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[Intervention Protocol]

Neurodevelopmental treatment approaches for children with cerebral palsy

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To evaluate the effectiveness of neurodevelopmental treatment approaches (NDT) for the treatment of children with cerebral palsy.

BACKGROUND

Description of the condition

Cerebral palsy, with its primary features of movement limitation and impairment of postural control, is a complex condition that results from damage to the immature brain. It is also the most prevalent type of physical disability in children (Cans 2000). High-income countries, such as Australia, Sweden, the United Kingdom (UK) and the United States of America (USA), report cerebral palsy rates of 2.0 to 2.5 per 1000 live births (Bhushan 1993; Himmelmann 2014; Paneth 1984; Paneth 2006; Reddihough 2003; Stanley 2008). According to a recent systematic review, the overall prevalence of cerebral palsy in high-income countries is 2.11 per 1000 live births (95% confidence interval (CI) 1.98 to 2.25 (Oskoui 2013)). In low- and middle-income countries, the few existing population-based studies report rates of cerebral palsy of between 2.0 and 2.8 per 1000 live births (Gladstone 2010). According to smaller surveys, the prevalence of cerebral palsy in Africa ranges from 3.8 to 10 per 1000 live births (Donald 2014; El-Tallawy 2014). In the USA, the rate of cerebral palsy increased by approximately 20% between 1960 and 1986 (Bhushan 1993), an increase that has been attributed to the survival of low and very low birth weight babies (Murphy 2003).

Causes of cerebral palsy can be classified as prenatal, perinatal or postnatal according to the timing of damage to the central nervous system (Nolan 2000). Prenatal events are responsible for 75% of cases of cerebral palsy whereas postnatal events account for 10% to 18% (Reddihough 2003). The cause of cerebral palsy is unclear in many children, though low birth weight and prematurity are known risk factors (Jan 2006).

Cerebral palsy is considered a static encephalopathy (i.e. permanent brain damage) in which the primary lesion is non progressive. However, clinical presentation can change over time due to the growth, plasticity, development, and maturation of the central nervous system (Sankar 2005). Cerebral palsy can lead to permanent disorders and abnormal movement patterns (Rosenbaum 2007).

The Surveillance of Cerebral Palsy in Europe (SCPE) Group classifies motor impairment in people with cerebral palsy as ataxic, dyskinetic (dystonia and choreoathetoid), or spastic (Cans 2000). Those with spastic cerebral palsy are further subcategorised as unilateral or bilateral. Other terms used to describe spastic cerebral palsy include hemiplegia (unilateral impairment), diplegia (total body involvement with lower limbs more affected than upper limbs), and quadriplegia (total body involvement with the four limbs affected). Individuals with cerebral palsy can also experience "disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy and by secondary musculoskeletal problems" (Rosenbaum 2007). The progression of the disease is influenced by the type of neuromotor abnormality, topographical classification, age, and associated deformities.

The earlier that cerebral palsy is diagnosed and treated, the better its prognosis (Hadders-Algra 2014; Köng 2008). The chances of motor incapacity are lower in children who are diagnosed and treated at an early age (Hutton 2006).

All children with cerebral palsy are at risk for contractures or deformities. However, because of their lack of (or reduced) active movements, non-ambulant children with cerebral palsy are more prone to develop muscle shortening and deformities such as scoliosis, dislocation, and sub dislocation (Porter 2007).

As cerebral palsy is a sensorial-motor disorder and may include associated problems (visual, auditory etc.), a multidisciplinary approach to rehabilitation is important. The team caring for these children usually includes neurologists, occupational therapists, orthopedic surgeons, paediatricians, physical therapists, and speech therapists (Brunstrom 2001). In this field, some authors favour the term ‘habilitation’ over 'rehabilitation', as children with cerebral palsy are not being rehabilitated. In this review, we will use these terms interchangeably along with ‘treatment’, which is also used frequently in this field.

The diagnosis of cerebral palsy is based on clinical evaluation (O’Shea 2008). It is possible for children with severe cerebral palsy to be diagnosed soon after birth. Others, however, often because of poor muscle tone, receive the diagnosis within the first two years of life (cerebralpalsy.org).

The motor function of children with cerebral palsy under 16 years of age is usually assessed using the Gross Motor Function Measure (GMFM)-88 (Russell 2002). This tool assesses five domains: (1) "Lie and roll", (2), "Crawling and kneeling"; (3) "Sitting", (4) "Standing", and (5) "Walk-jump-run" (Russell 2010). The test provides an overall percentage score as well as dimension scores. The GMFM-66 is a newer and shorter version of the GMFM-88 (Russell 2010).

The Gross Motor Function Classification System (GMFCS) is another tool used frequently with children with cerebral palsy that assesses the independent mobility and function of children according to chronological age (Palisano 2000). This test classifies children as Level I ("Walks without limitations"), Level II ("Walks with limitations"), Level III ("Walks using a hand-held mobility device"), Level IV ("Self-mobility with limitations", can use motorised mobility), and Level V ("Transported in a manual wheelchair") (Palisano 1997). See Appendix 1. Several investigators have suggested that the level of motor function should be analysed as a dichotomous outcome (researchrom.com; Vargus-Adams 2011). According to these investigators, children at Levels I to II should be categorised as having 'functional independence' while those at Levels III to V should be classified as having 'functional limitation'. An explanation describing the degree of motor function is provided for five different age bands (before 2 years, 2 to 4 years, 4 to 6 years, 6 to 12 years, and 12 to 18 years) within each level (GMFCS E&R - Expanded and Revised). For example, for the children in the last two age bands, the descriptions of motor function "reflect the potential impact of environment factors (e.g. distances in school), personal factors (e.g. energy demands and social preferences) on methods of mobility". According to the creators of this GMFCS, "the scale is ordinal, with no intent that the distances between levels be considered equal or that children and youth with cerebral palsy are equally distributed across the five levels" (motorgrowth.canchild.ca). A full description of GMFCS is presented in Appendix 2 (see also Palisano 1997).

Children with cerebral palsy may also have impaired hand and upper limb function. The Manual Ability Classification System (MACS; macs.nu) is a tool that is used to assess the manual ability of children between 4 and 18 years of age with adjustment for age (Eliasson 2006). This test classifies children as "Level I - Handles objects easily and successfully, Level II - Handles most objects but with somewhat reduced quality and/or speed of achievement,

Level III - Handles objects with difficulty; needs help to prepare and/or modify activities, Level IV - Handles a limited selection of easily managed objects in adapted situations, Level V - Does not handle objects and has severely limited ability to perform even simple actions" (Eliasson 2006). Often, the level of manual ability is presented as a dichotomous outcome also; Levels I to II are classified as 'independent' and Levels III to V are classified as 'dependent' (Arner 2008) (see Appendix 3).

Description of the intervention

Historically, the movement disorders of children with cerebral palsy has been treated with different rehabilitation interventions, including the Bobath Concept (dos Santos 2015). This method was developed in the 1940s by Dr Karel and Berta Bobath (a neuropsychiatrist and a physical therapist) and, since then, it has been used by therapists worldwide (IBITA, IBITA 2008). Bobath concept aims to improve gross motor function and postural control by facilitating muscle activity through key points of control assisted by the therapist (Bobath 1990; dos Santos 2015; Veličković 2005). Although the basic concept has not changed, it has evolved to reflect developments in understanding of movement dysfunction in children with central nervous system damage. In 1960, the Bobaths changed the name of the approach to neurodevelopmental treatment (or NDT); this term is used mostly in North America. In the scientific literature, both terms (the Bobath Concept and NDT) are used to describe the same intervention (Howle 2002; Raine 2009). In this review we will use NDT as the generic term to describe this intervention.

The first NDT interventions were based on the scientific understanding that prevailed in the 1940s and 1950s. At that time, the investigators thought that the central nervous system was 'hard-wired', which meant that voluntary movement was controlled by a higher level cortical centre, while lower centres controlled more primitive reflexes. This was known as a 'hierarchical/reflex model'. During that period, NDT interventions aimed to stop abnormal postures and movements by holding the child in fixed postures that were supposed to inhibit reflexes. This was abandoned because it was too passive, and it did not lead to improved movement or function, except in a few cases of very young children (Bobath 1984; Köng 1991; Mayston 1992).

NDT is currently defined as a client-centred, hands-on, 'problem solving approach'. It is used in the management and treatment of children who have disorders of function, movement or postural control because of damage in their central nervous system (NDTA 2012). The NDT approach does not involve exclusively the patients' sensory-motor problems. It involves the whole person, including the emotional, social and functional problems that the individual has to face in his or her daily life. The NDT approach also involves managing problems related to the development of the child, including impairments in perception and cognition (Veličković 2005)

This approach uses clinical reasoning rather than a series of standardised techniques (Graham 2009). Therapists of NDT must observe, analyse and interpret task performance before starting or adapting treatment. The approach is individualised and tailored to each child's specific problems, aims and goals.

Key elements in NDT are: facilitation (using sensory inputs to improve motor performance), management of compensatory motor behaviour , and an overall management strategy (a 24-hour interdisciplinary management approach) (Graham 2009; Veličković 2005). According to Kollen 2009, in NDT, *"the patient must be active while the therapist assists him. The therapist assists the patient to move using key points of control"*, such as the head, shoulders and pelvis, and guides the movement of the whole body.

NDT involves task-specific postures and movements. It centres on and emphasises functional activities and participation in relevant daily life situations. The main aim of NDT is to improve the quality of life of patients with neurological lesions by optimising their level of activity and participation (Mayston 2008).

NDT therapists prepare activities to improve specific functions of the child in the present. However, therapists will also prepare the child for specific functions that she will need to develop in the near future. This includes a thorough analysis of each task, taking into account the needs of each child.

NDT activities must also be practiced in the family context so that learning may occur (Mayston 2001; Veličković 2005). Therefore, family members and other caregivers receive education in NDT principles, which often includes written programmes to carry out at home (Mayston 2008). The objective of this continuous treatment is to maximise the quality of movements and the carry-over of functional skills to different environments, including the child's home, pre-school, school, and community settings.

Many people with neurological damage, including stroke victims, can benefit from NDT, regardless of their age or the severity of their neurological lesion (Raine 2006; Raine 2007). In the treatment of children with cerebral palsy, NDT can be used alone or with other techniques such as conductive education, animal therapy, neuromuscular electrical stimulation, or acupuncture.

How the intervention might work

During NDT evaluation and treatment sessions, the therapist interacts with the child in a dynamic and reciprocal way (ndta.org). This therapeutic handling and interaction is thought to activate optimal sensorimotor processing, task performance and skill acquisition, and ultimately lead the child to participate in meaningful activities and achieve an improved quality of life (Mayston 2008).

In other words, "NDT uses afferent input to re-educate the patient's internal reference systems to enable him or her to have more movement choices and greater efficiency of movement" (Gjelsvik 2008; Raine 2007).

The intervention works by learning functional activities, which involve sensorial, perceptive and adaptive components (Mayston 2008). Activities must involve sensorimotor experience because the learning comes from movement perception (Veličković 2005). Neurodevelopmental treatment is a hands-on, client-centred approach that seeks to improve gross motor function in children and adults with neurological problems (such as cerebral palsy), and thereby improve their independence in a variety of contexts. It is thought that by stimulating the affected side to promote the desired muscle action, abnormal movement patterns can be corrected, and normal movement patterns conducive to performing everyday activities restored. It is thought to works as follows:

"The therapist plans for the necessary preparatory work (e.g. muscle elongation) to enable the client to perform the task and will facilitate and guide the movement as needed to decrease or prevent posture and movement behaviours that would interfere with the functional abilities of the infant or child, Feedforward is developed as the child practices the skill or task with the therapist's guidance. The therapist provides less guidance and assistance as the infant or child takes over and anticipates postural and motor requirements" (Tecklin 2008).

Why it is important to do this review

NDT is one of the oldest and most frequently-used interventions to treat children with cerebral palsy (Webb 2008). However, there is no evidence that NDT can promote functional improvement of children with cerebral palsy (Novak 2013).

This review is important because it will be the first to identify, critically appraise, and synthesise the best, currently available evidence on the effectiveness of NDT for treating children with cerebral palsy. Previous reviews of interventions for children with cerebral palsy have either focused on specific types of motor disorders (Franki 2012), or were conducted over a decade ago and had several methodological limitations (Brown 2001). For example, Anttila 2008 conducted a systematic review of physical therapy treatments for children with cerebral palsy limited to studies published between 1990 and 2007. Novak 2013 performed a systematic review of systematic reviews, which included a wide range of interventions such as medication, physiotherapy, botulism injections and fitness training, among others. A relatively recent review on common, conventional physiotherapy interventions also had methodological limitations, such as the inclusion of observational studies along with randomised trials, and the authors did not assess the quality of the included primary studies or publication bias (Martin 2010). These limitations may have biased their results (NIHR 2014).

The findings of this review can help to inform healthcare professionals, families, and policy makers on the effectiveness of NDT for treating children with cerebral palsy.

OBJECTIVES

To evaluate the effectiveness of neurodevelopmental treatment approaches (NDT) for the treatment of children with cerebral palsy.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and quasi-randomised controlled trials (qRCTs).

Types of participants

Children and adolescents under 18 years of age with a clinical diagnosis of cerebral palsy, including those with any associated co-morbidities.

Types of interventions

We will include studies that use NDT as an intervention compared to no treatment, waiting list, placebo or treatment-as-usual. Studies that use NDT in conjunction with other types of treatments will also be included providing the participants in the control group receive only the other types of treatments (i.e. they do not receive NDT).

Types of outcome measures

Primary outcomes

1. Motor function, as assessed by measures such as the Gross Motor Function Measure (GMFM)-88 (Russell 2002); the GMFM-66 (Russell 2010); the Pediatric Evaluation of Disability Inventory (PEDI) (Haley 1992), and the Peabody Developmental Motor Scales, Second Edition (PDMS-2) (Palisano 1995). We remain mindful that there is limited evidence for the reliability and validity of the PDMS-2 and that the original PDMS is not recommended in children with cerebral palsy.
2. Participation, as assessed by measures such as the Children's Assessment of Participation and Enjoyment (CAPE) test (King 2007).
3. Any adverse outcomes, for example, pain, discomfort and tonus impairment.

Secondary outcomes

1. Changes in level of motor function, as assessed by measures such as the Gross Motor Function Classification System (GMFCS) (Palisano 2008). We will consider a change that results in an increase in the level of motor function (e.g. a change in GMFCS from Level III to Level IV after NDT), or no change, as 'worsening', and will consider a change that results in a decrease in the level of motor function (e.g. a change in GMFCS from Level III to Level II after NDT) as an 'improvement'. We acknowledge that the GMFCS was developed as a classification system and remains unvalidated.
2. Upper limb function, as assessed by measures such as the Melbourne Assessment of Unilateral Upper Limb Function (MAUULF) (Randall 1999).
3. Hand function, as assessed by measures such as the Assisting Hand Assessment (AHA) (Krumlinde-Sundholm 2007).
4. Changes in level of hand function, as assessed by measures such as the Manual Ability Classification System (MACS) (Eliasson 2006). We will consider a change that results in an increase in the level of hand function (e.g. a change in MACS from Level III to Level IV after NDT), or no change, as 'worsening', and will consider a change that results in a decrease in the level of hand function (e.g. a change in MACS from Level III to Level II after NDT) as an 'improvement'. We acknowledge that the MACS was developed as a classification system and remains unvalidated.
5. Quality of life, as assessed by measures such as the Cerebral Palsy Quality of Life Questionnaire for Children (CP QOL - Child; Chen 2013) and the Cerebral Palsy Quality of Life Questionnaire for Adolescents (CP QOL – Teen; Davis 2013).
6. Changes in level of function in everyday activities, as assessed by measures such as the Functional Independence Measure for Children (WeeFIM) (Ottenbacher 2000).

We will collect outcomes for the following time-point intervals: short term (zero to less than one month post-intervention), intermediate (one month to less than six months post-intervention), and long term (equal to or greater than six months post-intervention).

We will present all available results for the primary outcomes in a 'Summary of findings' table.

Search methods for identification of studies

Electronic searches

We will search the following electronic databases:

1. Cochrane Central Register of Controlled Trials (CENTRAL), current issue, part of the *Cochrane Library* (which includes the Specialised Register of the Cochrane Developmental, Psychosocial and Learning Problems Group).
2. MEDLINE (Ovid), 1946 to current.
3. EMBASE (Ovid), 1980 to current.
4. CINAHL (EBSCOhost), 1982 to current.
5. Science Citation Index (SCI; Web of Science), 1970 to current.
6. Conference Proceedings Citation Index - Science (CPCI-S; Web of Science), 1990 to current.
7. SciSEARCH, 1991 to current.
8. Cochrane Database of Systematic Reviews (CDSR), current issue, part of the *Cochrane Library.*
9. Database of Abstracts of Reviews of Effect (DARE), current issue, part of the *Cochrane Library.*
10. LILACS (lilacs.bvsalud.org).
11. OpenGrey (opengrey.eu).
12. PEDro (pedro.org.au).
13. ClinicalTrials.gov (clinicaltrials.gov).
14. World Health Organisation (WHO) International Clinical Trials Registry Platform (ICTRP) (who.int/ictrp/en).

We will not limit our searches by year, publication status or language of the publication. We will use the strategy in Appendix 4 to search Ovid MEDLINE. The strategy will be adapted for other databases using appropriate syntax and indexing terms.

Searching other resources

We will handsearch reference lists of relevant studies and will contact study authors and organisations about any ongoing or unpublished studies. We will also search Google Scholar to identify any relevant published or unpublished studies.

Data collection and analysis

Selection of studies

Two authors (MAZ and GJMP) will independently screen all titles and abstracts retrieved by the search strategy for eligibility. The same authors will then retrieve and independently assess full-text reports of those papers deemed potentially relevant, or for which more information is needed, and select studies that meet the aforementioned selection criteria (see Criteria for considering studies for this review). They will record reasons for excluding studies in the 'Characteristics of excluded studies' table. A third author (RR) will arbitrate any disputes.

Data extraction and management

MAZ and GJMP will independently extract data from the included studies on participant characteristics (age, gender, and type of cerebral palsy); intervention (type of intervention, frequency of treatment, and duration); methods (study design, randomisation, blinding, sample size, and unit of analysis); and outcomes (including motor function; upper limb function; hand function; quality of life; and participation). Disagreements will be resolved by a third author (RR).

We will seek assistance from the Cochrane Developmental, Psychosocial and Learning Problems Group for articles published in languages other than English. Where results are only available in graphs, we will extract the numeric information using SCaViS (Scientific Computation and Visualisation Environment) software (jwork.org/scavis). We will contact study authors in case of ambiguous or unclear results. We will describe each of these cases in the 'Characteristics of included studies' table.

Assessment of risk of bias in included studies

Using the Cochrane 'Risk of bias' tool (Higgins 2011, Section 8.5), two authors (MAZ, GJMP) will assess independently the risk of bias of each included study across the following seven domains.

1. Random sequence generation

For each included study we will describe the method used to generate the allocation sequence and assess whether it was reported in sufficient detail to allow an assessment of whether it should produce comparable groups.

We will categorise the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear risk of bias (insufficient information about the sequence generation process to permit a judgement of high or low risk of bias).

2. Allocation concealment

For each included study we will describe the method used to conceal allocation to interventions prior to assignment and will assess whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We will categorise the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively-numbered sealed opaque envelopes);
- high risk of bias (e.g. open random allocation; unsealed or non-opaque envelopes; alternation; date of birth); or
- unclear risk of bias (insufficient information to permit a judgment of high or low risk of bias, i.e. the method of concealment is not described or not described in sufficient detail to allow a definite judgment).

3. Blinding of participants and personnel

For each included study we will describe the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will assess blinding separately for different outcomes or classes of outcomes.

We will categorise the methods as:

- low risk of bias (participants and personnel are blinded, or we judge that the lack of blinding would be unlikely to affect results);

- high risk of bias (some participants or some key study personnel are not blinded, and the lack of blinding is likely to introduce bias; or blinding of key study participants and personnel attempted, but it is likely that the blinding could have been broken); or
- unclear risk of bias (insufficient information to permit a judgement of high or low risk of bias).

4. Blinding of outcome assessment

For each included study we will describe the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We will assess blinding separately for different outcomes or classes of outcomes.

We will categorise the methods as:

- low risk of bias (blinding of participants and key study personnel ensured, and it is unlikely that the blinding could have been broken);
- high risk of bias (no blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding); or
- unclear risk of bias (e.g. the study did not address this outcome).

5. Incomplete outcome data

For each included study and for each outcome or class of outcomes, we will describe the completeness of data, including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total number of randomised participants); if reasons for attrition or exclusion were reported; and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses that we undertake.

We will categorise the methods as:

- low risk of bias (no missing outcome data or missing outcome data balanced across groups);
- high risk of bias (numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation); or
- unclear risk of bias (insufficient reporting of attrition/exclusions to permit a judgment of high or low risk of bias, e.g. number randomised not stated; no reasons for missing data provided; or the study did not address this outcome).

6. Selective outcome reporting

For each included study we will describe how we investigated the possibility of selective outcome reporting bias and what we found.

We will categorise the methods as:

- low risk of bias (it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes was not pre-specified; outcomes of interest were reported incompletely and so cannot be used; the study failed to include results of a key outcome that would have been expected to have been reported); or
- unclear risk of bias (insufficient information to permit a judgment of high or low risk of bias).

7. Other potential sources of bias

For each included study we will describe any important concerns that we have about other possible sources of bias.

We will categorise the methods as:

- low risk of bias (the study appears to be free of other sources of bias);
- high risk of bias (the study has a potential source of bias related to the specific study design used; the study was stopped early due to some data-dependent process; the study has extreme baseline imbalance; or the study has been claimed to have been fraudulent); or
- unclear risk of bias (insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias).

We will make explicit judgments about whether studies are at high risk of bias according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias by undertaking sensitivity analyses (see Sensitivity analysis). Any disagreement will be resolved by a third evaluator (RR).

We will use the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach to assess overall quality of evidence (Schűnemann 2008), using the following ratings: high quality (RCTs and qRCTs with a very low risk of bias), moderate quality (RCTs and qRCTs with some evidence of risk of bias such as inadequate allocation concealment), and low and very low quality (RCTs and qRCTs that have significant threats to internal study validity such as failure to adequately randomise participants, lack of blinding of outcome assessors or selective outcome reporting) (Higgins 2011, Table 12.2.a).

Measures of treatment effect

Binary data

We will assess dichotomous data using the risk ratio (RR) and 95% confidence intervals (CI). We will consider a change that results in an increase in the level of motor function (e.g. a change in GMFCS from Level III to Level IV after NDT), or no change, as 'worsening', and will consider a change that results in a decrease in the level of motor function (e.g. a change in GMFCS from Level III to Level II after NDT) as an 'improvement'.

Continuous outcome data

For continuous data, we will calculate the mean difference (MD) for outcomes evaluated by the same instrument, or the standardised mean difference (SMD) for outcomes measured by different instruments for the same purpose, with a 95% CI.

Multiple outcome measures

When a study assesses the same outcome using different tools (e.g. GMFM-88 and PEDI for assessing motor function), at the same time point, we will conduct separate analyses. In other words, we will not pool the data from these tools in the same analysis.

When a study measures an outcome more than once during the same time interval, we will consider the last measure for analysis, in order to avoid double counting of participants (e.g. if a study provides data for GMFM at two months and at four months for the intermediate time point interval outcome, we will consider only the four-month data).

Unit of analysis issues

Cluster-randomised trials

For cluster-randomised trials, we will perform an approximately correct analysis if we can extract data on the following: the number of clusters randomised to each intervention group or the average (mean) size of each cluster; the outcome data ignoring the cluster design for the total number of individuals; an estimate of the intracluster correlation coefficient (ICC). If we are unable to obtain the individual participant data to allow us to calculate an estimate of the ICC, we will use external estimates obtained from similar studies. If this information is not available, we will analyse the results of cluster studies using a general summary considering each cluster as the unit of analysis.

Cross-over trials

In cross-over trials, to avoid the risk of counting the same child twice, we will include only data from the first period.

Studies with multiple treatment groups

For primary analyses we will pool results from relevant intervention (any NTD approach) groups and compare them with the pooled results from eligible control groups, creating single, pair-wise comparisons. When this strategy precludes exploration of potential causes of heterogeneity, we will assess each NTD approach individually (versus a common control group), and split the sample size for common comparator groups proportionately for each comparison (Higgins 2011, Section 16.5.4). This strategy enables the use of standard meta-analysis software and avoids double-counting of participants.

Dealing with missing data

We will try to contact the study authors to request any unreported data (e.g. standard errors and CI for group means or standard errors, CI, t values and P values for differences in means). When a study reports outcomes only for those participants who completed the trial or only those who followed the protocol, we will contact the authors and ask them to provide additional information that would enable us to conduct our analyses according to intention-to-treat principles. For dichotomous outcomes, we will carry out both a treated case analysis and an intention-to-treat analysis, and compare the results.

We will describe missing data and attrition for each study in the 'Risk of bias' table, and discuss the extent to which any missing data might affect the results or conclusions of the review.

For the included studies, we will conduct a Sensitivity analysis to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect.

Assessment of heterogeneity

We will consider clinical and methodological heterogeneity by examining factors such as similarity among participants and methodological aspects of the trial, which could lead to differences in the observed intervention effects. We will evaluate statistical heterogeneity using the Chi^2 test and the I^2 test (Higgins 2011). We will interpret a P value lower than 0.10 as evidence of statistical heterogeneity and an I^2 value greater than 50% as indicative of significant statistical heterogeneity.

Assessment of reporting biases

If we include a sufficient number of studies (more than 10), we will draw funnel plots to explore any small study effects, including publication bias. If we find any visual asymmetry of the funnel plot, we will discuss possible reasons (e.g. chance, publication bias or true heterogeneity).

If we suspect or find direct evidence for selective outcome reporting, we will contact study authors for additional information.

Data synthesis

We will carry out statistical analysis using Review Manager (RevMan) software (Review Manager 2014). We will use a fixed-effect model for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect (i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar). If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use a random-effects model to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will be treated as the average of the range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful, we will not combine trials and we will present a narrative description of the results.

If we use a random-effects model, the results will be presented as the average treatment effect with 95% CIs, and estimates of tau^2 and I^2.

Summary of findings

We will summarise the evidence in a 'Summary of findings' table, which we will construct using GRADEpro GDT 2015. We will categorise RCTs and qRCTs as high quality evidence and downgrade them according to the following criteria: risk of bias; inconsistency; indirectness; imprecision; and publication bias.

Subgroup analysis and investigation of heterogeneity

We will perform the following subgroup analyses:

1. Type of neuromotor abnormality (spastic, ataxic, and dyskinetic), since response to treatment may vary according to the type of abnormality.

2. Topographical distribution (hemiplegia, diplegia, and quadriplegia), since hemiplegia has a higher probability of responding to treatment than diplegia or quadriplegia.
3. Coexistence of postural deformities (e.g. scoliosis and subluxation), since response to treatment may vary in cases with and without postural deformities.

Sensitivity analysis

We will perform sensitivity analyses to assess the impact of the following.

1. Overall risk of bias, by comparing the results of studies deemed at high and unclear risk of bias with the results of studies at low risk of bias only.
2. Missing data for primary outcomes, by comparing the results of studies with imputed data to those without.
3. Use of a fixed-effect model versus a random-effects model, by comparing the impact of the type of model on the results of the meta-analyses.

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APPENDICES

Appendix 1. Description of gross motor function for children aged 6 to 12 years by Gross Motor Function Classification System (GMFCS level)

Level	Expected gross motor function between 6 and 12 years of age
Level I	Children walk indoors and outdoors, and climb stairs without limitations. Children perform gross motor skills including running and jumping, but speed, balance, and coordination are reduced.
Level II	Children walk indoors and outdoors, and climb stairs holding onto a rail, but experience limitations walking on uneven surfaces and inclines, and walking in crowds or confined spaces. Children have at best only minimal ability to perform gross motor skills such as running and jumping.
Level III	Children walk indoors or outdoors on a level surface with an assistive mobility device. Children may climb stairs holding onto a rail. Depending on upper-limb function, children propel a wheelchair manually or are transported (pushed by another person) when travelling for long distances or outdoors on uneven terrain.
Level IV	Children may maintain levels of function achieved before age 6 years or rely more on wheeled mobility at home, school, and in the community. Children may achieve self-mobility using a powered wheelchair.
Level V	Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and standing are not fully compensated for through the use of adaptive equipment and assistive technology. Children have no means of independent mobility and are transported (pushed by

(Continued)

	another person). Some children achieve self-mobility using a powered wheelchair with extensive adaptations.

Taken from: Palisano 1997.

Appendix 2. Gross Motor Function Classification System (GMFCS)

Level I: Walks without restrictions; limitations in more advanced gross motor skills	
Before 2nd birthday	Infants move in and out of sitting and floor sit with both hands free to manipulate objects. Infants crawl on hands and knees, pull to stand, and take steps holding onto furniture. Infants walk between 18 months and 2 years of age without the need for any assistive mobility device.
From age 2 to 4th birthday	Children floor sit with both hands free to manipulate objects. Children perform movements in and out of floor sitting and standing without adult assistance. Children walk as the preferred method of mobility without the need for any assistive mobility device.
From age 4 to 6th birthday	Children get into and out of and sit in a chair without the need for hand support. Children move from floor and chair sitting to standing without the need for objects for support. Children walk indoors and outdoors, and climb stairs. Emerging ability to run and jump.
From age 6 to 12th birthday	Children walk at home, school, outdoors, and in the community. Children are able to walk up and down curbs without physical assistance and stairs without the use of a railing. Children perform gross motor skills, such as running and jumping, but speed, balance, and coordination are limited. Children may participate in physical activities and sports depending on personal choices and environmental factors.
From age 12	Youth walk at home, school, outdoors, and in the community. Youth are able to walk up and down curbs without physical assistance and stairs without the use of a railing. Youth perform gross motor skills, such as running and jumping, but speed, balance, and coordination are limited. Youth may participate in physical activities and sports depending on personal choices and environmental factors.
Level II: Walks without assistive devices; limitations walking outdoors and in the community	
Before 2nd birthday	Infants maintain floor sitting but may need to use their hands for support to maintain balance. Infants creep on their stomach or crawl on hands and knees. Infants may pull to stand and take steps holding onto furniture.
From age 2 to 4th birthday	Children floor sit but may have difficulty with balance when both hands are free to manipulate objects. Children perform movements in and out of sitting without adult assistance. Children pull to stand on a stable surface. Children crawl on hands and knees with a reciprocal pattern, cruise holding onto furniture, and walk using an assistive mobility device as preferred methods of mobility.
From age 4 to 6th birthday	Children sit in a chair with both hands free to manipulate objects. Children move from the floor to standing and from chair sitting to standing but often require a stable surface to push or pull up on with their arms. Children walk without needing any assistive mobility device indoors and for short distances on level surfaces outdoors. Children climb stairs holding onto a railing but are unable to run or jump.
From age 6 to 12th birthday	Children walk in most settings. Children may experience difficulty walking long distances and balancing on uneven terrain, on inclines, in crowded areas, in confined spaces, or when carrying objects. Children walk up and down stairs holding onto a railing or with physical assistance if there is no railing. Outdoors and in the community, children may walk with physical assistance or a handheld mobility device or use wheeled mobility when travelling long distances. Children have at best

(Continued)

	only minimal ability to perform gross motor skills such as running and jumping. Limitations in performance of gross motor skills may necessitate adaptations to enable participation in physical activities and sports.
From age 12	Youth walk in most settings. Environmental factors (such as uneven terrain, inclines, long distances, time demands, weather, and peer acceptability) and personal preference influence mobility choices. At school or work, youth may walk using a hand-held mobility device for safety. Outdoors and in the community, youth may use wheeled mobility when travelling long distances. Youth walk up and down stairs holding a railing or with physical assistance if there is no railing. Limitations in performance of gross motor skills may necessitate adaptations to enable participation in physical activities and sports.
Distinctions between Levels I and II: Compared with children in Level I, children in Level II have limitations in the ease of performing movement transitions; walking outdoors and in the community; the need for assistive mobility devices when beginning to walk; quality of movement; and the ability to perform gross motor skills such as running and jumping.	
Level III: Walks with assistive mobility devices; limitations walking outdoors and in the community	
Before 2nd birthday	Infants maintain floor sitting when the low back is supported. Infants roll and creep forward on their stomachs.
From age 2 to 4th birthday	Children maintain floor sitting often by 'W-sitting' (sitting between flexed and internally rotated hips and knees) and may require adult assistance to assume sitting. Children creep on their stomach or crawl on hands and knees (often without reciprocal leg movements) as their primary methods of self mobility. Children may pull to stand on a stable surface and cruise short distances. Children may walk short distances indoors using an assistive mobility device and adult assistance for steering and turning.
From age 4 to 6th birthday	Children sit on a regular chair but may require pelvic or trunk support to maximise hand function. Children move in and out of chair sitting using a stable surface to push on or pull up with their arms. Children walk with an assistive mobility device on level surfaces and climb stairs with adult assistance. Children are frequently transported when travelling for long distances or outdoors on uneven terrain.
From age 6 to 12th birthday	Children walk using a hand-held mobility device in most indoor settings. When seated, children may require a seat belt for pelvic alignment and balance. Sit-to-stand and floor-to-stand transfers require physical assistance of a person or support surface. When travelling long distances, children use some form of wheeled mobility. Children may walk up and down stairs holding onto a railing with supervision or physical assistance. Limitations in walking may necessitate adaptations to enable participation in physical activities and sports, including a self propelling manual wheelchair or powered mobility.
From age 12	Youth are capable of walking using a hand-held mobility device. In comparison with individuals in other levels, youth in Level III demonstrate more variability in methods of mobility depending on physical ability and environmental and personal factors. When seated, youth may require a seat belt for pelvic alignment and balance. Sit-to-stand and floor-to-stand transfers require physical assistance from a person or support surface. At school, youth may self propel a manual wheelchair or use powered mobility. Outdoors and in the community, youth are transported in a wheelchair or use powered mobility. Youth may walk up and down stairs holding onto a railing with supervision or physical assistance. Limitations in walking may necessitate adaptations to enable participation in physical activities and sports, including self propelling a manual wheelchair or powered mobility.
Distinctions between Levels II and III: Differences are seen in the degree of achievement of functional mobility. Children in Level III need assistive mobility devices and frequently orthoses to walk, while children in Level II do not require assistive mobility devices after age 4.	
Level IV: Self mobility with limitations; children are transported or use power mobility outdoors and in the community	

(Continued)

Before 2nd birthday	Infants have head control but require trunk support for floor sitting. Infants can roll to supine and may roll to prone.
From age 2 to 4th birthday	Children floor sit when placed but are unable to maintain alignment and balance without using their hands for support. Children frequently require adaptive equipment for sitting and standing. Children achieve self mobility for short distances (within a room) through rolling, creeping on stomach, or crawling on hands and knees without reciprocal leg movement.
From age 4 to 6th birthday	Children sit on a chair but need adaptive seating for trunk control and to maximise hand function. Children move in and out of chair sitting with assistance from an adult or a stable surface to push or pull up on with their arms. Children may at best walk short distances with a walker and adult supervision but have difficulty turning and maintaining balance on uneven surfaces. Children are transported in the community. Children may achieve self mobility using a power wheelchair.
From age 6 to 12th birthday	Children use methods of mobility that require physical assistance or powered mobility in most settings. Children require adaptive seating for trunk and pelvic control and physical assistance for most transfers. At home, children use floor mobility (roll, creep, or crawl), walk short distances with physical assistance, or use powered mobility. When positioned, children may use a body support walker at home or school. At school, outdoors and in the community, children are transported in a manual wheelchair or use powered mobility. Limitations in mobility necessitate adaptations to enable participation in physical activities and sports, including physical assistance or powered mobility, or both.
From age 12	Youth use wheeled mobility in most settings. Youth require adaptive seating for pelvic and trunk control. Youth require physical assistance from one or two persons for transfers. Youth may support weight with their legs to assist with standing transfers. Indoors, youth may walk short distances with physical assistance, use wheeled mobility, or, when positioned, use a body support walker. Youth are physically capable of operating a powered wheelchair. When a powered wheelchair is not feasible or available, youth are transported in a manual wheelchair. Limitations in mobility necessitate adaptations to enable participation in physical activities and sports, including physical assistance or powered mobility, or both.
Distinctions between Levels III and IV: Differences in sitting ability and mobility exist, even allowing for extensive use of assistive technology. Children in Level III sit independently, have independent floor mobility, and walk with assistive mobility devices. Children in Level IV function in sitting (usually supported), but independent mobility is very limited. Children in Level IV are more likely to be transported or to use power mobility.	
Level V: Self-mobility is severely limited even with the use of assistive technology	
Before 2nd birthday	Physical impairments limit voluntary control of movement. Infants are unable to maintain antigravity head and trunk postures in prone and sitting. Infants require adult assistance to roll.
From age 2 to 12th birthday	Children are transported in a manual wheelchair in all settings. Children are limited in their ability to maintain antigravity head and trunk postures and control arm and leg movements. Assistive technology is used to improve head alignment, seating, standing, and/or mobility, but limitations are not fully compensated for by equipment. Transfers require complete physical assistance of an adult. At home, children may move short distances on the floor or may be carried by an adult. Children may achieve self mobility using powered mobility with extensive adaptations for seating and control access. Limitations in mobility necessitate adaptations to enable participation in physical activities and sports, including physical assistance and using powered mobility.
From age 12	Youth are transported in a manual wheelchair in all settings. Youth are limited in their ability to maintain antigravity head and trunk postures and control arm and leg movements. Assistive technology is used to improve head alignment, seating, standing, and mobility, but limitations are not fully compensated for by equipment. Transfers require physical assistance from one or two persons or a mechanical lift. Youth may achieve self mobility using powered mobility with extensive adaptations for seating and control access. Limitations in mobility necessitate adaptations to en-

(Continued)

	able participation in physical activities and sports, including physical assistance and using powered mobility.

Distinctions between Levels IV and V: Children in Level V lack independence even in basic antigravity postural control. Child achieves self mobility only if he or she can learn how to operate an electrically powered wheelchair.

Taken from: Ryan 2015.

Appendix 3. Manual Ability Classification System (MACS)

Level I: Handles objects easily and successfully. At most, limited in the ease of performing manual tasks requiring speed and accuracy. However, any limitations in manual abilities do not restrict independence in daily activities.

Level II: Handles most objects but with somewhat reduced quality or speed of achievement, or both. May avoid or achieve with some difficulty certain activities; might use alternative ways of performance, but manual abilities do not usually restrict independence in daily activities.

Level III: Handles objects with difficulty; needs help to prepare or modify activities, or both. The performance is slow and achieved with limited success regarding quality and quantity. Performs activities independently if they have been set up or adapted.

Level IV: Handles a limited selection of easily managed objects in adapted situations. Performs parts of activities with effort and with limited success. Requires continuous support and assistance or adapted equipment, or both, for even partial achievement of the activity.

Level V: Does not handle objects and has severely limited ability to perform even simple actions. Requires total assistance.

Distinctions between Levels I and II: Children in Level I may have limitations in handling very small, heavy, or fragile objects, which demand detailed fine motor control or efficient coordination between hands. Limitations may also involve performance in new and unfamiliar situations. Children in Level II perform almost the same activities as children in Level I, but the quality of performance is decreased or the performance is slower. Functional differences between hands can limit effectiveness of performance. Children in Level II commonly try to simplify handling of objects, for example, by using a surface for support instead of handling objects with both hands.

Distinctions between Levels II and III: Children in Level II handle most objects, although slowly or with reduced quality of performance. Children in Level III commonly need help to prepare the activity or require that adjustments be made to the environment, or both, since their ability to reach or handle objects is limited. They cannot perform certain activities and their degree of independence is related to the supportiveness of the environmental context.

Distinctions between Levels III and IV: Children in Level III can perform select activities if the situation is pre-arranged and if they receive supervision and plenty of time. Children in Level IV need continuous help during the activity and can at best participate meaningfully in only parts of an activity.

Distinctions between Levels IV and V: Children in Level IV perform part of an activity with continuous help. Children in Level V might at best participate with a simple movement in special situations, for example, by pushing a button.

Taken from: Ryan 2015.

Appendix 4. Ovid MEDLINE search strategy

1 Cerebral palsy/
2 Cerebral pals$.tw.
3 Little$ disease.tw.
4 CP.tw.
5 (unilateral adj3 spastic$).tw.

6 (hemiplegi$ adj3 spastic$).tw.
7 (diplegi$ adj3 spastic$).tw.
8 (tetrapleg$ adj3 spastic$).tw.
9 (triplegi$ adj3 spastic$).tw.
10 ((bilateral or bi-lateral) adj3 spastic$).tw.
11 (quadripleg$ adj3 spastic$).tw.
12 or/1-11
13 Physical therapy modalities/
14 musculoskeletal manipulations/
15 manipulation, chiropractic/
16 manipulation, orthopedic/
17 manipulation, osteopathic/
18 manipulation, spinal/
19 acupressure/
20 massage/
21 therapy, soft tissue/
22 Bobath$.tw.
23 (neurodevelopment$ adj3 (approach$ or habilit$ or rehabilit$ or technique$ or treat$ or therap$)).tw.
24 (neuro-development$ adj3 (approach$ or habilit$ or rehabilit$ or technique$ or treat$ or therap$)).tw.
25 (neurophysiological adj3 (approach$ or habilitat$ or rehabilit$ or technique$ or treat$ or therap$)).tw.
26 (neuro-physiological adj3 (approach$ or habilit$ or rehabilit$ or technique$ or treat$ or therap$)).tw.
27 (neuromuscular adj3 (approach$ or habilit$ or rehabilit$ or technique$ or treat$ or therap$)).tw.
28 (neuro-muscular adj3 (approach$ or habilit$ or rehabilit$ or technique$ or treat$ or therap$)).tw.
29 NDT.tw.
30 (neurofacilitation$ or neuro-facilitation$ or neuro$ facilitation$).tw.
31 (therap$ adj3 hand$).tw.
32 or/13-31
33 12 and 32

F E E D B A C K

Feedback on protocol of 'Neurodevelopmental treatment approaches for children with cerebral palsy'

Summary

Correspondence has been edited for length. A summary of substantive comments from Virginia Knox over many months, and responses from the authors, are presented below:

Comment 1

The Peabody Developmental Motor Scales (PDMS) is a norm-referenced test, which should not be used as an evaluative test until it is validated as having sufficient responsiveness in children with motor dysfunction. The original version had limitations in responsiveness when used as an evaluative measure in children with cerebral palsy and therefore is not recommended for this purpose (Palisano 1995). There has been one small study including 32 children with cerebral palsy using the revised version PDMS-2 (Wang 2006), which showed some promising results for reliability and responsiveness. ... Will it be made transparent that there is limited evidence for the reliability and validity of the PDMS-2 and that the original PDMS is not recommended in children with cerebral palsy?

Comment 2

The GMFCS (Gross Motor Fucntion Classification System) and MACS (Manual Ability Classification System) are NOT methods of assessing a child's gross or fine motor function – they are classification systems (Eliasson 2006; Palisano 2008). They are not outcome measures and not validated for that purpose, yet the authors ... repeatedly state they are tools for assessment and put them as secondary outcome measures.

Comment 3

Current practice of the Bobath approach. (The commenter is) ... concerned that (the protocol) ... is unclear about the Bobath approach or how it is practised clinically today. Many references are cited that contain information relating to how Bobath was practised many years ago, are related to using the Bobath approach in adult stroke rehabilitation and/or use outdated terminology. This may lead to significant difficulties determining the fidelity of the therapy as described in research articles identified in their search (was it or was it not therapy using the Bobath approach as it is applied now). For example:

a) (there is) an out of date definition of Bobath/NDT, which has been taken from a reference describing treatment for adults with strokes: "This concept relies on a neurophysiological approach to rehabilitation and emphasises that "the patient must be active while the therapist assists the patient to move using key points of control and reflex inhibiting patterns" (Kollen 2009)". Kollen 2009 follows that sentence in that paper with this: "Since 1984, the Bobaths conceded that reflexes were not primitive responses, but essential reactions to support

movement; as a consequence, the missing components of the normal developmental sequence were no longer facilitated during Bobath therapy in either adults or children". So the definition was conceded as out of date in the reference the authors cite, and not how Bobath is currently practised within the adult stroke population or with children.

b) This terminology is no longer used: "inhibition of abnormal movement patterns". "Inhibition" was recognised to be a confusing term in the 1990s and no longer used in the paediatric approach as it was not an accurate description of intervention. See Mayston 2002: "This has implications for the explanation of handling techniques applied during treatment/management, such that the word 'inhibition' is no longer a relevant explanation for the ways Bobath therapists stretch and activate muscles."

c) The example of Bobath therapy does not appear to represent therapeutic intervention – it is unclear what the clinical reasons for this activity might be:

"For example, to help a child develop the functional patterns involved in combining posture with arm and hand movements, the therapist, sitting on a chair, will place the child seated on the floor between his or her legs and surrounded by interesting objects such as small pots, lids and spoons. In this position, the child is free to use his or her hands and develop various ways to explore the objects to figure out how things 'work' by stacking, nesting, and combining various items. With this positioning, the therapist can encourage appropriate body alignment, trunk stability and weight shifting, and at the same time guide shoulder protraction (by limiting scapular retraction) so that the child can reach and play using her hands."

Comment 4

The commenter was concerned that the outcome of '"any adverse outcomes'" is too non-specific – would it be possible to provide an example of what one might expect to find in this category?

Comment 5

Measures of Treatment effect. ... The authors have confused the Gross Motor Function Measure (GMFM) outcome measure with the GMFCS classification system e.g. they refer to the GMFM levels, which do not exist. They mean Gross Motor Function Classification System (GMFCS) levels.

Comment 6

The commenter was concerned on looking at the protocol again about the accuracy of text relating to Kollen 2009 and work by Lennon 1996.

Comment 7

The commenter was concerned that Franki 2012 was misattributed as a source review, asserted that the work contained no relevant studies of neurodevelopmental treatment approaches, and wondered if Desloovere 2012 were, in fact, meant instead.

Comment 8

The commenter expressed concerns that the authors might:

"have incorrectly cited a reference (Singhi 2004) as evidence that Bobath cannot promote functional improvement in children. … To justify this statement, the authors of this Cochrane Review reference a general article on the management of cerebral palsy from the Indian Journal of Paediatrics by Singhi (2004). Singhi (2004) states there is no evidence to state there is superiority of one method over another (he does not state to which methods he is referring or on what evidence this statement is based). Using this reference to suggest there is no evidence to suggest that the Bobath approach can promote functional improvement in children is very misleading. The text in the article is not referring to Bobath at that point and refers to no research evidence".

I agree with the conflict of interest statement below:

I certify that I have no affiliations with or involvement in any organization or entity with a financial interest in the subject matter of my feedback.

Reply

Comment 1

Thank you for this comment. We agree with you. We removed PDMS tool as an option for assessing global motor function. We retained the PDMS-2. If, in a further version, we include a study using PDMS-2, we will highlight and discuss its limitation for this purpose (cerebral palsy), and we have been explicit about this under Types of outcome measures.

Comment 2

We understand your concern. We had already discussed this amongst ourselves and the peer reviewers at protocol stage. We are aware that these tools were originally developed as classification systems. However, over time, they became useful methods to assess the effects of physical therapy interventions on motor function in children with cerebral palsy both in practice and clinical trials settings. Other examples

of this can be found in medicine: NYHA (New York Heart Association) criteria - formally a classification system, but has been used to assess the effectiveness of treatments for chronic heart failure. So, at protocol phase, we decided to include them as tools for assessing motor function. Nevertheless, we acknowledge these remain unvalidated classification systems and have changed the text in the protocol to indicate this fact for both instruments.

Comment 3a

We updated the references and clarified the concept of Bobath approach as follows:

"Historically, the movement disorders of children with cerebral palsy has been treated with different rehabilitation interventions, including the Bobath Concept (dos Santos 2015). This method was developed in the 1940s by Dr Karel and Berta Bobath (a neuropsychiatrist and a physical therapist) and, since then, it has been used by therapists worldwide (IBITA, IBITA 2008). Bobath concept aims to improve gross motor function and postural control by facilitating muscle activity through key points of control assisted by the therapist (Bobath 1990; dos Santos 2015; Veličković 2005). Although the basic concept has not changed, it has evolved to reflect developments in understanding of movement dysfunction in children with central nervous system damage. In 1960, the Bobaths changed the name of the approach to neurodevelopmental treatment (or NDT); this term is used mostly in North America. In the scientific literature, both terms (the Bobath Concept and NDT) are used to describe the same intervention (Howle 2002; Raine 2009). In this review we will use NDT as the generic term to describe this intervention."

Comment 3b

We agree. We have deleted the term.

Comment 3c

We have exchanged the existing reference with a section from a more recent textbook, thus:

Neurodevelopmental treatment is a hands-on, client-centred approach that seeks to improve gross motor function in children and adults with neurological problems (such as cerebral palsy), and thereby improve their independence in a variety of contexts. It is thought that by stimulating the affected side to promote the desired muscle action, abnormal movement patterns can be corrected, and normal movement patterns conducive to performing everyday activities restored. It is thought to works as follows:

“The therapist plans for the necessary preparatory work (e.g. muscle elongation) to enable the client to perform the task and will facilitate and guide the movement as needed to decrease or prevent posture and movement behaviors that would interfere with the functional abilities of the infant or child, Feedforward is developed as the child practices the skill or task with the therapist's guidance. The therapist provides less guidance and assistance as the infant or child takes over and anticipates postural and motor requirements" (Tecklin 2008).

Comment 4

We have included the following examples of adverse events: pain, discomfort and tonus impairment.

Comment 5

Confusion regarding the Gross Motor Function Measure (GMFM) outcome measure and the GMFCS classification system levels has been corrected in the text.

Comment 6

We rewrote the text and removed the reference to Kollen 2009 at this point, as this study is related to the Bobath approach as used for adult stroke rehabilitation. We cited a new and more specific reference (dos Santos 2015) to support the text.

Comment 7

We believe that Franki 2012 does indeed include relevant NDT studies, and have retained it in the text.

Comment 8

We have replaced the Singhi 2004 reference with one to a more recent and comprehensive work, Novak 2013.

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CDPLPG

Jane Dennis, Feedback Editor, CDPLPG.
Joanne Wilson, Managing Editor, CDPLPG.

WHAT'S NEW

Date	Event	Description
21 August 2017	Feedback has been incorporated	Feedback incorporated.

CONTRIBUTIONS OF AUTHORS

MAZ was the contact person with the editorial base and has overall responsibility for the review. MAZ co-ordinated the contributions from the co-authors and wrote the final draft of the protocol. MAZ, GP, and RR contributed to writing the methods and statistical analysis sections of the protocol. MAZ, GP and RR drafted the clinical sections of the protocol. MAZ, GP, and RR contributed to writing the final draft of the protocol.

DECLARATIONS OF INTEREST

Márcia A Zanon - none known.
Gustavo JM Porfirio - none known.
Rachel Riera - none known.
Ana Luiza C Martimbianco - none known.

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