Efficacy of intensive versus nonintensive physiotherapy in children with cerebral palsy: a meta-analysis

Carla Arpino[a], Maria Fenicia Vescio[b], Angela De Luca[a] and Paolo Curatolo[a]

A commonly used treatment for cerebral palsy in children is so-called 'conventional therapy', which includes physiotherapy or the neurodevelopmental approach. Although more intensive rehabilitative treatment is thought to be more effective than less intensive interventions, this assumption has not been proven. In this study we compared the efficacy of intensive versus nonintensive rehabilitative treatment in children with cerebral palsy. A meta-analysis of the studies published between January 1996 and July 2007 was performed. Inclusion criteria: infants/children/adolescents (1–18 years old); randomized controlled trials using, as outcome measure, the Gross Motor Function Measure score. Exclusion criteria: studies that included therapies not generally used in 'so-called' conventional treatment (i.e. constraint, taping). Treatment effects were combined using the weighted mean difference method. Fixed and random effect meta-analyses were carried out and results were compared. Heterogeneity was also assessed. Funnel plots were examined and the presence of small-study effects was tested. Intensive therapy tended to have a greater effect than nonintensive therapy (1.32; 95% confidence interval: 0.55–2.10). The effect of intensive treatment tended to be apparently stronger for children 2 years of age. Our meta-analysis shows that, in children with cerebral palsy, intensive conventional therapy may improve the functional motor outcome, but the effect size seems to be modest.

Eine häufig angewandte Behandlungsmethode bei infantiler Zerebralparese ist eine sogenannte 'konventionelle Therapie' mit Physiotherapie und/oder Vorgehensweise auf neurophysiologischer Grundlage. Auch wenn eine intensivere Rehabilitationsmaßnahme effektiver sein soll als weniger intensive Interventionen, so gilt diese Annahme als nicht belegt. In dieser Studie verglichen wir die Wirksamkeit von intensiven Behandlungsmethoden mit nicht-intensiven Rehamaßnahmen bei infantiler Zerebralparese. Eine Metaanalyse der zwischen Januar 1996 und Juli 2007 veröffentlichten Studien wurde durchgeführt. Einschlusskriterien: Kleinkinder/Kinder/Jugendliche (im Alter von 1–18 Jahren); kontrollierte, randomisierte Studien unter Zuhilfenahme des GMFM-Instruments, mit dem die körpermotorischen Fähigkeiten gemessen werden. Ausschlusskriterien: Studien mit Therapien, die i.d.R. nicht im Rahmen sogenannter 'konventioneller' Behandlungsmaßnahmen (d.Orthesen, Taping) angewandt werden. Die Auswirkungen der Behandlung wurden mittels der gewichteten mittleren Differenzmethode kombiniert. Metaanalysen mit Fixed- und Random-Effects-Modell wurden durchgeführt, und ihre Ergebnisse wurden verglichen. Ebenfalls untersucht wurde die Heterogenität. Man untersuchte Funnel-Plots und prüfte die Präsenz von Small-Study-Effects. Eine intensive Therapie erzielte i.d.R. eine größere Wirkung als eine nicht-intensive Therapie (1.32; 95% Konfidenzintervall: 0.55–2.10). Die Wirkung der intensiven Behandlung schien bei Kindern im Alter von zwei Jahren angeblich stärker. Unsere Metaanalyse verdeutlicht, dass eine intensive konventionelle Therapie bei Kindern mit Zerebralparese das funktionelle Motorikergebnis zwar verbessert, dass die Effektgröße aber eher bescheiden scheint.

Un tratamiento frecuentemente utilizado en niños con parálisis cerebral infantil se denomina «terapia convencional» en el cual se utiliza la psicoterapia o la terapia del neurodesarrollo, o ambas. Si bien se considera que el tratamiento de rehabilitación más intensivo resulta más eficaz que las intervenciones menos intensivas, esta hipótesis no se ha demostrado. En este estudio comparamos la eficacia del tratamiento de rehabilitación intensivo frente al no intensivo en niños con parálisis cerebral infantil. Se realizó un metaanálisis de los estudios publicados entre enero de 1996 y julio de 2007. Los criterios de inclusión fueron lactantes/niños/adolescentes (1 a 18 años de edad); ensayos aleatorizados de comparación en los que se utilizó como medida de los resultados la escala de medida del funcionamiento motor general. Los criterios de exclusión fueron: estudios en los que se utilizaron tratamientos no utilizados, forma general, en la llamada terapia convencional (esto es, restricción física, fijación con cinta adhesiva). Los efectos del tratamiento se combinaron utilizando el método de diferencia media ponderada. Se valoró también la heterogeneidad. Se estudiaron los gráficos en embudo y la presencia de efectos de estudios pequeños. Por lo general, el tratamiento intensivo solió tener un efecto mayor que el tratamiento no intensivo (1.32; intervalo de confianza de 95%: 0.55 a 2.10). El efecto del tratamiento intensivo solió ser aparentemente más fuerte en niños de 2 años de edad. Nuestro metaanálisis muestra que en los niños con parálisis cerebral infantil, el tratamiento intensivo convencional podría mejorar los resultados del funcionamiento motor, pero la magnitud del efecto parece ser moderada.

Un traitement couramment utilisé pour la prise en charge de la paralysie cérébrale chez l'enfant est la thérapie dite «conventionnelle» qui inclut la physiothérapie et/ou l'approche du développement neurologique. Bien que les

0342-5282 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/MRR.0b013e328332f617

traitements de rééducation plus intensifs soient souvent considérés plus efficaces que les interventions moins intensives, cette hypothèse n'a pas été avérée. Dans cette étude, nous avons comparé l'efficacité d'un traitement de rééducation intensif par rapport à un traitement non intensif chez les enfants atteints de paralysie cérébrale. Une méta-analyse des études publiées entre janvier 1996 et juillet 2007 a été effectuée. Critères d'inclusion : enfants en bas âge/enfants/adolescents(1 à 18 ans) ; des essais randomisés contrôlés utilisant comme mesure des résultats le score GMFM (Gross Motor Function Measure). Critères d'exclusion : les études incluant des thérapies n'étant pas généralement utilisées dans le traitement dit «conventionnel» (par exemple attaches, sangles et bandes). Les effets du traitement ont été combinés en utilisant la méthode de différence moyenne pondérée. Des méta-analyses d'effets fixes et aléatoires ont été effectuées, et les résultats ont été comparés. L'hétérogénéité a également été évaluée. Les tracés en entonnoir ont été examinés et la présence de petits effets dus à l'étude a été testée. La thérapie intensive a tendance à avoir un effet plus important que la thérapie non intensive (1.32 95 % intervalles de confiance : 0.55–2.10). L'effet du traitement intensif tend à être en apparence plus important pour les enfants de 2 ans. Notre méta-analyse montre que, chez les enfants atteints de paralysie cérébrale, la thérapie conventionnelle intensive peut améliorer les résultats fonctionnels moteurs, mais l'ampleur de l'effet semble modeste. ***International Journal of Rehabilitation Research*** **00:000–000 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

International Journal of Rehabilitation Research 2009, **00**:000–000

Keywords: cerebral palsy, children, intensive treatment, meta-analysis, physiotherapy

[a]Child Neurology Unit, Department of Neuroscience, University of Tor Vergata and [b]Epidemiology Unit, Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy

Correspondence to Professor Carla Arpino, MD, PhD, Department of Neurosciences, Pediatric Neurology Unit, Tor Vergata University of Rome, Via Montpellier 1, 00133 Rome, Italy
Tel: +39 06 20900249; fax: +39 06 20900018; e-mail: carla.arpino@uniroma2.it

Received 14 June 2009 **Accepted** 11 September 2009

Introduction

Cerebral palsy (CP) has complex causal pathways. The prevalence of CP is about 2.5% live births worldwide and tends to be higher among infants with an extremely low birth weight (< 1000 g) (Himpens *et al.*, 2008). The majority of children with CP present a disabling condition (i.e. there is a high rate of comorbidity for cognitive deficits, epilepsy, sensorineural disorders, and behavioural disorders), and they require rehabilitative treatment, in addition to pharmacological therapy for spasticity and comorbid disorders, toxin botulinum, and orthopaedic surgery (Andersen *et al.*, 2008; Venkateswaran and Shevell, 2008; Pueyo *et al.*, 2009).

Neuroplasticity, regeneration, and recovery represent the basic biological assumption for rehabilitation, and a growing number of small experimental studies (i.e. functional magnetic resonance imaging studies and animal models) have shown that plastic phenomena occur in the injured neuronal network, in the cerebral cortex, and in subcortical structures, at the synaptic and cellular level (Krägeloh-Mann, 2004; McQuillen and Ferriero, 2005; Di Filippo *et al.*, 2008). Although there exists some knowledge on the basic mechanisms underlying neuroplasticity, the strength of the effect of rehabilitative treatment needs to be defined. Nonetheless, the majority of children with CP are currently under treatment; in fact, children with CP are routinely referred for management/rehabilitation of their physical disability and there is a general consensus that such services should be available as a basic right in a caring society (Bax, 2003). In the past 10–15 years, the development of standardized outcome measures of change in gross motor functioning has contributed to the evaluation of the effects of rehabilitation. To this end, the Gross Motor Function Measure (GMFM) has proven to be a reliable and valid tool in children with CP (Russell *et al.*, 1993, 2000).

Conventional therapy for CP in children includes physiotherapy and neurodevelopmental approaches and may be administered in regimens of different intensity. Although it has been hypothesized that the effectiveness of conventional therapy in children with CP may depend on the intensity of treatment (i.e. with intensive regimens being more effective), this assumption is far from proven. We conducted a systematic review and meta-analysis of published studies to assess whether intensive 'conventional therapy' is more effective than nonintensive 'conventional therapy' in children with CP whose clinical outcome was assessed with the GMFM.

Methods

A meta-analysis of studies published between January 1996 and July 2007 was carried out.

Type of study: randomized controlled trial (RCT).

Type of participants: infant/children/adolescents (1–18 years old) affected by any type of CP.

Outcome measure: GMFM.

Definitions of 'intensive treatment' and 'conventional therapy'

With regard to 'intensive treatment', we first selected the manuscripts that mentioned the treatment intensity in

the title or abstract. In all but one study included in the meta-analysis, 'intensive' treatment was defined as any treatment provided more than three times per week; in a single study, additional sessions provided by an assistant defined the 'intensity' of the treatment. We defined as 'conventional therapy' that which included physiotherapy or a neurodevelopmental approach. We excluded studies that included practices not generally used in conventional therapy (i.e. constraint, taping).

Search methods

Only manuscripts written in English were considered. We used Medline and Embase to identify all RCTs published between January 1996 and July 2007, using extended terms for CP and rehabilitation/physical therapy/neurodevelopmental approach in infants/children/adolescents and GMFM. Reference lists of articles were also examined. Four RCTs fulfilled the inclusion criteria and were included in the meta-analysis.

Data extraction

Two reviewers independently selected articles and extracted the data. Controversies were solved by discussion. Data on the following study characteristics were extracted: author, date of publication, inclusion and exclusion criteria, country, study design, duration of the intensive treatment, mean (or median) age of the study population, mean values and standard deviations (SD) of the outcomes at baseline, mean values and SD of the outcomes at the end of follow-up, the number of persons for whom the outcome was assessed, GMFM change score, and SD of the GMFM change score. We also extracted data on the adequacy of the randomization and allocation concealment processes, the potential for selection bias, and the level of masking. The meta-analyses were based on change scores (differences between score at baseline and scores at points in time following the intervention).

Description of studies

Three of the four RCTs were conducted in the United Kingdom (Bower *et al.*, 1996, 2001; Weindling *et al.*, 2007) and one was conducted in Greece (Tsorlakis *et al.*, 2004). In the RCT conducted by Bower *et al.* in 1996, 44 children (number of males and females not specified) between the age of 3 and 11 years with confirmed diagnosis of quadriplegic CP were enrolled (Bower *et al.*, 1996). The paediatric superintendent physiotherapists of different health districts in England were invited to participate in the study, enrolling one child each. The study used a 2×2 factorial design. Children were observed for a period of 6 months and randomized into four treatment groups, each of which contained 11 children: (i) 2 weeks of conventional therapy; (ii) 2 weeks of intensive therapy; (iii) specific goals negotiated and 2 weeks of conventional therapy; and (iv) specific goals negotiated and 2 weeks of intensive therapy. The results from groups 2 and 4 (intensive therapy) were compared with those from groups 1 and 3 (nonintensive therapy). Intensive therapy was 1 h of individual treatment per day Monday to Friday.

In the RCT carried out by Bower *et al.* in 2001, 56 children (31 males and 25 females) between the ages of 3 and 12 years with bilateral CP were enrolled (Bower *et al.*, 2001). The children were randomized into the same four treatment groups used in the RCT conducted in 1996. Twenty-eight children received intensive treatment (groups 1 and 3) and 28 nonintensive treatment (groups 2 and 4). Intensive and nonintensive treatments were defined as 1 h of individual treatment per day Monday to Friday, and as conventional therapy.

In the RCT carried out by Weindling *et al.* 85 (52 males and 33 females) children who were not older than 4 years upon enrolment took part in the baseline assessment (Weindling *et al.*, 2007). The children had been referred to the study by their paediatrician or by the senior paediatric physiotherapist. A few parents self-referred in response to posters placed in toy libraries. Children were eligible if they had CP of perinatal origin that was predominantly spastic in type. If the brain damage causing CP occurred after the age of 6 months, the children were excluded. Children were randomly allocated to three groups: (i) nonintensive treatment in the routine manner used in their health centre ($n = 29$ children); (ii) intensive treatment for 6 months focused on the needs and goals of the individual child (conventional treatment and one extra session of physiotherapy lasting for around 1 h each week from a physiotherapy assistant; the extra session was done at home for most children) ($n = 31$ children); and (iii) family support on the basis of the parent adviser model ($n = 28$ children). The results from group 1 (nonintensive treatment) were compared with those from group 2 (intensive treatment).

The RCT of Tsorlakis *et al.* was carried out among 38 children (14 females and 24 males) between the ages of 3 and 14 years with an established diagnosis of CP which had been confirmed by a consultant (Tsorlakis *et al.*, 2004). The children were recruited from the Hellenic Society for Care and Rehabilitation of Children with Disability (Tessaloniki, Greece). They were assigned to two treatment groups: (i) nonintensive therapy for 16 weeks (two sessions a week for 50 min each session); and (ii) intensive therapy for 16 weeks (five sessions a week for 50 min each session).

Before randomization, the children were stratified on the basis of the following: their GMFM score and age in the two RCTs of Bower; (Bower *et al.*, 1996, 2001) the mother's education, patterns of spasticity and the geographical area where the treatment was performed in the RCT of Weindling; (Weindling *et al.*, 2007) and their

age, sex, and the distribution of their impairment in the RCT of Tsorlakis *et al.* (2004). In all RCTs, randomization was carried out by a person not otherwise involved in the study.

Before treatment, the conventional and intensive treatment groups were similar for the characteristics considered (e.g. sex, age) within each RCT. During follow-up, in the two RCTs of Bower and that of Tsorlakis, the groups remained similar, (Bower *et al.*, 1996, 2001; Tsorlakis *et al.*, 2004) whereas in the RCT of Weindling there was an unequal distribution in the number of multiple births (Weindling *et al.*, 2007).

The length of follow-up and number of evaluations varied, in particular, in 1996 Bower *et al.* performed only one evaluation, immediately after treatment, which lasted 2 weeks; (Bower *et al.*, 1996) for the 2001 RCT, they performed an evaluation after treatment, which lasted 2 weeks, and 6 months later; (Bower *et al.*, 2001) in the RCT of Weindling, evaluation was performed immediately after the intervention (which lasted 6 months) and at 12 and 18 months; (Weindling *et al.*, 2007) finally, in the RCT of Tsorlakis, evaluation was performed after the intervention (which lasted 16 weeks), though it was not specified exactly how many days after the intervention (Tsorlakis *et al.*, 2004). To facilitate comparisons, for the 2001 RCT of Bower *et al.* (2001) we only considered the first evaluation (i.e. that immediately following the 6 months of treatment). Similarly, for the RCT of Weindling *et al.* (2007) we only considered the data collected at the end of the 6 months of treatment (T2: short term effects of the intervention: the main analysis) because by the end of the 18-month follow-up period more than half of the study participants had been lost to follow-up.

With regard to drop-outs, there were none in the 1996 RCT of Bower *et al.* (1996) one in the 2001 RCT of Bower *et al.* (2001) 12 in the RCT of Weindling *et al.* (at the end of the intervention period), (Weindling *et al.*, 2007) and four in the RCT of Tsorlakis *et al.* (2004) Intention to treat analysis was performed in both of the RCTs of Bower *et al.* and in that of Weindling *et al.* (Bower *et al.*, 1996, 2001; Weindling *et al.*, 2007).

In all four RCTs, motor skill acquisition was assessed by an independent investigator who was blinded to the intervention group (Bower *et al.*, 1996, 2001; Tsorlakis *et al.*, 2004; Weindling *et al.*, 2007).

The results had not been adjusted for potential confounders, apart from those extracted from the 2001 article by Bower *et al.* (2001) which had been adjusted by age and severity of GMFM at baseline. When information was incomplete or missing, we contacted some of the authors (e.g. to verify that the two RCTs of Bower *et al.* were independent).

Statistical analyses

The mean difference between the intensive and conventional treatments was used as measure of effect. Fixed (inverse variance) and random effect meta-analyses were carried out, and the results were compared. Heterogeneity was assessed by the I^2 statistic. The possible reasons for heterogeneity were explored by meta-regression and stratified analyses (age less than 2 years and age of at least 2 years; treatment duration less than 60 days and treatment duration of at least 60 days). The presence of small study effects was visually assessed by funnel plots and formally tested by the Egger's regression and rank correlation tests (Sterne *et al.*, 2001).

Results

The type and severity of CP differed among the studies (Table 1). The pooled GMFM change score is reported in Fig. 1. The meta-analysis showed that the GMFM change score was higher for the intensive treatment group, compared with the nonintensive treatment group [difference of 1.32; 95% confidence interval (CI): 0.55–2.10]. There was no evidence of heterogeneity ($I^2 = 0$), though the effect of intensive treatment tended to be stronger for children who were 2 years of age or younger (difference of 5; 95% CI: −0.45–10.45). When the meta-analysis was restricted to studies of children greater than 2 years of age, the difference between the change scores for the two groups was 1.25 (95% CI: 0.47–2.03). In the RCTs in which treatment lasted less than 60 days, (Bower *et al.*, 1996) the GMFM change score did not vary (difference of 0.96; 95% CI: −0.71–2.63), whereas in the RCTs in which treatment lasted for at least 60 days, (Bower *et al.*, 2001; Tsorlakis *et al.*, 2004; Weindling *et al.*, 2007) it was higher in the intensive treatment group than in the nonintensive treatment group (difference of 1.42; 95% CI: 0.55–2.30). There was no evidence of small study effects (Begg's test: $P = 0.902$; Egger's test: $P = 0.630$).

Discussion

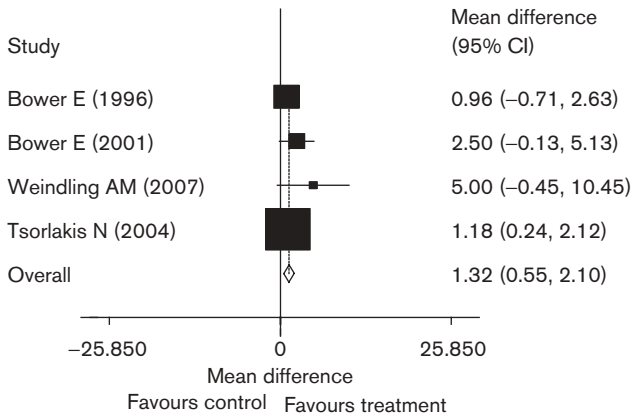
The evaluation of the efficacy of so-called 'conventional therapy' in children with CP is extremely important, since during their lifetime nearly all of these children undergo this type of therapy. This evaluation is even more crucial when considering intensive treatment, which is not only tiring and stressful for children and their families, with a consequent low compliance, but also rather expensive for national healthcare systems. The medical community concords that treatment should not only have an impact on impairment but also improve daily life functional activities and participation, as defined by the International Classification of Functioning, Disability and Health (World Health Organization, 2001). Full participation in society and equal opportunities should be a key concept in any rehabilitation policy

Table 1 Characteristics of randomized controlled trials included in the meta-analysis

Author	Country	Year of publication	Type of intervention	Length of intervention	Concealment of treatment allocation	Completeness of follow up (No. lost to follow-up)	Blinding of outcome measures	No. partici-pants	Mean age (months)	CP type[a]	CP severity
Bower *et al.* (1996, 2001)	UK	1996	Conventional therapy	14	Yes	0	Yes	44	72	Bilateral CP	NA
Bower *et al.* (1996, 2001)	UK	2001	Conventional therapy	180	Yes	1	Yes	56	72	Bilateral CP	Level III: 17 Level IV: 29 Level V: 10
Weindling *et al.* (2007)	UK	2007	Conventional therapy	180	Yes	12	Yes	88	19,75	Hemiplegia 33 Diplegia 18 tetraplegia 36	NA
Tsorlakis *et al.* (2004)	Greece	2004	Conventional therapy	112	Yes	4	Yes	38	86	Hemiplegia 10 Diplegia 12 Tetraplegia 12	Level I: 10 (six hemiplegia, four diplegia) Level II: 10 (six diplegia, four hemiplegia) Level III: 14 (two diplegia, 12 quadriplegia)

CP, cerebral palsy.
[a]According to the classification used by the authors.

Fig. 1



Test for heterogeneity: $Q = 2.79$ (d.f. = 3), $P = 0.425$
I^2 (% variation attributable to heterogeneity) = 0.0%

Gross Motor Function Measure change score and 95% confidence intervals (CI) for children with cerebral palsy. Summary estimates were obtained using a fixed-effect model. Squares are proportional to the amount of information contributed; 95% CI are represented by the horizontal line. Overall results are represented in diamond shape. d.f., degree of freedom.

(Brodin and Fasth, 2001). Moreover, quality of life should be adequately assessed and monitored (Bullinger *et al.*, 2002).

The results of our meta-analysis, in which the functional outcome of intensive and nonintensive conventional therapy was compared, show a modest effect in favour of children who underwent intensive therapy (i.e. a change of 1.32 on GMFM score). However, the clinical significance of this difference is unclear. According to the GMFM-88 manual (Russell *et al.*, 1993) an increase of 1.82% points seems to be the smallest change of clinical importance according to parents' perception. The studies considered in the meta-analysis included different types and severity of CP and did not mention comorbidity for perceptual/cognitive disorders, which might influence motor function. Thus, considering that treatment outcome may vary depending on the severity of CP and comorbidity, whether the change of 1.32 on GMFM score represents the true extent of the effect of intensive treatment remains to be determined. If the effect of therapy was small, only trials including homogeneous types of CP, also in terms of the presence of comorbidity, might be able to detect it. In the 1996 RCT of Bower *et al.* (Bower *et al.*, 1996) there was an advantage of about four percentage points conferred by 2 weeks of intensive treatment. In the 2001 RCT of Bower *et al.* (Bower *et al.*, 2001) it was hypothesized that, if the effect observed after 2 weeks consisted of a true gain in motor skills, and not simply a 'ceiling effect' (i.e. raising of the child's motor ability to the ceiling of his/her day-to-day range of ability), a gain of at least 15% points would have been expected after 6 months of treatment. Given that the 2001 RCT (Bower *et al.*, 2001) showed no effect in that direction, the authors interpreted their results as a 'ceiling effect' and not as a true acquisition of motor skills. This can now be seen as misleading, as typical motor progress of children in therapy can be viewed on the GMFM motor growth curves and percentiles, and

gains of 15 points or more within some motor levels at the ages the children were tested would be very unlikely (Hanna *et al.*, 2008).

Regarding the intensity of treatment, most studies included in the meta-analysis defined 'intensive treatment' as that which was provided more than three times a week during the trial, though intensity could be defined in different ways, also including the total length of exposure to therapy even before the trail. In fact, in our opinion, early initiation of therapy may be considered as a proxy of higher intensity. We were not able to study the potential effect of early exposure to therapy because only Bower (Bower *et al.*, 1996, 2001) stratified, before randomization, for the length of time the child had been undergoing physiotherapy; in the other two RCTs, (Tsorlakis *et al.*, 2004; Weindling *et al.*, 2007) no information on participation in the earlier therapeutic programmes was available.

Precise information on the number of sessions per week was lacking for one study. However, we decided to include the study in the meta-analysis since a definition of 'intensive' treatment was provided (i.e. additional sessions provided by an assistant). Moreover, the difference in the GMFM change score between the intervention and the control group did not change after including or excluding this study, being 1.32 (95% CI: 0.55–2.10) and 1.25 (95% CI: 0.47–2.03), respectively.

Our results suggest that the effect of intensive therapy is stronger for children who are 2 years of age or younger. However, this affirmation is based on the results of a single study only (Weindling *et al.*, 2007) which, together with the lack of information on therapy before enrolment in the RCT, did not allow us to answer the question of whether 'earlier' means 'better'.

Finally, not all the studies included in the meta-analysis specified whether or not the children were, or had been, exposed to other forms of treatment, such as pharmacologic therapy for spasticity, orthopaedic surgery or the use of specific treatment modalities (e.g. splint, casting). However, Tsorlakis *et al.* (2004) excluded children who underwent pharmacologic therapy or orthopaedic surgery, whereas Bower *et al.* (1996, 2001) conducted the data analysis by first including and then excluding children exposed to these interventions, and the results did not differ.

Although our results show evidence of a modest effect of intensive conventional therapy, it is important to stress that, as mentioned by Weindling, the maintenance of the GMFM score (i.e. an absence of worsening) could also be seen as a satisfactory outcome in children affected by severe CP (Weindling *et al.*, 2007). In our meta-analysis, more than 50% of the children enrolled in the RCTs of Bower (Bower *et al.*, 1996, 2001) and about 41% of those in the RCT of Weindling (Weindling *et al.*, 2007) presented severe CP; only in the RCT of Tsorlakis *et al.* (2004) did the majority of children have mild CP (i.e., 59% of patients were classified as level I and II), and of note is the finding that the greatest effect in favour of intensive therapy was observed in this RCT. It should also be mentioned that, by limiting the meta-analysis to RCTs that used the GMFM as the outcome measure, we excluded studies that report positive results in favour of intensive conventional therapy using other scales (Mayo, 1991) Moreover, the use of GMFM as outcome measure does not provide information on daily life functional activities and participation, as defined by WHO (World Health Organization, 2001). This limit should be addressed by further studies. Finally, publication bias deriving from selective exclusion of trials with negative results cannot be ruled out.

In conclusion, the results of our meta-analysis suggest that there is limited evidence to support additional physiotherapy. However, because of the limited number of studies, rather than considering these results as proof that intensive conventional therapy is poorly effective compared to routine physiotherapy, this meta-analysis may be considered as a useful exercise in identifying areas in which additional research is needed.

Acknowledgement

The authors wish to thank Mark Kanieff for useful suggestions and editing.

References

Andersen GL, Irgens LM, Haagaas I, Skranes JS, Meberg AE, Vik T (2008). Cerebral palsy in Norway: prevalence, subtypes and severity. *Eur J Paediatr Neurol* **12**:4–13.

Bax MC (2003). Management of physical disability. *Dev Med Child Neurol* **45**:435.

Bower E, McLellan DL, Arney J, Campbell MJ (1996). A randomised controlled trial of different intensities of physiotherapy and different goal-setting procedures in 44 children with cerebral palsy. *Dev Med Child Neurol* **38**:226–237.

Bower E, Michell D, Burnett M, Campbell MJ, McLellan DL (2001). Randomized controlled trial of physiotherapy in 56 children with cerebral palsy followed for 18 months. *Dev Med Child Neurol* **43**:4–15.

Brodin J, Fasth A (2001). Habilitation, support and service for young people with motor disabilities. A Swedish perspective. *Int J Rehabil Res* **24**:309–316.

Bullinger M, Schmidt S, Petersen C, DISABKIDS Group (2002). Assessing quality of life of children with chronic health conditions and disabilities: a European approach. *Int J Rehabil Res* **25**:197–206.

Di Filippo M, Tozzi A, Costa C, Belcastro V, Tantucci M, Picconi B, Calabresi P. (2008). Plasticity and repair in the post-ischemic brain. *Neuropharmacology* **55**:353–362.

Hanna SE, Bartlett DJ, Rivard LM, Russell DJ (2008). Reference curves for the gross motor function measure: percentiles for clinical description and tracking over time among children with cerebral palsy. *Phys Ther* **88**:596–607.

Himpens E, Van den Broeck C, Oostra A, Calders P, Vanhaesebrouck P (2008). Prevalence, type, distribution, and severity of cerebral palsy in relation to gestational age: a meta-analytic review. *Dev Med Child Neurol* **50**:334–340.

Krägeloh-Mann I (2004). Imaging of early brain injury and cortical plasticity. *Exp Neurol* **190** (**Suppl 1**):S84–S90.

Mayo NE (1991). The effect of physical therapy for children with motor delay and cerebral palsy. A randomized clinical trial. *Am J Phys Med Rehabil* **70**:258–267.

McQuillen PS, Ferriero DM (2005). Perinatal subplate neuron injury: implications for cortical development and plasticity. *Brain Pathol* **15**:250–260.

Pueyo R, Junqué C, Vendrell P, Narberhaus A, Segarra D (2009). Neuropsychologic impairment in bilateral cerebral palsy. *Pediatr Neurol* **40**: 19–26.

Russell DJ, Rosenbaum P, Gowland C, Hardy S, Lane M, Plews N, *et al.* (1993). *Gross motor function measure manual*. Hamilton: McMaster University.

Russell DJ, Avery L, Rosenbaum P, Raina P, Walter S, Palisano R (2000). Improved scaling of the gross motor function measure for children with cerebral palsy: evidence of reliability and validity. *Phys Ther* **80**:873–885.

Sterne JAC, Bradburn MJ, Egger M (2001). Meta-Analysis in STATA. In: Egger M, Davey Smith G, Altman DG, editors. *Systematic reviews in health care, meta-analysis in context*. London: BMA Books; pp. 346–347.

Tsorlakis N, Evaggelinou C, Grouios G, Tsorbatzoudis C (2004). Effect of intensive neurodevelopmental treatment in gross motor function of children with cerebral palsy. *Dev Med Child Neurol* **46**:740–745.

Venkateswaran S, Shevell MI (2008). Comorbidities and clinical determinants of outcome in children with spastic quadriplegic cerebral palsy. *Dev Med Child Neurol* **50**:216–222.

Weindling AM, Cunningham CC, Glenn SM, Edwards RT, Reeves DJ (2007). Additional therapy for young children with spastic cerebral palsy: a randomised controlled trial. *Health Technology Assessment* **11**:1–71.

World Health Organization (2001). *International Classification of functioning, disability and health (ICF)*. Geneva, Switzerland: World Health Organization.