FULL/LONG TITLE OF THE TRIAL

A prospective, single arm, pre-post trial to investigate whether quality of life (QOL) in children with cerebral palsy (GMFCS IV-V) can be effected using a robotic rehabilitation trainer (RRT) for 30minutes, 4 times a week for 6 weeks. The primary outcome will measure QOL using the Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD). Secondary outcomes are: range of movement (ROM) of hip and knee extension, popliteal angle, and dorsiflexion of the ankle using a goniometer; and spasticity of Hamstrings, rectus femoris, gastrocnemius and soleus using the Modified Tardieu Scale(MTS). Participant function using the Goal Attainment Scale (GAS) will also be measured. Outcomes will be assessed before and after intervention and then re-assessed at 6 weeks and 3months after intervention.

SHORT TRIAL TITLE / ACRONYM

Does t**he** use of a **R**obotic rehabilitation trainer (RRT) improve Q**O**L, ROM & functional goals **I**n children with **C**P? The 'heROIC' Trial.

- **This protocol has regard for the HRA guidance and order of content**

  Could make it closer to RCT unblinded if randomised to a waitlist, randomised to waitlist to controls baseline and then do 6 weeks can I create a control group

How can we capture staff feedback to capture feasibility:

Bowen – 8 domains of feasibility, use framework of how to look at feasibility overall. 5 questions to rate acceptability: to send an amendment to ethics to add consent for staff.

Contact Northern rep, CAHPR

-Is there a process for fidelity checks for the intervention: each participant was checked, and if anyone is concerned to message. They are checked at certain timepoints.

is there a process for reliability checking if multiple physios are doing assessments: everyone is trained to CPIP standards, second check in for reliability.

Unable to blind QOL questionnaire therefore is it relevant that physios are blinded to assessment.

RESEARCH REFERENCE NUMBERS

TRIAL REGISTRY NUMBER AND DATE

PROTOCOL VERSION NUMBER AND DATE

OTHER RESEARCH REFERENCE NUMBERS

SPONSOR / CO-SPONSORS / JOINT-SPONSORS

RESEARCH REFERENCE NUMBERS

IRAS Number:	**260371**
ISRCTN Number / Clinical trials.gov Number:	ISRCTN92095509
SPONSORS Number:	**NA**
FUNDERS Number:	**NA**

SIGNATURE PAGE

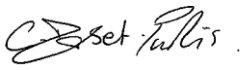
The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the trial publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

Chief Investigator:

Date:
..18../12./19..



Signature:
.....

Name: (please print):

.....Clare Dorset-Purkis.....

KEY TRIAL CONTACTS

Chief Investigator	Clare Dorset-Purkis Email: clare.dorset-purkis@nhs.net Tel: 02032270602 / 02077864804
Trial Co-ordinator	Clare Dorset-Purkis Email: clare.dorset-purkis@nhs.net

	Tel: 02032270602 / 02077864804
Sponsor	Whittington Health NHS Trust
Joint-sponsor(s)/co-sponsor(s)	Full contact details including phone, email and fax numbers of ALL organisations assuming sponsorship responsibilities as a joint- or co-sponsor/s (If applicable)
Funder(s)	NA
Clinical Trials Unit	NA
Key Protocol Contributors	Alesha Southby Email: aksouthby@gmail.com Tel: 07429935777
Statistician	Paul Bassett Email: paul@statsconsultancy.co.uk
Trials Pharmacist	NA
Committees	REC TBC

i. LIST of CONTENTS

ii. LIST OF ABBREVIATIONS

Define all unusual or 'technical' terms related to the trial. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.

AE	Adverse Event
AR	Adverse Reaction
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
EC	European Commission
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.
ISF	Investigator Site File (This forms part of the TMF)
ISRCTN	International Standard Randomised Controlled Trials Number
MA	Marketing Authorisation
NHS R&D	National Health Service Research & Development
NIMP	Non-Investigational Medicinal Product
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
QA	Quality Assurance
QP	Qualified Person
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification

SOP	Standard Operating Procedure
SSI	Site Specific Information
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee

iii. TRIAL SUMMARY

Trial Title	Does the use of a robotic rehabilitation trainer improve QOL, ROM & functional goals in children with CP?	
Trial Design	Single arm pre-post intervention study	
Trial Participants	Children age 5-18 with a diagnoses of CP GMFCS IV-V	
Planned Sample Size	25	
Treatment duration	6 weeks	
Follow up duration	3 months	
Planned Trial Period	4 months (per participant)	
	Objectives	Outcome Measures
Primary	QOL	CPCHILD
Secondary	• ROM of Lower limbs • Spasticity in lower limbs • Functional goals	• Goniometry measurement • Tardieu scale • GAS

iv. FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this trial)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
N/A	**N/A**

v. ROLE OF TRIAL SPONSOR AND FUNDER

This trial is not receiving any financial funding. The trial sponsor is Whittington Health with the support of NoClor.

The sponsor is supporting with components of the trial design and ethics and is the reporting body in the event of SAEs, SARs AND SUSARs. They will also support in components of the conduct, data analysis and interpretation, manuscript writing, and dissemination of results. The sponsor will work in collaboration with the PI/CI to make any final decisions on any aspect of the trial.

vi. ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

The protocol will be sent to the ethics committee who are completely uninvolved in the running of the trial and who cannot be unfairly influenced (either directly or indirectly) by people, or institutions, involved in the trial.

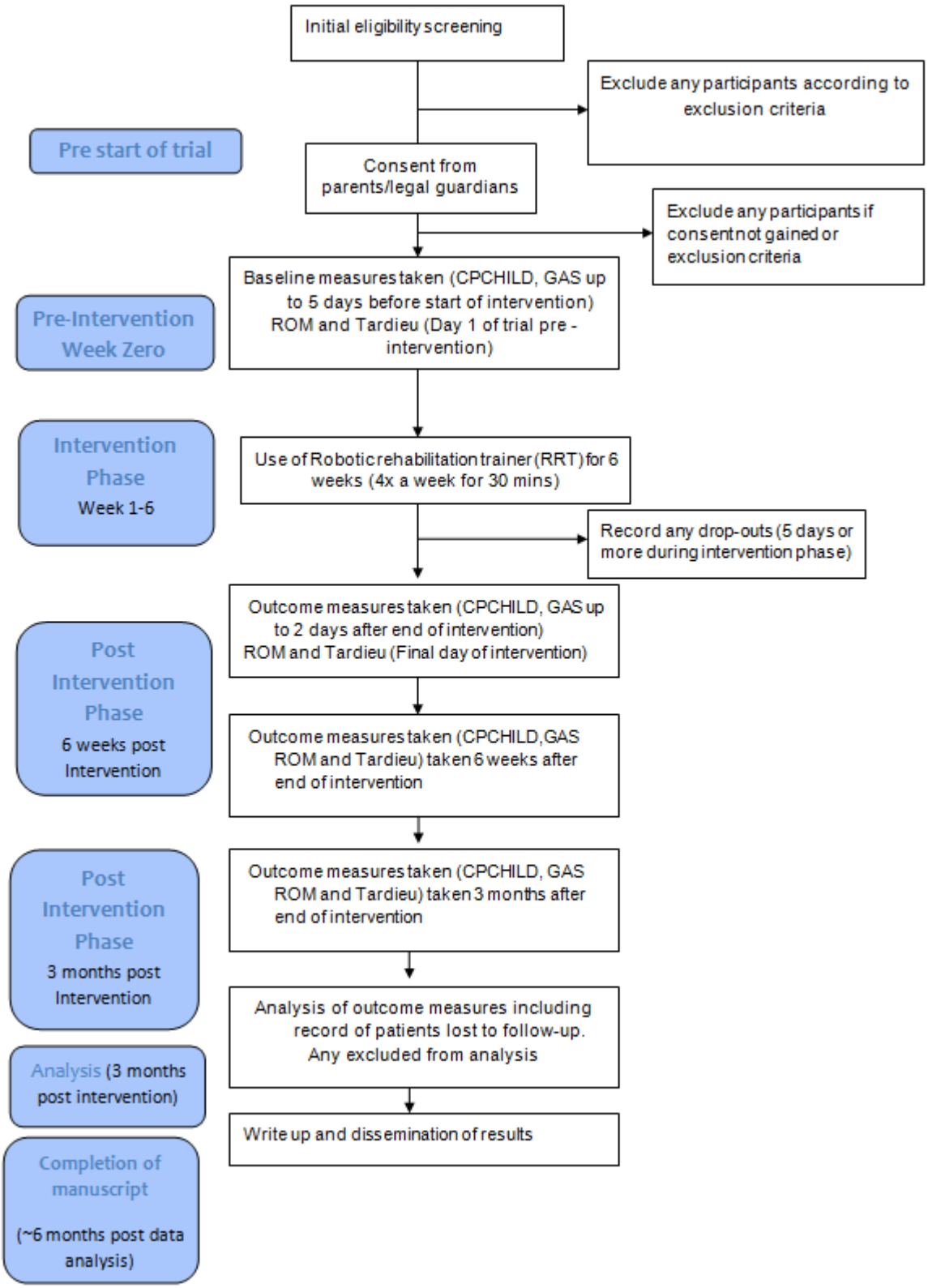
vii. PROTOCOL CONTRIBUTORS

- Clare Dorset-Purkis, Paediatric Physiotherapist. PI. Overview of protocol design
- Alesha Southby, Lead Paediatric Physiotherapist. PI support. Overview of protocol design
- Paul Bassett, Statistician.
- NoClor – protocol review
- Sally Douglas, Speech and Language therapist. Review of Patient Information sheets
- Caroline Brown. Head of Richard Cloudesley Primary School. Review of feasibility of intervention

viii. KEY WORDS:

Robotic rehabilitation trainer
Quality of Life
Cerebral Palsy (GMFCS IV/V)
Paediatric/Child
Physiotherapy
Range of Movement

ix. TRIAL FLOW CHART



1 BACKGROUND

CP is a disorder of the development of movement and posture, causing activity limitations attributed to non-progressive disturbances of the fetal or infant brain that may also affect sensation, perception, cognition, communication and behaviour (Richards). It is the most common physical disability in childhood occurring in 1 in 500 live births (Novak).

The Gross Motor Function Classification System (GMFCS) has become an important tool to describe motor function in children with CP (Carnahan). The GMFCS is based on self-initiated movement with emphasis on sitting, transfers, and mobility. The distinctions between levels are based on functional limitations, the need for hand-held mobility devices (such as walkers, crutches or canes) or wheeled mobility, and to a much lesser extent, quality of movement (Palisano).

There are five clinical levels with children in level 1 having the least limitations. A child or young person over the age of 5 years is unlikely to improve their GMFCS level.

There is no current cure for CP which is a permanent, but not unchanging condition; nonetheless, various treatments and therapies exist to enable individuals with CP to reach their fullest cognitive, emotional and physical potential. Due to the nature of CP, children have a high risk of developing musculoskeletal problems related to abnormal muscle tone, weakness, a lack of mobility, poor balance and loss of selective motor control which affects them differently as they are growing (Novak).

Physiotherapy management focuses on improving or maintaining gross motor function, activities of daily living and preventing secondary complications such as the development of contractures and deformity. It has been shown that an increase in intensity of therapy, repetition and motivation in children with CP increases rehabilitation potential (Mayer-Heim).

In recent years the development of dynamic or robotic-based therapies for children with CP is receiving more attention as it allows physical and cognitive integration, a combination which is expected to lead to better treatment results (Bayon).

Wu IN et al (2011) combined passive stretching and active movement rehabilitation in children with CP using a portable robot. They demonstrated improvements in joint bio-mechanical properties, motor control performance and functional capability in balance and mobility.

The IP is a robotic rehabilitation trainer (RRT) allowing patients with severe physical disability to stand and move in an upright position with natural weight-bearing. It provides assisted, guided and repetitive movements giving the user flexibility in adjustment and support, allowing for mobilisation with high intensity (Made for Movement, 2019).

Through clinical practice it has been widely noted that children with significant physical impairments related to their cerebral palsy often have issues with pain and physical wellbeing. Positioning and activity whether that be passive or active, has often helped to

improve pain and wellbeing and is recommended by Physiotherapists to reduce the severity of postural deformities and subsequent pain. In the literature it has been found that there were strong associations in poorer parent-reported QoL in the domains of physical wellbeing for children with cerebral palsy with higher severity of motor impairments (Arnaud et al, 2007). This study will attempt to show if the Innowalk can be helpful in this population to improve overall quality of life as reported by parents. Based on a recently published systematic review it has been reported that the Innowalk improves passive motion of the joints, muscle tone and general well-being associated with physical exercise (Schmidt-Lucke, 2019). This author has noted that the review is based on 11 studies which were mainly case studies, and therefore do not have a sufficiently powered analysis. The recommendations from the systematic review is that there is further more robust research into the Innowalk as it has been proposed that there are positive impacts to the wellbeing of children with cerebral palsy. This would therefore be the first cohort study looking at the effectiveness of the Innowalk Pro in a school setting.

The author believes the ability to move does not just improve physical health but also feelings of wellbeing and joy. Being active is an important part of child development. From our clinical practice it has been noted that children are more interactive when in more upright positions and performing physical activity, and in theory this would lead to improved communication, reduced discomfort and overall improved quality of life. Being on the same level as their peers can help with social interaction and give a child a sense of what is happening in the world around them enabling them to feel included and giving them a sense of personal achievement (Goodwin et al 2017). This study aims to capture any changes in these domains using the CPCHILD.

This prospective trial aims to investigate whether the quality of life (QOL) in children with cerebral palsy (CP) GMFCS level 4 and 5, who demonstrate more significant difficulties with their gross motor function, can be improved using the Innowalk Pro (IP), a robotic rehabilitation trainer (RRT). Secondary outcomes will assess range of movement (ROM) and spasticity in the lower limbs as well as patient specific goals and patient satisfaction. Outcomes will be re-assessed at 6 weeks and 12 weeks post intervention. The proposed study will be based in a special school across both the primary and secondary sites. The IP has been designed to adjust quickly and easily to different clinical users so it can be utilised in settings such as clinics and schools. This trial could also be used to evaluate the effectiveness of the IP in a multi-user setting and provide training recommendations within a school or clinic context.

2 RATIONALE

There are limited available peer-reviewed publications addressing the efficacy of robotic based therapy in CP (Wu 2011). Although a study (Wu 2011) did demonstrate that the combination of passive stretching and active movements using a portable robot has demonstrated improvements in joint biomechanical properties for children with CP; no platforms have yet evaluated this concept in a meaningful trial. (Bayon, 2016)

The intervention will be completed for 6 weeks for both clinical and feasibility reasons; each school half term is around 6 weeks long therefore if a child is having a block of physiotherapy intervention in the school setting, it will last for 6 weeks. The trial will investigate if the intervention is beneficial over this period. Studies have shown that children with CP can show benefits from having a 6 week standing programme. Paleg et al (2013) completed a systematic review on static standing in children with atypical development, and recommended that standing programs 5 days per week positively effect range of motion of hip, knee and ankle (45-60 min/day); and spasticity (30 to 45 min/day) with Gibson et al (2009) finding that hamstring length improved with an hour of static standing a day for 5 days a week for 6 weeks in children with non-ambulatory CP.

Current case study design research into the Innowalk shows positive effects of using it for a minimum of 30 minutes 5 times a week for 4 weeks (Schmidt-Lucke, 2019). This study will review possible long term carry over effects of the innowalk by re-assessing participants three months post completion of their intervention period of six weeks.

a. Assessment and management of risk

The Innowalk Pro is a robotic rehabilitation trainer (RRT) offering the possibility for assisted repetitive walking movements close to normal gait in an upright weight-bearing position. This movement generates flexion and extension of the hip, knee and ankle joints. The Innowalk Pro comprises of a motor-driven gait orthosis for legs, a weight support system, neck support, shoulder straps and side-support with a belt. When the participant transfers into the device it is in a sitting position and once secured with belts and straps he/she is moved from sitting into a position of weight-bearing. When the participant has reached the level of standing they can tolerate, the chest/hip belt is secured, and the device can start to move the legs. Accessories can be added and attached if needed such as a tray, supports to reduce over-stretching, shoulder straps and handles to encourage arm movement. The intervention of using the Innowalk Pro is not perceived to involve higher risk than what is known from their usual physiotherapy treatment as it offers movement through their available range of movement of their lower limbs. Representatives from the company supplying the Innowalk Pro will train physiotherapists involved in the research in how to correctly use the equipment. In turn physiotherapists will train members of school staff /other health professionals who will be supporting the participants with the equipment in accordance to the producer's user manual which includes observation of potential contraindications. A trained physiotherapist will either be present or on site during each session to resolve any concerns. If the participant feels any discomfort and/or pain during the session it will be stopped immediately and recorded appropriately, and then reviewed by the physiotherapist as to whether they can continue the study.

Potential contraindications will be reflected in the exclusion criteria and includes:

- Surgery within one year prior to study start
- Severe spasticity/tone which does not allow safe access to the equipment
- Advice from medical professionals not to stand
- Fixed flexion deformity of the hip >40 degrees, knee >50 degrees
- Severe scoliosis, windswept deformity, contractures or other deformities interfering with positioning of user in the Innowalk Pro
- Epilepsy not controlled by medication
- Lack of head control which is not possible to support in the Innowalk Pro
- Skin lesion/pressure areas in the contract areas of the padding/contact with the device
- Osteoporosis with previous or suspected spontaneous fractures of the lower extremities
- Lack of compliance of acceptance of dynamic standing
- Intolerance, pain or not able to cooperate or be positioned adequately within the Innowalk Pro

The Innowalk Pro will be used 4x a week for a 30 minute period for 6 consecutive weeks. Current research using the Innowalk Pro has used a similar duration and frequency of treatment and has not reported any adverse effects (Schmidt-Lucke, 2019).

Parents/caregivers will have consented to and understand their child's involvement in the study so both they and teaching staff will be aware to monitor for any adverse reactions and report this appropriately and in a timely manner.

The proposed trial design allows participants to continue their usual physiotherapy input with additional use of the Innowalk Pro for 4x sessions of 30 minutes per week. It is therefore considered that the trial is categorised as Type A = No higher than the risk of standard medical care.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

The primary research question is to assess the effect of the Innowalk Pro in a special school setting on QOL of children with CP (GMFCS IV-V), to address the hypothesis that the Innowalk Pro will improve QOL over a 6 week period of being used 4x a week for 30minutes. Secondary objectives will assess the effect of the Innowalk Pro over a 6 week period on range of movement and spasticity in the lower limbs as well as patient specific goals and whether any effects are sustained at 6 weeks and at 3 months after the intervention has stopped.

3.1 Primary objective

The primary research question is to assess the effect of the Innowalk Pro 4x a week for 30 mins in school as an adjunct to their usual physiotherapy care on QOL in children with CP (GMFCS IV-V), to address the hypothesis that the Innowalk Pro will improve QOL over a 6 week period of use.

The null hypothesis is that there is no change in QOL in children with CP (GMFCS IV-V) after using the Innowalk Pro 4x a week for 30 mins for 6 weeks.

3.2 Secondary objectives

Secondary objectives will review the effect of the Innowalk Pro 4x a week for 30 mins over a 6 week period on ROM and spasticity in the lower limbs as well as patient specific goals. Secondary objectives will also look at the long term effect of the Innowalk-Pro by re-assessing all outcomes at 6 weeks and 3 months after the participant has completed the 6 week block of using the Innowalk-Pro to see if there is any carryover in effect.

3.3 Outcome measures/endpoints

The main interest for the trial is looking to see if QOL can be affected by using the innowalk pro in addition to their normal physiotherapy routine in school. When working with CP, many different therapeutic approaches are used, however the basic principles recognised have; an emphasis on normalisation of the quality of movement, emphasis on functional activities and a focus on the skills necessary for performance of activities of daily living which all aim to improve the quality of life for the patient (Novak). QOL will be assessed using the Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD) questionnaire. The questionnaire is based on recommendations from caregivers, healthcare professionals experienced in the management of children with severe CP, and a review of other questionnaires. The 36-item questionnaire, has 6 domains: 1) Personal Care, 2) Positioning, Transfer, and Mobility, 3) Communication and Social Interaction, 4) Comfort, Emotions, and Behaviour, 5) Health, and 6) Overall Quality of Life. The questionnaire is a reliable and valid disease-specific measure of the caregivers' perspective on activity limitations, health status, well-being, and ease of care for children with severe CP (Mercado et al 2007).

Secondary end points will assess: hamstring length, measuring the popliteal angle; ROM of hip and knee extension, and dorsiflexion of the ankle with the knee flexed and extended using a goniometer; and spasticity of hamstrings, rectus femoris, gastrocnemius and soleus using the Modified Tardieu Scale (MTS). Despite best clinical practices, children with CP often develop contractures that limit their ROM, decrease their mobility and may be painful. Contractures occur when there is a unique muscle adaptation in which the muscle increases passive stiffness such that ROM around a joint is limited without active force production of the muscle. Muscle contractures are therefore a common secondary disability affecting patients with CP (Bache *et al.* 2003 and Smith et al 2011). Active and passive movement training is incorporated into therapeutic programs to improve functional ROM. Passive stretching is a critical component of maintaining muscle flexibility; however, stretching alone may not be enough. For children with CP, the possible reasons for insufficient effect may be due to immobility and/or undesired muscle activations associated with spasticity or dystonia (Wu 2011)

Wu (2011) investigated the efficacy of combined passive stretching and active movement training with motivating games using a portable rehabilitation robot. Children with mild to moderate spastic CP participated in robotic rehabilitation 3 times per week for 6 weeks and results showed significant improvement in both passive and active ankle dorsiflexion as a result of the 6-week training program. It is therefore predicted that the use of innowalk may have a beneficial effect on range of movement for participants in the study.

Secondary end points will also assess any improvement in patient specific goals using the GAS. The GAS allows functional goals to be assessed more individually than other standardised assessments in children with CP (Steenbeck 2011).

All end points will be assessed:

- On the day the trial begins
- On the day of completion of the intervention
- At 6 weeks and at 3 months after the trial is completed

All end points will look at the amount of change in quantitative data from baseline to the end of the intervention and then followed up at 6 weeks and 3 months of completion of the intervention phase to see if there is any long term effect. All data will be assessed using the mean scores to compare any effect between outcomes.

3.4 Primary endpoint/outcome

The primary endpoint is the mean change in quantitative data collected from the CPCHILD from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

3.5 Secondary endpoints/outcomes

Secondary endpoints will be:

Mean change in the popliteal angle (degrees) from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in ROM of hip extension (degrees) from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in ROM of knee extension (degrees) from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in ROM dorsiflexion with knee extended (degrees) from baseline immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in ROM dorsiflexion with knee flexed (degrees) from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in the spasticity of the rectus femoris muscle using the MTS from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in the spasticity of the hamstrings using the MTS from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in the spasticity of the gastrocnemius muscle using the MTS from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in the spasticity of the soleus muscle using the MTS from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

Mean change in perceived improvement in function using the GAS from baseline to immediately after stopping the 6 week intervention, and repeated at 6 weeks and 3 months following the end of the intervention phase.

3.6 Exploratory endpoints/outcomes

There are no other endpoints/outcomes which will be explored.

3.7 Table of endpoints/outcomes

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
Primary Objective **To assess the effect of the use of the Innowalk Pro over a 6 week period on QOL.**	Measurement of QOL of each participant using the CPCHILD:	Before (-3/5 days) the Intervention starts, immediately when the intervention ends after 6 weeks, and repeated 6 weeks and 3 months following the completion of using the Innowalk pro.
Secondary Objectives **To assess the effect of the use of the Innowalk Pro over a 6 week period on hamstring length.**	Measurement of popliteal angle of each participant using a goniometer.	Immediately pre and post intervention period of 6 weeks and repeated at 6 weeks and 3 months on completion of using the Innowalk Pro
To assess the effect of the use of the Innowalk Pro over a 6 week period on hip and knee extension	Measurement of hip and knee extension of each participant using a goniometer	
To assess the effect of the use of the Innowalk Pro over a 6 week period on	Measurement of dorsiflexion with knee flexed and knee extended of each participant using a goniometer	

dorsiflexion with the knee flexed and knee extended		
To assess the effect of the use of the Innowalk Pro over a 6 week period on spasticity of rectus femoris, hamstrings, gastrocnemius and soleus	Measurement of spasticity in the rectus femoris, hamstrings, gastrocnemius and soleus of each participant using the MTS.	
To assess the effect of the use of the Innowalk Pro over a 6 week period on perceived function	Measurement of perceived improvement in function for each participant using GAS.	Before (-3/5 days) the Intervention starts, immediately when the intervention ends after 6 weeks, and repeated at 6 weeks and 3 months following the completion of using the Innowalk pro.

4 TRIAL DESIGN

This prospective single-arm, pre-post design trial allows the researcher to evaluate the effect of the use of the Innowalk Pro as an adjunct to the participant's physiotherapy care allowing them to review its effectiveness in the school setting over a six week period and whether it has any effects at 6 weeks and 3 months post intervention.

As per the statistical power analysis (see 10.1), to achieve 90% power, 23 participants are required. The population that meet the inclusion criteria who attend the school is only 32 students and we anticipate that some families may not consent to being involved therefore a recruitment sample of 25 students is our aim. Due to low participant numbers it is therefore not possible to complete a randomised trial without significantly effecting the power calculation.

5 TRIAL SETTING

The trial will be run in a Whittington Health site in a special school in London with Primary and Secondary provision. The Whittington Health physiotherapists work in the special school alongside education staff. Training given to the staff supporting the students into the Innowalk Pro will be consistent and all outcome measures across the trial will be assessed by the same Physiotherapists meaning it is classed as a single centre trial.
The participants will all be recruited using a convenience sample from the special school who are all under the Whittington Health caseload. Their school based physiotherapy care is provided by the education staff at school who have been taught their physiotherapy

programme by a qualified physiotherapist. Students routinely access their standing frames or walker up to 3x a week and attend PE 1x a week in which a physiotherapist is present to review their activities – this includes full body stretches and a range of functional activities such as bridging/rolling/sitting, depending on the participant's ability. As a part of standard practice, teaching assistants will support the participant to perform their physiotherapy programme. For the intervention of utilising the Innowalk Pro, there will be a team of staff trained to support the participants in and out of the device and be able to recognise any signs of discomfort or contraindications to its use. The team will compile of 3x physiotherapists, 1x physiotherapy assistant, 2x teachers and up to 8 teaching assistants across the site. All staff are DBS checked and are known to the potential participants, understanding their individual needs. Training will be provided to all staff on equipment use and trained physiotherapists will administer the outcome measures. The Whittington Health physiotherapists are fully responsible for the running of this trial.

6 PARTICIPANT ELIGIBILITY CRITERIA

The trial population are selected using a convenience sample of students who attend a special school in London and are all under the Whittington Health caseload. The trial population will all have a diagnosis of CP and be classified as GMFCS IV/V.

6.1 Inclusion criteria

Any child aged 5-18 who attends the special school (primary and secondary) who has a diagnosis of CP classified at level IV-V whose parents/legal guardians give consent to partake in the trial.

6.2 Exclusion criteria

Any child who has had orthopaedic surgery in the last year to their lower limbs
Any child who meets the criteria but has had botox in their lower limbs within 3 months of the trial
Any child who meets the criteria however is younger than 5 or older than 18
Any contractures that don't allow access to the innowalk
Any orthopaedic/medical advice not to stand
Fixed flexion deformity of the hip >40 degrees, knee >50 degrees
Severe scoliosis, windswept deformity, contractures or other deformities interfering with positioning of user in the Innowalk Pro
Epilepsy not controlled by medication
Lack of head control which is not possible to support in the Innowalk Pro
Skin lesion/pressure areas in the contract areas of the padding/contact with the device
Osteoporosis with previous or suspected spontaneous fractures of the lower extremities
Lack of compliance of acceptance of dynamic standing
Intolerance, pain or not able to cooperate or be positioned adequately within the Innowalk Pro

7 TRIAL PROCEDURES

7.1 Recruitment

As the trial uses a convenience sample the participants are identified by the principal investigator as any student who attends a named special school (Richard Cloudesley Primary and Secondary) who meets the inclusion criteria. All students who attend the school will be screened and students who do not meet the inclusion criteria will have the data collected and reported on anonymously according to the exclusion criteria.

Sampling bias will be reduced by giving all students who meet the inclusion criteria the opportunity to take part in the study and those parents who consent to this will be eligible for the trial. A letter will be sent to all eligible participants parents/legal guardians with the contact details of the PI for them to express interest in their child participating in the trial. Once the number of participants needed to meet trial numbers has been met (first come first served basis), students will be placed on a waiting list as a reserve for any dropouts of the trial.

7.1.1 Participant identification

As the trial is using a convenience sample the participants will already be identifiable to the researchers as they are working in the school and therefore it is known that the students are eligible for the trial. It is known by the PI that there are 32 possible students that meet the inclusion criteria.

7.1.2 Screening

As all the medicals records are accessible by the researcher (lead physiotherapist at school) they will be screened to make sure that the participants are eligible for meeting the inclusion criteria for the trial and reviewing any exclusion criteria prior to families giving their consent. Medical records will include all the information needed to decide their eligibility including ROM of lower limbs taken in the last year. If students are deemed appropriate for involvement in the study by the PI, the parent/guardian will also sign consent that their child does not have any of the exclusion criteria.

7.1.3 Payment

As the participants will be a part of the trial during their normal school hours, there is not intent to pay any of the participants for any travel expenses as there will be no additional visits need to be made for the trial to be complete.

7.2 Consent

As the participants are either under the age of 16 or are 16-18 and have a level of cognitive impairment as a result of their diagnosis of Cerebral Palsy, their parent/legal guardian are able to give consent for them to participate in the trial. For the participants over the age of 16, although they are legally adults, due to their level of impairment it is deemed that they do not have the capacity to fully comprehend the full outline of the study and therefore a consultee declaration form will need to be completed by parents'/legal guardians.

The Department of Health Reference Guide to Consent for Examination or Treatment (2009) stated that: 'Where the person is an adult who lacks capacity or a child, then the experimental treatment cannot be given, unless it would be in their best interests'. The study hypothesises that the intervention would be in the best interest of the young person to use the equipment. There is no known harm for the young person and if there is any perceived pain then they would stop using the equipment immediately and be reassessed by the physiotherapist.

All of the participants in the study will have a patient information sheet (PIS), created alongside a speech and language therapist, presented to them at an appropriate language level to help them understand what is involved in the study, which will differ depending on age and cognitive ability. Parents/Legal guardians will also be given a PIS with the full details of the study to be able to give fully informed consent for their child. All written material must be approved by the REC and be in compliance with GCP, local regulatory requirements and legal requirements before being sent out.

The principal investigator (PI) has full responsibility for gaining consent for the research and has a certificate in Good Clinical Practice (GCP) and Informed Consent in Clinical Research conducted by Noclor. All of the proposed parents/legal guardians will be sent a PIS and invited to a presentation with a question and answer session, this will allow them to see the equipment being used during the trial as well as learn about the objectives and any possible risks and how these would be managed. They will then be questioned by the PI to make sure they fully understand the purpose and process of the research before giving consent and given the right to refuse their child to participate without reason with respect. For parents/legal guardians of potential participants age 16-18 a consultee declaration form will need to be completed in line with the Mental Capacity Act 2005. For any parents who do not understand English, a verbal interpreter will be booked via the NHS service. Any signed consent forms and patient identifiable information will be stored in a locked cupboard separate to the protocol and any data collected during the trial.

The participant and the parent have the right to withdraw at any time from the trial without giving reasons and without prejudice to his/her further treatment in the future. All participants' parents will be given the contact number and email of the PI where they can obtain further information about the trial at any time. If during the study any participants/families withdraw, any data collected up to that point can be used if consent is gained and this will be outlined within the consent literature. If at any time new information is required to be provided to a participant or re-consent is required, it is the responsibility of the PI to ensure this is done in a timely manner.

All of the participants in the trial are vulnerable due to being under 18 and having cognitive impairments. It is therefore the PI's responsibility to ensure that all participants are protected and participate in the study voluntarily in an environment free from coercion or undue influence. This will be ensured through the training process of all members of staff involved in the trial. This will mean if any participant during the process of the trial refuses to take part, staff cannot force them to take part and must document this appropriately. The PI will then contact the parents/legal guardians to find out whether they would like their child to continue to take part in the trial, but if the participant continues to refuse to take part their rights must be respected.

7.3 Method of implementing the randomisation/allocation sequence

This trial will not use randomisation due to it being a single arm pre-post intervention using a convenience sample. All eligible participants' parents/legal guardians at the special school will be sent a letter outlining the purpose of the trial and a contact number to express their interest. The participants will be then selected on a first come first served basis to enter the trial and begin the consent process until the number of participants required for the study is met.

7.6 Baseline data

There are a number of outcome measures that need to be collected as a baseline before the intervention begins. The following listed below are of interest in the study as we hypothesise the intervention may have some effect on them. The same outcomes will be followed up post intervention.

Measurement of QOL will be completed using the CPCHILD which is a paper based survey, completed independently by the child's parents with a pre- explanation by a member of the research team. This can be taken up to 5 days before the intervention period takes place.

All ROM measurements will be taken in accordance with the CPIP-UK standardised assessment protocol and taken on the day the intervention period starts. This will be completed by two trained members of the research team.

- Measurement of popliteal angle of each participant using a goniometer in both legs in supine.
- Measurement of hip extension of each participant using a goniometer in both legs in a prone position
- Measurement of knee extension of each participant using a goniometer in both legs in supine
- Measurement of dorsiflexion with knee flexed and knee extended of each participant using a goniometer in both legs in supine

Measurement of spasticity in the hamstrings, gastrocnemius and soleus of each participant using the MTS in both legs in supine will be taken on the day the intervention starts and rectus femoris for both legs will be taken in prone.

Setting of individual goal for the intervention of using the RRT with parents using Goal Attainment Scale can be taken up to 5 days before the intervention period starts. This will be done by the parent in collaboration with a member of the research team.

7.7 Trial assessments

All participants in the study will receive their usual level of physiotherapy care before during and after the trial is completed, this includes the use of standing frames/walkers/direct physiotherapy sessions as needed, and this will not change due to them being involved in the study.

The CPCHILD and GAS data will be taken up to 5 days before the intervention of using the RRT starts. The students will be assessed before the trial begins to assess the set up for each child which will be carried out by the physiotherapist, this requires measurements of the length of knee crease to sole of the foot, and the height of the student to be taken. The measurement of the popliteal angle, hip and knee extension, dorsiflexion with knee extended and knee flexed, and spasticity of the rectus femoris, hamstrings, gastrocnemius and soleus will all happen on day of the trial before the participants begin using the RRT. All measurements will be taken by trained members of the research team. The study will be

single blinded so that the outcome measures will be carried out by physiotherapists at the opposite school (primary/secondary) who do not know who has started the intervention and who has finished the intervention so as to reduce researcher bias.

Each participant will receive the intervention of using the RRT for 30 minutes a day, 4 times a week for 6 weeks. The RRT has a tablet which will record the time each participant has spent using the equipment, what angle they stood at, how far they technically travelled in metres and the participants' satisfaction when using it using a 4 point scale of smiley faces – sad, indifferent, happy and very happy. This is recorded at the end of every session the participant has using the equipment. If the desired 30 minutes using the RRT is not reached for a reason this will be recorded.

On the final day of using the RRT, within an hour after completing the session of 30 minutes; all measurements of the popliteal angle, hip and knee extension, dorsiflexion with knee extended and knee flexed, and spasticity of the rectus femoris, hamstrings, gastrocnemius and soleus will be repeated by a physiotherapist within one hour. The CPCHILD and GAS data will also be re-collected from parents within 2 days of the participants completing the intervention.

7.8 Long term follow-up assessments

All outcome measure data will be re-collected at 6 weeks following the last day of intervention (+/-3 days) and again at 3 months (+/- 3days). All ROM measurements of the popliteal angle, hip and knee extension, dorsiflexion with knee extended and knee flexed, and spasticity of the rectus femoris, hamstrings, gastrocnemius and soleus will be repeated by a physiotherapist in school. The CPCHILD and GAS data will also be re-collected from parents again at this time. The CPCHILD data is collected via a questionnaire which is intended to be self-administered (Narayanan 2007). They can complete it at home and send it back via their child to school or complete it at the school if they prefer. If the questionnaires are not sent back within 5 days of it being sent out, then the Physiotherapist will call the parents to ask the information over the phone. The collection of data from the GAS goals should be completed by the physiotherapist in conjunction with speaking to the parents and therefore establishing if they have met their goal set prior to the intervention taking place.

Once the intervention is completed there will be no change in the provision of physiotherapy within school to what they normally receive and therefore they will receive their usual standard of care.

In an event where the participant is not in school for a prolonged period and missed the follow-up window at 6 weeks (+/-3days) and 3 months (+/-3days) the participants will then be identified as 'lost to follow up.' Retention strategies that will be used will be a message sent to parents reminding them that assessments will be repeated and if there is any problems with attending school at that time to let us know immediately. Home visits can be carried out with permission from parents, by the physiotherapist, to collect the data if absolutely necessary. Home visits are carried out as part of the care package from the physiotherapist and lone worker policy is always followed.

Data can still be recorded and analysed for each participant up until the point of being lost to follow-up.

7.9 Qualitative assessments

The tablet on the RRT automatically records the participants' satisfaction when using it using a 4 point scale of smiley faces – sad, indifferent, happy and very happy which is recorded after every use. This encourages the participant to portray how they feel about using the device each time they use it. It will give an overall picture at the end of the trial of how much satisfaction each participant had out of using the RRT. It is noted that this is not a standardised scale and could be subject to interpretation depending on the cognitive level of the participant but can be commented on in the case report following the trial.

7.10 Withdrawal criteria

Participants will be withdrawn from the trial if:

- They are off school for 5 or more days during the intervention phase.
- The parents withdraw consent for the participant to participate in the study
- The participant develops any kind of pressure areas and pain relating to the RRT they need to stop using it and therefore be withdrawn from the trial for further intervention
- Where possible participants who are withdrawn from the trial will be replaced with another participant who meets the inclusion criteria, recruited from the same school.
- The trial will be prematurely stopped if there are any SUSARs.
- Any data collected up until the point of withdrawal will still be collected and unless the parent's have withdrawn consent data will still be collected 6 weeks and 3 months following the end of the intervention period.

7.11 Storage and analysis of clinical samples

Not applicable

7.12 End of trial

The trial will end after the last set of data is collected from the last student 3 months following the end of their intervention period using the RRT.

8 TRIAL TREATMENTS

8.1 Name and description of measures, assessments and treatments(s)

The CPCHILD is an objective measure used for children and their care givers to quantify health related quality of life. It has been used in previous research as a pre and post intervention measure (Narayanan 2007)

The CPCHILD© currently consists of 37 items distributed over among 6 sections representing the following domains:

1. Activities of Daily Living/Personal Care (9 items)
2. Positioning, Transferring & Mobility (8 items)
3. Comfort & Emotions (9 items)
4. Communication & Social Interaction (7 items)
5. Health (3 items)
6. Overall Quality of Life (1 item)

The CPCHILD questionnaire has been demonstrated to have excellent reliability and appears to be a valid measure of caregivers' perspectives on the health status, functional limitations, and well-being of children with severe non-ambulatory cerebral palsy. Overall reliability was excellent with an intraclass correlation coefficient ICC for CPCHILD© total score of 0.85 (95% CI: 0.68-0.93) (Narayanan UG 2007)

ROM assessments: Passive joint ROM will be assessed pre and post intervention in standardised positioning following the Cerebral Palsy Integrated Pathway(CPIP)-UK protocol- reference

- Hip extension and flexion using a goniometer
- Knee extension using a goniometer
- Popliteal angle (hamstring length) using a goniometer
- Ankle dorsi-flexion in knee extension and knee flexion using a goniometer

These will be assessed by experienced (more than 3 years practicing) Physiotherapists and has been shown to be a reliable way of measuring joint ROM with proven high inter-test reliability in children with spastic cerebral palsy (Mutlu, 2007)

Spasticity assessment: Spasticity will be assessed in the same standardised position as joint range of motion following the CPIP-UK protocol. The MTS will be used by trained experienced Physiotherapists (more than 3 years' experience) to record spasticity in the following muscles

- Rectus femoris
- Hamstrings
- Gastrocnemius
- Soleus

The MTS is a measure for spasticity used in children with CP and has high inter and intra rater reliability (Gracie, 2010)

The Goal Attainment Scale (GAS) will be used to determine specific functional goals for each participant and has shown to be applicable to this patient group Law 2004. The GAS has good inter rater reliability for use with children with CP (Steenbeek, 2010)

The scale is rated between -2 'much less than expected to +2 'much more than expected level of attainment of a goal. Goals will be set with parents/caregivers in collaboration with Physiotherapists prior to the start of the intervention and then scored by parents/care givers in collaboration with Physiotherapists at the end of the intervention period and at 6 weeks and 3 months after the intervention period.

8.2 Intervention(s)

For the intervention of utilising the Innowalk Pro, there will be a team of staff trained to support the participants in and out of the device and be able to recognise any signs of discomfort or contraindications to its use. The team will compile of 3x physiotherapists, 1x physiotherapy assistant, 2x teachers and up to 8 teaching assistants across both the primary

and secondary sites. Training will be provided to all staff on equipment use and trained physiotherapists will administer the outcome measures.

The innowalk Pro small will be used for participants who are of a height: 100-145 cm and a weight: max 65 kg.

The Innowalk Pro large will be used for participants who are of a height: User height: 145-190 cm
User weight: max 95 kg

Assessment for the Innowalk Pro will be carried out by the Physiotherapist and then trained Teaching assistants (TA's), will support the participant to use the equipment for the 30 minutes a day 4 days a week alongside their usual routine for 6 weeks.

The participant will be hoisted on and off the equipment, fully supported in the equipment by the chest and leg supports and supervised at all times during the process.

8.3 Control

There will be no control group.

8.4 Drug storage and supply

Not applicable

8.5 Preparation and labelling of Investigational Medical Device.

The Innowalk PRO is listed as Grade 1 classification on the Medical Device Directive registered with notified body of conformity through assessment with NEMKO AS Identification No. 0470

Made for Movement Group AS are certified ISO13485 management system standards and are registered with certification body DNV GL Presafe AS.

Innowalk PRO

Hereby, Made for Movement Group AS, declares that the above listed products with accessories are in risk class I and are in compliance with the essential requirements and other relevant provisions of directive:

93/42-EEC Council directive of medical devices, Annex VII / MDD 93/42 ECC

- FOR-2005-12-15-1690 Forskrift om medisinsk utstyr
- NEK IEC 60601-1 3.1 edition
- NEK IEC 60601-1-2 4. edition
- NEK IEC 60601-1-6 3. edition
- NEK IEC 60601-1-11 1. edition
- NEK EN 62366 :2016 1. edition
- NS-EN ISO 14971 :2012

- NS-EN ISO 13485 :2016
- NS-EN 12182 :2012
- NS-EN 60529 :2013

8.6 Treatment schedules/plan

Participants will use the RRT for 30 mins a day for 4 days a week during school hours for 6 weeks during the course of the trial. Time using the RRT will not exceed 30 minutes each time. If the participant misses a session for any reason, they may restart the trial as long as they do not miss more than 5 days of intervention over the course of 6 weeks – any missed intervention will be documented accordingly.

8.9 Concomitant treatment(s)

As written in the exclusion criteria, concomitant treatments are:

-Botox injections given 3 months prior or during the trial period

-Spinal or lower limb surgery within the year leading up to the trial or during the trial period.

8.10 Trial restrictions

If at any point during the trial the participant meets any of the exclusion criteria they will then be excluded from the trial for example the participant has active botulinum toxin injections during the trial phase.

8.11 Assessment of compliance with treatment

Each participant will be asked if they are agreeable to the intervention each time. They will also be asked for feedback during the intervention to ensure it is suitable to continue. The participants who have expressive and receptive communication difficulties will use alternative forms of communication to express consent. An individualised communication passport will be used and trained staff will communicate with the participant using the passport as needed.

Participants will be encouraged by members of the research team and positive feedback from school staff to complete the intervention as described to improve compliance and any missed sessions or reduced sessions of the intervention will be recorded.

If a participant is non-compliant for 20% or more (5days) during the intervention phase, they will be withdrawn from the trial and data will be recorded accordingly.

A trained member of staff will record compliance via the tablet attached to the Innowalk Pro. If there is non-compliance it will be reported to the PI/CI and at the end of the trial period this will be reported to the sponsor.

9 EVENT MANAGEMENT and REPORTING

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.
Adverse Reaction (AR)	An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions. It is important to note that this is entirely separate to the known side effects listed in the SmPC. It is specifically a temporal relationship between taking the drug, the half-life, and the time of the event or any valid alternative etiology that would explain the event.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.

9.2 Operational definitions for (S)AEs

We do not anticipate any (S)AE's, and if they were to occur we would use the SAE CRF form provided by NoClor to report such an event to Whittington Health and NoClor.

Exceptions to reporting (S)AE's may include hospitalisation for:

- Routine treatment or monitoring of the studied indication not associated with any deterioration in condition.
- Any admission to hospital or other institution for general care where there was no deterioration in condition.
- Treatment on an emergency, outpatient basis for an event **not** fulfilling any of the definitions of serious as given above and not resulting in hospital admission.

9.3 Recording and reporting of SAEs, SARs AND SUSARs

All SAEs / SUSARs occurring from the time of written informed consent until completion of the final outcome measures (3 months post intervention) must be recorded on the SAE report form and emailed securely to the Sponsor within 24 hours of the research staff becoming aware of the event. Once all resulting queries have been resolved, the Sponsor will request the original form should also be posted to the Sponsor and a copy to be retained on site.

For each SAEs/ SUSARs the following information will be collected:

- full details in medical terms and case description
- event duration (start and end dates, if applicable)
- action taken
- outcome
- seriousness criteria
- causality (i.e. relatedness to investigation), in the opinion of the investigator
- whether the event would be considered anticipated.

Any change of condition or other follow-up information should be emailed securely to the Sponsor as soon as it is available or at least within 24 hours of the information becoming available. Events will be followed up until the event has resolved or a final outcome has been reached.

All SAEs assigned by the PI or delegate (or following central review) as both suspected to be related to IMP-treatment and unexpected will be classified as SUSARs and will be subject to expedited reporting to the Medicines and Healthcare Products Regulatory Agency (MHRA). The sponsor will inform the MHRA, the REC and Marketing Authorisation Holder (if not the sponsor) of SUSARs within the required expedited reporting timescales.

9.4 Responsibilities

Principal Investigator (PI):

Checking for AEs and ARs when participants attend for treatment and follow-up.

1. Using medical judgement in assigning seriousness, causality and whether the event/reaction was anticipated.

2. Using medical judgement in assigning seriousness and causality and providing an opinion on whether the event/reaction was anticipated.

3. Ensuring that all SAEs are recorded and reported to the sponsor within 24 hours of becoming aware of the event and provide further follow-up information as soon as available. Ensuring that SAEs are chased with Sponsor if a record of receipt is not received within 2 working days of initial reporting.

4. Ensuring that AEs and ARs are recorded and reported to the sponsor in line with the requirements of the protocol.

Chief Investigator (CI):

1. Clinical oversight of the safety of patients participating in the trial, including an ongoing review of the risk / benefit.

2. Using medical judgement in assigning the SAEs seriousness, causality and whether the event was anticipated (in line with the Reference Safety Information) where it has not been possible to obtain local medical assessment.

3. Using medical judgement in assigning whether and event/reaction was anticipated or expectedness.

4. Immediate review of all SUSARs.

5. Review of specific SAEs and SARs in accordance with the trial risk assessment and protocol as detailed in the Trial Monitoring Plan.

6. Central data collection and verification of AEs, ARs, SAEs, SARs and SUSARs according to the trial protocol onto a database.

7. Reporting safety information to the TSC, sponsor and regulatory authorities for the ongoing assessment of the risk / benefit according to the Trial Monitoring Plan.

8. Reporting safety information to the independent oversight committees identified for the trial (Data Monitoring Committee (DMC) and / or Trial Steering Committee (TSC)) according to the Trial Monitoring Plan.

9. Notifying site Investigators of SUSARs that occur within the trial.

10. Checking for and notifying PIs of updates to the Reference Safety Information for the trial.

Sponsor:

1. Labelling of proposed amendments as substantial or non-substantial

2. Approval of proposed amendments

3. Verification of AEs, ARs, SAEs, SARs and SUSARs according to the trial protocol onto a database

4. Monitoring and auditing of research

5. Verification of research data

Trial Steering Committee (TSC):

In accordance with the Trial Terms of Reference for the TSC, periodically reviewing safety data and liaising with the DMC regarding safety issues.

Data Monitoring Committee (DMC):

In accordance with the Trial Terms of Reference for the DMC, periodically reviewing overall safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

9.5 Notification of deaths

All deaths will be reported to the sponsor irrespective of whether the death is related to disease progression, the IMP, or an unrelated event.

9.6 Reporting urgent safety measures

If any urgent safety measures are taken the CI/Sponsor shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant REC of the measures taken and the circumstances giving rise to those measures.

9.7 The type and duration of the follow-up of participants after adverse reactions.

If any adverse reactions occur during the trial period the participant will be reviewed as specified above by the PI and CI and the participants parents/legal guardian notified immediately. Any medical intervention deemed appropriate will be advised and the research team will support the participant and their parent/legal guardian to seek this out. The head of the school as loco parentis will also be advised.

The participant with any adverse reaction will be followed up by the PI/CI until it is deemed the adverse reaction is resolved. This will be completed with verbal or written communication with parents/legal guardians

Any SUSAR will need to be reported to the Sponsor irrespective of how long after treatment administration the reaction has occurred until resolved

10 STATISTICS AND DATA ANALYSIS

10.1 Sample size calculation

The sample size was based on detecting a change from pre-intervention to immediately post intervention at 6 weeks for the primary outcome, the CPCHILD score. Previous research from three papers (Narayanan 2007, Zalmstra 2014, Kraus 2017*)* were used to estimate the baseline score in the patient group. Based on this research, pre-intervention, the mean CPCHILD score was estimated to be 53, with a standard deviation of 14. The standard deviation of the change in score from pre to post-intervention is unknown, but is conservatively estimated to the same as the pre-intervention standard deviation, namely 14

units. A change in score between time points of 10 units is regarded as being of clinical importance. Using a 5% significance level and 90% power, it is calculated that 23 subjects are required to detect this level of difference. To allow for a possible dropout of the study of 5%, 25 subjects will be recruited into the study.

The CP Child is scored out of 100 therefore using a change between time points of 10 units is felt to be clinically important by the research team as a lower change in scores would not be clinically significant and would require a higher number of subjects which is not feasible. For example it is calculated to detect a difference in scores between time-points of:

- 5 units would require 85 subjects
- 7 units would require 44 subjects

The researchers believe in this case a lower change in scores of e.g. 5 units would not be clinically important to this population. It would also not be feasible to have any higher participant numbers due to the school population.

10.2 Planned recruitment rate

As the participant group is a convenience sample it is estimated adequate sample size of 25 recruited participants will be able to gained within one month of ethics approval. The participants will be recruited from one school site which has a primary and secondary campus. It is expected that all parents/guardians will consent to the intervention.

10.3 Statistical analysis plan

10.3.1 Summary of baseline data and flow of patients

As we are comparing the same participants pre and post interventions outcomes there is no intergroup comparison to comment on and therefore baseline comparability is controlled.

The demographic and baseline characteristics of the patient group will be summarised. The number and percentage in each category will be reported for categorical measures. Continuous variables will be summarised by the mean and standard deviation if normally distributed, and the median and inter-quartile range if not.

10.3.2 Primary outcome analysis

The primary outcome is the CPCHILD score at 6-weeks post intervention. The change from baseline will be assessed using the paired t-test if the changes in scores between time points is found to be normally distributed. If not, the Wilcoxon matched-pairs test will be used. Only observed data will be analysed with, no imputation of missing data.

10.3.3 Secondary outcome analysis

All secondary outcomes are continuous in nature meaning they will be analysed in the same way as the primary outcome. The change from baseline will be assessed using the paired t-test if the changes in scores between time points is found to be normally distributed. If not,

the Wilcoxon matched-pairs test will be used. Only observed data will be analysed with, no imputation of missing data

10.4 Subgroup analyses

All patients will be analysed together, and no subgroup analyses will be performed

10.5 Adjusted analysis

This is not relevant as the study only plans to analyse a single group of patients and therefore this reduces confounding variables as the patients data is being compared against themselves. Due to the nature of cerebral palsy the participants will have some different characteristics/comorbidities, however, as the same participants are being compared at both time-points and receiving the same level of intervention, the characteristics of these participants should be the same on both occasions and therefore this controls for confounding variables.

It is noted that if any characteristics change in the participants during the course of the study (in addition to the training programme received) that any changes in outcomes could be due to these factors and not wholly due to the intervention (e.g. the child becomes unwell). This would be discussed in the write up and analysis of the study. It is acknowledged that this is a general weakness of pre/post design with a single group of patients.

10.6 Interim analysis and criteria for the premature termination of the trial

No interim analysis will be performed. A single analysis will be performed at the end of the study.

10.7 Participant population

All participants who received the intervention will be subjected to the trial analysis.

10.8 Procedure(s) to account for missing or spurious data

Any missing data will be omitted from analysis.

11 DATA MANAGEMENT

11.1 Data collection tools and source document identification

Any source data collected will be stored in the Investigator Site File which will be electronic. Any original source data which has been written will be scanned in and the PI needs to check that they are:

- Accurate
- Legible
- Contemporaneous
- Original
- Attributable
- Complete
- Consistent
- Enduring
- Available when needed

There will be an electronic case report form (eCRF) to record individual patient data required by the protocol. The eCRF will be stored on an excel spreadsheet so it can be easily read and understood with any coding clearly explained. It will have no identifiable information so that if sent to the sponsor, data protection is maintained. It will be saved on the Whittington Health NHS secure database which only members of the research team will be able to access on Whittington Health NHS computers via a personal login with a username and password. If any mistakes are made and need to be adjusted on the eCRF, this will be written clearly to allow for traceability and vanity of the trial. The only data needed in the eCRF is that if the outcome measures using the standardised tools: CPCHILD, GAS, ROM and MTS. There will be an optional free text field for investigators to record additional information if needed.

To maximise completeness of data, parents/legal guardians of the participants will be telephoned if their CPCHILD questionnaires or GAS goals have not been returned. All other data will be collected by trained members of the research team in school.

All records of participants, original case record forms, signed informed consent forms, consultee declaration forms, and hospital records will be kept by the investigator separate from the eCRF to ensure patient confidentiality in the trial. Any paper records will be kept in a locked filing cabinet in the school where the trial is taking place.

11.2 Data handling and record keeping (If this information is included in a data management plan then there is no requirement to duplicate this information in the protocol)

GCP requires that any operating systems are validated and SOP's are written for the use of the system. The PI/CI:

- will create the investigator site file, and eCRF
- be responsible for training members of the research team for data handling and record keeping.
- Maintain an audit trail ensuring that there is no deletion of entered data
- maintain a security system to protect against unauthorised access with the support of Whittington Health IT team
- maintain a list of the individuals authorised to make data changes
- maintain adequate backup of the data with the support of Whittington Health IT team
- Archive any source data (i.e. hard copy and electronic) through Whittington Health NHS trust.

11.3 Access to Data

Direct access will be granted to authorised representatives from the Sponsor, and the regulatory authorities to permit trial-related monitoring, audits and inspections- in line with participant consent.

11.4 Archiving

All trial documentation will be archived securely for 25 years in accordance with the MRC guidelines for studies with children who lack capacity to consent. It will be stored securely, electronically through the Whittington Health R&D team. All notes relating to the patient will also be written in their e-medical records.

Destruction of any essential documentation in relation to the trial will require authorisation from the sponsor.

12 MONITORING, AUDIT & INSPECTION

The study will be subject to monitoring, auditing and inspection by the sponsor or the sponsor's delegated representatives, and the relevant authorities responsible for each of the sites where the research will take place. The purpose of the monitoring is to ensure that the study is conducted in accordance with the authorised study protocol, the principles of GCP and all applicable regulations. The sponsor/sponsor's delegated representatives and regulators will require access to the study site for these inspections which will be supervised by the site investigator(s). The inspection activities apply to the following, and associated, areas in order to:

· review the investigator site file (hard and soft copies);

· review the study participant consent forms;

· review research documents as approved by applicable regulatory body and those referenced in protocol;

· review participant facing, current and superseded versions;

· view the storage facilities/spaces for research documentation (paper and electronic);

· review site delegation of duties log;

· review trial amendment log.

13 ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee (REC) review& reports

- Before the start of the trial, approval will be sought from a REC for the trial protocol, informed consent forms and patient/staff/parent information sheets.
- If any substantial amendments are made to the protocol, it will require review by REC before being implemented in the trial
- all correspondence with the REC will be retained in the Investigator Site File
- an annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended
- it is the Chief Investigator's responsibility to produce the annual reports as required.
- the Chief Investigator will notify the REC of the end of the trial
- if the trial is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination
- within one year after the end of the trial, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC

13.2 Peer review

The full trial report will be submitted to relevant journals to be peer reviewed and/or abstracts submitted to relevant conferences.

Peer review must be independent, expert, and proportionate:

a) **Independent**: At least two individual experts should have reviewed the trial. The definition of independent used here is that the reviewers must be external to the investigators' host institution and not involved in the trial in any way. Reviewers do not need to be anonymous.

b) **Expert**: Reviewers should have knowledge of the relevant discipline to consider the clinical and/or service based aspects of the protocol, and/or have the expertise to assess the methodological and statistical aspects of the trial.

c) **Proportionate**: Peer review should be commensurate with the size and complexity of the trial.

13.3 Public and Patient Involvement

The special school which will be involved in the research has trialled the Innowalk Pro for a period of 6 weeks. The feedback from the students, parents and school staff was positive leading the head of the school to agree to be involved in the proposed trial.

Participants will be actively involved in the active phase of the trial (outcome measure collection and intervention) and the participants parents/legal guardians will be involved in outcome measure collection.

Members of staff at the special school will be involved in the intervention phase of the research by supporting participants on and off the equipment and recording the time they use it and any concerns they may have.

Once the full trial report has been published and peer reviewed the school staff and families may be involved in disseminating its findings by word of mouth, emails or posters.

13.4 Regulatory Compliance

- The trial will not commence until receipt a Favourable REC opinion and Approval from the Health Research Authority (HRA).
- Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator will ensure that appropriate approvals from participating organisations are in place. The special school named as the institution for the study to take place has agreed for the trial to take place with their students in their institution.
- For any amendment to the study, the Chief Investigator, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator will work with NoClor so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

13.5 Protocol compliance

All members of the research team and all school staff who are involved in supporting the participants during the intervention phase of the trial will have access to the protocol.

- Prospective, planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials and will not be used.
- Any accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.
- Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.

13.6 Notification of Serious Breaches to GCP and/or the protocol

A “serious breach” is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial

- the sponsor will be notified immediately of any case where the above definition applies during the trial conduct phase
- the sponsor of a clinical trial will notify the licensing authority in writing of any serious breach of

  (a) the conditions and principles of GCP in connection with that trial; or
  (b) the protocol relating to that trial, as amended from time to time, within 7 days of becoming aware of that breach

13.7 Data protection and patient confidentiality

Patient confidentiality will be maintained throughout the trial and on publication of the research. All investigators and trial site staff will comply with the requirements of the Data Protection Act 2018 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

All identifiable information for each participant is accessible to the research team via their health record, using RIO which is the electronic notes system used by the staff of Whittington Health, and is only accessible via an encrypted card with individual usernames and passwords.

Any data collected for the purposes of the trial will be written in the participants own individual electronic health record systematic well as being anonymised in the eCRF. Personalised information will be replaced with an unrelated sequence of characters which is codes. The code linking this data to their personal files will be kept separate from the eCRF in a separate password protected folder.

Access to the files related to the trial will be kept to the minimum number of individuals necessary for quality control, audit and analysis.

Confidentiality of data will be preserved when the data is transmitted to the statistician or the sponsor as identifiable information will continue to be replaced with a code that is not known to the sponsor or other readers.

Data will be stored securely for 25 years in accordance with the MRC guidelines for studies with children who lack capacity to consent.

The data custodian will be Whittington health.

13.8 Financial and other competing interests for the chief investigator, PIs at each site and committee members for the overall trial management

Made for Movement, the producers of the Innowalk Pro, are loaning the use of the equipment to the named school for the purpose of the trial for free, however they have had no input into the study design and will have no access to data around the trial until it has been peer reviewed and published.

13.9 Indemnity

Made for Movement Limited who are providing the trial with the Innowalk Pro for the purpose of the trial operates with fully comprehensive Public Liability and Products Liability Insurance provided from Zurich Insurance under Sections G1 &G2 - Public And Products Liability. Policy Number 127/H02/JR906359/1

TABLE OF COVER:

Sub-Section	Description	Limits of Indemnity
I	Public Liability	£1,000,000
II	Products Liability	£1,000,000

Insured	Broker	Provider
Made for Movement Limited Office 22, 3rd Floor The Blade Abbey Square Reading Berkshire RG1 3BA	Finch Insurance Brokers Limited St Ann's House St Ann's Place Manchester M2 7LP	ZURICH INSURANCE Norfolk House 7 Norfolk Street Manchester M2 1ZU

13.10 Amendments

The C.I. will contact the sponsor advising of the proposed amendment, specifically:

- The nature of the amendment
- The rationale for the amendment
- Which phase of the study it relates to if this is not clear
- Which sites the proposed amendment relates to if this is not clear
- When the proposed amendment should take effect
- Has sought advice from the statistician to ensure that the proposed amendment will not compromise the efficacy of any part of the research
- Has modified the protocol to reflect the proposed amendment including any statistical changes.

The C.I. will await the sponsor's confirmation of whether the amendment is 'substantial' to non-substantial' and submit the amendment form and modified research document set to the sponsor for review prior to any submission.

Both substantial and minor, non-substantial amendments are signed by the sponsor representative.

If applicable, other specialist review bodies (e.g. CAG) need to be notified about substantial amendments in case the amendment affects their opinion of the trial.

Amendments also need to be notified to the national coordinating function of the UK country where the lead NHS R&D office is based and communicated to the participating organisations (R&D office and local research team) departments of participating sites to assess whether the amendment affects the NHS permission for that site. Note that some amendments that may be considered to be non-substantial for the purposes of REC still need to be notified to NHS R&D (e.g. a change to the funding arrangements).

Any request to make amendments to the protocol will be discussed with the PI/CI and it is then their responsibility to contact the sponsor to decide whether the amendment is substantial or non-substantial and contact the REC if relevant.

If any amendments are made the protocol version will be updated and everyone in the research team will be made aware via email of which protocol version to be working from.

13.11 Post trial care

The Declaration of Helsinki states that “In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process” and that “in clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.”

After the trial if the intervention is deemed as beneficial the named school will purchase the Innowalk Pro for future use with their students.

13.12 Access to the final trial dataset

The PI/CI and named members of the research team who are GCP trained will have access to the full dataset. There are no known restrictions for the other trial investigators to access the data as it is a single centre trial and therefore it known that no results will be disclosed prior to the main publication.

14 DISSEMINATION POLICY

14.1 Dissemination policy

Trial results will be disseminated to participants and their parents/legal guardians on completion of the final trial report via a summarised report. Parents/legal guardians can request data for their child at any time during the trial.

On completion of the trial, the data remains the property of the research team and the sponsor. It will be submitted to relevant journals to be peer reviewed and/or abstracts submitted to relevant conferences.

Only the full trial report will be available to the public once it has been published in a relevant peer reviewed journal.

14.2 Authorship eligibility guidelines and any intended use of professional writers

- Identification of authors and other contributors is the responsibility of the people who did the work (the researchers) not the people who publish the work (editors, publishers). Researchers should determine which individuals have contributed sufficiently to the work to warrant identification as an author: Clare Dorset-Purkis and Alesha Southby
- Individuals who contributed to the work but whose contributions were not of sufficient magnitude to warrant authorship should be identified by name in an acknowledgments section: Other members of the physiotherapy team supporting with data collection. Noclor staff who are supporting with statistics and reviewing the final trial report.
- Editors should require authors and those acknowledged to identify their contributions to the work and make this information available to readers: at the stage of peer review editors will inform authors of any required changes.

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16 APPENDICIES

16.1 Appendix 1-Risk (categorisation from MHRA GCP 2012 page 70-72)

Risks associated with trial interventions

☒ A ≡ Comparable to the risk of standard medical care

The trial intervention of using the RRT is in conjunction with the participant's usual level of physiotherapy care. The intervention of using the RRT is not perceived to involve higher risk than what is known from their usual physiotherapy treatment as it offers movement through their available range of movement of their lower limbs and with correct training staff will be able to support the participant safely using the equipment.

What are the key risks related to therapeutic interventions you plan to monitor in this trial?		**How will these risks be minimised?**		
IMP/Intervention	**Body system/Hazard**	**Activity**	**Frequency**	**Comments**
Use of Innowalk Pro 4x week for 30 minutes	Musculoskeletal pain	Staff will monitor for any signs of pain in the participant	During and after intervention.	Intervention will be stopped and equipment will be adjusted if the child is experiencing any pain.
Use of Innowalk Pro 4x week for 30 minutes	Pressure areas on skin	Staff will review skin integrity of participant after every use of Innowalk Pro	After every intervention	Staff will report any pressure areas to the physiotherapy team to adjust settings as needed.

All staff supporting the participants during the trial will be specially trained into using the equipment and know the participants well to recognise first signs of any concerns and react accordingly by stopping the intervention and informing a member of the research team.

16.2.1 Patient registration/randomisation procedure

Potential participants will be given details of the trial and will be signed up to the trial on a first come first served basis by contacting Chief Investigator at clare.dorset-purkis@nhs.net or calling 02077864804. There is no randomisation in this trial.

16.2.2 Data management

All data management will be looked after by the research team and supported by Noclor.

16.2.6 Trial documentation and archiving

Whittington Health NHS Trust will be responsible for archiving the trial documentation.

16.3.1 Required documentation

All documentation is attached to this submission including consent forms, participant information sheets and CV'S.

16.3.2 Procedure for initiating/opening a new site

N/a

16.3.3 Principal Investigator responsibilities

The Principal Investigator will ensure any new members of the trial team are trained accordingly and if any adjustments are made to the protocol that all members of the research team are aware of such changes and disseminate it appropriately. They have full responsibility for the safe running of the trial.

16.4 Appendix 4 – Schedule of Procedures

Procedures	**Visits (insert visit numbers as appropriate)**				
	Screening	**Baseline**	**Treatment Phase**		**Follow Up**
Informed consent					

Demographics					
Medical history					
Physical examination					
Measurement of QOL of each participant using the CPCHILD:					
Measurement of popliteal angle of each participant using a goniometer. Measurement of hip and knee extension of each participant using a goniometer Measurement of dorsiflexion with knee flexed and knee exteded of each participant using a goniometer Measurement of spasticity in the rectus femoris, hamstrings, gastrocnemius and soleus of each participant using the MTS. Measurement of perceived improvement in function for each participant using GAS.					
Compliance					
Adverse event assessments					
Physician's Withdrawal Checklist					

16.6 Appendix 6 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

1	1.1	18.12.19	Clare Dorset-Purkis	Section 3 and 7.7 of the protocol to add in about single blinding the assessor.

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee.