

Evidence-based Perspective on CP Rehabilitation – Reviews on physiotherapy, physiotherapy-related motor-based interventions and orthotic devices

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ABSTRACT

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Objectives

This thesis utilises an evidence-based approach to critically evaluate and summarize effectiveness research on physiotherapy, physiotherapy-related motor-based interventions and orthotic devices in children and adolescents with cerebral palsy (CP). It aims to assess the methodological challenges of the systematic reviews and trials, to evaluate the effectiveness of interventions in current use, and to make suggestions for future trials

Methods

Systematic reviews were searched from computerized bibliographic databases up to August 2007 for physiotherapy and physiotherapy-related interventions, and up to May 2003 for orthotic devices. Two reviewers independently identified, selected, and assessed the quality of the reviews using the Overview Quality Assessment Questionnaire complemented with decision rules.

From a sample of 14 randomized controlled trials (RCT) published between January 1990 and June 2003 we analysed the methods of sampling, recruitment, and comparability of groups; defined the components of a complex intervention; identified outcome measures based on the International Classification of Functioning, Disability and Health (ICF); analysed the clinical interpretation of score changes; and analysed trial reporting using a modified 33-item CONSORT (Consolidated Standards of Reporting Trials) checklist.

The effectiveness of physiotherapy and physiotherapy-related interventions in children with diagnosed CP was evaluated in a systematic review of randomised controlled trials that were searched from computerized databases from January 1990 up to February 2007. Two reviewers independently assessed the methodological quality, extracted the data, classified the outcomes using the ICF, and considered the level of evidence according to van Tulder et al. (2003).

Results

We identified 21 reviews on physiotherapy and physiotherapy-related interventions and five on orthotic devices. These reviews summarized 23 or 5 randomised controlled trials and 104 or 27 observational studies, respectively. Only six reviews were of high quality. These found some evidence supporting strength training, constraint-induced movement therapy or hippotherapy, and insufficient evidence on comprehensive interventions. Based on the original studies included in the reviews on orthotic devices we found some short-term effects of lower limb casting on passive range of movement,

and of ankle-foot orthoses on equinus walk. Long term effects of lower limb orthoses have not been studied. Evidence of upper limb casting or orthoses is conflicting.

In the sample of 14 RCTs, most trials used simple randomisation, complemented with matching or stratification, but only three specified the concealed allocation. Numerous studies provided sufficient details on the components of a complex intervention, but the overlap of outcome measures across studies was poor and the clinical interpretation of observed score changes was mostly missing. Almost half (48%) of the applicable CONSORT-based items (range 28–32) were reported adequately. Most reporting inadequacies were in outcome measures, sample size determination, details of the sequence generation, allocation concealment and implementation of the randomization, success of assessor blinding, recruitment and follow-up dates, intention-to-treat analysis, precision of the effect size, co-interventions, and adverse events.

The systematic review identified 22 trials on eight intervention categories. Four trials were of high quality. Moderate evidence of effectiveness was established for upper extremity treatments on attained goals, active supination and developmental status, and of constraint-induced therapy on the amount and quality of hand use. Moderate evidence of ineffectiveness was found for strength training's effect on walking speed and stride length. Conflicting evidence was found for strength training's effect on gross motor function. For the other intervention categories the evidence was limited due to the low methodological quality and the statistically insignificant results of the studies.

Conclusions

The high-quality reviews provide both supportive and insufficient evidence on some physiotherapy interventions. The poor quality of most reviews calls for caution, although most reviews drew no conclusions on effectiveness due to the poor quality of the primary studies. A considerable number of RCTs of good to fair methodological and reporting quality indicate that informative and well-reported RCTs on complex interventions in children and adolescents with CP are feasible. Nevertheless, methodological improvement is needed in certain areas of the trial design and performance, and the trial authors are encouraged to follow the CONSORT criteria. Based on RCTs we established moderate evidence for some effectiveness of upper extremity training. Due to limitations in methodological quality and variations in population, interventions and outcomes, mostly limited evidence on the effectiveness of most physiotherapy interventions is available to guide clinical practice. Well-designed trials are needed, especially for focused physiotherapy interventions.

Keywords: cerebral palsy, children, adolescents, physical therapy, conductive education, orthotic devices, systematic review

Heidi Anttila. Evidence-based Perspective on CP Rehabilitation – Reviews on physiotherapy, physiotherapy-related motor-based interventions and orthotic devices. [Näyttöön perustuva näkökulma CP-kuntoutukseen – Katsauksia fysioterapiasta, fysioterapiaan liittyvistä motorista menetelmistä ja ortooseista] STAKES, Research Report 180. Helsinki 2008. ISBN 978-951-33-2249-6.

Tavoitteet

Tässä väitöskirjassa arvioidaan kriittisesti tutkimuksia CP-lasten ja -nuorten kuntoutuksessa käytetystä fysioterapiasta ja muista liikkumisen harjoitteista sekä ortooseista näyttöön perustuvasta näkökulmasta. Tutkimuskysymyksinä on, millaisia menetelmällisiä haasteita liittyy tämän aihealueen järjestelmällisiin katsauksiin ja satunnaistettuihin tutkimuksiin, ja mikä on erilaisten nykyisin käytössä olevien fysioterapiamenetelmien vaikuttavuus.

Menetelmät

Sähköisistä tietokannoista haettiin järjestelmällisiä katsauksia erilaisista fysioterapian menetelmistä (elokuuhun 2007) ja ortooseista (toukokuuhun 2003). Kaksi arvioijaa valitsi, keräsi tiedon ja arvioi katsausten laadun ”Overview Quality Assessment Questionnaire” -kriteereillä, joihin oli lisätty valmiit vastausvaihtoehdot.

Neljästätoista satunnaistetusta vertailututkimuksesta, jotka oli julkaistu tammi-kuun 1990 ja kesäkuun 2003 välillä, analysoitiin niissä käytettyjä menetelmiä: otanta, rekrytointi ja ryhmien välinen vertailtavuus; monimuotoisen intervention määritellyt osatekijät; tulostimet toimintakyvyn, toimintarajoitteiden ja terveyden kansainvälisen luokituksen (ICF) mukaan; muutoksen kliinisen merkittävyyden tulkinta; ja raportoinnin laatu 33-osioisen CONSORT:iin (Consolidated Standards of Reporting Trials) perustuvan tarkistuslistan avulla.

Fysioterapiamenetelmien vaikuttavuusselvitystä varten haettiin satunnaistettuja vertailututkimuksia sähköisistä tietokannoista vuodesta 1990 helmikuuhun 2007 asti. Kaksi arvioijaa arvioit itsenäisesti tutkimusten laadun, keräsi tiedot tutkimuksista, luokitteli tulokset ICF:n mukaan ja arvioi näytön asteen van Tulder ym. (2003) mukaan.

Tulokset

Hauissa löytyi 21 katsausta erilaisista fysioterapiamenetelmistä ja 5 katsausta ortooseista. Fysioterapiakatsauksissa oli arvioitu yhteensä 23 satunnaistettua vertailututkimusta ja 104 havainnoivaa tutkimusta CP-lapsilla ja -nuorilla. Ortoosikatsauksissa tutkimuksia oli vastaavasti 5 ja 27. Kuusi fysioterapiakatsausta oli laadultaan hyviä. Niissä todettiin, että on jotain näyttöä voimaharjoittelun, pakotetun yläraajan käytön ja ratsastusterapian hyödyistä, ja että tieteellinen näyttö on riittämätöntä kokonaisvaltaisista fysioterapia- tai toimintaterapiainventioista. Ortoosikatsauksissa olevien tutkimusten mukaan löytyi lyhyen ajan näyttöä siitä, että kipsaus voi lisätä passiivista liikelaajuutta, ja että plantaarifeksiota rajoittavilla ortooseilla voi olla suotuisa vaiku-

tus varvaskävelyyn. Alaraajaortoosien pitkäaikaisvaikutuksia ei ollut tutkittu. Näyttö yläraajan kipsien tai -lastojen vaikuttavuudesta on ristiriitaista.

Neljäntoista satunnaistetun tutkimuksen otoksessa useimmissa tutkimuksissa oli käytetty yksinkertaista satunnaistamista täydennettynä matching- ja stratifikaatio-tekniikoilla, mutta vain kolmessa tutkimuksessa ryhmäjoon salausta varmistettiin. Monet tutkimukset määrittivät selkeästi monimuotoisen intervention eri osia. Eri tutkimusten mittarit olivat harvoin samoja, eikä niissä tapahtuneiden muutosten kliinistä merkitystä tulkittu. Puolet soveltuvista CONSORT:iin pohjautuvista kysymyksistä (vaihteluväli 28–32) oli raportoitu riittävän hyvin. Puutteita oli tulostittareiden, ryhmäkoon määrittämisen, satunnaistamismenetelmän, ryhmäjoon salaamisen ja satunnaistamisen, mittaajien sokkouttamisen, tutkimuksen tekemisen ajankohtien, ryhmäkohtaisen analyysin (intention-to-treat), tuloksen luottamusvälien, muiden samanaikaisten interventioiden ja mahdollisten haittojen raportoinnissa.

Järjestelmälliseen katsaukseen hyväksyttiin 22 satunnaistettua tutkimusta, jotka luokiteltiin kahdeksaan terapialuokkaan. Neljä tutkimusta oli laadultaan hyviä. Kohtalaista näyttöä löytyi kahdesta terapialuokasta: 1) yläraajojen terapia lisäsi tavoitteiden saavuttamista, käsivarren aktiivista ulkokiertoa ja vaikutti lapsen kehitystasoon, sekä 2) pakotettu käden käyttö lisäsi käden käytön määrää ja laatua. Voimaharjoittelun vaikuttamattomuudesta kävelynopeuteen ja askelpituuteen löytyi kohtalaista näyttöä ja karkeamotoriikkaan ristiriitaista näyttöä. Muissa terapialuokissa tutkimusnäyttö oli heikkoa, ja huolimatta tutkimusten heikosta laadusta tutkittujen ryhmien välillä ei ollut eroja.

Johtopäätökset

Parhaiden katsausten johtopäätökset näytöstä joidenkin fysioterapiamenetelmien sekä vaikuttavuudesta että näytön riittämättömyydestä ovat luotettavia. Menetelmällisesti heikkojen katsausten tuloksia kannattaa tulkita varoen. Kaikkiaan katsausten mukaan tieteellinen näyttö useimmista fysioterapiamenetelmistä ja ortooseista oli riittämättömä heikkojen alkuperäistutkimusten takia. CP-lasten ja -nuorten satunnaistetuista tutkimuksista huomattava määrä oli sekä menetelmiltään että raportoinniltaan hyviä tai melko hyviä. Tämä osoittaa, että hyvin toteutettu ja raportoitu satunnaistettu tutkimus monimuotoisissa interventioissa voidaan toteuttaa heterogeenisessä potilasryhmässä. Tutkimusmenetelmissä ja toteuttamisessa on silti parannettavaa tietyin kohdin, ja tutkijoiden kannattaa noudattaa raportoidessaan CONSORT -suosituksia. Järjestelmällisessä katsauksessa yläraaja-harjoittelun vaikuttavuudesta löytyi kohtalaista tutkimusnäyttöä. Muiden tutkimusten heikkouksista ja tutkittujen potilasryhmien, interventioiden ja käytettyjen tulostittareiden erilaisuudesta johtuen useista fysioterapian menetelmistä on saatavilla vain rajoitetusti käytäntöön soveltuvaa tietoa. Uusia tutkimuksia tarvitaan erityisesti kohdennetuista interventioista.

Asiasanat: CP-vamma, lapset, nuoret, fysioterapia, konduktiivinen opetus, ortoosit, järjestelmällinen katsaus

Heidi Anttila. Evidence-based Perspective on CP Rehabilitation – Reviews on physiotherapy, physiotherapy-related motor-based interventions and orthotic devices [Evidensbaserat perspektiv på rehabilitering av cp-skadade – Översikter över fysioterapi, fysioterapirelaterade motorikbaserade metoder och ortoser]. STAKES, Research Report 180. Helsinki 2008. ISBN 978-951-33-2249-6.

Mål

I doktorsavhandlingen utvärderas kritiskt ur evidensbaserat perspektiv studier om användning av fysioterapi och andra rörelseövningar samt ortoser i rehabilitering av cp-skadade barn och ungdomar. Målet är att bedöma de metodiska utmaningarna i systematiska översikter och randomiserade studier, att utvärdera vilken effekt metoder som används för närvarande har och att lägga fram förslag till framtida studier.

Metoder

Genom sökningar i elektroniska databaser hittades systematiska översikter över olika fysioterapimetoder (fram till augusti 2007) och ortoser (fram till maj 2003). Två utvärderare valde och samlade översikterna och utvärderade kvaliteten på dem med hjälp av "Overview Quality Assessment Questionnaire"-kriterier kompletterade med färdiga svarsalternativ.

Metoderna i 14 randomiserade kontrollerade studier, som publicerades mellan januari 1990 och juni 2003, analyserades: urval, rekrytering och gruppernas jämförbarhet; den mångformiga interventionens fastställda delfaktorer; resultatmätare enligt den internationella klassifikationen av funktionstillstånd, funktionshinder och hälsa (ICF); analys av förändringens kliniska betydelse; och analys av kvaliteten på rapporteringen med hjälp av en checklista med 33 punkter enligt CONSORT (Consolidated Standards of Reporting Trials).

För utredningen av fysioterapimetodernas effekt hittades randomiserade kontrollerade studier från 1990 till februari 2007 genom sökningar i elektroniska databaser. Två utvärderare utvärderade självständigt studiernas kvalitet, samlade uppgifter ur studierna, klassificerade resultaten enligt ICF och utvärderade evidensgraden enligt van Tulder m.fl. (2003).

Resultat

Genom sökningarna hittades 21 översikter över olika fysioterapimetoder och fem översikter över ortoser. I fysioterapiöversikterna hade totalt 23 randomiserade studier och 104 observerande studier av cp-skadade barn och ungdomar utvärderats. I ortosöversikterna var antalet studier 5 respektive 27. Sex fysioterapiöversikter var av god kvalitet. I dem konstaterades det att det finns viss evidens för att styrketräning, CI-terapi och ridterapi är till nytta, och att den vetenskapliga evidensen för övergri-

pande fysioterapi- eller ergoterapiinterventioner är otillräcklig. Enligt studierna i ortosöversikterna hade det hittats evidens för att gipsning kan öka den passiva rörlighetsgraden på kort sikt och att fotledsortoser kan ha en gynnsam kortvarig effekt på equinusfelställning. Långvariga effekter av ortoser för de nedre extremiteterna har inte undersökts. Evidensen för behandlingseffekten av gipsning av eller ortoser för de övre extremiteterna är motstridiga.

I urvalet av 14 randomiserade studier hade man i de flesta av studierna använt enkel randomisering kompletterad av matchnings- och stratifikationsteknik, men endast i tre studier hade det säkerställts att gruppindelningen är hemlig. Många studier definierade tydligt den mångformiga interventionens olika delar. De olika studiernas mätare var sällan desamma, och den kliniska betydelsen av observerade förändringar analyserades inte. Enligt rapporteringen räckte hälften av de tillämpliga CONSORT-baserade frågorna (variationsintervall 28–32) väl till. Det förekom brister i rapporteringen om resultatmätare, fastställande av gruppstorlek, randomiseringsmetod, hemlighållande och randomisering av gruppindelning, blindning av utvärderare, tidpunkterna för genomförandet av studien, den gruppvisa analysen (intention-to-treat), precisionen av effektens storlek, andra samtidiga interventioner och eventuella olägenheter.

Till den systematiska översikten godkändes 22 randomiserade studier, som delades in i åtta terapiklasser. Fyra studier var av god kvalitet. Medelmåttig evidens hittades i två terapiklasser: 1) terapi för de övre extremiteterna förbättrade uppnåendet av mål liksom armens aktiva utåtrotation och påverkade barnets utvecklingsnivå, samt 2) CI-terapi ökade användningen av handen och kvaliteten på användningen. Det hittades medelmåttig evidens för att styrketräning inte har någon effekt på gånghastigheten och steglängden, medan evidensen för hur styrketräning påverkar grovmotoriken var motstridig. I de övriga terapiklasserna var forskningsevidensen svag. Oberoende av den låga kvaliteten på studierna förekom det inga skillnader mellan de undersökta grupperna.

Slutsatser

De bästa översikternas slutsatser om evidensen för vissa fysioterapimetoders effekt och otillräckliga evidens är tillförlitliga. Resultaten från översikterna med svag metodik bör tolkas med försiktighet. Allmänt sett ansågs det i de flesta av översikterna att den vetenskapliga evidensen för de flesta av fysioterapimetoderna och ortoserna var otillräcklig på grund av att de ursprungliga studierna var av dålig kvalitet. Ett stort antal av de randomiserade studierna om cp-skadade barn och ungdomar var goda eller rätt goda när det gäller både metoder och rapportering. Detta visar att en väl genomförd och rapporterad randomiserad studie om mångformiga interventioner kan genomföras i en heterogen patientgrupp. Forskningsmetoderna och genomförandet kan dock förbättras på vissa punkter, och det lönar sig för forskarna att följa CONSORT-rekommendationerna i rapporteringen. I den systematiska översikten hittades måttlig forskningsevidens för effekten av att träna de övre extremitete-

terna. På grund av de övriga studiernas svagheter och skillnaderna mellan undersökta patientgrupper, interventioner och använda resultatmätare var tillgången på sådan information som är till nytta i det praktiska arbetet begränsad i fråga om många fysioterapimetoder. Nya studier behövs särskilt om fokuserade interventioner.

Nyckelord: cp-skada, barn, ungdomar, fysioterapi, konduktiv undervisning, ortoser, systematisk översikt

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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original articles, which are referred to in the text by Roman numerals (I to V).

- I. Anttila H, Suoranta J, Malmivaara A, Mäkelä M, Autti-Rämö I:
Effectiveness of physiotherapy and conductive education interventions in children with cerebral palsy: a focused review. *Am J Phys Med Rehabil* 2008;87:478–501.
- II. Autti-Rämö I, Suoranta J, Anttila H, Malmivaara A, Mäkelä M.
Effectiveness of Upper and Lower Limb Casting and Orthoses in Children with Cerebral Palsy. *Am J Phys Med Rehabil* 85(1): 89–103, 2006.
- III. Kunz R, Autti-Rämö I, Anttila H, Malmivaara A, Mäkelä M.
A systematic review finds that methodological quality is better than its reputation but can be improved in physiotherapy trials in childhood cerebral palsy. *J Clin Epidemiol* 59:1239–1248; 2006.
- IV. Anttila H, Malmivaara A, Kunz R, Autti-Rämö I, Mäkelä M.
Quality of reporting randomized, controlled trials in cerebral palsy. *Pediatrics* 117(6): 2222–2230, 2006.
- V. Anttila H, Autti-Rämö I, Suoranta J, Mäkelä M, Malmivaara A.
Effectiveness of physiotherapy interventions for children with cerebral palsy: a systematic review. *BMC Pediatrics* 2008, 8:14.

ABBREVIATIONS

AACPDM	American Academy for Cerebral Palsy and Developmental Medicine
AFO	ankle-foot orthosis
CONSORT	Consolidated Standards of Reporting Trials
CP	cerebral palsy
GMFCS	Gross Motor Function Classification System
GMFM	Gross Motor Function Measure
ICF	International Classification of Functioning, Disability and Health
ICIDH	International Classification of Impairments, Disabilities and Handicaps
NDT	neurodevelopment therapy
PICO	Acronym of words: Patient, Intervention, Comparator, Outcomes
QUOROM	The Quality of Reporting of Meta-analyses
RCT	randomized controlled trial

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Introduction

The Finnish rehabilitation-research agenda identifies effectiveness, outcomes, benefits, and conceptual, theoretical and methodological issues as necessary information (Kuntoutuksen tutkimuksen kehittämissuunnitelma 2004). More resources are considered necessary for researching good and efficient rehabilitation practices, and the effectiveness in terms of desired outcomes of different rehabilitation services.

The evidence-based perspective can help to set realistic questions on treatment effectiveness or efficacy in any field (Sackett et al. 2000). The best evidence can be drawn from randomized controlled trials (RCT) and systematic reviews of such trials. The possible benefits or harms of treatments should always be considered together with the costs and the patients' own values and preferences. These principles of evidence-based practice are widely accepted among health care professionals. However, many physiotherapists and other professionals often have limited time, skills and resources to search for evidence and to interpret effectiveness studies (Haynes & Haines 1998; Maher et al. 2004). Thus systematic summaries of the highest quality research are warranted. Previous Finnish analyses on the effectiveness of physiotherapy interventions have focused on major public health problems for adults (Aalto et al. 2002; Sariola 2002; Mälkiä et al. 2004; Alaranta & Malmivaara 2007).

Children with cerebral palsy (CP) present a heterogeneous group of children with complex disabilities. The common unifying feature is a defect or injury to an immature central nervous system that adversely affects motor function, accompanied by additional impairments. In the field of CP rehabilitation, a number of contemporary conceptual frameworks—such as the International Classification of Functioning, Disability and Health (ICF), family-centred care, and models of motor change for children—have prompted a shift from individual interventions that focus on impairments and activity limitations to interventions that optimize participation in daily activities and environments (Rosenbaum & Stewart 2004). Modern rehabilitation services involve a partnership between the child, the family, health professionals and the community (Rosenbaum & Stewart 2004; Koivikko & Sipari 2006). Thus there is a need to consider a wide spectrum of child and family interventions and outcomes (Majnemer & Mazer 2004).

A wide variation of rehabilitation services are often available for children with CP. Scarce resources and the increasing demands by caregivers and the treating

professionals for the best care for the child have led to a desire to create an evidence base to assist in the selection of and prioritising between various therapeutic options for children and adolescents with cerebral palsy. Nevertheless, a comprehensive view of the advantages of the therapeutic alternatives is lacking. Therefore, the Hospital for Children and Adolescents in Helsinki (HUUS) proposed to the Finnish Office for Health Technology Assessment (Finnohta) at the National Research and Development Centre for Welfare and Health (STAKES) the collection and summarizing of such evidence to assist clinical decision-making at the hospitals. Soon after the project was launched in 2003, it became evident that methodological problems could pose challenges when evaluating the reviews and intervention studies of various physiotherapy or physiotherapy-related treatments used in children and adolescents with CP.

This thesis focuses on the methodological challenges that are often present in rehabilitation research on complex interventions for multifaceted problems. This study is a retrospective observational analysis on review articles and randomized controlled trials, the methods of which are compared to best available standards, the QUOROM (The Quality of Reporting of Meta-analyses) and the CONSORT (Consolidated Standards of Reporting Trials) statements (Begg et al. 1996; Moher et al. 1999a; Altman et al. 2001). Issues of generalizability are made clearer through comprehensive analyses of the patients, interventions and outcomes.

The first chapter provides a traditional literature review of the concepts of evaluation research, the current understanding of the wide spectrum of cerebral palsies and its consequences for functional abilities, contemporary therapeutic approaches, and outcome measures to evaluate therapeutic interventions in the field of CP. Chapters 2–6 form the main study. Chapter 2 presents the study questions, and Chapter 3 the materials and methods. The results section (Chapter 4) combines the results of the five original papers. The two overviews of reviews (I, II) summarize the quality of the reviews and the key findings of the literature identified by the reviews. The two methodological papers take a closer look at a sample of RCTs in this field and evaluate how the methodological challenges that are often present are managed (III) and how the authors have succeeded in reporting the conduct of the trial in terms of the standards set out by the CONSORT statement (IV). The last paper (V) provides a systematic evaluation of the characteristics, quality, methods and results of the RCTs published since 1990. Finally, Chapter 5 discusses the study results and limitation, and practical implications, as well as suggestions for future studies. Chapter 6 sets out the conclusions.

1 Review of the literature

1.1 Evidence-based evaluation of interventions

Definitions

Evidence can broadly be defined as “any empirical observation about the apparent relation between events” (The Evidence-Based Medicine Working Group et al. 2002). Evidence-based medicine involves two fundamental principles in clinical decision-making. First, the evidence is always interpreted together with the patient's values and preferences by weighing the benefits and risks, and the costs associated to the treatment compared to the alternatives. Second, the strength of the available evidence may be variable, constituting a hierarchy of evidence on the basis of the ability of the study to avoid systematic bias (Table 1.1). This hierarchy implies a clear course of action to seek the highest available evidence for clinical decision-making. Systematic reviews potentially provide the best syntheses of the available evidence, when more than one methodologically sound trial provides consistent results (Egger et al. 2001; Khan et al. 2001). Somewhat weaker inferences can be drawn from a single RCT, unless it is very large and studies a diverse population. Observational studies are far less trustworthy as they may under- or overestimate treatment effects in an unpredictable way. Unsystematic observations and physiological studies provide the weakest inferences about treatment effects (Table 1.1). Evidence from systematic reviews can further be summarized to guidelines or evidence-based textbooks, and to various high-technology easy-available systems such as computerized decision-making support software (The Evidence-Based Medicine Working Group et al. 2002; Haynes 2006).

Systematic reviews are studies where the analytic unit is a study. Such reviews apply sound scientific methodology with an a priori defined protocol. It defines a focused and structured study question, and the strategies and methods for the searches, study selection, critical appraisal, data collection, and analysing and summarizing of the results (Green et al.; Oxman et al. 1994; Khan et al. 2001). Table 1.2 outlines the step-by-step approach (Khan et al. 2001; Khan et al. 2003) and the differences between a systematic and traditional review (Petticrew 2001). The results are summarized either qualitatively or quantitatively by a meta-analysis. The main aim is to reduce data from clinical trials into simple statements about treatment effects (Egger et al. 2001).

Randomized controlled trials (RCTs) are the “gold standard” for providing evidence on the effects of interventions. They can separate the effects of the inter-

TABLE 1.1 Hierarchy of study designs for questions about effectiveness for healthcare interventions modified from (Khan et al. 2003).

Description of the design	Levels assigned to evidence based on soundness of design
Experimental study - RCT (with concealed allocation) - Experimental study without randomisation	I
Observational study with control group - Cohort study - Case-control studies	II
Observational study without control groups - Cross-sectional study - Before-after study - Case-series	III
Case reports Pathophysiological studies or bench research Expert opinion or consensus	IV

vention from those of extraneous factors such as natural recovery and statistical regression (Sackett et al. 2000). In an RCT people with similar clinical characteristics are allocated at random to two or more types of treatment (or placebo or sham treatments) (Begg et al. 1996; Altman et al. 2001). Whenever possible, both the participants and the treatment providers should remain unaware (blinded) as to who is receiving the intervention. During the trial as much as possible is kept similar between the groups (co-interventions). After an appropriate time for the treatment to work, the functional status is measured in the original groups (intention-to-treat principle) by trained assessors, who also are blinded as to what interventions the participants have received. Adequate group sizes to detect statistically significant changes should be determined prior the study. These and many other steps in the conduct of a randomized trial increase the internal validity and the credibility of the results (Begg et al. 1996; Altman et al. 2001).

The quality of clinical trials may refer to different aspects: the quality of design, conduct and analysis of a trial (internal validity), its clinical relevance (external validity) or quality of reporting. Internal validity refers to the extent of avoidance of systematic error (bias), which potentially falls into four categories: systematic differences between comparison groups (selection bias), unequal provision of care apart from the treatment under evaluation (performance bias), biased outcome assessment (detection bias) and biased occurrence and handling of protocol deviations and loss to follow up (attrition bias) (Jüni et al. 2001). The external validity of a trial is a matter of judgement. It refers to the extent to which the results provide a correct basis for applicability to other circumstances, its generalisability to other groups of patients or to usual care (patients, settings, and treatment and

TABLE 1.2 Systematic reviews and traditional narrative reviews compared (Khan et al. 2001; Petticrew 2001; Khan et al. 2003).

	Good quality systematic reviews	Traditional narrative reviews
Step 1		
Deciding on review question	Start with clear question to be answered or hypothesis to be tested	May also start with clear question to be answered, but they more often involve general discussion of subject with no stated hypothesis
Step 2		
- Searching for relevant studies	Strive to locate all relevant published and unpublished studies to limit impact of publication and other biases	Do not usually attempt to locate all relevant literature, and describe why certain studies are included and others excluded
- Defining which studies to include and exclude	Involve explicit description of what types of studies are to be included to limit selection bias on behalf of reviewer	
Step 3		
Assessing study quality	Examine in systematic manner methods used in primary studies, and investigate potential biases in those studies and sources of heterogeneity between study results	Often do not consider differences in study methods or study quality
Step 4		
Synthesising study results	Base their conclusions on those studies which are most methodologically sound	Often do not differentiate between methodologically sound and unsound studies
Step 5		
Interpreting the findings	Inferences and recommendations for practise are based on the strength of the evidence and clinical relevance of the findings.	Do not clearly link the conclusions and the data.

measurement variables) (Jüni et al. 2001). The acronym PICO provides a useful way to specify the trial circumstances for both reviews and clinical studies: population (P), interventions (I), comparison interventions (C), and outcomes (O) (Sackett et al. 2000; Malmivaara et al. 2007). Trials should provide adequate information on all aspects of the PICO to assist interpretation and deciding the applicability to clinical practice (Malmivaara et al. 2007).

Intervention trials are either explanatory or pragmatic. Explanatory trials test the intervention efficacy i.e. whether beneficial effects can be reached under carefully controlled ideal conditions. Pragmatic trials measure effectiveness i.e. the degree of beneficial effect in real clinical practice (Gold et al. 1996; Roland & Torgerson 1998). There is no validated definition to separate effectiveness studies from efficacy studies, but Gartlehner et al. have proposed a few general criteria for effectiveness studies: populations in primary care, less stringent eligibility criteria, health outcomes, long study duration, assessment of adverse events, adequate sample size to assess minimally important difference from a patient perspective, and an intention-to-treat analysis (Gartlehner et al. 2006).

Appraisal of trials

There is debate on how the methodological rigour or trial quality should best be assessed. Although some aspects (such as blinding and proper allocation) have been shown to quantitatively affect the results of a study (Schulz et al. 1995; Moher et al. 1998; Chalmers et al. 1999; Jüni et al. 1999; Kjaergard et al. 2001; Egger et al. 2003), others have not. The most important aspect for preventing bias appears to be the concealment of treatment allocation (Schulz et al. 1995; Chalmers et al. 1999).

Many different scoring systems exist (Moher et al. 1995), but consensus is lacking as to which components to include and what tool would be best to assess trial quality (Sutton et al. 1998; Jüni et al. 1999; Moher et al. 1999b). Most tools are variations of the series of appraisal questions originally presented in the User's Guides to the Medical Literature or the criteria suggested in the Cochrane handbook (The Evidence-Based Medicine Working Group et al. 2002; 2008). In Finland, the quality assessment checklist by Guyatt et al. (The Evidence-Based Medicine Working Group et al. 2002) is frequently used in technology assessment (Mäkelä et al. 2007) and guideline development (Käypä hoito -toimitus 2004).

Quality scales combine information on several features into a single numerical value. Published scales vary considerably in terms of dimensions covered, size, and complexity. This makes the interpretation of the summary score problematic. The study results may be associated with one or several components of a scale, or there may be an association between two or more components of a scale. Using different scales, the same trial may receive inconsistent quality scores (Jüni et al. 1999). Different reviewers using the same scale may find little inter-rater reliability (Hopayian 2001). Thus incorporation of quality data by weighting trials or using summary scores is controversial. Quality may best be evaluated qualitatively based on the individual components related to study quality, so that a judgement of the quality of any given study as good or bad is presented in a transparent and easily understood language (Shapiro 1997; Egger et al. 2003).

Inadequate reporting may hamper the quality assessment of the trials (DerSimonian et al. 1982; Schulz et al. 1994; Moher et al. 1996; Thornley & Adams 1998), and thus have profound consequences for the decision-making in health care. Discrepancies between the actual conduct of the trial and the trial report suggest that characterizing RCTs as good or poor on the basis of the report is likely to be inappropriate (Hill et al. 2002). Pildal et al. (Pildal et al. 2005) found discrepancies and unclear descriptions of allocation concealment both in the study protocol and the resulting publications. Well-conducted trials may not be reported adequately (Huwiler-Müntener et al. 2002). On the other hand, treatment effects may be exaggerated in inadequately reported trials. For example, a systematic review of 1147 trials concluded that trials with inadequate reporting of allocation concealment showed 25% greater estimates of the interventions effectiveness than trials with

adequately reported allocation concealment (Egger et al. 2003).

An International standard for reporting randomized trials, provided in 1996 by the CONSORT (Consolidated Standards of Reporting Trials) statement seeks to ensure valid reporting of trial methods and conduct (Begg et al. 1996). It comprises a flow chart and a checklist of 22 items on trial methods (such as blinding, concealment, and adequate randomisation) and elements that relate to reporting (such as description of protocol violations). The checklist items have further been explored in an extension document (Altman et al. 2001), and most recently in a book (Keech et al. 2007). The CONSORT statement has been associated with improvements in the quality of RCT reporting (Moher et al. 2001). Many scientific journals have adopted the CONSORT statement and endorsed its use for authors seeking to submit an RCT report to be considered for publication (Altman 2005). Moreover, the CONSORT is endorsed by the International Committee of Medical Journal Editors (International Committee of Medical Journal Editors 2006) and the World Association of Medical Editors.

Appraisal of systematic reviews

An essential feature of systematic reviews is critical appraisal of the methodological quality of the included primary studies (Oxman et al. 1994; Jüni et al. 2001). Lack of adherence to defined quality criteria may explain different results of studies on the same topic (Egger et al. 2003). Published systematic reviews have heterogeneous approaches to assess methodological quality; their reporting of trial quality has been infrequent or lacking, and when done seldom incorporated into the analyses (Moher et al. 1995; Moher et al. 1999b; Moja et al. 2005). The quality of a review can be defined as the confidence that the design, conduct and analysis of the review have minimised bias. Despite guidelines for the procedural path when conducting a systematic review (Deeks et al. 1996; 2008), all reviews may not have been carried out in a rigorous way (Mulrow 1987; Sacks et al. 1987). Previous evaluations of systematic reviews in many fields imply that readers should not accept them uncritically and there is a need to improve the methodological quality and guidelines of reporting (Sacks et al. 1987; Jadad & McQuay 1996; McAlister et al. 1999; Jadad et al. 2000; Bandhari et al. 2001; Moher et al. 2002; Glenny et al. 2003; Delaney et al. 2005). Cochrane reviews are usually more rigorously conducted and reported than non-Cochrane reviews (Moher et al. 1999b; Shea et al. 2002; Moher et al. 2007).

Because the effectiveness of interventions may be masked or exaggerated by reviews that are not rigorously conducted, quality assessment is important. A systematic review yielded 21 published checklists and 3 scales designed to assess the quality of systematic reviews and meta-analyses (Shea et al. 2001). These instruments were developed between 1984 and 1997, and generally contained items that should be included in the methods section of a systematic review. The most rigor-

ously developed scale was the 'Overview Quality Assessment Questionnaire' by Oxman and Guyatt (Oxman & Guatt 1991), complemented with an analysis of the inter-observer validity of the index (Oxman et al. 1991). Hoving et al. (Hoving et al. 2001) incorporated decision rules for this scale to be used in the field of rehabilitation.

Differences in quality may not always explain all discordance in results between reviews on the same topic (Jadad et al. 1997). Generic discordances such as the clinical question asked, the selection and inclusion of studies, data extraction, assessment of study quality, ability to combine studies, and statistical methods for data analysis may also explain different results. Other potential challenges for reviewers are missing data and the role of observational studies (Sutton et al. 1998). Recent research has provided evidence that results of systematic reviews on effectiveness can be overestimated because of publication bias (Dickersin 2005; Sutton 2005) or language bias (Egger et al. 1997; Moher et al. 2000). A newer rigorously developed and validated instrument for the 'assessment of multiple systematic reviews' (AMSTAR) also addresses these biases (Shea et al. 2007a; Shea et al. 2007b).

The rigour and clinical interpretability of systematic reviews may be enhanced by consistent reporting of the features of the included RCTs (Moher et al. 1999b). The quality of reporting of a systematic review can be assessed by means of the QUOROM (Quality Of Reporting Of Meta-analyses) statement, which describes the preferred way to present the abstract, introduction, methods, results, and discussion sections of a meta-analysis report, including a flow diagram of the article identification and selection process (Moher et al. 1999a). Similar guidance is available for health technology assessment reports (Hailey 2003).

Presenting and interpreting the results

Reviews usually provide information of the included studies in tables, where the PICO characteristics are collected. Results of the individual studies should be reported in terms of the between-group differences and their confidence intervals of all measured outcomes, as in the original studies (Begg et al. 1996). For binary data, the results can be presented as relative measures, such as risk ratios, odds ratios, and relative risk reduction, or as absolute measures i.e. absolute risk reduction. The latter can be converted to the number needed to treat (NNT) or events per thousand patients. As the relative and absolute effect measures have complementary interpretations, both of them should be reported. Results from continuous data can be presented as standardized mean differences or weighted mean differences (The Evidence-Based Medicine Working Group et al. 2002; 2008). The preferred approach for statistical comparisons of continuous data is the analysis of covariance (ANCOVA) (Vickers 2001; Vickers & Altman 2001).

TABLE 1.3 Questions for appraising clinical applicability (The Evidence-Based Medicine Working Group et al. 2002; van Tulder et al. 2003).

Population	Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practise?
Intervention	Are the interventions described well enough so that you can provide the same for your patients?
Intervention	Are the treatment settings described well enough so that you can provide the same for your patients?
Outcome	Were all clinically relevant outcomes measured and reported?
Outcome	Is the size of the effect clinically important?
Benefit	Are the likely treatment benefits worth potential harms and costs?

A balanced interpretation of the benefits and harms of the intervention takes the context of the patient into account (Guyatt & Drummond 2002; van Tulder et al. 2003; Malmivaara et al. 2006). Thus the clinical applicability of the results of a systematic review or a trial comes back to the definition of the study question and the basic trial determinants in terms of PICO. Table 1.3 outlines questions that may be used to appraise the clinical applicability of a trial (The Evidence-Based Medicine Working Group et al. 2002; van Tulder et al. 2003).

1.2 Children and adolescents with cerebral palsy

Definition

CP is a clinical descriptive term. Diagnosis of CP is based on developmental history and neurological examination (Stanley et al. 2000). After 150 years of international debate there are still differences in the terminology used to describe and classify CP (The Definition and Classification of Cerebral Palsy 2007; Morris 2007). The most widely accepted definitions have been those of Bax et al. (Bax 1964), defining CP as “a disorder of posture and movement due to a defect or lesion in the immature brain” and Mutch et al. (Mutch et al. 1992) “an umbrella term covering a group of non-progressive but often-changing motor impairment syndromes secondary to lesions or abnormalities of the brain arising in the early stages of development”.

The most recent definition underlines the idea that the concept of CP needs to be multidimensional and that management of CP always requires a multidisciplinary setting. It recognizes activity restrictions as part of CP and other commonly accompanying disorders, and broadens the definition of CP to “a group of permanent disorders of the development and movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication,

and behaviour, by epilepsy, and by secondary musculoskeletal problems.” (Rosenbaum et al. 2006)

Aetiology

CP has a complex and multifactorial etiology, where many questions still remain unanswered. A vast majority of cases are caused by an interplay of a number of less dramatic, often cumulative risk factors and events occurring pre- peri- or post-natally. Single factors are seldom sufficient to cause cerebral damage, unless present to an overwhelming degree, e.g. only 10% of cases can be ascribed to perinatal hypoxia. The strongest risk factors are prematurity and low birth weight (Stanley et al. 2000; Lawson & Badawi 2003). Multiple birth infants have a four times higher rate of CP than singletons, because of the higher risk of preterm birth (Topp et al. 2004).

In preterm infants CP is most commonly associated with gestational age, periventricular leucomalasia (with or without severe periventricular haemorrhage or infarction), bronchopulmonary dysplasia and hypotension (Martens et al. 2003). An investigation of a cohort of 753 very preterm infants showed inflammatory prenatal events (occurring during the last days or weeks before the delivery) were strongly associated with periventricular leucomalasia, especially the combination of intra-uterine infection and premature rupture of membranes, and prolongation of pregnancy for more than 24 hours with tocolysis (Zupan et al. 1996). Other identified risk factors include maternal diabetes mellitus, threatened abortion, pre-eclampsia, chorioamnionitis, intrauterine growth restriction, maternal black ethnicity, or maternal age older than 25 (Aicardi & Bax 1998; Wu et al. 2003).

CP with a post-neonatal origin (arising between 28 days and 25 months after birth) is most often caused by infection, vascular episodes and head injury (Cans et al. 2004).

Prevalence

The prevalence of CP has risen in time to well above 2.0 per 1000 live births according to a review of the published literature from 1964 to 2004 (Odding et al. 2006). In Europe, the CP prevalence has ranged from 1.49 to 2.63 per 1000 live births in the period 1980–1990, excluding postnatal cases (Surveillance of Cerebral Palsy 2002). The prevalence of post-neonatal CP has decreased to 1.26 per 10 000 live births in children born in the period 1976–1990 (Cans et al. 2004). Recent European data shows that the prevalence of CP has fallen from 6% of live births in 1980 to 4% in 1996 in very low-birth-weight infants (weighing less than 1500 g) and those born after less than 32 week's gestation (Platt et al. 2007). The decline occurred mainly among children with bilateral spastic CP weighing 1000–1499 g, whereas there were no changes in prevalence for children with a birth weight less than 1000 g.

In the Finnish population the overall rate has ranged from 1.6 to 2.5 per 1000 live births, including postnatal cases for children born between 1947–1986 (Tuuteri et al. 1967; Riikonen et al. 1989; Lano 2002). Higher prevalences have been reported for the northernmost Finnish provinces (5.7 per 1000 live births) (von Wendt 1985) and among infants with a birth weight less than 1000 g (11–12%) (Tommiska et al. 2007).

Classification

There are several international classification systems that define and provide terms for the types of movement abnormalities in CP differently. Clinical subtypes of CP have been classified according to topographical distribution of the affected extremities (monoplegia, diplegia, triplegia, hemiplegia, and quadriplegia) and the predominant type of muscle tone: spastic, dyskinetic (mainly choreoathetotic or mainly dystonic forms) or ataxic (diplegic or congenital forms) (Hagberg et al. 1975; Hagberg & Hagberg 1993). Since 1998, Surveillance of Cerebral Palsy (SCPE), consisting of European CP registers, proposed a new classification into CP subtypes (Table 1.4) (Cans 2000). Instead of using the terms diplegia and quadriplegia for spastic CP subtypes, only bilateral and unilateral CP are separated. In addition, the children's motor function are described using the Gross Motor Function Classification System (GMFCS) for the lower limb function (Palisano et al. 1997) (Table 1.5) and the Bimanual Fine Motor Function for the upper limb function (Beckung & Hagberg 2002), while, of the associated impairments, epilepsy and the cognitive, visual, and hearing impairments are recorded.

To assess functional motor abilities, the GMFCS provided the first standardized classification of the severity of motor disability in children with CP aged 1 to 12 years, focusing on functional disability and the need for assistive devices (Table 1.6) (Palisano et al. 1997). Parallel classification scales for upper extremities are the Bimanual Fine Motor Function scale (Beckung & Hagberg 2002) and the Manual Ability Classification System (Eliasson et al. 2006).

In Finland the syndrome is termed according to the International Classification of Diseases (ICD-10) as to spastic quadric- or tetraplegic, spastic diplegic, spastic hemiplegic, dyskinetic (athetoid or ataxic), and other or mixed cerebral palsy syndromes (World Health Organization 2007).

The most recent international classification continues to cover the multidimensional characteristics of the condition, including understanding of its neuropathophysiology gained from new uninvasive brain imaging techniques (Rosenbaum et al. 2006). It widens the description to two other dimensions: the anatomical and neuro-imaging findings of the affected body parts and brain, and the causation and timing of the brain injury.

TABLE 1.4 SCPE classification of CP subtypes and definitions for movement abnormalities (Cans 2000).

<p>1. Spastic CP (at least two of the following):</p> <ul style="list-style-type: none"> - abnormal pattern of posture and/or movement - increased muscle tone (not necessarily constant) - pathological reflexes (hyperreflexia and/or positive Babinski sign) <p>Spastic CP is divided into unilateral (i.e. limbs on one side of the body are involved) and bilateral (i.e. limbs on both sides of the body are involved)</p>
<p>2. Ataxic CP:</p> <ul style="list-style-type: none"> - abnormal pattern of movement and/or posture - loss or orderly coordination (movements executed with abnormal rhythm, accuracy and force)
<p>3. Dyskinetic CP</p> <ul style="list-style-type: none"> - abnormal pattern of movement and/or posture - involuntary, uncontrolled, recurring, occasionally stereotyped movements <p>Dyskinetic CP is divided into dystonic (comprises both hypokinesia/stiffness and hypertonia) or choreoathetotic (comprise both hyperkinesia and hypotonia).</p>
<p>4. Unclassifiable</p>

TABLE 1.5 An example of classification scales: The Gross Motor Function Classification System (Palisano et al. 1997)

GMFCS	
Level I	Walks without restriction, limitations in more advanced gross motor skills
Level II	Walks without restrictions, limitations in walking outdoors and in the community
Level III	Walks with assistive mobility devices, limitations in walking outdoors and in the community
Level IV	Self-mobility with limitations, children are transported or use power mobility outdoors and in the community
Level V	Self-mobility is severely limited, even with the use of assistive technology

Clinical implications of the motor disorder and additional impairments

The most prevalent form of CP is spasticity. According to a review by Odding et al. (Odding et al. 2006) the distribution of CP subtypes has changed over time to more cases with hemiplegia, and fewer with diplegia. Depending on the ethiological causes and brain pathology, 25-80% have additional impairments, such as epilepsy, cognitive difficulties, impaired sensibility in hands, chronic pain, behavioural, speech, visual, gastrointestinal and feeding problems. Many children (25–50%) are under- or overweight, have impaired growth, urinary incontinence and lower physical fitness compared to healthy peers (Odding et al. 2006).

More severe CP is associated with functional limitations in mobility, dexterity, speech and vision (Kennes et al. 2002), larger proportions of accompanying impairments, adverse peri- and neonatal events such as intracranial haemorrhage or stroke, cerebral infarction, and hypoxic-ischaemic encephalopathy in children born at term (Himmelmann et al. 2006). Comorbidities, such as mental retarda-

tion, epilepsy, visual impairment, and hydrocephalus are related to restrictions in mobility, educational achievement, and social relations (Beckung & Hagberg 2002). Pain is more prevalent, with moderate to severe impairment and is associated with educational and social consequences (Houlihan et al. 2004).

In recent Swedish data the children's gross motor function was 32% at level I, 29% at level II, 8% level at III, 15% at level IV, and 16% at level V as measured by the GMFCS (Himmelman et al. 2006). The gross motor function severity varied in CP subtypes as follows: GMFCS levels I and II mainly contain children with diplegia, whose gross and fine function is more homogeneous than in children with hemiplegia. GMFCS level V consists of children with mainly dyskinesia and tetraplegia (Beckung et al. 2007). In Norway 33% had spastic unilateral, 49% spastic bilateral, 6% dyskinetic, 5% ataxic CP subtype, and 7% were not classified (Andersen et al. 2008). Of the additional impairments, 40% have learning disabilities, 28–33% epilepsy, 31% mental retardation, 28% severe speech disturbances, and 19% severe visual impairment (Beckung et al. 2007; Andersen et al. 2008). Gross motor function and manual ability are often discrepant and varying in CP subgroups (Himmelman et al. 2006; Carnahan et al. 2007).

Functional limitations

CP contributes to lifelong functional limitations. Functional limitations that are often associated with CP, as mentioned in the literature, are grouped in Table 1.6 in terms of the International Classification of Functioning, Disability and Health (ICF) (World Health Organization 2001).

Impairments in *body functions and structures* include problems in neuronal structures, muscles, joints and bones. The primary physical pathology in the central nervous system is known as the upper motor neuron syndrome. It is characterized by loss of inhibition and connections to lower motor neurons and other pathways that are responsible for the control of motor activity. Interaction of positive (spasticity, clonus, hyperreflexia, co-contraction) and negative features (weakness, loss of selective motor control, sensory impairment) of the upper motor neuron syndrome result in a combination of neural and mechanical changes. In the musculoskeletal system this leads to shortened muscles, fixed contractures, bony torsions, joint instability and ultimately to premature degenerative arthritis (Graham & Selber 2003; Graham 2004). These changes limit motor skills to varying degrees. The muscles may be weak and the motor development delayed. The impaired motor sequencing, dexterity, and anticipatory control causes inappropriate and associated postures (Lin 2004).

Significant *activity limitations* can also be present, for example in postural control, functional mobility and activities of daily living. Children with CP are often not able to adjust their posture successfully to meet the demands of a task and environment. The children often seem to have stereotyped motor behaviour, which

TABLE 1.6 Common functional limitations in CP disorders.

Impairments in body functions & structures	Activity limitations & participation restrictions
<p>Muscle</p> <ul style="list-style-type: none"> - Atrophy, hypertrophy, deposits of fat and connective tissue, decreased number of sarcomeres, inadequate muscle length, slow muscle growth – weakness - Tone: spasticity, stiffness, contracture of muscle-tendon units and supporting connective tissues – slow activation, reduced speed, low force production, high energy cost, muscular fatigue, weakness - Reflexes: excitability and spasms <p>Joint</p> <ul style="list-style-type: none"> - Contracture of joint capsule and collateral ligaments, changes in joint shape, loss of articular cartilage, intra-articular deformity, instability, subluxation, displacement, pain, poor joint alignment, scoliosis, degenerative arthritis <p>Bone</p> <ul style="list-style-type: none"> - Torsional and angular deformities, osteoporosis, fractures, growth inhibition 	<p>Mobility limitations: poor anticipatory planning and postural control – compensatory postures, stereotyped motor behaviour</p> <p>Less physical activity</p> <p>Limitations in ADL (e.g. dressing, feeding, toileting, playing)</p> <p>Participation restrictions in school, hobbies, social relations)</p> <p>Vulnerable self-concept (e.g. physical appearance, social acceptance, athletic and scholastic competence)</p> <p>Overuse syndromes, loss of independent walking, educational and social consequences</p>

according to Hadders-Algra (Hadders-Algra 2001) is produced by a limited repertoire of primary cortical or subcortical neuronal networks and in processing sensory information, creating problems in selecting the most efficient neuronal activity.

The functional abilities in communication, emotional contact, self-care and cognitive performance, especially at school age, are often affected by visual disturbances (Schenk-Rootlieb & et al 1993; Mercuri et al. 2004). The children may have varying degrees of visual impairments in tasks requiring eye-hand co-ordination, fingertip-force and anticipatory planning when manipulating objects limiting the performance of daily activities (Steenbergen & Gordon 2006; Steenbergen et al. 2007).

Mobility and locomotion may be hampered by muscle weakness and imbalance across joints (Wiley & Damiano 1998). The variability of daily walking and activities is decreased as functional walking levels decrease (Bjornson et al. 2007). During walking the children have low force production and they move at a reduced speed, which may increase muscle co-contractions and limit stride length. Thus children with CP need to expend excessive energy to overcome body mass and inertial forces. The high energy cost and muscular fatigue limit endurance (Palisano et al. 2004). Further, physical growth and changes in physical and social environments may contribute to secondary impairments, including pain, poor joint alignment, scoliosis, osteoporosis, fractures, overuse syndromes, and loss of independent walking (Palisano et al 2004). Children with CP with similar capability have demonstrated differences in performance within the home, school, and outdoors or community settings (Tieman et al. 2004).

Participation restrictions may be diverse in various social and community roles for the child (Simeonsson et al. 2003). In an Australian study the intensity of participation in activities outside school was low. The children with CP in all levels of GMFCS and MACS undertook a diversity of activities (median of 26.5 activities) which were commonly informal rather than formal (Imms et al. 2008). Compared to other Australian children, more children participated in organized sport, but with lower frequency.

Quality of life

Children with CP can have multiple health-related quality of life problems, including physical functioning, pain, and poorer general health, as well as impacts on the parents. Many children use more medication and feeding tubes, and they are shorter and thinner compared to the general population (Liptak et al. 2001; Wake et al. 2003). Children classified at different levels in the GMFCS seem to have similar quality of life (Oeffinger et al. 2007). Motor and other activity limitations indicate lower physical, but not psychosocial well-being. Adolescents with CP may have decreased quality of life or they may report similar life quality to their non-disabled peers, indicating that their quality of life may be satisfactory in spite of significant deficits (Livingstone et al. 2007; Majnemer et al. 2007). The lower scores are associated with the parent's emotional state, time constraints, and interruption of family activities (Majnemer et al. 2007). Ambulatory youths with CP report lower health status than typically developing youth, though their quality of life was not different (Bjornson et al. 2008).

Natural course

Most CP children have near normal length of life expectancy, but the age-adjusted death rate is higher with more severe disability. Severe cognitive, motor (ambulation, manual dexterity), and visual disabilities each have an independent effect on the probability of survival. The severely impaired children have approximately a 35 to 50% probability of surviving to the age of 40 years (Hutton & Pharoah 2006). The influence of epilepsy, impaired ability to eat, and social and economic circumstances may also be deleterious to survival.

As the rehabilitation services are usually available to all children with CP in western countries, the “natural” course of CP will always be influenced by current intervention strategies (Rosenbaum 2007). The gross motor development of different severities of CP can be predicted by motor growth curves for children that are classified in the GMFCS and assessed longitudinally by GMFM (Palisano et al. 2000; Rosenbaum et al. 2002). Longitudinal analyses show that the gross motor development appears in distinct curves in each of the GMFCS levels and reaches a plateau at the age of 6 to 7 years (Rosenbaum et al. 2002; Beckung et al. 2007). The knowledge of normal developmental progress underlines the need for comparison groups in intervention research.

Adolescents with CP are less physically active than their peers without disability, and their physical activity level is related to GMFCS levels (Maher et al. 2007). In another study of adolescents with CP, a lower level of physical activity was associated with older age, female gender, and hip dysplasia (van Eck et al. 2008).

A systematic review up until 2005 shows that adolescent females with CP have a more vulnerable self-concept than females without disability (Shields et al. 2006). Their self-concept was lower in the domains of physical appearance, social acceptance, athletic and scholastic competence. The evidence on changes in self-concept for children with CP in general was insufficient and variable.

Studies on adults with CP indicate an alarming trend towards deterioration in physical, social and emotional well-being with increasing age (Stevenson et al. 1997; Andersson & Mattsson 2001; Bottos et al. 2001). Their contact with rehabilitation services decreases and fewer social relationships and experiences contribute to poor development of social skills, which increases the demands upon carers (Stevenson et al. 1997). Many experience deformity and deterioration in their motor performance and walking ability (Andersson & Mattsson 2001; Bottos et al. 2001) and lack of higher education and full employment (Stevenson et al. 1997; Andersson & Mattsson 2001).

Costs

The considerable long-term disability is associated with substantial costs to the health care system and society. In Finland, rehabilitation of children with severe CP belongs to the group of the most expensive rehabilitation services (Snellman & Pekurinen 2005). In the USA, non-reimbursed costs to families for services, equipment, and lost family income can amount to thousands of dollars each year (Salkever 1985), and lifetime costs associated with cerebral palsy is estimated to be 800 000 dollars per person (Honeycutt et al. 2003).

1.3 Therapeutic management

Rehabilitation can be defined as the multi- and interdisciplinary management of a person's functioning and health. Its goal is to minimize symptoms and disability (Stucki et al. 2003). In paediatric rehabilitation, best practice service delivery is considered to be family-centred, incorporate instruction and practice into daily activities and routines, and promote outcomes that are meaningful to the child and family life (King et al. 2004; Palisano 2006). Common treatment options to relieve muscle dysfunction include physiotherapy, occupational therapy, medical therapy and surgery (Koman et al. 2004; Krigger 2006; Steinbok 2006). The children should also have access to orthotic services, a paediatric speech and language therapist (Bakheit et al. 2001), a psychologist and special teachers (Rosenbaum et al. 2006).

Physiotherapy and physiotherapy-related interventions

Physiotherapy often constitutes a major part of the team approach in the management of CP. Physiotherapists use physical approaches and techniques to promote, maintain and establish physical, psychological and social well-being. The therapy includes strategies to improve posture and mobility and to prevent formation of deformities. Physiotherapists also teach parents how to handle their child at home for feeding, bathing, dressing and other daily and age-appropriate activities, and advise on mobility devices (World Confederation for Physical Therapy 1999; The Bobath Approach 2007). According to Mayston et al. (Mayston 2004) the main aim is to improve the quality of life for the child and their family, to maximise their potential for participation in daily life activities, and to prepare for improved quality of life in adulthood.

Physiotherapy methods are chosen according to agreed therapy goals. Many therapists use an eclectic approach, that is, they integrate and adapt different techniques to meet the needs of a child (Mayston 2004). The patient-related factors that may influence the choice, frequency and duration of the intervention are: chronicity, stability or severity of the current condition, level of impairment and physical function, age, anatomical and physical changes related to growth and development, cognitive status, comorbidities, complications, secondary impairments, decline in functional independence, multisite or multisystem involvement, nutritional status, overall health status, premorbid conditions, probability of prolonged impairment, functional limitation or disability, psychosocial and socio-economic factors, and psychomotor abilities (Guide to physical therapy practise 2001).

The choices and availability of various techniques may vary between therapists and from country to country. Table 1.7 lists some of the most common physiotherapy and physiotherapy-related approaches to the management of CP described in textbooks and articles during the past few decades (Scrutton 1984; Siebes et al. 2002; Rosenbaum 2003; Mayston 2004). Some approaches are more multidisciplinary and may thus be provided by different professionals e.g. occupational therapists or special teachers.

Many myths surround the various therapeutic approaches (Logan 2002) and new therapeutic alternatives or complementary therapies are constantly emerging (Rosenbaum 2003). For decades the physiotherapy management has been dominated by top-down philosophical approaches, whose bases have uncertain scientific validity. Typically the philosophies are package approaches that incorporate several different treatment strategies, of which some may be effective whereas others may not (Damiano 2004). Examples of such approaches are the commonly used neurodevelopmental therapy or Bobath therapy (NDT), sensory integration and conductive education (Kozma 1995). All these approaches have changed and evolved since their origin in the 1940s and 1960s. For instance, as new informa-

TABLE 1.7 Therapeutic approaches to the management of CP.

Bobath/Neurodevelopmental therapy (NDT)
Conductive education
Sensory integration
Adeli suit
Aim-oriented management
Advance neuromotor rehabilitation
Biofeedback
Dohsa-Hou (a Japanese psychorehabilitation technique)
Electrical stimulation
Early intervention (e.g. Portage project)
Functional physical therapy
Movement Opportunities via Education (MOVE)
Patterning (Doman-Delacato, i.e. IAHP/BIBIC/Brainwave)
Pelvic positioning
Physical activity training
Strength training
Targeted training
Vojta
Training program (15 modalities) by Phelps
Recreational therapies (e.g. hippotherapy/saddle riding, hydrotherapy/swimming programmes)
Alternative therapies (e.g. hyperbaric oxygen therapy, acupuncture, and osteocraniosacral therapy)

tion, theories and models emerge in the sciences related to motor control, motor development and motor learning, NDT has incorporated them and evolved into a concept for the examination and management of the whole child (Bly 1991; Howle 2002; The Bobath Approach 2007; Mayston).

While these philosophies still have a strong influence both internationally and nationally (Mayston 2008), a bottom-up approach, based on treatment principles, has gradually gained acceptance (Damiano 2004). A phase-oriented approach first explores and chooses the relevant theory to ensure the best choice of intervention and hypothesis for treatment. Next, the active components and the underlying mechanisms by which they will influence outcomes or relate to and interact with each other are identified. These preliminary and modelling phases are necessary in describing and defining the constant and variable components of an intervention (Campbell et al. 2000; Medical Research Council 2000).

Components of a physiotherapy intervention

Physiotherapy can be characterized as a complex intervention where a number of components act both independently and interdependently (Medical Research Council 2000). Even seemingly straightforward interventions have inherent complexities, not to mention package approaches. Many details require definition, for example, what are the series of exercises (type, frequency, duration), and what

changes to what exercises are needed at what stages? In addition to the exercises, elements of interaction may make an important contribution to the effectiveness of a physiotherapy intervention. The physical therapist has a role in rebuilding the child's confidence, training and teaching the family in how to help with care, and possibly influence the future behaviour of the child through advice and health education. Other complexities include the skills and experience of the therapists, and the modes of organizing and delivering the interventions (types of settings, locations, accessibility and availability of resources), adherence to the intervention program, caregiver consistency or expertise, concurrent medical, surgical and therapeutic interventions, living environment, social support, and potential discharge destinations (Guide to physical therapy practice 2001).

In practice, the therapists select, apply and modify the interventions based on the diagnosis, prognosis and the examination data of the child. The therapy goals are anticipated and expected outcomes are evaluated continuously. Physiotherapy can be integrated at home or into the community and leisure time. Generally physiotherapy interventions consist of 1) co-ordination, communication, and documentation; 2) patient-related instruction; and 3) the procedural interventions. The latter include therapeutic exercise; functional training in self-care; manual therapy techniques; prescription, application and fabrication of devices and equipment; airway clearance techniques; electrotherapy modalities; and various physical agents and mechanical modalities (Guide to physical therapy practice 2001). Therapeutic exercises include training of aerobic capacity, strength, power, endurance, balance, co-ordination, agility; stabilization of body mechanics and postural; flexibility exercises; gait and locomotion training; neuromotor development training; and relaxation (Guide to physical therapy practise 2001).

Problems in defining current practices

Despite the variety of approaches there are only a few studies that describe the current therapy choices and contents, while studies on actual treatment practices are lacking. In an American round table discussion, 62 paediatric physiotherapists described paediatric physiotherapy practices for a boy with spastic diplegia as a case example (Chiarello et al. 2005). The most typical direct intervention strategies included use of motor learning principles, functional training especially related to gait, range of motion, strengthening and balance exercises, use of equipment and orthotics, environmental adaptations, and a variety of therapeutic approaches, including NDT treatment, sensory integration, myofascial release, and proprioceptive neuromuscular facilitation. The strategies varied depending the age of the child. For the youngest children (aged 0–3 years) the caregivers were involved in the therapy sessions and caregiver-child interactions were emphasized. The activities often included play, and daily activities, and information on positioning provided by the therapist. For preschoolers the therapy focused on peer interaction

and endurance activities. For school-aged children the therapy sessions occurred in a variety of environments and include sports, games and aquatics. For older adolescents and young adults the therapy focus was often mobility training (Chiarello et al. 2005.)

Another survey from Scotland on rural community physiotherapy environments and specialized child development units described the management of CP as interdisciplinary, but lacking input from the educational and social care professions (Craig 1999). The therapists advocated passive parental involvement, and only a marginal majority of physiotherapists applied outcome evaluation.

In Finland children with CP are treated, at least until preschool age, at one of the 21 secondary or tertiary hospitals. The treatment of the children varies depending on the severity of the disability. Although many rehabilitation services for children and adolescents should be integrated into everyday life (Veijola 2003; Veijola 2004), the role of the local community often remains secondary and dependent on the rehabilitation teams at the hospitals (Koivikko & Sipari 2006). A recent Dutch evaluation of clinical paediatric practice related to therapy goal-setting shows that the integration of the children's needs and problems into their shared rehabilitation goals was not optimal (Nijhuis et al. 2008).

The Finnish rehabilitation practices are variable and the intensity of physiotherapy varies a lot, as shown in a national survey on rehabilitation practices for children with CP in 2003 (Autti-Rämö et al. 2005). Hospital rehabilitation teams designed individual therapy programs, and named the three most important objectives for rehabilitation for three children with CP based on patient videos and medical record summaries. The intensity of recommended therapies comprising physiotherapy, occupational therapy, speech therapy and hippotherapy (45–60 minute sessions) ranged from once a month to three times a week. The total amount of recommended therapies increased with the severity of the disability, and the highest recommended total amount of therapies per year was 225 hours, meaning 4 to 5 weekly 60-minute therapy sessions. Physiotherapy was recommended for all the three cases, and the annual intensity varied almost four-fold per patient. In addition, some hospitals recommended other specified form of therapies, for example hydrotherapy, group therapy in the form of conductive education, and training for functional vision. The main goals for future rehabilitation were mostly stated as improvements of body structures and functions, or in a specified function. A minority of goals were on activity and participation level and on the well-being of the child or the family only seldom. Only a few teams named environmental factors, optimal assistive technology, and consultation with day care personnel as important objectives for future rehabilitation. (Autti-Rämö et al. 2005)

Orthotic devices

Physical therapists prescribe, apply, and when possible, fabricate orthotic devices including braces, casts, shoe inserts or splints (Guide to physical therapy practice 2001). Orthoses are used for upper and lower limbs often for years to correct or prevent structural deformities, address pain and discomfort, to promote function by supporting normal joint alignment, and to facilitate or substitute for function (Malick 1982; Knutson & Clark 1991; Stuberg 1995; Coppard & Lohman 1996; Fish et al. 2001). Casting is primarily used in the lower or upper limb for short periods of time to stretch the shortened muscles and increase the range of movement.

Various treatment protocols have been suggested as to what kind of orthotic device should be prescribed for a particular child (Malick 1982; Knutson & Clark 1991; Condie 1995; Stuberg 1995; Coppard & Lohman 1996; Greene 2000; Fish et al. 2001; Goldstein 2001). The type of orthosis may vary according to the needs of the developing child. The orthoses can cover a different number of joints and include hinges, while the materials can range from flexible to rigid.

1.4 Outcome evaluation

Definitions

Outcome measurement provides objective information on the magnitude of changes over a period of time associated with the natural course of the disease or a treatment's effectiveness. A successful outcome in physical rehabilitation includes "improved or maintained physical function when possible, slowed functional decline where the status quo cannot be maintained, and is considered meaningful to the client." (Finch et al. 2002)

Outcome measures are various measurement tools (instruments, questionnaires, rating forms, etc.) that are used to document change in one or more constructs over time. Patient-based outcomes refer to the array of tools assessing health, illness and benefits of health care interventions from the patient's perspective (Fitzpatrick et al. 1998). When applying patient-based measures, the following eight criteria should be considered: appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability, and feasibility (Fitzpatrick et al. 1998). These criteria are not consistently defined in the literature, which poses a challenge when ranking the relative order of the criteria for selecting measures to include in a trial.

Kirshner and Guyatt (Kirshner & Guyatt 1985) provided a methodological framework for health measures that distinguishes evaluative indexes from discriminative and predictive indexes based on their purposes. An evaluative measure must contain items that are relevant to changes in health status and responsive to

clinically significant change. The item-scaling should have sufficient gradations to register change. The reliability of evaluative measures is shown with small within-subject variance in stable subjects and a large change-score when functional status improves or deteriorates. The most convincing validity of an evaluative index is demonstrated in a relationship between changes with other external measures over time. Moreover, the measure should be applicable to the population for whom it is developed and feasible to use.

Indexes that are developed for discriminative or predictive purposes are not necessarily useful for detecting changes over time as the prerequisites for each role are complementary and competing. Discriminative instruments are used to distinguish between individuals or groups on an underlying dimension when no external criterion or gold standard is available for validating these measures. A predictive index is used to classify individuals into a set of predefined measurement categories when a gold standard is available, to determine whether individuals have been classified correctly (Kirshner & Guyatt 1985).

Domains of outcome measurement

Physiotherapists have always advocated and respected patient-level goals in their rhetoric (Rothstein 1994), but the outcome evaluation has for a long time been focused on impairment level. In the 1990s, strong arguments were made for the need to examine the conceptual bases for treatment and the nature of the relationship assumed to exist between the different outcome domains (Jette 1995; Butler et al. 1999). Conceptual thinking with the help of multidimensional models of disability (Jette 1994) broadened the selection of outcomes to include functional limitations, disability, or outcomes related to individuals behaviour, or functioning in social roles within society (Rosenbaum et al. 1990; Fetters 1991; Jette 1995; Butler et al. 1999). A number of models conceptualized disability as a consequence of disease or injury. For example, the World Health Organization taxonomy, ICIDH (International Classification of Impairments, Disabilities, and Handicaps) (World Health Organization 1980; 1999) was a linear and causal model linking impairments, disabilities, and handicaps without accounting for the role of environment.

In the last decade the International Classification of Functioning, Disability, and Health (ICF) (World Health Organization 2001) has become a global standard for discussing disability and defining domains in outcome measurement (Stucki et al. 2003; Üstün et al. 2003; Rosenbaum & Stewart 2004; Jette 2006). This classification, revised from the original ICIDH, was initially referred to as ICIDH-2 (De Kleijn-De Vrankrijker 2003). The ICF is a biopsychosocial framework that recognizes person-environment interaction. In the ICF the components of functioning and disability include body functions and structures, and activities and participation. Further, the ICF considers contextual factors, including environmental and

personal factors that interact with health conditions to influence functioning and disability (World Health Organization 2001). The proper use of environmental factors can ensure appropriate policies, systems and services and more sustainable development that recognizes human rights (Hurst 2003).

In the field of CP rehabilitation, the ICF has promoted a broader application of outcome measures from solely impairments at organ levels, to the individual (activity limitations) and societal (participation restrictions) levels. Also the contextual factors are more likely to be taken into account (Majnemer & Mazer 2004; Rosenbaum & Stewart 2004). Between 1992 and 2002 the number of intervention studies increased and the range of outcomes measured widened, including participation, satisfaction, quality of life, and the use of medical and rehabilitation services (Majnemer & Mazer 2004).

The linking of instruments to ICF components is however not straightforward, as many measures, particularly those developed before ICF, may reflect different constructs. Thus the existing measures' comprehensiveness and correspondence to one or more ICF components vary (Simeonsson et al. 2003). The linking can be conducted by fitting single items to relevant ICF categories (Cieza et al. 2002; Cieza et al. 2005).

The determinants of motor change for children with CP may be considered to be both directly and indirectly linked. Based on the ICF, general systems theory, theories of human ecology and family-centred care, Bartlett and Palisano (Bartlett & Palisano 2000) proposed a multivariate model for understanding what aspects affect motor changes for children with CP. In this model the child characteristics relating to *primary impairments* (motor, sensory, or cognitive) are assumed to have a strong direct influence on changes in motor abilities and an indirect influence through a causal path associated with *secondary impairments* (e.g. skeletal alignment, range of motion, force production, aerobic capacity). *Child personality* (e.g. temperament, motivation) is hypothesized as influencing change in motor abilities through an effect in secondary impairments. The construct of *family ecology* includes both family demographics and function (e.g. parents' interaction, expectations, resources, and supports). It is proposed to influence changes in motor ability through the experiences and opportunities that the family provides the child. *Health care services* (availability, accessibility, intervention options, child and family satisfaction with the care) are proposed to have an effect on motor abilities through family ecology (Bartlett & Palisano 2000).

Evaluative outcome measures

Until 1990, there were no available measures on motor function that had been validated for their capacity to detect change in children with CP (Rosenbaum et al. 1990). Since then some measures have been more rigorously studied and new measures developed, and there is literature that have screened and evaluated the

psychometric properties of various outcomes used in children with CP. This literature was searched via Pubmed for the last 10 years up to February 2008 with the following search terms: (cerebral palsy OR CP) AND (treatment outcome OR quality of life OR disability evaluation OR motor skills OR activities of daily living OR outcome measurement) AND ((valid* OR reliab* OR reproducib* OR repeatab* OR responsiv*) OR (sensitiv* OR specificity OR psychometr*)). From this search, complemented with other sources, a selection of relevant reviews and studies are summarized here, with a particular focus on finding evidence on evaluative outcome measures.

Measures on body structures and functions

Scholtes et al. (Scholtes et al. 2006) reviewed the available clinical assessment instruments to measure spasticity. The 13 identified instruments were categorized into 3 groups according to their assessment technique and quantification: 4 to Ashworth-like scales, 2 to Tardieu-like scales, and 4 to other clinical grading scales. To quantify spasticity, most instruments grade the intensity of the muscle tone and range of motion with different grading and score ranges. None of the instruments complied with the definition of spasticity “velocity-dependent increase in muscle tone”, as they mostly grade muscle tone intensity only at one (often not-specified) velocity of passive stretch. Only the Tardieu-like scale is suited to measuring spasticity, but it lacks a standardisation for the muscle stretch velocities, and its intensity rating measures not only spasticity, but also clonus.

Measures on activities and participation

Ketelaar et al (Ketelaar et al. 1998) reviewed functional outcome measures applicable to children with CP from the literature published between 1978 and 1996, and identified 17 instruments. Only two measures are valid, reliable and responsive to changes: the Gross Motor Function Measure (GMFM) and the Pediatric Evaluation of Disability Inventory (PEDI). Ten other measures were developed and validated for discriminative purposes. Some of these, the Alberta Infant Motor Scale, the Barthel Index, the Movement Assessment Battery for Children (the Movement ABC), the Peabody Developmental Motor Scale (PDMS), and the Functional Independence Measure for Children are also characterized in their manuals as evaluative measures, but no evidence on their responsiveness to change had been published.

The GMFM-66 is an interval-level measure of gross motor function for cerebral palsy, with improved scoring, interpretation, and overall clinical and research utility over the original GMFM with 88 items (Avery et al. 2003). The GMFM-66 is more responsive than the GMFM-88 with respect to consistency in the therapist's clinically meaningful judgements (Wang & Yang 2006). The GMFM-66 has been extended by preference percentiles (at the 3rd, 5th, 10th, 25th, 50th, 75th,

90th, 95th, and 97th percentiles) to allow a consideration of the large variability in change that is typical among children with CP within GMFCS levels (Hanna et al. 2008). Both the GMFM and the Pediatric Evaluation of Disability Inventory detect change most in children younger than 4 years of age (Vos-Vromans et al. 2005), but they are limited by a ceiling effect when assessing higher-functioning children, and the Pediatric Evaluation of Disability Inventory is restricted to children who are 7 years old or less (Damiano et al. 2005).

Boyce et al. (Boyce et al. 1991) reviewed measures published between 1964 and 1990 that incorporated quality of movement or motor performance. This review identified 10 measures that were originally developed for discriminating and predictive purposes. Two of them (Peabody Developmental Gross Motor Scale and Objectives-Based Motor Skill Assessment Instrument) were developed with the stated purpose of evaluating change, but neither had published evidence of responsiveness in detecting clinically important change. In a subsequent study, the Gross Motor Performance Measure was validated to detect changes in the quality of movement in children with cerebral palsy aged 0 to 12 years (Boyce et al. 1995). The Peabody Developmental Gross Motor Scale has been shown to be comparable with the GMFM in measuring change in infants with CP (Kolobe et al. 1998).

Sakzewski (Sakzewski et al. 2007) identified 6 measures in which at least 30% of their content is participation. Of these, the Canadian Occupational Performance Measure and the Goal Attainment Scaling instruments are responsive to measuring change in paediatric rehabilitation (Cusick et al. 2006), as is an adapted Canadian Occupational Performance Measure (Cusick et al. 2007). To evaluate a conductive education programme, the GMFM, Quality of Upper Extremity Skills Test, Pediatric Evaluation of Disability Inventory (Caregiver Assistance) and the Impact on Family Scale were demonstrated as most responsive to physical, functional and psychosocial changes (Wright et al. 2005). The Pediatrics Outcomes Data Collection Instrument Global Function Scale was responsive to changes only after muscle-tendon lengthening (Damiano et al. 2005).

Most recently, Harvey et al. (Harvey et al. 2008) systematically reviewed the psychometric properties and clinical utility of evaluative outcome measures for activity limitations of CP children aged 0 to 18 years. The 8 identified measures examining different dimensions of activity limitation were: the Activities Scale for Kids, the Child Health Questionnaire, the Gillette Functional Assessment Questionnaire, the Functional Mobility Scale, the GMFM, the Pediatric Evaluation of Disability Inventory, the Pediatric Outcomes Data Collection Instrument, and the Functional Independence Measure for Children. Of these, the Activities Scale for Kids and the GMFM showed sound psychometric properties, while the other measures need further examination of their validity and responsiveness. Another recent review (Spittle et al. 2008) assessed measures for motor development of preterm infants within the first year of life. They identified nine measures reported

TABLE 1.8 Some validated and evaluative outcome measures for children with CP.

Activities

- Activities Scale for Kids (ASK) (Young et al. 1995)
- Canadian Occupational Performance Measure (COPM) (Law et al. 1990)
- Child Health Questionnaire (CHQ) (Landgraf et al. 1996)
- Functional Independence Measure for Children (WeeFIM) (Msall et al. 1994)
- Functional Mobility Scale (FMS) (Graham et al. 2004)
- Gillette Functional Assessment Questionnaire (FAQ) (Novacheck et al. 2000)
- Goal Attainment Scaling (GAS) (Maloney et al. 1978)
- Gross Motor Function Measure (GMFM) (Russell et al. 2002)
- Gross Motor Performance Measure (Boyce et al. 1995)
- Peabody Developmental Gross Motor Scale (PDMS-GM) (Palisano et al. 1995)
- Pediatric Evaluation of Disability Inventory (PEDI)(Haley et al. 1992) (Feldman et al. 1990)
- Pediatric Outcomes Data Collection Instrument (PODCI; also referred to as the Pediatric Orthopedic Society of North America scales) (Daltroy et al. 1998)
- Quality of Upper Extremities Skills Test (QUEST) (DeMatteo et al. 1993)
- Test of Infant Motor Performance (TIMP) (Campbell et al. 2002)

Environmental factors

- Impact on Family Scale (IFS) (Wright et al. 2005)
- Measure of Processes of Care (MPOC) (King et al. 1995)

Quality of life

- Pediatric Quality of Life Inventory (PedsQL) (Varni et al. 2001)
- Child Health Questionnaire (CHQ) (Landgraf et al. 1996)

to be evaluative, but only one of them, the Test of Infant Motor Performance, showed evidence of measuring changes over time.

Measures on environmental factors

The Measure of Processes of Care is a validated self-report tool to assess family-centred behaviours of health care providers (King et al. 1995).

Measures on quality of life

Quality of life is often the most important treatment outcome that covers many components of the ICF. However, the conceptual underpinnings of various quality-of-life instruments are variable (Davis et al. 2006). Earlier there were no disease-specific health-related quality-of-life instruments available for children with CP (Bjornson & McLaughlin 2001; Schneider et al. 2001). Available generic quality-of-life measures include the Child Health Questionnaire, the Pediatric Outcomes Data Collection Instrument, the Goal Attainment Scaling and Canadian Occupational Performance Measure (Bjornson & McLaughlin 2001). The Pediatric Quality of Life Inventory has excellent validity, responsiveness and reliability (Varni et al. 2001). A recent review on quality of life measures found 17 measures,

two of which were developed specifically for children with CP, the Quality of Life Questionnaire for children for CP and the DISABKIDS module CP, but did not assess the responsiveness of these measures (Viehweger et al. 2008).

To sum up, these reviews and studies identified some evaluative outcome measures, mainly on “activities and participation” in terms of the ICF. These measures are outlined in Table 1.8. Recently, a large multicentre prospective population-based study (Bagley et al. 2007) examined the discriminatory ability of outcome measures representing all aspects of the ICF and quality of life: the Pediatric Outcomes Data Collection Instrument (parent version), the Gillette Functional Assessment Questionnaire Walking subscale, GMFM (dimension E), Functional Independence Measure for Children Self-care and Mobility subscales, spatio-temporal parameters and O2 cost. The responsiveness to change of these measures will be tested in the second phase of the study (Sullivan et al. 2007).

2 Aims of the study

This study is based on a project evaluating the effectiveness of rehabilitation in children with cerebral palsy (CP) carried out by the Finnish Office for Health Technology Assessment (Finohta). Therapists, doctors and parents need critically evaluated information on the effects of widely used therapeutic interventions for evidence based-decision making. Systematic reviews and randomized controlled trials are considered to provide the best evidence for clinical decision-making. However, there are intricate problems related to the heterogeneity of the patients, complex interventions, and the multitude of outcomes in therapeutic intervention trials in children with CP. This thesis aims to assess the methodological challenges of the systematic reviews and effectiveness trials in this field and to evaluate the effectiveness of interventions in current use, as established in well-designed randomized studies.

The specific aims of this study are:

1. To critically appraise the methodological quality of systematic reviews on various physiotherapy interventions, physiotherapy-related motor based interventions and orthotic devices in children with CP, and the effectiveness of the reviewed interventions, and clinical applicability of the reviews (I, II).
2. To investigate how randomized controlled trials in children with CP have managed methodological challenges related to patient characteristics, outcomes assessment, and key components of physiotherapy as a complex intervention (III).
3. To determine the quality of reporting randomized controlled trials in physiotherapy and occupational therapy in children with CP using the CONSORT recommendations (IV).
4. To critically appraise the methodological quality and the effectiveness of current physiotherapy interventions (i.e. published since 1990) on functioning, according to randomized controlled trials (V).

3 Materials and methods

This study was based on two types of data: systematic review articles and randomized controlled trials.

3.1 Inclusion criteria and literature searches (I–V)

The inclusion criteria for study types, population, intervention and outcomes for all papers are shown in Table 3.1.

TABLE 3.1 Inclusion and exclusion criteria in the five original publications (I–V).

	Inclusion criteria	Exclusion criteria
Study types	<ul style="list-style-type: none"> • Published systematic review articles (I, II) • Published, full-length articles or full written reports of randomized controlled trials (RCT) since 1990 (III, IV, V) 	<ul style="list-style-type: none"> • If the reviews had no description of the searched databases or the search time period, and selection criteria for population and interventions (I, II) • Non-randomized trials, other designs (III, IV, V)
Population	<ul style="list-style-type: none"> • Children or adolescents with diagnosed CP, aged 3 months to 20 years at the start of the program. (I–V) 	<ul style="list-style-type: none"> • If more than 20% of the study population consisted of other conditions than CP or exceeded the age limits and the data could not be separated (I–V)
Interventions	<ul style="list-style-type: none"> • Clinically justifiable physiotherapy interventions, e.g. neurodevelopmental therapy (NDT), strength training, saddle riding, physical activity, swimming programs, functional therapy, targeted training (I, III–V), conductive education and interventions that may be used both by physiotherapist and occupational therapist (I), all types of upper and lower limb orthoses, casts and splints (II). • Physiotherapy intervention or a combination of these, as compared to placebo, sham therapy, or other physiotherapy interventions. Adjunct interventions (biofeedback, electrical stimulation, or behavioural or educational approaches such as conductive education), if given for all study groups. (V) 	<ul style="list-style-type: none"> • Surgical or pharmaceutical interventions, dental care, oral motor control (drooling, swallowing, speech and communication), nutrition, acupuncture, psychotherapy, and hyperbaric oxygen therapy (I–V), orthotic and assistive devices (I, III–V) • Other adjuncts to physiotherapy, such as selective dorsal rhizotomy, botulinum injection therapy, or intrathecal baclofen. (V) • If more than 20% of the included interventions were on orthotic or assistive devices and the results could not be separated (I).
Outcomes	<ul style="list-style-type: none"> • Any reported outcomes of functioning or disability according to the International Classification of Functioning, Disability and Health (ICF) (I–V). 	<ul style="list-style-type: none"> • None (I–V)
Language	<ul style="list-style-type: none"> • Danish, English, Finnish, German, Norwegian, or Swedish (I–V); and Spanish, French (III, IV). 	<ul style="list-style-type: none"> • Other languages (I–V)

TABLE 3.2 Search periods, terms and sources in the original publications (I–V).

Search period	Search terms for intervention	Searched databases	Additional sources	Articles found
Publication I				
Until June 2003, and updated from January 2003 to August 2007.	Exp physical therapy techniques, physical therapy, physiotherap\$, exp exercise therapy, physical activity, exp physical therapy, exp physical education and training, rehabilitation, vojta, bobath. neurodevelop\$, NDT, Rood, Kabat, vibroacoust\$, early intervention, conductive education, conservative therap\$, muscle strength\$, muscle training, motion, therapeutic exercise, exercise training, physical exercise, fitness, aerobic training, kinetic chain, movement, exercise movement techniques, swimming, hydrotherapy, functional therapy, self care training, motor control, motor learning, occupational therapy, constraint induced, restraint, physical, forced treatment, psychomotor performance, sensation, sensory integration, sensory perceptual, parent-child relations, parents, parent education, physical stimulation, posture, positioning, facilitate\$.*	Medline, Cinahl, CDSR, DARE, ACP Journal Club, HTA, and PEDro.	Personal files of studies and reviews on children with CP. Reference lists of included reviews.	1188
Publication II				
Until May 2003.	Exp. orthotic devices.	Medline, Cinahl, PreMedline, CCCT, CDSR, DARE, ACP Journal Club, and PEDro.	The search until June 2003 (as in article I). Reference lists of included reviews.	55
Publications III, IV				
Until June 2003.	As in article I.	As in article I.	Included articles of an unpublished systematic review of controlled trials that compared two different intensities (hours/week) of the same type of physiotherapy. Reference lists of the included reviews.	767 + 349
Publication V				
From January 1990 to February 2007.	As in article I, except: posture, positioning, motor control, motor learning. Additional search terms: hippo\$, hors\$.	Medline, Cinahl, CCCT, and PEDro.	Reference lists of the included trials.	163

CCCT=the Cochrane Central Register of Controlled Trials, CDSR=the Cochrane Database of Systematic Reviews, DARE=Database of Abstracts of reviews of Effects, HTA=Health Technology Assessment database, ACP=American College of Physicians Journal Club, PEDro=Physiotherapy Evidence Database.

* The different writing modes of some search terms are not listed here.

An experienced information scientist (Riitta Grahn, MSc Chemistry) planned the search strategies for all searches. The key characteristics of the search strategies are shown in Table 3.2. The search terms also included terms for population “cerebral palsy”, and filters to identify review articles and randomized trials. The exact search strategies are in Appendix A. All searches were made without language restrictions. The searches were conducted from the earliest year available in each database, except in study V, where the searches were made from 1990 onwards.

3.2 Article identification and data extraction (I–V)

The author’s work distribution in the conduct of the five original publications is presented in Table 3.3. In all articles (I–V) two reviewers independently screened the titles or abstracts of citations identified in the searches for inclusion and exclusion criteria. When the title and abstract did not clearly indicate whether an article should be included, two reviewers evaluated the full article for inclusion criteria.

Two reviewers independently extracted the data in reviews II–V. In review I the included articles were allocated equally to two reviewers. One review was done by both reviewers to ensure similarity. After data extraction the results were checked by the other reviewer.

In the overview of reviews on physiotherapy and conductive education (I) we tabulated the search strategies and inclusion criteria, data of the included populations, interventions, settings, outcome measures; number of studies and the study designs in each review; methods used in the quality assessment and analyses (qualitative or quantitative); the main results and conclusions, and reported adverse effects. For quantitative data we extracted the effect sizes of all outcome measures used. In the overview of reviews on orthotic devices (II) we extracted information on study design, type of orthotic intervention, number of patients and the outcomes of each study as reported in the reviews. The original studies were not retrieved. Both reviewers applied the same data extraction sheet.

In the review of physiotherapy and physiotherapy-related RCTs (V) we extracted detailed information on populations, interventions, outcomes and results using a predefined data extraction sheet (Appendix B). The feasibility of the data extraction form was tested with a sample of three articles eligible for this review.

TABLE 3.3 Work distribution.

	(I) Overview of reviews on physiotherapy and conductive education	(II) Overview of reviews on orthotic devices	(III) Are RCTs feasible?	(IV) Reporting Quality	(V) Review of physiotherapy and physiotherapy-related RCTs
Conception and design	All authors	All authors	All authors	All authors	All authors
Selection by titles and abstracts	HA, RK, IAR	IAR, JS	HA, RK	HA, RK	HA, IAR
Selection by full texts	HA, IAR	IAR, JS	HA, RK, IAR	HA, RK, IAR	HA, IAR
Data extraction	HA, JS	IAR, JS, HA	RK, HA	HA, RK	HA, IAR, JS
Methodological quality assessment	HA, JS, AM	IAR, JS, AM	–	–	HA, IAR, JS, AM
Selection of issues/ operationalisation of the CONSORT checklist	–	–	All authors	HA, AM	–
Analyses and interpretation of the data	All authors	All authors	All authors	All authors	All authors
Drafting the article	HA	IAR	RK	HA	HA
Critical revision and final approval of the article	All authors	All authors	All authors	All authors	All authors

All authors = Heidi Anttila (HA), Ilona-Autti-Rämö (IAR), Antti Malmivaara (AM), Marjukka Mäkelä (MM), Jutta Suoranta (JS). Regina Kunz (RK) co-authored in articles III and IV.

3.3 Analysis of the performance of RCTs (III)

The analyses of the trial performance was based on our comprehensive collection of narrative reviews, editorials and commentaries from the field of outcomes research in CP, the framework of complex interventions (Medical Research Council 2000) and long experience in child neurology rehabilitation. The list of possible issues often claimed as challenging in terms of trials was exhaustive. By a group consensus we chose to focus on issues that best represented the patients, interventions, comparison interventions and outcomes (PICO) complemented with important factors of internal validity.

For the population characteristics, we collected data on the recruitment of patients, including the sampling frame of the studies, the sample size, and the approaches to generating comparable groups. To analyse different aspects of the complex intervention as outlined in the Medical Research Council’s framework (Medical Research Council 2000) we developed and piloted a questionnaire, modifying it to the specific situation of physiotherapy interventions in children with CP. This questionnaire contained eight aspects of the complexity of physiotherapy: (1) expertise and skills of therapists, (2) interaction between physiotherapist and

TABLE 3.4 Questionnaire for assessing various components of physiotherapy as a complex intervention.

Which of the following components of physiotherapy in children with CP have been addressed in the study?
Please answer with: yes – partly – no / not reported

Health care professionals

Expertise and skills of physiotherapists

1. The procedures depend upon the therapist's skill level and her/ his specific aims. Is the previous experience and skills of the therapists presented in a transparent way?

Interaction between physiotherapist and child

2. This item is reduced to the question: Was the pair "child and his or her own physiotherapist" included in the study (assuming that therapist and child had developed a relationship over time) or was the intervention performed by a study physiotherapist previously unknown to the child?

Intervention and control intervention

Standardisation of the delivery of the intervention

3. Lack of standardisation of the delivery of the intervention is a common complaint in studies of therapy in CP-children: this refers to the fact that the procedures of physiotherapy are generally not standardised; there is no defined dosage; no constant environment or conditions. Did the investigators address those issues within the context of the individual study?

Active component of the intervention

4. A complex intervention is characterised by diverse simultaneous influences on an outcome where it is difficult to define the individual share of each influence on a possible effect. Did the investigators specify what they regarded as the "active component" of their intervention?

Attitudes of parents and children

Child's satisfaction with / attitude towards therapy

5. Dissimilar levels of patient commitment between intervention and control groups and behaviours such as differential drop out have been raised as a concern in complex interventions. A child's expression of dissatisfaction could be non-compliance with the intervention. Dissatisfaction could arise from a number of sources such as travelling, discomfort, or stress because of more intense therapies; Assessment of the child's satisfaction with the therapy seems relevant. Did the investigators attempt to assess the child's satisfaction with / attitude towards therapy? (This question might not be applicable in studies where the child is very young).

Parents' satisfaction with / attitude towards therapy

6. Integration of a child in a trial also means interaction with a child's family, their attitude, their (un-) realistic expectations in the intervention or the degree of additional support. Did the investigators attempt to assess the parents' satisfaction with and their attitude towards therapy?

Other determinants of Outcome ("Background noise")

Description of background therapy

7. Some studies might have tested a new type of therapy in addition to the background therapy which continues to be applied to both, the treatment and the control group. Was the "background therapy" sufficiently well and reproducibly described?

Potential co-interventions

8. This refers to interaction with potential co-interventions (such as additional physiotherapy, home training of the parents with the children) known or not known to the investigators. Did the investigators check whether additional therapy was administered outside the study?

child, (3) standardization of the delivery of the intervention, (4) active component of the intervention, (5) child's satisfaction with therapy, (6) parent's satisfaction with therapy, (7) description of routine therapy, and (8) potential co-interventions (Table 3.4). The answering options were: yes, partly, no/not reported. In addition, we collected detailed information on particularly successful solutions descriptively.

Of the outcome measurements, we analysed the choice of endpoints and the applied instruments according to the ICF components (World Health Organization 2001). The relationship between the type of endpoint (body function and structure, or activities and participation) and the finding of a statistically significant result was explored using the Fisher's exact test. Frequencies were reported as mean and standard deviation or as median and range, respectively. One follow-up publication (Steinbok & McLeod 2002) and one study with behavioural and psychological outcomes only (Palmer et al. 1990) were excluded from this analysis. Further, we assessed whether the identified differences were interpreted in a clinical context. The behavioral and psychological effects assessed in one study (Palmer et al. 1990) did not match the other outcomes, thus it was not considered in this analysis.

3.4 Analysis of the reporting quality of RCTs (IV)

We operationalized the 22 items of the CONSORT statement checklist (Altman et al. 2001) to 34 questions, which can be scored as "yes", "partly", "no", "unclear" or "not applicable". The questions were piloted and corrections were made to the wording of three items, and three items of the conclusion section were excluded because the operationalisation of these proved to be difficult. Two extra items were added: validation of the outcome measures and co-interventions. Thus the modified CONSORT-based checklist comprised 33 items (Article IV, Appendix A).

We analysed the number and overall proportion of adequately reported items (scored as "yes") and insufficiently/inadequately (scored as "no", "partly", "unclear") for each trial. Items that were not applicable in some of the trials were excluded from the analysis. Trials published from 1990–1997 were compared to trials published from 1998–2002 to examine whether there was any improvement in the quality of reporting after the publication of the CONSORT statement. In addition, the flow of participants throughout each trial according to the stages of the CONSORT flow charts was examined, and the validity of the outcomes measures used in the trials was examined by searching the bibliographies for references confirming that the instrument had been validated, or checking the Internet for this information.

3.5 Methodological quality assessment (I, II, V)

Two reviewers independently assessed the quality of the reviews (I, II) or trials (V). The discrepancies in evaluations were solved by discussion and remaining disagreements were decided by a third reviewer.

In both overviews (I, II) the methodological quality of the included reviews was analysed using a modified version (Hoving et al. 2001) of the method described by Oxman et al. (Oxman & Guatt 1991; Oxman et al. 1991). This checklist evaluates nine items covering search methods, selection of the articles, validity assessment and methods for synthesis. Each item is scored from 0 to 2, with a maximum total score of 18 (Table 3.5).

In the review of physiotherapy and physiotherapy-related RCTs (V) we used criteria and decision rules modified from Van Tulder et al. (van Tulder et al. 2003) (Table 3.6). These include internal validity criteria (n=11) related to selection bias (criteria a and b), performance bias (criteria d, e, g, and h), attrition bias (criteria i and k) and detection bias (criteria f and j). All items were rated as “yes”, “no” or “don’t know”. We counted a summary score for “yes” answers and considered studies as of high quality if they had adequate randomisation and group allocation concealment, similar prognostic factors at baseline, and a described and acceptable drop-out rate.

3.6 Synthesis methods

In the two overviews (I, II) we used a qualitative approach to group the studies according to intervention types and to draw a synthesis of the results of the reviews. In the overview of reviews on physiotherapy and conductive education (I) we analysed the conclusions of the systematic reviews according to their methodological quality. We also analysed the number and type of the included studies and their overlaps between the reviews. In the overview of reviews on orthotic devices (II) evidence of the effectiveness of the various types of orthotic devices was presented both as reviewers' conclusions and based on our own data extraction from the reported information of the original studies.

In the review of physiotherapy and physiotherapy-related RCTs (V) the diversity among studies with regard to participants, interventions, outcome measures and methodological quality of the studies did not allow us to perform a quantitative analysis (meta-analysis). For a qualitative summary, the interventions were grouped and analysed separately for each intervention category. The outcomes were divided into ICF components (body functions and structures, activities and participation, environmental factors and personal factors) according to the major focus of measurement. The results for all outcomes of each trial were grouped

TABLE 3.5 Quality assessment criteria for review articles (Hoving et al. 2001).

Search methods	
1. Were the search methods used to find evidence (primary studies) on the primary question(s) stated?	<p>2 points: Yes; includes description of databases searched, search strategy, and years reviewed. Described well enough to duplicate.</p> <p>1 point: Partially; partial description of methods, but not sufficient to duplicate search</p> <p>0 points: No; no description of search methods</p>
2. Was the search for evidence reasonably comprehensive?	<p>2 points: Yes; must include at least one computerized database search as well as a search of unpublished or non-indexed literature (for example: manual searches or letters to primary authors)</p> <p>1 point: Cannot tell; search strategy partially comprehensive (for example: at least one of the strategies in the foregoing section were performed)</p> <p>0 points: No; search not comprehensive or not described well enough to make a judgment</p>
Selection methods	
3. Were the criteria used for deciding which studies to include in the review reported?	<p>2 points: Yes; inclusion and exclusion criteria clearly defined</p> <p>1 point: Partially; reference to inclusion and exclusion criteria can be found in the paper but are not defined clearly enough to duplicate</p> <p>0 points: No; no criteria defined</p>
4. Was bias in the selection of articles avoided?	<p>2 points: Yes; key issues influencing selection bias were covered. Two of three of the following bias avoidance strategies were used: two or more assessors independently judged study relevance and selection using predetermined criteria, reviewers were blinded to identifying features of study (i.e., journal title, author(s), funding source), and assessors were blinded to treatment outcome.</p> <p>1 point: Cannot tell; if only one of the three strategies above were used</p> <p>0 points: No; selection bias was not avoided or was not discussed</p>
Validity assessment	
5. Were the criteria used for assessing the validity for the studies that were reviewed reported?	<p>2 points: Yes; criteria defined explicitly</p> <p>1 point: Partially; some discussion or reference to criteria but not sufficiently described to duplicate</p> <p>0 points: No; validity or methodological quality criteria not used or not described</p>
6. Was the validity for each study cited assessed using appropriate criteria (either in selecting studies for inclusion or in analysing the studies that are cited)?	<p>2 points: Yes; the criteria used address the major factors influencing bias (for example: population, intervention, outcomes, follow-up)</p> <p>1 point: Partially; some discussion of methodological review strategy but not clearly described with predetermined criteria</p> <p>0 points: No; criteria not used or not described</p>
Synthesis	
7. Were the methods used to combine the findings for the relevant studies (to reach a conclusion) reported?	<p>2 points: Yes; qualitative or quantitative methods are acceptable</p> <p>1 point: Partially; partial description of methods to combine and tabulate; not sufficient to duplicate</p> <p>0 points: Methods of combining studies not stated or described</p>
8. Were findings of the relevant studies combined appropriately relative to the primary question that the review addresses?	<p>2 points: Yes; combining of studies appears acceptable</p> <p>1 point: Cannot tell; should be marked if in doubt</p> <p>0 points: No; no attempt was made to combine findings, and no statement was made regarding the inappropriateness of combining findings; should be marked if a summary (general) estimate was given anywhere in the abstract, the discussion, or the summary section of the paper, and the method of deriving the estimate was not described, even if there is a statement regarding the limitations of combining the findings of the studies reviewed</p>
9. Were the conclusions made by author(s) supported by the data or analysis reported in the review?	<p>2 points: Yes; data, not merely citations, were reported that support the main conclusions regarding the primary question(s) that the overview addresses</p> <p>1 point: Partially</p> <p>0 points: No; conclusions not supported or unclear.</p>

Maximum total score is 18.

TABLE 3.6 Quality assessment criteria and decision rules for randomized controlled trials (van Tulder et al. 2003).

Criteria list	
A	Was the method of randomization adequate?
B	Was the treatment allocation concealed?
C	Were the groups similar at baseline regarding the most important prognostic indicators?
D	Was the patient blinded to the intervention?
E	Was the care provider blinded to the intervention?
F	Was the outcome assessor blinded to the intervention?
G	Were co-interventions avoided or similar?
H	Was the compliance acceptable in all groups?
I	Was the drop-out rate described and acceptable?
J	Was the timing of the outcome assessment in all groups similar?
K	Did the analysis include an intention-to-treat analysis?
Decision	
A	A random (unpredictable) assignment sequence. Examples of adequate methods are computer-generated random number table or similar. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation should not be regarded as appropriate.
B	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.
C	In order to receive a "yes," groups have to be similar at baseline regarding demographic factors (age, setting), type and severity of CP, types of co-morbidities, and value of main outcome measure(s).
D-F	The reviewer determines if enough information about the blinding is given in order to score a "yes."
G	Co-interventions should either be avoided in the trial design or similar between the index and control groups.
H	The reviewer determines if the compliance to the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s).
I	No dropouts; or the number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a "yes" is scored.
J	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.
K	All randomized patients are reported/analysed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of noncompliance and co-interventions.

according to the presence of statistically significant differences between groups: 1) a difference in favour of the intervention group 2) a difference in favour of the control group, 3) no difference, 4) not analysed. We also considered the level of evidence in the synthesis based on the method by van Tulder et al. (van Tulder et al. 2003) (Table 3.7).

TABLE 3.7 Levels of evidence (adapted and modified from (van Tulder et al. 2003).

Strong	Consistent findings among multiple high-quality RCTs
Moderate	Consistent findings among multiple low-quality RCTs and/or one high-quality RCT
Limited	One low-quality RCT
Conflicting	Inconsistent findings among multiple trials
No evidence	No RCTs

4 Results

4.1 Yield of the reviews and trials (I–V)

Figures 4.1 and 4.2 show the article selection flow for the two overviews of reviews on physiotherapy and conductive education, and orthotic devices (I, II) and the review of physiotherapy and physiotherapy-related RCTs (V), respectively. The sample of RCTs for the two methodology articles (III, IV) was selected from the search results of the two overviews (I, II) before updating the search for article I and from the search results of an unpublished review on different intensities of the same type of therapy. We identified fifteen articles (Palmer et al. 1990; Law et al. 1991; Mayo 1991; Girolami & Campbell 1994; O'Dwyer et al. 1994; MacKinnon et al. 1995; Bower et al. 1996; Law et al. 1997; Steinbok et al. 1997; Reddihough et al. 1998; Chad et al. 1999; Bower et al. 2001; Bumin & Kayihan 2001; Ketelaar et al. 2001; Steinbok & McLeod 2002). One trial was reported in two stages (Steinbok et al. 1997; Steinbok & McLeod 2002), so there were 14 RCTs in total.

The final lists of the included systematic reviews comprised 21 reviews on physiotherapy and conductive education (I) (Tirosh & Rabino 1989; Horn 1991; Parette et al. 1991; French & Nommensen 1992; Hur 1995; Darrah et al. 1997; Woolfson 1999; Ludwig et al. 2000; Pedersen 2000; Boyd et al. 2001; Brown & Burns 2001; Butler & Darrah 2001; Dodd et al. 2002; Darrah et al. 2003; Steultjens et al. 2004; Harris & Roxborough 2005; Getz et al. 2006; Pin et al. 2006; Hoare et al. 2007; Snider et al. 2007; Sterba 2007), and of 5 reviews of orthotic devices (II) (Vermeer & Bakx 1990; Hur 1995; Boyd et al. 2001; Morris 2002; Teplicky et al. 2002). Two reviews (Hur 1995; Boyd et al. 2001) were included in both overviews.

In the review of physiotherapy and physiotherapy-related RCTs (V) published since 1990, 25 articles describing 22 trials were finally included (Palmer et al. 1990; Law et al. 1991; MacKinnon et al. 1995; Bower et al. 1996; Hallam 1996; Law et al. 1997; van den Berg-Emons et al. 1998; Chad et al. 1999; Bower et al. 2001; Bumin & Kayihan 2001; Ketelaar et al. 2001; Benda et al. 2003; Dodd et al. 2003; 2004; Taub et al. 2004; Tsorlakis et al. 2004; Ledebt et al. 2005; Bar-Haim et al. 2006; Charles et al. 2006; Unger et al. 2006; Patikas et al. 2006a; Patikas et al. 2006b; Liao et al. 2007; Wallen et al. 2007).

In three trials the analysis of different outcomes was divided into two reports (Palmer et al. 1988; Palmer et al. 1990; Dodd et al. 2002; Dodd et al. 2003; Patikas et al. 2006a; Patikas et al. 2006b), and thus one article of further outcomes from the same trial published before 1990 was included in the analysis (Palmer et al.

**Overview of reviews on
physiotherapy and conductive
education (I)**

**Overview of reviews on orthotic
devices (II)**

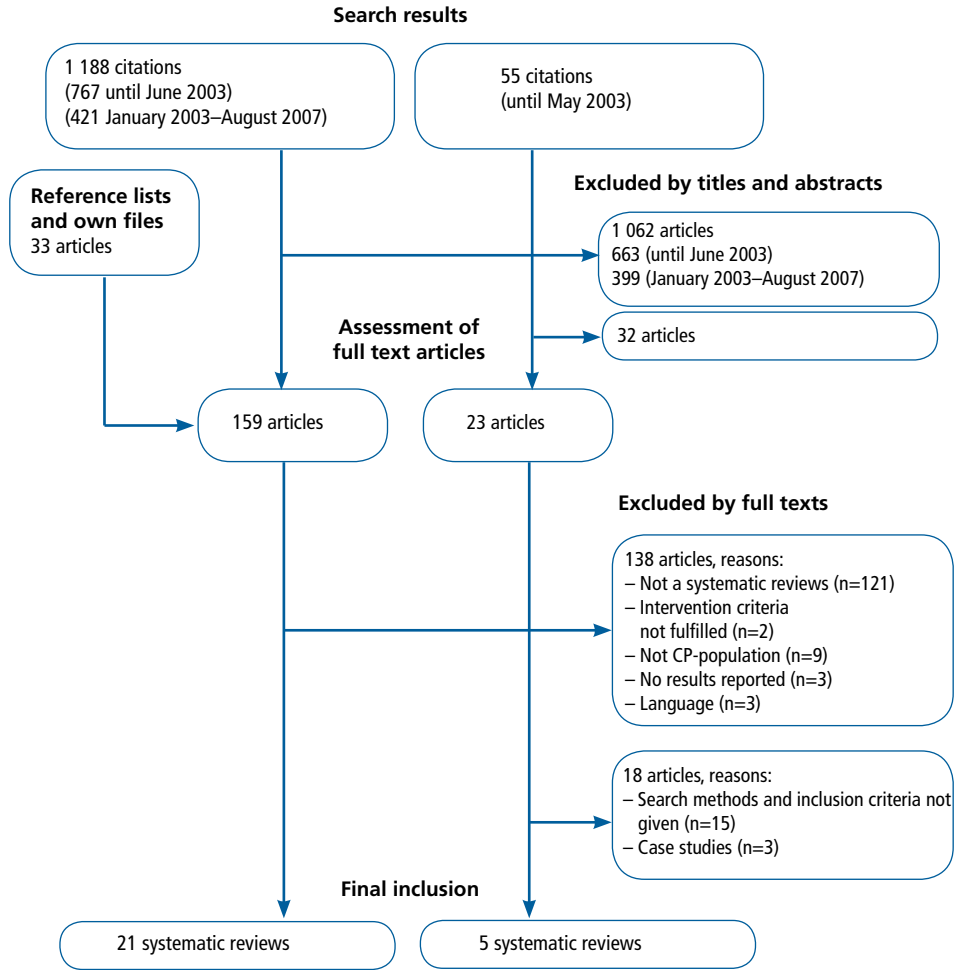


FIGURE 4.1 Flow chart of the article selection process in the two overviews on physiotherapy and conductive education (I) and on orthotic devices (II).

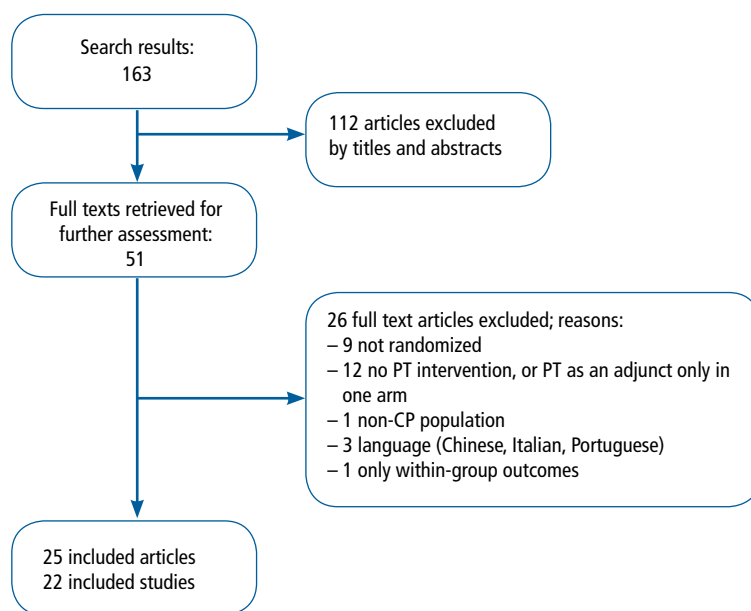


FIGURE 4.2 Flow chart of the article selection process in the review of RCTs (V).

1988). In one trial we analysed the data only for the first period, which presented a randomized intervention contrast (van den Berg-Emons et al. 1998).

The review of RCTs (V) identified 16 trials that were not evaluated in the previous reviews. There were also some overlaps. Five trials published between 1990 and 1998 had been evaluated in several reviews (Palmer et al. 1988; Palmer et al. 1990; Law et al. 1991; MacKinnon et al. 1995; Law et al. 1997; Reddihough et al. 1998), and two trials (Benda et al. 2003; Taub et al. 2004) in two reviews, by Hoare and by Snider, respectively. A thorough presentation of the RCTs identified in the overviews (I, II), and included in the sample (III, IV) and the review of RCTs (V) is in Appendix C. Reasons for exclusions are listed in Appendix D.

4.2 Methodological quality and characteristics of reviews (I, II)

Methodological quality

The methodological quality scores of the reviews (I, II) are shown in Table 4.1. The mandatory criteria for inclusion, search methods and inclusion criteria, were at least partially described in all reviews. Six reviews, fulfilling all criteria other than blinding reviewers from author and outcome information, were regarded as of high quality (Brown & Burns 2001; Dodd et al. 2002; Steultjens et al. 2004; Harris & Roxborough 2005; Hoare et al. 2007; Snider et al. 2007). Altogether twelve

reviews (Tirosh & Rabino 1989; Ludwig et al. 2000; Boyd et al. 2001; Brown & Burns 2001; Dodd et al. 2002; Darrah et al. 2003; Steultjens et al. 2004; Harris & Roxborough 2005; Pin et al. 2006; Hoare et al. 2007; Snider et al. 2007; Sterba 2007) had defined quality assessment criteria, and all but one (Sterba 2007) used these in their analyses. Many reviews had inadequacies in the search and synthesis methods. The median quality score was 11 out of 18 points (range 3–17). The methodological quality assessment was based on the other content of the two reviews (Hur 1995; Boyd et al. 2001) included in both overviews (I, II). Thus the quality scores differ.

Characteristics of the reviews

Summaries of the reviews' focus, their methods and conclusions as stated by the reviewers are given in Table 3 (in article I) for reviews on physiotherapy and conductive education and in Table 4.2 for reviews on orthotic devices. All reviews applied qualitative syntheses methods, those these varied considerably. The results were classified into different categories in 19 reviews: outcomes (n=6), interventions (n=4), interventions and outcomes (n=2), study designs (n=3), dichotomized findings (n=3), or participants (n=1). In two reviews, studies were analysed separately. The analysis methods were either descriptive (n=12) or levels of evidence analyses (n=9). One review applied meta-analysis on RCTs (Boyd et al. 2001). Effect sizes and confidence intervals were available only from three reviews (Dodd et al. 2002; Bjornson et al. 2007; Hoare et al. 2007).

The 21 reviews (I) were based on altogether 31 randomized controlled trials (RCTs) and 199 observational studies. Because ten reviews included studies on non-CP children (Tirosh & Rabino 1989; Horn 1991; Parette et al. 1991; French & Nommensen 1992; Hur 1995; Pedersen 2000; Brown & Burns 2001; Getz et al. 2006; Pin et al. 2006; Sterba 2007) and four reviews on interventions that were outside the scope of this review (Hur 1995; Boyd et al. 2001; Steultjens et al. 2004; Harris & Roxborough 2005), these studies were excluded from our analyses of the characteristics and effectiveness of the reviewed interventions. Thus 23 RCTs and 104 observational studies were on children with CP; of these 13 RCTs and 29 observational studies were included in more than one review (Article I, Table 4).

The five reviews on orthotic devices (II) included 5 RCTs and 27 published observational studies. The reviews included another 24 studies as abstracts or as only references with no further details, thus these were excluded from our analysis.

Characteristics of the population, interventions and outcomes

The reviews of physiotherapy and conductive education interventions (I) were categorized to 1) comprehensive therapy, 2) constraint-induced movement therapy, 3) aquatic therapy, 4) hippotherapy, 5) strength training, 6) postural control training, 7) stretching, 8) conductive education and 9) various (several of the above interventions in one review). The population in terms of age, type and severity of CP, the interventions, and the outcome measures were heterogeneous in all reviews and intervention groups. Altogether 702 children with CP were studied in the 23 RCTs (range 12–73). The total number of CP children was 2365 (range 1–626), as available from 88 observational studies. The age ranged from 3 months to 26 years, reported in 17 reviews. In 4 reviews the ages were not reported for some or any of the original studies (Article I, Appendix B).

The included studies were conducted in various settings (clinic, home, school or community), as reported in 4 reviews (Ludwig et al. 2000; Dodd et al. 2002; Darrah et al. 2003; Steultjens et al. 2004). The content of the interventions were described in the reviews with short titles only, except in the one Cochrane review (Hoare et al. 2007). In thirteen reviews, intervention doses varied from 8 minutes to 13½ hours per day, and sessions from 1 to 7 days per week. The interventions lasted from one session to 4 years, including possible follow-up periods. The number of different outcome measures reported varied from 6 to 30 per review, while two reviews did not report any outcomes (Hur 1995; Pedersen 2000). The reviews provided no data on possible adverse effects of the reviewed interventions. (Article I, Appendix B).

In the overview of reviews on orthotic devices (II), the sum of the total population was 551 children (Article II, Table 3). The studies included in the reviews were categorized to lower limb casting, lower limb orthosis, upper limb casting and upper limb orthosis. The number of different outcome measures reported in the reviews varied from 2 to 17 (Article II, Table 3).

TABLE 4.1 Methodological quality of systematic reviews on physiotherapy, conductive education (I, n=21) and orthotic devices (II, n=5).

First author (year)	Search methods		Selection methods		Validity assesment		Synthesis			Total points (max 18)
	Search methods	Search comprehensive-ness	Inclusion criteria	Avoid-ance of selection bias	Defini-tion of the validity assess-ment criteria	Use of the quality assess-ment criteria	Synthesis methods	Accept-ability of the synthesis methods	Conclu-sions supported by data analysis	
Comprehensive physiotherapy (I)										
Brown (2001)	2	2	2	1	2	2	2	2	2	17
Butler (2001)	2	2	2	0	0	0	2	1	2	11
Parette (1991)	1	1	1	0	0	0	0	0	0	3
Tirosh (1989)	1	1	1	0	2	2	0	1	2	10
Strength training (I)										
Dodd (2002)	2	2	2	1	2	2	2	2	2	17
Darrah (1997)	2	1	1	1	0	0	2	2	2	11
Constraint induced movement therapy (I)										
Hoare (2007)	2	2	2	1	2	2	2	2	2	17
Postural control (I)										
Harris (2005)	2	2	2	1	2	2	2	2	2	17
Soft tissue treatment (I)										
Pin (2006)	2	1	2	0	2	2	2	0	0	11
Hydrotherapy (I)										
Getz (2006)	2	2	2	1	0	0	2	2	2	13
Hippotherapy (I)										
Snider (2007)	2	2	2	0	2	2	2	2	2	16
Sterba (2007)	2	1	2	0	2	0	0	0	0	7
Conductive education (I)										
Darrah (2003)	2	1	2	0	2	2	2	1	2	14
Ludwig (2000)	2	2	2	1	2	2	0	1	0	12
Pedersen (2000)	1	1	1	0	0	0	0	0	0	3
French (1992)	1	2	2	0	0	0	1	1	2	9
Various interventions (I)										
Stultjens (2004)	2	2	2	1	2	2	2	2	2	17
Boyd (2001)	2	2	2	0	2	1	1	1	0	11
Woolfson (1999)	1	2	2	0	0	0	0	0	1	6
Hur (1995)	1	1	1	0	0	0	0	1	2	6
Horn (1991)	2	2	2	0	0	0	0	1	2	9
Orthotic devices (II)										
Morris (2002)	2	2	1	0	0	0	0	1	2	8
Teplicky (2002)	1	1	1	0	0	0	0	1	1	5
Boyd (2001)	2	2	2	0	2	2	2	2	2	16
Hur (1995)	1	1	1	0	0	0	0	0	2	5
Vermeer (1990)	1	1	1	0	2	2	0	0	0	7

TABLE 4.2 Characteristics of methods and conclusions of systematic reviews on orthotic devices (n=5).

First author (year)	Objectives of the review	Designs included*	Methods of analyses (Search period, methodological quality assessment (QA), categorisation of the results, synthesis method)	Quality score	Conclusions of review*
Orthotic devices					
Boyd (2001)	Efficacy of different treatments (including orthotic devices) for the management of upper limb dysfunction in children with CP.	RCT (5) ObD (51)	Search (1966–December 2000). QA: only RCTs by PEDro scale (Verhagen et al. 1998) Categorisation by interventions, ICIDH-2. Meta-analysis of 3 studies with same outcome measure. Levels of evidence analyses (Sackett 1989).	11	All physiotherapy interventions: ? Casting combined with adjuncts: ±
Hur (1995)	Effect of physiotherapy interventions (including orthotic devices) for children with CP.	RCT (7) CCT (2) ObD (28)	Search (1966–1994). QA: - Categorisation by study designs. Descriptive analyses.	6	Therapeutic interventions: ? Lower limb orthotic devices: ?
Morris (2002)	Efficacy of lower limb orthoses used for children with CP.	RCT (1) ObD (26) Abstracts (15)	Search period (1994–2000) QA: - Descriptive analyses.	8	Lower limb orthoses: prevention of deformities ±, prevention of equinus, if plantarflexion is restricted +, long term benefits or harm ?
Teplicky (2002)	Effectiveness of casts, orthoses, and splints for upper and lower limbs when used in children with CP or brain injury.	RCT (5) ObD (27) Not described (11)	Search period nr. QA: - Categorization by the orthotic device. Descriptive analyses.	5	Lower limb casting: ankle movement + Lower limb orthoses (ankle-foot orthosis): ankle movement during walking +, walking pattern ? Upper limb casting: range of motion +, tone ±, hand function ? Upper limb orthosis (hand splints): grasping +, hand use in functional tasks ?
Vermeer (1990)	Improvement of scientific quality of intervention research with children.	ObD (4) Other articles (29)	Hand search of 13 English and 4 Dutch journals since 1978. QA: 13 criteria for description of population, treatment and methodological aspects. Categorization by interventions. Descriptive analyses.	7	Lower limb casting: balance +, walking symmetry + Lower limb inhibitive orthoses: balance +, walking symmetry +

*as stated by the author; +, improved outcome; ±, indications for improvement; -, evidence for ineffectiveness; ?, insufficient evidence. CP, cerebral palsy; NDT, neurodevelopmental therapy; CIMT, constraint-induced movement therapy; RCT, randomised controlled trial; CCT, clinical controlled trial; ObD, observational design; ICIDH-2, International Classification of Impairments, PEDro scale, Physiotherapy Evidence Database Scale; Disabilities and Handicaps; QA, quality assessment methods.

4.3 Feasibility of a randomised controlled trial in a CP context (III)

Characteristics of the sample trials

All trials (n=14) were small with a median sample size of 34 (range 15–72) and the studied populations, interventions and outcomes differed between the trials. Nine trials had an NDT treatment in one arm, compared to less intensive NDT, casting, infant stimulation, functional physiotherapy or conductive education. The other interventions comprised various physiotherapy methods. Most studies used a two-arm design, while some had three (Girolami & Campbell 1994; Chad et al. 1999) or four (Law et al. 1991; Bower et al. 1996; Bower et al. 2001) groups (factorial design). One study chose a cross-over design (Law et al. 1997).

Sampling, recruitment and treatment allocation

The sampling frame was sufficiently described in detail in 8 out of 14 trials so as to allow an interpretation of the results and a transfer to other settings. In two studies the description was partly reproducible while four studies did not provide any information. The recruitment settings were population-based, covering the population of a defined area (n=4) or including two or more specialized centres (n=6). Six trials were performed in a single centre, whereas three studies did not describe their setting at all (Table 4.3).

Only three trials specified concealed allocation of treatment. The used randomization methods included simple or block (of four to eight) randomization. Other trials assigned the children according to date of admission or did not specify the randomization process. Nine trials applied matched pairs or stratification for one or two prognostic or risk factors (e.g. severity of disease or age). Eleven studies reported the baseline characteristics of the groups by comparing socio-demographic factors, disease severity or functional deficits. (Table 4.3)

Individual components of the complex intervention

No trial presented the eight key components of a complex intervention in a systematic or standardized way (Figure 4.3). Most trials standardized their intervention (86%) and specified 'the active ingredient' of the therapy (57%). The other six important components were mentioned only in one to five studies, and rarely described in a standardized way. Five trials described the therapist's expertise and skills or detailed the interaction between the therapist and the child. In five trials the researchers checked and clarified what co-interventions were ongoing during the study. The routine therapy both for the experimental and control groups was defined only in two trials. Similarly, discussion on child- or parent-related issues, such as their attitudes toward the study and satisfaction with the therapy, was very limited. Parents' attitudes or satisfaction were addressed descriptively in four studies and children's attitudes only in one.

TABLE 4.3 Population — Recruitment and comparability

Author, year	Study size (group size)	Sampling Frame		Comparability			
		Reproducible description	Setting	Mode of randomisation	Stratification or similar action	Concealed allocation	Baseline comparability
Bower 1996	44 (11/11/11/11)	Y	Multi-centre Population	Computer programme Blocks of 8	Stratification (severity)	Y	Y
Bower 2001	56 (15/13/13/15)	Y	Multi-centre Population	Computer programme Blocks of 4	Stratification (severity; age)	Y	Y
Bumin 2001	41 (16/16/9)	N	Single centre	Quasi-randomisation	N	N	N
Chad 1999	18 (9/9)	N	Unclear	Unclear	N	n.r.	N
Girolami 1994	27 (10/ 9/ 8)	Y	Single centre	Simple	N	n.r.	Y
Ketelaar 2001	55 (27/28)	Y	Multi-centre Population	Blocks of 6 Incomplete	Stratification (age; type of CP)	n.r.	Y
Law 1991	72 (19/17/18/18)	Y	Multi-centre	Blocks of 4	n.r.	n.r.	Y
Law 1997	50 (cross-over)	Y	Multi-centre Population	Blocks of 4	Stratification (age; hand function)	n.r.	Y
MacKinnon 1995	19 (9/10)	N	Unclear	Simple	Stratification (walking abilities)	n.r.	Imbalances on sex and age
Mayo 1991	29 (17/12)	P	Single centre	Simple	Stratification (severity)	n.r.	Y
O'Dwyer 1994	15 (7/8)	P	Two centres	Simple	Matched pairs (spasticity; age)	n.r.	N
Palmer 1990	48 (25/23)	Y	Single centre	Simple	Stratification (mental development)	n.r.	Y
Reddihough 1998	34 (17/17) (randomised); 26 (13/13) (preferred)	N	Unclear	Simple	Matched (age; type + severity; cognitive abilities)	n.r.	Y
Steinbok 1997 / 2002	29 (15/14)	Y	Single centre	Simple	n.r.	Y	Y

n.r. = not reported; Y = yes, N=no, P = partly

We also evaluated how well the individual studies depicted those potentially relevant components of a complex intervention. Eight of 14 studies covered 50% or more of the predefined complexity items and four of them even managed to cover 80% or more (Article III, Figure 3), implying that many research teams were aware of the intrinsic complexity issues and the ongoing interactions and tried to control or at least describe these elements. Examples of such solutions are collected in the Appendix of the Article III.

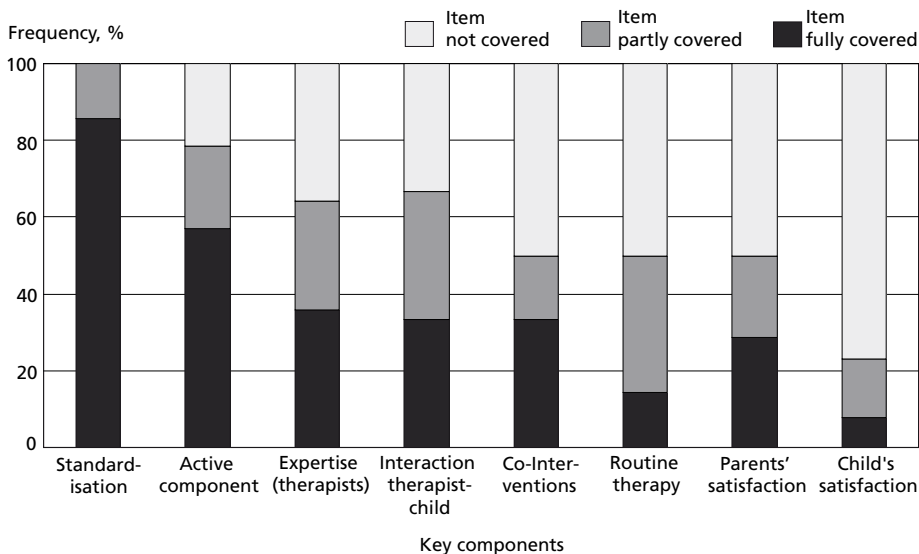


FIGURE 4.3 Physiotherapy as a complex intervention: How well were the 8 key components of complexity taken into account in the 14 studies?

Outcomes and their interpretation

A summary of the interventions, instruments, results, and the authors' clinical interpretation are given in article III (Supplemental Table 4). Twenty-seven different instruments and scales for motor outcomes were used. A majority of studies did not distinguish between primary and secondary outcomes. Four studies (Bower et al. 1996; Law et al. 1997; Bower et al. 2001; Ketelaar et al. 2001) exclusively used activity outcomes such as the GMFM, whereas two studies (Girolami & Campbell 1994; Chad et al. 1999) limited their assessment to body function and structures (such as bone density or muscle strength) only. The overlap for the instruments measuring body structures and functions was poor: 15 of 16 instruments (94%) were administered only once across all studies. Only "range of motion" measures were used twice. This makes any comparison of results across studies unfeasible.

A more homogeneous selection of assessment tools was observed for activity items where three of the 12 instruments were applied in more than one study: the GMFM in six, the Peabody Fine Motor Scale in three, and the Quality of Upper Extremities Skills Test in two trials. There was a statistically significant difference between the intervention groups in a third of outcomes, more frequently in outcomes measuring mainly "body functions and structures" than "activities and participation" ($p=.0007$) (Table 4.4).

There was only one instrument where the clinical interpretation of the score had an empirical foundation, based on parents' judgement on what minimum score change they would regard as relevant (Russell et al. 2002). This difference was

TABLE 4.4 Relationship between endpoint domain according to the International Classification of Functioning, Disability, and Health (ICF) and the probability of a significant test result.

	Endpoint domain (according to the ICF)		Total	
	Body structures and functions	Activities and participation		
Significant result	9	2	11	
Nonsignificant result	5	15	20	
	14	17	31	p=0.007*

* Fisher's exact test.

picked up in the discussions of three of the studies (Bower et al. 1996; Steinbok et al. 1997; Bower et al. 2001). Two studies with outcomes on body functions and structures made speculations about the meaning of their positive findings. One compared the findings to another study with healthy adults, where a decrease in bone mineral content was associated with an increased risk of hip fracture (Chad et al. 1999). The other discussed the clinical value of an isolated change in spasticity (O'Dwyer et al. 1994). Three other studies acknowledged the discrepancy between a statistically significant difference in score and its clinical importance (Palmer et al. 1990; Law et al. 1991; Law et al. 1997). The remaining studies did not address these issues regardless of their findings.

4.4 Reporting quality (IV)

Agreement of the evaluations and overall results

Using the CONSORT checklist the evaluators disagreed in 23% of the evaluations. After consensus discussions the remaining disagreements (9%) were resolved by a third researcher. Nine percent of evaluations were not applicable in some of the trials, The reasons for not being applicable were that the trials had no stopping rules or interim analyses (CONSORT descriptor item 10), could not blind the therapists and patients (17), and thus could not assess the success of it (19), or did not do any ancillary analyses (21, 30). These non-applicable evaluations were not counted in the calculations.

Of all evaluations of the applicable 31 items based on the CONSORT checklist, nearly half (48%) were reported adequately (Table 4.5). The remaining items were either not reported at all (37%), or were reported partially (13%) or not clearly (2%). Only seven trials employed validated outcome measures and five trials reported on co-interventions. Adding these two items did not change the overall results.

More than half of the items were reported adequately in seven trials, while four trials reached an adequate score in less than 10 items (30%). Comparing tri-

als published between 1990 and 1997 (n=9) and between 1998 and 2002 (n=6) showed no clear differences in the quality of reporting. The percentages of adequately reported items were 45.5% (SD 30.6; range 0–88.9) and 40.9% (SD 29.8; range 0–83.3), respectively. Assessment scores for each CONSORT item in the 15 trials are shown in Article IV, Appendix 2.

Adequately and inadequately reported items

Most trials reported adequately items that were descriptive. These included problem definitions and descriptions of research subjects, objectives, settings, and trial locations, details of the actual administration of the interventions (intensity and short descriptions of the type of therapy), methods to enhance the quality of measurements, for example training of assessors, and statistical procedures in analysing the results. Trials (n=7) using subgroup or adjusted analyses provided clear specifications of the choice of the variables adjusted, but did not specify whether these were planned in the protocol or whether they were data driven. From most trials we found adequate tables reporting baseline demographic characteristics, such as type of CP, age and mean values of the main outcome measure, and numbers of participants of each group in each analysis and a summary of the results and effect sizes for each group and for each of the outcomes. Detailed charts of participant flow were not available in any trial, but based on the numbers of participants reported in both text and tables of the papers, we could construct the participant flow starting from the randomization process in eleven trials (Article IV, Table 3). In nearly half of the trials it remained unclear as to how many children were assessed and excluded prior to the randomization.

Items that seldom were reported adequately were mostly research methodological items. We identified major shortcomings in the descriptions of the trial methods, particularly in reporting the randomisation process. These items included concealment of the allocation, implementation of the randomisation, methods to generate the random allocation sequence. Further reporting inadequacies were found in the definition of primary outcomes, application of only validated outcome measures, precision of the effect size, full rationale for sample-size calculation, blinding of therapist and participants (was not applicable for most trials) details on how its success of assessor blinding was evaluated, whether the results were analysed with the intention-to-treat principle, and whether there were co-interventions or adverse events.

TABLE 4.5 The 31 CONSORT-based items and items on validation of the outcome measures and co-interventions reported in 15 physical or occupational therapy intervention trials on children with cerebral palsy.

Original CONSORT item	Descriptor item	Item content	Yes	No	Partly	Unsure	N.a.
Title & abstract							
1	1	Word "random or "randomized" mentioned	12 ^a	3	0	0	0
Introduction and protocol							
2	2	Nature, scope and severity of the problem	13 ^a	0	2	0	0
3 - 1	3	Eligibility criteria for participants	9 ^a	0	6	0	0
3 - 2	4	Settings and locations	10 ^a	1	4	0	0
4	5	Intervention description	11 ^a	0	4	0	0
5	6	Objectives	12 ^a	0	3	0	0
6 - 1	7	Primary and secondary measures defined	5	3	7	0	0
6 - 2	8	Quality enhancement of the outcome measurement	9 ^a	4	2	0	0
7 - 1	9	Sample size determination	4	9 ^a	2	0	0
7 - 2	10	Interim analysis and stopping rules	0	0	0	0	15 ^a
Assignment and masking							
8 - 1	11	Method of generating a randomization sequence	5	10 ^a	0	0	0
8 - 2	12	Details of restriction	9 ^a	6	0	0	0
9	13	Concealment of allocation	0	12 ^a	1	2	0
10 - 1	14	Who generated the allocation sequence?	1	13 ^a	1	0	0
10 - 2	15	Who enrolled the patients?	2	13 ^a	0	0	0
10 - 3	16	Who assigned the patients to groups?	0	15 ^a	0	0	0
11 - 1	17	Were the participants and therapists blinded?	0	0	1	0	14 ^a
11 - 2	18	Were the assessors blinded?	11 ^a	3	1	0	0
11 - 3	19	If blinded: how success of blinding was evaluated?	2	10 ^a	0	0	3
12 - 1	20	Statistical methods	13 ^a	0	2	0	0
12 - 2	21	If applicable: ancillary analysis methods	8 ^a	2	0	0	5
Participant flow and recruitment							
13 - 1	22	Participants flow	11 ^a	1	3	0	0
13 - 2	23	Report of study violations	9 ^a	5	1	0	0
14	24	Recruitment and follow-up dates defined	1	14 ^a	0	0	0
Results							
15	25	Demographic and clinical characteristics	8 ^a	1	6	0	0
16 - 1	26	Number of participants in each group	12 ^a	2	0	1	0
16 - 2	27	Was it an Intention to treat analysis?	5	4	2	4	0
17 - 1	28	Effect sizes for each group for each outcome measure	11 ^a	3	1	0	0
17 - 2	29	Precision of the effect sizes	4	11 ^a	0	0	0
18	30	If applicable: ancillary analysis stated in the study protocol	4	2	4	0	5
19	31	All important adverse events	3	11 ^a	1	0	0
		Sum	204	158	54	7	42
		Percentage of applicable CONSORT descriptor items (n=423)	48.2	37.4	12.8	1.6	
Added items							
-	32	Validation of the outcome measures	7	0	5	3	0
-	33	Co-interventions	5	9 ^a	1	0	0
		Sum	216	167	60	10	42
		Percentage of all applicable items (n=453)	47.7	36.9	13.2	2.2	

N.a.=not applicable.

^a Score in the majority of the trials (≥ 8)

4.5 Characteristics of the trials (V)

Participants

The sample sizes of the 22 trials varied from 10 to 100 children, and the age from 7 months to 18 years (Appendix E). Different CP subgroups were represented: spastic diplegia (n=255), hemiplegia (n=238), tetraplegia (n=180), bilateral (n=56), ataxic or mixed di- or quadriplegia (n=20), and triplegia (n=7), or they were not reported in three studies for 52 children (MacKinnon et al. 1995; Chad et al. 1999; Benda et al. 2003). The severity of the children's motor deficit was defined by the GMFCS in 7 trials as follows: 21% of level I, 20% of level II, 33% of level III, 21% of level IV and 5% of level V. In 10 trials the children were mildly (51%) or moderately (39%) impaired. Five trials did not report the severity of motor impairment. In three trials some participants were reported to have cognitive impairments (van den Berg-Emons et al. 1998; Taub et al. 2004; Wallen et al. 2007).

Prior to randomisation, all children had undergone multilevel surgery on lower extremities in one trial (Patikas et al. 2006a; Patikas et al. 2006b), and 18 children had had surgery and three botulinum toxin treatment in another trial (Dodd et al. 2003; 2004). Stratification techniques were used in twelve trials (Palmer et al. 1988; Palmer et al. 1990; Law et al. 1991; MacKinnon et al. 1995; Bower et al. 1996; Law et al. 1997; van den Berg-Emons et al. 1998; Bower et al. 2001; Ketelaar et al. 2001; Tsorlakis et al. 2004; Ledebt et al. 2005; Bar-Haim et al. 2006; Liao et al. 2007), usually by age and severity or type of CP and also by sex. One trial stratified the children by cognitive status defined by Bayley Scales of Infant Development Mental Developmental Index (Palmer et al. 1988; Palmer et al. 1990), and one by activity and mental function (van den Berg-Emons et al. 1998).

Interventions

Eight intervention categories were formed: comprehensive physiotherapy approaches, upper extremity treatments, strength training, cardiovascular fitness or aerobic programs, constraint-induced therapy, sensorimotor training, balance training, and hippotherapy (Appendix E). The trials described the interventions quite accurately and in detail (Appendix F). The studied interventions lasted from eight minutes to 12 months (most typically six months). Nine trials had a post-intervention follow-up period (range from one to 18 months from baseline).

In 11 trials the index intervention was compared to no-training (n=4), or to no extra therapy (n=7). In these trials the children in all groups continued their usual physiotherapy (n=8) or customary care (n=1). In the 8-minute trial there were no add-on interventions (Benda et al. 2003), or the add-on therapies were not reported in three trials (Chad et al. 1999; Ledebt et al. 2005; Unger et al. 2006). The other 11 trials compared the index intervention to other types of intervention (n=5), or another intensity of the same intervention (n=5), or both (n=1). Seven

TABLE 4.6 Measurements or outcome measures (n=57) used in the included 22 trials.

Outcome category	Outcome measure
Body Structures and functions (n=19)	Bone mineral content
	Energy expenditure Index
	Fat mas
	Hand grip (by dynamometer)
	Maximum load of the loaded sit-to-stand test
	Mean aerobic power
	Metabolic cost of stair climbing
	Modified Asworth Scale
	Muscle asymmetry by EMG
	Muscle strength (knee extensor)
	Muscle strength by dynamometer (ankle plantar flexors, knee extensors, hip extensors)
	Oxygen consumption
	Peak aerobic power
	Peak anaerobic power
	Physiological cost index (PCI)
	Range of motion (ROM)
	Tardieu Scale
Two-point discrimination (sensibility)	
Volumatic bone mineral content	
Activity and participation (n=32)	3D Gait analysis (various parameters)
	Attained motor skills (no scale)
	Ayres Southern California Sensory Integration test (ACSIT)
	Bayley Scales of Motor Development
	Bertoti, sitting posture
	Bruininks-Oseretsky Test of Motor Proficiency (BOTMP)
	Caregiver Functional Use Survey
	Child Behaviour Checklist
	Child Health Questionnaire (CHQ)
	Canadian Occupational Performance Measure (COPM)
	Dynamic stance on force plate
	Emerging Behaviors Scale (EBS)
	Gait speed (self-selected walking speed in 10m)
	Gross Motor Function Measure (GMFM-66, GMFM-88)
	Gross Motor Performance Measure (GMPM)
	Goal Attainment Scale (GAS)
	Griffith Mental Development Scale (GMDS)
	Jebsen-Taylor Test of Hand function
	Level of daily physical activity
	Measure of Processes of Care (MPOC)
	Peabody Developmental Motor Scales - Fine Motor (PDMS-FM)
	Peadiatric Evaluation of Disability Inventory (PEDI)
	Pediatric Motor Activity Log (PMAL)
	Physical Ability Test
	Quality of Upper Extremity Skills Test (QUEST)
	Quiet stance on force plate
	Step length
	Step length asymmetry
	Timed stair test
	Toddler Arm Use Test (TAUT)
Vineland Adaptive Behaviour Scale	
Environmental factors (n=2)	Carey Infant Temperament Questionnaire
	Harter Self-perception Profile
Personal factors (n=4)	HOME
	Self perception questionnaire
	Self-perception Profile for Children
	The Mother-Child Relationship Evaluation
Overall improvement	Parent questionnaire for overall improvement

of these trials also included add-on interventions for both groups, whereas four trials did not report on this issue (Bower et al. 1996; Law et al. 1997; Ketelaar et al. 2001; Tsorlakis et al. 2004).

Outcomes

Fifty-seven different endpoints were analysed in the 22 trials as roughly categorised by their major measurement goals to ICF components in Table 4.6. Three measures were used in more than one trial: the Gross Motor Function Measure in nine, the Quality of Upper Extremity Skills Test in four, and the Peabody Fine Motor Scales in three trials. The other measures were used in one or two trials. Three trials did not analyse the between-group differences for subjective well-being (Wallen et al. 2007), sensory integration (Bumin & Kayihan 2001), and hand-grip force (Hallam 1996).

4.6 Methodological quality of the trials (V)

The methodological quality scores of the trials are shown in Table 4.7. The number of fulfilled quality items ranged from 1 to 8. No trial could blind the participants or therapists, and all trials, except one, succeeded in similar outcome assessment timing. Four trials fulfilled the four criteria that were considered to constitute high quality (Bower et al. 1996; Hallam 1996; Taub et al. 2004; Wallen et al. 2007). Four other studies fulfilled seven or eight of the quality criteria, but these trials failed to report the randomization method (Tsorlakis et al. 2004), concealment of allocation (Ketelaar et al. 2001), or the groups were different at baseline (Bower et al. 2001; Dodd et al. 2003; 2004).

4.7 Effects of the reviewed interventions (I, II, V)

The results of the 22 trials fall into eight intervention categories. The measured outcomes are classified according to the ICF components and a level of evidence is assigned to each outcome. A full description of the reviewed interventions is shown in Appendix E and full details of the baseline values and changes on all measured outcomes in Appendix G. The conclusions from the existing reviews (I, II) complement four of the same intervention categories covered in the trials and provide insights into nine additional intervention categories that were established based on the 22 trials. Thus the results on the effects of the interventions comprise altogether 17 intervention categories. Because of the variety of review methods and presentation modes of the results in the analysed reviews, their results could not be presented according to the ICF categories and the levels of evidence. A full

TABLE 4.7 Methodological quality of the trials (n=22).

First author (year)	Adequate randomization ^c	Allocation concealment ^c	Prognostic similarity ^c	Subject blinding	Therapist blinding	Assessor blinding	Co interventions avoided or similar	Acceptable compliance	Acceptable and described dropout rate ^c	Similar outcome assessment timing	Intention to treat analysis	No of "yes" scores
Comprehensive physiotherapy programs												
Bar-Haim (2006)	yes	?	yes	no	no	?	yes	?	yes	no	yes	5
Tsolakis (2004)	?	yes	yes	no	no	yes	?	yes	yes	yes	yes	7
Ketelaar (2001)	yes	?	yes	no	no	yes	yes	yes	yes	yes	yes	8
Bower (2001)	yes	yes	no	no	no	yes	yes	no	yes	yes	yes	7
Bower (1996)	yes	yes	yes	no	no	yes	?	yes	yes	yes	yes	8
Palmer (1990, 1988)	?	?	yes	no	no	no	?	yes	yes	yes	yes	5
Upper extremity treatments												
Wallen (2007)	yes	yes	yes	no	no	no	?	yes	yes	yes	yes	7
Law (1997)	?	?	yes	no	no	yes	?	yes	yes	yes	yes	5
Law (1991)	?	?	yes	no	no	yes	?	yes	yes	yes	yes	6
Hallam (1996)	yes	yes	yes	no	no	?	yes	yes	yes	yes	yes	8
Strength training programs												
Liao (2007)	?	?	yes	no	no	yes	?	yes	yes	yes	yes	6
Patikas (2006a, b)	yes	yes	?	no	no	no ^a , yes ^b	yes	?	yes	yes	no	6
Unger (2005)	yes	?	yes	no	no	yes	?	?	yes	yes	?	5
Dodd (2003, 2004)	yes	yes	no	no	no	yes	yes	yes	yes	yes	yes	8
Cardiovascular fitness and aerobic programs												
Chad (1999)	?	?	yes	no	no	?	?	?	yes	yes	yes	4
Van Den Berg-Emons (1998)	?	?	yes	no	no	?	?	yes	yes	yes	yes	5
Constraint induced therapy												
Charles (2006)	?	?	yes	no	no	yes	?	yes	no	yes	?	4
Taub (2004)	yes	yes	yes	no	no	no	?	yes	yes	yes	yes	7
Sensorimotor training												
Burnin (2001)	no	no	?	no	no	no	?	?	no	yes	yes	2
Balance training												
Ledebt (2005)	?	?	no	no	no	no	?	?	no	yes	?	1
Therapy with animals												
Benda (2003)	?	yes	?	no	no	no	yes	yes	yes	yes	yes	6
MacKinnon (1995)	?	?	?	no	no	yes	?	yes	yes	yes	yes	5

Yes=criteria fulfilled, no=criteria not fulfilled, ?=don't know. ^cThese four items were considered to constitute "high quality".

description of the reviews' conclusions on effectiveness from the studies on children with CP can be found in Appendix B of the Article I.

Table 4.8 summarizes the available moderate and conflicting evidence of the 22 trials, based on the levels of evidence as outlined in Table 3.7. We found no strong evidence on the reviewed interventions, but established some moderate and conflicting evidence on some particular outcomes in a few intervention categories. For most interventions the evidence remains limited.

Moderate evidence on the effectiveness of upper extremity treatments and constraint induced movement therapy was found based on three high-quality trials complemented with one lower-quality trial. In one high-quality trial comparing three months NDT to no therapy with young children (from 2 to 11 years), the NDT group improved more on attained goals and range of motion in active supination at six months. The other high-quality trial investigated very young children (1.5–2 years) with an extra session of prehensile hand treatment as combined to NDT and compared it to two groups: NDT twice a week or NDT once a week. After the intervention at six months the intervention group and the group having NDT twice a week improved more in the developmental quotient of the Griffith's Mental Developmental Scales than the group having NDT once a week only. Neither of these two trials reported, however, on how big the difference was between the intervention and comparison groups. Constraint induced therapy was studied in one high-quality and one lower-quality trial amongst hemiplegic children under the age of eight years with interventions lasting three weeks and one week, with a cast or a sling, respectively. The results from both these trials showed concordant improvements on the amount and quality of hand use after the intervention. The effect sizes, as reported in the one-week trial with a sling, were modest.

Moderate evidence of ineffectiveness of strength training on walking speed was established based on four, and on stride length on two lower-quality trials. The children's ages ranged from five to 18 years and the interventions lasted from six weeks to nine months.

There was *conflicting evidence of the effectiveness of strength training* among school-aged children (5–18 years) on gross motor function, as measured by the GMFM. One trial showed improvements of home-based sit-to-stand exercises at six weeks, whereas two trials on home-based strength training exercises found no between-group differences at six, 12 or 18 months.

For the other outcomes measured in the upper extremity treatments, strength training and constraint induced movement therapy trials, the evidence was limited. For the other five intervention categories (comprehensive physiotherapy, cardiovascular fitness and aerobic programs, sensorimotor training, balance training, therapy with animals) there was only one trial per intervention or per measured outcome, so these trials contributed only to limited evidence.

TABLE 4.8 The evidence synthesis of the systematic review on 22 RCTs.

First author (year)	Intervention vs. control (intervention length), age range of participants	Outcome measure	Difference between the groups
Moderate evidence on effectiveness			
Upper extremity treatment (1 high-quality trial with Goal Attainment Scale and range of motion as an outcome, and 1 high-quality trial with GMDS as an outcome)			
Wallen (2007)	OT vs. no treatment (3 mo) 2–11 y	Goal Attainment Scale Range of motion in active supination	6 mo: p=0.054 6 mo: p=0.008
Hallam (1996)	Prehensile hand treatment+NDT vs. NDT (twice a week) vs. NDT (once a week) (6 mo) 1.5–2 y	GMDS developmental quotient	6 mo: p<0.002*
Constraint induced (CI) therapy (1 high-quality and 1 lower-quality trial with amount and quality of hand use as an outcome)			
Charles (2006)	CI therapy with a sling vs. no therapy (1 wk) 4–8 y	Amount of hand use † Quality of hand use †	1 wk: effect size 0.3, p<.01 1, 6 mo: effect size 0.2, p<0.01
Taub (2004)	CI therapy with a cast vs. early intervention program (3 wk) 7 mo–8 y	Amount of hand use ‡ Quality of hand use ‡	3 wk: p<0.0001 3 wk: p<0.0001
Moderate evidence on ineffectiveness			
Strength training (4 lower-quality trials with walking speed, and 2 lower-quality trials with stride length as an outcome)			
Liao (2007)	Home-based loaded sit-to-stand exercise vs. no training (6 wk) 5–12 y	Self-selected walking speed	6 wk: NS
Dodd (2003)	Home-based strength training vs. no training (6 wk) 8–18 y	Self-selected walking speed	6, 18 wk: NS
Patikas (2006a)	Strength training vs. no training (9 mo) 6–16 y	Walking speed Stride length	9 mo: NS 9 mo: NS
Unger (2006)	Circuit training vs. no training (9 wk) 13–18 y	Walking speed Stride length	9 wk: NS 9 wk: NS
Conflicting evidence			
Strength training (3 lower-quality trials with GMFM as an outcome)			
Liao (2007)	Home-based loaded sit-to-stand exercise vs. no training (6 wk) 5–12 y	GMFM	6 wk: effect size 1.17, p=0.02
Patikas (2006b)	Home-based strength training vs. no training (9 mo) 6–16 y	GMFM	12 mo: NS
Dodd (2003)	Home-based strength training vs. no training (6 wk) 8–18 y	GMFM	6, 18 wk: NS

wk=weeks, mo=months, y=years, GMDF=Griffith's Mental Developmental Scales, GMFM=Gross Motor Function Measure, * For the prehensile hand treatment+NDT and extra NDT groups compared to NDT group, † Caregiver Functional Use Survey (14 items, 6-point Likert scale), ‡ Paediatric Motor Activity Log (22 items, scale 0-5).

Some of the findings from the trials confirm the conclusions of the previous reviews. In a review of NDT interventions the only positive conclusion was that NDT immediately improved dynamic range of motion (Butler & Darrah 2001). In the Cochrane review on constraint induced movement therapy and its modifications the conclusions concordantly supported the effects of these interventions (Hoare et al. 2007). In a previous review on strength training (Dodd et al. 2002) however, the conclusions differed from ours. In that review the effects on walking speed were contradictory and on gross motor function positive, analysed on the basis of a few observational studies.

Comprehensive physiotherapy (I, V)

Trials: One of the six trials was of high quality (Bower et al. 1996). Significant between-group differences were observed in four trials, all of them contributing to limited evidence of the studied interventions (Palmer et al. 1988; Palmer et al. 1990; Ketelaar et al. 2001; Tsorlakis et al. 2004; Bar-Haim et al. 2006). Use of an Adeli suit in addition to intensive NDT resulted in better metabolic cost in stair climbing (limited evidence) (Bar-Haim et al. 2006). A functional therapy group reached better GMFM scores in standing, walking, running and jumping, and in Pediatric Evaluation of Disability Inventory for functional skills and caregiver assistance scales, than an NDT group (limited evidence) (Ketelaar et al. 2001). Infant stimulation followed by NDT resulted in better motor and mental developmental quotients and independent walking than NDT alone, which had better outcomes only in one sub-item on emotional and verbal responsiveness of the mother (limited evidence) (Palmer et al. 1988; Palmer et al. 1990). The high-quality trial and one lower-quality trial compared individual and measurable treatment goals to generalized aims and intensive physiotherapy (5 times a week) to routine amounts (2 times a week) for 2 weeks (Bower et al. 1996) and six months (Bower et al. 2001). The intensive goal-directed group improved more than the other groups after two weeks (Bower et al. 1996), but this trend was not maintained in the 6-month trial that found no between-group differences in gross motor function or in the Measure of Processes of Care (limited evidence) (Bower et al. 2001). In a trial with milder affected children an intensive NDT group reached better GMFM-66 scores than a less intensive NDT group, but there was no between-group difference measured with GMFM-88 (limited evidence) (Tsorlakis et al. 2004).

Reviews: Four systematic reviews (Tirosh & Rabino 1989; Parette et al. 1991; Brown & Burns 2001; Butler & Darrah 2001) had evaluated 15 RCTs and 28 observational studies, of which 9 RCTs (Wright & Nicholson 1973; Carlsen 1975; Scherzer et al. 1976; Sommerfeld et al. 1981; Palmer et al. 1988; Palmer et al. 1990; Law et al. 1991; Law et al. 1997; Steinbok et al. 1997) and 19 observational studies were on children with CP. Seven of the 9 RCTs (N=309) and 5/19 observational studies (total number of children, N=493) were included in more than one review.

The only high-quality review (Brown & Burns 2001) concluded on no evidence of the efficacy or inefficacy of NDT. Conclusions in the lower-quality reviews were similar (Tirosh & Rabino 1989; Butler & Darrah 2001), or pointed to some support for the efficacy of therapeutic interventions (Parette et al. 1991).

Strength training (I, V)

Trials: All the four trials were of lower quality (Dodd et al. 2003; 2004; Unger et al. 2006; Patikas et al. 2006a; Patikas et al. 2006b; Liao et al. 2007) evaluating various body functions and activities. The maximum load of the loaded sit-to-stand test, gross motor function, the physiological cost index (Liao et al. 2007), and ankle plantar flexor and knee extensor strength (Dodd et al. 2003) improved more in the training than in the no-training groups (limited evidence). In one trial the strength training group performed better in gait analysis and in an analysis of the sum of ankle, knee and hip angles at mid-stance than the controls, though no differences were found in any of these angles when analysed separately (limited evidence) (Unger et al. 2006). There were no between group differences in knee extensor strength or gait speed (Liao et al. 2007); muscle tone, range of motion in the knee, oxygen consumption, energy expenditure, gross motor function or various gait analysis parameters (Patikas et al. 2006a; Patikas et al. 2006b); and in the strength of ankle plantar flexors, knee and hip extensors separately or combined, gross motor function, self selected walking speed or Timed Stair Test (Dodd et al. 2003) (limited evidence).

To combine these results, no between-group differences were seen in self-selected walking speed (Dodd et al. 2003; Unger et al. 2006; Patikas et al. 2006a; Patikas et al. 2006b; Liao et al. 2007) or in stride length (Unger et al. 2006; Patikas et al. 2006a) measured by gait analysis (moderate evidence). One trial (Liao et al. 2007) found significant differences between the study groups in gross motor function using the GMFM, while two trials (Dodd et al. 2003; Patikas et al. 2006b) did not (conflicting evidence).

Personal factors were considered in two trials (Dodd et al. 2004; Unger et al. 2006). Circuit training improved the children's body image but not functional competence on a self-perception scale, as compared to the non-training control group in an African school setting (limited evidence) (Unger et al. 2006). In a Canadian home-based training program (Dodd et al. 2004) the results on a Self-perception Profile for Children favoured the non-training control group. Their scores improved more in scholastic competence and social acceptance, whereas these scores worsened for the children in the training group (limited evidence). No between-group differences were observed in other sub-items (athletic competence, physical appearance, behavioural conduct) or global self-worth on the same measure (limited evidence).

Reviews: The one high-quality (Dodd et al. 2002) and one lower-quality (Darrah et al. 1997) review included one RCT and 11 observational studies, where the total number of patients was 102. Four studies were included in both reviews, including the RCT (McCubbin & Shasby 1985). The conclusions in both reviews were similar: strength training programs improve muscle strength with no adverse effects on spasticity (Darrah et al. 1997; Dodd et al. 2002).

Upper extremity treatments (V)

Trials: Two (Wallen et al. 2007; Hallam 1996) of the four trials (Law et al. 1991; Hallam 1996; Law et al. 1997; Wallen et al. 2007) were of high quality. Significant differences between groups were found in three trials on some outcomes. Occupational therapy increased active hand supination (moderate evidence) and goals on various activities (leisure, dressing, eating, postural/weight bearing, school/preschool, other self-care, or other) were achieved more than with no treatment (moderate evidence) (Wallen et al. 2007). NDT with prehensile hand treatment twice a week improved the children's developmental status on the Griffiths Mental Developmental Scales as compared to NDT once a week (moderate evidence) (Hallam 1996). NDT with cast increased the quality of hand movement as measured by Quality of Upper Extremities Skills Tests and wrist extension compared to NDT with no cast (limited evidence) (Law et al. 1991).

All four trials observed no between-group differences in other measured outcomes. The high-quality trials found no between-group differences in spasticity measured by Tardieu Scale, passive elbow range of motion, the Child Health Questionnaire, the Canadian Occupational Performance Measure, the Melbourne Assessment of Unilateral Upper Limb Function, the Pediatric Evaluation of Disability Inventory, the Peabody Fine Motor Scales, and the Quality of Upper Extremities Skills Test (Wallen et al. 2007) or in chronological and mental age subquotients of the Griffith Mental Development Scale (Hallam 1996) (limited evidence). The two lower-quality trials observed no differences between NDT with cast compared to regular OT on Peabody Developmental Fine Motor Scales (limited evidence) (Law et al. 1991; Law et al. 1997).

Cardiovascular fitness and aerobic programs (V)

Trials: Two lower-quality trials (van den Berg-Emons et al. 1998; Chad et al. 1999) measured only outcomes on body functions or structures. An eight-month weight-bearing physical activity program had a positive effect on bone mineral density (limited evidence) (Chad et al. 1999). Nine-months of physical training four times per week on top of the normal school sport activities and therapy program had a positive effect on peak aerobic power and improved weight control as compared to a control group (limited evidence) (van den Berg-Emons et al. 1998). No effects on physical activity or anaerobic power were observed during the nine-month period (limited evidence).

Sensorimotor training programs (V)

Trials: One lower-quality trial measured only body functions (Bumin & Kayihan 2001). The between-group differences were not analysed, but group treatment had positive short-time within-group effects on sensory integration and physical ability compared to individual therapy (limited evidence).

Balance training (V)

Trials: One lower-quality trial (Ledebt et al. 2005) analysed dynamic and quiet stance on a force plate and step length of the spastic and non-spastic legs. After six to seven weeks of balance training the children had positive results in displacement in forward and backward direction in quiet stance, in leaning to all directions in dynamic stance, and in the non-paretic leg step length (limited evidence).

Constraint induced movement therapy (I, V)

Trials: One high-quality (Taub et al. 2004) and one lower-quality (Charles et al. 2006) trial measured both body functions and structures, and activity and participation outcomes. Constraint induced movement therapy with a cast showed positive effects in the frequency and quality of functional hand use and new emerging behaviour as compared to the no-therapy group, but no effects were found on the Quality of Upper Extremities Skills Test (Taub et al. 2004). Constraint induced movement therapy with a sling had positive effects on functional hand use, time to complete tasks, and speed and dexterity, but no effects on sensibility, handgrip force, or elbow and wrist muscle tone (Charles et al. 2006). Thus there is moderate evidence for the effectiveness of constraint induced movement therapy on functional hand use.

Reviews: The high-quality Cochrane review (Hoare et al. 2007) analysing 2 RCTs (DeLuca 2002; Taub et al. 2004; Sung et al. 2005) and one controlled clinical study (CCT) (N=94) found similar effects. They found a significant treatment effect [on bimanual performance] using modified constraint induced movement therapy in a single trial, and a positive trend favouring constraint-induced movement therapy and forced use.

Postural control (I)

Reviews: From one high-quality review (Harris & Roxborough 2005) on interventions aiming to improve postural control, we included four observational studies on NDT, rocker platform, and massed practice (total number of children, N=22). This review concluded suggestive evidence for the effectiveness of interventions comprising externally generated movement on the development of postural control, promising evidence for postural perturbations improving reactive balance when a high number of repetitions is provided, and moderately strong evidence for the lack of group-level effects of one week NDT or practice.

Soft tissue treatment (I)

Review: One lower-quality review (Pin et al. 2006) evaluated 3 RCTs (Tremblay et al. 1990; Richards et al. 1991; O'Dwyer et al. 1994) and 2 observational studies on passive stretching in children with CP (N=89). The conclusion was that the effectiveness of passive stretching remains weak, although some evidence indicates that sustained stretching is preferable to manual stretching in improving range of motion and reducing spasticity.

Hydrotherapy (I)

Review: From one lower-quality review on aquatic interventions (Getz et al. 2006) we included 1 RCT (Dorval et al. 1996) and 4 observational studies on children with CP (N=68). The conclusion was that hydrotherapy might improve respiratory function in children with cerebral palsy.

Hippotherapy (I, V)

Trials: Two lower-quality trials (MacKinnon et al. 1995; Benda et al. 2003) on saddle riding on a horse found no between-group differences in muscle symmetry (Benda et al. 2003) or in any of the seven different outcome measures, except on a sub-item of grasping (MacKinnon et al. 1995) (limited evidence).

Reviews: One high-quality (Snider et al. 2007) and one lower-quality (Sterba 2007) review compared therapist-directed hippotherapy to recreational horseback riding therapy (HBRT). These reviews included 3 RCTs (MacKinnon et al. 1995; Benda et al. 2003; Cherng et al. 2004) and 7 observational studies (N=100). Of these 2 RCTs (MacKinnon et al. 1995; Cherng et al. 2004) and 6 observational studies were included in both reviews. Snider et al.'s (Snider et al. 2007) results indicate that hippotherapy has short-term positive effects on muscle symmetry in the trunk and hip and that therapeutic horseback riding is no more effective than other therapies for improving muscle tone. Evidence from observational studies showed positive effects of both hippotherapy and therapeutic horseback riding on activities. The lower-quality review (Sterba 2007) stated that clinicians and therapists can recommend hippotherapy as an efficacious, medically-indicated therapy for gross motor rehabilitation of children with CP.

Conductive education (I)

Reviews: The effectiveness of conductive education has been evaluated in four reviews (French & Nommensen 1992; Ludwig et al. 2000; Pedersen 2000; Darrah et al. 2003). One RCT (Reddihough et al. 1998) and 21 observational studies (N=1264) were included in the four reviews, seven of the observational studies being included in more than one review. The overall conclusions of these reviews were concordant: the number of studies was too small and the quality too low to draw conclusions about the effectiveness or ineffectiveness of CE.

Various interventions (I)

Reviews: One high-quality (Stultjens et al. 2004) and four lower-quality reviews (Horn 1991; Hur 1995; Woolfson 1999; Boyd et al. 2001) included many different types of interventions from 13 RCTs (Wright & Nicholson 1973; Carlsen 1975; Scherzer et al. 1976; Sellick & Over 1980; Sommerfeld et al. 1981; Talbot & Junkala 1981; McCubbin & Shasby 1985; Palmer et al. 1988; Hanzlik 1989; Palmer et al. 1990; Law et al. 1991; Law et al. 1997; Reddihough et al. 1998; McConachie et al. 2000) and 47 observational studies. Reviewers' conclusions unanimously pinpointed the paucity of evidence. According to Stultjens et al. (Stultjens et al. 2004) there was insufficient evidence for the efficacy of occupational therapy in all intervention categories. Focusing on basic motor skill interventions, Horn et al. (Horn et al. 1991) found "no evidence of the effectiveness or ineffectiveness of NDT, sensory integration or naturalistic programming". No conclusions could be made in the reviews on treatment approaches for upper limb dysfunction (Boyd et al. 2001), on training and behaviour modification techniques in conjunction with physiotherapy (Hur 1995), and on multi-domain developmental and conductive education programs (Woolfson 1999) due to paucity of evidence and methodological limitations.

Lower Limb Casting (II)

Reviews: Based on three lower-quality reviews (Vermeer & Bakx 1990; Hur 1995; Teplicky et al. 2002) 3 RCTs (Bertoti 1986; Corry et al. 1998; Fleet et al. 1999) and 4 observational studies had evaluated the effects of lower limb casting (e.g. short leg-cast, tone-reducing cast). All studies consistently showed an increase in the range of ankle dorsiflexion after lower limb casting. It remains unclear whether the effect is of clinical significance (i.e., no operation needed) and whether it solely affects the passive range of motion or also the active range of motion either negatively (decreased strength in ankle dorsiflexors after a period of immobilization) or positively (decreased resistance in ankle plantar flexors).

Lower Limb Orthoses (II)

Reviews: Four lower-quality reviews (Vermeer & Bakx 1990; Hur 1995; Morris 2002; Teplicky et al. 2002) included twelve observational studies that evaluated nine different types of orthoses (rigid or hinged ankle-foot orthosis (AFO), posterior leaf spring AFO, spiral graphite AFO, hinged AFO with tone-reducing footplate and calf cut-out, rigid AFO with tone-reducing footplate, dynamic AFO, dynamic AFO with plantarflexion stop, supramalleolar orthosis) (Ounpuu et al. 1996; Carlson et al. 1997; Hainsworth et al. 1997; Radtka et al. 1997; Wilson et al. 1997; Abel et al. 1998; Brunner et al. 1998; Burtner et al. 1999; Hall 1999; Retlefsen et al. 1999; Crenshaw et al. 2000; Matthews 2000). The orthoses were compared against barefoot walking in 6 studies (Ounpuu et al. 1996; Radtka et al. 1997; Wil-

son et al. 1997; Abel et al. 1998; Brunner et al. 1998; Crenshaw et al. 2000) or with shoes only in 2 studies (Carlson et al. 1997; Retlefsen et al. 1999).

According to these studies evidence to support the hypothesis that orthoses can prevent deformities or improve function is weak. Orthoses that restrict plantar flexion were more often reported to prevent equinus during walking than orthoses with supramalleolar designs. Restrictive orthosis may hamper functional activities in children with less severe motor involvement. It is unclear whether reported biomechanical changes (gait kinematics and kinetics, energy consumption) are associated with functional benefits or of clinical significance compared to, for example, good supportive shoes with or without individual foot soles.

The possible negative effects of orthoses with restrictive components on other areas of gross motor functions should also be considered. The role of good, supportive shoes with or without an individual foot sole therefore remains unclear and ought to be studied. Tone-relieving AFOs (with thin, well-fitting footplates enclosing the foot fully and tightly) did not seem to improve any functional outcome measurements.

Upper Limb Casting (II)

Reviews: Two reviews (Boyd et al. 2001; Teplicky et al. 2002) included 2 RCTs (Law et al. 1991; Law et al. 1997) and one observational study (Copley et al. 1996) on upper limb casting as an adjunct to therapy. The length of casting varied from 4 weeks to 6 months, but it remained unclear for how long the casts were worn per day. Upper limb casting combined with physiotherapeutic or occupational therapeutic intervention may have a short-term effect on quality and range of motion in some children with a hemiplegic or tetraplegic type of CP, but it is unclear whether the effect is clinically important.

Upper Limb Orthoses (II)

Reviews: One review (Teplicky et al. 2002) included three observational studies that had analysed different types of upper limb orthosis: orthokinetic cuff, short opponens thumb splint, MacKinnon splint, or non-specified hand splint (Exner & Bonder 1983; Flegle & Leibowitz 1988; Reid 1992). This research suggests that the choice of a splint or orthosis for the upper limb needs to be task specific, but the effects on children's general ability to use their hands for function or play has not been studied.

5 Discussion

This thesis intended to enhance and facilitate the appropriate use of proper and valid methods of clinical trials and systematic reviews to fully address the information needs of professionals and patients in the field of CP rehabilitation. It appraised critically systematic reviews and randomized controlled trials on physiotherapy, physiotherapy-related motor-based interventions and orthotic devices in children and adolescents with CP. The methodological quality and clinical usefulness of 24 systematic review articles was evaluated. Methodological problems in trial performance and reporting quality were analysed from a sample of 14 RCTs. The effectiveness of interventions was evaluated based on the 22 RCTs published since 1990, complemented with conclusions of the high-quality reviews. The best available evidence evaluated in this thesis provides insights into the current scientific basis for clinical decision-making and the future research agenda in this field.

5.1 Main findings

We identified 21 systematic reviews on physiotherapy and physiotherapy-related motor-based interventions (I) and 5 reviews on orthotic devices (II) on children and adolescents with CP. The reviews were based altogether on 23 RCTs and 104 observational studies, and on 5 RCTs and 27 observational designs, respectively. Many reviews also included studies on non-CP children. The reviewed populations were heterogeneous, interventions often vaguely defined, and outcome measures incomparable across studies. No review had excluded studies based on quality. Twelve reviews had defined quality assessment criteria, and all but one used these. The qualitative synthesis were based on categories of different aspects across the reviews, for example, by outcomes, interventions, study designs, study quality or populations, which were each summarized descriptively or by levels of evidence analyses. Most of these methods hid important factors, such as the number of patients included and the real effect sizes and confidence intervals. Six reviews were of high quality (Brown & Burns 2001; Dodd et al. 2002; Steultjens et al. 2004; Harris & Roxborough 2005; Hoare et al. 2007; Snider et al. 2007). In most of the reviews, the methodological deficiencies and clinical heterogeneity together with insufficient reporting complicates the determining of which patient groups may benefit from the studied interventions. According to the studies included in the five reviews on orthotic devices, lower limb casting may have a short-term effect

on passive range of motion. For other outcomes there is a paucity of evidence on the effect of using upper and lower limb orthoses in children with CP.

The evaluation of the performance (III) and reporting quality by a CONSORT-based checklist (IV) of 14 trials suggests that a high-quality RCT on the effectiveness of a complex intervention in this heterogenic population is possible. Examples of particularly successful solutions on difficult methodological problems on sampling and recruitment of population, defining complex interventions and the choice of endpoints were found. Half of the sample trials succeeded in adequate reporting at least sixteen particular items and almost all the CONSORT items were reported in at least one trial. Nevertheless, several crucial issues relating to the trial methods were reported poorly or not reported at all, such as outcome measures, sample size determination, details of the sequence generation, allocation concealment, and implementation of the randomisation, success of assessor blinding, recruitment and follow-up dates, and intention-to-treat analysis, precision of the effect size, co-interventions, and adverse effects.

The review of physiotherapy and physiotherapy-related RCTs published since 1990 (V) identified 22 trials, of which four trials were of high quality (Bower et al. 1996; Hallam 1996; Taub et al. 2004; Wallen et al. 2007). Using a levels of evidence synthesis (van Tulder et al. 2003) we established moderate evidence for the effectiveness of two intervention categories: upper extremity treatments and constraint induced movement therapy. Occupational therapy resulted in better active supination and individualized goals achieved for various activities compared to no treatment (Wallen et al. 2007), and prehensile hand treatment with NDT or NDT alone both provided twice a week improved the children's developmental status as compared to NDT once a week (Hallam 1996). Constraint-induced movement therapy resulted in better functional use of the spastic upper extremity compared to conventional therapy (Taub et al. 2004; Charles et al. 2006). In these four trials the studied children were young (ages between 1.5 to 11 years) and the interventions lasted from three to six months for the upper extremity treatments and one to three weeks in constraint-induced therapy. Such short-term intensive interventions can thus be helpful for these subgroups of CP children, but their long-term relevance with respect to the children's whole life span remains to be studied.

We also found moderate evidence that strength training had no effects on self-selected walking speed based on four trials (Dodd et al. 2003; Unger et al. 2006; Patikas et al. 2006a; Liao et al. 2007) or on stride length based on two trials (Unger et al. 2006; Patikas et al. 2006a) compared to no training. Conflicting evidence was found on the effectiveness of strength training on gross motor function as measured by GMFM compared to no training based on three trials (Dodd et al. 2003; Patikas et al. 2006b; Liao et al. 2007). These findings apply to school-aged children for home-based exercises and only for these few outcomes that were similar in the strength training trials. For any of the other outcomes and any other interven-

tion categories the evidence remains limited. Thus many interventions and their outcomes on many different aspects of functioning need to be studied in further good-quality research. This available evidence may be complemented by findings from the high-quality reviews, which based on earlier literature found some supportive evidence for some outcomes of strength training, constraint-induced movement therapy and hippotherapy, and insufficient evidence on comprehensive physiotherapy or occupational therapy.

5.2 Methodological considerations

Overviews of systematic reviews

Analyses using validated criteria complemented with analyses of heterogeneity may become increasingly necessary as reviews are now produced in high volumes in many fields (Moher et al. 2007). Earlier overviews of systematic reviews in other fields have pointed out there is lot of scope for improvement in methods and reporting (Mulrow 1987; McAlister et al. 1999; Jadad et al. 2000; Bandhari et al. 2001; Glenny et al. 2003; Delaney et al. 2005; Moja et al. 2005). A recent similar overview of reviews on acute asthma in children found that despite the quality of the reviews being good, their clinical usefulness was threatened by insufficient handling of heterogeneity (Boluyt et al. 2007). In our overview only six reviews were of high quality, but their clinical applicability was similarly hampered by a lack of clear definitions for the included populations and clinically important health outcomes, and also by insufficient descriptions of the intervention components. These reviews may thus provide only limited help for clinical decision-makers searching for evidence of specific interventions for their patients.

Nevertheless, systematic reviews are usually based on critically appraised high-quality effectiveness research; all reviews in this study (I, II) included a wide range of observational studies with mixed terminology for the various designs. The RCTs were not always recognized among the included studies (Parette et al. 1991; Brown & Burns 2001; Sterba 2007). Previous research on the role of non-randomized studies and case series in reviews in other fields has been hampered by both paucity and the poor quality of these studies (MacLehose et al. 2000; Dalziel et al. 2005). Also in this field there is scope for more research on the methods required to minimise bias in observational studies. If observational studies are to be included in a review, the authors should clearly define how to deal with the possible biases. Recent guides may enhance the quality of the study reports of observational designs (Vandenbroucke et al. 2007). More research is needed to determine how the methodological features of observational studies affect outcomes in this field (Sanderson et al. 2007).

Twelve reviews assessed the quality of studies with variable criteria, reflecting the lack of consensus as to which components and what tools would best assess trial quality (Sutton et al. 1998; Jüni et al. 1999; Moher et al. 1999b). Most of the used quality criteria only suit RCTs, not observational studies. Three reviews applied a tool (Butler 1998-1999) that raised single-case studies to the level of RCTs in the evidence hierarchy, but later the American Academy for Cerebral Palsy and Developmental Medicine (AACPDMD) methodology was updated (O'Donnell et al. 2004) to meet the criteria of evidence-based evaluation (Phillips et al. 2001).

The reviews on the same topics also included somewhat different studies, but no review had excluded studies on the basis of quality. The discrepancies between the reviews may be explained by differences in the search periods, the search terms and databases, and the inclusion criteria. The qualitative synthesis methods, built on different combinations of different aspects across the reviews, hid important factors, such as the number of patients included and the real effect-sizes. Only three reviews provided effect sizes together with the confidence intervals. Reporting the results with p-values says nothing about the magnitude of the possible change or its clinical implications to similar patient groups. A common understanding of how to summarise findings on individual studies in a qualitative synthesis is obviously needed, as found previously in analyses of Cochrane reviews of physio- and occupational therapy (van den Ende et al. 2006). Further, a systematic review in this field can be further improved by focusing on more narrowly defined interventions, as is the case in the recent reviews (Darrah et al. 1997; Dodd et al. 2002; Harris & Roxborough 2005; Getz et al. 2006; Pin et al. 2006; Hoare et al. 2007; Snider et al. 2007; Sterba 2007)

Empirical evaluation of feasibility and methodological aspects of an RCT in this field

Previous methodological reviews have evaluated the scientific quality of motor intervention studies in children with CP, one covering the period from 1980 to 1989 (Vermeer & Bakx 1990) and the other from 1990 to 2001 (Siebes et al. 2002). Fundamental research with adequate methodology was more often applied in the latter time period, but these developments did not substantially improve the scientific foundations for the studied interventions. Single-case studies combined with efforts to develop high sensitivity measures were recommended (Siebes et al. 2002). A few other papers have discussed the value and special problems in conducting RCTs in the fields of physiotherapy (Koes & Hoving 1998) and occupational therapy (Nelson & Mathiowetz 2004). The physiotherapy paper identified methodological challenges in creating prognostic homogeneous study groups, standardization of interventions, blinding of patients, therapist and outcome measurement, small sample sizes, drop-outs or losses to follow-up (Koes & Hoving 1998). In terms of the importance of theory, background, and rationale, the occupational

therapy paper identified intervention fidelity; theory-based outcomes; management of non-blinded intervention and participants; and the multiplicity of statistical analyses (Nelson & Mathiowetz 2004). Considering this body of literature on methodological issues, our study may add knowledge about the specific challenges in conducting trials in the field of CP rehabilitation, and what solutions there may be to solve some of the problems.

Heterogeneity of population

In the analysed reviews and trials, children with diagnosed CP of all ages between 7 months and 18 years were represented, as well as all CP types and severities. In Europe SCPE recommends to register only cases of five-year-olds or older as CP, to fully exclude progressive diseases or diseases that mimic CP in younger children. In the analysed trials we trusted the authors diagnoses and noted no “amazing improvement or disappearance” of CP signs. We are thus assuming that the patients included in these trials had permanent signs indicative of damage to the central nervous system and were clinically diagnosable as CP.

The available moderate evidence of the upper extremity treatments apply to young or school-aged (5–12 years) or to very small (1.5–2 years) children, whereas the strength training was mostly studied amongst school-aged children aged from 5 up to 18 years. Evidence on any other age group remained limited.

Not all studies described the patient characteristics equally clearly. In particular many reviews included non-CP children, which can bias conclusions when results are not analysed separately. Most trials used matching or stratification to ensure a more equal distribution of risk, but not all provided informative baseline characteristics to show the degree of group similarity at baseline. This leaves the possibility for patient variables like age, gender, cognitive, and functional level to explain the change during an intervention program. Consequently, if the patient characteristics are not described, it is impossible to determine which patient groups may benefit from the studied interventions.

Complexity and variability of interventions

Physiotherapy interventions may need a thorough conceptualization of the intervention prior the definitive RCT (Medical Research Council 2000). Findings of other research or preliminary qualitative or modelling studies could be used to provide considerations of the components and quality of the intervention. When other research strongly suggests an intervention should be administered in a particular way, that research can be used to guide the delivery of the intervention (Herbert & Bø 2005). One example is a recently published clinical practice improvement study in adult stroke patients that tried to open the black box of physiotherapy through careful analysis of the various components of interventions used during therapy sessions and beyond (DeJong et al. 2004). Another good

example for development of a complex intervention is using the Medical Research Council's phases prior to the main trial (Byrne et al. 2006). Further, the CONSORT statement recommends reporting the precise details of the interventions intended for each group and the mode and timing of their actual administration (Begg et al. 1996). Sufficient detailed reporting may thus advise the readers of possible changes in their own practice.

In systematic reviews a formal assessment of the quality of the intervention is potentially problematic. The analysed reviews (I, II) often summarized and shortened information, providing superficial definitions of the interacting intervention components or types of the orthotic devices. Specific types of orthoses (such as hinged or tone-relieving AFO) may not be generalized to all orthoses similarly named. Further, in many of the within-participant studies in the reviews of orthotic devices (II), the effect of orthoses was most often compared against barefoot walking, while a good shoe might have been a more meaningful comparison for clinical decision-making. Thus conclusions on the effectiveness of the interventions based on the name labels only, as is often the case in review articles, may be seriously hampered. Also the QUOROM statement exhorts reviewers to describe details of the intervention provided in each trial (Moher et al. 1999a).

The analysed trials (V) provided much more detailed intervention descriptions that may assist a busy clinician in the application of the described intervention in their own patients. However, the comparison interventions should also be fully described. Children often continued their usual therapy, named as “traditional physiotherapy” or “conventional physiotherapy”, which content and intensity may vary in different contexts and countries. Proper information on the type of conventional therapy used is needed to assist application in different contexts. Also much of the missing information on co-interventions and many other environmental factors such as parental support, home and leisure time activities, or the qualifications of therapists, would be easy to monitor and collect. This would instantly improve the quality of the studies, and would promote the transfer of the intervention to other settings. This type of additional information has been highly preferred for physiotherapy trials published in leading journals, who can publish more information in their online formats (Foster et al. 2007).

Given the variability of the interventions, their categorisation proved to be a challenge. In the analysed trials there were no two exactly similar interventions (V). Because no readily available categorisation of interventions for children and adolescents with CP are available, we chose a post-hoc approach to include only categories based on published trials, not on current practice or patient needs. Thus relevant and currently used interventions may have been ignored from the analysis and also from our conclusions. Future reviews should consider more comprehensive intervention classification, defined a priori in the review protocol. Encouraging steps towards international physiotherapy intervention categories

using the ICF have been taken already with adults (Finger et al. 2006), and similar approaches are needed for children and adolescents in neurology.

Variety of outcome measures

We identified a large diversity of outcome instruments both in the reviews and trials, which complicated meaningful comparisons across studies. Many of the measures used in older trials may fall short of the standards we now expect of modern research. Thus results from older studies may be less reliable, and not comparable to newer studies, as found also in the field of musculoskeletal and back rehabilitation (Hopayian 2001). Primary research and consensus-type processes are needed to improve the use of outcome measures that are clear in terms of their appropriateness, reliability, validity, responsiveness, precision interpretability, acceptability and feasibility (Fitzpatrick et al. 1998).

The ICF provides a useful framework for selecting outcomes. Most outcomes measured in the included reviews and trials (I–V) were on various aspects of body structures and functions or activities and participation. Very little structured information was collected about environmental factors, for example, the children's and parents' satisfaction, family functioning, coping, motivation, health service supports, and societal attitudes with various treatment options or overall well-being. The increasing agreement on a limited set of instruments as noticed in our sample of 15 trials (III) and further in the reviewed 22 RCTs (V) is encouraging. In future studies, an agreement on standard, validated instruments in the research community for all ICF components and their common use in studies would be crucial for an adequate comparison of results from interventions across studies. A worldwide initiative in rheumatology, a discipline with similar problems, had a major impact on the quality of clinical research (Tugwell et al. 2007), as well in other fields (Cooney et al. 2007). Initiatives on outcome measures in CanChild (CanChild Centre for Childhood Disability Research 2008) and AACPD (Treatment Outcomes Committee 2008) provide important steps into this direction. An increasing amount of standardized evaluative measures are already available and using these will increase the ability to more accurately determine the effectiveness of the interventions.

For many children a beneficial intervention may be the one which maintains their functional ability and prevents further deterioration e.g. deformity. In a case where a gain is observed, we need to know whether it is also clinically important or whether the possible improvement in a specific motor performance happens at the cost of hindering more complex performance. We also need to evaluate when the effects are also meaningful for the children—for example, what was the effect on their overall well-being. In most trials this type of clinical interpretation was widely omitted. In most cases the implication that any observed difference was also of clinical importance seemed unfounded (IV). Only a few instruments (e.g.,

GMFM (Russell et al. 2002)) referred to an empirical assessment of the minimum difference that would be important to children. Further development of this area of research is urgently needed.

Reporting quality

The CONSORT statement has been associated with improvements in the quality of reports of RCTs (Moher et al. 2001). Our findings on the poor quality of reporting the methodological choices in particular are very similar to the previous findings using CONSORT-based evaluations in other fields, confirming the need for enhanced reporting (DerSimonian et al. 1982; Adetugbo & Williams 2000; Sanchez-Thorin et al. 2001; Khan et al. 2002; Moher et al. 2002; Piggot et al. 2004). In previous analyses in the field of physiotherapy, only a few trials have been shown to report adequately methods such as concealment of allocation, blinding and adequate follow-up (Moseley et al. 2002). The poor quality of some of the literature has been noted before in a systematic review of occupational therapy interventions (Steultjens et al. 2004). The CONSORT statement may have been rather unknown in this field, as the journals where the sample trials were published did not even mention the CONSORT statement in their web instructions for authors and reviewers as of September 2005. Further, many of the trials were conducted well before this recommendation was published in 1996, so authors of these trials did not even have the possibility to follow the CONSORT recommendations. Looking at this issue again in September 2008 showed, however, that five of the nine journals where the trials included in the review (V) were published now require the authors to follow the CONSORT statement.

Although CONSORT-based checklists to assess reporting quality have been developed previously (Adetugbo & Williams 2000; Sanchez-Thorin et al. 2001; Khan et al. 2002; Moher et al. 2002; Piggot et al. 2004), we created a checklist that follows the CONSORT items literally. We excluded questions on the discussion section from our checklist, and added two items, asking whether the outcome measures had been validated and if there had been co-interventions. Adding these did not change the overall results. The piloting process successfully improved the wording of three items. Still, some of the original CONSORT items were not applicable in all trial contexts (participant and therapist blinding, success of assessor blinding, interim analyses and stopping rules, and items on ancillary analysis methods).

Reviewed evidence in the context of evolving evidence

Despite the many existing reviews of various physiotherapy and physiotherapy-related interventions in children and adolescents with CP (I), our review (V) intended to address specifically the questions on the effects of the interventions and to provide detailed descriptions of the available research to enhance clinical applicability. Such reviews are relevant especially in the development of clinical

practice guidelines. Recently, some such guidelines for children with CP have been published. An Italian guideline, however, did not consider scientific evidence (Ferrari et al. 2005), and the New York State Department of Health recommendations for motor disorders for young children are based on studies published up to 1998 (Rogers et al. 2006).

Our review was able to capture 16 trials that were not evaluated in the previous reviews. However, as scientific evidence for treatments addressing motor dysfunction is continually and rapidly accumulating, at least three systematic reviews and three RCTs on physiotherapy and two RCTs on orthotic devices have been published since our searches. These studies were found by running the same search strategies again in Medline in May 2008.

A review on all types of exercise programs focusing on cardiovascular fitness and lower extremity muscle strength identified five of the same RCTs (van den Berg-Emons et al. 1998; Dodd et al. 2003; 2004; Unger et al. 2006; Patikas et al. 2006a) in our study (V), complemented with 15 observational studies (Verschuren et al. 2008). With the support of the findings from the observational studies, they concluded that the children may benefit from improved exercise programs that focus on lower-extremity strength or cardiovascular fitness, or their combination, as measured mainly in body functional & structural or activity levels. This differed from our conflicting findings based on RCTs only; including one extra RCT (Liao et al. 2007) that in fact was the only trial that contributed to the benefits at the activity level.

An AACPDPM review on the effects of casting on equinus (Blackmore et al. 2007) found only little evidence of the superiority of casting compared to no casting, with improvements only in stride length based on one small RCT (Bertotti 1986). The third review was a meta-analysis of spatiotemporal measures of a number of interventions to improve gait based on prospective studies with small convenience samples (Paul et al. 2007). Separate analyses with Hedge's G of 26 studies on orthotic prescription of some types of AFOs favoured velocity improvements, but the data was insufficient for clinical recommendations. Similar to our findings on orthotic devices (II), these two reviews show the paucity of good-quality research.

The three new RCTs studied the effects of additional therapy and family support (Weindling et al. 2007), intermittent physiotherapy compared to continuous physiotherapy (Christiansen & Lange 2008), and strength training (Verschuren et al. 2007). Using a well-designed multi-centre design, with a 6-month intervention period and 12 and 18 months follow-ups, no support was found for the effectiveness of additional once-a-week intervention (physiotherapy assistant or family support worker) on the motor or general development of young children with CP (Weindling et al. 2007). In the other trial, the same amount of physiotherapy (30 weeks) was administered either intermittently (4 times a week for 4 weeks with

6-week treatment pauses) or continuously (1–2 per week), with these regimens showing identical outcome with GMFM-66 (Christiansen & Lange 2008). These studies will add to the evidence base on the effects of various intensities, suggesting that more therapy is not necessarily better or that therapy sessions may be scheduled in various ways.

The third trial was also well-designed, utilizing a pragmatic 8-month intervention, recruiting 65 children and adolescents aged 7–18 years from 4 schools either to a control group or to circuit training focusing on aerobic and anaerobic exercises twice a week for 45 minutes per session (Verschuren et al. 2007). Outcomes were measured for all ICF levels and health-related quality of life and improvements were found in the training group in physical fitness, intensity of activities, participation, and quality of life.

The high-quality of these three trials further strengthens the case that a trial in this field can be well conducted. Weindling et al., however, experienced problems in recruitment and group similarity and acknowledged the impossibility of standardising the type of intervention they evaluated (an individualized NDT treatment and the family setting, with a variety of existing services available) (Weindling et al. 2007). Nevertheless, new research in this area is already ongoing, as shown in recently published protocols for RCTs on endurance and limb strengthening exercises (Fowler et al. 2007), and context-focused versus child-focused therapy approaches (Law et al. 2007).

The two recent RCTs on orthotic devices evaluated short-term effects of a dynamic AFO (Bjornson et al. 2006) and dynamic AFO compared to AFO (Lam et al. 2005). Both studies were cross-over designs evaluating the same participants in random order twice over the course of a single day. Bjornson et al. (Bjornson et al. 2006) assessed 23 ambulatory children aged 1.9–7.3 years. Their GMFM percentage scores were higher with dynamic AFOs than without them, thus showing immediate improvements. In the other study (Lam et al. 2005) thirteen 3.3–9.7 year-old children with spastic diplegic CP had eighteen age-matched controls. Biomechanical and electromyographic evaluations were taken from the participants in barefoot, wearing AFOs, or wearing dynamic AFOs. Both AFOs and dynamic AFOs increased stride length, provided better foot pre-positioning for initial contact and control of equinus during gait, and limited plantarflexion at push off. The dynamic AFOs restricted ankle joint movements less than AFOs, but the AFOs reduced the median frequency of the electromyographic signal more, suggesting better walking endurance (Lam et al. 2005). These studies add to the understanding of the very short-term effects of the AFOs, but the long-term effects remain to be evaluated in further studies.

5.3 Strengths and limitations of the present study

The most important factors relating to the validity of systematic reviews are the inclusion of all relevant studies, and an assessment of the methodological quality of component studies. A legitimate weakness relates to the retrospective nature of this type of analysis and reliance on what the authors of the original reviews and trials have reported. Nevertheless, the results reported here reflect the situation typical to a busy clinician who has to rely on the published information, and which is available in the databases most typically accessed.

This study focused solely on the quality and applicability of the available scientific literature. Other aspects often important to clinical and health policy decisions were not addressed, for example, the costs or cost-effectiveness of the various treatment alternatives, and the organisational, social, legal and ethical consequences of various choices (Mäkelä et al. 2007). Complementary analyses of some of these aspects evaluated in Finnish circumstances can be found elsewhere (Koivikko & Sipari 2006).

Inclusion and exclusion criteria

This study focused on the evidence-based perspective, and thus study designs other than systematic reviews and randomized controlled trials were excluded. The searches for the systematic reviews (I, II) were designed to identify every existing review, and were thus considered to cover the literature from as far back as possible. In the review of RCTs (V) and the two samples (III, IV) we then restricted the studies to be published in 1990 or later. This decision was made on the basis of earlier systematic evaluations, which have found that weaknesses in the methodological quality of cerebral palsy research (Vermeer & Bakx 1990) had improved in the 1990s (Siebes et al. 2002). The aim was also to include only those physiotherapy interventions that are currently in use and to avoid overlaps with the existing reviews.

Many reviews on physiotherapy and conductive education interventions included non-CP children (Tirosh & Rabino 1989; Horn 1991; Parette et al. 1991; French & Nommensen 1992; Hur 1995; Pedersen 2000; Brown & Burns 2001; Getz et al. 2006; Pin et al. 2006; Sterba 2007). We excluded all trials with non-CP participants from our analyses, because of the possibility of bias in the conclusions if the results were not analysed separately. Thus our analysis of the results may differ from the reviewer's own conclusions.

There remains some debate as to what interventions to include or exclude in the category of physiotherapy interventions. It is not always clear as to which interventions are strictly physiotherapy and which should be considered to belong to other professions, as in different countries various motor-based interventions are delivered by different professionals e.g. physical therapist, occupational therapists

or special teachers. These borderline interventions include the upper extremity interventions, sensory integration, and conductive education. Some other interventions, such as swimming programs or hippotherapy may be considered merely as recreational, but nevertheless they are motor-based, aiming to improve the functional and overall well-being of the child, and are frequently provided by physical therapists, too. Considering these ambiguities we chose to apply broad inclusion criteria for interventions, as also suggested in the field of stroke rehabilitation (Greener & Langhorne 2002). However, we excluded all assistive devices or other therapeutic modalities that are provided with a device (e.g. electrical stimulation) which are frequently part of physiotherapeutic management in everyday practice. Thus the analyses and results in this review comprise various handling, exercise and managing techniques of motor-based physiotherapy or physiotherapy-related interventions rather than all aspects of physiotherapy.

Searches

Inclusion of relevant studies in systematic reviews is crucial to avoid bias and to maximise precision. We searched only databases that most likely would include the relevant papers, complemented with screening the reference lists of included studies and reviews for additional papers. We may thus have missed articles if attainable only through Embase or other specialized databases. No language restrictions were applied in the searches, but because of our limited language skills, we were not able to judge whether one systematic review (I) and three studies (V) would have fulfilled our inclusion criteria. No attempt was made to identify unpublished studies or to contact authors or researchers in the field to identify more studies. Thus there is scope for publication bias, as we may have omitted relevant studies in other languages and unpublished studies. In previous analyses the results of unpublished studies have found to be inconclusive or negative (Egger et al. 2003), similar to the results of most published studies identified in our review.

The analyses of reporting quality (III) and methodological issues on population, interventions and outcomes (IV) were based on a sample of 15 publications (III, IV) that was identified from searches of the overview article (I), complemented by a separate unpublished review search that compared different intensities of the same intervention. Although not comprehensive, we believe that this sample of trials up until 2002 represents the variability in reporting and the key challenges in physiotherapy or occupational therapy trials among children with cerebral palsy.

Selection and data extraction

Decisions regarding the inclusion or exclusion of individual studies always involve some degree of subjectivity. We did not apply any blinding of the reviewers to the names of the authors and institutions, sources of funding or acknowledgements. All but one (IAR) author had no previous experience in the field of CP rehabilita-

tion, ensuring different perspectives (Greener & Langhorne 2002). Thus blinding the author information was considered time consuming with unjustifiable additional costs (Berlin & Cirigliano 1997).

We had two reviewers independently to extract the data (II–V), or one reviewer to check all data extracted by another reviewer (I), and pre-developed standard forms to avoid errors in data collection. This process, requiring multiple cross-checking from both reviewers, is time consuming. Future reviews may gain from the development and testing of electronic data collection forms that allow automatic detection of inconsistencies between data recorded by different observers. We did not ask for further details from authors, except for one study that did not provide between-group comparisons in the results section (Bumin & Kayihan 2001).

Quality assessment

The assessment of methodological quality of clinical trials and reviews is widely recommended, although the methodology for the assessment is a matter of continuous debate. We chose to apply criteria that evaluate the four categories of internal validity, with defined decision rules in clinical trials (van Tulder et al. 2003) and systematic reviews (Hoving et al. 2001). To avoid errors, the quality assessment of all reviews and trials was performed by two reviewers. As the use of summary scores has proven to be problematic (Jüni et al. 2001), we preferred to display the individual components of methodological quality to allow full interpretation of the methodological rigour of the trials and reviews.

A few limitations should be taken into account when interpreting the statements of effectiveness of the interventions. Although all the evaluated items are important indicators of trial quality, we chose four distinct criteria (adequate randomisation, allocation concealment, prognostic similarity, and acceptable compliance) to constitute high quality (V). With this choice, emphasis was given to an avoidance of selection and attrition bias, while possible performance and detection biases were not regarded as equally important. For systematic reviews (I), fulfilment of all criteria, except blinding of reviewers, was expected to constitute high quality. No review fully avoided selection bias, defined as use of two reviewers and blinding information of authors and results from the reviewers. In the earlier overview of reviews on orthotic devices (II) the quality of the included reviews was also displayed item-by-item, but not actually utilized in the synthesis. The synthesis was solely based on the results of the observational studies included in the reviews, thus relying on the information provided by the reviewers. The quality of the primary studies could not be assessed, nor did we take into account the quality of the review articles. This review may thus be of more limited value.

Synthesis methods

In the overview of physiotherapy & conductive education reviews (I) the synthesis on effectiveness was based on the review quality and the reviewers' conclusions. In the reviews of trials we based the evidence synthesis on trial quality and statistical differences in the between-group comparisons in each intervention category (V). In most studies, however, the differences were reported only using p-values, which do not allow any interpretations of the size and direction of the effects. In order to draw clinical conclusions one must rely on the reported baseline and change values for the groups (Article V, Additional file 9).

Small sample sizes in many trials also meant a possibility for type II error i.e. that real group differences could not be detected. A further limitation is that intervention lengths and the timing of measurements varied across the trials. Thus caution is necessary when interpreting the results. New trials may change the strength and direction of the evidence.

5.4 Clinical and health policy implications

The evidence-based perspective suggests that selection and use of rehabilitation interventions should be based on research evidence. Many reviews and trials of good and reasonably good quality are available. The improvements in methodological quality in the recent reviews and trials are encouraging. Findings from this study could be utilized when developing clinical practice guidelines in Finland or other countries. However, evidence alone is never sufficient to clinical decision-making. Clinicians and decision-makers need to weigh up the benefits against possible risks, and the costs associated with the therapy together with the values of the children or adolescents and their family.

The four high-quality reviews posing targeted questions may be clinically easier to apply, as they included a limited number and type of interventions and outcomes. For example, in the strength training review the interventions, outcome measures and patient inclusion criteria were fairly unambiguous (Dodd et al. 2002). The positive evidence on effectiveness was based on only one RCT (McCubbin & Shasby 1985) supported by several concordant observational studies, in line with the evidence grading system by the GRADE Working Group (Oxman & for the GRADE Working Group 2004). The GRADE suggests upgrading for cohort studies, when two or more observational studies show a consistent association, with no plausible confounders.

The evidence from the low-quality reviews should be interpreted more cautiously due to the methodological limitations. In many reviews the authors' concordantly stated that they can reach no conclusion on the effectiveness or ineffec-

tiveness of the reviewed interventions. Some reviews, however, drew conclusions on the indicative evidence of passive and sustained stretching on range of motion and spasticity (Pin et al. 2006), hydrotherapy on respiratory function (Getz et al. 2006), and hippotherapy and horseback riding therapy for gross motor performance (Sterba 2007). Moreover, our searches for the two overviews (I, II) revealed a large number of items in the literature consisting of narrative and historical reviews presenting a more or less personal experiences or views of the authors. Clinical inferences from these types of studies may be much weaker, because of the high probability of selection bias.

To be applicable, the clinicians need to know what types of participants were studied, how the interventions were administered, and what functional benefits can be expected. This type of information was very limited in many of the existing systematic reviews. In our review (V), we tried to fill this gap by detailed PICO descriptions of the included trials (see additional files 6 and 7). We believe that proper knowledge of the trial characteristics increase external validity and thus their clinical applicability. However, the effect sizes and the confidence intervals of the observed results were mostly not provided, which makes the clinical interpretation of the size and importance of the results difficult.

Because evidence of the effectiveness of many of the reviewed interventions is currently limited, the clinical implications on what interventions to use or not to use in children with CP remain mostly inconclusive and limited. The lack of evidence does not mean that the interventions are ineffective, but calls for further research on this area. New evidence is rapidly accumulating, and there is a need to consider when this type of summary should be updated and whose responsibility it would be. For a further enhancement of decision-making, complementary analyses of the costs or cost-effectiveness of the various treatment alternatives, and their organisational, social, legal and ethical implications may be warranted (Mäkelä et al. 2007).

5.5 Scientific implications

How could reporting be enhanced?

The low methodological quality was too often a consequent of insufficient details in the trial reports (V), as described in the analysis of reporting quality (IV). In many clinical instances, however, the only way to assess the quality of a report is by relying on the information contained in the report. Reports of reviews and trials would benefit greatly if the authors adhered to the internationally widely agreed reporting standards, the QUOROM and the CONSORT statements, respectively. A common journal policy that requires the authors and reviewers to use these checklists in writing and evaluating the reports would be required to improve re-

porting. Moreover, as the methodology should be taken into consideration already during planning and execution of the trial, institutional review boards should require researchers to complete methodological checklists already as part of the trial proposal.

Is an RCT feasible, under what circumstances?

The substantial number of excellent trials confirms that RCTs on complex interventions are feasible, even in diseases with multifaceted disorders such as CP. Analysis of the trials revealed important prerequisites, such as a general understanding of the need for trials by parents, patients, and health care professionals, more research expertise in the various fields of therapy, and standardized assessments of commonly agreed outcome measures.

In Finnish circumstances a legitimate concern is the difficulty in recruiting enough children in a single study, thus running the risk of an underpowered study. There is a possibility to perform multicenter studies, these requiring careful modelling and standardisation of the intervention delivery. In the case of small studies, the technique of meta-analysis allows for collating small studies, provided the interventions and outcome assessments are sufficiently similar across studies (Pogue & Yusuf 1998). This strengthens the case for more standardization.

More comprehensive treatment approaches that include everything in an undefined fashion may be difficult to evaluate in RCT designs. The treatment goals may vary notably between the participants, and thus active components of the intervention may be different. A randomized design may more easily be used to evaluate more narrowly defined interventions, such as strength, aerobic, or balance training, or riding. Even these interventions should be carefully determined by modelling studies. The confounders, for example, hobbies or other activities that may happen at day care, school, or home, should be carefully monitored and reported.

What should be done to enhance the quality and applicability of the trials?

A fundamental issue for future studies is to enhance the quality of the trials in this field. Researchers should have a clear plan of how to address the methodological validity issues to avoid systematic bias. Future trials would gain from an agreement of a CP definition and more detailed characterisations of the clinical presentation and activity limitations (The Definition and Classification of Cerebral Palsy 2007). Careful compiling of the intervention's components using a phase-oriented approach may be useful (Campbell et al. 2000). The various interventions in all groups should be defined more clearly, detailing the various components and skills needed to provide the intervention, its intensity and setting, and types, materials, and methods of applying or manufacturing of the therapy equipment.

Complementary qualitative analyses may be relevant to monitor the progress of the intervention delivery and the role of the interaction and family situation for the child's progress. The many single components of physiotherapy interventions could be studied separately. Cohort studies can add information about the long-term prognosis and help to integrate trial findings into routine care. Evidence from studies on more focused interventions, such as strength training and constraint induced movement therapy could be utilized when developing complex interventions. A consensus on clinically relevant outcome measures to apply in CP would be required to combine results across studies. Future studies should apply validated measures that are responsive to changes covering all ICF components and health-related quality of life.

The applicability of the trial findings would be enhanced by detailed reporting of the trial methods, as well as the characteristics of the studied populations, interventions and the evaluative ability of the outcome measures. Such information is also essential to assist replication of the studied interventions in clinical settings.

Where are the research gaps?

Most currently used treatment approaches have not been rigorously evaluated for their effectiveness in pragmatic trials. Well-designed studies on the various motor-based physiotherapy or physiotherapy-related interventions and orthotic devices are urgently needed. First of all, it would be important to study what type and level of therapeutic input is necessary and sufficient to prevent deformities and to maintain optimal progress in functioning and quality of life in the various types and severities of CP. Secondly, it would be useful to evaluate what type of add-on therapy (e.g. various training programs, swimming programs, hippotherapy) would be suitable and provide further improvements for the children.

6 Conclusions and future considerations

What was already known on this topic?

- Systematic reviews and randomised controlled trials are valuable and powerful tools for decision-makers to cope with information overload and for evidence-based decisions
- Children with cerebral palsy represent a heterogeneous population
- Different philosophies and doctrines surround physiotherapy interventions, and the effectiveness of the physiotherapy interventions has remained ambiguous due to methodological weaknesses in related studies.
- A wide variation of functional outcome measures exist; only partly validated in research settings
- Many problems of reporting trials or reviews can be avoided using guides such as the CONSORT and the QUOROM statements.

What this study adds?

About reviews:

- Systematic reviews of physiotherapy or conductive education interventions in children with CP require cautious interpretation of the findings.
- The low number of RCTs had resulted in the inclusion of a large variety of observational studies in reviews.
- Based on six high-quality reviews, conclusions on the effectiveness of some interventions on specific outcomes could be made. Otherwise the effects remain unclear or unsupported by data.
- Even the high-quality systematic reviews may overlook important clinical details in the papers reviewed, thereby diminishing their applicability

About trials:

- Good quality RCTs addressing motor dysfunction in children and adolescents with CP are feasible and currently being produced despite the well-described challenges.
- More multiprofessional work is needed to improve the quality of the trial methods and reporting these with descriptions of the participants and interventions to facilitate the transfer of findings into clinical practice.

About the effectiveness:

- Some moderate, but mostly limited evidence was established on the effectiveness of the various physiotherapy interventions.
- The lack of long-term follow-up prevents conclusions on any effect of any orthotic devices or intermittent casting on structure during growth in children with CP.
- Because of the small number of trials and mostly limited evidence in almost all intervention categories there is a need for original, well-designed, and long-term studies on the effects of many currently used and novel physiotherapy interventions in children with CP, as are also new methods for analysing the effects of comprehensive physiotherapy interventions.

Notes

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Figure 4.3 and Tables 4.3 and 4.4 were reprinted from *Journal of Clinical Epidemiology*, vol. 59, Kunz R, Autti-Rämö I, Anttila H, Malmivaara A, Mäkelä M., A systematic review finds that methodological quality is better than its reputation but can be improved in physiotherapy trials in childhood cerebral palsy, pages 1239-1248 (Figure 2, Table 1 and Table 3), Copyright © 2006, with permission from Elsevier.

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The appendices B and D-G are reprinted from additional materials of *BMC Pediatrics* 2008, 8:14, Anttila H, Autti-Rämö I, Suoranta J, Mäkelä M, Malmivaara A. Effectiveness of physiotherapy interventions for children with cerebral palsy: a systematic review, under the terms of Biomed Central open access license.

Appendices

Appendix A. Search strategies.

Article I

Databases: Ovid MEDLINE (1966 to June Week 3 2003), ACP Journal Club (1991 to January/February 2003), Cochrane Database of Systematic Reviews (1st Quarter 2003), Database of Abstracts of Reviews of Effects (1st Quarter 2003)

Date: 27.6.2003

Search strategy:

1. cerebral palsy/rh, th [Rehabilitation, Therapy]
2. cerebral palsy.mp. or Cerebral Palsy/
3. exp physical therapy techniques/
4. (physical therapy or physical therapies).ab,ti.
5. physiotherap\$.ab,ti.
6. exp exercise therapy/
7. (physical activity or physical activities).ab,ti.
8. exp "physical therapy (specialty)"/
9. exp "physical education and training"/
10. rehabilitation.mp. or REHABILITATION/
11. (vojta or bobath or neurodevelop\$ or NDT or Rood or Kabat or vibroacoust\$).ab,ti.
12. "Early intervention (education)"/
13. conductive education.ab,ti.
14. conservative therap\$.ab,ti.
15. (muscle strength\$ or muscle training or motion or therapeutic exercise or exercise training or physical exercise or fitness or aerobic training or kinetic chain).ab,ti.
16. movement.mp. or EXERCISE MOVEMENT TECHNIQUES/ or MOVEMENT/
17. SWIMMING/ or swimming.mp. or hydrotherapy.mp.
18. (functional therapy or functional therapies).ab,ti.
19. (self care training or motor control or motor learning).ab,ti.
20. occupational therapy.mp. or Occupational Therapy/
21. (constraint adj induced).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
22. restraint, physical/
23. (forced adj2 treatment).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
24. (psychomotor performance or sensation).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
25. sensory integration.ab,ti.
26. (sensory adj perceptual).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
27. Parent-Child Relations/ or Parents/ or parent education.mp.
28. physical stimulation.mp. or Physical Stimulation/
29. (posture or positioning).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw]
30. facilitat\$.ti,ab.
31. 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32. 2 and 31
33. 1 or 32
34. controlled.ab.
35. design.ab.
36. evidence.ab.
37. extraction.ab.
38. randomised controlled trials/
39. meta-analysis.pt.

- 40. review.pt.
- 41. sources.ab.
- 42. studies.ab.
- 43. or/34-42
- 44. letter.pt.
- 45. comment.pt.
- 46. editorial.pt.
- 47. or/44-46
- 48. 43 not 47
- 49. 33 and 48

Databases: Ovid MEDLINE(R) (2003 to August Week 1 2007), ACP Journal Club (1991 to July/August 2007), Cochrane Database of Systematic Reviews (3rd Quarter 2007), Database of Abstracts of Reviews of Effects (3rd Quarter 2007)

Date: 8.8.2007

Search Strategy: Lines 1-49 as above

50. Limit 49 to systematic reviews

51. limit 49 to "review articles"

52. 51 and 52

Database: HTA

Date: 15.08.2007

Search strategy: search terms were "cerebral palsy" or "CP"

Database: CINAHL – Cumulative Index to Nursing & Allied Health Literature (1982 to June Week 3 2003)

Date: 27.6.2003

Search strategy:

1 meta analysis/

2 systematic review/

3 systematic review.pt.

4 (metaanaly\$ or meta-analy\$).tw.

5 metanal\$.mp. [mp=title, cinahl subject headings, abstract, instrumentation]

6 nursing interventions.pt.

7 (review\$ or overview\$).ti.

8 literature review/

9 exp literature searching/

10 cochrane\$.tw.

11 (synthes\$ adj3 (literature\$ or research\$ or studies or data)).tw.

12 (medline or medlars or embase or scisearch or psycinfo or psychinfo or psyclit or psychlit).tw,sh.

13 pooled analy\$.tw.

14 ((data adj2 pool\$) and studies).tw.

15 ((hand or manual\$ or database\$ or computer\$) adj2 search\$).tw.

16 reference databases/

17 ((electronic\$ or bibliographic\$) adj2 (database\$ or data base\$)).tw.

18 (review or systematic-review or practice-guidelines).pt.

19 (review\$ or overview\$).ab.

20 (systematic\$ or methodologic\$ or quantitativ\$ or research\$ or literature\$ or studies or trial\$ or effective\$).ab.

21 18 and 20

22 ((review\$ or overview\$) adj 10 20).ab.

23 or/1-17,21-22
 24 editorial.pt.
 25 letter.pt.
 26 case study.pt.
 27 record review/
 28 peer review/
 29 (retrospective\$ adj2 review\$).tw.
 30 (case\$ adj2 review\$).tw.
 31 (record\$ adj2 review\$).tw.
 32 (patient\$ adj2 review\$).tw.
 33 (patient\$ adj2 chart\$).tw.
 34 (peer adj2 review\$).tw.
 35 (chart\$ adj2 review\$).tw.
 36 (case\$ adj2 report\$).tw.
 37 exp case control studies/
 38 exp prospective studies/
 39 case studies/
 40 animal studies/
 41 "edit and review"/
 42 (rat\$ or mouse or mice or hamster\$ or animal\$ or dog\$ or cat\$ or rabbit\$ or bovine or sheep\$).tw.
 43 or/24-42
 44 43 not (43 and 23)
 45 23 not 44
 46 cerebral palsy/rh, th [Rehabilitation, Therapy]
 47 cerebral palsy.mp. or Cerebral Palsy/
 48 exp physical therapy techniques/
 49 (physical therapy or physical therapies).ab,ti.
 50 physiotherap\$.ab,ti.
 51 exp exercise therapy/
 52 (physical activity or physical activities).ab,ti.
 53 exp "physical therapy (specialty)"/
 54 exp "physical education and training"/
 55 rehabilitation.mp. or REHABILITATION/
 56 (vojta or bobath or neurodevelop\$ or NDT or Rood or Kabat or vibroacoust\$).ab,ti.
 57 "Early intervention (education)"/
 58 conductive education.ab,ti.
 59 conservative therap\$.ab,ti.
 60 (muscle strength\$ or muscle training or motion or therapeutic exercise or exercise training or physical exercise or fitness or aerobic training or kinetic chain).ab,ti.
 61 movement.mp. or EXERCISE MOVEMENT TECHNIQUES/ or MOVEMENT/
 62 SWIMMING/ or swimming.mp. or hydrotherapy.mp.
 63 (functional therapy or functional therapies).ab,ti.
 64 (self care training or motor control or motor learning).ab,ti.
 65 occupational therapy.mp. or Occupational Therapy/
 66 (constraint adj induced).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
 67 restraint, physical/
 68 (forced adj2 treatment).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
 69 (psychomotor performance or sensation).mp. [mp=title, cinahl subject headings, abstract, instrumentation]

70 sensory integration.ab.ti.
71 (sensory adj perceptual).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
72 Parent-Child Relations/ or Parents/ or parent education.mp.
73 physical stimulation.mp. or Physical Stimulation/
74 (posture or positioning).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
75 facilitat\$.ti.ab.
76 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75
77 47 and 76
78 46 or 77
79 45 and 78

Database: CINAHL (1982 to August Week 1 2007)

Date: 8.8.2007

Search strategy: Lines 1-79 as above

80 limit 78 to "systematic review"

81 (systematic adj2 review\$).mp. [mp=title, subject heading word, abstract, instrumentation]

82 (meta-anal\$ or metaregression or metasynthesis or synthesis).mp. [mp=title, subject heading word, abstract, instrumentation]

83 81 or 82

84 78 and 83

85 80 or 84

Database: The Physiotherapy Evidence Database (PEDro)

Date: 15.8.2007

Search strategy: Search terms were "cerebral palsy" or "CP" and "systematic review"

Article II

Databases: Ovid Pre-MEDLINE, Ovid MEDLINE (1966 to Present), CDSR, ACP Journal Club, DARE, CCTR

Date: 12.5.2003

Search strategy:

1. review.ab.

2. review.pt.

3. meta-analysis.ab.

4. meta-analysis.pt.

5. meta-analysis.ti.

6. or/ 1-5

7. letter.pt.

8. editorial.pt.

9. comment.pt.

10. or/ 7-9

11. (cerebral palsy or Cerebral Palsy).mp. [mp=ti, ab, rw, sh]

12. exp Orthotic Devices/

13. 12 and 11

14. 6 not 10

15. 13 and 14

Database: CINAHL (1982 to May Week 1 2003)

Date: 12.5.2003

Search strategy:

1. meta analysis
2. systematic review/
3. systematic review.pt.
4. (metaanaly\$ or meta-analy\$).tw.
5. nursing interventions.pt.
6. (review\$ or overview\$).ti.
7. literature review/
8. exp literature searching/
9. cochrane\$.tw.
10. (synthes\$ adj3 (literature\$ or research\$ or studies or data)).tw.
11. (medline or medlars or embase or scisearch or psycinfo or psychinfo or psyclit or psychlit).tw,sh.
12. pooled analy\$.tw.
13. ((data adj2 pool\$) and studies).tw.
14. ((hand or manual\$ or database\$ or computer\$) adj2 search\$).tw.
15. reference databases/
16. ((electronic\$ or bibliographic\$) adj2 (database\$ or data base\$)).tw.
17. (review or systematic-review or practice-guidelines).pt.
18. (review\$ or overview\$).ab.
19. (systematic\$ or methodologic\$ or quantitativ\$ or research\$ or literature\$ or studies or trial\$ or effective\$).ab.
20. 17 and 19
21. ((review\$ or overview\$) adj 9 19).ab.
22. or/1-16,20-21
23. editorial.pt.
24. letter.pt.
25. case study.pt.
26. record review/
27. peer review/
28. (retrospective\$ adj2 review\$).tw.
29. (case\$ adj2 review\$).tw.
30. (record\$ adj2 review\$).tw.
31. (patient\$ adj2 review\$).tw.
32. (patient\$ adj2 chart\$).tw.
33. (peer adj2 review\$).tw.
34. (chart\$ adj2 review\$).tw.
35. (case\$ adj2 report\$).tw.
36. exp case control studies/
37. exp prospective studies/
38. case studies/
39. animal studies/
40. "edit and review"/
41. (rat\$ or mouse or mice or hamster\$ or animal\$ or dog\$ or cat\$ or rabbit\$ or bovine or sheep\$).tw.
42. or/23-41
43. 42 not (42 and 22)
44. 22 not 43
45. exp Cerebral Palsy/ or cerebral palsy.mp.
46. exp Orthotic Devices/ or orthotic devices.mp.

47. 45 and 46

48. 44 and 47

Database: The Physiotherapy Evidence Database (PEDro)

Date: 2.6.2003

Search strategy: The search terms were "cerebral palsy" and "systematic review".

Article V

Databases: Ovid MEDLINE(R) (1950 to January Week 5 2007), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (February 12, 2007), Ovid MEDLINE(R) Daily Update (February 12, 2007),

Cochrane Central Register of Controlled Trials (1st Quarter 2007)

Date:13.2.2007

Search strategy:

1. cerebral palsy.mp. or Cerebral Palsy/
2. exp physical therapy techniques/
3. (physical therapy or physical therapies).ab,ti.
4. physiotherap\$.ab,ti.
5. exp exercise therapy/
6. (physical activity or physical activities).ab,ti.
7. exp "physical therapy (specialty)"/
8. exp "physical education and training"/
9. cerebral palsy/rh, th [Rehabilitation, Therapy]
10. rehabilitation.mp. or REHABILITATION/
11. (vojta or bobath or neurodevelop\$ or NDT or Rood or Kabat or vibroacoust\$).ab,ti.
12. "Early intervention (education)"/
13. conductive education.ab,ti.
14. (conservative therap\$ or hippo\$).mp. or hors\$.ab,ti. [mp=ti, ot, ab, sh, hw, kw, it, nm]
15. (muscle strength\$ or muscle training or motion or therapeutic exercise or exercise training or physical exercise or fitness or aerobic training or kinetic chain training).ab,ti.
16. movement.mp. or EXERCISE MOVEMENT TECHNIQUES/ or MOVEMENT/
17. SWIMMING/ or swimming.mp. or hydrotherapy.mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
18. (functional adj therap\$).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
19. (self adj care adj training).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
20. occupational therapy.mp. or Occupational Therapy/
21. (constraint adj induced).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
22. restraint, physical/
23. (forced adj2 treatment).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
24. (psychomotor performance or sensation).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
25. sensory integration.mp. or sensory-integration.ab,ti. [mp=ti, ot, ab, sh, hw, kw, it, nm]
26. (sensory adj perceptual).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
27. Parent-Child Relations/ or Parents/ or parent education.mp.
28. physical stimulation.mp. or Physical Stimulation/ or infant stimulation.mp. or Infant Stimulation/
29. exp facilitation/
30. exp Randomized Controlled Trials/
31. randomized controlled trial.pt.
32. (random\$ or rct?).mp. [mp=ti, ot, ab, sh, hw, kw, it, nm]
33. 30 or 31 or 32
34. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29

- 35. 1 and 33 and 34
- 36. 1 and 10
- 37. 9 or 36
- 38. 33 and 37

Database: CINAHL (1982 to February Week 1 2007)

Date: 13.2.2007

Search strategy:

- 1. cerebral palsy.mp. or Cerebral Palsy/
- 2. (physical therapy or physical therapies).ab,ti.
- 3. physiotherap\$.ab,ti.
- 4. exp exercise therapy/
- 5. (physical activity or physical activities).ab,ti.
- 6. exp "physical education and training"/
- 7. cerebral palsy/rh, th [Rehabilitation, Therapy]
- 8. rehabilitation.mp. or REHABILITATION/
- 9. (vojta or bobath or neurodevelop\$ or vibroacoust\$).ab,ti.
- 10. conductive education.ab,ti.
- 11. conservative therap\$.ab,ti.
- 12. (muscle strength\$ or muscle training).ab,ti.
- 13. movement.mp. or EXERCISE MOVEMENT TECHNIQUES/ or MOVEMENT/
- 14. SWIMMING/ or swimming.mp.
- 15. (functional adj therap\$).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 16. (self adj care adj training).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 17. occupational therapy.mp. or Occupational Therapy/
- 18. (constraint adj induced).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 19. restraint, physical/
- 20. (forced adj2 treatment).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 21. (psychomotor performance or sensation).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 22. sensory integration.ab,ti.
- 23. (sensory adj perceptual).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 24. Parent-Child Relations/ or Parents/ or parent education.mp.
- 25. physical stimulation.mp. or Physical Stimulation/
- 26. (posture or positioning).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 27. exp "play and playthings"/
- 28. toy?.mp.
- 29. exp clinical trials/
- 30. double-blind method/ or meta-analysis/ or random allocation/ or single-blind method/
- 31. (clinical trial or randomized controlled trial).pt.
- 32. (rct\$ or random\$).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
- 33. systematic review?.ab,ti.
- 34. exp cohort studies/
- 35. cohort?.ab,ti.
- 36. physical education, adapted/ or home physical therapy/ or physical mobility/ or pediat-

ric physical therapy/ or physical medicine/ or physical therapy/
37. (early adj intervention).mp. [mp=title, cinahl subject headings, abstract, instrumentation]
38. intervention.mp. or EARLY INTERVENTION/ or EARLY CHILDHOOD INTERVENTION/ or INTERVENTION TRIALS/
39. exp comparative studies/
40. exp prospective studies/
41. confidence intervals.mp. or Confidence Intervals/
42. systematic review.pt.
43. 2 or 3 or 4 or 5 or 6 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 36 or 37 or 38
44. 1 and 43
45. 7 or 44
46. 29 or 30 or 31 or 32 or 33 or 34 or 35 or 39 or 40 or 41 or 42
47. 45 and 46

Database: The Physiotherapy Evidence Database (PEDro)

Date: 13.2.2007

Search strategy: The search terms were "cerebral palsy" or "CP" and "clinical trial".

Appendix B. Data extraction form

Data extraction form

1. IDENTIFICATION

1.1 Evaluation date: _____

1.2 Reviewer: _____

1.3 Endnote number: _____

1.4 Primary author, year: _____

2. VERIFICATION OF STUDY ELIGIBILITY

- Randomized controlled trial
- Children with CP aged 3months - 20 years* at the start of the programme. (* ≥80% of the study population and the data has to be separable.)
- Evaluates physical therapy interventions
- Outcome assessed: functioning

3. STUDY POPULATION

3.1 Severity and type

Severity scale	Hemiplegia					Diplegia					Tetraplegia				
What scale?	Spastic	Dystonic	Ataxic	Mixed	Not specified	Spastic	Dystonic	Ataxic	Mixed	Not specified	Spastic	Dystonic	Ataxic	Mixed	Not specified

3.2 Gender and Age

Group	Gender			Age			
	Male	Female	Both	Mean	SD	Median	Range
Exercise ()							
Control 1 ()							
Control 2 ()							
Control 3 ()							
SUM (all groups)							

3.3 Comorbidities

- No
- Yes, list: _____
- Not specified

4. STUDY INFORMATION

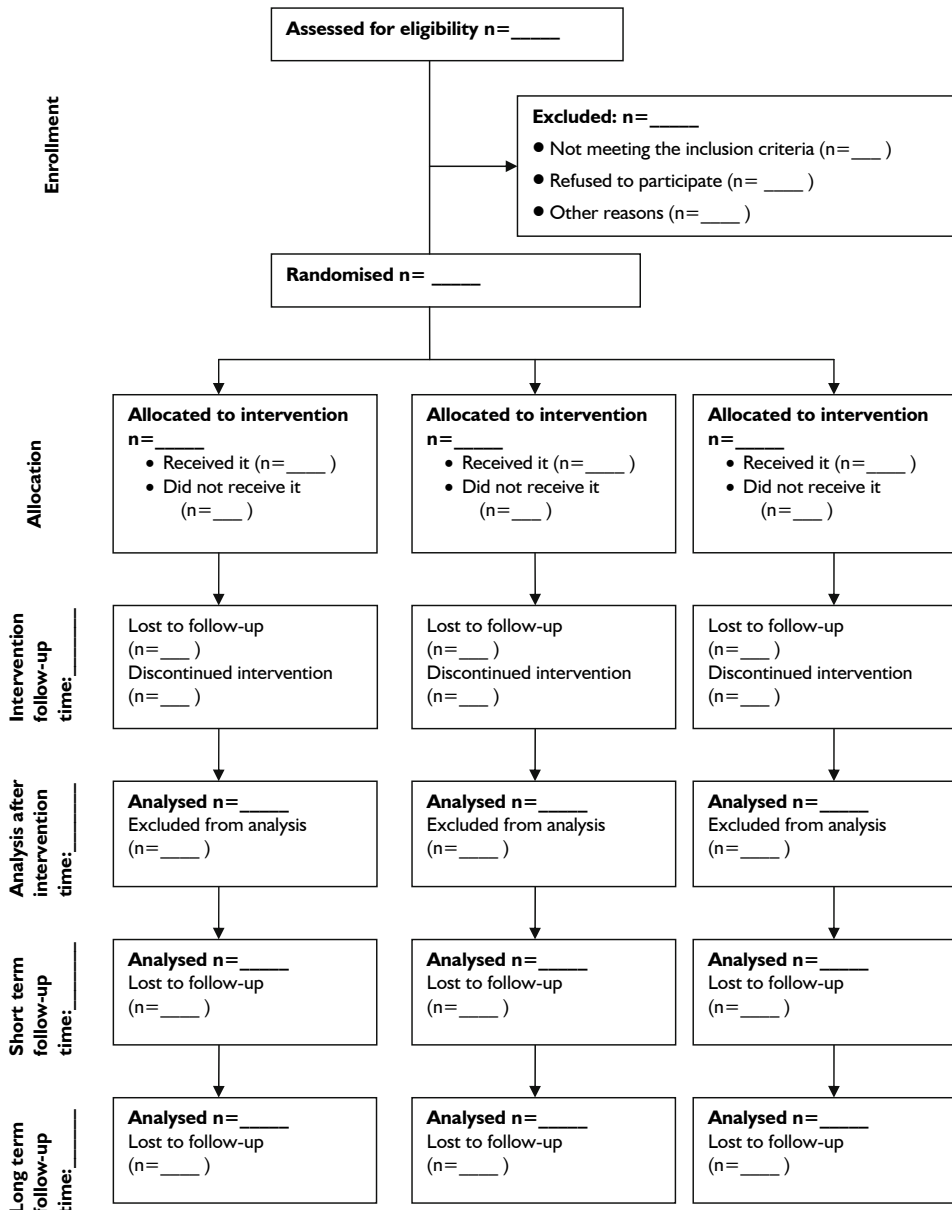
4.1 Inclusion and exclusion criteria (page: _____)

- Inclusion criteria: _____
- Exclusion criteria: _____

4.2 Stratification

- No
- Yes, according to what? _____

4.3 Flow chart (? = not reported)



Reason(s) for lost to follow-up:

5. INTERVENTIONS

5.1 Index intervention

5.1.1 The type of intervention according to authors' definition (Description in page: _____)

- Neurological intervention
- Other physical therapy intervention
- Therapy with animals

5.1.2 Dose (intended and actual length and number of sessions, duration of intervention)

	Length of session	Length of session	or hours/week	Number of sessions	Intervention period
PRE					
POST					

5.1.3 Setting

Specify: _____

5.1.4 Delivery type

- Parent or self-led (e.g. home exercise program)
- Professionally led (1:1)
- Group participation
- Not specified

5.1.5 Addition of other intervention(s) to index

- Yes LIST: _____ DOSE: _____
- No
- Not specified

5.2 Control group I

5.2.1 The type of intervention according to authors' definition (Description in page: _____)

- Neurological intervention
- Other physical therapy intervention
- Therapy with animals

5.2.2 Dose (*intended and actual length and number of sessions, duration of intervention*)

	Length of session	Length of session	or hours/week	Number of sessions	Intervention period
PRE					
POST					

5.2.3 Setting

Specify: _____

5.2.4 Delivery type

- Parent or self-led (e.g. home exercise program)
- Professionally led (1:1)
- Group participation
- Not specified

5.2.5 Addition of other intervention(s) to comparison intervention

- Yes LIST: _____
DOSE: _____
- No
- Not specified

5.3 Control Group 2

5.3.1 The type of intervention according to authors' definition

- Neurological intervention
- Other physical therapy intervention
- Therapy with animals

5.3.2 Dose (*intended and actual length and number of sessions, duration of intervention*)

	Length of session	Length of session	or hours/week	Number of sessions	Intervention period
PRE					
POST					

5.3.3 Setting

Specify: _____

5.3.4 Delivery type

- Parent or self-led (e.g. home exercise program)
- Professionally led (1:1)
- Group participation
- Not specified

5.3.5 Addition of other intervention(s) to comparison intervention

- Yes LIST: _____
DOSE: _____
- No
- Not specified

5.4 Comparisons

- Sham or ineffective treatments
- Effective treatments
- No treatment

6. OUTCOME

6.1 Outcome measure(s) assessed

- Body function & structures
- Activity limitation & participation restriction

6.2 Measures and timing (underline the primary)

Measures	Before baseline	Baseline	At the end	Short term	Long term (<6m)

6.3 Outcome assessments

Instrument _____

Scale: _____

Clinical significance level: _____

AFTER THE INTERVENTION _____ weeks/months	Physical therapy	Control 1 ()	Control 2 ()	Control 3 ()
Total number of patients				
Number improved*				
Percentage improved				
Baseline mean (SD) (Range)				
Post-mean (SD) (Range)				
Mean change (SD) (Range)				
(95% CI) of mean change				
Statistical test:				
p-value				

* How improvement was described / defined? _____

FOLLOW-UP _____ wk/mo	Physical therapy	Control 1 ()	Control 2 ()	Control 3 ()
Total number of patients				
Number improved*				
Percentage improved				
Baseline mean (SD) (Range)				
Follow-up mean (SD) (Range)				
Mean change (SD) (Range)				
(95% CI) of mean change				
Statistical test:				
p-value				

* How improvement was described / defined? _____

6.4 Adverse Effects

No adverse effects

Adverse effects

Type: _____

Number of index group: _____

Number of control group: _____

Not specified

7. CONCLUSIONS

Outcome measure	Index outcome			
	Positive	Neutral	Negative	Unclear
Body structure/function				
Activity limitation				
Participation restriction				
Environmental factors				
Personal factors				
Authors' overall				
Reviewer's overall				

NOTES: _____

Appendix D. Articles excluded after reviewing full texts and reasons for exclusions

References (n=26)	Reason for exclusion
Adams MA, Chandler LS, Schuhmann K. Gait changes in children with cerebral palsy following a neurodevelopmental treatment course. <i>Pediatr Phys Ther.</i> 2000;12:114-20	Not randomized
Catanese AA, Coleman GJ, et al. Evaluation of an early childhood programme based on principles of conductive education: the Yooralla project. <i>J Paediatr Child Health.</i> 1995;31:418-22	Not randomized
Cherng R, et al. The effectiveness of therapeutic horseback riding in children with spastic cerebral palsy. <i>Adapt Phys Act Q</i> 2004; 21:103-21	Not randomized
Fetters L, Kluzik J. The effects of neurodevelopmental treatment versus practice on the reaching of children with spastic cerebral palsy. <i>Phys Ther</i> 1996;76: 346-58	Not randomized
Palisano RJ, Tieman BL, et al. Environmental setting on mobility methods of children with cerebral palsy. <i>Dev Med Child Neurol</i> 2003; 45:113-20	Not randomized
Ross SA, Engsborg JR, et al. Ankle strengthening to improve gait and function in cerebral palsy – a pilot study. <i>Pediatr Phys Ther.</i> 2006;18:80-1	Not randomized
Sung IY, Ryu JS, et al. Efficacy of forced-use therapy in hemiplegic cerebral palsy. <i>Arch Phys Med Rehabil</i> 2005;86:2195-8	Not randomized
Thorpe DE, Valvano J. The effects of knowledge of performance and cognitive strategies on motor skill learning in children with cerebral palsy. <i>Pediatr Phys Ther.</i> 2002;14:2-15	Not randomized
Tieman BL, Palisano RJ, et al. Changes in mobility of children with cerebral palsy over time and across environmental settings. <i>Phys Occup Ther Pediatr.</i> 2004; 24:109-28	Not randomized
Mayo NE. The effect of physical therapy for children with motor delay and cerebral palsy. A randomized clinical trial. <i>Am J Phys Med Rehabil.</i> 1991;70:258-67	Population: over 20% of participants non-CP.
Burditt CA. The effects of therapeutic taping on seated postural control in children with cerebral palsy, quadriplegia. Dissertation. University of Miami, 1999.	Intervention: taping as an adjunct to physiotherapy
Coleman GJ, King JA, et al. A pilot evaluation of conductive education-based intervention for children with cerebral palsy: the Tongala project. <i>J Paediatr Child Health</i> 1995;31:412-7	Intervention: conductive education
Duff SV, Gordon AM. Learning of grasp control in children with hemiplegic cerebral palsy. <i>Dev Med Child Neurol.</i> 2003; 45:746-57	Intervention: grasp control as an adjunct to physiotherapy
Duncan B, Barton L, et al. Parental perceptions of the therapeutic effect from osteopathic manipulation or acupuncture in children with spastic cerebral palsy. <i>Clin Pediatr.</i> 2004;43:349-53	Intervention: osteopathic manipulation vs. acupuncture
Dursun, E, Dursun N, Alican D. Effects of biofeedback treatment on gait in children with cerebral palsy. <i>Disabil Rehabil.</i> 2004; 26:116-20	Intervention: biofeedback as an adjunct to physiotherapy
Kramer JF, Ashton B, et al. Training of head control in the sitting and semi-prone positions. <i>Child: Care, Health & Development.</i> 1992;18:365-76	Intervention: training of head control semi prone vs. sitting training position

McConachie, H, Huq S, et al. A randomized controlled trial of alternative modes of service provision to young children with cerebral palsy in Bangladesh. <i>J Pediatr</i> . 2000; 137:769-76	Intervention: center-based mother-child group vs. monthly training of parents along with a pictorial guidance manual
Reddihough, DS, King J, et al. Efficacy of programmes based on conductive education for young children with cerebral palsy. <i>Dev Med Child Neurol</i> . 1998; 40:763-70	Intervention: conductive education vs no treatment.
Steinbok P, McLeod K. Comparison of motor outcomes after selective dorsal rhizotomy with and without preoperative intensified physiotherapy in children with spastic diplegic cerebral palsy. <i>Pediatr Neurosurg</i> . 2002;36(3):142-7	Intervention: selective dorsal rhizotomy as an adjunct to physiotherapy
Steinbok P, Reiner AM, et al. A randomized clinical trial to compare selective posterior rhizotomy plus physiotherapy with physiotherapy alone in children with spastic diplegic cerebral palsy. <i>Dev Med Child Neurol</i> . Mar 1997;39(3):178-84.	Intervention: selective dorsal rhizotomy as an adjunct to physiotherapy
Stiller C, Marcoux BC, et al. The effect of conductive education, intensive therapy, and special education services on motor skills in children with cerebral palsy. <i>Phys Occup Ther Pediatr</i> . 2003;23:31-50	Intervention: conductive education, intensive therapy and special education
Wallen MA, O'Flaherty SJ, et al. Functional outcomes of intramuscular botulinum toxin type A in the upper limbs of children with cerebral palsy: a phase II trial." <i>Arch Phys Med Rehabil</i> . 2004;85:192-200	Intervention: botulinum toxin A, no PT
Liu J. The influence of the early interference in the convalescence on the infantile cerebral palsy. <i>Modern Rehabil</i> . 2000;4:844-5	Language: Chinese
Pisaturo C, et al. La paralisi cerebrale ipotonica. Quale trattamento? [Hypotonic cerebral palsy. Which treatment?]. <i>Minerva Pediatrica</i> . 1997;49:551-8	Language: Italian
Tudella E, Formiga CKM, et al. Comparison of the effectiveness of the early and late physical therapy intervention in infants with cerebral palsy. <i>Fisioterapia em Movimento</i> . 2004;17:45-52	Language: Portuguese
DeLuca SC, Echols K, Law CR, Ramey SL. Intensive pediatric constraint-induced therapy for children with cerebral palsy: randomized, controlled, crossover trial. <i>J Child Neurol</i> . 2006;21(11):931-8.	Reports only within-group data of the trial by Taub et al.[53]

Appendix E. Summary of participants, interventions and outcomes of the 22 RCTs (V).

First author (year) study length (follow-up),	Participants	Interventions	Outcomes by ICF components	
	a. N (group n) b. Age-range, mean (\pm SD) c. Sex distribution d. Type of CP e. Severity of motor deficit	Intervention comparisons A: add-on interventions in all groups S: setting and provider	Difference in favor of the intervention group	No between group differences
Comprehensive physiotherapy programs				
Bar-Haim (2006) 1 mo (10 mo)	a. 24 (12/12) b. 5y2mo-12y 11mo, 8y2mo l: 8.3y (\pm 2.0), C: 8.1y (\pm 2.2) c. l: 8 M, 4 F, C: 9 M, 3 F d. l: 6 spastic/ataxic diplegia, 1 triplegia, 5 spastic/mixed quadriplegia C: 5 spastic diplegia, 7 spastic/mixed quadriplegia e. GMFCS l: 2 II, 6 III, 4 IV; C: 2 II, 5 III, 5 IV.	I: NDT with Adeli suit (120 min, 5 d/wk for 4 wk; 20 sessions) C: NDT (120 min, 5 d/wk for 4 wk; 20 sessions) A: Both groups stopped their routine physiotherapy treatments, but continued educational and recreational activities (dose, intensity and number not defined). S: Russian pts, experts in Adeli suit application, same environment for all children (l); physiotherapists with \geq 7y experience and training of NDT basic and advanced courses; rehabilitation centre (C).	Body functions & structures: Metabolic cost of stair climbing (10mo) \uparrow p=0.0004 Activity & participation:- Contextual factors:-	Body functions & structures:- Activity & participation: GMFM-66 Contextual factors:-
Tsoralakis (2004) 4 mo	a. 34 (17/17) b. 3-14y, 7y 3mo (\pm 3y6mo) c. 14 F, 24 M d. 10 spastic hemiplegia, 12 diplegia and 12 tetraplegia. e. GMFCS: 10 I, 10 II, 14 III.	I: Intensive NDT (50min, 5 d/wk) C: NDT (50 min, 2 d/wk) A: Not reported S: 17 physiotherapists with NDT certification for at least 5 years and at least 10 year clinical experience.	Body functions & structures:- Activity & participation: GMFM-66 \uparrow p=0.018, ES=0.8 Contextual factors:-	Body functions & structures:- Activity & participation: GMFM-88 Contextual factors:-
Ketelaar (2001) 6 mo (12, 18 mo)	a. 55 (28/27) b. 24-87mo, 55mo (\pm 20) c. Not reported d. 32 hemi-, 11 di- and 12 tetraplegia. e. 43 mild and 12 moderate.	I: Functional physiotherapy (mean 3.4 sessions/ mo) C: Continued previous physiotherapy regime (mean 3.8 sessions/mo) A: Not reported S: Pediatric physiotherapists working in primary health care, number not given.	Body functions & structures:- Activity & participation: GMFM: standing (6+18mo) \uparrow p=0.01, walking, running, jumping (6mo) \uparrow p=0.04; PEDI (18mo): functional skills, self-care \uparrow p=0.01, mobility \uparrow p<0.05; caregiver assistance: self-care \uparrow p<0.01, mobility \uparrow p<0.05 Contextual factors:-	Body functions & structures:- Activity & participation: GMFM: walking, running, jumping (18mo); PEDI (6mo) Contextual factors:-
Bower (2001) 6 mo (9, 12, 18 mo)	a. 56 (15/13/13/15) b. 3-12y c. Not reported d. Bilateral CP. e. GMFCS: 17 III, 29 IV, 10 V.	I: Intensive physiotherapy + generalized aims (60min, 5 d/wk) C1: Intensive physiotherapy + individual and measurable treatment goals (60min, 5d/wk) C2: Routine physiotherapy + generalized aims C3: Routine physiotherapy + individual and measurable treatment goals A: Routine amounts of therapy on equipment, orthotics, and on consultation. Large individual variation in the amounts activities e.g. hydrotherapy, horse riding, occupational therapy, school physical education, conductive education. S: 56 physiotherapists (child's own) at current praxis.	Body functions & structures:- Activity & participation:- Contextual factors:-	Body functions & structures:- Activity & participation: GMFM, GMPM Contextual factors:-

Bower (1996)	a. 44 (11/11/11/11) b. 3–11y c. Not reported d. Quadriplegic CP. e. SRCMD: 28 moderate, 16 severe.	I: Conventional physiotherapy + generalized aims C1: Intensive physiotherapy + generalized aims (60 min, 5d /wk) C2: Conventional physiotherapy + individual and measurable treatment goals C3: Intensive physiotherapy + individual and measurable treatment goals (60 min, 5d /wk) A: Not reported S: 44 physiotherapists (child's own) at current praxis.	Body functions & structures:- Activity & participation:- Contextual factors:-	Body functions & structures:- Activity & participation: GMFM Contextual factors:-
Palmer (1990, 1988)	a. 48 (25/23) b. 12–19mo c. Not reported d. Spastic diplegia. e. Mild to severe.	I: NDT (60min in 14 d; home prg ?) C: Infant stimulation (6 mo) + NDT (6 mo) (60 min in 14 d, home prg ?) A: No additional therapies S: parents at home and therapist at the Clinical Research Unit of the Kennedy Institute for Handicapped Children.	Body functions & structures:- Activity & participation: in favour of the control group: Attained motor skills: independent walking p=0.01; BSID: motor ↑ (6mo)p=0.02, (12mo) p<0.01; mental ↑ (6mo) p=0.05 Contextual factors: HOME sub item: emotional and verbal responsivity of mother ↑ p=0.04	Body functions & structures:- Activity & participation: Attained motor skills; BSID (12mo): mental ; VABS social quotient Contextual factors: HOME total, mother–child relationship, Infant temperament
Upper extremity treatments				
Wallen (2007)	a. 32 (17/15)* b. 2–11y, I: 5y2mo (±2y11mo); C: 5y11m (±2y10mo) c. I: 53% M, C: 73% M. d. I: 8 hemiparesis, 3 triplegia, 6 quadriparesis; (C) 8 hemiparesis, 2 triplegia, 5 quadriparesis. MAS score of 2: I: 77%, C: 73%. e. Motor control scale developed for study†: I: I 12%, II 47%, III 35%, IV 6%, C: I 6%, II 33%, III 53%, IV 13%.	I: Occupational therapy (60min, 1d/wk, for 12 wk.) C: No extra occupational therapy. A: Pre-existing levels of regular therapy was maintained (dose, intensity and number not defined). S: the children's usual occupational therapist, at the Children's Hospital at Westmead.	Body functions & structures: ROM: active supination ↑ p=0.008 Activity & participation: GAS ↑ p=0.054 Contextual factors:-	Body functions & structures: Tardieu scale: spasticity; ROM: passive elbow Activity & participation: PEDI; QUEST; COPM; MA; CHQ Contextual factors:-
Law (1997)	a. 50 (26/24) b. 18mo – 4y, 32.92mo c. Not reported d. 19 hemiplegia, 9 diplegia, 22 tetraplegia. e. Not reported.	I: Intensive NDT (45min, 2d/wk) + casting (minimum 4 h daily) + home prg (30min daily) C: Regular occupational therapy (45min, 1-4d/ mo) A: Not reported S: 8 different rehabilitation centres in Ontario, Canada; occupational therapists, number not given.	Body functions & structures:- Activity & participation:- Contextual factors:-	Body functions & structures: - Activity & participation: PDMS-FM; QUEST; COPM Contextual factors:-

Appendix E. Summary of participants, interventions and outcomes of the 22 RCTs (V). Continues

Law (1991)	a. 72 (19/17/18/18) b. 18mo – 8y c. Not reported d. 44 Spastic hemiplegia, 28 tetraplegia. e. Not reported.	I: Intensive (45 min, 2d/wk) + home prg (30min/d) + Casting (≥ 4 h/d) C1: Intensive NDT (intensity as above) C2: Regular NDT (1-4xmo) + Home prg (15min, 3d/wk) + Casting (≥ 4 h/d) C3: Regular NDT (intensity as above) A: Records were kept of other type of interventions during six mo intervention. S: 3 regional occupational therapycentres; ots, number not given.	Body functions & structures: ROM: wrist extension \uparrow $p=0.02$ (I + C2) Activity & participation: QUEST (6mo) \uparrow $p=0.03$ (I + C2) Contextual factors:-	Body functions & structures:- Activity & participation: PDMS-FM; QUEST (9mo) Contextual factors:-
Hallam (1996)	a. 100 (33/33/34) b. Not reported c. 58 M, 42 F d. 13 diplegia, 18 right hemiplegia, 22 left hemiplegia, 37 quadriplegia, 10 double diplegia (arms affected more than legs). e. Not reported.	I: Prehensile hand treatment (1d/wk) C1: NDT (1d/wk) C2: No extra NDT or hand therapy A: Traditional physiotherapy (NDT) 1 x wk by the child's own pt. S: the researcher physiotherapist (I, C1).	Body functions & structures:- Activity & participation: GMDS developmental quotient \uparrow $p<0.002$ (for I, C1 groups) Contextual factors:-	Body functions & structures:- Activity & participation: GMDS: chronological and mental age Contextual factors:-
Strength training programs				
Liao (2007)	a. 24 (12/12) b. 5–12y; I: 85.6mo (± 20.8), C: 91.3mo (± 17.5) c. 8 F, 12 M d. Spastic diplegia. e. GMFCS: I: 4 I, 6 II, C: 6 I, 4 II.	I: Home-based loaded sit-to-stand resisted exercise prg (3 sets/session, 3 d/wk for 6 wk with increasing loads every 2 wk) C: No extra prg A: Physiotherapy including passive ROM exercises, positioning, balance training, functional training, NDT. [I: 1xwk (n=4), 2xwk (n=2), discontinued physiotherapy (n=4); C: 1xwk (n=5), 2xwk (n=1), no physiotherapy (n=3).] S: Home with caregiver assistance. Trainer taught and checked the exercises other every other wk visits at home or laboratory.	Body functions & structures: PCI \uparrow $p=0.005$, ES=1.34 Activity & participation: GMFM-88: standing, walking, running, jumping \uparrow $p<0.02$, ES=1.17; Loaded sit-to-stand test: maximum load \uparrow $p=0.001$, ES=1.78 Contextual factors:-	Body functions & structures: Knee extensor strength Activity & participation: Gait speed Contextual factors:-
Patikas (2006)	a. 43 (21/22) b. 6–16y, 9.7y (± 2.8) c. 12 F, 27 M d. Spastic diplegia. e. GMFCS: 12 I, 18 II, 9 III.	I: Strength training (30–45 min, 3-4 d/wk, for 9 mo) C: No training A: Conventional physiotherapy after surgery as soon as mobilization was possible. S: At home, self-led with help of parents (I); 4 physiotherapists during hospital stay and after that by the children's own physiotherapists (I, C).	Body functions & structures:- Activity & participation:- Contextual factors:-	Body functions & structures: MAS; Muscle tone; knee extension, flexion and ROM; oxygen consumption; energy expenditure Activity & participation: GMFM: standing, walking, running, jumping Gait analysis: e.g. stride length, gait speed Contextual factors: -
Unger (2005)	a. 31 (24/13) b. 13–18 y; I: 13.5–18.92y (± 15.86); C: 14–18.33y (± 16.28) c. 12 F, 19 M d. Spastic CP. 16 hemiplegic, 14 diplegic, 1 triplicgia. e. Independently ambulant with or without aids. Assistive devices: I: crutches (n=1), wheelchair in occasional use (n=1), supra-malleolar orthosis (n=1).	I: Circuit training (1-3d/ wk for 8 wk during school hours.) C: No training. A: Not reported. S: at school, consultation by therapist, research assistant.	Body functions & structures: 3D gait analysis (free speed): sum of ankle, knee and hip angles at midstance \downarrow (p value unclear) Activity & participation:- Contextual factors: Self-perception: body image \uparrow (p value unclear)	Body functions & structures: 3D gait analysis: ankle, knee and hip angles separately at midstance, knee angle at heel strike Activity & participation: 3D gait analysis: velocity, stride length, cadence Contextual factors: Self-perception: functional competence

Dodd (2003, 2004)	a. 21 (11/10) b. 8–18y, 13y1mo ($\pm 3y1mo$) c. 10 F, 11 M	I: Home-based strength-training prg (20-30min, 3d/wk) C: Normal daily activity	Body functions & structures: Hand-held dynamometer: ankle plantar flexor and knee extensor strength \uparrow (6wk) $p=0.046$, (18wk) $p=0.041$ Activity & participation:- Contextual factors: in favor of the control group: Self-perception profile for children: scholastic competence \uparrow (6wk) $p=0.04$, (18wk) $p=0.016$, social acceptance \uparrow (18wk) $p=0.03$	Body functions & structures: Hand-held dynamometer: combined ankle plantar flexor, knee and hip extensor strength Activity & participation: GMFM, gait speed, timed stair test Contextual factors: Self-perception: athletic competence, physical appearance, behavioral conduct and global self-worth
6 wk (18 wk)	d. Spastic diplegia. e. GMFCS: 7 I, 5 II, 9 III.	A: Normal physiotherapy (45min 1-2 x mo), normal daily activities, including school and sport. S: I: Home, self-led. C: At school, physiotherapist checked exercise performance and adjusted the load at 2 wk intervals (I).		

Cardiovascular fitness and aerobic programs

Chad (1999)	a. 18 (9/9) b. range not given; I: 9.0y (± 2.9); C: 9.0 y (± 2.7) c. 13 F, 5 M	I: Physical activity prg (2 sessions /wk for 2 mo, 3 sessions/ wk for 6 mo) C: Maintenance of normal lifestyle habits. A: Not reported.	Body functions & structures: Femoral neck bone mineral content \uparrow $p=0.03$, density \uparrow $p=0.02$ Activity & participation:- Contextual factors:-	Body functions & structures: Proximal femur bone mineral content Activity & participation:- Contextual factors:-
8 mo	d. Spastic CP. e. 2 independent ambulators, 5 independent ambulators with an aid, 5 ambulators with an assistant, 6 non-ambulators.	S: not reported, physiotherapist one-on-one, number not given (I).		
Van den Berg-Emons (1998)	a. 20 (10/10) b. 7–13y, 9y (± 1.4) c. 9 F, 11 M	I. Physical training prg (45 min, 4 d/wk) C: No training. A: 45 min gymnastic lessons 2xwk at school; individual therapy based on personal needs, frequency varying from no therapy to >2.5 hours/wk. S: Not reported (I)	Body functions & structures: Peak aerobic power \uparrow (9mo) $p=0.05$; Fat mass \downarrow $p<0.05$ Activity & participation:- Contextual factors:-	Body functions & structures: Peak anaerobic and mean aerobic power Activity & participation: Physical activity Contextual factors:-
9 mo	d. 14 spastic diplegia and 2 mixed spastic and ataxic diplegia, 4 tetraplegia. e. 10 ambulant, 10 wheelchair-bound.			

Constraint induced therapy

Charles (2006)	a. 33 (19/14) b. 4–8y, 6y 8mo ($\pm 1y 4mo$) c. 8 F, 14 M	I: CI-therapy with a sling (6 h/session for 10 out of 12 consecutive d, altogether 60 h) C: No treatment. A: The children continued to receive their usual and customary care that the children were receiving elsewhere. S: Columbia university, a trained interventionist involving specific practice of designated target movements (I).	Body functions & structures:- Activity & participation: Caregiver Functional Use Survey: hand use: frequency \uparrow (1wk) $p<0.01$, ES=0.3 quality \uparrow (1+6mo) $p<0.01$, ES=0.2; Jebsen-Taylor Test of Hand Function: time to complete tasks \downarrow (1wk) $p=0.01$, ES=0.3; BOTMP: speed, dexterity \uparrow (1wk) $p=0.005$, ES=0.4 Contextual factors:-	Body functions & structures: Sensibility; hand-grip; shoulder, elbow and wrist muscle tone Activity & participation: Hand function (1+6mo); BOTMP: speed and dexterity (1+6mo) Contextual factors:-
1 wk (1 mo, 6 mo)	d. Hemiplegic CP. Involved side I: 8 left, 3 right, C: 4 left, 7 right. e. Moderate hand involvement \pm , a 50% difference between the involved and non-involved hand on the Jebsen-Taylor Test.			

Appendix E. Summary of participants, interventions and outcomes of the 22 RCTs (V). Continues

Taub (2004) 3 wk (3 mo, 6 mo)	a. 18 (9/9) b. 7mo–8y, 41.5mo c. 5 F, 13 M d. Spastic or low muscle tone hemiparesis. e. 2 mild, 7 moderate, 2 moderate-severe, 7 severe.	I: CI-therapy with a bivalved cast (6 h/ session, 7 d/wk for 21 days) C: Early intervention prg ,OT and/or physiotherapy (1–2 h/wk) (+ crossover to CI therapy for 21 d) A: Not reported S: Natural settings, ots and pts, or a pt assistant; 1 method developer trained and supervised the therapists 2 x wk (I), previously established school-based services or private therapy sessions (C).	Body functions & structures:- Activity & participation: Emerging Behaviours Scale↑ p<0.0001; Pediatric Motor Activity Log: frequency and quality of hand use ↑ (3wk) p<0.0001 Contextual factors:-	Body functions & structures:- Activity & participation: QUEST Contextual factors:-
Sensorimotor training				
Bumin (2001) 3 mo	a. 41 (16/16/9) b. range not given; I: 7,06y (±1,88); C1: 7,68y (±1,70); C2: 7,00y (±1,22) c. Not reported d. Spastic diplegia. e. Not reported.	I: Sensory perceptual motor (SPM) training individually (90 min, 3 d/wk) C1: SPM training in groups of 4 (intensity as above) C2: Home prg A: Some activities as a home prg. S: At the School of Physiotherapy and Rehabilitation Hacettepe University occupational therapyUnit (I, C1), at home, physiotherapist, number not given (C2).	Body functions & structures:- Activity & participation:- Contextual factors:-	Body functions & structures:- Activity & participation:- Contextual factors:-
Balance training				
Ledeht (2005) 6–7 wk (10 wk)	a. 10 (???) b. 5–10 y; I: 7y2mo, C: 7y7mo c. Not reported d. Hemiplegic CP e. GMFCS: I 10.	I: Balance training (30 min, 3 d/wk for 6 wk (18 sessions) C: No balance training. A: Own shoes including ankle-foot orthoses or insoles to correct leg-length discrepancies. S: University laboratory in Amsterdam, 2 trainers (I).	Body functions & structures:- Activity & participation: Force Plate: displacement ↓ forward p=0.01, backward p=0.006 Leaning ↓ forward p=0.003, backward p=0.001, parietic side p=0.022 and non-parietic side p=0.001; step length of non-parietic leg ↑ p=0.017 Contextual factors:-	Body functions & structures:- Activity & participation: Force plate (quiet stance): time on target, displacement toward parietic and non parietic sides; step length of parietic leg Contextual factors:-
Therapy with animals				
Benda (2003) 8 min	a. 15 (7/8) b. 4–12y c. Not reported d. Spastic CP. e. Not reported.	I: Equine-assisted therapy (Hippo therapy) (one 8 min session) C: Stationary barrel (one 8 min session) A: No additional therapies. S: Therapeutic Riding of Tuscon, 1 physiotherapist certified as a hippo therapy clinical specialists (I).	Body functions & structures:- Activity & participation:- Contextual factors:-	Body functions & structures: Muscle asymmetry Activity & participation:- Contextual factors:-
MacKinnon (1995) 6 mo	a. 19 (10/9) b. 4–12y, 6.5y ; I: 7.2 (±2.39), C1: 5.7y (±1.46), C2: 6.8y (±2.05), C3: 6.0 (±1.87) c. 10 F, 9 M d. Spastic CP. e. 10 mild, 9 moderate.	I: Horseback riding, moderate (60 min, 1 d/wk) C1: No hippo therapy (waiting list), moderate C2: Horseback riding, mild (60 min, 1 d/ wk) C3: No hippo therapy (waiting list), mild A: Routine therapies and activities continued, no attempt to stop them was made. S: not reported; 1 therapeutic riding instructor and 1 pt (I, C2).	Body functions & structures:- Activity & participation: PDMS-FM sub item: grasping ↑ p=0.045 Contextual factors:-	Body functions & structures: Sitting posture§ Activity & participation: GMFM; PDMS-FM total; VABS-ADL: socialization; CBC; BOTMP Contextual factors: HSPC

I=intervention group, C=control group, F=females, M=males, min=minutes, h=hours, d=day/s, wk=week/s, mo=month(s), y=year(s), CP=cerebral palsy, prg=program, CI=constraint inducement, NDT=neurodevelopmental treatment, SPM=sensory perceptual motor, MAS=Modified Ashworth scale, DASI-II=Developmental Activities Screening Inventory, SRCMD = Standard Record of Central Motor Deficit: section 7; GMFCS = Gross Motor Function Classification System (levels I-V),

↑=improvement or increase of the outcome, ↓=deterioration or decrease of the outcome.

ADL=activities of daily living, BSID=Bayley Scales of Infant Development, BOTMP=Bruininks-Oseretsky Test of Motor Proficiency, CBC=Child Behaviour Checklist, ES=effect size, GMDF=Griffith's Mental Developmental Scales, GMFM = Gross Motor Function Measure, HOME=Home Observation for Measurement of the Environment, HSPC=Harter Self-perception Profile for Children, MA=Melbourne assessment of unilateral upper limb function, MAS=Modified Asworth Scale, MPOC=Measure of Processes of Care, PCI=Physiological Cost Index, PEDI=Pediatric Evaluation of Disability Inventory, PDMS-FM=Peabody Developmental Motor Scales Fine Motor , TACQOL-PF=The TNO-AZL Questionnaire for Children's Health-Related Quality of Life – Parent Form, QUEST=Quality of Upper Extremity Skills Test, ROM=range of motion, mo=months, VABS=Vineland Adaptive Behavior Scale.

* The Wallen 2007 trial included a total of 80 participants who were randomized to four groups. The 2 other groups (BTX-A plus occupational therapy and BTX-A) were not included in this review.

† I=manipulate small objects, pincer, opposition of most fingers, II=useful grasp and release for holding larger objects, III=can flex and extend fingers and wrist, IV=movement that is not useful for activity.

‡ type IIa by Zancolli & Zancolli (Zancolli & Zancolli 1981)

§ by a scale developed by Bertoti et al (Bertoti 1988)

Appendix F. Detailed intervention descriptions

First author (year)	Type of therapy
Comprehensive physiotherapy programs	
Bar-Heim (2006)	<p>Adeli suit treatment: The treatment approach included the Adeli suit (from Zvezda Corporation, Moscow, Russia, and sized in accordance with the anthropometrical measures) and an intensive, well-structured treatment protocol. Treatment was "conducted in accordance with the original Russian protocol that included the following: 1) massage before fitting the suit; 2) passive stretching of all limb muscles; 3) application of the suit by placing the body into proper alignment and restricting limb positions, thereby loading the patient's musculature; and 4) rigorous exercises in the suit, following an individual program based on functional weight-bearing gross motor activities primarily related to locomotion. Each session included walking activities suited to individual abilities, standing up from sitting, playing with a ball while standing, walking on different terrains, jumping on a trampoline, and climbing stairs and ladders."</p> <p>Neurodevelopmental therapy (NDT): targets "the central nervous and neuromuscular system and 'teaching' the brain to improve motor performance skills and achieve 'as normal function as possible', in view of the specific lesion in the central nervous system." No strict protocol of treatment, rather an orientation to reacting "in real time to the tone and movement patterns of the patient". Individual functional aims and goals were determined and a structured program was set for each child. The program included: passive stretching of lower limb muscles, techniques of reducing spasticity and facilitating more normal patterns of movements while working on motor functions (walking, standing up from sitting and sitting on a bench).</p>
Tsorlakis (2004)	<p>NDT: was based on the fundamental and current principles of the approach, as it has evolved more recently. Therapy was individualized for each child's condition and dictated by the child's unique needs.</p>
Ketelaar (2001)	<p>Functional physical therapy: "directed at promoting functional skills instead of normalization of movement". Emphasizes the learning of motor abilities that are meaningful to the child's environment and perceived as problematic by the child or the parents. Children practice these motor abilities in functional situations, with the child having an active role in finding solutions for motor problems rather than having the physical therapist's handling result in a solution. Functional goals, in terms of skills, are established with parents and children based on their priorities. Functional activities are assumed to be learned by repetitive practice of goal-related tasks in functional situations. Content of the therapy varies between the children.</p> <p>Reference group: previous physical therapy regimen, which content varied between the children. 19 of 27 children were treated according a neurophysiological treatment method (NDT or Vojta), with focus on the principle of normalization of motor performance and quality of movement.</p>
Bower (2001)	<p>Physiotherapy: was described by each physiotherapist involved and was found to consist of a mixture of muscle stretching, passive corrective manual handling, positioning, including the use of equipment, orthoses and casting as considered necessary, muscle strengthening and active movement in addition to gross motor skill training along developmental and functional lines as considered appropriate by the child's physiotherapist. Treatment was primarily targeted at gross motor abilities and not manual dexterity. There were remarkable similarities in the documented treatment descriptions between the therapists. For half of the children the [general] aims of the therapy were defined, while specific goals were set for the other half.</p>
Bower (1996)	<p>Physiotherapy: "eclectic or comprising a mixture of different ingredients considered appropriate by each individual physiotherapist for each individual child and family". In other groups general aims were documented, and in others specific individual and measurable treatment goals were negotiated, assessed and documented.</p>

Palmer (1990, 1988)	<p><u>Physical therapy</u>: focused on motor development, designed to “optimize expression of components of righting and equilibrium believed to be necessary for continued development of gross motor milestones”.</p> <p><u>The infant stimulation program</u>: learning games, a curriculum designed to “address a broad range of infant developmental domains: 100 explicitly defined and illustrated cognitive, sensory, language, and motor activities of increasing developmental complexity appropriate for children from birth to 3 years. Fine motor activities include puzzles, crayons, form-matching, and block-building tasks”.</p>
Upper extremity treatment	
Wallen (2007)	<p><u>Occupational therapy</u>: a broad range of intervention modalities in order to mirror usual clinical practice. The therapy component was not standardized but “determined by treating clinicians to ensure that the intervention appropriate for participants to meet their individual goals. Intervention techniques included those aimed at improving impairment (e.g. stretching, casting, splinting), and enhancing activities (e.g. motor training, environmental modification, practice of specific goal activities).”</p>
Law (1997)	<p><u>Intensive therapy + casting</u>: facilitation and handling by principles of NDT, focus on changing impairments and improving upper-extremity quality of movement. Bivalved fiberglass upper-extremity cast extended from below the elbow to the palm of the hand. The wrist was held in a position of neutral to 10 degrees extension and the thumb and fingers were free so that their movement was not affected.</p> <p><u>Regular occupational therapy</u>: focused on task analysis and facilitating changes in functional skills: self-care, feeding and play.</p>
Law (1991)	<p><u>Regular and intensive NDT</u>: All occupational therapists attended a training workshop on the guidelines for therapy. Although principles for intervention were similar for all children, each child’s program was dictated by their unique clinical needs. Additional home programs consisted of specific NDT therapy activities.</p> <p><u>Casting</u>: Bivalved fiberglass inhibitive upper-extremity cast extended from below the elbow to the palm of the hand, immobilizing the wrist from neutral to 10 degrees extension. The thumb and fingers were not included. Casts were worn for at least 4 hours per day.</p>
Hallam (1996)	<p><u>Prehensile hand treatment</u>: a treatment program intended to advance the children’s prehensile and fine motor skills. Prior to the start of therapy parents received a handbook on the importance of hand function in relation to daily life and on ideas and suggestions to help the parents to get involved with the research while helping and playing with their child. The exercises in the handbook were intended as guides to aid purposeful play rather than as definitive routines to be followed rigidly. The therapy program followed the regime described in the handbook given to the parents. At the beginning of each session the child was either placed or requested to sit in a good position, usually in a specially adapted chair or a good small seat with the feet flat on a footrest or the floor. If the child demonstrated marked spasticity that inhibited correct posture or movement, time was spent counteracting it with general physiotherapy before attempting any specific hand therapy. The therapy program included 14 different toys and play equipment: threading cotton reels, shape sorter, balls to roll and catch with bells/chimes inside, stacking humpty dumpty, rocking ring stacker, more difficult shape sorter, cup and spoons for pretend play, cardboard picture books (to practice page turning), stacking beakers, mirror, picture form boards, square blocks for threading and building, balls for color matching and throwing/catching, building blocks.</p> <p><u>General physiotherapy</u>: was modeled Bobath NDT, combined with any specific exercises requested by the child’s regular therapist to ensure continuity and constancy of treatment. The aims were: “to give the child all possible mobility, to help the child develop without excessive effort which will increase spasticity, to [have] control over their own abnormal sensori-motor patterns with a view to obtaining more normal functional activity.” Securing such changes in postural tone and abnormal patterns that lead towards the normal state cannot be achieved unless the degree and distribution of hypertonus is capable of being altered by handling and stimulation.</p>

Strength training programs

Liao (2007)	<p>Loaded sit-to-stand (STS) group: The trainer demonstrated and instructed the loaded STS exercise, provided a body vest and weight to the children and their caregivers, and educated the caregivers to motivate children and to encourage the child to perform as many repetitions as possible. 1 repetition maximum (1-RM) was tested prior to training, and was defined as "the maximal load a child is capable of carrying while standing up one time from a sitting position without falling". Each session consisted of: 1) 5 to 10 minute warm-up activities: active movements of lower extremities, stretching of hip abductors, ankle plantar flexors, hamstring muscles, and lumbar extensors, 2) STS 10 times with body vest at 20% of 1-RM STS load, 3) 1–2 minute rest, 4) STS with the load at 50% 1-RM STS repeatedly without stopping until fatigue, 5) 2–3 minute rest, 6) STS activities again for 10 times with 20% of 1-RM STS weight, and 7) cooling down exercises, similar to warm-up exercises. The height of the chair the child sat in and performed the STS exercises at home was similar for that used for the maximum load of the loaded STS test. The progressive increasing of weight was adjusted to 50% 1-RM STS every 2 weeks according to the latest loaded STS tests.</p>
Patikas (2006)	<p>Training: started 3 to 4 weeks after surgery (no longer painful to perform the exercises and no danger of recurring injury). The children were instructed to carry out the training program at least 3 times a week, with an optimal target of 4 times a week. Each session was 30-45 minutes long (depending on the child) and consisted of 7 exercises: 1) pelvis raised lying supine knees flexed at 90°, 2) unilateral knee extension lying supine with the hip flexed at 30°, 3) sit-ups approaching with the hands to the left, center and right, 4) unilateral hip and knee flexion from lying supine, 5) knee flexion from prone position, 6) knee flexion from kneeling position with the trunk in upward position, 7) sitting down and standing up from a chair with the hands projected to the front. Sitting position at 90° of knee and hip flexion. For exercises 1 and 7 the tights fastened together distally with rubber bans to prohibit excessive hip abduction. Two sets of 5 repetitions were performed for each exercise, and for both legs with a 1-minute rest between each set and drill. The movement velocity was 4 to 5 seconds per repetition, including slow return to the initial position in order to evoke eccentric muscle activation. The resistance was progressively increased by gradually eliminating the external support during the exercise. As soon as the children succeed in overcoming the resistance against gravity without assistance, the parents increased further resistance for exercises 2, 4 and 5 using elastic bans. Additional rubber band layers were applied if the child could repeat the whole set without compensatory movements from other muscle groups. 2 physiotherapists taught and supervised the training protocol and gave instructions to the child's parents about executing the exercises following hospital discharge, as well as giving a detailed written description of the exercises. The research team contacted the parents at home by telephone at least twice a month to clarify potential issues related to the training and to learn of possible adverse effects.</p>
Unger (2005)	<p>Individually designed circuit training: 1–3 times a week for 8 weeks in school hours. Individually designed in consultation with the children's therapists to ensure correct selection exercises. The training program included a 5-min warm-up on a stationary bicycle and 8-12 exercises (selected for each subject from a 28-station circuit targeting upper and lower limbs and trunk). The circuit was completed at the subject's own pace, with self-selected speed for each exercise. Movements had to be controlled and smooth. Exercises were progressive according to guidelines by McArdle et al. (1996). Initial resistance was set to allow at least one set of 6–10 repetitions. When 3 sets of 12 repetitions were reached resistance was increased and repetitions reduced. This process was repeated as soon as the subject could complete 3 sets of 12 repetitions. Resistance was provided by body weights or free weights (dumbbells, ankle and wrist cuff weights, elastic and rubber bands).</p>

Dodd (2003, 2004)	<p>Strength-training: Target muscle groups were ankle plantar flexors, knee extensors and hip extensors. The program included: "1) bilateral heel raises in which the participant stood on the edge of a stable, light-weight portable step (height 20cm) and raised and lowered his or her heels through the full available range, 2) bilateral half squats in which from a standing position, the participant slowly squatted until knees were flexed to between 30 and 60 degrees. A large inflatable ball (55cm diameter) was placed between the lower back of the participant and the wall to help guide and standardize the exercise; 3) step-ups where the participant stepped onto and off portable steps." The training load was adjusted by adding free weights to a backpack worn by the participants to ensure optimal strengthening benefit. Once the initial load was determined, participants were instructed to complete three sets of 8 to 10 repetitions of each exercise, 3 times a week.</p> <p>Control group: continued normal daily activities, including school and sport. Participants were also able to attend their normal physiotherapy program, provided therapy did not include a progressive resistance exercise program.</p>
Cardiovascular fitness and aerobic programs	
Chad (1999)	<p>Physical activity program: Each session: exercise for upper extremities 20min, lower extremities 20 min, truncal region 20 min; exercise focused on the facilitation of normal movement and weight-bearing activities.</p>
Van den Berg-Emons (1998)	<p>Physical training: Activities consisted of predominantly aerobic exercises: cycling, wheelchair driving, running, swimming, training on "flying-saucer", and mat exercises. Four times per week above the normal school and therapy program. Therapy program was according to personal needs (varied from 0 to 2.5 hrs/week for all children included in the study).</p>
Constraint induced therapy	
Charles (2006)	<p>CI-therapy with a sling: The intervention was provided on 10 out of 12 consecutive days during summer or school vacations (typically 2 weeks of weekdays) with groups of 2–4 children. Children wore a sling on the non-involved upper extremity for the 6 hour-session. After the session the sling was removed. The sling was strapped to the child's trunk and the distal end was sewn shut to prevent use of the non-involved hand.</p>
Taub (2004)	<p>CI-therapy with a cast: 2 components: 1) child's less-impaired upper extremity was casted from upper arm to fingertips by using a lightweight fiberglass cast. The cast was bivalved to enable easy weekly removal to check skin integrity and allow range of motion, 2) intensive treatment (shaping) for the involved upper extremity for 6 hours each day for 21 consecutive days. Training procedures: Shaping involved presenting interesting and useful activities to the child that provided immediate rewards. When a new skill emerged the therapist proceeded to shape this by increasing demands in quality. "Tasks such as reaching, grasping, holding, manipulating an object, bearing weight on the arm, and making hand gestures were divided into their small component skills, which were worked on individually and later chained together to comprise a target activity. The CI therapist also incorporated everyday tasks (e.g. dressing/undressing, eating, bathing, and grooming). Parents were encouraged to join in therapy-related activities and encourage their child to use newly acquired skills when the therapist was not present. When a child showed signs of fatigue, frustration, or reduced interest, the therapist adapted the activities but did not cease the therapy. Rest intervals were given as needed." On average, a child participated in at least 2 distinct upper extremity activities each hour. The therapist was responsible for ensuring that the full dose of 6 hours of active treatment per day was provided.</p> <p>Control group: continued their participation in conventional PT and/or OT, which was established earlier. After 6 weeks the control group crossed over to receive CI-therapy for 21 days.</p>

Sensorimotor training programs	
Bumin (2001)	<p>Sensory-perceptual-motor training (SPM) protocol: 1) sensory systems input activities (wheelbarrow hand walk, swimming/drying off); 2) activities for body awareness (window game, body pushing); 3) vestibular system activities (swing, jumping on a trampoline, climbing the wall bar); 4) tactile system activities (stereo gnosis training, textured road); 5) motor planning activities (statue spinning, mystery writing); 6) balance and postural responses activities (balance activities used were: two knees and two hands, two hands and one foot, two elbows and one knee, two knees and kneel hand push); postural responses and ocular control activities (ball catch, two person ball catch, ball foot toss, throwing a ball into a basket and a target); 8) bilateral motor co-ordination and motor planning (Inchworm art, stick ball); 9) visual spatial perception (matching the geometric shapes, puzzle activities); 10) fine motor skills and motor planning (bead stringing, pegboard activities, writing at different positions, tear art on knee position, button up, knotting, design copying); 11) right - left discrimination training; and 12) standing and walking training. Also home program (not specified).</p> <p>Control group: home training, not specified.</p>
Balance training	
Ledebt (2005)	<p>Balance training: static and dynamic tasks on a force plate in 30-minute sessions, 3 sessions per week for 6 weeks (a total of 18 sessions). "The force plate was displayed as a square (40x40cm) on a vertical screen (2.5x2.5m), situated at a distance of 1.3m in front of the child standing at the center of the force plate. The center of pressure was represented by a red dot. The children were required to either keep the dot within a target area located directly in front of them at an eye height that corresponded to the center of the base of support (static task), or to move the dot towards successive positions occupied by the target area (dynamic tasks). Three dynamic tasks were performed: a) a "circle task", in which the target areas appeared at regular distances along a circular path in either a clockwise or counter-clockwise direction, b) a "random task", in which the targets appeared at unpredictable places, and c) a "lateral weight-shifting task", in which the target area moved continuously to and from the center and either to a position to the left or right of the center. During the latter task the distance was gradually increased. The distance was also progressively increased from one trial to the next when the participant was able to reach the most distant located target." The children wore their own shoes including ankle-foot orthoses or insoles that corrected leg-length discrepancies.</p>
Therapy with animals	
Benda (2003)	<p>Hippotherapy: 2 trained therapy horses with similar stride lengths, one small and one medium size were selected for the study in order to accommodate both the smaller and larger children. The horse was tacked with a fleece pad and flat surcingle (a belt to secure pad), and the child was mounted on the horse sitting forward astride the fleece. A horse handler led the horse on a designated track at a steady walk for 4 minutes clockwise and 4 minutes counterclockwise. A physical therapist and assistant walked aside the horse but no postural support was provided.</p> <p>Stationary barrel: made from a 55-gallon drum approximating the girth of horse, was covered with the fleece and mounted on supports at the approximate height of an average horse. A television with VCR was mounted in front of the barrel to encourage the child to maintain forward attention and quiet sitting. The child sat astride the barrel, as he would on a horse with three assistants in identical places to previously.</p>
MacKinnon (1995)	<p>Horseback riding: focused on the development of functional riding skills, basic horse and stable knowledge, and skills at games on horseback. Children in the mild group rode using saddles and were encouraged to use reins, holding one in each hand. The children in the moderate group rode on saddle pads with surcingles.</p>

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

First author, year; length of intervention (follow-up)	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
Comprehensive physiotherapy programs						
Bar-Haim 2006		I: NDT with Adeli suit		C: NDT		
4 wk (1mo, 10mo)	1) GMFM-66	54.0 (SEM 4.0)	1mo: 1.0* 10mo: 0.7	52.2 (SEM 3.0)	1mo: 0.7 10mo: 1.9*	NS
	2) Metabolic cost of stair climbing (mechanical efficiency index, units are 100xkg. m per beat)	12.7 (SEM 3.5)	1mo: 2.4 10mo: 6.9*	11.1 (SEM 5.0)	1mo: 1.4 10mo: 2.0	10 mo: I > C (p=.0004)
Tsoralakis 2004		I: Intensive NDT (5xwk)		C: NDT (2xwk)		
16 wk	1) GMFM -88 (% points, scale 0–100), Total score	77.36 (15.89) [range 44.43–97.07]	16wk: 2.63	80.31 (15.15) [range 52.46–98.65]	16wk: 1.69	NA
	2) GMFM -66 (% points, scale 0–100), Total score	62.17 (12.24) [range 44.03–84.05]	16wk: 2.36*, Paired t-test, t=5.433 (P<0.001)	65.85 (14.47) [range 45.91–87.99]	16wk: 1.18*; Paired t-test, t = 4.449 (p<0.001)	I > C (Cohen's d effect size 0.8, p=.018)
	3) Improvement in GMFM -88 (score over 1.825 clinically significant)		10 out of 17		7 out of 17	NA
Ketelaar 2001		I: Functional PT (n=28)		C: Previous PT continued (n=27)		
6 mo (12mo, 18mo)	1) GMFM (% points, scale 0–100)					
	- Standing	82.8 (15.7)	6mo: 3.1 12mo: 5.7 18mo: 7.8	81.2 (20.3)	6mo: 5.9 12mo: 6.4 18mo: 9.6	6 mo: I > C (p=.01) 18mo: I > C (p=.01)
	- Walking, running, jumping	70.2 (18.2)	6mo: 6.5 12mo: 13.9 18mo: 16.3	70.8 (24.4)	6mo: 5.5 12mo: 11.3 18mo: 14.0	6mo: I > C (p=.04) 18mo: NS
	2) PEDI functional skills (scale 0–100)					
	- Self-care	68.3 (14.9)	6mo: 3.6 12mo: 8.4 18mo: 11.4	67.3 (10.1)	6mo: 3.0 12mo: 4.4 18mo: 9.2	6mo: NS 18mo: I > C (p=.01)
	- Mobility	78.2 (11.3)	6mo: 2.2 12mo: 7.9 18mo: 9.9	75.8 (11.6)	6mo: 0.9 12mo: 4.1 18mo: 5.4	18mo: I > C (p<.05)
	3) PEDI caregiver assistance					
	- Self-care	58.7 (13.7)	6mo: 4.3 12mo: 12.7 18mo: 15.2	59.2 (11.6)	6mo: 1.4 12mo: 7.3 18mo: 9.1	6mo: NS 18mo: I > C (p<.01)
	- Mobility	72.7 (13.7)	6mo: 6.1 12mo: 13.7 18mo: 16.0	74.0 (15.7)	6mo: 3.7 12mo: 7.9 18mo: 10.4	6mo: NS 18mo: I > C (p<.05)

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
Bower 2001						
		I: Aim-directed therapy (n=28)		C: Goal-directed therapy (n=27)		
6 mo (9mo, 12 mo, 18mo)	1) GMFM total score (% points, scale 0–100)	No data	12 mo: 4.4	No data	12 mo: 4.6	NS
	2) GMPM total score (% points, scale 0–100)	No data	6 mo: 2.9	No data	6 mo: 1.8	NS
	3) MPOC (scale 0–7)					
	- Enabling and partnership	5.4 (1.5)	6 mo: 0.1 12mo: -0.3	5.7 (1.4)	6mo: 0 12mo: -0.2	NA
	- Providing general information	3.0 (1.6)	6 mo: 0,5 12mo: 0.6	3.4 (2.0)	6mo: 0,5 12mo: 0.4	NA
	- Providing specific information	5.3 (1.6)	6 mo: 0,1 12mo: -0.3	5.4 (1.6)	6mo: 0,2 12mo: -0.3	NA
	- Coordinated comprehensive care	6.0 (1.2)	6 mo: -0,1 12mo: -0.2	5.5 (1.5)	6mo: 0,3 12mo: 0	NA
	- Respectful and supportive care	5.7 (1.4)	6 mo: 0,1 12mo: -0.1	6.0 (1.3)	6mo: 0,1 12mo: -0.2	NA
Bower 1996						
		I: Conventional PT+aims (n=11)		C1: Intensive PT+aims (n=11)		
2 wk	1) GMFM (Number of aims set and improved / deteriorated >1.825% points)	No of aims set	No of aims improved/ deteriorated	No of aims set	No of aims improved/ deteriorated	NS
	- Lying & rolling	2	0/1	3	2/0	
	- Sitting	4	2/2	7	4/1	
	- Crawling & kneeling	1	0/1	0	0/0	
	- Standing	4	1/3	5	3/0	
	- Walking, running, jumping	2	1/0	4	2/0	
	- Total score (% points, SD)	36.3 (17.9)	2	31.9 (21.5)	2	
		C2: Conventional PT+goals (n=11)		C3: Intensive PT+goals (n=11)		
	1) GMFM (Number of aims set and improved / deteriorated >1.825 % points)	No of goals set	No of goals improved/ deteriorated	No of goals set	No of goals improved/ deteriorated	NS
	- Lying & rolling	1	1/0	4	3/1	
	- Sitting	9	8/1	7	6/1	
	- Crawling & kneeling	0	0/0	2	1/0	
	- Standing	3	2/1	6	5/0	
	- Walking, running, jumping	2	1/0	2	1/0	
	- Total score (% points, SD)	32.4 (16.2)	2	39.8 (21.2)	4	

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
Palmer 1990, 1988		I: NDT		C: Infant stimulation + NDT		
12 mo	1) HOME (45 items)					
	- Emotional and verbal responsiveness of mother	8.16	12mo: 1.20	8.87	12mo: 0.32	I > C p=0.04 (95% CI 0.13 to 1.63)
	- Avoidance of restriction and punishment	5.88	12mo: 0.0	6.00	12mo: -0.18	NS
	- Organization of the physical and temporal environment	5.08	12mo: -0.12	5.13	12mo: -0.18	NS
	- Provision of appropriate play materials	5.88	12mo: 1.88	5.78	12mo: 1.86	NS
	- Maternal involvement with child	4.2	12mo: 0.6	4.65	12mo: 0.14	NS
	- Opportunities for variety in daily stimulation	2.64	12mo: 1.0	2.96	12mo: 0.64	NS
	- Total score	31.8	12 mo:3.32	33.39	12mo: 2.59	NS
	2) The Mother-Child Relationship Evaluation (48 items)					
	- Acceptance	40.12	12mo: 1.0	41.83	12mo: 2.14	NS
	- Overprotection	36.76	12mo: -1.52	35.65	12mo: -2.00	NS
	- Overindulgence	33.52	12mo: -1.20	33.09	12mo: -1.32	NS
	-Rejection	35.68	12mo: 0.12	33.35	12mo: 0.77	NS
	3) Carey Infant Temperament questionnaire					
	- Activity	3.04	12mo: 0.08	3.70	12mo: 0.64	NS
	- Rhythmicity	3.72	12mo: 0.24	3.43	12mo: -0.36	NS
	- Adaptability	6.84	12mo: -1.52	6.57	12mo: -1.36	NS
	- Approach	4.92	12mo: -0.36	4.39	12mo: -0.59	NS
	- Threshold	8.20	12mo: -0.04	7.35	12mo: 0.09	NS
	- Intensity	11.12	12mo: 2.00	12.04	12mo: 0.14	NS
	- Mood	8.00	12mo: -0.64	7.22	12mo: -0.64	NS
	- Distractibility	4.00	12mo: 0.44	3.17	12mo: 0.27	NS
	- Persistence	3.72	12mo: 0.28	3.91	12mo: -0.86	NS
	4) Bayley Scales of Infant Development					
	- Motor quotient	53.0 (8.5)	6mo: -3.8 12mo: -5.0	53.0 (9.4)	6mo: +5.1 12mo: +9.6	6mo: C > I (95% CI -16.2 to -1.7, p=0.02) 12mo: C > I (95% CI -24.2 to -5.1, p<0.01)
	- Mental quotient	62.0 (15.6)	6mo: +3.6 12mo: +5.0	66.1 (18.3)	6mo: +9.4 12mo: +9.0	6mo: C > I (95% CI -11.5 to -0.1, p=0.05) 12mo: NS

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
	5) VABS					
	- Social quotient	60.9 (15.4)	6mo: 67.8 (19.0) 12mo: 67.5	65.2 (17.1)	6mo: 12mo:	6mo: NS 12mo: NS
	6) Attained motor skills (% of children attaining skill)					
	- Roll from supine to prone position	83	6mo: 100 12mo: 100	87	6mo: 95 12mo: 100	NS
	- Sit tripod	70	6mo: 92 12mo: 100	78	6mo: 96 12mo: 100	NS
	- Sit alone	61	6mo: 83 12mo: 92	65	6mo: 91 12mo: 91	NS
	- Creep in prone position	56	6mo: 96 12mo: 100	56	6mo: 96 12mo: 95	NS
	- Crawl on hands and knees	9	6mo: 56 12mo: 88	9	6mo: 65 12mo: 77	NS
	- Come to sitting position	0	6mo: 54 12mo: 80	0	6mo: 61 12mo: 86	NS
	- Pull to standing position	17	6mo: 62 12mo: 92	4	6mo: 78 12mo: 86	NS
	- Cruise	9	6mo: 58 12mo: 84	9	6mo: 74 12mo: 86	NS
	- Walk with one hand held	0	6mo: 33 12mo: 52	0	6mo: 48 12mo: 77	NS
	- Walk independently	0	6mo: 12 12mo: 36	0	6mo: 35 12mo: 73	6mo: NS 12mo: C > I (p=0.01)
	- Walk backward	0	6mo: 4 12mo: 20	0	6mo: 4 12mo: 45	NS
Upper extremity treatment						
Wallen 2007						
		I: OT		C: No extra OT		
12 wk (2 wk, 3mo, 6mo)	1) COPM (scale 0-10)	3.5±1.3	3mo: 2.1±1.7 (95% CI 1.2-3.0)	3.2±0.7	3mo: 1.2±1.2 (95% CI 0.6-1.8)	NS
	-Performance scores		6mo: 2.7±1.8 (95% CI 1.8-3.6)		6mo: 1.7±1.5 (95% CI 0.8-2.6)	
	-Satisfaction scores	3.6±1.5	3mo: 2.5±1.9 (95% CI 1.6-3.5) 6mo: 3.3±2.2 (95% CI 2.2-4.5)	4.0±2.1	3mo: 1.4±1.4 (95% CI 0.6-2.1) 6mo: 2.1±1.7 (95% CI 1.1-3.2)	NS
	2) Goal Attainment Scale (normalized T scores, whereby a score of 50 means that goals, on average, are achieved)	Goals identified	3mo: 42.2±10.6 (95% CI 26.8-47.7) 6mo: 51.4±11.1 (95% CI 45.7-57.1)	Goals identified	3mo: 32.9±10.3 (95% CI 27.2-38.7) 6mo: 51.6±12.0 (95% CI 33.4-47.9)	3mo: NA 6mo: I>C (p=.054)
	3) Melbourne Assessment of unilateral upper limb function	No data	3mo: No data	No data	3mo: No data	NS
	4) QUEST (dissociated movement, grasp, protective extension, weight bearing, scale -12 to 106)	No data	No data	No data	No data	NS

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
	5) PEDI (scale 0-100) -Functional skills -Caregiver assistance	No data	No data	No data	No data	NS
	6) CHQ	No data	No data	No data	No data	NS
	7) Tardieu scale (Proportion of potentially available change of spasticity at each muscle group that was actually achieved)					
	- Elbow flexors	No data	2we: -4.8±42.6 (95% CI -29.5-19.8) 3mo: -3.0±26.2 (95% CI -17.5-11.5) 6mo: -12.7±86.9 (95% CI 59.0-33.6)	No data	2we: -15.0±89.6 (95% CI -79.1-49.1) 3mo: 28.2±29.9 (95% CI 10.9-45.4) 6mo: 28.1±36.6 (95% CI 4.8-51.4)	NS
	- Pronators	No data	2we: -12.3±37.5 (95% CI -33.1-8.4)	No data	No data	NS
	8) ROM passive elbow flexors and pronators	No data	No data	No data	No data	NS
	9) ROM active supination	No data	6mo: +1.5	No data	6mo: -19.5	I > C (p=.008)
	10) Parent questionnaire (rating of the child's arm compared with baseline: much worse, a bit worse, much the same, a bit better, much better)	-	2we: 3mo: 6mo:	-	2we: 3mo: 6mo:	NA
Law 1997		I: Intensive NDT+casting		C: Regular OT		
4 mo	1) PDMS-FM	20.4 (9.0)	4mo: 1.4	19.2 (8.6)	4mo: 1.7	NS
	2) QUEST	51.3 (22.3)	4mo: 2.0	41.5 (25.3)	4mo: 5.8	NS
	3) COPM performance scores	3.2 (1.5)	4mo: 3.3	3.4 (1.0)	4mo: 2.3	NS
Law 1991		I: Intensive NDT+ cast		C1: Intensive NDT		
6 mo (9 mo)	1) PDMS-FM (age equivalent in mo)	30.3 (13.2)	6mo: 5.26 9mo: 6.33	25.0 (17.5)	6mo: 3.11 9mo: 3.24	NS NS
	2) QUEST (percentage score)	61.9 (21.9)	6mo: 4.89 9mo: 4.1	47.1 (26.4)	6mo: 0.8 9mo: 1.55	I, C2 > C1, C3 (p=0.03) NS
	3) ROM (wrist extension)	No data	No data	No data	No data	I, C2 > C1, C3 (p=0.02)

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
		C2: Regular NDT + cast		C3: Regular NDT		
	1) PDMS-FM (age equivalent in mo)	30.6 (18.4)	6mo: 3.05 9mo: 2.44	27.3 (20.3)	6mo: 3.44 9mo: 4.94	
	2) QUEST (percentage score)	43.9 (25.7)	6mo: 7.02 9mo: 6.11	45.8 (29.6)	6mo: 1.34 9mo: 1.47	
	3) ROM (wrist extension)	No data	No data	No data	No data	
Hallam 1996		I: prehensile hand treatment + NDT		C1: NDT 2xweek		
6mo	1) GMDS					
	- Chronological age in mo	18.3 (.352)	6mo: +6	18.3 (.387)	6mo: -6.1	NS
	- Mental age in mo	12.1 (4.58)	6mo: +5.1	12.5 (4.29)	6mo: +5.6	NS
	- Locomotor score	60 (23.2)	6mo: +3	59 (24.3)	6mo: +9	I, C1 > C2 (p<0.000)
	- Personal-social score	73 (25.6)	6mo: 0	78 (22.7)	6mo: +4	C1 > C2 (p<0.0010)
	- Hearing-speech score	73 (21.8)	6mo: +5	76 (21.3)	6mo: +6	I, C1 > C2 (p<0.005)
	- Eye-hand co-ordination score	67 (25.6)	6mo: +1	64 (28.4)	6mo: +7	I, C1 > C2 (p<0.001)
	- Performance	63 (25.7)	6mo: +8	67 (24.6)	6mo: +9	I, C1 > C2 (p<0.003)
	- Total: developmental quotient (average of all sub-quotients)	66 (23.4)	6mo: +5	68 (21.1)	6mo: +7	I, C1 > C2 (p<0.002)
	2) Hand-grip force (Dynamometer)	(n=21)		(n=17)		
	- Median peak power	No data	No data	No data	No data	NA
		C2: NDT 1xweek				
	1) GMDS					
	- Chronological age in mo	18.4 (.392)	6mo: +5.9			
	- Mental age in mo	11.3 (4.56)	6mo: +1.6			
	- Locomotor score	50 (28.7)	6mo: -9			
	- Personal-social score	65 (25.1)	6mo: -4			
	- Hearing-speech score	68 (27.4)	6mo: -8			
	- Eye-hand co-ordination score	51 (28.1)	6mo: -3			
	- Performance	57 (24.8)	6mo: -5			
	- Developmental quotient (average of all sub-quotients)	58 (24.1)	6mo: -6			
	2) Hand-grip force (Dynamometer)	(n=13)				
	- Median peak power	No data	No data			

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
Strength training programs						
Liao 2007		I: Home-based Loaded sit-to stand exercise		C: No extra exercise		
6 wk	1) GMFM-88, dimensions D, E	76.6±4.4	+3.2	83.1±3.2	+0.4	I > C (Effect size 1.17, p=0.02)
	2) Gait speed (m/min, self selected speed, 10m distance)	56.9±5.1	+1.5	63.8±3.0	-1.8	NS
	3) Maximum load of the loaded sit-to-stand test (kg, 1-RM of the max load the child is capable of carrying while standing up 1 time from a sitting position without falling)	9.6±1.6	+3.9	11.3±1.8	+0.9	I > C (Effect size 1.78, p=0.001)
	4) Maximum knee extensor strength (average torque of 3 separate trials of both legs)	5.3±0.8	+0.7	5.7±1.1	+0.7	NS
	5) PCI (difference between the resting and walking heart rates divided by the walking speed)	1.14±0.14	-0.13	1.02±0.09	+0.05	I > C (Effect size 1.34, p=0.005)
Patikas 2006 a,b		I: Strength training + PT		C: No training + PT		
9 mo	1) MAS (0-4 nominal scale)	No data	6mo: 95% CI -1.1 to -0.3* 12mo: 95% CI -1.1 to -0.3*	No data	6mo: 95% CI -1.0 to -0.2* 12mo: 95% CI -1.0 to -0.3*	NS
	2) Knee extension deficit (°)	-5.0±9.8	6mo: -1.1±4.4 12mo: -1.1±4.7	-5.0±8.3	6mo: -0.3±6.6 * 12mo: -0.5±8.6	NS
	3) Knee flexion (°)	No data	6mo: 95%CI -14.2 to 2.1 12mo: 95%CI -12.3 to -0.0*	No data	6mo: 95% CI -19.4 to -3.6* 12mo: 95% CI -12.4 to -0.4*	NS
	4) Knee ROM (°)	No data	6mo: 95% CI -10.9 to 6.7 12mo: 95% CI -9.7 to 5.2	No data	6mo: 95% CI -15.4 to 1.9 12mo: 95% CI -9.1 to 5.4	NS
	5) GMFM (% points)	No data		No data		NS
	- Standing (% of maximum)	No data	6mo: no data 12mo: 95%CI -8.5 to 5.0	No data	6mo: no data 12mo: 95%CI 6.1 to 19.3*	NS
	- Walking, running, jumping (% of maximum)	No data	6mo: no data 12mo: 95%CI -13.0 to -0.4*	No data	6mo: no data 12mo: 95%CI -5.5 to 6.9	NS

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
	- Total score	No data	6mo: no data 12mo: 95%CI -4.8 to 1.1	No data	6mo: no data 12mo: 95%CI 0.7 to 6.5*	NS
	6) Oxygen consumption	No data	No data	No data	No data	NS
	7) Energy expenditure index (heart beats/min)	No data	No data	No data	No data	NS
	8) Gait analysis	No data	No data	No data	No data	NS
	- Walking speed (cm/s), stance phase duration (% of gait cycle), stride duration (s), stride length (cm), normalcy index, max. hip extension, min. knee flexion during terminal swing, max. plantarflexion during stance-swing transition, max. hip power absorption (W/kg), max. knee power absorption during loading response (W/kg), max. plantarflexion moment (Nm/kg), max. plantarflexion power generation (W/kg)					
Unger, 2005		I: Circuit training		C: No training		
9 wk	1) 3D gait analysis (free speed)					
	- Knee angle at mid-stance phase (°)	19.3 (10.1)	-1.5	19.1 (5.5)	+0.1	NS
	- Ankle angle at mid-stance phase (°)	-8.6 (6.1)	+0.9	-9.6 (2.2)	-1.4	NS
	- Hip angle at mid-stance phase (°)	20.1 (8.9)	-1.7	14.6 (7.7)	+1.2	NS
	- Sum of ankle, knee and hip angles at mid-stance (°)	49.7 (16.9)	-4.9	43.4 (14.3)	+2.6	I > C (p value unclear)
	- Knee angle at heel strike (°)	26.7 (6.6)	-1.3	26.6 (6.7)	-1.4	NS
	- Velocity (mm/s)	1075.6 (235.4)	+43.7	1128 (132.0)	+43.4	NS
	- Stride length (mm/s)	1111.9 (207.3)	+17.5	1112.8 (149.2)	+31.1	NS
	- Cadence (steps/min)	114.6 (15.1)	+2.3	119.2 (11.6)	+3.9	NS

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
	2) Self-perception (questionnaire, 11 items)					
	- Body image (composite score/30)	23.9 (4.1)	+2	23.2 (4.6)	-0.9	I > C (p value unclear)
	- Functional competence (composite score/25)	19.9 (3.4)	+1.4	19.3 (3.2)	+1.5	NS
Dodd 2003, 2004		I: Home-based strength-training		C: Normal daily activity		
6 wk (18w)	1) Hand-held dynamometer (Nicholas Manual Muscle Test), kg					
	- Ankle plantar flexors	11 (15.8)	6wk: 0.1 18wk: 5.6	17.5 (13.1)	6wk: -2.1 18wk: -3.7	NA
	- Knee extensors	27.5 (10.9)	6 wk: 5.6 18wk: 5.0	23.7 (11.5)	6wk: 1.8 18wk: 1.5	NA
	- Hip extensors	7.9 (7.6)	6wk: 2.7 18wk: 2.9	8.5 (8.4)	6wk: 3 18wk: 2.1	NA
	- Ankle plantar flexion+knee extensors	38.5 (23.2)	6wk: 5.7* 18wk: 10.7*	41.1 (20.0)	6wk: -0.2 18wk: -2.2	6wk: I > C (p=.046) 18wk: I > C (p=.041)
	- Total extensors (combined ankle plantar flexor knee extensor, and hip extensor strength)	46.5 (29.6)	6wk: 8.3* 18wk: 13.5*	49.6 (25.9)	6wk: 2.8 18wk: -0.1	NS
	2) GMFM (results are presented in % of 13 items, scale 0-100)					
	- Standing	75.2 (14.4)	6wk: 4.9 18wk: 5.2	74.6 (20.9)	6wk: 5.9 18wk: 6.1	NS
	- Running, walking, jumping	52.8 (31.3)	6wk: 4.4 18wk: 5.4	68.3 (30.1)	6wk: 1.2 18wk: -0.5	NS
	- Sum score of standing and running, walking, jumping	64.2 (27.8)	6wk: 4.8 18wk: 5.4	71.7 (24.9)	6wk: 3.6 18wk: 2.6	
	3) Self-selected walking speed (standardized instructions, m/min)	47.4 (23.3)	6wk: 0.6 18wk: 1.2	49.5 (24.5)	6wk: 1.0 18wk: 1.9	NS
	4) Timed stair test (s)	27.4 (34.7)	6wk: -6.3* 18wk: -2.3	22.4 (20.5)	6wk: -0.7 18wk: -2.7	NS
	5) Self-Perception Profile for Children (scale 0-4)					
	- Scholastic competence	3.33 (0.32)	6wk: -0.23 18wk: -0.16	2.57 (0.7)	6wk: 0.29* 18wk: 0.32*	6wk: C > I (p=.04) 18wk: C > I (p=.016)
	- Social acceptance	3.22 (0.79)	6wk: -0.09 18wk: -0.01	2.72 (0.62)	6wk: 0.32* 18wk: 0.64*	NS 18wk: C > I (p=.03)
	- Athletic competence	2.46 (0.8)	6wk: 0.07 18wk: -0.05	2.38 (0.81)	6wk: 0.33* 18wk: 0.45*	NS
	- Physical appearance	3.25 (0.63)	6wk: 0.17 18wk: 0.02	3.26 (0.6)	6wk: -0.17 18wk: 0.04	NS

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
	- Behavioral conduct	3.42 (0.45)	6wk: 0.21 18wk: 0.33	2.97 (0.59)	6wk: 0.04 18wk: 0.11	NS
	- Global self-worth	3.41 (0.38)	6wk: 0.14 18wk: 0.16	3.27 (0.52)	6wk: 0.06 18wk: 0.14	NS
Cardiovascular fitness and aerobic programs						
Chad 1999		I: Physical activity program		C: No program		
8 mo	1) Proximal femur BMC (g)	8.55 (1.32)	8mo: 0.98*, 11.5 %	6.79 (0.59)	8mo: 0.24, 3.5 %	NS
	2) Femoral neck BMC (g)	1.57 (0.18)	8mo: 0.15*, 9.6 %	1.37 (0.10)	8mo: -0.08, -5.8 %	I > C (p=.03)
	3) Femoral neck vBMD (g/cm³)	0.36 (0.02)	8mo: 0.02*, 5.6 %	0.32 (0.01)	8mo: 0.02, -6.3 %	I > C (p=.02)
Van den Berg-Emons 1998		I: Physical training program		C: No program		
9 mo	1) Level of daily physical activity	1.34 (0.25)	2mo: -0.03 9 mo: 0.21, +16%	1.24 (0.21)	2 mo: 0.10 9 mo: 0.10	NS
	2) Fat mass (kg)	8.1 (6.2)	2 mo: decreased 9 mo: no changes	5.7 (2.2)	2 mo: increased* 9 mo: +1.1 (SD 1.6)	I > C (p<0.05)
	3) Peak aerobic power Watt per kg fat-free mass (FFM)	0.91 (0.83)	2 mo: 0.11 9 mo: 0.32*, 35%, range -9 to 376, 12 mo: 0.11, -17%*	1.11 (0.96)	2 mo: -0.10 9 mo: 0.06 12 mo: 0.04	9mo: I > C (p=.05)
	4) Peak anaerobic power (watt per kg FFM)	2.16 (1.94)	2 mo: 0.16 9 mo: 0.32, +15% 12 mo: 0.25	2.35 (1.75)	2 mo: -0.09 9 mo: 0.25, +11%*	NS
	5) Mean aerobic power (watt per kg FFM)	1.77 (1.58)	2 mo: -0.01 9 mo: 0.20, +11% 12 mo: 0.13	1.92 (1.45)	2 mo: -0.04 9 mo: 0.25, +13%* 12 mo: 0.2	NS
Constraint induced therapy						
Charles 2006		I: CI-therapy with a sling		C: No therapy		
1 wk (1mo, 6mo)	1) Jebsen-Taylor Test of Hand Function (modified, max time to complete tasks 720 seconds)	361.2 (205.4)	1wk: -82.7 1mo: -92.6 6mo: -88.7	314.2 (177.5)	1wk -13.2 1mo: -53.9 6mo: -17.2	1wk: I > C (effect size 0.3, p<.01) 1mo and 6mo: NS
	2) BOTMP (subtest 8: speed and dexterity)	4.8 (3.0)	1wk: +2.4 1mo: +2.8 6mo: +2.1	4.8 (3.7)	1wk: +0.4 1mo: +0.7 6mo: +1.5	1wk: I > C (effect size 0.4, p<.005) 1mo and 6mo: NS
	3) Caregiver Functional Use Survey (14 items, 6-point likert scale) - How frequently	2.6 (0.7)	1wk: +0.4 1mo: +0.7 6mo: +0.7	2.6 (0.6)	1wk: -0.3 1mo: -0.1 6mo: 0	1wk: I > C (effect size 0.3, p<.01) 1mo and 6mo: NA

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
	- How well	2.0 (0.5)	1wk: +0.5 1mo: +1 6mo: +0.9	2.2 (0.5)	1wk: +0.2 1mo: +0.1 6mo: +0.1	1wk: NS 1mo and 6 mo: I > C (Effect size 0.2, p<.01)
	4) Sensibility (two point discrimination)	7.5 (3.1)	1wk: -0.9 1mo: -1 6mo: +0.1	5.7 (3.2)	1wk: -1.3 1mo: -1.1 6mo: 0	NS
	5) Hand-grip force (hand-held dynamometer)	2.1 (2.0)	1wk: -0.1 1mo: -0.2 6mo: +0.3	2.2 (2.4)	1wk: -0.1 1mo: +0.7 6mo: -0.4	NS
	6) MAS					
	- Shoulder	0.5 (0.5)	1wk: -0.4 1mo: -0.1 6mo: -0.3	0.9 (0.8)	1wk: 0 1mo: -0.2 6mo: -0.1	NS
	- Elbow	1.3 (0.6)	1wk: -0.2 1mo: -0.1 6mo: -0.2	1.3 (1.0)	1wk: -0.2 1mo: -0.2 6mo: -0.1	NS
	- Wrist	1.2 (0.6)	1wk: 0 1mo: +0.1 6mo: 0	1.1 (1.0)	1wk: +0.4 1mo: +0.3 6mo: +0.5	NS
Taub 2004		I: Constraint-induced therapy		C: Early intervention program		
3 wk (3wk, 3mo, 6mo)	1) QUEST	No data		No data		NS
	1) Emerging Behaviors Scale (scale 0-31, number of new behaviors emerging)	12.2 (5.64)	3wk: 9.3 (range 7-12)	12.7 (6.5)	3wk: 2.3 (range 0-6)	I > C (p<.0001)
	2) Toddler Arm Use Test (22 tasks, 2wo raters, 4 scales: arm selection (R/L), amount of participation (0-2), how well 0-5, willingness (0-3), global rating 0-10.					
	- Increased first time use of the more impairment arm	No data	53.9% improved (SD 35.64)	No data	18% improved (SD 31.12)	NA
	- Overall independent functional use of the more-impaired arm	No data	16.8% improved (SD 21.53)	No data	5% improved (SD 15.4)	NA
	3) Pediatric Motor Activity Log (22 items, scale 0-5)					
	- Amount of use: "how often"	0.8 (0.44)	post treatment: 2.0 3wk: 1.8 3mo: 1.3 6mo: 1.6	1.1 (0.75)	post treatment: 0.1 3wk: 0.1	I > C (p<.0001)
	- Quality of use: "how well"	0.9 (0.62)	post treatment: 1.8 3wk: 1.7 3mo: 1.7 6mo: 1.8	1.6 (1.2)	post treatment: 0.3 3wk: 0.2	I > C (p<.0001)
	- Overall score					I > C (p<.0001)

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
Bumin 2001		I: SPM training individually		C1: SPM training in groups		
3 mo	1) ASCSIT					
	- Double tactile stimuli perception	29.13 (3.58)	-2.50 (3.31)		-1.50 (2.34)	NA
	- Localization of tactile stimuli, total score	22.71 (7.94)	6.77 (4.73)		5.48 (6.09)	NA
	- Graphesthesia, total score	9.13 (5.21)	-3.38 (2.03)		-3.13 (1.50)	NA
	- Kinesthesia, total score	51.51 (17.77)	-17.72 (13.75)		-6.04 (11.64)	NA
	- Finger identification	13.69 (2.82)	-1.19 (1.64)		-2.63 (3.42)	NA
	- Manual form perception	9.88 (0.50)	-0.13 (0.50)		-0.19 (0.54)	NA
	- Design copying	2.75 (5.13)	-2.13 (1.71)		-2.19 (2.10)	NA
	- Position in space	8.56 (5.46)	-1.81 (1.22)		-2.19 (2.90)	NA
	- Imitation of posture	2.81 (6.72)	-2.44 (2.06)		-3.06 (1.48)	NA
	- Motor accuracy	96.31 (31.64)	10.15 (17.24)		14.63 (15.07)	NA
	- Right-left discrimination	10.69 (5.67)	-2.94 (3.30)		-1.69 (2.00)	NA
	2) Physical Ability Test	90.50 (26.30)	-11.25 (24.30)		-3.94 (3.55)	NA
		C2: Home program				
	1) ASCSIT					
	- Double tactile stimuli perception	29.56 (5.27)	-0.78 (1.20)			
	- Localization of tactile stimuli, total score	28.39 (13.79)	-1.83 (4.49)			
	- Graphesthesia, total score	7.78 (6.92)	-0.44 (0.53)			
	- Kinesthesia, total score	58.78 (22.70)	4.24 (9.60)			
	- Finger identification	12.78 (3.49)	-0.89 (0.78)			
	- Manual form perception	9.22 (1.20)	-0.11 (0.33)			
	- Design copying	2.56 (3.40)	-0.11 (0.33)			
	- Position in space	8.67 (7.92)	0.00 (0.71)			
	- Imitation of posture	9.22 (7.24)	-0.67 (0.87)			
	- Motor accuracy	78.54 (43.39)	-10.37 (33.21)			
	- Right-left discrimination	9.78 (4.76)	0.22 (1.79)			
	2) Physical Ability Test	95.33 (14.20)	-2.44 (1.33)			

	Outcome measure	Intervention group		Control group		Statistical difference between the groups
		Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
Balance training						
Ledebt, 2005		I: Balance training		C: No training		
6-7 wk (10 wk)	1) Quiet stance on force plate (time, maximum amplitudes)					
	- Time on target during quiet standing	No data	No data	No data	No data	NS
	- Displacement in the forward direction	No data	No data	No data	No data	I > C (p=.01)
	- Displacement in the backward direction	No data	No data	No data	No data	I > C (p=.006)
	- Displacement toward the paretic side	No data	No data	No data	No data	NS
	- Displacement toward the non-paretic side	No data	No data	No data	No data	NS
	2) Dynamic stance on force plate (maximum amplitudes of COP displacement)					
	- Leaning forward	No data	No data	No data	No data	I > C (p=.003)
	- Leaning backward	No data	No data	No data	No data	I > C (p<.001)
	- Leaning toward the paretic side	No data	No data	No data	No data	I > C (p=.022)
	- Leaning toward the non-paretic side	No data	No data	No data	No data	I > C (p<.001)
	3) Step length (cm)‡					
	- Paretic leg	No data	No data	No data	No data	NS
	- Non-paretic leg	No data	No data	No data	No data	I > C (p=.017)
	4) Step length asymmetry (percentage of the average step length in forward swinging of both legs)	No data	No data	No data	No data	NA
Therapy with animals						
Benda 2003		I: Equine-assisted therapy (hippo therapy)		C: Stationary barrel		
8 min	1) Muscle asymmetry with EMG§	No data	8min: 55.5 (82.5), 64.6% (28.3)	No data	8min: 11.9 (29.9), 12.8% (88.8)	NS
Mackinnon 1995		I: Horseback riding, moderate		C1: No hippo therapy, moderate		
6 mo	1) GMFM (scale 0-100)					
	- Sitting	No data	-0.40	No data	2.00	NS
	- Standing	No data	0.40	No data	-0.50	NS
	- Walking	No data	0.40	No data	0.00	NS
	- Total score	No data	0.40	No data	1.50	NS
	2) Bertoti (posture measured in sitting position)	No data	1.20	No data	1.00	NS

Appendix G. Full details of the baseline values and changes on all measured outcomes of each trial. (Table continues)

Outcome measure	Intervention group		Control group		Statistical difference between the groups
	Mean baseline value (SD)	Mean change from baseline (SD)	Mean baseline value (SD)	Mean change from baseline (SD)	
3) BOTMP	No data	No data	No data	No data	NS
- fine motor, item 6					
- Fine motor, item 8	No data	No data	No data	No data	NS
4) PDMS-FM	No data		No data		
- Grasping	No data	1.80	No data	-0.50	I > C1 (p=.045)
- Hand use	No data	3.40	No data	1.25	NS
- Eye-hand coordination	No data	4.20	No data	4.50	NS
- Manual dexterity	No data	1.00	No data	2.25	NS
- Total score	No data	9.80	No data	8.50	NS
5) VABS - ADL	No data	-18.73	No data	-19.33	NS
- Socialization	No data	-3.00	No data	-5.75	NS
6) HSPC	No data	-3.00	No data	2.80	NS
7) CBC	No data		No data		NS
- Activities	No data	-0.70	No data	0.42	NS
- School	No data	0.63	No data	-0.25	NS
- Social	No data	-0.90	No data	0.13	NS
- Total prob	No data	-1.40	No data	-4.67	NS
- Total COMP	No data	-1.73	No data	-9.50	NS
	C2: Horseback riding, mild		C3: No hippo therapy, mild		
1) GMFM (scale 0-100)					
- Sitting	No data	-0.20	No data	-2.05	NS
- Standing	No data	1.40	No data	2.55	NS
- Walking	No data	0.60	No data	0.50	NS
- Total score	No data	1.40	No data	1.00	NS
2) Posture measured in sitting position¶	No data	-0.20	No data	-1.30	NS
3) BOTMP					
- Fine motor, item 6	No data	-0.75	No data	-1.67	NS
- Fine motor, item 8	No data	0.60	No data	5.33	NS
4) PDMS-FM	No data		No data		
- Grasping	No data	0.00	No data	0.60	NS
- Hand use	No data	0.40	No data	0.10	NS
- Eye-hand coordination	No data	2.60	No data	2.30	NS
- Manual dexterity	No data	0.20	No data	2.05	NS
- Total score	No data	3.20	No data	5.05	NS
5) VABS: - ADL	No data	-1.80	No data	-0.45	NS
- Socialization	No data	-2.80	No data	-5.40	NS
6) HSPC	No data	2.20	No data	3.55	NS
7) CBC	No data		No data		NS
- Activities	No data	1.00	No data	-0.62	NS
- School	No data	0.00	No data	-0.25	NS
- Social	No data	0.30	No data	-0.97	NS
- Total prob	No data	3.20	No data	2.40	NS
- Total COMP	No data	-7.0	No data	-10.0	NS

* Statistically significant difference to the baseline values in the within group analysis,

† total energy expenditure/sleeping metabolic rate or total energy expenditure/resting metabolic rate,

‡ distance of 2 successive foot contacts when swinging forward, calculated from the displacement of the COP along the progressive axis during walking,

§ asymmetry score for the muscle group most affected during the pretest activity in sitting, standing or walking, and the mean change in percentage (pre-test asymmetry score/post-test asymmetry score x 100). 16 surface electrodes (posterior cervical, posterior thoracic, posterior lumbar, adductor and abductor muscle groups of upper thigh) connected to 2 transmitters.

Absolute differences in mean microvolt readings between left and right-side individual muscle groups were calculated during sitting, standing and walking and recorded as asymmetry scores. The highest pre-test asymmetry score for the most affected muscle group for each child was used and compared with post-test value and converted into a percentage score.

¶ by a scale developed by Bertoti DB: Therapeutic riding conferences-Positive progress. In Proceedings of the 6th International Therapeutic Riding Congress; August 23-27; Toronto, Ontario. 1988: 400-405.

wk=week/s, mo=month/s, SD=standard deviation, SEM=standard error of mean, NDT=neurodevelopmental therapy, PT=physiotherapy, SPM=sensory perceptual motor, CI=confidence interval, NS= no statistically significant difference between the groups, I > C=Statistically significant difference in favor of the intervention group, C > I =Statistically significant difference in favor of the control group.

ASCSIT=Ayres Southern California Sensory Integration Test, BMC=Bone mineral density, vBMD = Volumetric bone mineral density, BOTMP=Bruininks-Oseretsky Test of Motor Proficiency, CHQ=Child health Questionnaire, CBC=Child Behavior Checklists, EMG=Electromyography, GMDS=Griffith's Mental Developmental Scales, GMFM = Gross Motor Function Measure, GMPM=Gross Motor Performance Measure, HOME=Home Observation for Measurement of the Environment, HSPC=Harter Self-perception Profile for Children, MAS=Modified Asworth Scale, MPOC=Measure of Processes of Care, PCI=Physiological Cost Index, PEDI=Pediatric Evaluation of Disability Inventory, PDMS-FM= Peabody Developmental Motor Scales Fine Motor, QUEST=Quality of Upper Extremity Skills Test, ROM=range of motion, VABS=Vineland Adaptive Behavior Scale.

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