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Prenton, Sarah, Hollands, Kristen L. and Kenney, Laurence P.

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## TITLE PAGE

**Running Head:** FES versus AFO for foot-drop

**Title:** Functional electrical stimulation versus ankle foot orthoses for foot-drop: a meta-analysis of orthotic effects

### **Authors:**

1. Mrs Sarah Prenton. BSc (Hons) Physiotherapy, PGCert Higher Education Research and Practice. [1] [s.prenton@hud.ac.uk](mailto:s.prenton@hud.ac.uk)
2. Dr. Kristen L. Hollands. PhD. [2] [k.hollands@salford.ac.uk](mailto:k.hollands@salford.ac.uk)
3. Professor Laurence P.J. Kenney. PhD. [2] [l.p.j.kenney@salford.ac.uk](mailto:l.p.j.kenney@salford.ac.uk)

### **Institutions:**

1. University of Huddersfield, School of Human and Health Sciences, Department of Health Sciences, Health and Rehabilitation division, England.
2. University of Salford, School of Health Sciences, England.

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**Corresponding author:** Mrs Sarah Prenton, Room RG/23, Ramsden Building University of Huddersfield, Queensgate, Huddersfield, West Yorkshire, HD1 3DH. [S.Prenton@hud.ac.uk](mailto:S.Prenton@hud.ac.uk)  
+44 (0)1487473861

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## ABSTRACT

***Objective:*** To compare the effects on walking of Functional Electrical Stimulation (FES) and Ankle Foot Orthoses (AFO) for foot-drop of central neurological origin, assessed in terms of unassisted 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 Randomised Controlled Trials (RCTs).

***Data Synthesis:*** Seven RCTs were eligible for inclusion. Two of these reported different results from the same trial and another two reported results from different follow up periods so were combined; resulting in five synthesised trials with 815 stroke participants. Meta-analyses of data from the final assessment in each study and three overlapping time-points showed comparable improvements in walking speed over ten metres ( $p=0.04-0.95$ ), 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, AFOs 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.

## MAIN TEXT

### 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 United Kingdom (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 stabilise 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-randomised control trial (RCT) evidence. AFOs have been criticised for detrimental effects on the adaptability of walking, propulsion, aesthetics and comfort (14-16) which can impact 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 to 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:

- a) Immediate-orthotic effects where same-day comparisons are made between AFO/FES unassisted and assisted walking behaviours (16, 27).

- b) Therapeutic effects (19, 28) where unassisted walking behaviours are compared with unassisted walking on a day some period later (16, 27).
- c) Training effects (16) where assisted walking behaviours are compared with assisted walking on a day some period later.
- d) 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 (a) (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 hypothesised 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 versus 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 to 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](http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=9892&UserID=6114)

Nine electronic databases were searched. These were 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 one reviewer (SP) screened titles and abstracts categorising each as ‘possibly’ or ‘clearly not’ relevant against the inclusion criteria (Table I). Full length articles were retrieved for ‘possibly relevant’ studies and two 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).

Table I. *Inclusion Criteria.*

SP extracted data using a predesigned proforma; trial details extracted related to the characteristics of the included studies, participant 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 two 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 Organisation'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 categorised 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 hypothesised 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 so was converted as necessary (15).

Meta-analyses were performed using RevMan 5.3® software. Where the same measurement was used across more than two trials, outcomes were combined using mean difference (MD) with 95% confidence intervals (CIs). Where an outcome was measured using different approaches, such as functional exercise capacity (distance walked in metres measured over two, three or six minutes), standardised 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 extracted (15).

Heterogeneity was examined using visual inspection of forest plot,  $\chi^2$  test and  $I^2$  statistic. If the  $\chi^2$  test showed heterogeneity which 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 of >50%.

## RESULTS

1836 citations were found of which seven were eligible for inclusion. Two of these reported outcomes from the same participants (44, 53) so were grouped, and subsequently referred to by the first publication date (44). One trial published results up to six months (14) and had another publication reporting results at 12 months (51); so were 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 five RCTs, published between 2007 and 2015 with 815 participants, were available for meta-analysis (*Fig. 1*).

*Fig. 1.* Flowchart of trial selection.

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

### *Characteristics of included trials*

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

### *Participant details*

All the participants were over the age of 18 years and had suffered a stroke. Average 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 four 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 one 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 study used surface FES systems (44), one trial highlighted that “clinicians” setup FES for measurement (45) but no trial reported details of setup parameters such as electrode placement, ramping, amplitude or frequency. The setting where interventions were used varied with participants from three of the studies

using the devices within their own environment (14, 15, 44, 51). One trial used them in both the participants own environment and under supervision (16) and one 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. Risk of Bias*

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

#### *Table IV. Outcome measurements and intervention effects*

### *Outcome Measurements*

All trials utilised ICF activity domain measurements; most commonly the 10-metre 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 six weeks (15) – 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 summarised below. Final-assessment meta-analyses are presented first. There were three overlapping data time-points found at 4-6 weeks, 12-13 weeks and 26-30 weeks for activity domain measurements. These are categorised as short, medium and longer-term respectively (Table IV); meta-analyses at these time-points are then presented.

### *BFS*

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-metre walking speed (all five trials,  $n=789$ ) and functional exercise capacity (three 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.

*Fig. 2. Activity domain measurement: 10-metre (m) walk test metres per second (m/s)*

*Fig. 3. Activity domain measurement: functional exercise capacity metres (m).*

The timed up-and-go test was used in two 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-metre walk test using data at short (four trials,  $n=771$ ), medium (three trials,  $n=699$ ) and longer-term (three trials,  $n=713$ ) time-points (*Fig. 2b-d*). It 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= -0.00 [-0.04, 0.04];  $I^2=14\%$ ;  $p=0.95$ , *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 (three trials,  $n=761$ ) and medium-term (two trials,  $n=692$ ) time-points (*Fig. 3b and c*). Meta-analyses revealed between-group comparable improvement (SMD= -0.12 [-0.26-0.02];  $I^2=0\%$ ;  $p=0.10$ , *Figure 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 three 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*).

*Fig. 4.* Participation domain measurement: Stroke Impact Scale (mobility sub-scale).

Activity monitoring was used by two trials (16, 44) (Table IV) but their data collection methods varied too significantly (steps taken compared to 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 ( $p=0.04$ ).

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 to FES as interventions for people with CNO foot-drop which focusses 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-metre 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 two 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.

### *BFS*

The majority of measurements used in the reviewed trials suggest that there are no differences between the two interventions. However, given the suggestions of a negative influence of AFO and a positive influence of FES on volitional muscle activation 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) which compared EMG activity between FES and AFO treatments. This trial reported that EMG activity was greater following a period of FES than AFO use (56).

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, that 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 & Participation*

Meta-analysis of three 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 one trial highlight another potential explanation. Kluding et al (16) found that the number of steps taken per day increased with use of either intervention (1891-2069, AFO and 2092-2369, FES at six 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 which 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 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, two 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 versus 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 setup 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 hypothesised 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 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.

## REFERENCES

1. Sheean G, McGuire JR. Spastic Hypertonia and Movement Disorders: Pathophysiology, Clinical Presentation, and Quantification. *Phys Med Rehabil* 2009; 1: 827-833.
2. National Institute for health and Clinical Excellence (NICE). Functional electrical stimulation for drop foot of central neurological origin. NICE interventional procedure guidance (IPG 278) [Internet]. 2009 [cited 2016 May 15]. Available from: <https://www.nice.org.uk/guidance/ipg278>
3. Stroke Association. State of the Nation. Stroke Statistics- January 2016 [Internet]. 2016. [cited 2016 May 21]. Available from: [https://www.stroke.org.uk/sites/default/files/state\\_of\\_the\\_nation\\_2016\\_110116\\_0.pdf](https://www.stroke.org.uk/sites/default/files/state_of_the_nation_2016_110116_0.pdf)
4. BMJ Best Practice. Chronic Spinal Cord Injury [Internet]. 2015 [cited 2016 May 21]. Available from: <http://bestpractice.bmj.com/best-practice/monograph/1176/basics/epidemiology.html>
5. Headway- the brain injury association [Internet]. 2015 [cited 2016 May 21]. Available from: <https://www.headway.org.uk/brain-injury-statistics.aspx>.

6. NHS Choices. Cerebral palsy [Internet]. 2015 [cited 2016 May 21]. Available from: <http://www.nhs.uk/conditions/cerebral-palsy/pages/introduction.aspx>
7. Graham J. Foot drop: Explaining the causes, characteristics and treatment. *Br J Neurosci Nurs* 2010; 6: 168-172.
8. Burridge JH, Elessi K, Pickering RM, Taylor PN. Walking on an uneven surface: the effect of common peroneal stimulation on gait parameters and relationship between perceived and measured benefits in a sample of participants with a drop-foot. *Neuromodulat* 2007; 10: 59-67.
9. Bosch PR, Harris JE, Wing K, American Congress of Rehabilitation Medicine Stroke Movement Interventions S. Review of therapeutic electrical stimulation for dorsiflexion assist and orthotic substitution from the American Congress of Rehabilitation Medicine stroke movement interventions subcommittee. *Arch Phys Med Rehabil* 2014; 95: 390-396.
10. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011; 305: 50-58.
11. Geboers JFM, Geboers JFM, Wetzelaer WLH, Seelen HAM, Spaans F. Ankle-foot orthosis has limited effect on walking test parameters among patients with peripheral ankle dorsiflexor paresis. *J Rehabil Med* 2002; 34: 80-85.
12. Tyson SF, Kent RM. Effects of an Ankle-Foot Orthosis on Balance and Walking After Stroke: A Systematic Review and Pooled Meta-Analysis. *Arch Phys Med Rehabil*. 2013; 94: 1377-1385.
13. Tyson S, Sadeghi-Demneh E, Nester C. A systematic review and meta-analysis of the effect of an ankle-foot orthosis on gait biomechanics after stroke. *Clin Rehabil* 2013; 27: 879-891.
14. Bethoux F, Rogers HL, Nolan KJ, Abrams GM, Annaswamy TM, Brandstater M, et al. The Effects of Peroneal Nerve Functional Electrical Stimulation Versus Ankle-Foot Orthosis in Patients With Chronic Stroke: A Randomized Controlled Trial. *Neurorehabil Neural Repair* 2014; 28: 688-697.
15. Everaert DG, Stein RB, Abrams GM, Dromerick AW, Francisco GE, Hafner BJ. Effect of a foot-drop stimulator and ankle-foot orthosis on walking performance after stroke: a multicenter randomized controlled trial. *Neurorehabil Neural Repair* 2013; 27: 579-591.
16. Kluding PM, Dunning K, O'Dell MW, Wu SS, Ginosian J, Feld J, et al. Foot Drop Stimulation Versus Ankle Foot Orthosis After Stroke: 30-Week Outcomes. *Stroke* 2013; 44: 1660-1669.
17. Liberson WT, Holmquest HJ, Scot D, Dow M. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. *Arch Phys Med Rehabil* 1961; 42: 101-105.
18. Kottink AIR, Oostendorp LJM, Burke JH, Nene AV, Hermens HJ, MJ IJ. The orthotic effect of functional electrical stimulation on the improvement of walking in stroke patients with a dropped foot: A systematic review. *Artific Organs* 2004; 28: 577-586.
19. Robbins SM, Houghton PE, Woodbury MG, Brown JL. The Therapeutic Effect of Functional and Transcutaneous Electric Stimulation on Improving Gait Speed in Stroke Patients: A Meta-Analysis. *Arch Phys Med Rehabil* 2006; 87: 853-859.
20. Taylor PN. How long do Dropped foot stimulator users continue to use FES and how much does it cost? An eleven and six year clinical audit [Internet]. 10<sup>th</sup> International workshop of functional electrical stimulation and 15<sup>th</sup> International FES Society Conference; 2010 Sept 8-12; Vienna, Austria [cited 2016 Jan 17]. Available from: [http://www.odstockmedical.com/sites/default/files/how\\_long\\_do\\_dropped\\_foot\\_stimulator\\_users\\_continue\\_to\\_use\\_fes\\_and\\_how\\_much\\_does\\_it\\_cost.pdf](http://www.odstockmedical.com/sites/default/files/how_long_do_dropped_foot_stimulator_users_continue_to_use_fes_and_how_much_does_it_cost.pdf)

21. NHS Purchasing and Supplies Agency. Market Review: Functional electrical stimulation for drop foot of central neurological origin (CEP10011) [Internet]. 2010 [cited 2016 March 24]. Available from: <http://www.cedar.wales.nhs.uk/sitesplus/documents/1091/CEP10011%20FES%20market%20review.pdf>
22. Intercollegiate Stroke Working Party. National clinical guidelines for stroke. 4<sup>th</sup> edition. [Internet]. London: Royal College of Physicians (RCP). 2012 [cited 2016 May 21]. Available from: <https://www.rcplondon.ac.uk/guidelines-policy/stroke-guidelines>
23. Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning: A national clinical guideline. SIGN publication no. 118 [Internet]. Edinburgh; 2010 [cited 2016 May 21]. Available from: <http://www.sign.ac.uk/pdf/sign118.pdf>
24. National Institute of health and Clinical Excellence (NICE). Multiple Sclerosis in adults: management. NICE guidelines [CG186] [Internet]. 2014 [cited 2016 May 15]. Available from: <https://www.nice.org.uk/guidance/cg186?unlid=7618266092016224183024>
25. National Institute of health and Clinical Excellence (NICE). Spasticity in under 19s: management [CG145] [Internet]. 2012 [cited 2016 May 21]. Available from: <https://www.nice.org.uk/guidance/cg145?unlid=334144086201652914464>
26. Scottish Intercollegiate Guidelines Network (SIGN). Brain injury rehabilitation in adults. A national clinical guideline. SIGN publication no. 130 [Internet]. Edinburgh; 2013 [cited 2016 May 21]. Available from: <http://www.sign.ac.uk/pdf/sign130.pdf>
27. Street TD, Taylor PN, Swain ID. The Practical Use of Functional Electrical Stimulation in the Treatment of Foot Drop. UK Stroke Forum. Harrogate; 2014.
28. Roche A, o'Laighin G, Coote S. Surface-applied functional electrical stimulation for orthotic and therapeutic treatment of drop-foot after stroke - a systematic review. *Phys Ther Rev* 2009; 14: 63-80.
29. Hesse S, Werner C, Matthias K, Stephen K, Berteau M. Non-Velocity-Related Effects of a rigid Double-Stopped Ankle-Foot Orthosis on Gait and Lower Limb Muscle Activity of Hemiparetic Subjects With and Equinovarus Deformity. *Stroke* 1999; 30: 1855-1861.
30. Alam M, Choudhury IA, Mamat AB. Mechanism and Design Analysis of Articulated Ankle Foot Orthoses for Drop-Foot. *Sci World J* 2014; 1-14.
31. Dunning K, O'Dell M, Kluding P, Wu SS, Feld J, J. G, et al. The Functional Ambulation: Standard Treatment versus Electrical Stimulation Therapy (FASTEST) trial for stroke: study design and protocol. *Op Acc J Clin Trials* 2013; 5: 39-49.
32. Beckerman H, Becher J, Lankhorst GJ, Verbeek AM. Walking ability of stroke patients: Efficacy of tibial nerve blocking and a polypropylene ankle-foot orthosis. *Arch Phys Med Rehabil* 1996; 77: 1144-1151.
33. Howlett OA, Lannin NA, Ada L, McKinstry C. Functional Electrical Stimulation Improves Activity After Stroke: A Systematic Review With Meta-Analysis. *Arch Phys Med Rehabil* 2015; 96:934-943.
34. Everaert DG, Thompson AK, Chong SL, Stein RB. Does functional electrical stimulation for foot drop strengthen corticospinal connections? *Neurorehabil Neural Repair* 2010; 24: 168-177.
35. Thompson A, Lapallo B, Duffield M, Abel B, Pomerantz F. Repetitive common peroneal nerve stimulation increases ankle dorsiflexor motor evoked potentials in incomplete spinal cord lesions. *Exp Brain Res* 2011; 210: 143-152.
36. Rushton DN. Functional electrical stimulation and rehabilitation-a hypothesis. *Med Eng Phys* 2003; 25: 75-78.

37. Kottink AI, Hermens HJ, Nene AV, Tenniglo MJ, Groothuis-Oudshoorn CG, MJ IJ. Therapeutic effect of an implantable peroneal nerve stimulator in subjects with chronic stroke and footdrop: a randomized controlled trial. *Phys Ther* 2008; 88: 437-448.
38. Dunning K, O'Dell MW, Kluding P, McBride K. Peroneal Stimulation for Foot Drop After Stroke. A Systematic Review. *Am J Phys Med Rehabil* 2015; 94: 649-664.
39. Grant MJ, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. *Health Info Lib J* 2009; 26: 91-108.
40. Johnson CA, Burridge JH, Strike PW, Wood DE, Swain ID. The effect of combined use of botulinum toxin type A and functional electric stimulation in the treatment of spastic drop foot after stroke: a preliminary investigation. *Arch Phys Med Rehabil* 2004; 85: 902-909.
41. Burridge JH, Taylor P, Hagan S, Wood D, Swain I. The effects of common peroneal stimulation on the effort and speed of walking: a randomized controlled trial with chronic hemiplegic patients. *Clin Rehabil* 1997; 11: 201-210.
42. The Cochrane Collaboration. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [Internet]. 2011 [cited 2016 March 24]. Available from: [www.cochrane-handbook.org](http://www.cochrane-handbook.org)
43. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 2009; 6: 1-6.
44. Kottink AI, Hermens HJ, Nene AV, Tenniglo MJ, van der Aa HE, Buschman HP, et al. A randomized controlled trial of an implantable 2-channel peroneal nerve stimulator on walking speed and activity in poststroke hemiplegia. *Arch Phys Med Rehabil* 2007; 88: 971-978.
45. Salisbury L, Shiels J, Todd I, Dennis M. A feasibility study to investigate the clinical application of functional electrical stimulation (FES), for dropped foot, during the sub-acute phase of stroke - A randomized controlled trial. *Physiother Theory Prac* 2013; 29: 31-40.
46. Higgins JPT, Altman DG, P.C. G, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; 343: d5928.
47. World Health Organization. *International Classification of Functioning, Disability and Health*. Geneva; 2001.
48. Brehm M, Bus SA, Harlaar J, Nollet F. A candidate core set of outcome measures based on the international classification of functioning, disability and health for clinical studies on lower limb orthoses. *Prosthet Orthot Int* 2011; 35: 269-277.
49. Mudge S, Stott NS. Outcome measures to assess walking ability following stroke: a systematic review of the literature. *Physiother* 2007; 93: 189-200.
50. Sullivan JE, Crowner BE, Kluding PM, Nichols D, Rose DK, Yoshida R, et al. Outcome Measures for Individuals With Stroke: Process and Recommendations From the American Physical Therapy Association Neurology Section Task Force. *Phys Ther.* 2013; 93: 1383-1396.
51. Bethoux F, Rogers HL, Nolan KJ, Abrams GM, Annaswamy T, Brandstater M, et al. Long-Term Follow-up to a Randomized Controlled Trial Comparing Peroneal Nerve Functional Electrical Stimulation to an Ankle Foot Orthosis for Patients With Chronic Stroke. *Neurorehabil Neural Repair* 2015; 29: 911-922.
52. Geroïn C, Mazzoleni S, Smania N, Gandolfi M, Bonaiuti D, Gasperini G, et al. Systematic review of outcome measures of walking training using electromechanical and robotic devices in patients with stroke. *J Rehabil Med* 2013; 45: 987-996.



53. Kottink A, Tenniglo M, de VW, Hermens H, Buurke J. Effects of an implantable two-channel peroneal nerve stimulator versus conventional walking device on spatiotemporal parameters and kinematics of hemiparetic gait. *J Rehabil Med* 2012; 44: 51-57.
54. Condie E, Campbell J, Martina J. Report of a consensus conference on the orthotic management of stroke patients. Copenhagen, Denmark; 2004.
55. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *Annals Int Med* 2009; 151: W65-W94.
56. Kottink AIR, Hermens HJ, Nene AV, Tenniglo MJ, Groothuis-Oudshoorn CG, Ijzerman MJ. Therapeutic effect of an implantable peroneal nerve stimulator in subjects with chronic stroke and footdrop: a randomized controlled trial. *Phys Ther* 2008; 88: 437-448.
57. Voigt M, Sinkjaer T. Kinematic and kinetic analysis of the walking pattern in hemiplegic patients with foot-drop using a peroneal nerve stimulator. *Clin Biomech* 2000; 15: 340-351.
58. Hausdorff JM, Ring H. Effects of a new radio frequency-controlled neuroprosthesis on gait symmetry and rhythmicity in patients with chronic hemiparesis. *Am J Phys Med Rehabil* 2008; 87: 4-13.
59. Kim CM, Eng JJ, Whittaker MW. Effects of a simple functional electric system and/or a hinged ankle-foot orthosis on walking in persons with incomplete spinal cord injury. *Arch Phys Med Rehabil* 2004; 85: 1718-1723.
60. Van Swigchem R, Vloothuis J, Den Boer J, Weerdesteyn V, Geurts ACH. Is transcutaneous peroneal stimulation beneficial to patients with chronic stroke using an ankle-foot orthosis? A within-subjects study of patients' satisfaction, walking speed and physical activity level. *J Rehabil Med* 2010; 42: 117-121.
61. Scott SM, van der Linden ML, Hooper JE, Cowan P, Mercer TH. Quantification of gait kinematics and walking ability of people with multiple sclerosis who are new users of functional electrical stimulation. *J Rehabil Med* 2013; 45: 364-369.
62. Levin MF, Kleim JA, Wolf SL. What Do Motor "Recovery" and "Compensation" Mean in Patients Following Stroke? *Neurorehabil Neural Repair* 2009; 23: 313-319.
63. Meilahn JR. Tolerability and effectiveness of a neuroprosthesis for the treatment of footdrop in pediatric patients with hemiparetic cerebral palsy. *Phys Med Rehabil* 2013; 5: 503-509.
64. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: a systematic review. *Lancet Neurol* 2009; 8: 741-754.
65. French B, Thomas L, Leathley M, Sutton C, McAdam J, Forster A, et al. Does repetitive task training improve functional activity after stroke? A Cochrane systematic review and meta-analysis. *J Rehabil Med*. 2010; 42: 9-14.
66. Peurala SH, Karttunen AH, Sjogren T, Paltamaa J, Heinonen A. Evidence for the effectiveness of walking training on walking and self-care after stroke: a systematic review and meta-analysis of randomized controlled trials. *J Rehabil Med*. 2014; 46: 387-399.
67. Thompson AK, Estabrooks KL, Chong S, Stein RB. Spinal reflexes in ankle flexor and extensor muscles after chronic central nervous system lesions and functional electrical stimulation. *Neurorehabil Neural Repair* 2009; 23: 133-142.
68. Sanchez MC, Bussmann J, Janssen W, Horemans H, Chastin S, Heijnenbrok M, et al. Accelerometric assessment of different dimensions of natural walking during the first year after stroke: Recovery of amount, distribution, quality and speed of walking. *J Rehabil Med*. 2015; 47: 714-721.
69. Miller L, Rafferty D, Paul L, Mattison P. A comparison of the orthotic effect of the Odstock Dropped Foot Stimulator and the Walkaide functional electrical stimulation systems

- on energy cost and speed of walking in Multiple Sclerosis. *Disabil Rehabil Assist Tech* 2014; 10: 482-485.
70. Mulroy SJ, Eberly VJ, Gronely JK, Weiss W, Newsam CJ. Effect of AFO design on walking after stroke: Impact of ankle plantar flexion contracture. *Prosthet Orthot Int* 2010; 34: 277-292.
71. Lam WK, Leong JCY, Li YH, Hu Y, Lu WW. Biomechanical and electromyographic evaluation of ankle foot orthosis and dynamic ankle foot orthosis in spastic cerebral palsy. *Gait Posture* 2005; 22: 189-197.
72. Lowe CM, Wilson M, Sackley C, Barker K. Blind outcome assessment: the development and use of procedures to maintain and describe blinding in a pragmatic physiotherapy rehabilitation trial. *Clin Rehabil* 2011; 25: 264-274.
73. Harlaar J, Brehm M, Becher JG, Bregman DJ, Buurke J, Holtkamp F, et al. Studies examining the efficacy of ankle foot orthoses should report activity level and mechanical evidence. *Prosthet Orthot Int* 2010; 34: 327-335.
74. Bregman DJ, De Groot V, Van Diggele P, Meulman H, Houdijk H, Harlaar J. Polypropylene ankle foot orthoses to overcome drop-foot gait in central neurological patients: a mechanical and functional evaluation. *Prosthet Orthot Int* 2010; 34: 293-304.
75. Bregman DJ, van der Krogt MM, de Groot V, Harlaar J, Wisse M, Collins SH. The effect of ankle foot orthosis stiffness on the energy cost of walking: A simulation study. *Clin Biomech* 2011; 26: 955-961.
76. Heller BW, Clarke AJ, Good TR, Healey TJ, Nair S, Pratt EJ, et al. Automated setup of functional electrical stimulation for drop foot using a novel 64 channel prototype stimulator and electrode array: Results from a gait-lab based study. *Med Eng Phys* 2013; 35: 74-81.
77. Prenton S, Kenney LP, Stapleton C, Cooper G, Reeves ML, Heller BW, et al. Feasibility Study of a Take-Home Array-Based Functional Electrical Stimulation System With Automated Setup for Current Functional Electrical Stimulation Users With Foot-Drop. *Arch Phys Med Rehabil*. 2014; 95: 1870-1877.

Table I. *Inclusion Criteria.*

<p>Design</p> <ul style="list-style-type: none"><li>• Randomised Controlled Trials (RCT)</li></ul>
<p>Participants</p> <ul style="list-style-type: none"><li>• Participants with foot-drop of a central neurological origin</li></ul>
<p>Intervention</p> <ul style="list-style-type: none"><li>• Common peroneal nerve FES to address the specific impairment of foot-drop, with or without other areas of stimulation</li><li>• Stimulation eliciting a muscular contraction</li><li>• Trials where common peroneal stimulation is used during walking (overground or treadmill) as part of the intervention</li><li>• Trials studying combined-orthotic effects of foot-drop FES</li><li>• Trials where foot-drop FES and another intervention are used in combination but foot-drop FES is measured independently</li></ul>
<p>Comparator</p> <ul style="list-style-type: none"><li>• Trials comparing foot-drop FES with AFO (the term therapy was allowed as might involve AFO)</li></ul>
<p>Outcomes</p> <ul style="list-style-type: none"><li>• Measures of walking</li></ul>

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

	Trial design	N Diagnosis (R):(L)	Men: Women	Age (years)	Time since diagnosis	Current or new AFO users	AFO	Mechanical properties reported	FES	Setup for measurement done by	Use
<b>Bethoux (2014 &amp; 2015)+</b>	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=6.9yrs (6.43) AFO=6.86yrs (6.64)	New	Customized	No	Surface Walkaide	Not specified	Home 2wk progressive wearing schedule then AD
<b>Everaert (2013)*</b>	3 arm crossover Multiple sites	78 (43 FES: 35 AFO) CVA Not specified	FES=32:6** AFO=19:12**	FES=57.1 (12.9)** AFO=55.6 (11.9)**	FES=6.4mos (3.8)** AFO=6.9mos (3.2)**	New	Customized	No	Surface Walkaide	Not specified	Home AD
<b>Kluding (2013)+</b>	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=4.77yrs (5.29) AFO=4.34yrs (4.1)	Current	Customized*** PLUS TENS for 2wks	No	Surface NESS L300	Not specified	Both <ul style="list-style-type: none"> <li>• Bioness clinical protocols followed 15mins-AD</li> <li>• Training: 15mins x2 day 1wk then 20mins 2xday next 2wks</li> </ul>
<b>Kottink (2007)*~</b>	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=9.07yrs (9.29) AFO=5.67yrs (4.64)	Current	Combination***	No	Implanted 2-channel implant	Not specified	Home Gradual increase over 2wks, then AD
<b>Salisbury (2013)†</b>	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 20mins, 5 x wk with supervised/ independent walking as appropriate.

2 Abbreviations: FES= functional electrical stimulation; AFO=ankle-foot orthosis; \*=post intervention/dropout characteristics; +=ITT completed; ~~=based on 2007 not 2012 data; †= Pre intervention/drop out  
3 characteristics; CVA= Cerebrovascular accident/Stroke; \*\* post intervention/drop characteristics at later time point than is included in this review (12 weeks); yrs=years; mos=months; Customized= custom made/  
4 modified AFO; Combination= Different AFOs used by different participants; off the shelf= prefabricated/unmodified AFO; \*\*\*= both groups continued with physical therapy alongside intervention; TENS=  
5 transcutaneous electrical nerve stimulation with no motor response; wk=week; NESS L300=Bioness model; ODFS= Odstock foot-drop system; AD=all day.

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9 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 2014/2015	U	H	H	L	L	L
Everaert 2013	U	U	U	H	L	L
Kluding 2013	L	L	U	L	U	L
Kottink 2007	H	U	H	U	L	L
Salisbury 2013	H	L	H	U	L	L

10 Abbreviations: L= Low; U=Unclear; H=High.

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22 Table IV. *Outcome measurements and intervention effects.*

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	Walking outcome measures used & ICF level	Outcome collection points	Combined-orthotic effects
<b>Bethoux et al (2014/2015+)</b>	Activity: <ul style="list-style-type: none"> <li>• 10MWT<sup>1</sup></li> <li>• 6min walk test (distance)</li> <li>• Gaitrite Functional Ambulation Profile+</li> <li>• mEFAP (including TUG)</li> </ul> Participation+: <ul style="list-style-type: none"> <li>• SIS (Mobility, ADL/IADL &amp; social participation domains combined)<sup>1</sup></li> <li>• SIS mobility sub-scale</li> <li>• Perry ambulation categories based on 10MWT results</li> </ul>	0 Short: 1mos (not published) Medium: 3mos (not published) Long: 6mos 12 mos+	<ul style="list-style-type: none"> <li>• FES ↑ = AFO ↑</li> </ul>
<b>Everaert et al (2013)</b>	BFS: <ul style="list-style-type: none"> <li>• PCI over 4min test<sup>1</sup></li> </ul> Activity: <ul style="list-style-type: none"> <li>• 4min walking test (speed)<sup>1</sup></li> <li>• 10MWT</li> <li>• Modified RMI</li> </ul>	0, 3wks Short: 6wks	<ul style="list-style-type: none"> <li>• Modified RMI: between-group, post-intervention differences not reported</li> <li>• FES ↑ = AFO ↑: for other measures</li> </ul>
<b>Kluding et al (2013)</b>	BFS: <ul style="list-style-type: none"> <li>• LL Fugl Meyer</li> </ul> Activity: <ul style="list-style-type: none"> <li>• 10MWT (self and fast)<sup>1</sup></li> <li>• TUG</li> <li>• 6min walk test (distance)</li> </ul> Participation: <ul style="list-style-type: none"> <li>• SIS mobility sub-scale</li> <li>• Activity monitoring (Stepwatch @)</li> </ul>	0 Short: 6 weeks Medium: 12 weeks Long: 30wks (only change data published)	<ul style="list-style-type: none"> <li>• FES ↑ = AFO ↑</li> </ul>
<b>Kottink et al (2007)</b>	BFS: <ul style="list-style-type: none"> <li>• stride time*</li> <li>• stride length*</li> <li>• stride width*</li> <li>• step length*</li> <li>• stance phase %*</li> <li>• 1<sup>st</sup> double support phase %*</li> <li>• 1<sup>st</sup> single support phase %*</li> <li>• kinematics=hip, knee &amp; ankle*</li> </ul> Activity: <ul style="list-style-type: none"> <li>• 10MWT</li> <li>• 6min walk (speed)</li> <li>• Speed*</li> </ul> Participation:	0 Long: 26wks	<ul style="list-style-type: none"> <li>• FES &gt; AFO: Longer 1<sup>st</sup> single support phase %*; shorter Stance phase; 1<sup>st</sup> double support phase %*; Speed*; 10MWT; 6min walk (speed) at 26 wks</li> <li>• AFO spent less time less in sitting/lying than FES</li> <li>• FES ↑ = AFO ↑: all other measures</li> </ul>

- Activity monitoring (ActivPAL®)

<b>Salisbury et al (2013)</b>	BFS:	0	• FES ↑=AFO ↑
	<ul style="list-style-type: none"> <li>• Cadence (10MWT)</li> </ul>	Short: 6wks	
	Activity:	Medium: 12wks	
	<ul style="list-style-type: none"> <li>• Speed (10MWT)</li> <li>• FAC</li> </ul>		
	Participation:		
	<ul style="list-style-type: none"> <li>• SIS mobility sub-scale</li> </ul>		

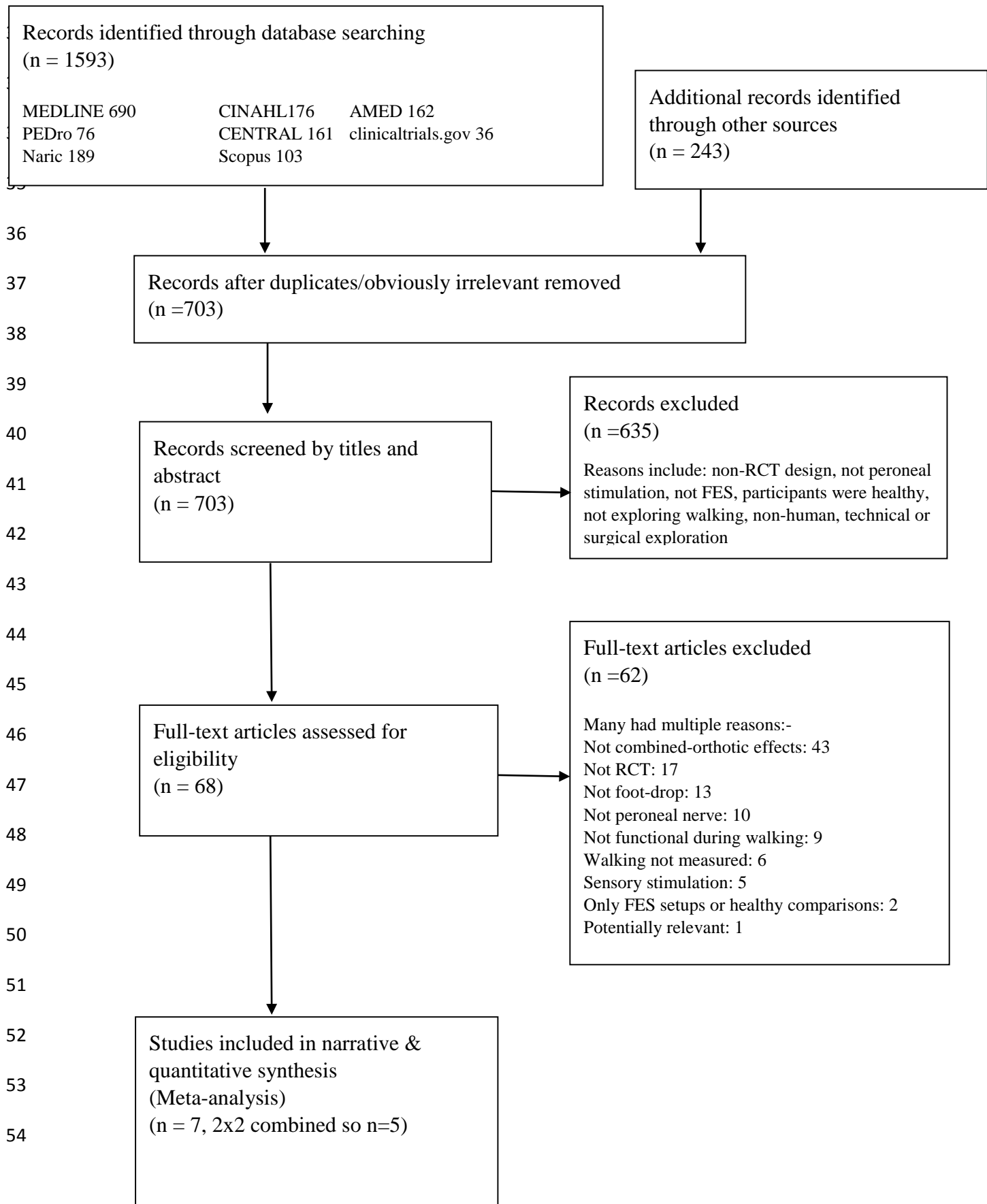
24 Abbreviations: wks=weeks; mos=months; min(s)=minute(s); mEFAP=modified Emory Functional Ambulation Profile; TUG=Timed Up and Go; QoL=Quality of Life; SIS=Stroke Impact Scale; ADL/IADL=  
 25 Activities of Daily Living/ Instrumental Activities of Daily Living; 10MWT=10-metre walk test; PCI=Physiological Cost Index; RMI=Rivermead Mobility Index; BBS=Berg Balance Scale; \*=from Kottink et al  
 26 (2012); FAC=Functional Ambulation categories; <sup>1</sup>=identified as primary outcome measure by authors; += not reported in Bethoux 2015 12 month follow up publication; ↑=increase; >=greater than; = =equal to; <=less  
 27 than.

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30 *Fig. 1.* Flowchart of trial selection.

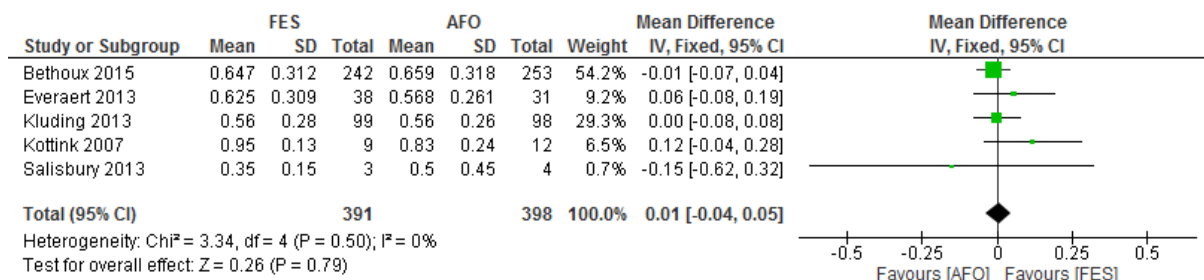
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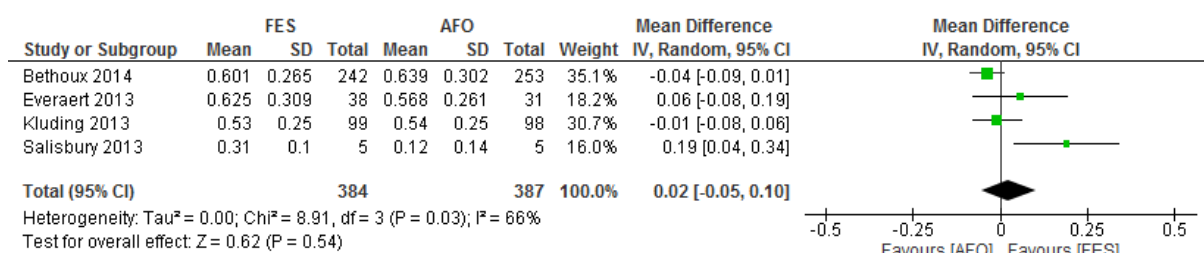
55 Fig. 2. Activity measure: 10-metre (m) walk test metres per second (m/s).

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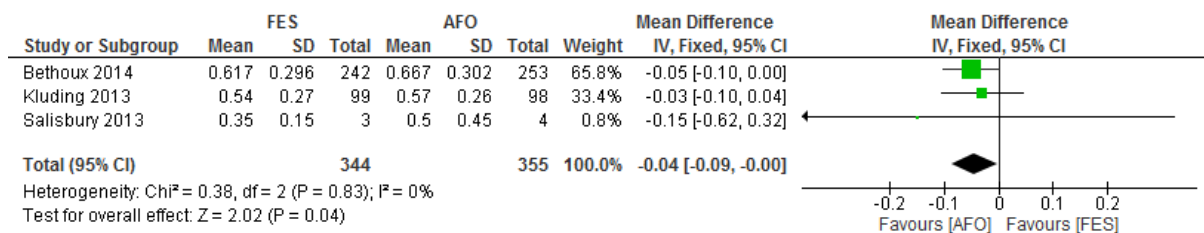
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58 2a) Final-assessment



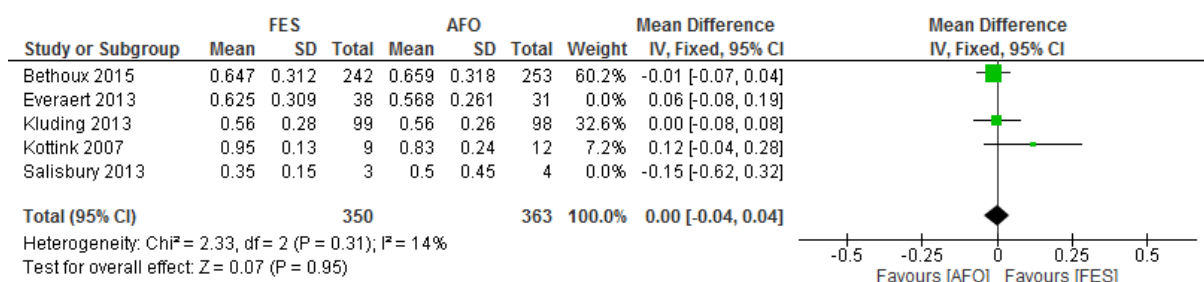
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60 2b) Short-term. Bethoux et al (2014) and Kluding et al (2013) data obtained via  
61 correspondence with authors



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63 2c) Medium-term. Bethoux et al (2014) and Kluding et al (2013) data obtained via  
64 correspondence with authors



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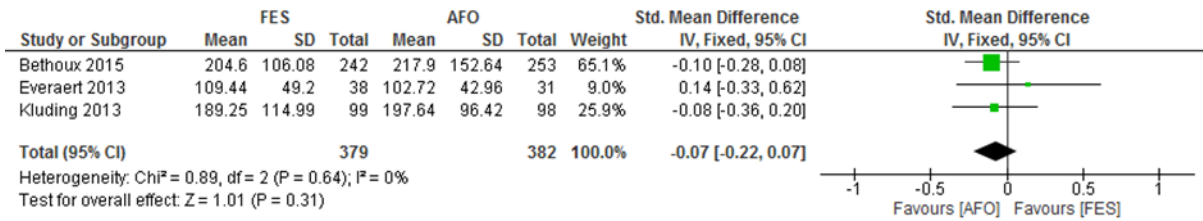
66 2d) Longer-term. Kluding et al (2013) data from correspondence with authors

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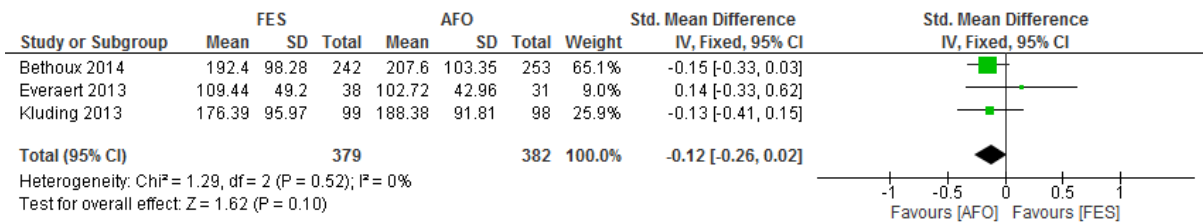
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70 *Fig. 3. Activity measure: Functional exercise capacity metres (m).*



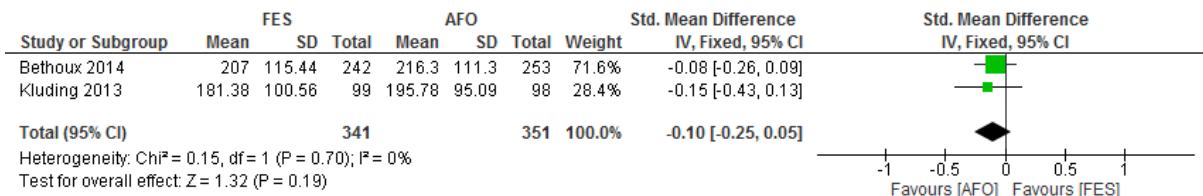
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72 3a) Final-assessment. Kluding et al (2013) data obtained via correspondence with authors.



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74 3b) Short-term. Bethoux et al (2014) and Kluding et al (2013) data obtained via  
75 correspondence with authors



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77 3c) Medium-term. Data obtained via correspondence with authors

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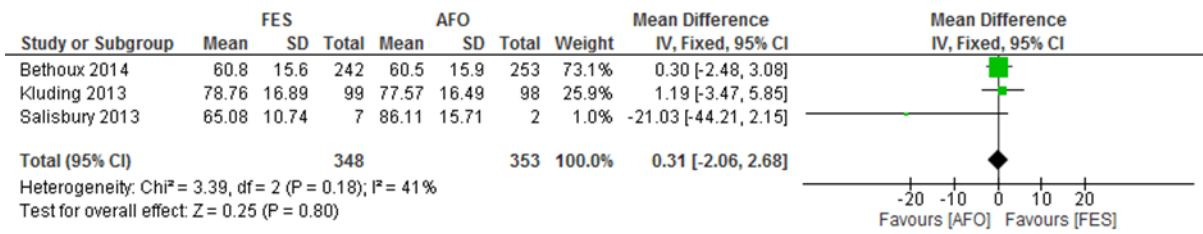
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86 *Fig. 4.* Participation measure: Stroke Impact Scale (mobility sub-scale).



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## APPENDIX I

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### 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 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 (metres per second) for Everaert et al (15).