatarsophalangeal joint during mid-swing. Our use of virtual markers at different points of the sole of shoe takes into account that collision between the foot and ground may occur at points on the shoe other than the fifth metatarsophalangeal joint. Further, by capturing the location of virtual markers on the perimeter of the sole of the shoe it takes into account shoe shape, providing an accurate representation of shoe-floor clearance, rather than anatomical joint-ground clearance, as used by Kim et al. (2004). Ankle kinematics during swing have been reported on (Scott, van der Linden, Hooper, Cowan, & Mercer, 2013; Voigt & Sinkjaer, 2000) but are not a suitable substitute for clearance as they cannot indicate whether this reduces trip risk whereas toe clearance has been reported as crucial for safe walking and shown to relate to the probability and risk of tripping (Thies, Jones, et al., 2011). As such this study presented a unique insight into a fundamental FES mechanism-of-action. Since the completion of this

study the candidate has come to recognise that foot clearance within the participants own environment might have been captured with the use of inertial sensors (Dadashi et al., 2014) and this approach is worth investigating in the future. Walking speed is one of the most commonly used measures of walking capacity (Mudge & Stott, 2007), its inclusion allowed for comparison to other studies in the field as well as it being shown that it is a key prognostic indicator (Studenski, Perera, Patel, & et al., 2011). The use of obstacle avoidance or step targeting, and/or carrying out a dual task whilst walking might have been more functionally relevant than walking speed alone, but the candidate was mindful of the length of visits for participants. The speed, kinematic and foot clearance results were reported to two decimal places which on reflection was inappropriate as this suggested a higher resolution of the measurement systems than was the case.

The choice of some novel evaluation measures (usage, timed setup/donning diary in real time, QUEST 2.0, foot clearance) advanced the field of research by addressing the second identified gap in the evidence base. Prior to this study the focus within the literature had tended to be on laboratory measures of capacity (WHO, 2001) as the sole indicators of benefit (Prenton et al., 2016). This study moved the focus towards measures that evaluated potential relevant mechanisms-of-action, actual usage and usability. However, it restricted comparison with previous studies. Use of the more commonly used CQ measure of efficacy, walking speed, allowed for a comparison to previous studies; which were also clinically meaningful (Perera, Mody, Woodman, & Studenski, 2006). This was also true for the kinematics at IC. The similarity in the effect sizes described in this study with these other studies further supported the case that ShefStim® warranted a definitive efficacy trial, once the issue with the hydrogel array electrodes had been solved.

The study therefore met its aims and would appear to have provided a case for a Phase III comparative trial (Medical Research Council, 2000). The results gave product development and user training guidance, with regards the voice command clarity on the remote control and the skip-site function that was not used by participants, to inform such a trial. However, the issue of the array electrode-skin interface meaning that new arrays were required daily was not resolved. This, along with the lack of an appropriate commercial stimulator development partner meant that the device was not developed further at that time. Overall this article contributed to the knowledge base by using new and directly relevant

approaches to device evaluation. The study considered the fundamental deficits caused by foot-drop, addressing also the key issues of device usage and usability. This has the potential to impact the associated clinical guidelines if future studies in both the FES and AFO fields emulates this approach.

2.4 Article 4

Kenney, L.P.J., Heller, B., Barker, A.T., Reeves, M.L., Healey, J., Good, T.R., Cooper, G., Sha, N., Prenton, S., Liu, A. and Howard, D. (2016). A review of the design and clinical evaluation of the ShefStim array-based functional electrical stimulation system. *Medical Engineering & Physics*, *38*(11), 1159-1165. doi: 10.1016/j.medengphy.2016.08.005

2.4.1 Article summary and Publication

This article sought to address the first identified gap in the evidence base (an alternative FES foot-drop device developed to address the cited electrode placement difficulties with conventional systems).

This article charts the design, development and evaluation of the ShefStim® FES device, the challenges that were faced, with particular reference to the design of the electrode array, the choice of hydrogel, the array search algorithm and how iterations of the device were tested first within a laboratory (Heller et al., 2013) and then in the community (Article 3). It reiterated what limited ShefStim® from being manufactured and studies on a larger-scale and suggested alternatives for the prohibitive electrode-skin interface problem.

A review of the design and clinical evaluation of the ShefStim array-based functional electrical stimulation system

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ABSTRACT

Functional electrical stimulation has been shown to be a safe and effective means of correcting foot drop of central neurological origin. Current surface-based devices typically consist of a single channel stimulator, a sensor for determining gait phase and a cuff, within which is housed the anode and cathode. The cuff-mounted electrode design reduces the likelihood of large errors in electrode placement, but the user is still fully responsible for selecting the correct stimulation level each time the system is donned. Researchers have investigated different approaches to automating aspects of setup and/or use, including recent promising work based on iterative learning techniques. This paper reports on the design and clinical evaluation of an electrode array-based FES system for the correction of drop foot, ShefStim. The paper reviews the design process from proof of concept lab-based study, through modelling of the array geometry and interface layer to array search algorithm development. Finally, the paper summarises two clinical studies involving patients with drop foot. The results suggest that the ShefStim system with automated setup produces results which are comparable with clinician setup of conventional systems. Further, the final study demonstrated that patients can use the system without clinical supervision. When used unsupervised, setup time was 14 min (9 min for automated search plus 5 min for donning the equipment), although this figure could be reduced significantly with relatively minor changes to the design.

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1. Introduction

Functional electrical stimulation has been shown to be a safe and effective means of correcting foot drop of central neurological origin [1–3]. Surface-based devices typically stimulate via a cathode placed over the common peroneal nerve immediately distal to where it bifurcates into the deep and superficial branches, and an anode placed over tibialis anterior. Appropriate levels of stimulation delivered via accurately placed electrodes should result in suitably weighted recruitment of the two nerve branches, leading to a useful and safe foot response during the swing phase of walking (dorsiflexion with a small degree of eversion). However, in certain individuals even very small electrode positioning errors can lead to a poor foot response. Indeed, a 1999 survey of users of drop foot stimulators reported over 40% of respondents finding

electrode positioning problematic [4]. Some current systems such as the WalkAide (Innovative Neurotronics Inc., Austin, Texas, USA) embed electrodes in a cuff, worn below the knee (the reader is referred to the work of Melo et al. [5] for a recent review of current systems). Such an approach greatly reduces the likelihood of large errors in electrode placement, but the user is still fully responsible for selecting the correct stimulation level each time the system is donned. Interestingly, despite improvements in both stimulator designs and patient education, two recent studies demonstrated that when patients set up their stimulators without clinician support, the resultant foot response is often less than optimal [6,7].

One approach to the challenge of stimulator setup is to implant the electrodes on the nerve(s), thereby removing the electrode placement problem from the user [8,9]. However, an invasive approach carries risks and the implantable devices and surgical costs remain relatively expensive. As a result, a number of groups have been investigating the possibility of automating the surface-based drop foot setup process through a two-channel stimulation approach to software steering of the foot [10–12],

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or electrode array-based approaches [13–18]. Both approaches feature a 'setup space' which can be automatically searched, either through replacing single electrode(s) with one or two arrays of discrete electrodes, or by allowing modulation of pulse waveform. Both approaches also use measurement of foot orientation, usually derived from foot-worn inertial sensors, to guide the search.

Elsaify proposed an automatic array element search algorithm, but using array elements with separate gel layers (a matrix of small single electrodes) [14]. More recently, Valtin et al. [17] demonstrated an array search algorithm that takes roughly two minutes using two flexible PCB electrode arrays (one over the nerve and one over Tibialis Anterior), each interfaced with a continuous, high-resistivity hydrogel layer. However, in contrast to the work presented here, only preliminary results with a healthy subject were presented. In the most recent work, Seel reported on a system using a foot-mounted inertial sensor to adjust the steering based on realtime measurements of the foot orientation [11]. The system uses only two electrodes and, in laboratory studies with stroke participants, demonstrates convergence on a suitable foot response within one or two strides. However, studies of the system outside of the laboratory setting have yet to be published.

In this paper we expand on a recent conference paper [19] to report on the design, development and demonstration of a system for automated setup of drop foot FES (ShefStim). The paper extends the conference paper by presenting the model used to define the initial electrode array geometry design (Section 2) and provides discussion of the merits and limitations of ShefStim compared with alternative systems. The ShefStim design concept was proposed by Heller et al. [20] in 2003. For this study the Department of Medical Physics at Sheffield Teaching Hospitals initially developed a 'proof-of-concept' multi-electrode stimulator, which could simultaneously stimulate any manually-selected subset out of a conveniently sized, 8 by 8 rectangular array of metal electrodes. The subset of activated electrodes is termed a virtual electrode (VE). In order to develop this concept into a clinically usable system for automated setup a series of design problems needed to be solved. The first problem was the electrode array design; the second problem was the development of an array search algorithm. The remaining part of the paper summarises the results from two studies of the ShefStim involving people with drop foot of central neurological origin.

2. Design of the electrode array

For clinical applications a moderately electrically conductive hydrogel interface between the electrodes and skin provides the benefits of hydration of, and adhesion to, the skin. However, in array applications a continuous hydrogel layer also introduces the issue of spatial selectivity loss due to transverse currents in the hydrogel. Spatial selectivity is defined as the ability to activate discrete groups of nerve fibres in a localised region without stimulating nerve fibres in neighbouring regions.

In order to achieve a satisfactory degree of spatial selectivity, it was necessary to identify an appropriate electrode geometry and interface layer properties. Two finite-element models were therefore developed to investigate the effects of electrode geometry and hydrogel layer properties on spatial selectivity, characterised in our model by the activation area (see below). Model 1 was developed to explore the effects of hydrogel resistivity and electrode size on activation area under a single cathode electrode and; Model 2 extended Model 1 through the addition of electrodes surrounding the cathode, to allow investigation of activation area under a multi-electrode array. The results of the second model, together with practical constraints imposed by the stimulator, led to the array geometry and interface layer properties used in part 3 of this paper.
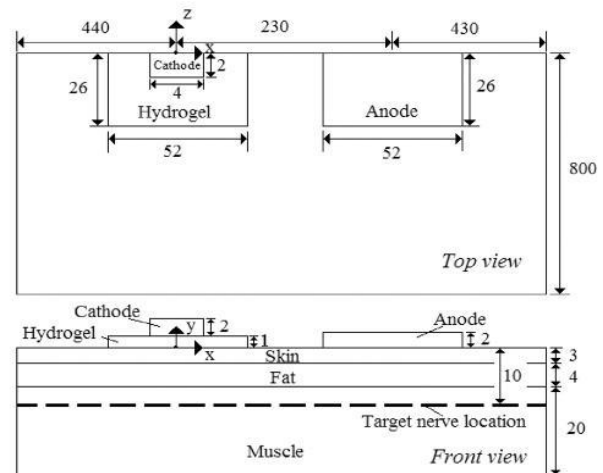

Fig. 1. Schematic of the geometry of the selectivity FE model (not to scale) (dimensions in mm).

2.1. Model 1

Fig. 1 shows the 3D finite-element model, developed using ANSYS Multiphysics (Version 10.0, Ansys, Inc, Canonsburg, PA, USA) to predict the effects of electrode geometry and hydrogel properties on electric field distribution in the underlying tissue [21]. The model represents a cathode, an anode, a hydrogel layer, skin, fat and muscle. The skin, fat and muscle were modelled as flat, extended layers, whose thicknesses were based on their anatomical dimensions. As bone has much higher resistivity than the other media, it was assumed to be non-conductive volume underlying the muscle, and hence was represented as the lower boundary of the model. Structures of smaller dimension, such as hair follicles or blood vessels, were not explicitly modelled, as their influence on stimulation at the depth of the motor nerve branches could be considered negligible.

Appropriate electrical conductivity properties were assigned to the elements, based on values from Duck [22] (Table 1). Although the skin's capacitance cannot normally be neglected, the skin in the model was assumed to be hydrated due to intimate contact with the hydrogel layer. Hence capacitive effects were not included in this model.

The calculation of whether a point in the model was deemed to be stimulated was based on the stimulation function [23]. To explore spatial selectivity we first defined a stimulus pool to be a volume over which the value of the stimulation function exceeds a threshold at which action potentials in a nerve fibre are generated. The maximum stimulation function always appears in the stimulus pool centre, just underneath the cathode, and the amplitude of the stimulation function decreases from the centre to the edge of the stimulus pool. Although the value of the maximum stimulation

Table 1
Model parameters.

Biological tissues and materials	Resistivity (Ωm)
Bone	7×10^4
Muscle	2 in X and Z directions
	4 in Y direction
Fat	62.5
Skin (hydrated)	833
Hydrogel	Model variable
Cathode and Anode	1.5×10^{-8}
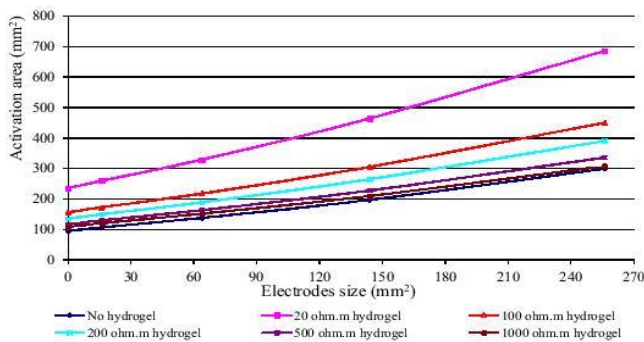
Fig. 2. The effects of electrode size on activation area for a range of hydrogel resistivities.

Fig. 3. Model 2. The electrode gap (g) is the edge-to-edge distance between any two neighbouring electrodes in the array; 2a is the dimension of each square electrode.

Table 2
Electrode gap and size evaluated in the FE model, and resultant overall electrode array size.

Electrode gap (mm)	Electrode size (mm)	Electrode array size (mm)
1	8×8	71×71
2	7×7	70×70
3	6×6	69×69
4	5×5	68×68
5	4×4	67×67

Table 3
Hydrogel materials represented in the model. Note that the different sheet thicknesses modelled were chosen to represent the sheet thicknesses provided by the manufacturers.

Hydrogel (abbreviation)	Approx thickness (mm)	Resisitivity at 1.67 kHz (Ωm)
AG703, Axelgaard manufacture Co., Ltd. Fallbrook, CA. USA (Hydrogel 703)	0.9	55
AG803, Axelgaard manufacture Co., Ltd. Fallbrook, CA. USA (Hydrogel 803)	0.9	206
SRBZAB-05SB, Sekisui Plastics, Co., Ltd. Tokyo, Japan (Hydrogel ST)	0.5	1363
AG, AG3AM03M-P10W05, Sekisui Plastics, Co., Ltd. Tokyo, Japan (Hydrogel AG)	0.3	25,185

function varies between models, it can always be scaled to the same value by changing the input current, and this scaling does not change the shape or size of the stimulus pool. Contours may be defined which connect points in the model with identical stimulation function values (expressed as a percentage of the maximum) and the 50% contour was selected to represent the boundary of the stimulus pool for the results presented here. The 50% contour choice was somewhat arbitrary, but avoided problems which would be associated with choice of a contour near 100% or 0% of maximum stimulation function (all contours converge to a point at 100% of maximum stimulation function and contours enclose infinitely large areas at 0%) As the electrical properties of the tissue were uniform, the current density distribution was symmetric along the plane normal to the skin surface and along the centres of the cathode and the anode. This symmetry allowed a study to be performed on a half model. To represent the location of the nerve, we defined a plane representing the anatomical depth of the target nerve (10 mm). The intersection of the stimulus pool with the plane defined an area; the smaller the area, the more focused is the stimulation and thus the better the spatial selectivity. Therefore, the area of the stimulus contour associated with 50% of maximal stimulation was used as the metric of spatial selectivity.

To explore the combined effect of hydrogel resistivity and electrode size on selectivity, a series of simulations were run with square electrodes from infinitely small (a point) to 16 mm × 16 mm with a range of interface layers. The first simulation considered the no interface layer case; subsequent simulations varied the 1 mm thick hydrogel layer resistivity from 20 Ωm to 1000 Ωm. The results are shown in Fig. 2.

Fig. 2 shows that there is a minimum limit to activation area of approximately 100 mm² at 10 mm depth, and that spatial selectivity becomes poorer (activation area increases) with increasing size of electrode and decreasing resistivity. When the resistivity reaches 500 Ωm or greater, the spatial selectivity is similar to that of the model without the hydrogel sheet.

2.2. Model 2

Model 1 had shown that the introduction of a 1 mm hydrogel interface layer did not significantly degrade selectivity providing the hydrogel resistivity was at least 500 Ωm. However, the model did not account for the presence of neighbouring electrodes which would surround an electrode in the array. The presence of these electrodes will lead to a decrease in selectivity compared with the single electrode condition, as current can flow from activated electrodes across inter-electrode gaps and into adjacent non-activated electrodes. These effects would be modulated by the size of the inter-electrode gap and hydrogel properties. Therefore, Model 1
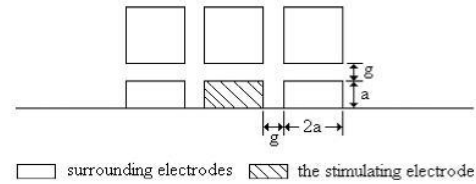
was used as the basis for a new model (Model 2) to enable the electrode array design to be finalised.

It was assumed that the magnitude of reduction in selectivity due to current passing across the inter-electrode gaps would be dominated by electrodes immediately surrounding any given electrode in the array. Hence, Model 1 was extended to include eight more electrodes surrounding the original cathode electrode (Fig. 3)[1]. The interface between the electrode array and the skin was a sheet of hydrogel. The initial geometry of Model 2 was informed by previous pilot experimental work carried out as part of a Master's research project, demonstrating the viability of using a 70 mm x 70 mm electrode array consisting of 64 electrodes (arranged in an 8×8 format) [24].

As the feasibility work suggested maintaining an overall array size of approximately 70 mm x 70 mm, we fixed the centre-to-centre spacing of electrodes in the model to be 9 mm (2a + g = 9, see Fig. 3). Five different gap sizes were modelled (Table 2) and for each of these, four commercial hydrogel sheets were modelled (Table 3). The set of hydrogel properties were informed not only by the results of Model 1, but also by earlier experimental work [25,26] which provided further evidence to support the use of a thin, high-resistivity hydrogel layer between the electrode and skin.

In order to quantify the effects of the surrounding electrodes on selectivity, two versions of each model were run. In the first version, the surrounding electrodes were not represented and in the

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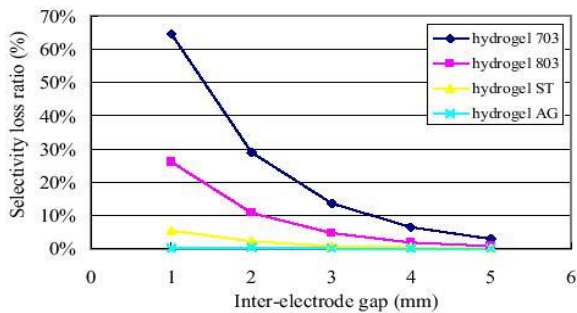[1] Note, as per Model 1, a half model was developed to take advantage of symmetry.

Fig. 4. Selectivity loss ratios with different hydrogels.

second, the surrounding electrodes were represented. The selectivity loss resulting from the introduction of surrounding electrodes was quantified by a selectivity loss ratio, defined in Eq. (1).

$$Selectivity\_loss\_ratio = \frac{A_2 - A_1}{A_1} \times 100\% \qquad (1)$$

where, A_1 is the activation area of the model without surrounding electrode and A_2 is the activation area of the model with surrounding electrode

Fig. 4 shows the selectivity loss ratio due to the surrounding electrodes calculated for each combination of hydrogel interface layer and inter-electrode gap.

The results suggested that for hydrogels ST and AG an electrode gap between 1 mm and 5 mm will result in an acceptably low selectivity loss (defined as less than 10%) in the presence of the surrounding electrodes. From a manufacturing perspective, an inter-electrode gap of less than 2 mm would make it very difficult to route the tracks between electrodes, so a 2 mm inter-electrode gap was chosen. A final practical test demonstrated that our stimulator (200 V drive voltage) could not drive the specified 8 mA per channel when using the more resistive of the two most promising materials (hydrogel AG) and hence hydrogel ST was selected.

3. Feasibility study of electrode array search strategy

Section 3 described the design of an 8×8 electrode array interfaced to the skin via a thin high-resistivity hydrogel layer. The next design problem was the development of a quick, reliable method of searching the set of all possible stimulation electrodes to find the optimal virtual electrode. In this section we report on two methods for searching the array used to identify appropriate virtual electrodes and their associated stimulation levels, which extended the work of Elsaify et al. [14]. In the first part of the work, we apply a slowly ramped stimulation through each virtual electrode while continuously monitoring the orientation of the foot relative to the leg. These data allow identification of electrode sets that, when appropriately stimulated, result in acceptable foot movement. The ramped stimulation results were used to investigate whether it is possible to reduce the search space through prediction of the location of the best subset of these electrodes based only on the response of the foot to short bursts of stimulation (twitch stimulation). We investigated use of a cost function to rank the response to short bursts of stimulation and examine whether this ranking may be used to isolate smaller groups of electrodes that contain one or all of the best subset of electrodes identified in the slow ramped stimulation search.

For brevity, here we only report on the search for appropriate single VEs. Additional work to identify suitable pairs of VEs is reported elsewhere [27]. Ethical approval for the study was granted by the University of Salford's Research Governance and Ethics committee (RGE06/102). Twelve healthy subjects were recruited from

within the University and a full set of results were obtained for ten (9 male) subjects (median 30 years)[2].

The stimulation system consisted of a constant current portable 64 channel stimulator designed and built by the Medical Engineering section of Sheffield Teaching Hospitals NHS Foundation Trust (size: 155 mm × 95 mm × 33 mm), an.8 × 8 electrode array, described in Section 2 and a 50 × 50 mm square conventional hydrogel electrode (PALS® Platinum electrode, Axelgaard Manufacturing Co. Ltd.), The charge-balanced asymmetrical biphasic stimulus pulses were software controllable via a graphical user interface, with the pulse width fixed at 300 μs, and the frequency at 35 Hz. Stimulation intensity through each electrode was software controlled and measured by an analogue to digital converter built-in to the stimulator itself. During the experiment, groups of 2 × 2 electrodes were activated simultaneously (the minimum number required to elicit adequate contractions, providing a total current of up to 32 mA), and act as a virtual electrode.

A 5-camera Qualisys motion capture system (Proreflex, Qualisys AB, Sweden) was used to record foot movement at 100 Hz and the motion data were transferred to and simultaneously analysed in Visual3D (Visual3D™, C-Motion Inc., USA). Hence the foot movement was captured, and ankle angles in sagittal, coronal and transverse planes were displayed in real-time. Synchronisation between the stimulator and the motion capture system was achieved using a data acquisition device via the stimulator control program. An electrically-isolated button was included to allow the user to stop stimulation at any stage in the experiment.

The experiment started with measurement of the neutral foot orientation for the subject while standing upright. He/she was then asked to sit in a chair and their right lower leg was strapped in the brackets to keep the shank in a consistent pose throughout. The stimulator and electrodes were then donned. The subject was then asked to maintain their sitting posture and relax the foot in a natural (dropped) position throughout the experiments. As the analysis of data did not dictate the order in which the tests were conducted, the foot twitch experiment was conducted first to reduce fatigue. However, here they are explained in reverse order for clarity.

Prior to beginning the slow ramped stimulation experiment a user-defined maximal current was identified. We assumed that sensation would be most acute over bony prominences and hence at the start of the experiment increased stimulation over these sites until a user-defined maximum was reached and the value noted. Next, current through each VE in turn was ramped from zero to the user-defined maximal current over 10 s. The twitch stimulation part of the experiment involved six different bursts of stimulation (1 and 4 pulses/burst, at 3 different levels of stimulation (16, 24 and 32 mA) being applied in turn through each of the 49 VEs. Ankle angles together with time-synchronised current data for each of the different electrodes were recorded for both experiments.

The target for foot orientation was defined as dorsiflexion at or above neutral, and inversion/eversion within − 1SD of the previously reported healthy subject mean foot orientation at heel strike [28]. All VEs which, when stimulated over the 10 s period, resulted in the foot reaching the target foot orientation were identified and the set of electrodes satisfying these criteria were labelled Set A.

When sitting relaxed in the chair the subject's foot was typically plantarflexed and inverted, compared with its neutral position. Hence, it was assumed that a twitch response that moved the foot towards dorsiflexion and eversion was desirable. A cost function was defined which used the maximum value of dorsiflexion

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[2] Two subjects could only tolerate 12.8 mA and 16 mA respectively, which was insufficient to produce target dorsiflexion when applied through any of the virtual electrodes electrodes during the slowly ramped stimulation

Table 4
Rank_any and Rank_all for different twitch stimuli.

	1 pulse @ 32 mA	4 pulses @32 mA	1 pulse @ 24 mA	4 pulses @ 24 mA
Rank_all Median (range)	5 (1–33)	4 (1–41)	11 (2–40)	8 (2–41)
Rank_any Median (range)	2 (1–19)	3 (1–15)	6 (1–15)	4 (1–29)

and inversion angles observed during the twitch response

$$\text{Cost} = -2 \cdot Dorsi + Inver$$

where *Dorsi* is the peak dorsiflexion angle (in degrees) measured during stimulation relative to the relaxed position. Dorsiflexion is positive and plantarflexion is negative. *Inver* is the peak inversion angle (in degrees) measured during stimulation relative to the relaxed position. Inversion is positive and eversion is negative. A weighting factor of 2 was applied to the dorsiflexion angle to reflect its relative importance compared to inversion/eversion.

This cost function was used to rank the foot responses to each of the different twitch stimulation bursts applied to each of the VEs. The cost function, which was applied to the positive peak value of dorsiflexion and inversion, maximises dorsiflexion and minimises inversion. The VE with the lowest cost was ranked 1st and each of the remaining 48 VEs were then assigned a rank based on their cost. To identify how well the cost function could be used to predict membership of Set A (the set of VEs which, when stimulated resulted in the foot reaching the target foot orientation) two metrics were derived. First, how far down the ranking it was necessary to go to include all of the members of Set A, defined as Rank_all; second, how far down the ranking it was necessary to go to include any member of Set A, defined as Rank_any.

In 9 out of the 10 subjects to complete the slow ramped stimulation study, at least 1 VE was identified which, when stimulated, produced the target foot response. The maximum number of acceptable VEs found for any individual subject was 4 (out of 49) and the minimum was 0.

The results of the twitch stimulation analysis for the 9 subjects are shown in Table 4. Note that stimulation at 16 mA produced no or minimal response.

Although there was significant inter-subject variability, the results showed that in most cases by using a cost function to rank responses to twitch stimulation it was possible to identify a much smaller set of electrodes containing one, or all of Set A. For example, using a 4 pulse burst of stimulation at 32 mA, a suitable electrode was identified in all cases within the first 15 of the responses ranked according to the slow ramped stimulation results. The data suggested therefore there could be advantage to using a twitch stimulation consisting of multiple pulses at high currents and a two stage search strategy was worth further investigation.

4. First lab-based demonstration of ShefStim

Further development work on both the stimulator and the search algorithm was carried out over the period 2009–11 resulting in the first demonstration of an array-based FES system with automated setup for the correction of drop foot. The study is reported in detail elsewhere [6], so in this paper, we focus on the improvements made to the stimulator hardware and implementation of the search algorithm, and provide an overview of the laboratory-based study involving subjects with drop foot.

4.1. Stimulator

Further stimulator development led to a new design weighing 200 g with a volume of 211 cc (130 mm x 65 mm × 25 mm). During automated setup the stimulator was controlled via an isolated
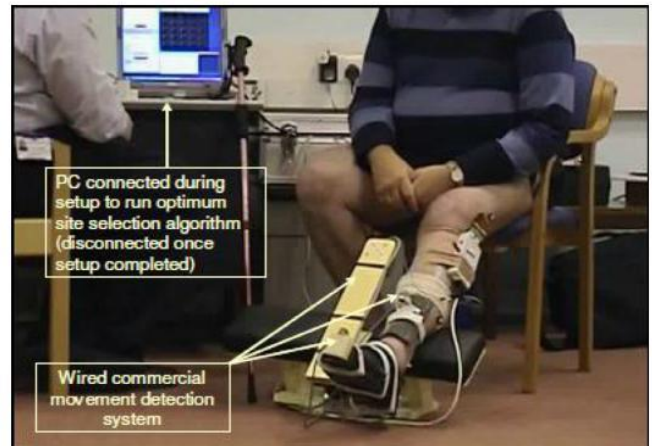

Fig. 5. Setup of ShefStim.

serial link by a program running on an external computer, the participant's leg was held in a brace, with the knee extended and foot movement was measured using an electromagnetic position and orientation sensor (Patriot, Polhemus Inc, Vermont) (Fig. 5). For walking trials the setup parameters were downloaded and the stimulator disconnected from the computer, enabling it to function as a standalone drop foot stimulator being triggered using a foot switch.

4.2. Search algorithm

The work described in Section 4 had been based on the use of a 2 × 2 VE. Following further pilot work it was found that a 4 × 4 VE still provided satisfactory resolution over foot response, but reduced sensation compared to a 2 × 2 arrangement and increased robustness to tissue movement during gait. The move to a 4 × 4 VE also served to reduce the array search space by a factor of ~2, compared with the original approach (25 VEs to be searched rather than 49).

As described in Section 4, we had already demonstrated the potential to use the response of the foot to short bursts of stimulation as a means of homing in on promising VEs. However, further work was needed to develop a clinically usable search algorithm. In the final system a three phase search strategy was implemented.

In phase one the level of stimulation at which the foot first responds is determined. Short bursts of stimulation are applied to each of the 25 virtual electrodes, a process taking about 2.5 s. The amplitude is automatically titrated until the threshold for repeatable foot movement, irrespective of direction, is determined. This threshold amplitude is used as the base for searches in subsequent phases. In phase two (twitch response), the algorithm searches for candidate stimulation sites, using twitches rather than tetanic contractions to speed-up search time and reduce sensation. Four pulses of stimulation are applied to each electrode in turn. The foot response is monitored for short periods after each stimulation, if there is a detectable response it is added to the list of candidate sites. Again the current is automatically adjusted until be-

tween 4 and 12 sites are found or the maximum current limit is reached. These sites are ranked in order of sensitivity using a cost function based on the angular displacement. The first two stages therefore allowed for rapid identification of the most sensitive VEs.

In phase three (tetanic testing), up to 8 of the sites identified in phase two were tested in rank order with an increasing stimulation intensity. Stimulation began at the level identified in phase two and incremented in steps until one of the following conditions were met: either plantarflexion was corrected to neutral dorsiflexion; or current reaching twice the starting value; or 150% of starting value with no movement detected; or motion saturation was detected. The algorithm included safeguards if unexpected movements occurred, enabling the system to temporarily wait if a leg spasm was detected or to pause the search process if repeated non-stimulated leg movement was detected. Once all the candidate sites were assessed, they were given a score based on a three-part cost function, designed to penalise solutions resulting in plantarflexion, excessive inversion or eversion, and high current If at any point during this phase the user found a site uncomfortable the clinician was able to skip that site. Once the tetanic testing phase was complete the first-ranked site was activated and, after initial testing of the site while sitting, the user then walked using the stimulator: If the foot response or stimulation sensation was not satisfactory it could be manually changed to an alternative site the ranking list. Finally, stimulus pulse width could be adjusted by the user, if necessary, to fine-tune the magnitude of foot response.

4.3. Laboratory-based clinical study

Ten participants with drop foot due to stroke (ages 53–71 years) and 11 due to MS (ages 40–80 years) were recruited to test the system. Each participant walked twice over 10 m under each of four conditions; (a) using their own stimulator setup by themselves; (b) using their own stimulator set up by a clinician, (c) using ShefStim with automated setup, and (d). no stimulation. Outcome measures were walking speed, foot angle at initial contact and the Borg Rating of Perceived Exertion. As described in Heller et al. [6], the results showed that when setup using ShefStim subjects' walking speed, dorsiflexion and frontal plane ankle angle at initial contact were all broadly comparable with clinician setup and, apart from walking speed, better than patient setup. The study demonstrated for the first time that fully automated setup of an array stimulator is feasible in a population with drop foot of central origin.

5. First take-home study of ShefStim

A final iteration of the stimulator design resulted in the CE-marked ShefStim system as shown in Fig. 6.

The ShefStim stimulator measures 142 mm x 50 mm x 14 mm (volume 99 cc) and weighs 125 g (including batteries). In contrast to the earlier versions of the system, it includes a combined foot angle sensor and remote control device, and setup does not involve holding the leg in a brace (Fig. 6). The remote control device is placed on the foot during set up and wirelessly provides triaxial accelerometer inputs to the search algorithm described in the previous section. Users are provided with an attachment, based on an iPod holder, which could be slipped onto the shoe prior to setup. Guidance is provided to the users on the correct mounting of the remote control on the shoe and the importance of aligning the ShefStim box with the long axis of the leg. Once setup is completed, the foot angle sensor device serves as a remote control with which the user can pause stimulation, adjust intensity or receive audible error messages. Stimulation timing during gait is con-

Fig. 6. ShefStim stimulator (left) being used by a subject during setup (right).

trolled using a conventional footswitch, located under the heel of the shoe. Integrating the foot angle sensor into the system enabled the stimulator to carry out the automated setup routine without requiring input from any external sensors or connection to a PC, making it suitable for use in the home environment.

In the final clinical study seven subjects with drop foot (3 subjects with MS, 3 with stroke and 1 with traumatic brain injury) used ShefStim over a 2 week period. The reader is referred to the work by Prenton et al. [7] for the experimental protocol and full results. Log data showed that all subjects were able to setup the stimulator outside of the laboratory environment without technical support. Automated setup time averaged 9 min, plus 5 min to don the equipment. Despite the challenges associated with unsupervised use, including the need for users to correctly align the ShefStim, placed in a pocket of a leg-mounted sleeve, and the remote on their shoe, speed and foot response with ShefStim, evaluated in a gait laboratory at the end of the 2 week period showed results comparable with the previous study by Heller et al. [6]. The study demonstrated, for the first time, that array-based automated setup FES system for foot-drop can be successfully used without technical support outside of the laboratory environment.

6. Discussion and conclusions

The work presented in this paper describes the evolution of the ShefStim design from initial concept in 2003 to evaluation of the CE-marked system by people with stroke in their own homes. A number of issues are worth discussing before conclusions are drawn on the revisions needed to be made to the design.

In Section 2 we introduced two models used for the identification of electrode array geometry. The activation area is similar in concept to the measure used by Kuhn et al. [29], who based their measure of selectivity on an activation volume. As our model assumes the nerve depth to be known (at 10 mm in this case), the cross-sectional area of the stimulation pool at 10 mm is the measure of the selectivity of stimulation. The larger this area is, the less selective the array stimulation is (i.e. the worse the ability to selectively stimulate neural structures). There are a number of limitations with the model, including the prismatic geometry and assumptions regarding the nerve depth, which undoubtedly varies significantly between subjects. Further, in contrast to Kuhn et al. [29], we did not experimentally validate the model. However, the array geometry and hydrogel properties derived using the model

proved to be similar to the array design successfully used in the final take-home study.

Although the ShefStim stimulator has been CE marked, there remain a small number of barriers to clinical uptake. By far the most significant of these is that sweat ingress to the hydrogel electrode interface layer leads to a significant drop in its resistivity and an inevitable decay in focality and stimulation efficiency with wear time [30]. These effects limit use of a given array to around one day of continuous wear. In the final study of ShefStim [7] we were able to provide participants with sufficient arrays to use a fresh hydrogel layer each day. However, the cost of such an approach is high and not a realistic solution in clinical practice. To address this we are exploring alternative solutions, including the use of dry electrodes (see, for example [31]). Other minor product development issues remain, including the development of an improved garment to house the stimulator on the leg and minor improvements to the firmware, all of which may be easily resolved. We believe that these improvements would lead to a significant reduction in setup time, as recorded in our final (unsupervised) study [7].

In conclusion, this paper has described the complete design, development and evaluation of an array-based FES system with automated setup for the correction of drop foot. The results demonstrate that an array-based stimulator with automated setup is a viable alternative to a conventional surface stimulator, or an implanted stimulator, for the correction of drop foot. Longer term clinical exploitation of ShefStim is dependent on identifying an acceptable alternative to the high-resistivity hydrogel electrode-skin interface layer.

Conflict of interest

There are no conflicts of interest for any of the authors of this study.

Acknowledgements

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2.4.2 Candidate involvement[5]

The candidate's central involvement in the HTD480 project is reflected in articles 1-3. However, the candidate also contributed to the review and feedback on this article (Article 4) with particular focus on the fifth section, about the take-home ShefStim® device (page 1164), and the the associated part of the discussion and conclusions relevant to this study (page 1165)

2.4.3 Critical Appraisal

This article allowed readers to follow the development of the ShefStim®, provided context and explained key decisions. It brought together the articles that studied iterations of the device and explained how the ShefStim® device works and what the main results were. As such the reader has this information in one place with clear links to the associated articles and conference proceedings. In essence it shows compliance with MRC guidelines (Medical Research Council, 2000) by confirming that the pre-clinical, phase 1 and phase 2 have been completed, as well as presenting evidence of project completion the funding body (NIHR/HTD).

The lay-advisory group (Article 1) and the DMO dorsiflex sock® (Article 2) were already in publication. Unlike the DMO dorsiflex sock® ShefStim® was a technological development explitly adhering to the MRC framework for trials of complex interventions (Medical Research Council, 2000). Therefore the article presents a technical narrative of the ShefStim®, including discussion around previously unpublished aspects of its development (Sha, 2008), which charts the progress to that point as well as aligning with the journal's, engineering, focus. Publication focussing on device development allowed a detailed report of the ShefStim® device, which is important in evaluations of complex interventions (Medical Research Council, 2000, 2006). Reporting the design, development and evaluation to date was also important given that further product development was indicated (by Article 3) before further definitive (Phase III) efficacy testing could occur. So this article provides a detailed frame of reference to any researcher wishing to address these limitations and/or carry out efficacy evaluation once the product limitations have been overcome. This article therefore contributes an approach to how a new technology can be initally but

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[5] A summary of the candidate's involvement in each article is presented in Table 1 on page 5

comprehensively developed and evaluated which, if adopted, could influence future clinical guidelines

<u>PART 2</u>

As stated in Chapter 1 the identified gaps in the AFO/FES foot-drop evidence base can be summarised as: 1) cited device limitations; 2) limitations in the evaluation of device effects and 3) a lack of good quality evidence with direct comparisons with which to further enhance clinical guidelines. The first of these gaps was addressed in **PART 1** through development and early phase evaluations of devices; which used a lay-advisory group in the co-design of the products and the evaluation studies. The development of ShefStim® was further reported in Article 4 to fill that first gap. The clinical evaluation studies of the DMO dorsiflex sock® (Article 2) and ShefStim® (Articles 3) were conducted by the candidate in such a way as to try and address the second gap, for these devices. The unclear effects of the DMO dorsiflex sock® found in Article 2 and the difficult problem related to the electrode array-skin interface for ShefStim® highlighted in Article 3 meant it was not possible to proceed to definitive trial for either. However, through the empirical study of the DMO dorsiflex sock® and ShefStim® and via the process of giving attention to how to most credibly evaluate the devices in order to more fully explore their mechanisms-of-action, their usability and the functional translation into the users own environment it became apparent that:

a) Some of the measures chosen for the two HTD480 empirical studies were not typically used in either the AFO or FES fields of research. The novel measures introduced in this thesis and which may be of value to the field include *foot*-clearance methods, detailed characterisation of use outside of the lab environment (logged usage, diary, donning/ setup times) and user satisfaction (face-to-face questionnaire, QUEST 2.0)

b) That the AFO and FES fields of research had been largely mutually exclusive until around the start of the PhD.

c) Clinical guidance did not extend to recommendations on which type of device to choose, or how they worked.

d) A number of RCTs comparing AFOs and FES had been conducted at the start of the PhD.

This part of the body of works therefore focussed on using the highest level of evidence, systematic review of RCT evidence with meta-analysis (Oxford centre for evidence-based medicine, 2009) to compare the orthotic and therapeutic effects of the devices on walking. The aim of the two reviews was to provide the highest level of evidence possible because any update in clinical guidelines would give greatest weight to RCT level evidence. Therefore Cochrane methodology of reviewing and meta-analysing was utilised (The Cochrane Collaboration, 2011). Given that national guidance about the devices has been applied to more conditions than just stroke (NICE, 2009; NICE, 2012; NICE., 2014; SIGN, 2013) there was a need for a synthesis of available evidence that included all CNO disorders. This meant that the work was not adoptable by a Cochrane review group which are organised according to single conditions (Stroke, Movement disorders and MS and rare diseases of the central nervous system). However their handbook (The Cochrane Collaboration, 2011; Higgins et al., 2011) and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Liberati et al., 2009; Moher, Liberati, Tetzlaff, & Altman, 2009) were utilised throughout for quality assurance purposes. Both reviews were registered with the International prospective register of systematic reviews (PROSPERO) for transparency, and to avoid any potential overlap. The candidate was mindful that a number of previous systematic reviews already existed. Most of these were focussed on one or other of the devices (AFO: (Ferreira et al., 2013; Leung & Moseley, 2003; Tyson & Kent, 2013; Tyson et al., 2013) and FES:(Kottink et al., 2004; Miller et al., 2017; Roche et al., 2009)). There was only one comparative RCT based systematic review (Dunning et al., 2015) which showed overall device comparability apart from preference which favoured FES but the breadth of the question asked by the authors prohibited meta-analysis and undermined its conclusions; as discussed in Chapter 1.

It was therefore timely to try and make more robust clinical comparisons and to try and develop a clearer understanding of whether either type of device was more effective and also to see whether studies comparing the devices reported on how the devices work (their mechanisms-of-action) with the aim to guide clinical choice and inform future guidelines to seek to fill this third identified gap in the evidence base.

2.5 Article 5

Prenton, S., Hollands, K., Kenney, L.P.J. (2016). Functional electrical stimulation versus ankle foot orthoses for foot-drop: a meta-analysis of orthotic effects. *Journal of Rehabilitation Medicine* 48(8): 646-656. doi: 10.2340/16501977-2136.

2.5.1 Article Summary and Publication

This article sought to fill the second gap in the evidence base identified by the candidate; that both devices lack foot-drop specific and user-important evaluation measures. It also sought to fill the third identified gap in the evidence base of a lack of clinical guidance about which device was better overall.

This first review (https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014009892) considered the devices as long-term orthotics which is how they are most commonly prescribed in clinical practice (Bosch, Harris, & Wing, 2014; National Research Council, 1973; Melo et al., 2015). As such the effects of interest were those which compared measurements with the device worn following a period of use to measurements taken at baseline while walking without the device (combined-orthotic effect (Figure 4)). Any measure of walking that captured this effect was considered and each measure was categorised according to the ICF domains of body functions and structures (BFS); activity/capacity qualifiers (CQ) and participation/performance qualifiers (PQ) (Brehm et al., 2011; WHO, 2001). Relevant databases were systematically searched alongside key author, citation and journal searches. 1593 studies were identified of which seven met the inclusion criteria. These reported results from 815, stroke, participants who participated in five trials.

Walking speed over ten metres (CQ); functional exercise capacity as determined by the six-minute walk test (CQ); timed up and go (CQ) and perceived mobility as captured by the stroke impact scale (SIS) mobility sub-scale (PQ) were used consistently enough amongst the included RCTs that meta-analyses were possible. Regardless of when comparisons were made and despite the hypothesized mechanisms-of-action that may have predicted FES to achieve greater benefits over time (Prenton, Hollands & Kenney, 2016) the take home message was that the two devices had comparable, favourable, effects. This was the first time this had been quantitatively demonstrated. BFS measures of mechanisms-of-action

were limited to single studies so whilst there was suggestion of equal improvement in energy cost, the lower limb Fugl Meyer and cadence and FES superiority with regards temporal-spatial aspects of gait pattern nothing further could be concluded about what mechanisms both/either used to achieve the observed equal functional gains. Potential reasons for the observed equal improvement in capacity and participation were discussed with one suggestion being that it might be as a result of both devices remedying foot-drop leading to greater levels of task-specific repetitive activity, i.e. walking, which is recognised as a necessary approach to promote recovery (Levin et al., 2009); albeit in the absence of usage data to show this occurred. An alternative offered rationale was that the trials did not collect data over a long enough period to highlight any differentiation, especially given the chronic populations studied.

Overall this article presented the first comparative meta-analysis of the two devices that was able to highlight, for the first time, their ability to produce statistically equal improvements in some activity and participation measures whilst simultaneously highlighting the failure of the RCT pool to evaluate how these improvements were achieved (mechanisms-of-action).

REVIEW ARTICLE

FUNCTIONAL ELECTRICAL STIMULATION VERSUS ANKLE FOOT ORTHOSES FOR FOOT-DROP: A META-ANALYSIS OF ORTHOTIC EFFECTS*

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Objective: To compare the effects on walking of functional electrical stimulation (FES) and ankle foot orthoses for foot-drop of central neurological origin, assessed in terms of un-assisted walking behaviours compared with assisted walking following a period of use (combined-orthotic effects).
Data sources: MEDLINE, AMED, CINAHL, Cochrane Central Register of Controlled Trials, Scopus, REHABDATA, PEDro, NIHR Centre for Reviews and Dissemination and clinicaltrials.gov, plus reference list, journal, author and citation searches.
Study selection: English language comparative randomized controlled trials (RCTs).
Data synthesis: Seven RCTs were eligible for inclusion. Two of these reported different results from the same trial and another 2 reported results from different follow-up periods and were therefore combined, resulting in 5 synthesized trials with 815 stroke participants. Meta-analyses of data from the final assessment in each study and 3 overlapping time-points showed comparable improvements in walking speed over 10 m ($p = 0.04–0.79$), functional exercise capacity ($p = 0.10–0.31$), timed up-and-go ($p = 0.812$ and $p = 0.539$) and perceived mobility ($p = 0.80$) for both interventions.
Conclusion: Data suggest that, in contrast to assumptions that predict FES superiority, ankle foot orthoses have equally positive combined-orthotic effects as FES on key walking measures for foot-drop caused by stroke. However, further long-term, high-quality RCTs are required. These should focus on measuring the mechanisms-of-action; whether there is translation of improvements in impairment to function, plus detailed reporting of the devices used across diagnoses. Only then can robust clinical recommendations be made.

Key words: electrical stimulation therapy; nervous system diseases; stroke; walking; foot drop; systematic review; meta-analysis.

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INTRODUCTION

Conditions such as stroke, brain injury (BI), multiple sclerosis (MS), spinal cord injury (SCI) and cerebral palsy (CP) affect upper motor neuronal pathways (1) and are collectively referred to as pathologies of central neurological origin (CNO) (2). In the UK there are approximately 1.2 million people living with stroke (3), 100,000 MS and 40,000 SCI (4), there are 160,000 BI admissions per year (5) and 1 in 400 people have CP (6). Foot-drop is a common impairment seen across these conditions (7) and although prevalence data in some of the CNO conditions is very limited, a commonly cited figure suggests that it is seen in 20–30% of people with stroke (7, 8).

Foot-drop is categorized as an inability to dorsiflex the foot, with or without excessive inversion and is most commonly caused by weakness in the dorsiflexor (and evertor) and/or overactivity in the plantarflexor (and invertor) muscle groups. Foot-drop results in walking being slower, less efficient and potentially unsafe (7); as foot clearance during swing and initial foot contact at the start of the stance phase are compromised. These factors have been associated with an increased risk of falls (7), reduced quality of life (7, 9) and increased levels of mortality (10).

Current practice in the treatment of foot-drop normally involves a form of ankle foot orthosis (AFO) (11). Functional electrical stimulation (FES) is also used but less frequently (9).

AFOs stabilize the foot and ankle and lift the toes when stepping (12). Meta-analyses have shown them to have positive effects on some aspects of walking (12, 13), but these analyses are primarily based on non-randomized control trial (RCT) evidence. AFOs have been criticized for detrimental effects on the adaptability of walking, propulsion, aesthetics and comfort (14–16), which can impact on compliance and satisfaction.

Foot-drop FES uses electrical pulse trains to stimulate the common peroneal nerve over key phases of the gait cycle to correct the foot-drop impairment (17). This phasic stimulation can be delivered via surface or implanted electrodes. Foot-drop FES has been shown to have positive effects on walking speed (18, 19), but meta-analyses have also, in part, been based on non-RCT evidence. For surface systems, limitations have been cited in relation to issues with effort of setup, skin irritation and pain (20), which again affects compliance and satisfaction. Implanted systems address some of these limitations, but are more costly (21).

Despite their limitations both are endorsed in the management of foot-drop, with clinical guidelines existing for AFO as a result of stroke (22, 23) MS (24), CP (25) and BI (26) and FES guidelines promoting use across all CNO diagnoses (2). However, these guidelines have had to rely on some non-RCT sources of evidence and as intervention specific guidelines, comparing with no treatment or physiotherapy, do not consider evidence from direct comparisons between these interventions. As a result, current guidelines do not provide clinicians with a clear patient pathway. Recently a number of RCTs providing direct comparisons have been published. Furthermore, these studies have advanced our understanding of the effects these interventions may produce:

- Immediate-orthotic effects where same-day comparisons are made between AFO/FES unassisted and assisted walking behaviours (16, 27).
- Therapeutic effects (19, 28) where unassisted walking behaviours are compared with unassisted walking on a day some period later (16, 27).
- Training effects (16) where assisted walking behaviours are compared with assisted walking on a day some period later.
- Combined-orthotic effects (15) where unassisted walking behaviours on one day are compared with assisted walking on a day some period later (16, 27).

The suggested mechanism-of-action for AFO is that the device remedies the loss of dorsiflexion/eversion by holding the foot in a neutral position, but this can result in negative effects on neuromuscular control and muscle biomechanics with long-term use (29–31). Therefore, it has been assumed that they only provide immediate-orthotic effects (12), a notion supported by the only known long-term AFO-specific RCT in the field (32).

In contrast, there are many reports of long-term neuromuscular control improvements with FES (19, 33), which are attributed to changes in neural plasticity, muscular strength and cardiovascular efficiency (31, 34, 35). The mechanism for these improvements has been hypothesized as being due to the coinciding of antidromic electrical stimulation-generated action potentials with volitional activity, leading to strengthening of modifiable Hebb-synapses at a segmental level (34, 36, 37).

Given these proposed mechanisms-of-action it could be assumed that FES will provide a distinct advantage over AFO with long-term use.

Two recent reviews (9, 38) have explored the long-term effects evidence for AFOs vs FES in stroke survivors; both concluding that there was a preference for FES but insufficient evidence to recommend one over the other. However, the first was not systematic (39) and included non-RCT studies (9) and the other did not meta-analyse; possibly due to the breadth of question posed (38). This review (38) reported that FES was superior at conserving energy but included a paper where FES was combined with botulinum toxin (40) and another that compared FES with therapy as opposed to AFO (41).

In order to provide improved clinical guidelines, which will help clinicians determine which of these interventions to prescribe and what the directly comparable effects are over a period of use, gold standard meta-analysis of RCT level evidence is required (42). Given that both interventions are most commonly prescribed as long-term orthotics (9, 30) and the assumption that studying long-term use will highlight any differences in walking behaviours resulting from the different mechanisms-of-action, we sought to perform a systematic examination of the evidence base to address the question: Are the combined-orthotic effects on walking for foot-drop of CNO greater for FES than AFO?

METHODS

This review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (43). The full review protocol can be found at: http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=9892&UserID=6114.

Nine electronic databases were searched: MEDLINE (Ovid), AMED (Ovid), CINAHL (EBSCO), Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, REHABDATA, PEDro, NIHR Centre for Reviews and Dissemination and clinicaltrials.gov. A search strategy including controlled vocabularies related to "electric stimulation", "walking" and "nervous system diseases" and terms such as "foot drop" and "electric* stimulat*" were used with no date limits (full search strategy available on request from the corresponding author). Reference list, citation, key author and journal searches were also completed and all searches were limited to the English language.

Once duplicates were removed 1 reviewer (SP) screened titles and abstracts, categorizing each as "possibly" or "clearly not" relevant against the inclusion criteria (Table I). Full-length articles were retrieved for "possibly relevant" studies and 2 unmasked reviewers (SP and KH) independently assessed their eligibility (Table I), classing them as "relevant", "definitely irrelevant" or "unsure". Different outcome measurements from the same trial reported in separate publications were treated as a single publication; as were separate publications that reported different data collection time-points within the same trial. Any disagreements or "unsure" publications were discussed (between SP and KH). A third reviewer was available to resolve any disagreements (LK).

SP extracted data using a predesigned pro forma; trial details extracted related to the characteristics of the included studies, participant

Table I. *Inclusion criteria*

Design
- Randomized controlled trials (RCT)

Participants
- Participants with foot-drop of a central neurological origin (CNO)

Intervention
- Common peroneal nerve functional electrical stimulation (FES) to address the specific impairment of foot-drop, with or without other areas of stimulation
- Stimulation eliciting a muscular contraction
- Trials where common peroneal stimulation is used during walking (overground or treadmill) as part of the intervention
- Trials studying combined-orthotic effects of foot-drop FES
- Trials where foot-drop FES and another intervention are used in combination but foot-drop FES is measured independently

Comparator
- Trials comparing foot-drop FES with ankle-foot orthosis (AFO) (the term therapy was allowed as might involve AFO)

Outcomes
- Measures of walking

and intervention details. Missing data and/or aspects that required clarification were requested from trial authors (14, 16, 44, 45), by SP (Appendix I). KH reviewed the extracted data for accuracy.

As an RCT-based review, and to avoid the limitations of scaled quality assessment tools (42, 46), the Cochrane risk of bias assessment tool (42) was used independently by 2 reviewers (SP and KH) with a third reviewer (LK) available if necessary. To ensure impartiality, risk of bias was based on published work only. Performance bias was not considered as the interventions precluded blinding of participants and measures were primarily objective (46).

Outcomes across the World Health Organization's (WHO) International Classification of Functioning, Disability and Health (ICF) (47) were extracted. This helped to identify if there was any comparative evidence to support the assumed mechanisms-of-action and whether they translated into function. Therefore, all measurements were categorized as either being within the body functions and structures (BFS), activity or participation domain (47) by SP, using supporting literature (47–50). All post-intervention data collection point assisted-walking means and standard deviations (SD) were extracted with final-assessment data pooled for data analysis. Given the hypothesized mechanisms-of-action suggesting that FES would have greater benefits than AFO with longer-term use; broadly overlapping time-point data was also grouped for meta-analysis where possible. Standard errors were converted to SDs (14, 42, 51) and functional exercise capacity (an activity domain measurement (52)) was considered as metres walked, and was converted as necessary (15).

Meta-analyses were performed using RevMan 5.3® software. Where the same measurement was used across more than 2 trials, outcomes were combined using mean difference (MD) with 95% confidence intervals (95% CIs). Where an outcome was measured using different approaches, such as functional exercise capacity (distance walked in m measured over 2, 3 or 6 min), standardized mean difference (SMD) with 95% CIs was used. For crossover trials only pre-crossover data was extracted (15). Where there was more than one arm looking at the same intervention the similarity at baseline to the other intervention and size were used to decide which to use, and the data from the most comparable group was extracted (15).

Heterogeneity was examined using visual inspection of forest plot, χ^2 test and I^2 statistic. If the χ^2 test showed heterogeneity that the I^2 statistic

identified as being moderate to low (< 50% (42)) a fixed-effects model was used. A random-effects model was used for heterogeneity > 50%.

RESULTS

A total of 1,836 citations were found, of which 7 were eligible for inclusion. Two of these reported outcomes from the same participants (44, 53) and were therefore grouped, and subsequently referred to by the first publication date (44). One trial published results up to 6 months (14) and had another publication reporting results at 12 months (51); and were therefore also grouped. For meta-analysis the relevant publication was used with the source identified by the date of the publication on the corresponding forest plot. Thus a total of 5 RCTs, published between 2007 and 2015 with 815 participants, were available for meta-analysis (Fig. 1).

Characteristics of included trials

One trial used a multiple-site crossover design (15) with 2 AFO arms. Data from arm 2 (AFO-FES) was used as it was larger and similar to the FES group at baseline. The remaining 4 trials used 2-arm parallel RCT design, 2 single-site (44, 45) and 2 multiple-site (14, 16) (Table II).

Participant details

All the participants were over the age of 18 years and had suffered a stroke. Mean time since diagnosis ranged from 51.7 days (45) up to 6.9 years (14, 51). Of those trials that reported hemiplegic side (16, 44, 45) there was a relatively even distribution (116: 47.9% right, 126: 52.1% left). Two of the trials recruited current AFO users (16, 44), whereas the remaining 3 introduced the interventions to both groups for the first time (Table II).

Intervention details

Three of the trials (14–16, 51) reported providing "customized" AFOs prescribed by an orthotist; plus a physiotherapist for Kluding et al. (16). One used off-the-shelf AFOs (45) which is appropriate practice with their, sub-acute, population (54) and 1 used a combination (44). No trial reported any further details of the AFOs or how prescription decisions were made; none were hinged. All but one trial used surface FES systems (44), one trial highlighted that "clinicians" set up FES for measurement (45), but no trial reported details of set-up parameters, such as electrode placement, ramping, amplitude or frequency. The setting where interventions were used varied, with participants from 3 of the trials using the devices within their own environment (14, 15, 44, 51). One trial used them in both the participant's own environment and under supervision (16) and 1 used them only under supervision (45). All-day-use was encouraged in all but one of the trials (45), some with a gradual introduction, although whether this was adhered to was not reported. Three trials provided concurrent therapy for both groups (16, 44, 45) (Table II).

Methodological quality

Table III summarizes the quality assessment, Kluding et al. (16) alone had no identified areas of high risk of bias.
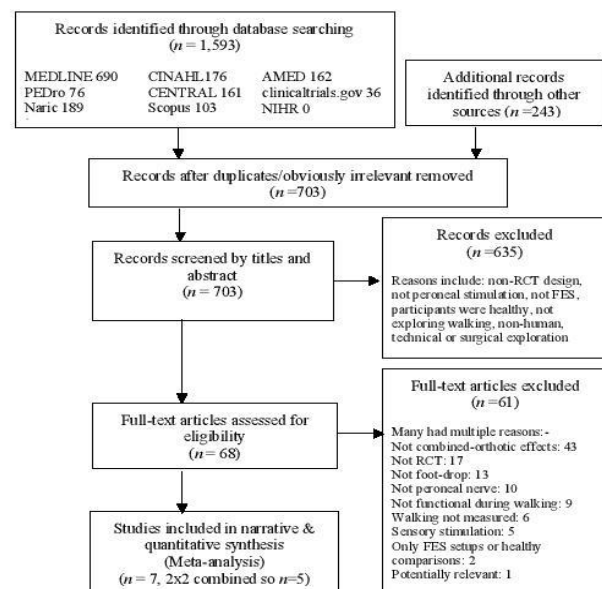

Records identified through database searching
(*n* = 1,593)

MEDLINE 690	CINAHL 176	AMED 162
PEDro 76	CENTRAL 161	clinicaltrials.gov 36
Naric 189	Scopus 103	NIHR 0

Additional records identified through other sources (*n* =243)

Records after duplicates/obviously irrelevant removed (*n* =703)

Records screened by titles and abstract (*n* = 703)

Records excluded (*n* =635)

Reasons include: non-RCT design, not peroneal stimulation, not FES, participants were healthy, not exploring walking, non-human, technical or surgical exploration

Full-text articles assessed for eligibility (*n* = 68)

Full-text articles excluded (*n* =61)

Many had multiple reasons:-
Not combined-orthotic effects: 43
Not RCT: 17
Not foot-drop: 13
Not peroneal nerve: 10
Not functional during walking: 9
Walking not measured: 6
Sensory stimulation: 5
Only FES setups or healthy comparisons: 2
Potentially relevant: 1

Studies included in narrative & quantitative synthesis (Meta-analysis) (*n* = 7, 2x2 combined so *n*=5)

Fig. 1. Trial selection.

Table II. *Characteristics of included trials, participant and intervention details*

	Trial design	N Diagnosis (R):(L)	Men: Women	Age (years)	Time since diagnosis Mean (SD)	Current or new AFO users	AFO	Mechanical properties reported	FES	Setup for measurement done by	Use
Bethoux et al. (14, 51)[a]	2-arm parallel Multiple sites	495 (242 FES: 253 AFO) CVA Not specified	FES=147:95 AFO=157:96	FES=63.87 (11.33) AFO=64.3 (12.01)	FES=6.9 years (6.43) AFO=6.86 years (6.64)	New	Customized	No	Surface Walkaide	Not specified	Home 2-week progressive wearing schedule then all day
Everaert et al. (15)[b]	3-arm crossover Multiple sites	78 (43 FES: 35 AFO) CVA Not specified	FES=32:6[e] AFO=19:12[e]	FES=57.1 (12.9)[e] AFO=55.6 (11.9)[e]	FES=6.4 months (3.8)[e] AFO=6.9 months (3.2)[e]	New	Customized	No	Surface Walkaide	Not specified	Home All day
Kluding et al. (16)[a]	2-arm parallel Multiple sites	197 (99 FES: 98 AFO) CVA 93:104	FES=51:48 AFO=67:31	FES=60.71 (12.24) AFO=61.58 (10.98)	FES=4.77 years (5.29) AFO=4.34 years (4.1)	Current	Customized[f] plus TENS for 2 weeks	No	Surface NESS L300	Not specified	Both Bioness clinical protocols followed 15min-all day Training: 15 min × 2 day 1 week then 20 min 2 × day next 2 weeks
Kottink et al. (44)[c]	2-arm parallel Single site	29 (14 FES: 15 AFO) CVA 13:16	FES=10:04 AFO=10:05	FES=55.2 (11.36) AFO=52.87 (9.87)	FES=9.07 years (9.29) AFO=5.67 years (4.64)	Current	Combination[f]	No	Implanted 2-channel implant	Not specified	Home Gradual increase over 2 weeks, then all day
Salisbury et al. (45)[d]	2-arm parallel Single site	16 (9 FES: 7 AFO) CVA 10:6	FES=03:06 AFO=03:04	FES=55.8 (11.3) AFO=52.6 (17.2)	FES=51.7 days (34.6)	New	Off the shelf	No	Surface ODFS	Clinician for FES	Supervised Part of physiotherapy 20 min, 5× week with supervised/ independent walking as appropriate

[a]ITT completed; [b]Post-intervention/dropout characteristics; [c]Post-intervention/dropout characteristics; CVA: cerebrovascular accident/stroke. [d]Pre-intervention/ dropout data. [e]Pre-intervention/ dropout characteristics at later time-point than is included in this review (12 weeks); customized: custom-made/modified AFO; Combination: different AFOs used by different participants; off the shelf: prefabricated/unmodified AFO; [f]Both groups continued with physical therapy alongside intervention. FES: functional electrical stimulation; AFO: ankle-foot orthosis; TENS: transcutaneous electrical nerve stimulation with no motor response; NESS L300: Bioness model; ODFS: Odstock foot-drop system; BFS: body functions and structures.

Outcome measurements

All trials utilized ICF activity domain measurements; most commonly the 10-metre (m) walk test (Table IV). However, one did not collect any BFS domain measurements (14, 51) and another lacked participation domain measurements (15). The intervention period studied ranged from 6 weeks (15) to 12 months (51).

To allow direct comparison of the assumed mechanisms-of-action and functional translation, the following results are presented according to ICF domains. The narrative comparison found in Table IV is summarized below. Final-assessment meta-analyses are presented first. There were 3 overlapping data time-points, at 4–6 weeks, 12–13 weeks and 26–30 weeks, for activity domain measurements. These are categorized as short, medium and longer-term respectively (Table IV); meta-analyses at these time-points are then presented.

Body functions and structures

Physiological cost index (PCI) (15), cadence (45), spatiotemporal/kinematics (44) and lower limb Fugl-Meyer (16) were reported by single trials; therefore pooled-analysis was not possible. All the trials found within-group improvements, but no significant statistical differences were reported for any of these measures by the primary authors except Kottink et al. (44), who found some spatiotemporal and kinematic differences in favour of FES ($p < 0.05$) (Table IV).

Activity

Final-assessment outcomes of 10-m walking speed (all 5 trials, $n = 789$) and functional exercise capacity (3 trials, $n = 761$) were pooled. Meta-analysis showed between-group comparable improvement (MD = 0.01, [−0.04, 0.05]; $I^2 = 0\%$; $p = 0.79$, Fig. 2a); and SMD −0.07 [0.22, 0.07], $I^2 = 0\%$; $p = 0.31$, Fig. 3a), respectively.

The timed up-and-go test was used in 2 trials (16, 51), both reported between-group comparable improvement ($p = 0.812$ and $p = 0.539$), therefore meta-analysis was not required (Table IV).

All other final-assessment activity measures were used in single trials with between-group comparable improvement in all cases (Table IV).

Meta-analysis was possible for the 10-m walk test using data at short (4 trials, $n = 771$), medium (3 trials, $n = 699$) and long-

Table III. *Risk of bias*

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bethoux et al. (14, 51)	Unclear	High	High	Low	Low	Low
Everaert et al. (15)	Unclear	Unclear	Unclear	High	Low	Low
Kluding et al. (16)	Low	Low	Unclear	Low	Unclear	Low
Kottink et al. (44)	High	Unclear	High	Unclear	Low	Low
Salisbury et al. (45)	High	Low	High	Unclear	Low	Low

Table IV. *Outcome measurements and intervention effects*

	Walking outcome measures used & ICF level	Outcome collection points	Combined-orthotic effects
Bethoux et al. (14, 51)	Activity: • 10MWT[a] • 6-min walk test (distance) • Gaitrite Functional Ambulation Profile[b] • mEFAP (including TUG) Participation[b]: • SIS (Mobility, ADL/IADL & social participation domains combined)[a] • SIS mobility sub-scale • Perry ambulation categories based on 10MWT results	0 Short: 1 month (not published) Medium: 3 month (not published) Longer: 6 month 12 month[b]	• FES↑=AFO↑
Everaert et al. (15)	BFS: • PCI over 4-min test[a] Activity: • 4-min walking test (speed)[a] • 10MWT • Modified RMI	0, 3 weeks Short: 6 weeks	• Modified RMI: between-group, post-intervention differences not reported • FES↑=AFO↑: for other measures
Kluding et al. (16)	BFS: • LL Fugl Meyer Activity: • 10MWT (self and fast)[a] • TUG • 6-min walk test (distance) Participation: • SIS mobility sub-scale • Activity monitoring (Stepwatch®)	0 Short: 6 weeks (not published) Medium: 12 weeks (not published) Longer: 30 weeks (only change data published)	• FES↑=AFO↑
Kottink et al. (44)	BFS: • stride time[c] • stride length[c] • stride width[c] • step length[c] • stance phase %[c] • 1st double support phase %[c] • 1st single support phase %[c] • kinematics = hip, knee & ankle[c] Activity: • 10MWT • 6-min walk test (speed) • Speed[c] Participation: • Activity monitoring (ActivPAL®)	0 Longer: 26 weeks	• FES>AFO: Longer 1st single support phase %[c]; shorter Stance phase; 1st double support phase %[c]; Speed[c]; 10MWT; 6-min walk (speed) at 26 weeks • AFO spent less time less in sitting/lying than FES • FES↑=AFO↑: all other measures
Salisbury et al. (45)	BFS: • Cadence (10MWT) Activity: • Speed (10MWT) • FAC Participation: • SIS mobility sub-scale	0 Short: 6 weeks Medium: 12 weeks	• FES↑=AFO↑

[a]identified as primary outcome measure by authors; [b]not reported in Bethoux et al. (51) 12-month follow-up publication; [c]From Kottink et al. (53).
mEFAP: modified Emory Functional Ambulation Profile; TUG: Timed Up and Go; QoL: Quality of Life; SIS: Stroke Impact Scale; ADL/IADL: Activities of Daily Living/Instrumental Activities of Daily Living; 10MWT: 10-metre walk test; PCI: Physiological Cost Index; RMI: Rivermead Mobility Index; BBS: Berg Balance Scale. FAC: Functional Ambulation categories; ↑increase; >greater than; =equal to; <less than; BFS: body functions and structures.

er-term (3 trials, $n=713$) time-points (Fig. 2b–d). This revealed comparable improvement in the short-term (MD = 0.02 [–0.05, 0.10]; $I^2=66\%$; $p=0.54$, Fig. 2b)) and longer-term (MD = –0.02 [–0.06, 0.03]; $I^2=50\%$; $p=0.43$, Fig. 2d)). In the medium-term there was a marginal, but significant, difference in favour of AFO (MD = –0.04 [–0.09, –0.00]; $I^2=0\%$; $p=0.04$, Fig. 2c)).

Functional exercise capacity meta-analyses were performed for short (3 trials, $n=761$) and medium-term (2 trials, $n=692$) time-points (Fig. 3b and c). Meta-analyses revealed between-group comparable improvement (SMD = –0.12 [–0.26–0.02]; $I^2=0\%$; $p=0.10$, Fig. 3b) and SMD = –0.10 [–0.25, 0.05]; $I^2=0\%$; $p=0.19$, Fig. 3c)).

Participation

The mobility domain of the Stroke Impact Scale (SIS) was collected by 3 trials ($n=701$) (14, 16, 45). Meta-analysis showed between-group comparable improvement (MD 0.31 [–2.06, 2.68]; $I^2=41\%$; $p=0.80$, Fig. 4).

Activity monitoring was used by 2 trials (16, 44) (Table IV), but their data collection methods varied too significantly (steps taken compared with time spent in different positions) to pool results. Kluding et al. (16) found no significant differences in the number of steps taken and Kottink et al. (44) found the FES group spent significantly more time in sitting/lying than the AFO group ($p=0.04$).
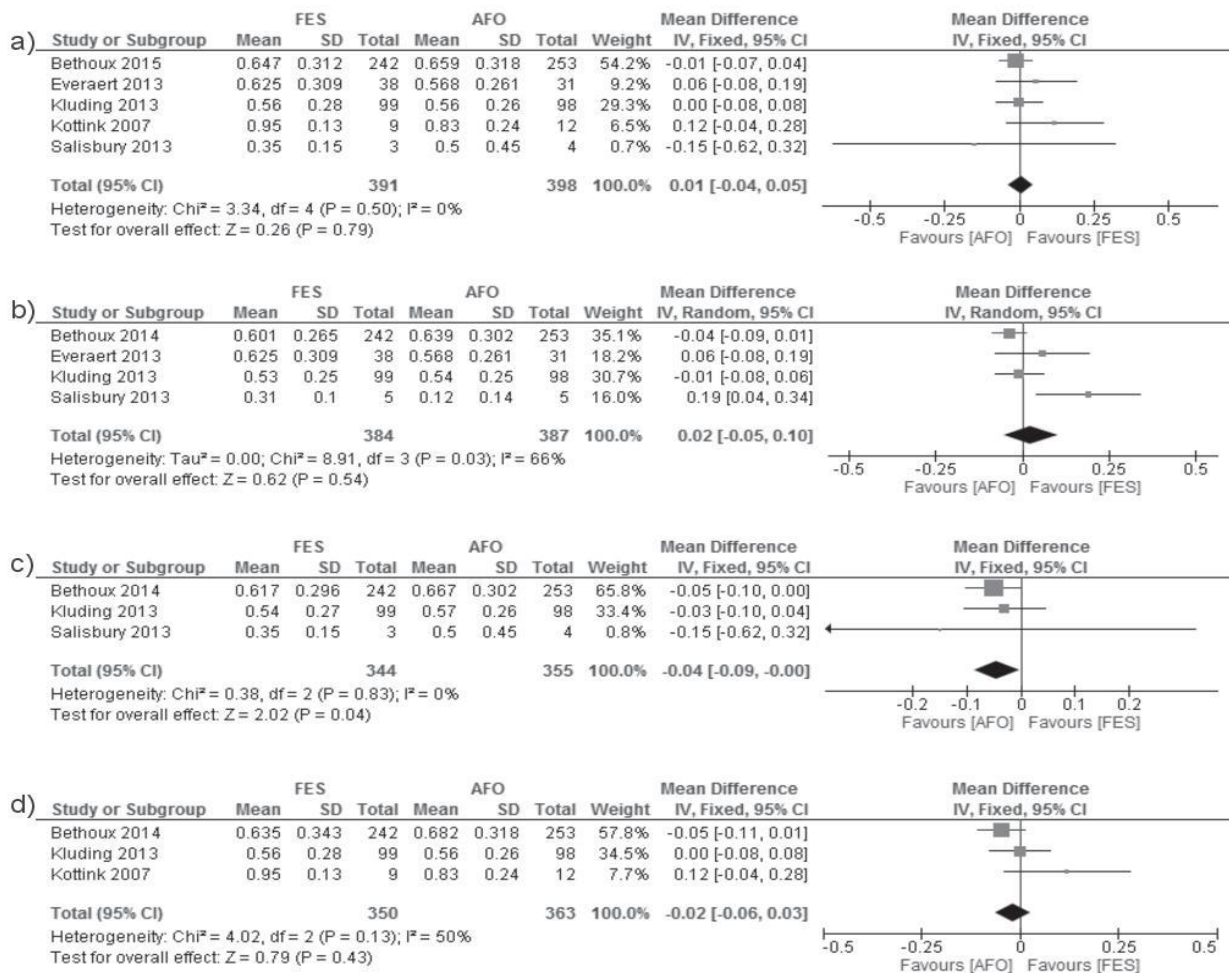
Fig. 2. Activity measure: 10-metre (m) walk test (metre/second). (a) Final assessment. (b) Short-term. Bethoux et al. (14) and Kluding et al. (16) data obtained via correspondence with authors. (c) Medium-term. Bethoux et al. (14) and Kluding et al. (16) data obtained via correspondence with authors. (d) Longer-term. Kluding et al. (16) data from correspondence with authors.
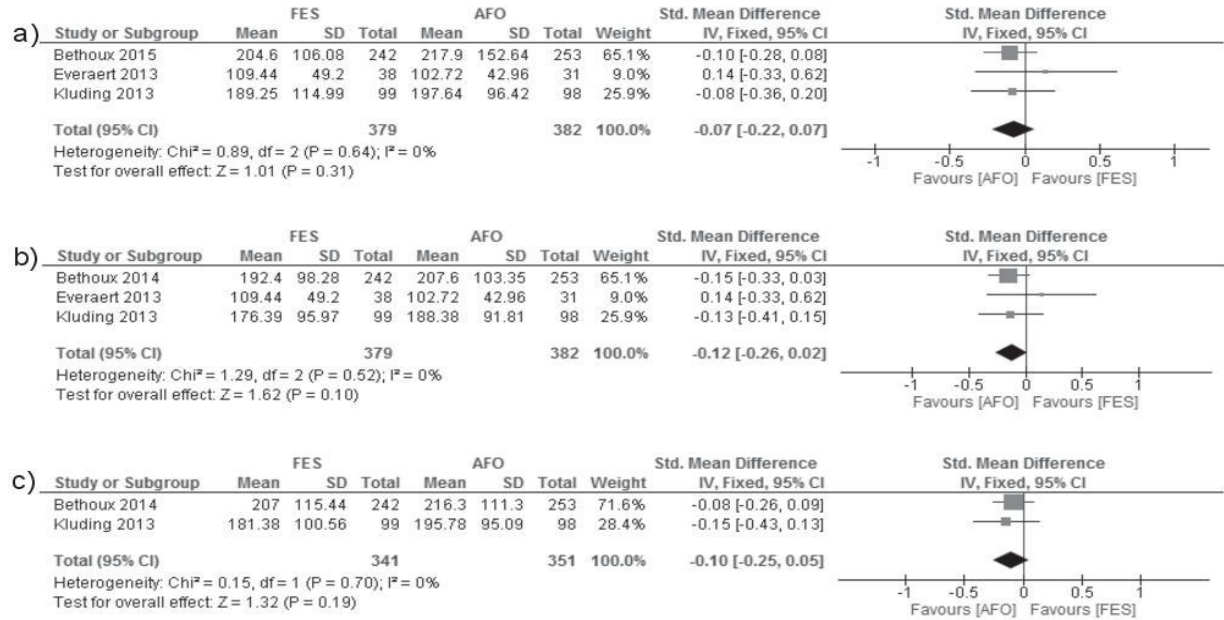
Fig. 3. Activity measure: functional exercise capacity metres (m). (a) Final-assessment. Kluding et al. (16) data obtained via correspondence with authors. (b) Short-term. Bethoux et al. (14) and Kluding et al. (16) data obtained via correspondence with authors. (c) Medium-term. Data obtained via correspondence with authors.

All other final-assessment participation measurements were used by a single trial (14) with between-group comparable improvements found (Table IV).

DISCUSSION

This is the first systematic review, including meta-analysis, of studies comparing AFO with FES as interventions for people with CNO foot-drop, which focuses on the clinically relevant combined-orthotic effects on walking. As a RCT-based review with meta-analysis guided by the PRISMA statement (55) the results provide the highest level of evidence currently available to support clinical decision-making (42).

The RCTs were deemed to be of medium-methodological quality, which provides some confidence in our results that both interventions demonstrate equal combined-orthotic improvements in 10-m walking speed, functional exercise capacity, timed-up-and-go and the mobility sub-scale of the SIS; regardless of the length of time used.

Given the different hypothesized mechanisms-of-action detailed in the introduction it is somewhat surprising that there was no differentiation between the 2 interventions for any of the pooled measurements. To explore this result we examined outcome measurements within the BFS domain (which directly reflect mechanisms-of-action (48)) and whether or not these changes in BFS coincide with changes in activity and participation differentially between the interventions and over different time-points of use.

Body functions and structures

The majority of measurements used in the reviewed trials suggest that there are no differences between the 2 interventions. However, given the suggestions of a negative influence of AFO and a positive influence of FES on volitional muscle activa-
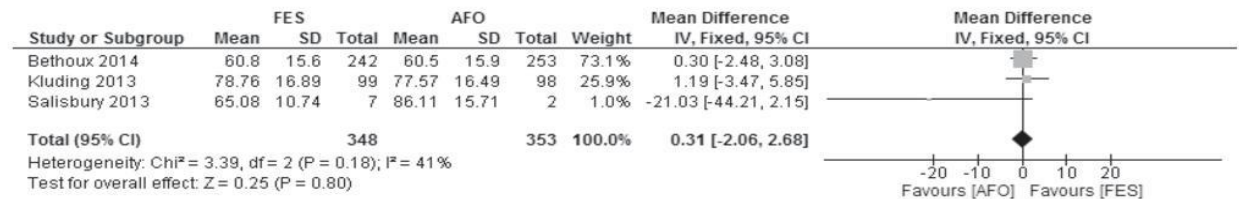

Fig. 4. Participation measure: Stroke Impact Scale (mobility sub-scale).

tion it was surprising that none of the included trials reported electromyography (EMG) or strength data. Throughout our systematic search of the literature we found only one RCT (which explored therapeutic as opposed to combined-orthotic effects) that compared EMG activity between FES and AFO treatments. This trial reported that EMG activity was greater following a period of FES than AFO use (37).

Kottink et al. (53) was the only reviewed trial to measure gait features and found differences between a FES group and an AFO group. Despite these findings, which are supported by results of non-RCT studies (57–61), no further inferences can be drawn at this time. Future trials should capture such measurements to determine whether restorative, as opposed to compensatory, changes are made (62) in order to more accurately understand the mechanisms-of-action.

Activity and participation

Meta-analysis of 3 validated measures of the activity domain (49, 52) and one mobility-specific participation domain measurement (49, 52) indicate that AFOs and FES produce equivalent functional improvements to walking for people with foot-drop as a result of stroke; regardless of length of use. The equivalency of effects between these interventions is supported by non-RCT studies, which have found no significant changes in activity domain measurements when FES is provided to AFO users (59, 60, 63).

Given the difference in hypothesized mechanisms-of-action between FES and AFO and the lack of BFS measurements, the question remains as to how these comparable effects on activity/participation are achieved. One explanation is that both simply correct the mechanical problem of foot-drop; as is suggested for AFO. However, this does not fully explain the differences between immediate-orthotic effect and orthotic effect after a period of use. The activity monitoring results from 1 trial highlight another potential explanation. Kluding et al. (16) found that the number of steps taken per day increased with use of either intervention (1,891–2,069, AFO and 2,092–2,369, FES at 6 and 30 weeks). This increase in repetition of walking in both FES and AFO intervention groups (facilitated by the correction of foot-drop) could explain the observed comparable improvements. Indeed intensity of task-specific repetition is widely accepted as critical for effective improvements of motor-impairments (64–66). This hypothesis is consistent with Kluding et al.'s suggestion that both interventions achieve combined-orthotic effects through immediate-orthotic and training effects (16).

A final hypothesis is that RCTs to date have not been long enough to detect differences given the predominantly chronic populations investigated (67). Bethoux et al. (51) did not find differences at 12 months, which may suggest even longer-term follow up is required (68). To facilitate comparisons, all future trials should ensure that data collection time-points are justified against physiological processes underlying treatment effects.

This review had some limitations. Firstly, it has revealed that, until 2007, research has been limited to examinations of a single intervention for a single diagnosis precluding comparisons between interventions that might usefully inform

clinicians which intervention may be most suitable. Since 2007 comparative RCTs have been undertaken, making this review timely. Whilst future FES- (9, 69) and AFO-specific studies (13, 70, 71) are necessary for intervention development, where possible, research should be impairment focused in order to facilitate more discerning prescription.

Secondly, despite the literature search encompassing all CNO diagnoses, the reviewed trials only included participants who had experienced a stroke and who were over the age of 18 years, so our results can only be applied to this population. Trials using different CNO populations are necessary, given that current clinical guidelines encompass them. Similarly, in order to form clinical guidelines indicating which subgroups of patients with any given CNO diagnosis (e.g. time points post-stroke, severity of foot-drop impairment) might benefit most from either intervention future studies with carefully defined inclusion/exclusion criteria are needed. This approach is of critical importance in subsequent trials so that potentially important clinical effects are not diluted in heterogeneous study groups. Until such a time as sufficient high-quality RCTs in specific groups of patients become available any meta-analyses will also suffer similar limitations.

Thirdly, risk of bias was present in the reviewed studies with detection bias (assessor blinding) the most common area. While this might impact our results this area of bias is common within rehabilitation research. Indeed, previous FES (28) and AFO (12) reviews have chosen to discount it, suggesting it is impractical to address in studies of medical devices. It can also be argued that objective measures minimize the risk of this source of bias. However, 2 trials (15, 16) attempted to control for this, suggesting that it is feasible to blind assessors and should at least be considered in future trials (72). We based the quality assessment on published material alone; so as not to advantage trial authors who respond to requests for additional data. Therefore a lack of reported methodological detail might account for some of the other unclear and high areas of bias found.

Finally, the reader should note that a range of different AFO and FES devices were used in the included trials and our analysis combined these. While combining data from different types of AFO/FES does not allow a detailed look at the possible different effects of each individual sub-type, assuming the prescription of devices within each trial was provided on the basis of clinical judgement and complies with current guidelines, this allows for a clinically relevant comparison. Furthermore, limited reports of the details of AFO and FES interventions preclude reliable sub-group analyses. The traditional description of AFOs on the basis of the material used (carbon fibre, plastic, metal) or mode of manufacture (customized vs off-the-shelf (54) as with our included trials) should be discontinued. The mechanical properties (stiffness, mass) of an AFO determine its behaviour (73) so it is these that should be measured and reported (73–75). Similarly, differences in outcome between therapist and patient FES set-up have been found (76, 77) so this should also be reported. None of the included trials reported details of FES setup parameters and it remains unclear

which set of parameters would be most useful when comparing across trials; further work is required in this area.

In conclusion, despite very different hypothesized mechanisms-of-action for AFO and FES this RCT, state-of-the-art review, with meta-analysis (39) conservatively indicates that AFOs have positive combined-orthotic effects on walking that are equivalent to FES for foot-drop caused by stroke. Methodological and reporting limitations within the current RCT pool preclude clinical recommendations regarding which type of AFO or FES set-up to use for particular patient groups from being made; as they do in guiding clinicians as to which intervention to prescribe for a specific patient. However, crucially, and for the first time, barriers to achieving such clinical recommendations within research design and reporting have been identified to progress future research. Furthermore long-term, high-quality RCTs are required across CNO diagnoses. These should focus on measuring the mechanisms-of-action, whether there is translation of improved impairment to function and reporting the correct device details; only then will discerning prescription be possible.

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Appendix I. *Unpublished data*

- Salisbury et al. (45) published results were a combination of assisted and unassisted walking data. On request assisted data was provided.
- Kluding et al. (16) published change as opposed to post-intervention data; this was provided on request.
- Kottink et al. (44) only displayed results from their 2007 study in graphical form and did not respond to request for raw data.
- Bethoux et al. (14) published standard error; these were converted to standard deviation (SD) (42).
- Both Bethoux et al. (14) and Kluding et al. (16) provided unpublished time-point data on request.
- Functional exercise capacity was converted from the speed (m/s) for Everaert et al. (15).

2.5.2 Candidate Involvement[6]

The candidate led all key processes, from PROSPERO registration to all methodological decisions, journal choices, manuscript writing and re-writes. The candidate also prepared a poster detailing some of this work that was presented at UKIFESS 2015 in Sheffield (Appendix 3c).

2.5.3 Critical Appraisal

This was the first meta-analysis that used RCT level evidence alone focussed on a specific clinically relevant effect (combined-orthotic). It therefore provided a more precise and robust estimate of effect in the direct comparison between AFO and FES (Grant & Booth, 2009). This along with the use of systematic searching, appraisal and synthesis using recognised good practice guidance (The Cochrane Collaboration, 2011; Liberati et al., 2009) gave confidence in the findings. The potential criticisms potentially levelled at this review article tie in with the limitations of the included RCTs, the decision to only focus on RCT evidence and walking measures and errors in the data extraction process.

"A meta-analysis cannot be better than its included studies allow" (Grant & Booth, 2009, p. 98). This systematic review included five trials, the results of which were reported in seven publications. These spanned a relatively short time span (2007-2015) with five of the seven publications, which resulted from four of the five trials, published within a two-year window (2013-2015). It could therefore be expected that trial authors were acting independent of each other, which might account for some of the common issues such as lack of evaluation measure justification and risks associated with bias that were found (i.e. that learning from each study could not be carried forward to improve the next). Conversely this shows that many authors identified that the need for RCT level comparison was necessary/timely at around the same period of time which, by extension, indicates the timeliness of this review article.

The review highlighted the predominant use of laboratory based measures of capacity (WHO, 2001) to compare the AFO and FES devices with one trial lacking any BFS measures (Bethoux et al., 2015; Bethoux et al., 2014) and another not considering participation

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[6] A summary of the candidate's involvement in each article is presented in Table 1 on page 5

domain/PQ measures (Everaert et al., 2013). Of those that did use measures that spanned the three ICF domains this framework alone was used in their justification of choices. With regards the lack of BFS measures, despite recommendations to include mechanistic measures (Harlaar et al., 2010), this is most likely explained by the fact that the primary aim of the included studies was not to determine the mechanisms-of-action. The lack of mechanistic alongside the lack of "real-world" evaluation measures did serve to further emphasise the second gap in the evidence base identified by the candidate; that both devices lack evaluations that would advance current clinical guidelines.

Despite guidelines about how best to report mechanical properties existing for some time (Ridgewell et al., 2010), none of the selected RCTs reported any of mechanical properties of the AFOs used. As such their mechanical properties are unknown (Condie et al., 2004; Ridgewell et al., 2010) and hence cannot be accurately recreated in the future. A similar criticism could be levelled at the FES studies, in which only one of the selected trials reported set-up parameters. The potential device heterogeneity feeds in to the inability of clinicians to replicate interventions for which evidence is provided. However, it did make combining them a more realistic estimate of the effect seen across clinical services where a range of devices and setups are used. In recognition of this the review proposed how AFOs should be reported in the future; discouraging the sole reporting of either the materials used or mode of manufacture while encouraging reporting of mechanical properties (Bregman et al., 2010; Bregman et al., 2011). It also suggested that, alongside setup parameters, who sets up the FES device should be reported given the marked differences in performance that have been noted by the candidate and research group involved in the HTD480 project when a user sets up their FES device versus a clinician (Heller et al., 2013; Prenton, Kenney, Stapleton, et al., 2014).

There is heterogeneity in clinical features amongst the stroke population (Louw, 2002). Large sample sizes, randomisation, a clear description of the participants according to appreciable subgroups and specific outcome measures address this by increasing the ability to generalise results (Louw, 2002). Although it is acknowledged that in relation to potential UK foot-drop population (approximately 240,000) the number of participants in this review was relatively small (n=815) it is very similar to the previous comparative review (Dunning et al., 2015) and larger than the device specific reviews (Ferreira et al., 2013; Kottink et al.,

2004; Miller et al., 2017; Roche et al., 2009; Tyson & Kent, 2013; Tyson et al., 2013). As evidenced by the risk of bias assessment in Article 5 (page 650 of the article) random sequence generation appears to have been considered by some, but not all, of the included trials resulting in an increased risk of selection bias. The description of participants was generally limited, primarily including side of hemiplegia, chronicity, age and, in some cases, mental capability. Walking speed at trial entry was also focussed upon by three trials (Bethoux et al., 2014; Everaert et al., 2013; Kluding et al., 2013) Kottink et al. (2007) focussed on outdoors walkers, no further description was provided and Salisbury et al. (2013) only mentioned distance walk required (five metres). It cannot be concluded whether these aspects provide sufficient demarcation of the stroke population. The meta-analyses, via the I^2 statistic, revealed that for some measures there was no significant effects of heterogeneity. Where there was heterogeneity this was accommodated for by using a random effects model. Until more good quality trials with adequate reporting of details this review therefore provided the best possible evidence to date.

This review demonstrated that both devices had equal positive combined-orthotic effects on the activity/CQ measures of walking speed (over 10 metres) and functional exercise capacity (6-minute walk test) plus walking participation/PQ (SIS). This has not been comprehensively shown before this article and so is field leading. It is accepted however that the limited range of evaluation measures chosen restricted the conclusions that could be drawn and thus how clinical guidelines could be updated. Nothing conclusive could be said about the mechanisms-of-action as no numerical analysis of BFS measures could be undertaken. This was disappointing, but not completely unsurprising given that was not the primary aim of the included studies.

Stroke is largest CNO population and importantly is not degenerative which might explain the tendency of researchers to focus on this population for participants. Research of the effects of AFO and FES devices was being done in other CNO disorders (Brehm, Harlaar, & Schwartz, 2008; Esnouf, Taylor, Mann, & Barrett, 2010; Mann, Finn, & Taylor, 2008; Paul et al., 2008; Sheffler et al., 2009) but at the time of the review there were no published comparative RCTs and so the generalizability of the systematic review could be questioned. The devices however are foot-drop impairment as opposed to diagnosis specific so the

impact of the results being from stroke participants alone on the generalizability of the conclusions drawn is unknown.

Participants of three of the 5 studies (Kluding et al., 2013; Kottink et al., 2007, 2012; Salisbury, 2013) received concurrent physiotherapy. Therapy is indicated up to a year post-stroke (Teasell et al., 2003) but Kluding et al (2013) and Kottink et al (2007; 2012) recruited participants on average 4.77 and 9.07 years' post-stroke respectively. Therefore, these two studies do not represent standard clinical practice which threatens their external validity and by extension this review.

Prior to commencing the review there was detailed consideration of whether to focus on RCT level evidence or open the study type. The candidate chose to focus on RCT level evidence alone for three reasons:

1. Consideration of the hierarchy of evidence and previous searches of the literature revealing the potential to focus at this level (1a) only (Oxford centre for evidence-based medicine, 2009).
2. Critique of other reviews in the field.
3. Any update in guidelines would give greatest weight to this level of evidence

However it is recognised that the decision to do this excluded device specific evaluation studies (Medical Research Council, 2006) which, although individually at higher risk of bias and likely underpowered, might have provided a more detailed insight into effects.

The included RCTs were primarily conducted in North America where the healthcare system differs significantly from the UK system. This could be construed to undermine the applicability of the review results to the UK. However, the purpose of this review was to compare efficacy and explore possible mechanisms-of-action of the foot-drop AT interventional devices based on RCT level evidence. Therefore, any variation in any other interventions participants received should not influence our findings as between group heterogeneity was not found.

Only measures that evaluated the combined-orthotic effects on walking were considered by the review. Given that both devices have been shown to positively influence balance (Dunning et al., 2015; Tyson & Kent, 2013) the decision to disregard postural sway and/or

functional balance measures might have been remiss. This was justified due the desire to keep a clear focus on walking effects. The combined-orthotic effect was chosen because of its clinical relevance given this is how most AFOs and indeed FES are prescribed (Bosch et al., 2014) and yet the guidelines lack advice on which of these to use for which patient to target combined-orthotic effects.

It is recognised by the candidate that there was an error in data extraction by reporting that one trial recruited new AFO users when in fact there was a combination of new and current users (Bethoux et al., 2015; Bethoux et al., 2014). Whilst this does not directly impact the results and conclusions of the review it is misleading to readers. This was an oversight by the candidate.

Despite some limitations this review provided the first gold standard comparison of the two devices used in a clinically applicable way (combined-orthotic). Quality was assured through the use of recognised guidelines (Higgins et al., 2011; Liberati et al., 2009) and therefore there can be confidence in the findings that AFOs produce equal improvements in some activity and participation walking measures. It was also able to highlight the limitations in the current RCT evidence base; most notably the lack of device details and the inability to further the understanding of the mechanism-of-action for either device. This article therefore has the potential to impact future clinical guidelines by providing direction for future comparative RCTs.

As previously discussed in Chapter 1, there is a view that FES use may encourage the return of voluntary control over foot and ankle musculature (Rushton, 2003); conversely some authors propose that the use of a passive AFO may lead to deterioration in volitional Tib Ant muscle activity (Hesse et al., 1999; Lairamore et al., 2011; Romkes et al., 2006). This review raised a further question for the candidate about whether these claims were substantiated.

2.6 Article 6

Prenton, S., Hollands, K., Kenney, L.P.J. Onmanee, P. (2018) Which to use for therapeutic improvement of foot-drop: functional electrical stimulation or ankle foot orthoses? A meta-analysis that gives clear direction for future research. *Journal of Rehabilitation Medicine*, *50*, 129-139. doi: 10.2340/16501977-2289.

As with Article 5 this article sought to fill the second gap in the evidence base identified by the candidate; that both devices lack foot-drop specific and user-important evaluation measures. It also sought to fill the third identified gap in the evidence base of a lack of clinical guidance about which device was better overall.

Based on this further question regarding the potential, conflicting, mechanisms-of-action on volitional muscle activation this review (https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015025967) compared the effects of the two devices whilst they were not being worn following a period use.

This review identified primary measures of interest based on those that could evaluate the hypothesised claims around the therapeutic effects on volitional muscle activity and those that were foot-drop specific and known to be used in the field. These were electromyography (EMG) to evaluate the effect on volitional muscle activity and ankle kinematics at IC to evaluate the effect on the transition from swing to stance. As the candidate knew they were the first to use foot clearance as an evaluation measure (ShefStim® study, Article 3), although (Kim et al., 2004) had previously reported on *toe* clearance, this was not identified.

Actual walking performance was the functional primary measure of interest to compare the effects in the users' own environment. As the candidate was already aware that device usage data was not routinely collected any form of activity monitoring was identified to capture actual walking performance. All walking measures, including those of primary interest, were extracted and categorised as BFS or functional.

Similar procedures to Article 5 were used to source, screen, data extract and then quality assess appropriate trials. This resulted in seven RCTs, from eight publications, with 464 participants. Only walking speed over 10 metres was collected frequently enough by the included RCTs to be meta-analysed. Sub-group analysis of overall effects on the walking speed over 10 metres for stroke and following four-six weeks' use was also possible. Meta-analysis indicated equal, positive, improvement for both devices both overall and after only four-six weeks use. This was also true for the sub-group analysis based on the six stroke

RCTs. None of the three identified primary measures of interest were used consistently enough to meta-analyse but were used sufficiently to allow a narrative summary. This narrative summary found equal changes for both devices with regards kinematics and the EMG findings from a single trial (Kottink et al., 2008) found therapeutic differences between FES and AFO use. The way in which activity monitoring was used proved to be problematic; two trials collected this data, but one did so during the intervention period which was more likely (but not explicitly defined) to indicate activity whilst the device was being worn rather than a therapeutic effect (when the device was not being worn). This meant that the ability to interpret the results was very limited.

This review was the first to statistically show that AFO use has a positive therapeutic effect on walking speed. This is a novel contribution to the field. It also demonstrated that the size of the improvement is the same as the observed improvement following FES use for non-progressive CNO disorders as well as for stroke alone and after four-six weeks use. Due to the measures used to comparatively evaluate the two devices the included RCTs were not able to show how these improvements were achieved or whether this translated into actual walking performance, as the primary measures of interest were not used sufficiently. As such it gave a very clear direction for future comparative RCTs, thereby extending the discipline and adding to the theoretical base.

REVIEW ARTICLE

FUNCTIONAL ELECTRICAL STIMULATION AND ANKLE FOOT ORTHOSES PROVIDE EQUIVALENT THERAPEUTIC EFFECTS ON FOOT DROP: A META-ANALYSIS PROVIDING DIRECTION FOR FUTURE RESEARCH*

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Objective: To compare the randomized controlled trial evidence for therapeutic effects on walking of functional electrical stimulation and ankle foot orthoses for foot drop caused by central nervous system conditions.
Data sources: MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, REHABDATA, PEDro, NIHR Centre for Reviews and Dissemination, Scopus and clinicaltrials.gov.
Study selection: One reviewer screened titles/abstracts. Two independent reviewers then screened the full articles.
Data extraction: One reviewer extracted data, another screened for accuracy. Risk of bias was assessed by 2 independent reviewers using the Cochrane Risk of Bias Tool.
Data synthesis: Eight papers were eligible; 7 involving participants with stroke and 1 involving participants with cerebral palsy. Two papes reporting different measures from the same trial were grouped, resulting in 7 synthesized randomized controlled trials (*n* = 464). Meta-analysis of walking speed at final assessment (*p* = 0.46), for stroke participants (*p* = 0.54) and after 4–6 weeks' use (*p* = 0.49) showed equal improvement for both devices.
Conclusion: Functional electrical stimulation and ankle foot orthoses have an equally positive therapeutic effect on walking speed in non-progressive central nervous system diagnoses. The current randomized controlled trial evidence base does not show whether this improvement translates into the user's own environment or reveal the mechanisms that achieve that change. Future studies should focus on measuring activity, muscle activity and gait kinematics. They should also report specific device details, capture sustained therapeutic effects and involve a variety of central nervous system diagnoses.

Key words: electric stimulation therapy; foot orthoses; walking; foot drop; central nervous system; therapeutic effects; systematic review; meta-analysis.

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Foot drop is a common motor impairment associated with many central nervous system (CNS) conditions (1). An estimated 20–30% of stroke survivors experience foot drop; thus approximately 240,000–360,000 people might be living with it in the UK alone (2). Foot drop is an abnormal activation of the musculature of the lower limb, resulting in inefficient foot clearance during swing (3) and reduced stability in stance (4). These impairments negatively impact the function of walking, which may restrict participation in many aspects of life.

There are 2 demonstrably effective orthotic interventions for foot drop: ankle-foot orthoses (AFO) (5–9) and functional electrical stimulation (FES) devices (10). AFOs address foot drop by changing the effective stiffness and neutral point of the ankle joint (11). FES devices stimulate lower motor neurones, in this case the common peroneal nerve, to assist muscle contraction over appropriate phases in the gait cycle (12).

Recent randomized controlled trials (RCT) have sought to compare the direct effects of using each device on various walking behaviours (13, 14). These comparisons have been made both with and without the devices being worn, at the point of provision and at various time-points after a period of use (15). Clinically the devices are commonly prescribed as orthotics for long-term use (16); the difference between walking behaviours without the device at baseline and walking with the device being worn after a period of use is called the combined-orthotic effects (14). RCTs (14, 17–19) reporting these effects have found that both devices achieve the same improvement at various time-points up 12 months (18). The combined results of individual RCTs, demonstrating equal combined-orthotic effects of AFO and FES, have also been confirmed in a recent meta-analysis (15). However, given the clinical importance of attempting to achieve therapeutic benefits (20, 21) (i.e. improvement in measured walking behaviours without a device being worn relative to baseline, called the therapeutic effects (13)), further work is required to establish whether there are differences in the therapeutic effects of the 2 devices.

The first study of FES reported that some users, following a period of use, experienced improvement even after the device was removed (22). More recently, a number of studies have suggested a range of possible peripheral and central neural mechanisms to explain these observations (23–26). In contrast, an AFO is a purely mechanical device and there appears to be an assumption that the effects of AFO on walking are seen only when the device is worn (27). In addition, some studies suggest that AFO use may lead to muscle weakening (4, 28–31), whereas FES has been suggested to improve volitional muscle activation (25).

These studies appear to predict differential therapeutic effects between the 2 devices, which makes the findings (18) of an equivalent combined-orthotic effect of the devices somewhat surprising; as one might expect improvements in therapeutic effects to be positively correlated with combined-orthotic effects. Therefore a review of therapeutic effects is needed to help inform guidelines for clinical use.

While a number of AFO- and FES-specific reviews have been published, only 2 of these have attempted to draw direct comparisons (16, 32). RCT-based direct comparisons are particularly important as they summarize current thinking about mechanisms-of-effect and how these impact on function. This information can then be used to advance clinical guidelines, which is timely in the face of increasing market choice for both devices. However, neither of the existing reviews (16, 32) could be considered a gold standard meta-analysis, due to methodological issues, and hence there remains a need to pool RCT-level evidence to answer the following specific questions:

1. Are the therapeutic effects on the function of walking for CNS foot drop different for FES and AFO?

    i) Does diagnosis impact these therapeutic effects?

    ii) Does time of use impact these therapeutic effects?

2. What are the mechanisms of therapeutic effects of AFO and FES on walking for CNS foot drop?

By answering these questions this review aims to guide clinical decision-making and the direction of future research.

METHODS

In line with best practice the full review protocol was developed a priori and registered with PROSPERO (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015025967).

Identification and selection of trials

Eight electronic databases were searched: MEDLINE (EBSCO), CINAHL (EBSCO), Cochrane Central Register of Controlled Trials (CENTRAL), REHABDATA, PEDro, NIHR Centre for Reviews and Dissemination, Scopus and clinicaltrials.gov.

Search terms included "walking","electric* stimulat*", equinovarus and Nervous system disease* ; The full search strategy is available from the lead author (SP).

One reviewer (SP) assessed titles and abstracts against the inclusion criteria (Table I) and those deemed potentially relevant were considered by 2 independent reviewers (SP and PO). Any disagreements or ambiguity were resolved through discussion with a third reviewer (LK).

Data extraction and analysis

A pre-designed pro forma was used to extract data about the characteristics of the included trials, participants and intervention details. Trial authors were contacted by SP if data were not readily available (Appendix I).

The Cochrane Risk of Bias Assessment Tool (33) was used independently by the 2 reviewers (SP and PO), with a third reviewer (LK) available if necessary. In order not to disadvantage authors who did not respond to information requests, risk of bias was based only on published work. It is not possible to blind participants to which device they are given during the trial; therefore the performance bias criterion was removed. *A post hoc* sensitivity analysis was undertaken if 3 or more trials showed a high risk of bias, in which the meta-analysis was recalculated with those trials temporarily excluded to check whether they had influenced the results.

A range of outcome measures could evidence therapeutic effects; therefore any measure that captured walking behaviours when a device was not being worn following a period of use was extracted (Table I). In order to compare the therapeutic effects on the function of walking (question 1), measures that sat within the Activity or Participation domains of the World Health Organization's (WHO) International Classification of Functioning, Disability and Health (ICF) model (34) were extracted. Activity monitoring was identified as the primary functional outcome measure (question 1) because, unlike more controlled functional walking measures, it captures actual performance (35, 36) as opposed to potential capacity (37).

Although foot drop manifests itself in the same way for all CNS disorders, the possible impact of diagnosis on therapeutic effects (question 1i) was explored by performing, where possible, sub-group analysis on individual CNS pathologies. This aimed to provide specific clinical guidance regarding which patients may benefit most from which device.

The time course of therapeutic effects (question 1ii) was explored by pooling data from trials that compared the devices

Table I. Inclusion criteria

Design
Randomized controlled trials
Participants
Participants with foot drop caused by a CNS disorder
Intervention
Common peroneal nerve FES to address the specific impairment of foot drop, with or without other areas of stimulation
Trials where common peroneal stimulation is used during walking (overground or treadmill) as part of the intervention
Trials studying the therapeutic effects of foot drop FES
Trials where foot drop FES and another intervention are used in combination, but foot drop FES is measured independently
Comparator
AFO (the term therapy was also included as might involve AFO)
Outcomes
Measures of walking

CNS: central nervous system; FES: functional electrical stimulation; AFO: ankle foot orthosis.

at similar time-points. Some authors suggest that a period of use of 3 months is required to observe any therapeutic effects of either device (24). Sub-group meta-analysis was therefore sought at 12–13 weeks, as an approximation of 3 months.

In order to evidence potential mechanisms-of-effect (question 2), measures reflecting the Body Functions and Structures (BFS) domain are required (38). Given the assumption that FES, but not AFO, has a therapeutic effect on volitional muscle activity, electromyography (EMG) was chosen as a primary BFS measure of interest. As another key measure of gait (quality) is its kinematics (39), which may be influenced by muscle activations in complex ways, we chose to complement the EMG analysis with gait kinematics as a second primary BFS measure. Any other walking measure was deemed secondary and categorized as a functional measure of walking or BFS measures by SP, using appropriate literature (34, 37, 40, 41). All primary and secondary end-point data were extracted.

Where possible, mean differences (MD) with 95% confidence intervals (95% CIs) were used, where outcome measurements were comparable. If data collection methods varied then standardized mean differences (SMD) with 95% CIs were used. RevMan 5.3® software was used.

Visual inspection of forest plot, χ^2 test and I^2 statistic were used to examine heterogeneity. Low heterogeneity (< 50%) resulted in a fixed-effects and high (> 50%) in a random-effects model being used.

Where meta-analysis was not possible a narrative summary of the overall effects was presented.

Fig. 1. Flowchart of trial selection. RCT: randomized controlled trial; FES: functional electrical stimulation; AFO: ankle foot orthosis.

RESULTS

A total of 1,725 possible citations were found as a result of the searches. Following title, abstract and full-paper screening, a total of 8 papers met the inclusion criteria. Two of these papers (42, 43) reported results from the same trial, and so were grouped and referred to by the first publication date (42), resulting in 7 RCTs, which included a total of 464 participants (Fig. 1).

Characteristics of included trials

Six (14) of the 7 trials had a parallel-group RCT design. The remaining trial had a cross-over design with 2 AFO arms. Only 1 AFO arm was used, to avoid any issues associated with multiplicity (44); arm 2 (AFO-FES) was chosen due to its larger size and comparability to the FES arm (arm 1, FES-AFO) and final assessment data was deemed to be at 6 weeks, pre-cross-over (45), given the carry-over observed by the trial authors (46). Two trials collected data from multiple sites (14, 17), with the other 5 based at a single site (Table II).

Participant details

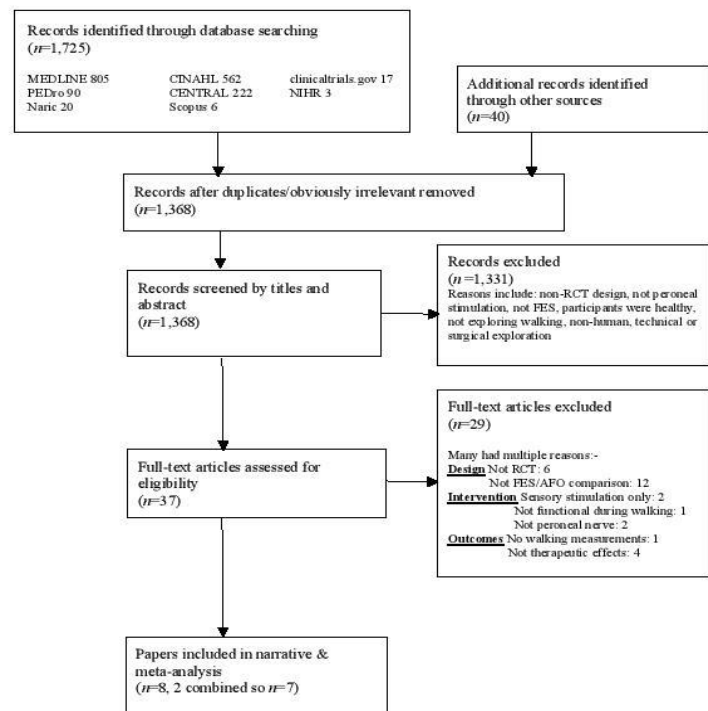Mean age ranged from 8 (47) to 61.58 (17) years, all participants had unilateral foot drop with an even distribution of right and left foot drop (182 right, 50.3%, and 180 left, 49.7%). Where reported, more men than women were recruited (262 men, 62%, and 159 women, 38%).

Although Van der Linden et al. (47) included participants with cerebral palsy (CP) (n = 14), the majority of participants (n = 450) had had a stroke (Table II). This allowed for sub-group analysis of this pathology (question 1i). There were no trials that included any progressive CNS diagnoses. Medication was considered by 2 trials (Table II) (14, 17), with 1 screening based on no expected change in medication during the intervention period (14); compliance with medication was not reported by this trial.

Device details

Three trials (14, 17, 42) used "customized" AFOs that were either made or modified for the participant, by an appropriate clinician, on inclusion to the trial (Table II). Participants in 2 of the other trials used a variety of different types of AFO (29, 47) and participants in another trial used off-the-shelf orthoses (48), which was appropriate for the acute/sub-acute population they investigated (49). Four trials recruited participants who did not already use an AFO (12, 14, 42, 48), while the other trials recruited current AFO users (17, 29,

Table II. Characteristics of included trials, participant and intervention details

Author/reference	Trial design	Subjects, n Diagnosis (R):(L)	Male:Female	Age (years)	Time since diagnosis	Medication	AFO	FES (all new AFO users)	Current or new AFO users	Current or AFO mechanical properties reported	FES set-up parameters reported	Prescribed usage: home vs supervised
Everaert et al. (2013)[a] [14]	3-arm crossover Multiple sites	78 (43 FES: 35 AFO) CVA not specified	FES = 32:6[b] AFO = 19:12[b]	FES = 57.1 (12.9)[b] AFO = 55.6 (11.9)[b]	FES = 6.4 months (3.8)[b] AFO = 6.9 months (3.2)[b]	No expected change (6mos)[b]	Customized	Surface Walkaide	New	No	No	Home AD
Kluding et al. (2013)[c] [17]	2-arm parallel Multiple sites	197 (99 FES: 98 AFO) CVA 93:104	FES = 51:48 AFO = 67:31	FES = 60.71 (12.24) AFO = 61.58 (10.98)	FES = 4.77 years (5.29) AFO = 4.34 years (4.1)	No botulinum toxin 6 weeks prior or planned for 2 weeks	Customized plus TENS for 2 weeks[g]	Surface NESS L300	Current	No	No	Home FES: Bioness clinical protocol followed: 15 min–AD over 3 weeks
Kottink et al. (2008)[a] [29]	2 arm parallel Single site	29 (14 FES: 15 AFO) CVA 13:16	FES = 10:04 AFO = 10:05	FES = 55.2 (11.36) AFO = 52.87 (9.87)	FES = 9.07 years (9.29) AFO = 5.67 years (4.64)	Not mentioned	Combination[f]	Implanted 2-channel implant	Current	No	No	Home FES: Gradual increase over 2 weeks, then AD
Morone et al. (2012) [12]	2-arm parallel Single site	20 (10 FES: 10 AFO)	Not specified	FES = 53.3 (±14.6) AFO = 61.2 (±16.2)	FES = 27 days (±27) AFO = 13 (±7)	Not mentioned	Not specified	Surface Walkaide	New	No	No	Supervised Both gps: This was the therapy = 20×40 min sessions, 5×week
Salisbury et al. (2013)[d] [48]	2-arm parallel Single site	16 (9 FES: 7 AFO) CVA 10:06	FES = 03:06 AFO = 03:04	FES = 55.8 (11.3) AFO = 52.6 (17.2)	FES = 51.7 days (34.6)	Not mentioned	Off the shelf	Surface ODFS	New	No	No	Supervised Both gps: Part of physiotherapy 20 min, 5×week with supervised/independent walking as appropriate
Sheffler et al. (2013) [42]	2-arm parallel Single site	110 (54 FES: 56 AFO) CVA 62:48	FES = 30:24 AFO = 37:19	FES = 52.8 (12.2) AFO = 53.2 (10.1)	FES = 44.7 months (97.5) AFO = 44.9 months (79.2)	Not mentioned	Customized	Surface ODFS	New	No	No	Supervised Both gps: This was the therapy that was received for 12/52
Van der Linden et al. (2008) [47]	2-arm parallel Single site	14 (7 FES; 7 AFO) CP 4:6	Not specified	FES = 8 (3.32) AFO = 8.14 (2.61)	Not specified	Not mentioned	Combination	Surface ODFS III plus TENS for 2 weeks	Current	No	Frequency: 40 Hz Pulse width: 3–350 Current: 20–70 mA Waveform: asymmetric biphasic	Home FES: AD apart from when doing sporting activities

[a]Participant characteristics collected after the intervention period; [b]Participant characteristics collected at later time-point than is included in this review (12 weeks); [c]ITT completed; [d]Participant characteristics collected before the intervention period; [e]=no dropouts; [f]both groups continued with physical therapy alongside intervention; [g]compliance with medication not reported. FES: functional electrical stimulation; AFO: ankle foot orthosis; CVA: cerebrovascular accident/stroke; CP: cerebral palsy; AD: all day; ODFS: Odstock Drop Foot System; NESS L300: Bioness model; Customized: custom-made/modified AFO; Combination: Different AFOs used by different participants; off the shelf: prefabricated/unmodified AFO; TENS: transcutaneous electrical nerve stimulation with no motor response; gps: groups.

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Table III. Risk of bias

Author/reference	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Everaert et al. (2013) (14)	Unclear	Unclear	Unclear	High	Low	Low
Kluding et al. (2013) (17)	Low	Low	Unclear	Low	Low	Unclear
Kottink et al. (2008) (29)	High	Unclear	High	Unclear	High	Unclear
Morone et al. (2012) (12)	High	High	Unclear	Low	Low	Low
Salisbury et al. (2013) (48)	Unclear	Low	High	Unclear	Low	Low
Sheffler et al. (2013) (42)	High	High	Unclear	Low	Low	Unclear
Van der Linden (2008) (47)	Low	Unclear	Unclear	Unclear	Low	Unclear

47). None of the trials reported any of the mechanical properties of the AFO (Table II).

All trials recruited new users of FES. One trial used an implantable FES system (29), while the others opted for surface systems from 3 different manufacturers. Set-up parameters were reported by only one trial (47) (Table II).

Four trials allowed use within the home/community setting (14, 17, 29, 47), whilst the remaining 3 trials provided devices only under supervision (12, 42, 48) (Table II).

Risk of bias

Table III shows the results of the Cochrane Risk of Bias Assessment. Kluding et al. (17) and Van der Linden et al. (47) were deemed to have no areas of high risk with Kottink et al. (29) showing the most high risk areas (three). Selection bias, as determined by the ability to generate an appropriately random sequence (33), was the area of risk least well addressed by the included trials (Table III). Based on these findings the trials were deemed to be at a moderate or lower risk of bias overall.

Outcome measures

All 7 trials used outcome measures that could be categorized as functional and BFS (Table IV). Four of the trials utilized measures that we had deemed to be of primary interest (17, 29, 42, 47). The most commonly used secondary measure was walking speed, which was primarily captured over

10 m. This was captured by 6 trials (12, 14, 17, 29, 42, 48) (*n*=450).

Therapeutic effects – meta-analysis of gait speed

Salisbury et al. (48) reported data that reflected orthotic and therapeutic effects in combination. Despite repeated communication no specific therapeutic data was shared and so their results could not be included in meta-analyses. Meta-analysis of final-assessment walking speed data (Fig. 2a) of the other 6 trials (*n*=437) showed that both interventions had equivalent positive therapeutic effects (MD=0.02 [–0.03, 0.06]: I² 0%; *p*=0.46). A sensitivity analysis was undertaken excluding the 3 trials (12, 29, 42) that showed high risk of bias (Table III) with regards random sequence generation (selec-
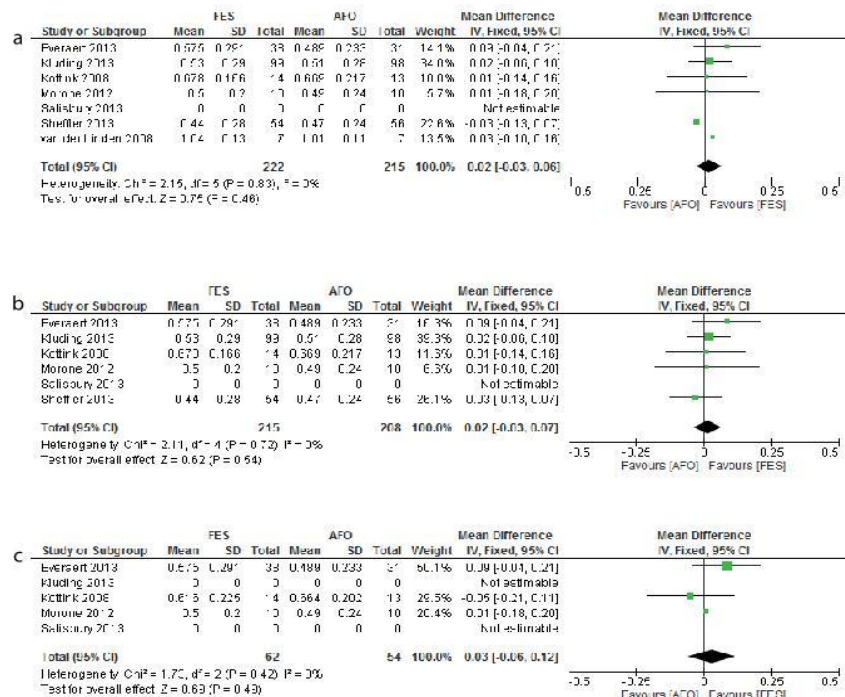

Fig. 2. (a) Final assessment of 10-m walking speed (m/s). (b) Sub-group analysis of 10-m walking speed for stroke (m/s). (c) Sub-group analysis of 10-m walking speed at 4–6 weeks (m/s).

Table IV. Walking outcome measures and therapeutic effects

Author/reference	Walking outcome measures used & ICF level	Outcome collection points	Therapeutic effects reported at final outcome collection point: Significant $p < 0.05$
Everaert et al. (2013) (14)	BFS: PCI over 4-min test[b] Functional: 4-min walking test (speed)[b] 10MWT Modified RMI	0, 3, 6 weeks	Insignificant ↑ in all measures for both groups
Kluding et al. (2013)[c] (17)	BFS: LE Fugl Meyer Functional: 10MWT (self and fast)[b] TUG 6-min walk test (distance) SIS mobility sub-scale Activity monitoring (Stepwatch®) for 7 consecutive days in weeks 6 and 24	0, 6, 12, 30 weeks	LE Fugl Meyer: both groups showed ↑, AFO group was significant (insignificant between-group difference) Self and fast 10MWT: both groups showed significant ↑ (insignificant between-group difference) TUG: both groups showed ↑, FES group was significant (insignificant between-group difference) 6-min walk test (distance): both groups showed significant improvement (insignificant between-group difference) SIS mobility sub-scale: both groups showed significant ↑ (insignificant between-group difference) Activity Monitoring: both groups showed improvement, significance was not reported
Kottink et al. (2008)[c] (29)	BFS: RMSMax TA[b], PL, GS, SL with knee flexed and extended RMSswing TA Functional: 10MWT[b]	0, 4, 8, 12, 26 weeks[e]	RMSMax TA: FES ↑ with knee flexed and extended. AFO did not have an effect. Significant between group difference with knee extended RMSMax PL and SL: Neither group showed an effect RMSMax GS: FES ↑ with knee flexed and extended, AFO caused an ↓ in flexion and did not have an effect in extension. Significant between group differences with knee flexed and extended RMSswing TA: remained constant for FES, significant ↓ for AFO 10MWT: neither group showed an effect
Morone et al. (2012) (12)	BFS MRC muscle strength Ashworth scale Functional: 10MWT[b] RMI FAC	0, approximately 1 month	MRC muscle strength: both groups showed significant ↑ Ashworth scale: both groups showed ↑, but not significant 10MWT: both groups showed significant ↑. FES group showed significantly more ↑ than AFO group. RMI: both groups showed significant ↑ FAC: both groups showed significant ↑. FES group showed significantly more ↑ than AFO group.
Salisbury et al. (2013) (48)	BFS: Cadence (10MWT) Functional: 10MWT FAC SIS mobility sub-scale	0, 6, 12 weeks	[a]Cadence: both groups showed insignificant ↑ [a]10MWT: both groups showed insignificant ↑ [a]FAC: both groups showed insignificant ↑ [a]SIS mobility sub-scale: both groups showed insignificant ↑
Sheffler et al. (2013)[c] (42)	BFS: LE Fugl Meyer[b] Spatiotemporal: cadence; stride length; double support time Proximal kinematic: peak hip flex in swing[b]; peak knee flex in swing[b]; peak hip ext in stance Distal kinematic: DF at IC; peak ankle DF in swing; peak ankle abd in swing; peak ankle ext rot in swing Kinetic: peak AP GRF; peak hip power in pre-swing; peak ankle power at push-off Functional: Walking speed mEFAP Activity Monitoring (ActivPAL®) for 3 consecutive days	0, 12, 24[d], 36 weeks[d]	LE Fugl Meyer: neither group showed ↑ Spatiotemporal: Cadence and stride length: both groups showed significant ↑. Double support time: both group showed insignificant ↑ Kinematic: peak hip flex in swing, peak knee flex in swing, DF at IC, peak ankle abd in swing, peak ankle ext rot in swing showed insignificant changes. Peak ankle DF in swing: both groups showed significant ↓ at 12 and 24 weeks but not 36 weeks. Peak hip ext in stance: not reported. Kinetic: AP GRF, peak hip power in pre-swing and peak ankle power at push-off had both groups showing significant ↑ Walking speed: both groups showed significant ↑ mEFAP: both groups showed significant ↑ Activity Monitoring: no change in either group
Van der Linden et al. (2008)[c] (47)	BFS: Kinematics: knee flex at IC; DF swing, foot floor angle Gilette Gait Index pROM: ankle DF with knee flex/ext Functional: Walking speed	0, 2, 10 weeks	Knee flex at IC: both groups showed insignificant ↑ DF swing: FES showed insignificant ↑, AFO showed insignificant ↓ Gilette gait Index: both groups showed insignificant effects pROM: both groups showed insignificant effects Walking speed: FES showed insignificant ↑, AFO remained constant.

[a]Published results were therapeutic and combined-orthotic effects data; [b]identified as primary outcome measure by authors; [c]used a primary outcome measure of interest, as identified by review authors; [d]post 12 weeks use at 12 and 24 weeks, respectively; [e]RMSswing only collected at weeks 0 and 26. ↑ = increase; ↓ = decrease.

abd: abduction; BFS: Body Functions & Structures; ICF: International Classification of Functioning Disability and Health; min: minute; LE: lower extremity; mEFAP: modified Emory Functional Ambulation Profile; TUG: Timed Up and Go; SIS: Stroke Impact Scale; 10MWT: 10-m walk test; PCI: Physiological Cost Index; RMI: Rivermead Mobility Index; FAC: Functional Ambulation Categories; MRC: Medical Research Council; FAC: Functional Ambulation categories; TA: tibialis anterior; GS: gastrocnemius; PL: peroneus longus; SL: soleus; RMSMax: root mean square during static maximum voluntary contraction; RMSswing: root mean square of activity during swing; DF: dorsiflexion; IC: initial contact; pROM: passive range of movement; AP: anterior-posterior; GRF: ground reaction force; flex: flexion; ext: extension; FES: functional electrical stimulation; AFO: ankle-foot orthosis.

tion bias). This showed no significant impact. Positive between-group comparability was also true for the stroke-specific analysis (question 1i) (*n* = 423) (MD = 0.02 [−0.03, 0.07]: I² 0%; *p* = 0.54) (Fig. 2b).

Sub-group analysis of walking speed was not possible at 12–13 weeks (question 1ii), as 1 of the 4 trials (17, 29, 43, 48) that collected at this time-point, Kluding et al. (17), were contacted by the lead author but could not access their unpublished AFO data and, as previously stated, Salisbury's (48) data was not in an accessible format. Five trials (12, 14, 17, 29, 48) collected walking speed data at 4–6 weeks (*n* = 116); meta-analysis of 3 of those trials (12, 14, 29) at this time-point showed a positive therapeutic effect with between-group comparability (MD = 0.03 [−0.06, 0.12]: I² 0%; *p* = 0.49) (Fig. 2c). Kluding et al. (17) and Salisbury (48) could not be included in the analysis due the aforementioned lack of access to data.

Therapeutic effects — narrative summary for activity (steps), EMG, Kinematics and Fugl-Meyer

Two trials monitored activity levels by collecting the mean number of steps taken per day, the primary functional measure identified to evidence therapeutic effects on walking (question 1) (17, 42). Kluding et al. (17) found equal improvement over the period of use (AFO group 1,891 steps/day at week 6 to 2,069 steps/day at week 30; FES group 2,092 steps/day at week 6 to 2,369 steps/day at week 30), whereas Sheffler et al. (42) found an equal lack of improvement (3,270 ± 2,947 steps/day at baseline to 4,038 ± 2,848 steps/day at 24 weeks post device use for AFO vs 3,223 ± 3,134 to 3,738 ± 3,211 steps/day for FES). These could not be meta-analysed due to the lack of data spread reported and because activity was monitored during the intervention period by Kluding et al. (17). Given that it was therefore not clear whether activity monitoring was performed with or without the devices being worn, the ability to interpret the outcome of activity monitoring is very limited.

With regards the mechanisms-of-effect (question 2), only 1 trial collected EMG data (29) (Table IV). This trial calculated the root mean square during static maximum voluntary contraction (RMSmax) of a filtered EMG signal and found that FES enhanced volitional activity of the tibialis anterior (TA), whereas AFO did not. This between-group difference was significant when the knee was extended (*p* = 0.006), after 26 weeks' use. The same was true for the gastrocnemius (GS) when the knee was in flexion (*p* = 0.002) and extension (*p* = 0.035), after 26 weeks' use. The RMS of TA during swing (RMSswing) was found to significantly decrease for the AFO group (*p* = 0.036) with no change for the FES group, after 26 weeks use.

Two trials captured kinematic data (43, 47), but each collected different parameters (Table IV). Sheffler et al. (43) found a comparable lack of effect on most measures, but an equal decrease in peak DF during swing after the 12-week device use period (*p* = 0.002). This equal decrease in peak dorisflexion (DF) was again found 12 weeks after participants had finished using either device (*p* = 0.0001). When measured for the final time 24 weeks after participants had finished using their device the decrease in peak DF was no longer statistically significant, for either device (*p* = 0.058). By contrast, van der Linden et al. (47) found equal, but insignificant, improvement in all measures.

With regards to secondary measures, the lower extremity (LE) Fugl-Meyer test was a BFS measurement reported by 2 trials (17, 42). There were differences in their findings, with Kluding et al. (17) reporting improvement in both groups that, despite only the AFO group showing within-group statistically significant improvement (*p* < 0.05), was statistically comparable (*p* = 0.178). Sheffler et al. (42) found an equal between-group lack of improvement (*p* = 0.321) (Table IV).

Across other measures used by single trials there was a mixture of therapeutic effects results reported across and/or within trials (Table IV).

DISCUSSION

This review shows, for the first time, that AFOs produce an equally positive therapeutic effect on walking speed to that of FES. These improvements are observed for stroke alone and are seen after 4–6 weeks of use. These findings are based on meta-analysis of RCT-level evidence (33) and those RCTs were deemed to be of moderate (or less) risk of bias (33), meaning that there can be confidence in these findings. Equality of therapeutic effect on walking speed has not been demonstrated previously, as the focus of previous reviews (16, 32, 45, 50) and primary studies (51, 52) has been on the therapeutic effects of FES alone. What the RCT evidence does not answer is whether this improvement translates into activity within the person's own environment.

It is essential to gain a better understanding of whether therapeutic effects on walking speed translate into activity in a home setting, and the mechanisms by which therapeutic effects are achieved, in order to better inform clinical guidelines about which device to use for which patients. However, the included trials do not provide the measures needed to identify the mechanisms by which the devices achieve speed increases (question 2). Narratively, there is a suggestion that FES, but not AFOs, lead to improvement in

voluntary muscle activity (29), although both produce equal effects on kinematic gait pattern (42, 47).

One possible explanation is that remedying foot drop using either device allows increased time spent walking, thereby facilitating task-specific repetitive practice; which is widely accepted as leading to therapeutic improvement (21). However, from the activity monitoring results of the included RCTs it is unclear whether this occurs (17, 43), with non-RCT studies also finding variable results (53–55).

An alternative explanation for equivalent effects on walking speed may lie in how the increased walking speed is achieved; i.e. via restoration of motor function or compensation (56). True motor recovery is defined as the reversal of an impairment such that it results in the restitution of the functions governed by it (20). Compensation is a restoration of function achieved through adaptation or substitution of remaining motor elements (20). Being able to distinguish between recovery and compensation facilitates clinical decision-making and potentially increases intervention efficiency (21). Crucially, recognizing the distinction relies on an understanding of the mechanisms-of-effects.

The mechanisms-of-effects ascribed to FES are based on the fact that it is seen as an active orthosis, whereby volitional muscle activity is combined with lower motor neurone stimulation. This leads to a number of possible neuromuscular plastic mechanisms, including: repeated muscle contractions leading to increased oxidative capacity; increased number of micro-capillaries and change in fibre type at a muscular level; convergence of orthodromic/antidromic impulses at the anterior horn leading to strengthening of synapses at a spinal level, as well as cortical changes (23–25). Structural cortical changes result from increased cortical excitability (26) are thought to strengthen the residual descending connections from motor-related areas of the cortex (24). In the case of therapeutic effects this culminates in increased volitional muscle activity of the weak dorsiflexors/evertors of the ankle, which is thought to positively influence other biomechanical features and therefore the restitution of associated functions.

In contrast, FES literature has asserted that AFOs, as passive devices, mask the abnormal muscle activation associated with foot drop impairment and so, whilst range of movement is maintained, neuromuscular plasticity mechanisms result in a loss of volitional activity in those muscle groups over time (17, 29). This would mean that, in the absence of the AFO, other muscle groups will have to compensate for this deficit.

In order to provide evidence for the hypothesis of differential changes in volitional muscle activation between FES and AFOs, both EMG and kinematic data of walking are needed. Only 1 trial included in this review provided EMG outcome measures (29), finding that FES use was associated with an increase in voluntary RMSmax for TA and GS, whereas AFO use was not. Similarly, with FES use voluntary activation of TA during swing was maintained relative to baseline, whereas following a period of AFO use TA activation declined during swing. This suggests that the ability to voluntarily activate TA and GS muscles may be maintained, or even improved by a period of FES use compared with AFO. Previous non-RCT studies and systematic reviews support this suggestion, as they have shown increased TA muscle activity, force and size with FES use (57–60) with the opposite occurring in AFO (4, 28, 30, 31). Further trials examining EMG following FES and AFO use are therefore needed if this potential mechanism-of-effect is to be more fully understood.

Despite the potential for differing effects on volitional muscle activity, the RCT-evidence suggests that both devices have equal therapeutic effects on kinematic measures (43, 47); whether the effects are positive, negligible or negative is unclear. Non-RCT studies examining gait kinematics are limited with regards to FES (39, 61) and AFO (62). Further kinematic comparative study is therefore required to identify whether improvement is compensatory or restorative and to correlate EMG data with functionally meaningful improvements.

These trials should consider how they both measure and define therapeutic effects. For example, in the included trials (17, 43) it was unclear whether activity (number of steps) was measured during walking while wearing the device, during walking when the device was not being worn, or a combination of both. Furthermore, the current definition of improvement in measured walking behaviours without the device being worn following a period of use (13) may not be clinically relevant.

In all the reviewed RCTs participants used the devices for a period of time, with measurement occurring immediately at the end of that period; with or without interim data collection points. This aligns with the definition of therapeutic effects and is consistent with its interpretation by non-RCT studies (63). However, these effects are clinically relevant only if the motor recovery effect is sustained for a meaningful period of time for the individual. The intervention period for the participants within Sheffler et al.'s trial was 12 weeks, at which point they measured walking behaviours. In contrast to the other included trials, they also invited participants to additional data collection sessions 12 and 24 weeks after they had finished using the devices (42). They found that the lack of effect on most measures reported after the intervention period was, unsurprisingly, sustained at these time-points. However, the equal decrease in peak DF during swing was sustained

12 weeks post-use, but not 24 weeks post-use. Justification of data collection time-points that align with an understanding of the mechanisms-of-effect and their clinical relevance are therefore needed. Only then will the time course of effects and the sustained therapeutic effects of the devices on measures, including kinematics, be understood.

Strengths and limitations

This review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria (64, 65) and guidance from the Cochrane Collaboration (33). This, coupled with the specific questions and inclusion of RCTs only (66), enhances its validity.

Our findings can only feasibly be generalized to a non-progressive CNS population, as data comes only from participants with stroke and CP. Further investigation into progressive CNS disorders is necessary, as the potential for therapeutic improvement has been shown to be limited with such conditions (54). Given that most individuals with CNS disorders will be on medication (e.g. anti-spasticity medication (67)), which could confound results, future trials should also consider how to control and report this variable.

Possible variability in the device design could limit the viability of the comparisons made by the primary trials and, by extension, this review. Lack of description of key aspects of either device means that the impact of pooling data from different FES set-up parameters and AFO mechanical properties cannot be explored (11, 25). However, given that both types of device were prescribed by qualified professionals, combining data from different trials reflects clinical practice and arguably improves the clinical validity of the findings.

The risk of selection bias in the included trials was the greatest threat to the internal validity of our findings. This could mean that the estimates of effect are exaggerated (68, 69) but the inclusion of a sensitivity analysis excluding trials with high selection bias (12, 29) as a result of un-randomized sequence generation suggests there was no impact. Care should be taken to avoid this risk in future RCTs. There were a number of areas deemed to be unclear areas of risk across and within the RCTs; detailed reporting might have avoided this. Overall however, the RCTs were of at only moderate (or less) risk of bias, providing confidence in our findings.

Two trials could not be included in the meta-analysis because data was reported in such a way as to not allow analysis for the purpose of obtaining therapeutic effects. One of these trials would have provided additional participants' data for only 6 FES and 3 AFO,

and so the effects are probably negligible (48). The absence of the full data-set from the 6- and 12-week data collection points from the other trial (17), $n=198$, meant that no sub-group analysis of walking speed could be performed at the 12–13-week point. It may also have impacted the 4–6-week analysis, meaning that this aspect of therapeutic effects comparison (question 1ii) could not be explored. Future RCTs should report the raw results for all planned primary and secondary end-points and separate data relating to different effects (70).

Conclusion

This meta-analysis shows, for the first time, that FES and AFO are statistically proven to have the same therapeutic effect on walking speed in CNS foot drop. This effect has also specifically been shown to occur for foot drop caused by stroke and is observed after 4–6 weeks' use. Nevertheless, whether this increase in walking speed translates into increased activity in the person's own environment, and how this improvement is achieved, remain unclear. Future research should therefore focus on the measures suggested in this review in order to address this gap in the evidence base and, with regards activity monitoring, address when the measures are captured. In addition to measurement, future trials must also report specific device details, capture sustained therapeutic effects and should involve a variety of CNS diagnoses with justified primary and secondary end-points. Only then can clinical decision-making be significantly advanced and supported by a robust evidence base.

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Appendix I. Unpublished data from trial authors

- Anke Kottink for raw walking speed data (29)
- Keith McBride for raw end-point walking speed data (comfortable speed) from Kluding et al. trial (17)
- Marietta van der Linden for walking speed data from participants who used foot drop FES (47)

2.6.2 Candidate involvement[7]

The candidate's involvement mirrored that for Article 5 (2.5.2). This work was a poster presentation at the International Society for Posture and Gait Research Conference (ISPGR) in Florida July 2017 (Appendix 3d).

2.6.3 Critical appraisal

This review is in many ways similar to Article 5 and therefore the same critique discussed in section 2.5.3 applies. As with Article 5 the publication dates of the included trials were clustered around a similar time period to the combined-orthotic studies (2008-2013) with five of the eight publications, from four of the seven trials, being published over 2 years (2012-2013). This is not surprising given that some of the same trials were included in both the combined-orthotic (Article 5) and therapeutic (Article 6) reviews (Everaert et al., 2013; Kluding et al., 2013; Salisbury et al., 2013). Therefore, the common issues around selection bias and choice of outcome measures might be due to studies not being able to learn from each other. Again device details were not reported and there was an overuse of standard functional measures, most prominently walking speed. No progressive CNO disorders were recruited with stroke primarily focused on although, unlike in Article 5, one RCT did focus on another diagnosis (CP) (van der Linden, Hazlewood, Hillman, & Robb, 2008). And here again 3 of the 7 studies (Kluding et al., 2013; Kottink et al., 2008; Salisbury et al., 2013) provided concurrent physiotherapy alongside the foot-drop device which threatens the external validity of the former two. The same rationale why only RCTs and walking measures presented for Article 5 applies. Again it should be noted that there was an inaccuracy in one aspect of the extracted data. It was wrongly reported that in the trial by Sheffler et al (Sheffler et al., 2015; Sheffler et al., 2013) the foot-drop devices were only used under supervision. Whilst this appeared to be the focus of the intervention participants also used the devices at home. This oversight was most probably due to the decision to allow a single author, the candidate, to extract data with a second person checking for accuracy rather than having two independent people doing this. Again errors such as these do not impact on the review results and conclusions but the candidate did in no way wish to misrepresent the included trial authors, so regrets this error.

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[7] A summary of the candidate's involvement in each article is presented in Table 1 on page 5

Where this article differed to the previous review on combined-orthotic effects of AFO versus FES was in relation to its specificity and findings. The development of this review benefitted from the knowledge of the relevant evidence base built up when writing the first review. Therefore, unlike Article 5, the candidate specifically chose and justified primary measures of interest. The chosen measures, activity monitoring, EMG and ankle kinematics at IC, were indeed found to be underused and overall there was a lack of justification as to the choice of measures used in the included trials. As such this review was able to very clearly direct future research to use similarly justified, credible and robust measures in future.

Although the narrative summary covered a range of evaluation measures the meta-analysis was limited to walking speed over ten metres. This limited the conclusions that could be drawn, but emphasised the variation in the measures chosen by the included trials and the need to address this if the second identified gap in the evidence base is to be filled. With respect to the primary measures of interest, narratively there was a suggestion that EMG is effected in different ways by the two devices in favour of FES, a view which was supported by other non-RCT sources. However, no further comment could be made about whether this indicated that FES produces recovery and AFOs compensation. The two trials that evaluated the therapeutic effects on kinematics found different results with (van der Linden et al., 2008) observing an equal, but insignificant, improvement in knee flex at IC and DF through swing. (Sheffler et al., 2015) found no significant effect from either device on peak hip flex in swing, peak knee flex in swing, DF at IC, peak ankle abduction in swing, peak ankle external rotation in swing. In contrast both groups showed a significant reduction in peak ankle DF in swing after 12 weeks use and 12 weeks' post-use; but this was not found 24 weeks after finishing using the device. This further highlighted the importance of future researchers adopting common and clearly justified measures. Whilst not appropriate to mention in the manuscript, the candidate believes that toe (Kim et al., 2004) or foot clearance should feature in this battery of mechanism-of-action measures (Prenton, Kenney, Stapleton, et al., 2014; Thies, Jones, et al., 2011) given its justification in the ShefStim® study of Part 1 (Article 3).

The final point that should guide the field was with regards the notion of therapeutic effect itself. Most RCTs captured this at the end of the intervention period, indeed this is when it

has been observed in other generic reviews (Pomeroy, King, Pollock, Baily-Hallam, & Langhorne, 2006). This review challenged the clinical applicability of this notion and introduced the concept of a sustained therapeutic effect that was detailed in Chapter 2 (Figure 3). Therefore, overall, and building on what was reported in Article 5, this article gives specific direction for future comparative RCTs which has the potential to influence future clinical guidelines.

2.7 Conclusions and Future Work

The articles that contribute to this thesis, and the thesis itself, sit within the body of evidence that seeks to evaluate and compare foot-drop AFO and FES devices. It adds to previous work which recognises that in order to do this in a meaningful way direct mechanistic measures of the foot-drop impairment (Tyson et al, 2013; Kottink et al, 2012; Kim et al, 2004; Voigt & Sinkjaer, 2000) alongside measures which capture the effects on the walking behaviours of the user in their own environment (Kluding et al, 2013, van Swigchem et al, 2010, Stein et al, 2006) and usability (Arthranat et al., 2007; Choi & Springle, 2011) are what are now needed in order to further develop our understanding of how the devices work and which is better overall; with a view to enhancing current clinical guidance.

The HTD480 project team members identified a researcher/user co-design process would be beneficial in the development of new interventional AT foot-drop devices. This approach was subsequently extended to user input to study design at the candidate's suggestion (Williamson et al, 2014). The co-design approach used by the HTD480 project was shown to be feasible and led to positive changes in both product and study design. However, how this approach compares with any alternative cannot be commented on, as no comparisons with other co-design methods were made. **PART 1** of this thesis charts the involvement of the candidate in a funded project focussed on doing this for both devices. The candidate recognises that the methodological decisions made in relation to the two empirical studies of the devices (Article 2 and 3) do not allow conclusions to be drawn regarding the efficacy of either device. However, the studies (Kenney et al, 2016; Prenton, Kenney, Cooper, et al, 2014; Prenton, Kenney, Stapleton, et al, 2014) demonstrated the feasibility of the devices for the first time using some methods and measures previously not used in the field that

might help to more fully understand the usability of these devices. There were many points to come from **PART 1** of my work, as discussed earlier in this Chapter of the thesis. Three key points that would be useful for future researchers in this field were:

1. The positive impact of user/researcher co-design processes to inform study design as well as the development of new devices.
2. The use of *foot*, as opposed to *toe*, clearance as a direct mechanism-of-action measure for arguably the fundamental issue caused by foot-drop; clearance through the swing phase of gait.
3. The importance of evaluating device usage and usability as ultimately foot-drop devices are only of any real value if they can and are used in the person's own environment.

The candidate then focussed on asking whether one type of device was more effective overall than the other (**PART 2**) so as to establish the evidence for clinical recommendations on which device to use for which purpose in the face of increasing numbers of manufacturers and versions of both devices. This was felt to be best served by making clinically relevant comparisons. Therefore, trials that compared both devices as long-term orthotics was the most logical focus of the first meta-analysis (Article 5). Due to the weight given to RCTs within guidelines, the availability of RCTs at this point in the candidate's work and the lack of any previous statistically robust reviews this was timely. There were opposing views on the long-term effects of each device on the lower limb when the devices were removed (therapeutic effects). Thus therapeutic comparisons were also clinically relevant (Article 6). The candidate acknowledges that both reviews in **PART 2** have limitations related to the reviewed trials, the decision to focus on a single level of evidence and minor errors in data extraction. However, and building on previous reviews in the field, both reviews showed device comparability with the meta-analyses importantly revealing statistically significant device comparability for speed, exercise capacity and the mobility sub-scale of the SIS with regards combined-orthotic effects (Prenton et al, 2016) and therapeutic speed increases (Prenton et al, 2018). These were surprising results which, as discussed in the articles themselves, the candidate suggests may be due to one of more of the following three reasons:

1. Both interventional AT foot-drop devices increase task-specific repetitive activity and it is this alone that produces the observed effects on walking behaviours. If this is the case then it does not matter which you use. Such an outcome could lead to AFOs being prescribed more frequently than FES, given their lower costs at the point of prescription, despite FES showing long term cost effectiveness (National Health Service Purchasing and Supply Agency, 2010; Taylor, Humphreys, & Swain, 2013) and bearing in mind that either device is only cost effective if it used.

2. Speed increases might be due to compensation as opposed to restoration of volitional muscle activity for either or both devices (Langhorne et al., 2009). Speed increase is of limited direct value unless there is translation into the real life of the user.

3. It might be due to the chronic, non-degenerative and hence relatively stable populations studied by the included trials. The data collection periods used in the included studies might therefore not be long enough to highlight any differences.

Due to their focus these reviews have shown the gaps in the comparative RCT evidence base in terms of the choice of measures used. Current clinical guidelines cannot comment on how each device works which might help to indicate which people they may be best used for (Tyson et al., 2013). While the primary aim of the included studies was not to determine the mechanisms-of-action of the devices the candidate examined the included studies for any evidence that might aid clinicians to choose the best device for their clients. It was concluded that further information regarding the biomechanical effects of both devices was needed to make this possible. Guidelines are also unable to comment on if and how devices are used outside of a laboratory or their usability. The reviews in **PART 2** (Articles 5 & 6) highlight that this lack of focus on foot-drop specific and user-important functional measures persists in more recent RCTs and suggest what measures might increase our understanding of the mechanisms-of-action and how the devices impact the user in their own environment. So although these reviews do not advance our understanding of how the devices work or if and how they impact the user in their "real-life" per se, the findings could inform the design of better future RCTs in this field.

The reviews also highlighted that the current RCTs recruited non-progressive populations (overwhelmingly stroke) which limit their generalizability to all CNO disorders where foot-

drop occurs as well as a lack of reported device details which would allow clinicians and/or further studies to replicate devices.

The application of novel ways of developing and evaluating new devices, with user/researcher co-design, in **PART 1** and the highlighting of the limitations with recent RCTs in **PART 2** has demonstrated the importance of measurement of both parameters which may reflect mechanisms-of-action and appropriate functional measures. **PART 1** in particular has also demonstrated how public involvement and a focus on usability may help with future device compliance. In contrast to the findings in **PART 2** of this thesis, which focused on the results from the limited RCT evidence base, it is clear that many users of either intervention do not consider them to be equivalent in their effect (Everaert et al., 2013; Kluding et al., 2013). Everaert et al (2013) found 70% (p<0.001) of their participants who were new users of either device chose FES (Walkaide®) over AFO after 12 weeks use citing function, confidence, comfort, convenience, easy donning/doffing and safety as reasons for preferring either device. Kluding et al (2013) used a self-developed user satisfaction survey finding significantly higher satisfaction in the FES (Bioness ®) group after 12 and again after 30 weeks use. This differences were significant for eight of the 12 questions relating to: enthusiasm about continuing to use; comparison to other walking devices, convenience in using all day long, confidence in performing tasks whilst wearing, confidence in walking on inclines and/or uneven ground, comfort in social situations, whether they would use the device daily and whether they would recommend the device. The results might have been influenced by the decision to recruit current AFO users and the use of a purposive survey using three point Likert scales or yes/ no responses. Nevertheless, it is imperative that further study is undertaken that explores this mismatch. Based on the work contained in this thesis, the candidate proposes that a Phase III trial (Medical Research Council, 2000) is required which uses foot-drop specific and user-relevant outcome measures to compare the two types, AFO and FES, of AT interventional foot-drop devices. Based on my work I recommend that the foot-drop specific measures should be foot-clearance and, given the potential impact of foot-drop devices on the entire lower limb and throughout the gait cycle, EMG, kinematic and kinetic measures. Further, device usage as well as the physical activity of the user when not wearing the device should be recorded to both capture a potential mechanism-of-action (task-specific repetitive activity) as well as the

impact of the devices on participation. Participant views whilst invaluable to understand user experience and to inform methodological decisions are susceptible to social desirability bias (Grimm, 2010) when captured in the context of an efficacy trial using purposive questionnaires (Everaert et al., 2013; Kluding et al., 2013; Prenton, Kenney, Cooper, et al., 2014). Due to validation processes data collection tools such as the QUEST 2.0 allow a more robust approach to the collection of user satisfaction data (Koumpouros, 2016). Although generic to any AT the questions asked by the QUEST 2.0 device sub-scale (Appendix 4) reflect what Kluding et al (2013) was also trying to explore by asking about comfort and convenience, but with the benefit of construct validity. An alternative would be to adopt a mixed methods approach. This combination of measures would shift the emphasis of evaluation from the laboratory to the real life of the user where effects are most important; which was apparent as being important to potential end-users during the lay-advisory group meetings that accompanied the HTD480 project (Williamson et al., 2013). Further lay-advisory work is needed to confirm whether this proposed raft of measures fully reflects user priorities. With regards recruitment the candidate suggests that all participants should be new users of either device so as to not bias preference. Recruitment should also focus on people who present with a range of CNO disorders; albeit progressive and non-progressive participants will require sub-group analysis. In addition to this, based on the work contained in this thesis, the candidate recommends that details of prescription processes (mechanical properties (AFO), setup parameters (FES)) must be reported and devices should be set up by users during data collection sessions to reflect real use. Due to the variation in types of AFO and FES used in clinical practice and the impact this heterogeneity has on the potential mechanisms-of-action, either one type of AFO and one type of FES system should be used, or the recruitment be sufficient to allow sub-group analysis. Both combined-orthotic and therapeutic effects should be evaluated. The study period should be at least 42 weeks in duration (Dunning et al., 2015) with data collected every 6 weeks. The reasons for this are linked to the findings of effects after 6 weeks and 12-13 weeks (Prenton et al., 2016) and the necessity of longer study periods to potentially differentiate between the devices if participants have chronic conditions (Prenton et al, 2016). However, it is recognised that 6 weekly data collection points is not indicative of clinical practice which could undermine external validity. The impact of more frequent data collection points would have to be weighed against the increased risk to recruitment and attrition; getting this balance right

might be best achieved by seeking lay advice. Post-device use follow-up is also necessary if sustained therapeutic effects are to be compared (Prenton et al, 2018).

If these recommendations are utilised the future trials undertaken will then create the opportunity for the development of more specific clinical guidance based on a clearer understanding of the devices' mechanisms-of-action, if/how they are used outside of a laboratory and whether/how that relates to the usability of the devices.

CHAPTER 3: IMPACT

The potential impact of the work presented in this thesis is best summarised according to identified gaps, how they have been addressed and the suggestions made regarding where future work in the field should focus. As stated in the conclusion & future work section in Chapter 2 (2.7) the substantial body of work within this thesis as based on the identified gaps in the evidence base, were underpinned by the candidate's focus of how devices for foot-drop are most credibly evaluated if future foot-drop clinical guidance is to be advanced. This was achieved through the creation of new knowledge in the form of the three studies that formed **PART 1** as well as the synthesis and interpretation of existing evidence presented in **PART 2**. The candidate conceptualised key elements within all of these studies and used applicable and rigorous techniques in the enquiry undertaken (Articles 2, 3, 5, 6). In so doing the candidate fulfils the four Quality Assurance Agency (QAA) Framework for Higher Education Qualifications (FHEQ) descriptors for higher education qualifications at level 8 (Quality Assurance Agency, 2008) and has the potential to redirect the device for foot-drop evidence base.

In addition to the overt conclusions related to the identified gaps in the evidence base to come from the presented body of works there are other areas of potential impact that three of the articles that constitute **PART 1** provide. The lay-advisory group study (Article 1), the DMO dorsiflex sock® study (Article 2) and the ShefStim® study (Article 3) could be used by future researchers as examples of user involvement in device development, study design development and participant feedback within this field of research. Use of these articles could therefore facilitate translation of evidence for device efficacy into implementation as they illustrate how to implement user involvement which is necessary if AT is to align with the needs and expectations of the user (Wilkinson & De Angeli, 2014).

It was recognised that the two devices that were studied (DMO dorsiflex sock® and ShefStim®) in **PART 1** were complex interventions and subsequently appropriate methodological approaches to preliminarily evaluate them in line with appropriate guidance (Medical Research Council, 2000) at Phase I (lay advisory group) and Phase II (empirical studies of the two devices) were utilised. The demonstration of where devices might not work as hoped, DMO dorsiflex sock® study (Article 2), and where product refinement is

required for commercial partnership, ShefStim® study (Article 3), is impactful so that future development and research into those devices can be specifically targeted.

Appendix 5 details the journals the body of work have been published in and some metrics pertaining to them. Citation metrics gauge the impact of individual scholarly impact. The Hirsch (h) index is the most useful summary measure of this (Birks et al., 2014) calculated based on the number of publications and the number of citations. The h-index for the candidate currently stands at 3. Whilst a low number (Birks et al., 2014) considering the timespan of the articles publications (2014-2018) and the proximity of thesis submission to that period of time there is evidence that the candidate is having some scholarly impact in a relatively short period (Saleem, 2011). The number of citations as a standalone metric is also relevant for consideration for a PhD by published works as an indication of author visibility (Nightingale & Marshall, 2013). It should be noted that Article 6 was in the process of publication around the time of submission. As such its impact cannot be judged at this time.

Article	Google scholar	SCOPUS	ResearchGate
1	8	4	4
3	9	6	8
4	2	1	1
5	4	2	2

Table 3: Article Citations[8]

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[8] Accurate as of 11/1/18

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Engineers	*Current, or last known, affiliation*	*Key Contributions*[9]
Professor Laurence Kenney	University of Salford. School of Health Sciences	Research Lead Rehabilitation technologies and biomedical engineering theme. Led HTD480 project. Co-author on all publications. PhD co-supervisor.
Professor David Howard	University of Salford. School of Computing, Science & Engineering	Research Lead Rehabilitation technologies and biomedical engineering theme. Advised on stimulator-skin interface components of HTD480 project. Co-author on articles 3 & 4
Professor Anthony Barker	Retired: Sheffield Teaching Hospitals NHS Foundation Trust	Conceptualised array FES approach. Part of HTD480 project. Co-author on Articles 3 & 4
Dr Ben Heller	Sheffield Hallam University	Conceptualised array FES approach. Part of HTD480 project. Involved in Completed phase 1 evaluation of ShefStim precursor. Co-author on Article 3 & 4
Dr Timothy Good	Sheffield Teaching Hospitals NHS Foundation Trust*	Helped refine array FES concept into ShefStim. Part of HTD480 project. Co-author on Articles 3 & 4
Dr Sibylle Thies	University of Salford. School of Health Sciences	Supported with foot clearance data analysis. Co-author on Article 3
Dr Glen Cooper	University of Manchester	Part of HTD480 project. Supported with data collection of the DMO dorsiflex sock (Article 2). Involved in researching the stimulator-skin interface components for the HTD480 project. Co-author on articles 2, 3 & 4
Dr Matty Majors	Northwestern Medicine: Feinberg School of Medicine	Supported with data collection for Article 2 (co-author).
Clinicians	*Current, or last known, affiliation*	*Key Contributions*
Dr Claire Stapleton (Physiotherapist)	Keele University	Assisted with recruitment and data collection for Article 3 (co-author)
Dr Tracey Williamson (Nurse)	University of Salford. School of Health Sciences	Part of HTD480 project. Lead researcher of the lay-advisory group (Article 1). Co-author Article 3
Dr Julia Ryan (Nurse)	University of Salford. School of Health Sciences	Co-researcher of the lay-advisory group (Article 1)
Martin Matthews (Orthotist)**	DMO orthotics™	Commercial partner in HTD480 project, with regards DMO dorsiflex sock®
Dr Mohammed Sobuh (Prosthetics & Orthotics)	University of Jordan	Constructed ShefStim units during data collection. Co –author Article 3.
Pornsuree Onmanee (Orthotist)	University of Salford. School of Health Sciences	Involved in article review process, quality assessment and manuscript development for Article 6. Co-author Article 6

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[9] This list is designed to give some indication of role but is by no means exhaustive for all those listed.

Clinical Scientists	*Current, or last known, affiliation*	*Key Contributions*
Mark Reeves	Sheffield Teaching Hospitals NHS Foundation Trust	Part of HTD480 project. Co-author Articles 3 & 4
Dr Jamie Healey	Sheffield Teaching Hospitals NHS Foundation Trust	Part of HTD480 project. Co-author Articles 3 & 4
Biomechanist	*Current, or last known, affiliation*	*Key Contributions*
Dr Kristen Hollands	University of Salford. School of Health Sciences	Senior Research Fellow. Co-author and contributor to Articles 5 & 6. PhD candidate co-supervisor.
Undergraduates (BSc (Hons) Physiotherapy)	*Current, or last known, affiliation*	*Key Contributions*
Helen Carrington	University of Salford. School of Health Sciences	Helped with data collection for Article 2
Samantha Carey	University of Salford. School of Health Sciences	Helped with data analysis for Article 3
Statistician	*Current, or last known, affiliation*	*Key Contributions*
John Stephenson	University of Huddersfield	Reviewed meta-analyses for Article 5

Appendix 2

ELECTRODE POSITION REVISION

Paul Taylor, Clinical Engineer

Finding the right electrode position for your patient is an important part of using FES in the clinic. We aim to produce dorsiflexion with a little eversion. Eversion is important as it enables safer weight bearing at heel contact. Here is a reminder of the positions commonly used in our clinic.

Finding the Head of Fibula

The head of fibula is the most important anatomical landmark for identifying electrode positions. It is important that the patient learns how to identify it for themselves. It can sometimes be confused with the tibial tuberosity so patients should remember that the fibula head is further round the side of the leg and is the lowest bony prominence. A good way to teach it is by asking the patient to find the ankle bone and run their fingers up the outside of the leg until the first bony prominence is found.
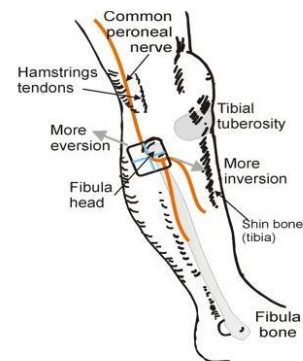
Standard Electrode Position

To place an electrode on the fibula head, imagine the electrode divided into 4 quarters. Place the top, front corner over the fibula head. This will result in the common peroneal nerve passing diagonally underneath the electrode. If you press with your finger on the 4 quarters, the top front quarter will feel hard while the other quarters will feel soft. This is a good exercise for the patient to do.

Place the second electrode over the belly of the anterior tibialis muscle. This is generally one fingers breadth to the side of the tibia bone and about one fingers breadth below the fibula head electrode. Often the corners of the electrodes will be in line with each other as shown. If the electrode goes over the tibia bone the stimulation can sting a little. Connect the black electrode lead plug to the top electrode and the red electrode plug to the other electrode: this is called the standard electrode position and is the most commonly used position. Moving the top electrode further forward and downwards will generally recruit proportionally more of the deep branch of common peroneal nerve and cause increased inversion. Moving the same electrode back and upwards will cause more eversion as a greater proportion of the superficial branch is stimulated. Moving the lower electrode further away from the tibia and more over the peroneii muscles may also increase the amount of eversion.
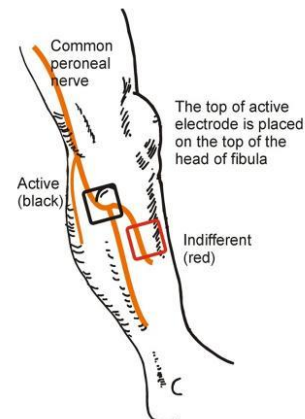
Reversing the Polarity

Sometimes the standard position produces too much eversion even after adjustment. Swapping over the electrode leads will make the electrode over the tibialis anterior the negative electrode and as there is always a stronger stimulation effect under the negative, a greater proportion of this muscle will be stimulated. This will produce greater inversion. This will often be suitable for patients with low calf tone. Patients with high calf tone will often require more eversion because excessive calf activity causes plantarflexion with inversion.
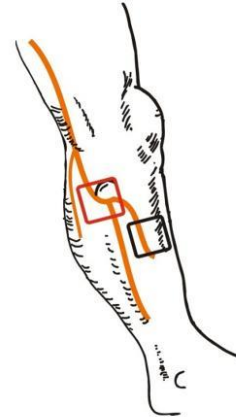
Symmetrical Biphasic.

Sometimes it is the case that the standard position causes too much eversion but reversed polarity causes too much inversion. A compromise can be achieved by changing the waveform from asymmetrical biphasic to symmetrical biphasic (second to last parameter on the FINETUNE menu of the ODFS® Pace). This will cause both electrodes to have equal stimulation effect, producing a balance of eversion and inversion.

Popliteal Fossa Positions

The common peroneal nerve can be stimulated more proximally than at the head of fibula by placing an electrode behind the knee. The nerve runs up the lateral side of the popliteal fossa, just to the inside of the biceps femoris tendon. Place an electrode with one edge along the tendon with the rest of the electrode within the fossa. If you place the electrode too far into the popliteal fossa, it is likely that the tibial nerve will be stimulated, causing plantarflexion from calf activation. Placing the electrode a little more proximal can sometimes be more comfortable but may also have less effect as the nerve will be deeper.

Stimulating the nerve in the popliteal fossa will generally produce a stronger effect, producing more dorsiflexion and more eversion. It is also the best electrode position for producing a withdrawal reflex, improving knee and hip flexion. Sometimes excessive hip external rotation can occur.

The strongest effect is produced by placing the active (black electrode plug) in the popliteal fossa with the indifferent on the head of fibula. A more moderate effect is achieved by reversing the polarity. If too much eversion is produced, move the electrode from the head of fibula to the motor point of anterior tibialis. If more eversion is required, the lower electrode can be moved towards the peronei group. These positions can be used with either polarity electrode. Further variation can be found by changing the waveform to symmetrically biphasic.

Electrode on the Biceps femoris tendon and lateral border of the popliteal fossa

Avoid the tibial nerve

Strongest effect

Moderate effect

Increased dorsiflexion, reduced eversion

Dorsiflexion without eversion

Motor point of anterior tibialis

Avoid tibia bone

Motor point stimulation requires high levels of stimulation and may be more uncomfortable
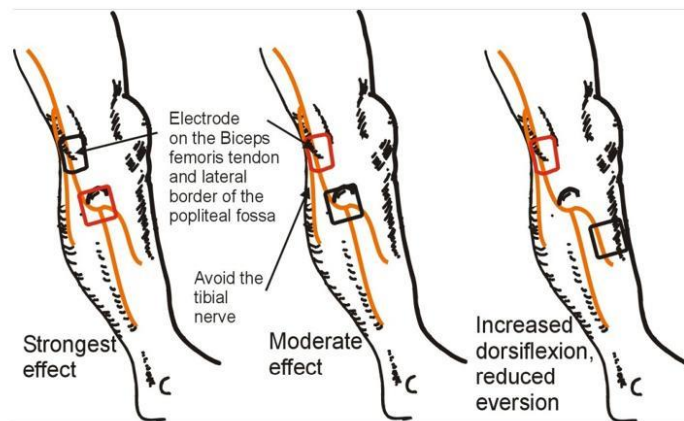
Motor Point Stimulation

If all the other electrode positions produce too much eversion, place the active electrode over the motor point of tibialis anterior with the indifferent electrode below it. If a little eversion is needed, either or both electrodes can be moved towards the peroneii group. It is common for a higher level of stimulation to be required for this electrode position because the nerve is less superficial. This may make the stimulation more uncomfortable
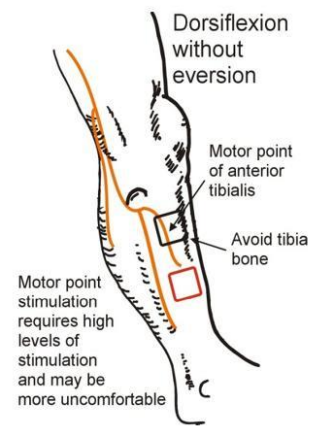
Toe clawing while walking

Sometimes a dropped foot stimulator user can experience toe clawing. This is generally a spastic response to walking and not caused by the FES. Sometimes it is possible to increase toe extension by stimulating the long toe extensors. This

can be achieved by placing one electrode over the common peroneal nerve as before and the other over the toe extensors, mid way down the lower leg (lower than the Standard position). Choose polarity and waveform depending on the response you find.

Finding the electrode positions again

Many patients ask us to mark the position of the electrodes on their legs with an indelible marker. While in the short term this helps ensure correct duplication of the positions, after a few days the marks will fade. While re-marking can help, the lines can drift in time resulting in incorrect positions. The best plan is for the patient to learn their own anatomy and understand why the electrodes are placed where they are. In this way, if the incorrect response is found, they will have a better idea of what to do to improve the movement of the foot. An aid to learning the anatomy is to mark the position of the head of fibula on the back of the electrode. The patient then learns to line up the mark with their fibula head and in this way learns the anatomical land mark. Likewise the position of the biceps femoris tendon can also be marked.
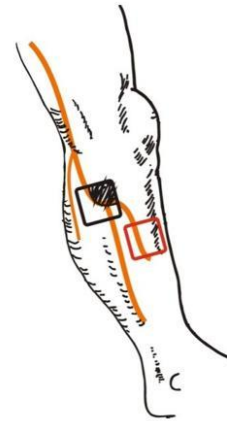
Conclusion

Our knowledge of electrode positions continues to expand as we see more patients and try out new ideas. As with all things with FES, don't be afraid to use your knowledge of anatomy and basic principles to experiment and find variations of your own.

Please let us know your own experiences and ideas so we can share practice through the FES Newsletter.

http://www.odstockmedical.com/sites/default/files/electrode_position_revision_0.pdf

Appendix 3

3a)

http://www.invo.org.uk/posttypeconference/impact-of-public-involvement-on-assistive-technology-design-experiences-and-formative-evaluation-findings/

3b)

FINAL PROGRAMME

Time	Friday 12th April
9.00-9.45	Coffee and tea on arrival and registration
9.45-10.00	Opening address and welcome by Professor Jane Burridge and conference team
10.00-12.30	INSPIRE DISSEMINATION EVENT: *'Exploring the views of the current and future use of FES in spinal cord injury'*
12.30-13.45	Lunch/Tradeshow Exhibition/Poster presentations
13.45-14.45	**Keynote Speaker** Professor Volker Dietz Spinal Cord Injury Center, Balgrist University Hospital, Zürich *'Neurorehabilitation after spinal cord injury: Significance of technology'*
14.45-15.30	Question time/Panel Discussion: *"What are the basic science questions that need to be understood for FES to make progress?"*
15.30-16.00	Tea & Coffee Break/Tradeshow Exhibition/ Poster presentations
16.00-17.15	Short Paper Presentations relating to <u>'Clinical application and new research developments involving FES'</u> a) Maura Whittaker: *'4 year follow-up survey of Canadian patients fitted with the Odstock dropped foot stimulator (ODFS)'* b) Dr Paul Taylor: *'A comparison of external and implanted EFS for correction of dropped foot. An audit of the STIMuSTEP service in Salisbury'* c) Sarah Prenton: *'The impact of an array based drop-foot FES system on speed & foot orientation following 2 weeks of home use'* d) Earl Merson: *'Point accelerometery alone is not an accurate measure of limb tilt when walking'*
19:00-22.30	Conference Dinner at the SeaCity Museum in Southampton City Centre.

3c)

Poster Presentations

3d)

Abstract Book

2017 ISPGR WORLD CONGRESS

June 25 to June 29, 2017
Fort Lauderdale, Florida, USA

Westin Fort Lauderdale
Beach Resort

3-O-77 Does functional electrical stimulation have greater therapeutic effects on walking than ankle foot orthoses for foot-drop?

Kristen Hollands[1], Sarah Prenton[2], Pornsuree Onmannee[1], Laurence Kenney[1]
[1]University of Salford, [2]University of Huddersfield

Background: Foot-drop of central neurological origin affects 20-30% of people who suffer a stroke and is also prevalent in other central nervous system (CNS) disorders. There are two commonly used devices for correcting foot-drop, ankle foot orthoses (AFO) [1] and functional electrical stimulators (FES) [2]. Meta-analysis of randomised controlled trials (RCT) comparing the effects of sustained use of FES or AFO on various outcome measures with them in-situ found no clear differences [3]. The use of either device for a sustained period of time is also believed to impact on a person?s unassisted walking (therapeutic effect), with authors suggesting FES may have positive and AFO negative effects. However, a direct comparison has yet to been done. Aim: To compare the therapeutic effects on walking of AFO versus FES for foot-drop caused by a CNS disorder through a systematic review of RCT literature, including meta-analysis. Methods: An a-priori strategy was used to search MEDLINE (Ovid), CINAHL (EBSCO), CENTRAL, Scopus (Elsevier), REHABDATA, PEDro & clinicaltrials.gov databases plus reference lists, citations, key authors and journals. Screening was performed by two reviewers independently and data were extracted using a pre-designed proforma; quality was assessed using the Cochrane risk of bias assessment tool. Meta-analysis was planned, where possible. Primary outcomes were activity (measured using monitors) and impairments in electromyography and kinematics; all other walking outcomes were classed as secondary. Results: Seven RCTs were included. These were deemed to be of

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moderate methodological quality overall. Meta-analysis was only possible for the secondary measure of walking speed, with data taken from five trials (N=327; MD= 0.03 [-0.02, 0.08]; I2=0%; p=0.24, Fig.1.) Conclusions: The therapeutic effects on walking speed for CNS foot-drop are not greater for FES than AFO. Therefore, if the aim of treatment is to increase unassisted walking speed, either can be used. However, none of the primary measures of interest could be analysed due to their inconsistent use. Therefore whether the observed gait speed increases are associated with increased activity in the users own environment remains answered. Further, it remains unknown whether the increase in speed was a result of motor recovery (e.g. improved volitional muscular activation) or compensatory strategies, or both. Further RCTs should use appropriately justified outcome measures that reflect actual performance and mechanisms-of-action. 1. Intercollegiate Stroke Working Party. National clinical guidelines for stroke. 2016, Royal College of Physicians (RCP): London. 2. National Institute for health and Care Excellence (NICE) Functional electrical stimulation for drop foot of central neurological origin. 2009. 3. Prenton, S., K.L. Hollands, and L.P. Kenney, Functional electrical stimulation versus ankle foot orthoses for foot-drop: A meta-analysis of orthotic effects. J Rehabil Med, 2016. 48(8): p. 646-656.

1	2	3	4	5
not satisfied at all	not very satisfied	more or less satisfied	quite satisfied	very satisfied

ASSISTIVE DEVICE					
How satisfied are you with,					
1. the **dimensions** (size, height, length, width) of your assistive device? Comments:	1	2	3	4	5
2. the **weight** of your assistive device? Comments:	1	2	3	4	5
3. the **ease in adjusting** (fixing, fastening) the parts of your assistive device? Comments:	1	2	3	4	5
4. how **safe and secure** your assistive device is? Comments:	1	2	3	4	5
5. the **durability** (endurance, resistance to wear) of your assistive device? Comments:	1	2	3	4	5
6. how **easy** it is to use your assistive device? Comments:	1	2	3	4	5
7. how **comfortable** your assistive device is? Comments:	1	2	3	4	5
8. how **effective** your assistive device is (the degree to which your device meets your needs)? Comments:	1	2	3	4	5

Article 1: Disability & Rehabilitation: Assistive Technology

Journal is UK based (Taylor and Francis)

Aims & Scope

Disability and Rehabilitation: Assistive Technology along with **Disability and Rehabilitation** seek to encourage a better understanding of all aspects of disability and to promote rehabilitation science, practice and policy aspects of the rehabilitation process. Taken together, both journals represent an important forum for the dissemination and exchange of ideas amongst global health practitioners and researchers.

The mission of Disability and Rehabilitation: Assistive Technology is to advance the practice and science of interdisciplinary and integrative assistive technology service delivery and product design internationally so that persons with disabilities, chronic illnesses, and challenges to the performance of activities and participation in life roles, achieve enhanced functioning and life quality.

Assistive technology focuses on both equipping individuals with the most appropriate technologies and also removing barriers to functioning that exist in the environment. Topics range from everyday/mainstream to specialized devices, and include: exoskeltons and robotics; smart homes; information and communication technologies and computerized systems; ergonomics; universal design; ambient assistive technology; telerehabilitation; job and environmental accommodations; and methods of service delivery.

Disability and Rehabilitation: Assistive Technology is an international and multidisciplinary journal, published six times a year. The Journal publishes review articles and original research on assistive technology devices, services, user experiences, education and training, and policies. The journal also publishes supplements, special issues and special sections. Because the field is broad, submissions include experimental investigations, survey research, case studies, systematic reviews and product development and testing. Theoretical and conceptual papers and the discussion of professional issues and international/national policies and standards are also published.

ISSN: 1748-3107

Article 2: Prosthetics & Orthotics International

Journal is operated from London, England

Aims & Scope

Prosthetics and Orthotics International is an international, multidisciplinary journal for all professionals who have an interest in the medical, clinical, rehabilitation, technical, educational and research aspects of prosthetics, orthotics and rehabilitation engineering, as well as their related topics.

The Journal publishes review articles, experimental and clinical research papers, case studies, technical notes, reports on prosthetics, orthotics and rehabilitation engineering

practice, and book reviews. Occasionally special issues on specific themes of interest to the Journal's readership are published. Information about ISPO activities and the outcomes of the ISPO consensus conferences and working groups that are held are also published.

Article 3: Archives of Physical Medicine and Rehabilitation

Journal is operated from Philadelphia, America (Elsevier), base in UK (W.B. Saunders Co. Ltd)

The *Archives of Physical Medicine and Rehabilitation* is the official journal of the ACRM | American Congress of Rehabilitation Medicine, an organization focused on the creation and use of knowledge in the rehabilitation process. The *Archives of Physical Medicine and Rehabilitation* publishes original, peer-reviewed research and clinical reports on important trends and developments in medical rehabilitation and related fields.

This international journal brings researchers and clinician's authoritative information on the therapeutic utilization of physical, behavioral, and pharmaceutical agents in providing comprehensive care for individuals with chronic illness and disabilities. The journal's content is relevant to all members of medical rehabilitation teams, including physicians, nurses, counselors, therapists, and case managers.

Mission Statement
The mission of the *Archives of Physical Medicine and Rehabilitation* is to disseminate original information, with the goal of advancing the art and science of interdisciplinary rehabilitation, thus improving the health and welfare of persons with chronic illness and disabilities and reducing the cost of care.

Article 4: Medical Engineering and Physics

Journal is operated from Amsterdam, Netherlands (Elsevier)

Medical Engineering & Physics provides a forum for the publication of the latest developments in **biomedical engineering**, and reflects the essential multidisciplinary nature of the subject. The journal publishes in-depth critical reviews, scientific papers and technical notes. Our focus encompasses the application of the basic principles of **physics** and **engineering** to the development of **medical devices** and **technology**, with the ultimate aim of producing improvements in the quality of health care. Topics covered include biomechanics, biomaterials, mechanobiology, rehabilitation engineering, biomedical signal processing and medical device development. *Medical Engineering & Physics* aims to keep both engineers and clinicians abreast of the latest applications of technology to health care.

Articles 5 and 6: Journal of Rehabilitation Medicine

This journal is published in Uppsala, Sweden.

Journal of Rehabilitation Medicine is the international peer-review journal published in English, with at least 10 issues published per year.

Original articles, reviews, case reports, short communications, special reports and letters to the editor are published, as also are editorials and book reviews. The journal strives to provide its readers with a variety of topics, including: functional assessment and intervention studies, clinical studies in various patient groups, methodology in physical and rehabilitation medicine, epidemiological studies on disabling conditions and reports on vocational and sociomedical aspects of rehabilitation.

The journal is read by a wide group of healthcare professionals including specialists in rehabilitation medicine, neurology, clinical neurophysiology, general medicine, psychologists, physiotherapists, occupational therapists and social workers.

Contributions from all parts of the world and from different professions in rehabilitation are welcome

Journal	Journal impact factor (Web of Science JCR®, 2015)	5-year journal impact factor (Web of Science JCR®, 2015)	Ranking (Web of Science JCR®, 2015)	h5-index (Google Scholar, June 2016)	h5-median (Google Scholar, June 2016)	Ranking (Google Scholar, June 2016)	SCImago Journal Ranking (SJR) (SCImago, 2015)	H index (SCImago, 2015)	Ranking (SCImago, 2015)
Disability & Rehabilitation-Assistive Technology (Article 1)	0.71#	Not found	Not found	*40	*55	*5th in Rehab Ther	0.591	23	77/321 Biomed Eng (Q2); 95/225 Ortho & Sports Med (Q2); Phys Ther, Sports Ther & Rehab (Q2); Rehab (Q2)
Prosthetics & Orthotics International (Article 2)	0.930	1.069	53/74 Ortho (Q3); 51/65 Rehab (Q4)	Not listed	Not listed	Not in top 20	0.567	37	7/27 Health Profs (Q1); 39/113 rehab (Q2)
Archives of Physical Medicine & Rehabilitation (Article 3)	3.045	3.315	4/65 Rehab (Q1); 9/82 Sports Sci (Q1)	51	62	1st in Rehab Ther	1.427	143	8/167 Phys Ther, Sports Ther & Rehab (Q1); 3/113 Rehab (Q1); 18/128 Sports Sci (Q1)
Medical Engineering & Physics (Article 4)	1.619	1.946	45/76 Biomed Eng (Q3)	38	51	13th in Biomed Tech	0.784	76	66/321 Biomed Eng (Q2); 50/123 Biophysics (Q2)
Journal of Rehabilitation Medicine (Articles 5 & 6✓)	1.595	2.261	25/65 Rehab (Q2); 37/82 Sport Sci (Q2)	34	47	10th in Rehab Med	0.911	71	25/167 Phys Ther (Q1); 41/128 Sports Sci (Q2).

#= based on ResearchGate data; *= relates to Disability and Rehabilitation as opposed to the Assistive Technology supplement; ✓= in process of publication. Rehab= rehabilitation; Ther= Therapy; Biomed= biomedical; Eng=Engineering; Ortho= Orthopaedics; Profs= Professions; Sci=Science; Tech= Technology.