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[Intervention Review]

# Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

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## ABSTRACT

### Background

Delayed motor development may occur in children with Down syndrome, cerebral palsy or children born preterm, which in turn may limit the child's opportunities to explore the environment. Neurophysiologic and early intervention literature suggests that task-specific training facilitates motor development. Treadmill intervention is a good example of locomotor task-specific training.

### Objectives

To assess the effectiveness of treadmill intervention on locomotor motor development in pre-ambulatory infants and children under six years of age who are at risk for neuromotor delay.

### Search methods

In March 2011 we searched CENTRAL (*The Cochrane Library* 2011, Issue 1), MEDLINE (1948 to March Week 2, 2011), EMBASE (1980 to Week 11, 2011), PsycINFO (1887 to current), CINAHL (1937 to current), Science Citation Index (1970 to 19 March 2011), PED*ro* (until 7 March 2011), CPCI-S (1990 to 19 March 2011) and LILACS (until March 2011). We also searched ICTRP, ClinicalTrials.gov, *m*RCT and CenterWatch.

### Selection criteria

We included randomised controlled trials, quasi-randomised controlled trials and controlled clinical trials that evaluated the effect of treadmill intervention in children up to six years of age with delays in gait development or the attainment of independent walking or who were at risk of neuromotor delay.

### Data collection and analysis

Four authors independently extracted the data using standardised forms. Outcome parameters were structured according to the "Body functions" and "Activity and Participation" components of the International Classification of Functioning, Disability and Health, Children & Youth version (ICFCY), which was developed by the World Health Organization.

**Main results**

We included five studies, which reported on treadmill intervention in 139 children. Of the 139 children, 73 were allocated to treadmill intervention groups, with the other children serving as controls. The studies varied in the type of population studied (children with Down syndrome, cerebral palsy or who were at risk for neuromotor delay); the type of comparison (for example, treadmill versus no intervention, high intensity treadmill versus low intensity); the time of evaluation (during the intervention or at various intervals after intervention), and the parameters assessed. Due to the diversity of the studies, we were only able to use data from three studies in meta-analyses and these were limited to two outcomes: age of onset of independent walking and gross motor function.

Evidence suggested that treadmill intervention could lead to earlier onset of independent walking when compared to no treadmill intervention (two studies; effect estimate -1.47; 95% confidence interval (CI): -2.97, 0.03), though these trials studied two different populations and children with Down syndrome seemed to benefit while it was not clear if this was the case for children at high risk of neuromotor disabilities. Another two studies, both in children with Down syndrome, compared different types of treadmill intervention: one compared treadmill intervention with and without orthotics, while the other compared high versus low intensity treadmill intervention. Both were inconclusive regarding the impact of these different protocols on the age at which children started to walk.

There is insufficient evidence to determine whether treadmill intervention improves gross motor function (two studies; effect estimate 0.88; 95% CI: -4.54, 6.30). In the one study evaluating treadmill with and without orthotics, results suggested that adding orthotics might hinder gross motor progress (effect estimate -8.40; 95% CI: -14.55, -2.25).

One study of children with Down syndrome measured the age of onset of assisted walking and reported those receiving the treadmill intervention were able to walk with assistance earlier than those who did not receive the intervention (effect estimate -74.00; 95% CI: -135.40, -12.60). Another study comparing high and low intensity treadmill was unable to conclude whether one was more effective than the other in helping children achieve supported walking at an earlier age (effect estimate -1.86; 95% CI: -4.09, 0.37).

One study of children at high risk of neuromotor disabilities evaluated step quality and found a statistically significant benefit from treadmill intervention compared to no treadmill intervention (effect estimate at 16 months of age: -15.61; 95% CI: -23.96, -7.27), but was not able to conclude whether there was a beneficial effect from treadmill training on step frequency at the same age (effect estimate at 16 months of age: 4.36; 95% CI: -2.63, 11.35). Step frequency was also evaluated in children with Down syndrome in another study and those who received high intensity rather than low intensity treadmill training showed an increased number of alternating steps (effect estimate 11.00; 95% CI: 6.03, 15.97).

Our other primary outcome, falls and injuries due to falls, was not measured in any of the included studies.

**Authors' conclusions**

The current review provided only limited evidence of the efficacy of treadmill intervention in children up to six years of age. Few studies have assessed treadmill interventions in young children using an appropriate control group (which would be usual treatment or no treatment). The available evidence indicates that treadmill intervention may accelerate the development of independent walking in children with Down syndrome. Further research is needed to confirm this and should also address whether intensive treadmill intervention can accelerate walking onset in young children with cerebral palsy and high risk infants, and whether treadmill intervention has a general effect on gross motor development in the various subgroups of young children at risk for developmental delay.

## PLAIN LANGUAGE SUMMARY

**Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay**

Children who have a diagnosis of Down syndrome or cerebral palsy, or who are born pre-term, may be delayed in their motor development. Delays in motor development limit children's ability to move and achieve motor milestones such as walking, running and jumping. Helping children to walk is often the focus of therapeutic intervention. There is a body of literature to suggest that the best way to do this is by getting the child to practice stepping with appropriate support. Treadmill training, in which the child is supported by a harness, provides an opportunity for children to walk with support for long enough periods of time to acquire the necessary motor abilities for independent walking.

This review included five trials involving children under six years of age with, or at risk for, neuromotor delay. The findings suggest that treadmill training may help children with Down syndrome to walk earlier than they would without the intervention. However, for

children with cerebral palsy and for pre-term infants, the evidence is not clear due to a lack of studies and differences in their design and focus. This makes it difficult to draw conclusions about treadmill interventions. Further investigation of the effects of treadmill training on children under six years of age, particularly pre-term infants and children with cerebral palsy, is essential in order to determine whether it can accelerate the onset of walking and improve motor development.

# BACKGROUND

## Description of the condition

### Typical gross motor development

The World Health Organization (WHO) describes the gross motor development of infants as the attainment of six gross motor milestones. These are: (1) sitting without support; (2) crawling on hands and knees; (3) standing with assistance; (4) walking with assistance; (5) standing alone, and (6) walking alone. Approximately 86% of children with typical development attain all six milestones, though the sequence of attainment may vary. For instance, crawling on hands and knees is the most variable milestone; it is observed at different ages during the infant's development and is sometimes even skipped. While infants are learning these temporary means of locomotion, they are gradually becoming able to support increasing amounts of weight while in a standing position until they eventually begin to walk at around 12 months of age. Attainment of this ultimate milestone has the widest age range at between eight and 18 months of age (WHO 2006) and may depend on various environmental factors, such as sensory or motor stimulation.

### Developmental delay

The *International Classification of Functioning, Disability and Health for Children and Youth* (ICFCY) (WHO 2005) describes developmental delay as retardation in the achievement of developmental milestones. The most plausible cause of the motor delay is an alteration in the typical development and function of the central nervous system. Motor delays in locomotor abilities are defined by standards used in clinical paediatric settings. For example, the onset of independent walking should occur prior to 18 months of corrected age, so the presence of a motor delay would not be considered before this age. Developmental delay in infants is usually diagnosed via routine screening (Case-Smith 1998) and/or the use of norm-referenced tests and/or criterion-referenced tests. Kinetic and kinematic analysis using force plates and video motion analysis may be used to further specify the delay; brain imaging techniques may be used to elucidate the etiology of the delay. Although used for both research and clinical purposes, the tests are typically not good predictors for later outcomes and generally lack sensitivity in detecting small changes in motor development (Heineman 2008). In addition, in the paediatric population the reliability of some of these tests may be affected by the child's emotional state, by daily fluctuations in performance or by the experience of the tester. Due to the continuous developmental changes occurring in the young brain, early diagnostic tests are relatively limited in predicting developmental outcomes (de Graaf-Peters 2006) and the high level of variation in motor developmental trajectories in healthy children means that care has to be taken when interpreting results from motor assessments (Roze 2010).

### Consequences of motor developmental delay

One of the major tasks in gross motor development is locomotion, the ability to move from one place to another (Bly 1995). The failure to attain walking or the late attainment of walking has consequences for the musculoskeletal system. The anatomy of the hip, for instance, needs weight bearing for proper bone growth and correct orientation of the femoral head, as well as for a correct alignment of the spine (Campbell 2006). As well as its importance for subsequent motor skill development, acquiring the ability to locomote is important for infants because of its impact on cognitive, social and emotional skills. Researchers have demonstrated that for infants with typical development, experience with locomotion is associated with the development of a broad array of cognitive skills, including the onset of wariness of heights; the concept of object permanence (objects hidden from sight still exist); a shift from self-centred to landmark-based spatial coding strategies; the ability to follow the pointing gestures and gaze of another person, and aspects of social referencing and detour reaching (Bertenthal 1984; Kermoian 1988; Campos 1989; Bertenthal 1990). This suggests that infants are better able to develop spatial cognition and learn about the world around them as they become able to locomote independently. Children who can walk independently show improved active exploration of their environment, as opposed to children who passively observe the environment when being held or carried through space. Rosenbloom 1971 further suggests that the quality of movement may affect subsequent development. He proposes that inefficient locomotion may hamper development by limiting the attention and energy that infants spend on explo-

ration of the environment. Moreover, early locomotor experiences may have a larger impact on the developing brain than similar experiences at a later age due to the brain's high plasticity during the first few postnatal years (Webb 2001; de Graaf-Peters 2006). Earlier achievement of developmental milestones, in particular independent walking, have also been associated with better intellectual performance in adulthood (Murray 2007). In summary, independent locomotion at early age not only facilitates the infant's motor development, but also impacts other developmental domains and affects quality of life for the child and his or her family (Lepage 1998).

### Population affected

There are various reasons for delays in typical motor development. Disorders affecting motor development during infancy include Down syndrome, cerebral palsy, spina bifida and a broad range of other neuromuscular disorders (Campbell 2006).

In addition, preterm birth, defined as childbirth occurring at less than 37 weeks or 259 days gestation (Beck 2010), is associated with a series of risk factors that make children vulnerable to delays in their developmental process (Formiga 2011). For instance, children who are born prematurely have higher rates of cerebral palsy, sensory deficits and learning disabilities compared with children born at term (Beck 2010).

The incidence of preterm birth rate is 6.2% in Europe, 6.4% in Australia and 10.6% in North America (excluding Mexico) (Beck 2010) and the incidence of cerebral palsy is 1.5 to 2 per 1000 live births (Surveillance CP Europe). However, more epidemiological studies are needed to reliably assess the incidence for cerebral palsy as its causes are not fully understood (Lie 2010). Approximately one in 800 children in the USA are born with Down syndrome, while the incidence in the UK is one in 1000 (Down's Syndrome Association).

## Description of the intervention

According to some authors, high levels of motor activity are the key to motor development (Adolph 1998; Damiano 2006). In order to best influence neural plasticity, it is important that any training is performed early in development and that it is specific to the task the child needs to master (Hodgson 1994; Blackman 2002). Intervention studies examining infants developing in a typical and atypical way show that task-specific training may best facilitate the development of postural control (Hadders-Algra 1996; Sveistrup 1997; de Graaf-Peters 2007).This concept of task-specificity can be considered an evidence-based concept based on neuroscientific principles (Hodgson 1994).

Although the optimal window of intervention within the motor domain is not clear (Nelson 2000), it is reasonable to think of independent walking as a motor task that needs to be achieved by six years of age if long-term negative effects are to be minimised.

Locomotor treadmill interventions, with or without partial weight support, have been used to promote the acquisition of independent walking in children with Down Syndrome (Looper 2006; Cherng 2007) and cerebral palsy (Richards 1997; Begnoche 2007; Mattern-Baxter 2009).

Protocols of treadmill interventions described in the literature vary with regard to training speeds, support provided, manual assistance with stepping, and frequency and duration of the intervention. In studies of infants, the majority had training speeds ranging from 0.1 m/s to 0.22 m/s (Davis 1994); whereas, older children were trained at higher speeds of 1.8 m/s (Begnoche 2007). The percentage of body weight used as partial weight support varied across studies and was provided either manually (the infant is supported under the arms, with the feet resting on the treadmill surface, bearing as much weight as comfortable) (Ulrich 2001), or with a commercially available pelvic harness or trunk harness, or both (Dodd 2007; Provost 2007). Only a few studies quantified the amount of body weight support provided during training (Schindl 2000; Meyer-Heim 2007; Provost 2007; Mattern-Baxter 2009). Training duration ranged between two weeks (Phillips 2007; de Bode 2007; Provost 2007) and 57 weeks (Ulrich 2001), with some studies including breaks during the training programme (Day 2004; Prosser 2007; Cernak 2008). Frequency of the training sessions varied between studies from two to six training sessions per week (Damiano 2009; Mattern-Baxter 2009a). Manual facilitation of gait varied from no assistance with leg advancement to assistance from up to three physical therapists (Mattern-Baxter 2009a).

In summary, the existing scientific literature exhibits wide variation in the parameters of treadmill interventions, indicating a need for systematic establishment of intervention protocols. Furthermore, research found in paediatric populations has used the treadmill for both prevention and rehabilitation purposes. Its use as a preventive tool mainly relates to infants who have no prior walking experience; whereas training in rehabilitation would be directed towards infants or children who, having walked independently, need to retrain that skill after injury/physical dysfunction and/or who need to improve their walking parameters.

## How the intervention might work

It is well established that brain plasticity exists and is particularly pronounced in the young nervous system (NS) (Stiles 2000; Stiles 2005). Experience-dependent and/or activity-dependent plasticity has been demonstrated in the human nervous system (Edgerton 1997; Eyre 2003) and postural control intervention studies (Harbourne 2003). The capacity for the nervous system to reorganise is one of the fundamental mechanisms by which therapeutic interventions may be effective.

The treadmill is one form of intervention used in physical therapy to enhance the locomotor capabilities of patients (Eng 2007; Verschuren 2008); however, most of the scientific knowledge related to this topic comes from animal models (already since the pio-

neering work of Sir Charles Scott Sherrington; Sherrington 1910) or interventions in adult human populations (Sullivan 2007). In fact, the use of treadmill interventions for people with neurological disorders has its roots in animal studies (Eidelberg 1980; Barbeau 1987) where adult cats were able to regain stepping skills after a complete lesion of the spinal cord. The underlying mechanism by which this technique is effective is thought to reside in the regenerating capacity (plasticity) of the central nervous system when task-specific motor practice is provided. Voluntary exercise and treadmill interventions specifically have been utilised in humans and in animal models to promote central nervous system (including spinal cord) plasticity and functional change (Jones 1999; Cotman 2002; Cotman 2002a). The underlying neuronal mechanisms responsible for such change are thought to be up-regulation of trophic factors, neurogenesis, synaptogenesis, pre- and post-synaptic modulation and angiogenesis, among others. These plasticity mechanisms are particularly active during early development. These neuroscience principles are the basis of the current motor learning theories (Newell 1991; Kleim 2008).

Plausible positive outcomes from treadmill interventions via central nervous system plasticity have been proposed in infants with Down syndrome and premature infants. Evidence from studies with children who have Down syndrome indicate statistically significant improvements in a variety of outcome measures including obstacle negotiation and onset of walking. For this population, two main benefits from treadmill interventions implemented during early development have been described. Firstly, it promotes the transition to continuous alternating steps in infants (including typically developing infants (Thelen 1986; Thelen 1991)), which is an important precursor to walking (Ulrich 1992; Ulrich 1995; Ulrich 2001). Secondly, it leads to an acceleration of the onset of independent walking and an improvement of the quality of gait (Ulrich 2001).

Observational studies suggest that infants born prematurely follow similar developmental trajectories to their full-term peers, although frequently with some delay (Luo 2009; Angulo-Barroso 2010). The neonatal period of preterm infants is stressful as the immaturity of vital physiological functions, such as respiration, blood pressure control, and autoregulation of cerebral blood flow, makes it difficult for the infant to adapt to the extrauterine situation. This results in vulnerability to delay in motor development and to developmental disorders (Goyen 2002; Pin 2010; Prins 2010; Formiga 2011), a vulnerability which in part is mediated by detectable lesions of the brain (Volpe 2009). The evidence available on the effect of treadmill interventions for this population is almost non-existent. A case study of a premature infant showed an increase in the number of steps, of which almost 100% were exclusively alternating steps, during the post-training phase (Bodkin 2003). However, encouraging as these results may seem, evidence of the effectiveness of treadmill interventions remains inconclusive.

### Why it is important to do this review

The importance of children attaining independent walking has been well documented. A range of interventions to improve motor development in children is currently used in practice (Riethmuller 2009). However, research on early interventions for children with physical disabilities is very limited and most studies have methodological limitations (Ziviani 2010).

Treadmill interventions are now being used in rehabilitation to prevent walking problems with children under six years of age. This intervention could have significant benefits in terms of preventing gross motor delays, promoting cognitive and social development, and promoting correct biomechanical function during gait. It is important to evaluate the effectiveness of treadmill training as an early intervention method designed to improve motor function and to prevent neuromotor delays in children.

Diagnoses that may result in a delay in the acquisition of walking (Down syndrome, cerebral palsy, among others) have different intrinsic characteristics. Because of this, a differentiation of interventions or parameters specific to the diagnosis may be required, indicating the need to perform subgroup analyses.

There are several existing systematic reviews on treadmill interventions in paediatric populations (Damiano 2009; Mattern-Baxter 2009a; Mutlu 2009; Willoughby 2009; Molina-Rueda 2010). However, these reviews evaluated published reports from 1980 to 2008 on treadmill training for children aged up to 21 years. In addition to their reliance on published reports in English, their search strategy did not include terms of specific diagnoses that are known to cause gross motor delay in childhood, and some were limited to children with cerebral palsy (Mattern-Baxter 2009a; Mutlu 2009; Willoughby 2009; Molina-Rueda 2010).

To date, there is no systematic review of treadmill intervention that examines its effectiveness on children before or during the acquisition of independent walking, and that encompasses both prevention and rehabilitation. A systematic review of the literature is needed in order to define the extent of the preventive and rehabilitative effectiveness of treadmill training, and to define optimal training parameters for this intervention.

This review aims to fill this gap and to review all relevant studies, irrespective of publication status or language.

## OBJECTIVES

To assess the effectiveness of treadmill interventions on locomotor motor development in pre-ambulatory infants and children under six years of age who are at risk of neuromotor delay.

## METHODS

## Criteria for considering studies for this review

### Types of studies

Randomised controlled trials, quasi-randomised controlled trials (that is, where participants are allocated in a way that is not strictly speaking random, such as by alternation or date of birth) and controlled clinical trials (that is, trials where random allocation seems likely to have occurred but is not explicitly stated).

### Types of participants

Children up to six years of age with delays in gait development or the attainment of independent walking (children who cannot walk independently by the age of 18 months), or who are at risk of neuromotor delay (primarily with non-progressive neurological disorder), however diagnosed.

We excluded children diagnosed with a condition for which physical activity is contraindicated, for example, infants with genetic degenerative diseases such as neuromuscular dystrophy (and those with diagnoses that preclude independent walking).

### Types of interventions

Treadmill intervention of any type, frequency or intensity aimed at (1) improving gait parameters such as walking speed, endurance, quality of step (how the foot lands on the floor surface) or (2) facilitating onset of independent walking or walking with assistance. Comparison groups received no treatment or another treatment. Control group treatments could include physical therapy or another intervention designed to improve gait. We included studies with treadmill intervention as an adjunctive treatment. We also reported on studies comparing different types of treadmill interventions, for example, low versus high intensity.

### Types of outcome measures

We accepted five types of outcome measures: standardised measures, questionnaires, self-report data, data from motion analysis systems and coded-video observations. We assessed the following outcomes, which are based on the International Classification of Functioning, Disability and Health, Children & Youth version (WHO 2005).

#### Primary outcomes

Body functions (neuromusculoskeletal and movement related functions - gait pattern functions)

- Step frequency (number of alternating treadmill steps per minute, cadence during independent walking).
- Step quality (foot doing toe versus flat contact during treadmill stepping).

Activities and participation functions

- Age of onset of independent walking.
- Age of onset of walking with assistance.
- Gross motor function.
- Falls and injuries due to falls.

#### Secondary outcomes

Body functions (neuromusculoskeletal and movement related functions - gait pattern functions)

- Inter- and intra-limb co-ordination.
- Other gait parameters, for example, speed, step width etc.

Activities and participation functions

- Infant or child quality of life.

There were insufficient data to examine outcomes by intervention type (preventive or rehabilitative). When data permitted, we examined outcomes by diagnosis (cerebral palsy, Down syndrome and other).

## Search methods for identification of studies

### Electronic searches

We searched the following databases. No date or language restrictions were applied.

The Cochrane Central Register of Controlled Trials ( CENTRAL) 2011(1), part of the Cochrane Library, searched 21 March 2011

MEDLINE (1948 to March Week 2, 2011), searched 21 March 2011

EMBASE (1980 to 2011, Week 11), searched 21 March 2011

CINAHL (1937 to current), searched 21 March 2011

PsycINFO (1887 to current), searched 21 March 2011

Science Citation Index (1970 to 19 March 2011), searched 21 March 2011

PED*ro* (last updated 7 March 2011), searched 21 March 2011

Conference Proceedings Citation Index -Science (1990 to 19 March 2011), searched 21 March 2011

LILACS (Latin American and Caribbean Health Sciences Literature) until March 2011, searched 22 March 2011

We also searched ClinicalTrials.gov, WHO ICTRP, CenterWatch and *meta*Register of Controlled Trials on 22 March 2011.

The search strategies used for each database are in Appendix 1.

### Searching other resources

1. We checked whether studies incorporated in previous systematic reviews and other reviews of the subject fulfilled inclusion criteria.
2. We checked whether bibliographies of articles identified through the search strategy contained potential studies for inclusion.

3. We evaluated unpublished abstracts and dissertations.

## Data collection and analysis

### Selection of studies

We divided the titles and abstracts yielded by the search strategy into two blocks. Two authors independently screened the first block of references (KMB and CB), while two other authors did the same with the second block (RA and MV), using the inclusion criteria described above. RA functioned as the arbiter for KMB and CB, while KMB fulfilled this role for RA and MV, in case of discrepancies. The selected titles were read in full text to determine their relevance for the review. We resolved disagreement about eligibility through discussion. We recorded the reasons for excluding trials.

### Data extraction and management

Four authors (MV, RA, CB and MG) independently extracted data for each trial using a data extraction form to collect information about the population, intervention, randomisation methods, blinding, sample size, outcome measures, follow-up duration, attrition and handling of missing data, and methods of analysis.

### Assessment of risk of bias in included studies

Three authors (CB, MV and RA) independently assessed the risk of bias of each included study using the Cochrane Collaboration's tool for assessing risk of bias (Higgins 2008). Review authors independently assessed each included study as low risk of bias, high risk of bias or unclear risk of bias in relation to the following six domains: sequence generation; allocation concealment; blinding; incomplete outcome data (including data on attrition and exclusions); selective outcome reporting, and other risks of bias**.** We entered these judgements into a 'Risk of bias' table in Review Manager 5.1 (Review Manager 2011), the latest version of the Cochrane Collaboration's meta-analysis software, with a brief rationale for the judgements.
Details on the possible sources of bias are described below.

#### Sequence generation

We described the method used to generate the allocation sequence in sufficient detail so as to assess whether or not the sequence was adequately generated and whether it should have produced comparable groups.

#### Allocation concealment

We described the method used to conceal allocation sequence in sufficient detail to assess whether intervention schedules could have been foreseen before or during recruitment. We judged whether or not there was adequate allocation concealment.

#### Blinding of participants and personnel

It is not possible to blind either those who deliver the therapy (treadmill training) or those infants who receive it, due to the nature of the intervention. Our assessment of risk of bias took into account the likely bias attributable to the inability to blind participants or personnel in such interventions.

#### Blinding of outcome assessment

We described any measures used to blind outcome assessors so as to assess whether knowledge of the allocated intervention was adequately prevented.

#### Incomplete outcome data

We extracted and reported data on attrition and exclusions, as well as the numbers involved (compared with the total randomised), reasons for attrition or exclusion (where reported or obtained from authors) and any re-inclusions in analyses performed by review authors. For each included study, we assessed whether incomplete outcome data were adequately addressed.

#### Selective reporting

We attempted to assess the possibility of selective outcome reporting by investigators. We evaluated if each study was free from selective outcome reporting by considering whether or not all collected data were reported.

#### Other risks of bias

We assessed the extent to which each study is apparently free of other problems that could put it at high risk of bias, by describing important concerns not addressed in the other domains with the Cochrane Collaboration's 'Risk of bias' tool. We assessed other threats to validity as 'low risk of bias' if the study appeared to be free of other sources of bias.

### Measures of treatment effect

We used Review Manager 5.1 (Review Manager 2011) to calculate the adjustments of measures of treatment effects.

#### Continuous data

We analysed continuous data if means and standard deviations had been reported, could be obtained from primary investigators or could be calculated from the available data. If continuous outcomes had been measured identically across studies, we calculated the mean difference (MD) with 95% confidence interval (CI).

#### Dichotomous data

As the studies did not use identical dichotomous data, we were unable to calculate summary statistics on these data.

### Unit of analysis issues

The authors planned to take into account the unit of analysis and determine whether: 1) individuals were randomised in groups (i.e. cluster-randomised trials); 2) results were reported at multiple time points, and 3) individuals simultaneously received multiple interventions. The only unit of analysis issue relevant for th analysis in this review was cross-over trials. We combined the results from the one cross-over trial with those of the parallel group trials, including only the first phase before the point of cross-over in the analyses. Please see Appendix 2.

### Dealing with missing data

We assessed missing data and dropouts in the included studies. We investigated and report the reasons, numbers and characteristics of dropouts (see Characteristics of included studies tables). We made efforts to contact the authors when further information or data were necessary.

We analysed missing continuous data either on an endpoint basis, including only participants with a final assessment, or using last observation carried forward to the final assessment if these data were reported by the trial authors. When the values for standard deviations where not detailed in the publications, we contacted the authors or else, if possible, they were calculated with the available data. For further details, see Characteristics of included studies tables.

### Assessment of heterogeneity

We assessed clinical heterogeneity by comparing the distribution of important participant factors among trials (for example, age, diagnosis), and trial factors (for example, randomisation concealment, blinding of outcome assessment, form of treadmill training, losses to follow-up).

### Assessment of reporting biases

We could not assess reporting biases due to the low number of studies.

### Data synthesis

We synthesised the data using Review Manager 5.1, the latest version of the Cochrane Collaboration's meta-analysis software (Review Manager 2011).

For continuous variables, we applied the mean difference approach where data allowed.

When meta-analysis was inappropriate, we provided a narrative description of the individual study results.

### Subgroup analysis and investigation of heterogeneity

Due to the data and the variables given in the included studies, we were unable to perform all the subgroup analyses we had planned. We did, where possible, conduct subgroup analysis by diagnosis: cerebral palsy, Down syndrome, risk of developmental delay.

### Sensitivity analysis

Due to having such a small number of studies and only two meta-analyses, we considered sensitivity analysis inappropriate.

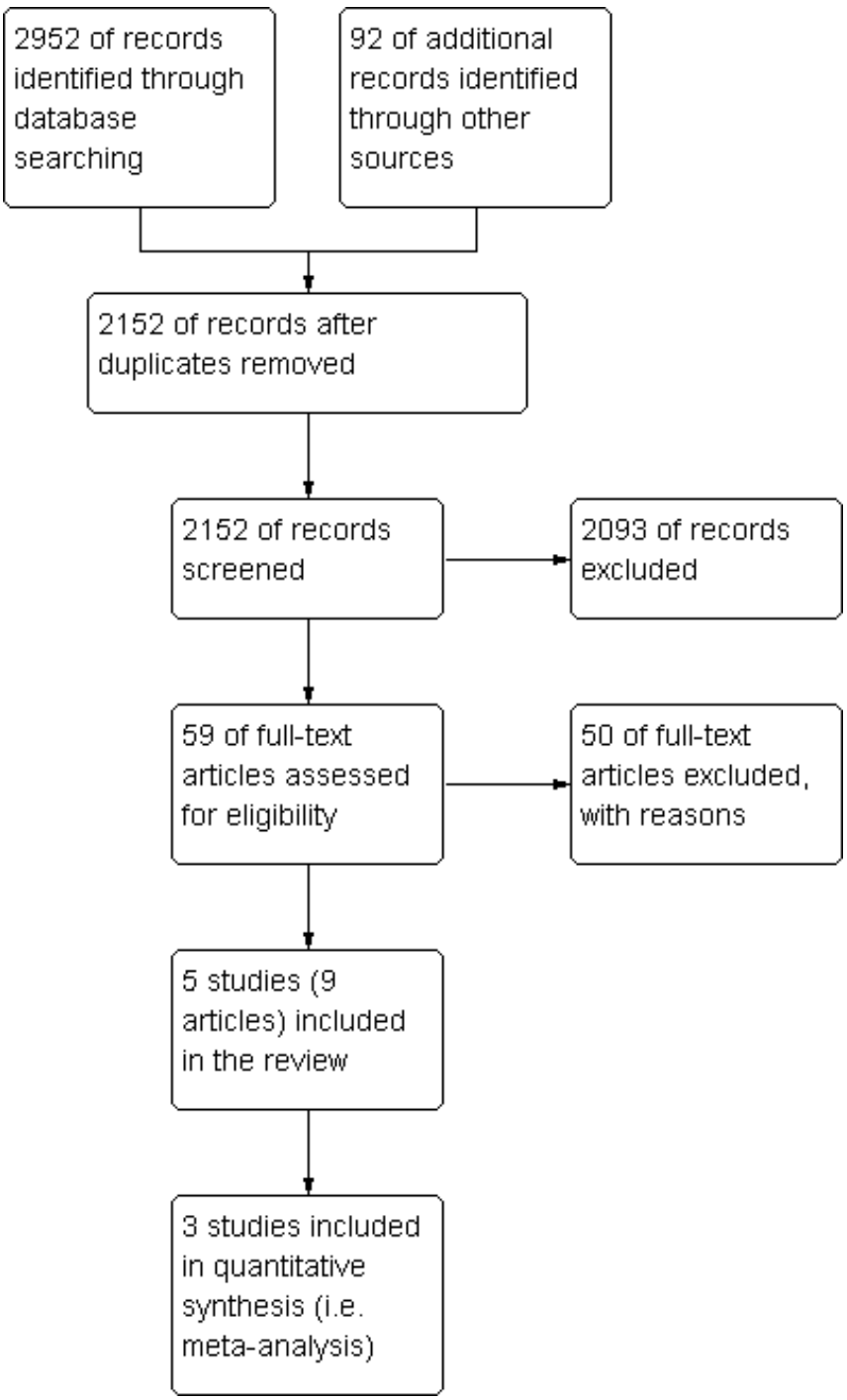
## RESULTS

## Description of studies

### Results of the search

Figure 1 shows the selection of studies. Database searches identified 2952 references and we found 92 references via other sources (ICTRP, CenterWatch, ClinicalTrials.gov and *meta* Register). After removal of duplicates, we examined 2152 references; of these, 2093 were excluded based on screening of their title and abstract. We examined the full text of the remaining 59 records and 49 of these were excluded because they did not meet the inclusion criteria. Although several of the excluded studies examined the effects of treadmill intervention, the main reasons for exclusion were the lack of a control group or that the children studied were older than six years.

**Figure 1. Study flow diagram.**



Of the remaining 10 records, six were original studies, with four being additional publications relating to one of the studies. One of these was excluded after consulting a trials registry as it was a nonrandomised trial with participants choosing whether to be in the intervention or control group (Schlittler 2011).
One of the included studies (Chen 2008) is unpublished and the data were obtained from personal communication with the author, who was also one of the review authors (RA).

## Included studies

We included five studies of treadmill intervention with partial body weight support in children under six years of age at risk for neurodevelopmental delay (Ulrich 2001; Cherng 2007; Chen 2008; Ulrich 2008; Looper 2010). Data from the Ulrich 2008 study were also presented in four further publications (Angulo-Barroso 2008; Wu 2007; Wu 2008; Wu 2010); therefore this review considers the information reported from a total of nine articles.

### Location

All studies were conducted in USA.

### Design

One study had a cross-over design (Cherng 2007), one was a quasi-randomised controlled trial (Looper 2010, personal communication) and the other three were reported as randomised controlled trials without additional information about the randomisation process.

### Sample sizes

The five studies included 139 children. Sample sizes ranged from eight (Cherng 2007) to 41 children (Chen 2008), with the remaining three studies comprising 22, 32 and 36 participants (Looper 2010; Ulrich 2001 and Ulrich 2008 respectively).
According to diagnosis, there were 41 infants at risk of developmental delay (in Chen 2008); 8 with cerebral palsy (in Cherng 2007) and 90 children with Down syndrome (22 in Looper 2010; 32 in Ulrich 2001; 36 in Ulrich 2008).

### Participants

Further details of participant characteristics can be found in the Characteristics of included studies tables.
Chen 2008 examined the effects of treadmill intervention on children at high risk for neuromotor disabilities. The children ranged from corrected age 6.2 months to 11.4 months at study onset As an inclusion criteria, infants entered into the study when they were able to take 10 steps on the treadmill in one minute. No information on ethnicity was reported.
Cherng 2007 focused on children diagnosed with cerebral palsy. Participants were between 42 and 75.6 months old at study onset and were diagnosed with spastic diplegic cerebral palsy. Two of the children were ambulatory without assistive devices; the remaining six children ambulated with assistive devices at study onset.No information on ethnicity was reported.
Three studies examined the effects of treadmill intervention on nonambulatory children with Down syndrome (Ulrich 2001; Ulrich 2008; Looper 2010).
Participants in Ulrich 2001 were children with Down syndrome who had a mean age of 10.1 months (SD 1.94) at study onset. Participantswere admitted into the study when they were able to sit for 30 seconds. Two infants were of mixed race with the remaining infants being white. Nine of the 32 infants (28.1%) had received surgery for congenital heart disease.
Ulrich 2008 examined a different group of children with Down syndrome with mean age ranging from 9.6 to 10.4 months. Two of the children were African-American, two were biracial and the remaining were white. Fourteen of the 36 (38.9%) children had congenital heart defects. An eligibility criterion for commencing treadmill intervention was the ability to take a minimum of six steps in one minute on a moving treadmill while supported under the arms by a parent. Looper 2010 examined children with Down syndrome with mean ages from 18.9 to 21.1 months old at study onset. There was no information on ethnicity or medical conditions. Children entered the study when they were able to pull to stand but unable to cruise.

### Intervention and comparisons

#### *Treadmill intervention versus no treadmill intervention*

This comparison was examined in a total of 81 children across three diagnoses: children at risk for neuromotor disabilities (Chen 2008), children with cerebral palsy (Cherng 2007) and children with Down syndrome (Ulrich 2001).
Chen 2008 randomly allocated high risk infants to a control group (n=16) or a treadmill intervention group (n=25). Infants in the treadmill intervention group engaged in home-based intervention for eight minutes a day, five days a week at an unspecified speed, whereas children in the control group received twice weekly physical therapy without treadmill intervention. Treadmill intervention was discontinued once the children could walk for eight to 10 continuous steps.
Cherng 2007 randomised eight children with cerebral palsy into two groups, each of whom received three 12-week blocks of in-

tervention with varying intervention schedules. Intervention A in the cross-over design was a regular therapeutic intervention without use of a treadmill, while intervention B consisted of treadmill intervention in addition to a traditional therapeutic intervention. Interventions were carried out in 12-week blocks for two to three sessions per week and for 30 minutes per session, with one group receiving intervention schedule AAB and the other group receiving intervention schedule ABA. Assessments were conducted at study entry and subsequently in 12 week increments.

Ulrich 2001 randomised 32 children with Down syndrome to a a treadmill training intervention (n=16) or a control group (n=16). The intervention group received treadmill intervention five days per week at a speed of 0.2 meters/second for up to eight minutes as tolerated. The intervention was carried out in the children's homes by the children's families on portable treadmills. Children were held under the arms over the moving treadmill by a parent. The control group received physical therapy intervention without treadmill intervention at least every other week.

#### *Treadmill intervention with the use of orthotics versus treadmill intervention without orthotic use*

Looper 2010 allocated 22 children with Down syndrome to a treadmill intervention, with and without use of orthotics. Both the intervention and control groups engaged in home-based treadmill intervention at a speed of 0.2 m/s for up to eight minutes a day, five days a week. This was carried out by the parents and the children were held over the moving treadmill. Treadmill intervention was discontinued when the children could take three independent steps. The difference in the intervention group was the use of orthotics. The children were measured for these on the first visit and received them on their second, thereafter wearing them for eight hours a day five days a week for the study duration. The control group received orthotics after the end of the intervention and wore them prior to the final developmental assessment.

#### *High-intensity treadmill intervention versus a low-intensity treadmill intervention*

Ulrich 2008 randomised 36 children with Down syndrome to two groups to compare the effects of high-intensity versus low-intensity treadmill intervention. The low-intensity group (n=18) received home-based treadmill intervention for five days a week, eight minutes per day at a speed of 0.15 meters/second until walking onset. The high-intensity group (n=18) received an individualised treadmill intervention protocol in which the speed of the treadmill was increased depending on the child's performance and additional ankle weights were added during treadmill intervention. Treadmill intervention was terminated in both groups when the children achieved independent walking for three steps. In addition to the information provided in Ulrich 2008, information about this study came from four other publications: Wu 2007, Angulo-Barroso 2008, Wu 2008 and Wu 2010. Wu 2007 also included comparisons of the high intensity and low intensity group data to no treatment using an historical control group from another included study (Ulrich 2001). We did not use data from these comparisons due to their being nonrandomised.

### Outcomes

The studies presented data on most of the outcomes identified in the protocol for this review, with the exception of falls and injuries due to falls, inter- and intra-limb coordination and child quality of life. Below we list below all outcomes measured in the studies, including those that are not relevant for this review.

Ulrich 2001, Ulrich 2008 and Chen 2008 used the standard assessment batteries BSID-II (Bayley Scales of Infant Development) (Bayley 1993) to assess onset of assisted and independent walking. Cherng 2007 and Chen 2008 used GMFM (Gross Motor Function Measure) (Russell 2002) to assess gross motor function. Video coding was used to count frequency of alternating steps (Chen 2008; Ulrich 2008). An instrumented gait mat (GaitRite mat, CIR systems) was used to compute the spatial-temporal gait parameters in both gait with and without an obstacle (Ulrich 2001; Chen 2008; Ulrich 2008), and a 3D motion analysis system (VICOM Peak) was used to obtain the gait kinematics variables (Ulrich 2008) .

Outcomes are presented separately by diagnosis because the effects of the treadmill intervention could vary given the different nature of each population. For instance, infants with Down syndrome are characterised by laxity, while children with cerebral palsy tend to have high tone. Therefore, repetition of the same movement (treadmill step) could have different neuromuscular consequences in a more compliant system versus a stiffer system.

#### *Infants at risk for developmental delay*

Chen 2008 examined children each month during the intervention period and at three and six months post intervention. During the treadmill period, they examined frequency of alternating steps on the treadmill, type of foot contact (step quality) and Gross Motor Function Measure (GMFM) (Russell 2002). After independent walking onset, spatiotemporal gait parameters measured by the GAITRite system, in addition to gait speed, were measured during the follow-up.

#### *Cerebral palsy*

Cherng 2007 used all dimensions of the GMFM, muscle tone, selective motor control and gait velocity and gait parameters, such as stride length and double limb support, as outcome measures.

***Down syndrome***

Ulrich 2001 assessed effectiveness using the number of days lapsed between entry into the study and the attainment of three developmental milestones as outcome measures: raising to stand, walking with help and walking independently for three steps.
In addition, follow-up data for gait spatiotemporal parameters were measured in the control and experimental groups but were not reported.
Looper 2010 examined the average time in study until the infants achieved independent walking and the infant's motor skill development after one-month follow-up (GMFM).
Ulrich 2008 compared high intensity with low intensity treadmill intervention and examined the onset of several gross motor milestones from the Bayley Scales of Infant Development motor subscale, i.e. moving forward using pre-walking methods (item 43), raising self to sitting position (item 47), raising self to standing position (item 52), walking sideways/cruising (item 54), walking with help (item 60), standing alone (item 61), walking alone (item 62) and walking alone with good coordination (item 63). In addition, videotape analysis was performed on the frequency of alternating steps per minute on the treadmill every two months until onset of independent walking.
Additional data from this study were reported in four other publications (Angulo-Barroso 2008; Wu 2007; Wu 2008; Wu 2010), some of which contained follow-up data for this group of children with Down syndrome.
Wu 2007 presented data for age of walking onset, average velocity, stride length, step width, stride time, stance time and dynamic base. In a follow-up article, Wu 2008 examined the ability and methods of obstacle clearance at walking onset, and at three, six, and 12 months after walking onset in 26 of the 30 children from the original high intensity versus low intensity treadmill intervention by Ulrich 2008. The ability to clear an obstacle was categorised as "refusal, crawl, fall, and walk." The five steps taken by the children leading up to the obstacle were analysed with the GAITRite system.
The long-term effects of high intensity treadmill and low intensity treadmill intervention in the same group of children with Down syndrome at three, six, nine and 12 months post intervention were reported in an article by Angulo-Barroso 2008. Six basic gait parameters were examined in a principal component analysis (normalised velocity, cadence, step length, step width, double support percentage and dynamic base).
Additionally, gait laboratory analysis was conducted during the one-year follow-up in these children with Down syndrome after walking onset following high intensity and low intensity treadmill intervention on 26 of the 30 analysed children with Down syndrome (Wu 2010). Timing and magnitude of peak extension and flexion at the hip, knee, and ankle joints, as well as peak adduction and abduction at the hip joint, were compared in the high intensity and low intensity intervention groups.

### Excluded studies

Thirteen studies appeared eligible to be included in this review when examining the full articles. All but four studies were excluded on the basis of the age of the participants, i.e. the participants were older than six years. Three (Pang 2003; Mussleman 2007; Teulier 2009) were excluded because they did not evaluate treadmill intervention but used the treadmill for other investigations. Lastly, one study was excluded because participants were not randomly assigned to the groups (Schlittler 2011).

## Risk of bias in included studies

A comprehensive description of the risk of bias for each study can be found in the Characteristics of included studies tables. This information is summarised in Figure 2 and Figure 3.

**Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**

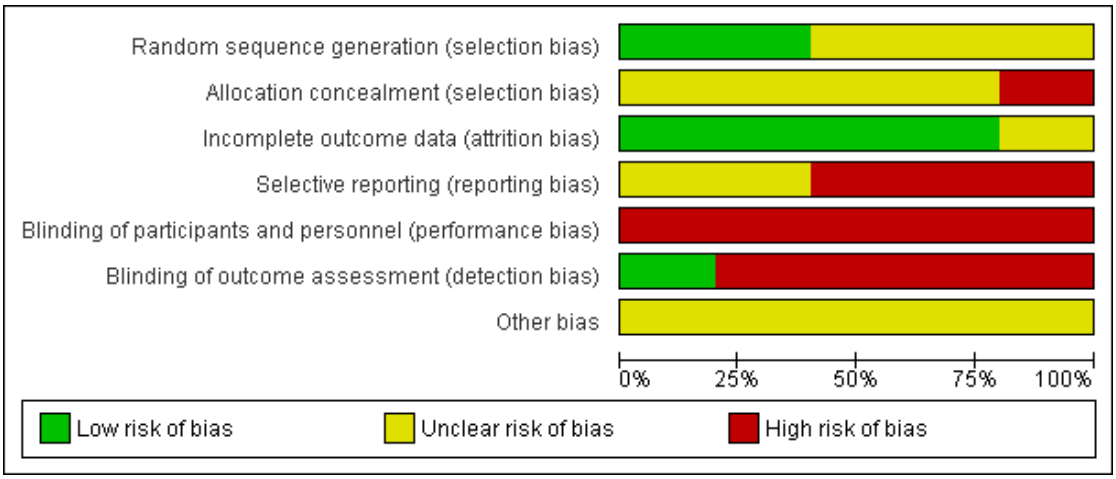
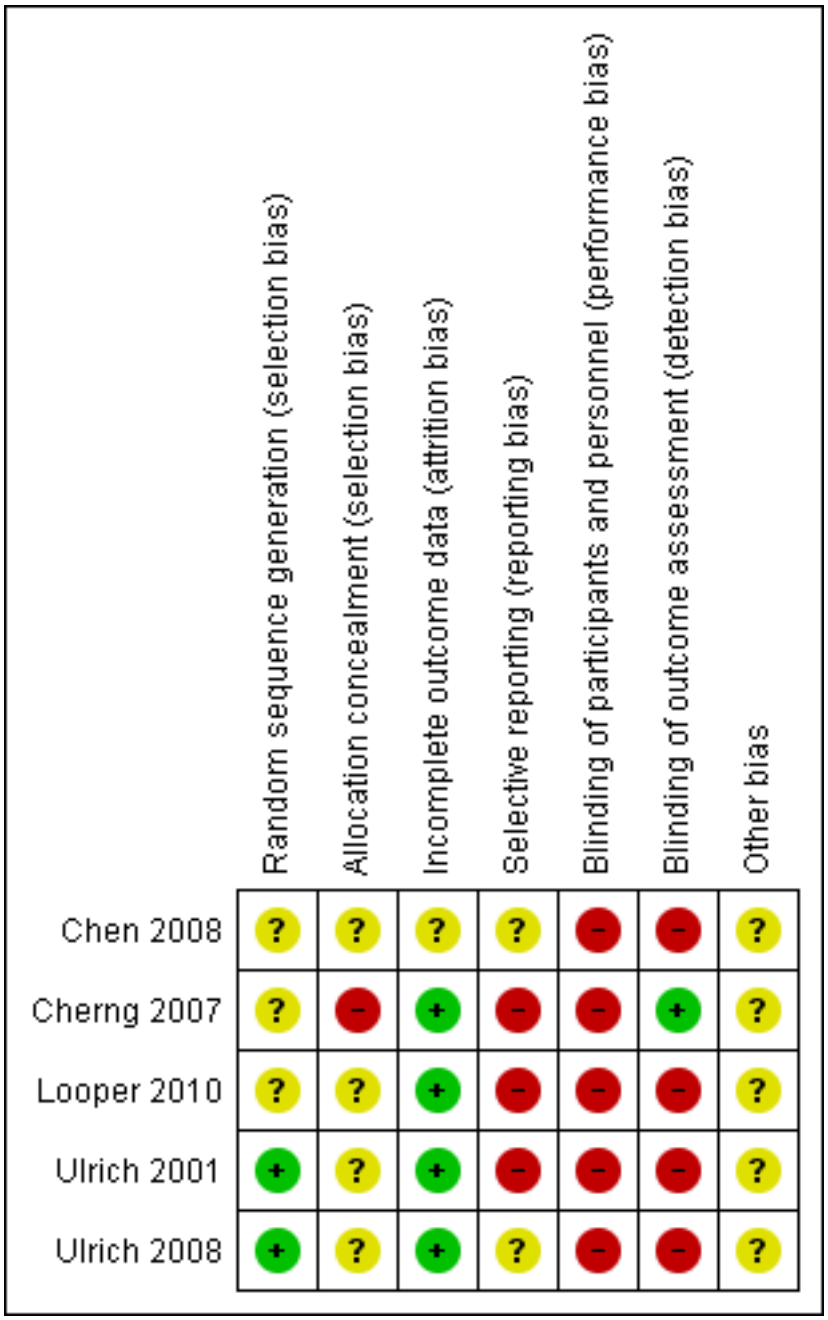


**Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. + = low risk, - = high risk, ? = unclear risk**



### Allocation

#### Random sequence generation

Ulrich 2001 and Ulrich 2008 were judged to be at low risk of bias as a table of random numbers was used to assign participants to the intervention or control group. Information on how the random sequence was generated was lacking in the other studies, which we therefore assessed as at unclear risk of bias for this domain.

#### Allocation concealment

In Ulrich 2001 and Ulrich 2008, one of the investigators used a table of random numbers to assign allocation, but this is not an acceptable method to ensure allocation concealment (Higgins 2008). In the absence of other information, we assessed this as unclear risk of bias. All other studies were also at unclear risk of bias as they did not report how the allocation process took place.

### Blinding

#### Blinding of participants and personnel

Performance bias was high, as parents, infants and personnel were aware of group allocation in all studies.

#### Blinding of outcome assessment

Most studies suffered from a high risk of detection bias as the assessors usually were aware of group allocation. In one study ( Cherng 2007) the risk of bias was low as there was one independent therapist who took gait parameter measurements and who was unaware of the therapy the children had received.

### Incomplete outcome data

Attrition was related to the duration of follow-up after treadmill intervention. In the four studies that assessed outcome during and/or immediately after the intervention, attrition and bias due to attrition was low (Ulrich 2001; Cherng 2007; Ulrich 2008; Looper 2010). The remaining study had an unclear risk related to intervention attrition and bias (Chen 2008).

### Selective reporting

In three studies reporting bias was high as not all data were reported (Cherng 2007; Looper 2010; Ulrich 2001). It was unclear whether all data had been reported in Ulrich 2008 and the unpublished study Chen 2008.

### Other potential sources of bias

In all studies, the risk of other sources of bias was unclear.

## Effects of interventions

We could only perform limited quantitative analysis due to the heterogeneous nature of the types of interventions used, the distinct nature of the diagnostic subgroups studied and differences in outcome measures and/or time periods when data were collected. Because all studies had continuous outcome measures, mean differences were calculated to determine the effect estimate of treadmill intervention on the various outcome measures in the different subgroups of children. There was high variability of outcome measures across studies, similar or identical outcome measures were assessed at different time points and different treadmill interventions were used across studies. Due to this heterogeneity, we could only perform limited quantitative analysis. Meta-analysis could only be conducted on the effects of treadmill intervention versus no treadmill intervention in children with different diagnoses for the GMFM percentage scores and the onset of independent walking in days. The effects of intervention are reported by type of treadmill intervention and outcomes.

### Treadmill intervention versus no treadmill intervention

This comparison was evaluated by three studies (Ulrich 2001; Cherng 2007; Chen 2008).

#### Primary outcomes

#### Step frequency (treadmill alternating steps)

In children at risk for motor delays, Chen 2008 found an increase of step frequency for both experimental and control groups, especially from 10 to 16 months of age. However, the differences between the two groups were not significant. There is no evidence that suggests that TM training helps to increase step frequency in children at risk for motor delays (effect estimate at 16 months of age: 4.36; 95% CI: -2.63, 11.35) (Analysis 1.9).

#### Step quality

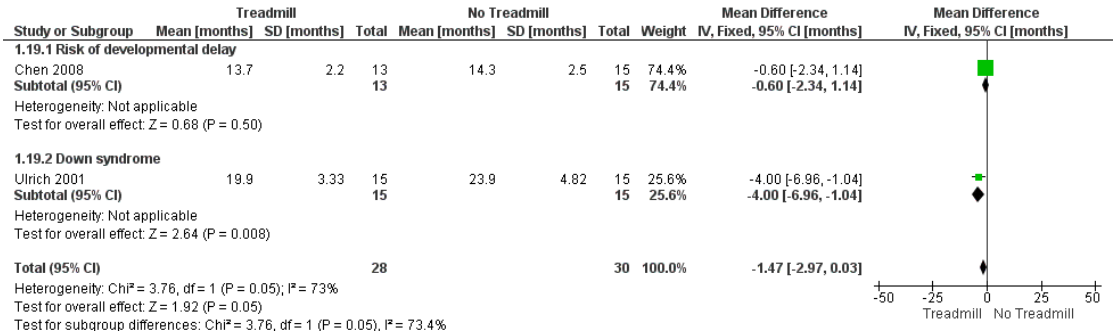
Chen 2008 found that treadmill training helped improve step quality for children at risk of neuromotor disabilities. In the experimental group, from 11 to 16 months of age, there was a significant decrease of foot toe contact during treadmill stepping (effect estimate at 11 months of age: -20.98; 95% CI: -26.87, -15.08 (Analysis 1.13); effect estimate at 16 months of age: -15.61; 95%

CI: -23.96, -7.27 (Analysis 1.18)), thus an increase of flat foot contact steps occurred.

### Age of onset of independent walking

The onset of independent walking was characterised across studies as the ability to take three to 10 independent steps. Meta-analysis of two studies (Ulrich 2001; Chen 2008) was conducted on a total of 58 children who had Down syndrome or were high-risk infants with an effect estimate of -1.47 (95% CI: -2.97, 0.03) (Figure 4), which suggests that the treadmill intervention was effective in promoting earlier independent walking; however, it must be noted that the studies examined children with different diagnoses.

**Figure 4. Forest plot of comparison: 1 No Treadmill vs Treadmill: Walking independently (months).**




Chen 2008 found that children both in the control and the experimental group attained independent walking at similar corrected ages and did not find support for an effect of treadmill intervention on the age of onset of independent walking in children at risk of motor delays (effect estimate -0.60, 95% CI -2.34, 1.14) (Analysis 1.19).

For children with Down syndrome, those in the treadmill intervention group learned to walk independently significantly faster (effect estimate -4.00; 95% CI: -6.96, -1.04) than the control group (Ulrich 2001) (Analysis 1.19).

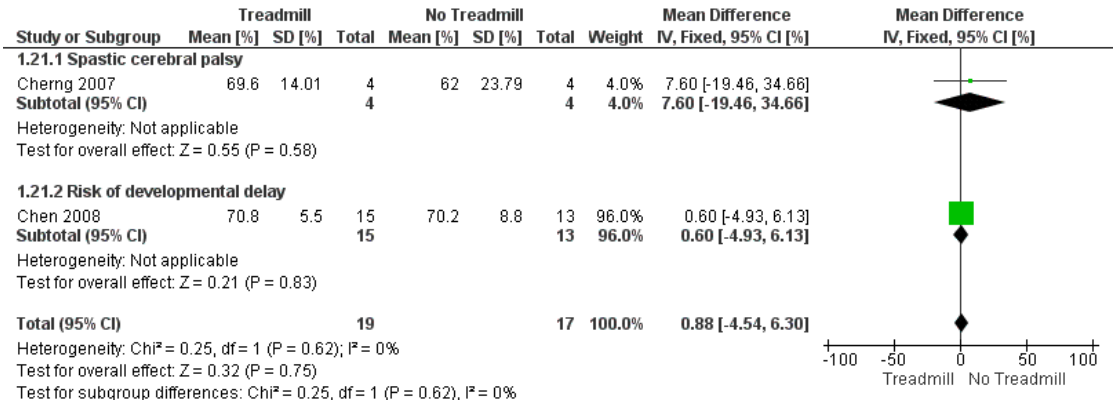
### Age of onset of walking with assistance

Ulrich 2001 found a significant effect of treadmill intervention on the onset of supported walking in a study of 30 children with Down syndrome (effect estimate -74.00; 95% CI: -135.40, -12.60) (Analysis 1.20).

### Gross motor function (GMFM)

Meta-analysis of two studies (Chen 2008; Cherng 2007) on the effects of treadmill versus no treadmill intervention for the GMFM percentage change suggested that treadmill intervention did not affect GMFM scores (effect estimate 0.88; 95% CI: -4.54, 6.30) (Analysis 1.21). The two studies were conducted on infants with different diagnoses (cerebral palsy and high-risk infants). The absence of evidence of an effect of treadmill intervention on GMFM scores was reported in both groups of infants: cerebral palsy (Cherng 2007: effect estimate 7.60; 95% CI: -19.46, 34.66) and high risk (Chen 2008: effect estimate 0.60; 95% CI: -4.93, 6.13) (Figure 5).

**Figure 5. Forest plot of comparison: 1 No Treadmill vs Treadmill: Gross motor function (GMFM as %).**




### Falls and injuries due to falls.

These were not measured.

### Secondary outcomes

### Inter- and intra-limb co-ordination.

These were not measured.

### Other gait parameters

Gait velocity, step length and double limb support were measured in two studies that examined treadmill versus no treadmill intervention in children with cerebral palsy and high-risk infants (Chen 2008; Cherng 2007). There was no effect across studies with respect to velocity (for children with cerebral palsy: effect estimate 0.39; 95% CI: -4.19, 4.97; Analysis 1.22; for high-risk infants: effect estimate 1.32; 95%CI: -0.53, 3.17; Analysis 1.23); step length (for cerebral palsy: effect estimate 0.37; 95% CI: -25.04, 25.75; Analysis 1.26; for high-risk: effect estimate 0.08; 95% CI: -0.02, 0.18; Analysis 1.27) or double limb support (for cerebral palsy: effect estimate 3.80; 95% CI: -21.52, 29.12; Analysis 1.30; for high-risk: effect estimate -4.19; 95%CI: -10.02, 1.64; Analysis 1.31) at time of walking onset.

### Infant or child quality of life

This was not measured.

## Treadmill intervention without orthotics versus treadmill intervention with orthotics

Only one study (Looper 2010) evaluated this comparison. In this study of children with Down syndrome, only two of our outcomes were measured: age of onset of independent walking and gross motor function. These were both primary outcomes.

### Age of onset of independent walking

No significant difference in the age of independent walking onset was found between the two intervention groups: effect estimate 0.10 (95% CI: -5.96, 6.16) (Analysis 2.1) .

### Gross motor function

The use of orthotics was associated with lower GMFM total scores one month after completion of treadmill intervention: effect estimate -8.40 (95% CI: -14.55, -2.25) (Analysis 2.2). The lower total scores were mainly brought about by lower scores on the dimensions D and E. The results suggest that early use of orthoses might hinder gross motor progress.

## High-intensity treadmill intervention versus low-intensity treadmill intervention

Ulrich 2008 was the only study to evaluate this comparison in their study of children with Down syndrome. Three of our primary outcomes were measured in this study: step frequency, age of onset of independent walking and age of onset of walking with assistance; and one of our secondary outcomes: other gait parameters.

**Step frequency (treadmill alternating steps)**

Ulrich 2008 calculated the values for frequency of alternating steps in both the high intensity and the low intensity groups. No differences in frequency of stepping were found prior to the training. After the intervention, those infants who received the high-intensity training protocol took a greater number of steps than those who belonged to the low-intensity group: effect estimate 11.00 (95%CI: 6.03, 15.97) (Analysis 3.1).

### Age of onset of independent walking or walking with assistance

No clear evidence of a differential effect was observed on either supported (effect estimate: -1.86, 95%CI: -4.09, 0.37) or independent walking (effect estimate: -2.13, 95% CI -4.96, 0.70) (Analysis 3.2).

### Other gait parameters

Various gait parameters were examined in Ulrich 2008 and three additional publications of the same sample of children with Down syndrome at three, six, nine and 12 months after walking onset (Angulo-Barosso 2008, Wu 2008, Wu 2010). There was a positive effect of high intensity treadmill intervention on children with Down syndrome on the ability to clear obstacles in the upright position compared to children who received low intensity treadmill intervention at follow-up visits after the onset of independent walking (effect estimate: -3.60, 95% CI: -6.77, -0.43 (Analysis 3.4) at three months; -4.00, 95% CI: -6.86, -1.14 (Analysis 3.5) at six months; -3.20, 95% CI: -6.34, -0.06 (Analysis 3.6) at nine months; -2.80, 95% CI: -5.89, 0.29 at 12 months (Analysis 3.7)). At follow-up visit two, there was a positive effect of high intensity treadmill intervention compared to low intensity treadmill intervention on gait velocity of 0.16, 95% CI: 0.01, 0.31 (Analysis 3.9) and on decreased double-limb support of -4.00, 95% CI: -7.91, -0.09 (Analysis 3.21); however, at follow-up visits one, three and four there was no clear difference in the effect of the two interventions on these two outcomes. Similarly, the high intensity treadmill intervention resulted in better timing of maximum ankle plantar flexion during gait compared to the low intensity group at the second follow-up visit (-4.80, 95% CI: -8.76, -0.84; Analysis 3.25), but not at follow-up visits one, three and four. There was no difference between the high intensity and low intensity treadmill intervention groups on other gait parameters, such as step length (effect estimate at follow-up visit four: 2.68, 95% CI -0.99, 6.35; Analysis 3.15), step width (effect estimate at follow-up visit four: -0.58, 95% CI -2.11, 0.95; Analysis 3.19), gait ankle dorsiflexion (effect estimate at follow-up visit four: 2.80, 95% CI: -5.96, 0.36; Analysis 3.31) and toe-off (effect estimate at follow-up visit four: -0.90, -5.49, 3.69; Analysis 3.35).

# DISCUSSION

We have included data from four randomised and one quasi-randomised controlled trials in which 139 children (73 of whom engaged in treadmill with the remainder acting as controls) below the age of six years participated. One trial (Ulrich 2008) was reported in multiple publications.

## Summary of main results

The studies varied in the type of population studied (children with Down syndrome or cerebral palsy or at risk for developmental delay), in time of evaluation (during the intervention, immediately after the intervention or during follow-up after three to 12 months after intervention) and in the parameters assessed. The latter varied from motor milestones such as the onset of independent walking to detailed gait parameters. Due to the heterogeneity of the studies, the meta-analyses were restricted to few studies and limited to the GMFM scores and the onset of independent walking in days.

### Body functions

The reported effect of treadmill intervention on gait parameters varied across studies, which makes it difficult to draw conclusions. For children with cerebral palsy or at high risk for developmental delay, no effect of treadmill intervention on gait velocity, step length and double limb support could be established. The studies on the effect of high intensity-individualised treadmill intervention in comparison to low intensity-generalised treadmill intervention in children with Down syndrome suggested that the high intensity intervention was associated with a better ability to take alternating steps and an improved ability to clear obstacles during the year post-intervention. Evidence of an effect on gait velocity and and decreased double-limb support was mixed. There was no evidence of a different effect of low and high intensity interventions on step length, step width or toe-off.

### Activity and participation functions

The results of this review indicate that treadmill intervention may be associated with an earlier onset of independent walking and supported walking in children with Down syndrome. In these children both a high intensity-individualised treadmill intervention and a low intensity-generalised treadmill intervention had a similar effect on onset of independent walking. The effect of treadmill intervention on GMFM scores in children with Down syndrome was not studied. However, it seemed the early application of supramalleolar orthoses in children with Down syndrome may have a negative effect on GMFM scores.

Treadmill intervention in children with cerebral palsy and children at risk for developmental delay was not associated with improved gross motor development measured with the GMFM. However, only two randomised controlled trials, one of which is unpublished to date, have been conducted on this population (Chen 2008; Cherng 2007).

## Overall completeness and applicability of evidence

Overall, there were few studies assessing the effect of treadmill intervention in young children with or at high risk for motor developmental delay. Three of the five studies examined treadmill intervention in children with Down syndrome (Ulrich 2001; Ulrich 2008; Looper 2010). One study (Chen 2008) assessed treadmill intervention in infants at high risk for developmental delay and one in children with cerebral palsy (Cherng 2007). Two of the five studies did not evaluate the effect of treadmill intervention versus no treadmill intervention, but assessed two modifications of treadmill intervention (high versus low intensity, with orthosis versus without orthosis) (Ulrich 2008; Looper 2010). This means that the evidence on the effect of treadmill intervention itself is limited. The effect has been most extensively studied in children with Down syndrome.

### Quality of the evidence

Most studies were designed as RCTs, a design which is associated with a high standard of evidence, all things being equal (Sacket level I: Sackett 1996; Butler 2001). However, the studies in this review suffered from methodological limitations, in particular from a high risk of bias due to the absence of blinding. Performance bias is inevitable in studies on treadmill intervention, but detection bias, from which most studies suffered, may be prevented. Another important methodological limitation was the risk of attrition bias. Attrition occurred in particular during follow-up after treadmill intervention. In general the extent of attrition was moderate, but it was unclear whether attrition was selective or not.

### Potential biases in the review process

One of the authors of the review (Angulo-Barroso) participated in the series of studies on the children with Down syndrome. Other potential biases have not been identified.

### Agreements and disagreements with other studies or reviews

The effects of treadmill intervention have been examined in previous reviews in children of all ages with or at risk of a motor developmental disorder, but most of the these reviews dealt with school-aged children and adolescents with cerebral palsy.
These reviews concluded that 1) treadmill intervention in children with Down syndrome accelerates development of walking (Damiano 2009) and 2) limited evidence on the effect of treadmill intervention in children with cerebral palsy is available, even though many studies in the reviews note some positive effect (Damiano 2009; Mattern-Baxter 2009; Mutlu 2009; Willoughby 2009; Molina-Rueda 2010). These conclusions are similar to the findings of the present review, which focuses on the effect of treadmill intervention on children with or at risk for developmental delay in a specific age group (six years or younger) and uses only high quality evidence, i.e. randomised controlled trials and controlled clinical trials, rather than including nonrandomised trials and single case studies.

## AUTHORS' CONCLUSIONS

### Implications for practice

Regular frequent practice of motor activity is the cornerstone of motor development. Evidence is accumulating that task-specific training is a useful tool to promote motor development in children with or at high risk for delayed motor development. The current review assessed the evidence for the effectiveness of treadmill intervention in young children with, or at high risk for, motor developmental delay under six years of age. Given the limited number of studies, and their heterogeneity, this review can provide no firm evidence for the clinical application of treadmill intervention. Nevertheless, the review indicates that treadmill intervention in children with Down syndrome may assist in facilitating an earlier onset of walking. Furthermore, the data suggest that children with Down syndrome who received more intensive treadmill intervention may be more accomplished in their gait parameters as compared to children who received less intensive treadmill intervention.

The evidence in this review also suggests that application of orthoses during treadmill intervention and before walking onset in children with Down syndrome may have a negative effect on gross motor development.

Home-based protocols, where the intervention is carried out by parents or caregivers with instruction/supervision by a physical therapist, appears to be a feasible intervention for children with Down syndrome. This type of home-based approach might more easily provide the necessary intensity of intervention for task-specific ambulation training. However, the effectiveness of a home-based model of intensive treadmill training has not been established for children with cerebral palsy or high-risk infants in the literature. From a clinical perspective, It is also important to consider the intrinsic differences of the studied populations. It is generally accepted that infants with DS are hypotonic and their neuromusculoskeletal systems may benefit from heavy repetition of a highly patterned movement. In contrast, infants at risk for neuromotor delay may present variable levels of muscle tone and frequently hypertonicity. An intervention with more variability of movement in individuals with less compliant neuro-muscular system would perhaps be more appropriate.

### Implications for research

Both neurophysiologic and early intervention literature suggest that task-specific training facilitates motor development. Treadmill

intervention is a good example of task-specific training. The current study highlights the need for RCTs on the effect of treadmill intervention. Given the limited evidence on the effect of treadmill intervention, it is ethically justified to assess the effect of treadmill intervention versus no treadmill intervention (and not only of its intensity). Well-controlled RCT studies are needed, of sufficient power, and enrolling children with a variety of diagnoses, such as Down syndrome, cerebral palsy and high risk infants Given the results in Down syndrome, and because the literature suggests that high intensity intervention has a larger effect on motor development than low intensity intervention in children with cerebral palsy (Gordon), it would be worthwhile to investigate the effect of treadmill intervention applied at higher dosages than applied in the studies reviewed, for instance increasing progressively minutes of training. Additionally, the effects of home-based treadmill intervention carried out by the parent or caregiver should be examined in young children with diagnoses other than Down syndrome. Important for future studies is to avoid bias through lack of blinding. Although blinding of parents, children and personnel applying treadmill intervention is impossible, masking of persons assessing outcomes is perfectly feasible.

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* *Indicates the major publication for the study*

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

**Chen 2008**

| | |
|---|---|
| Methods | Randomised controlled trial. |
| Participants | Information provided through a personal communication with the author<br>41 infants with moderate risk for neuromotor disabilities were initially randomised (25 on the experimental group and 16 on the control group), but only 28 finally analysed (13 control group: 9 male / 4 female vs. 15 treadmill-experimental group 9 male / 6 female). They entered the study when they were able to take 10 steps on the treadmill in 1 minute<br>Infants at risk include: low-birth-weight (<1250g), low gestational-age (<32weeks), brain insult, prolonged ventilator use or multiple births<br>Mean age: 9.0 mo (SD 1.4) control group; 9.7 (SD 1.3) experimental group<br>No information on ethnicity available. |
| Interventions | Experimental group: home-based treadmill training: 8min/day, 5days/week until onset of independent walking, defined as the ability to take 8-10 continuous steps without support. They were followed monthly to assess stepping performance on the treadmill until the onset of independent walking. Gait was re-examined 3 and 6 months later<br>Control group: twice weekly physical therapy without treadmill intervention |
| Outcomes | Treadmill step frequency<br>Treadmill step quality (type of foot contact)<br>Age at onset of independent walking<br>Step length<br>Step velocity<br>Cadence<br>Step width |
| Notes | Country: USA.<br>Unpublished trial, only data and abstract available from authors |

***Risk of bias*** ***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Moderate-risk infants were randomly assigned to either a control (C) or an experimental (treadmill) group |
| Allocation concealment (selection bias) | Unclear risk | No information provided regarding how the allocation process took place |
| Incomplete outcome data (attrition bias) Experimental group 1 | Unclear risk | Treadmill training:<br>n=25 allocated<br>n=10 discontinued intervention for the following reasons: |

**Chen 2008** (*Continued*)

| | | |
|---|---|---|
| | | n=6 did not follow the protocols; n=3 voluntarily withdrew; n=1 was diagnosed with genetic disorder<br>n=15 were analysed<br>Control:<br>n=16 allocated; n=1 unable to schedule for data collection<br>Data were collected from n=15<br>n=2 were excluded from the analysis due to the following reasons:<br>n=1 diagnosed with genetic disorder; n=1 received multiple occasions of Botox injections<br>n=13 were analysed |
| Selective reporting (reporting bias) | Unclear risk | As the trial is unpublished, we are not able to assess. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | No blinding. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | No blinding. |
| Other bias | Unclear risk | Since this trial has not been published, full details of methodology are not available to be evaluated |

**Cherng 2007**

| | |
|---|---|
| Methods | Randomised controlled trial (crossed design: AAB, ABA) |
| Participants | 8 children with spastic cerebral palsy<br>Age range: 3.5 - 6.3 years old<br>Ethnicity not reported. |
| Interventions | Experimental (B): Treadmill treatment (TBWS); 20 min/session, 2-3 sessions/wk, for a total of 12 weeks<br>Control (A): Regular therapeutic treatment (NDT, mat exercises of range of motion, stretching, strengthening, and motor function activities. Gross motor activities included changing positions, lie to sit, sit to stand, and standing); 2-3 times/wk, 30 min/session |
| Outcomes | GMFM total score<br>Gait speed<br>Gait stride length<br>Gait double-limb support |
| Notes | Country: Taiwan<br>This study was supported by NSC 92-2218-E-006-003 and through a collaboration of National Cheng Kung University and Chi Mei Medical Center |

**Cherng 2007** (*Continued*)

| *Risk of bias* | | *Risk of bias* |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | The children were equally divided into 2 groups and randomly assigned to the schedules |
| Allocation concealment (selection bias) | High risk | Cross-sectional trial. |
| Incomplete outcome data (attrition bias)<br>Experimental group 1 | Low risk | A: Regular therapeutic treatment.<br>n=1 dropped out of the program before the third assessment. Reasons are not reported<br>B: Treadmill training.<br>No dropouts. |
| Selective reporting (reporting bias) | High risk | "Outcomes measures included muscle tone...". No data about muscle tone are provided |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | No blinding. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | One independent therapist, who was not aware of any child's grouping or stage within the study, took all the measurements on gait parameters |
| Other bias | Unclear risk | We do not have enough information to make a judgement. |

**Looper 2010**

| | |
|---|---|
| Methods | Quasi-randomised controlled trial, according to a personal communication with the author |
| Participants | 22 infants with Down syndrome were randomised (10 to the experimental group; 12 to the control group). Five infants discontinued the intervention in the control group<br>Mean age: 21.4 mo (SD 4.0).<br>Ethnicity not reported. |
| Interventions | Experimental group: use of orthosis; co-interventions of treadmill training and regular physical therapy. Orthoses (SMOs, Surestep. 17530 Dugdale Dr, South Bend. IN 46635) . 8 hrs/wk, 5 days/wk, from entry to end of follow-up. Treadmill terminated at the onset of independent walking<br>Control group: treadmill training (5 days/week, 8 min/day, belt speed 0.2m/s; co-interventions of regular physical therapy) |

| | |
|---|---|
| Outcomes | Average time in study until the infants achieved independent walking<br>GMFM after one-month follow-up. |
| Notes | Country: USA<br>Funds provided by the Foundation for Physical Therapy PO Down syndrome II awards to Dr Looper, a grant from the Michigan Physical Therapy Association, and a grant from the Rackham Graduate School, University of Michigan |

***Risk of bias*** ***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The subjects were randomly assigned to groups based on a random list of 1 (treadmill) and 2 (treadmill plus orthoses) from random.org. The first subject who entered the study (convenience sample) was assigned to the first number on the list, the second subject to the second number, the third to the third etc. (personal communication) |
| Allocation concealment (selection bias) | Unclear risk | No information provided regarding how the allocation process took place |
| Incomplete outcome data (attrition bias) Experimental group 1 | Low risk | Orthosis and treadmill training.<br>n=10 allocated<br>All received the intervention and none discontinued the intervention<br>n=10 were analysed.<br>Treadmill training alone.<br>n=12 allocated<br>All received the intervention.<br>n=5 discontinued intervention for the following reasons:<br>n=1 emerging medical problems; n=1 did not tolerate the treadmill; n=3 received orthoses prior to the end of the study<br>n=7 were analysed. |
| Selective reporting (reporting bias) | High risk | Antrhopometric measurements were taken at each monthly visit, and treadmill training was videotaped. No information on these is reported. Also, age of onset of independent walking was not directly reported and the authors provided only information about study duration |

**Looper 2010** (*Continued*)

| | | |
|---|---|---|
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Only one assessor, who was aware of the children's allocation |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | No blinding. |
| Other bias | Unclear risk | We do not have enough information to make a judgement. |

**Ulrich 2001**

| | |
|---|---|
| Methods | Randomised controlled trial. |
| Participants | 32 infants with Down syndrome, randomised into 2 groups (16 experimental; 16 control) . Enrolled when able to sit for 30 seconds. 2 infants discontinued the intervention (one in each group) and 2 more were lost to gait follow-up (one in each group), as reported in Wu 2007. Any discrepancies in the paper were resolved through personal discussion with RA who was one of the authors involved in both this study and in Ulrich 2008, and who is also a review author<br>Average age at entry: 10.1 months (SD 1.94).<br>The 15 analysed infants in the control group who did not receive treadmill intervention (8 male, 7 female), had a mean age: 10.2 months (SD 2.2). The experimental group (15 infants) has a mean age of 9.9 months (SD 1.7) (no breakdown by sex is provided for this group)<br>2 mixed raced; remaining were white. |
| Interventions | Experimental: Parents were trained in the treadmill intervention and delivered it 5days/ week; 8min/session; belt speed 0.2m/s. It stopped when infants achieved independent walking (i.e. took 3 independent steps on the ground). They also received traditional physical therapy as well as any activity that was prescribed by their health care provider and early intervention team<br>Control: Traditional physical therapy as well as any activity that was prescribed by their health care provider and early intervention team<br>Researchers visited biweekly to measure growth and assess child. Parents kept a log book of the intervention and infant's response, which was shared with researcher |
| Outcomes | Length of time from entry into study until the raising up to stand, the onset of walking with help or independent walking (i.e. taking 3 steps), which are items from the Bayley Scales of Infant Development |
| Notes | Country: USA (Indiana, Tennesse, Ohio).<br>Founding sources: grants from the National Institute for Disability and Rehabilitation Research and from the March of Dimes Birth Defects Foundation<br>The control group from this study is also used in another paper (Wu 2007) that relates to Ulrich 2008 |

**Ulrich 2001** (*Continued*)

| *Risk of bias* | | *Risk of bias* |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Low risk | Infants were randomised into two groups. "Given that there were no group differences on the 11 anthropometric measures at entry, it appears that randomisation process resulted in producing comparable treatment groups. " In addition, Wu 2007 report on the use of a table of random numbers |
| Allocation concealment (selection bias) | Unclear risk | This information is obtained from another publication of the same study (Wu 2007):<br>"The randomisation procedure was conducted by the fourth investigator for the two cohorts separately via a table of random numbers." This means that each randomisation was conducted separately with the involvement of only the 4th author and with the use of a table of random numbers. This does not give us enough information to make a judgement |
| Incomplete outcome data (attrition bias)<br>Experimental group 1 | Low risk | Treadmill training. All outcome measures are reported. There was one dropout not reported on this paper but in Wu 2007 (used the same control group) |
| Selective reporting (reporting bias) | High risk | Not all data are reported. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Neither participants or personnel were blinded. Infants in the treadmill intervention group had treadmills placed in their homes. Parents were trained to implement the training. A team of researchers visited all participants biweekly throughout the study: infants were videoed on the treadmill and their growth was assessed and parents shared log book |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Assessors were aware of infant's group assignment. |
| Other bias | Unclear risk | All parents were asked to keep a log book including information regarding the treadmill training (for those in the experimental group) and any other information relevant information regarding the infant's health state and daily activities, including any therapeutic session administered other than treadmill training |

**Ulrich 2008**

| | |
|---|---|
| Methods | Randomised controlled trial. |
| Participants | 36 infants with Down syndrome were randomised into two groups: low-intensity and high-intensity. They were included when they were able to take 6 steps per minute on a treadmill while being supported<br>30 children were analysed in the final sample (16 experimental group: high-intensity training 12 males / 4 female, 14 control group: low-intensity training 6 males / 8 females) ; (28 with trisomy 21; two with mosaic type)<br>6 infants discontinued the intervention, 4 in the low-intensity and 2 in the high-intensity group. An additional 5 infants were lost to gait follow-up (2 in the low-intensity and 3 in the high-intensity group). Any discrepancies in the paper were resolved through personal discussion with RA who was one of the authors involved in both Ulrich 2001 and this study, and who is also a review author<br>Corrected age at entry: 9.65 (SD 1.61) months for the higher-intensity group; and 10. 40 (SD 2.14) months for the lower-intensity group<br>2 African American, 2 biracial, and remaining infants were white |
| Interventions | Experimental group (high-intensity treadmill training): 5days/week, with two treadmill parameters (minutes/day, treadmill belt speed) individualised, as well as an ankle weight being added as the infant progressed in frequency of alternating steps; co-interventions: early intervention services and any other activities that were prescribed by their health care providers<br>Control group (low-intensity treadmill training): 5 days/week, 6min/session, belt speed 0.18m/s; co-interventions: early intervention services and any other activities that were prescribed by their health care providers<br>The training stopped when infants could take 3 independent steps overground<br>Four additional publications (Wu 2007; Angulo-Barroso 2008; Wu 2008; Wu 2010) dealt with the follow-up from this intervention including assessments from 1 to 15 months post walking onset (i.e. after termination of the intervention) |
| Outcomes | The study reported frequency of alternating TM steps and onset of assisted and independent walking. The follow-up publications reported on spatio-temporal variables, joint kinematics, and gait adaptation parameters, In addition, Wu 2007 presented follow-up spatio-temporal gait variables including a historical control group from Ulrich 2001, which we did not use this data as it was not randomised)<br>**Publication Wu 2007**<br>Gait follow-up assessment, between 1 and 3 months after walking onset (training groups) and 1 month after walking onset (control group)<br>Age at walking onset (decreased when any training, with further decreases in high-intensity group = positive effects of training at higher intensities)<br>Elapsed time from entry to walking onset.<br>Gait speed.<br>Gait stride length.<br>Gait stride width.<br>**Publication Angulo-Barroso 2008**<br>Measured after the onset of independent walking during 4 home-visits scheduled at the following infant's age (low-intensity group: 24.9 mo SD 5.1; 28.4 mo SD 4.6; 30.5 SD 5.1; 36.5 SD 4.9 - high-intensity group: 21.3 mo SD 2.4, 24.4 mo SD 2.4, 27.3 SD 2.3, 33.7 SD 2.5). The walking experience prior to visit one had been 3.3 mo (SD 1.2 |

| | |
|---|---|
| | mo) for the low-intensity group and 2.6 mo (SD 0.9 mo) for the high-intensity group<br>Velocity (increased after hi-intensity training = positive effect)<br>Cadence (increased after hi-intensity training = positive effect)<br>Step length (increased after hi-intensity training = positive effect)<br>Step width (decreased after hi-intensity training = positive effect)<br>Gait double-limb support.<br>**Publication Wu 2008**<br>Age at onset of independent walking<br>**Publication Wu 2010**<br>Toe-off as % of gait cycle<br>Joint angle (ankle: plantar flexion and dorsiflexion; hip: extension and flexion and abduction and adduction; knee: extension and flexion) |
| Notes | Country: USA (Michigan, Ohio, Indiana).<br>Funding sources: research grant from the US Office of Special Education and Rehabilitative Services (H324C010067), a US Office of Special Education Programs Leadership Training Grant (H325D020028), and the Steelcase Foundation in Michigan |

***Risk of bias*** ***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Random numbers table was used to assign to either low intensity training group or high intensity training group (described in Wu 2007) |
| Allocation concealment (selection bias) | Unclear risk | This information is obtained from another publication of the same study (Wu 2007):<br>"The randomisation procedure was conducted by the fourth investigator for the two cohorts separately via a table of random numbers." This means that each randomisation was conducted separately with the involvement of only the 4th author and with the use of a table of random numbers. This does not give us enough information to make a judgement |
| Incomplete outcome data (attrition bias) Experimental group 1 | Low risk | High-intensity treadmill training.<br>20 allocated<br>3 excluded from the analyses because their parents routinely did not adhere to the protocol<br>1 also excluded from the analysis because of emerging medical conditions<br>Low-intensity treadmill training.<br>16 allocated<br>1 excluded from the analyses because their parents routinely did not adhere to the protocol<br>1 also excluded from the analysis because of emerging medical conditions |

**Ulrich 2008** (*Continued*)

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Unclear risk | It is not clear if all data are reported. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | No blinding of participants or personnel. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | No blinding of outcome assessment. |
| Other bias | Unclear risk | We do not have enough information to make a judgement. |

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Borggraefe 2007 | The participants were older children. |
| Borggraefe 2010 | The participants were older children. There was no control group |
| Dodd 2007 | The participants were older children. |
| Maltais 2003 | The participants were older children. |
| Matsuno 2010 | The participants were older children. |
| Meyer-Heim 2007 | The participants were older children. |
| Mussleman 2007 | No training with the treadmill, it was used for investigation purposes |
| Pang 2003 | No training with the treadmill, it was used for investigation purposes |
| Phillips 2007 | The participants were older children. |
| Schindl 2000 | The participants were older children. |
| Schlittler 2011 | Allocation to groups not random. |
| Smania 2011 | The participants were older children. |
| Teulier 2009 | No training with the treadmill, it was used for investigation purposes |

## DATA AND ANALYSES

### Comparison 1. Treadmill vs No Treadmill

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Step frequency (8 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 4.91 [-1.78, 11.61] |
| 1.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 4.91 [-1.78, 11.61] |
| 2 Step frequency (9 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -10.23 [-16.53, -3.93] |
| 2.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -10.23 [-16.53, -3.93] |
| 3 Step frequency (10 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 7.72 [2.57, 12.86] |
| 3.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 7.72 [2.57, 12.86] |
| 4 Step frequency (11 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -1.63 [-6.69, 3.42] |
| 4.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -1.63 [-6.69, 3.42] |
| 5 Step frequency (12 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -9.20 [-14.54, -3.86] |
| 5.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -9.20 [-14.54, -3.86] |
| 6 Step frequency (13 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 7.53 [2.24, 12.82] |
| 6.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 7.53 [2.24, 12.82] |
| 7 Step frequency (14 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -6.60 [-12.51, -0.69] |
| 7.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -6.60 [-12.51, -0.69] |
| 8 Step frequency (15 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 7.90 [1.58, 14.22] |
| 8.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 7.90 [1.58, 14.22] |
| 9 Step frequency (16 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 4.36 [-2.63, 11.35] |
| 9.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 4.36 [-2.63, 11.35] |
| 10 Step quality (8 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 8.44 [0.46, 16.42] |
| 10.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 8.44 [0.46, 16.42] |
| 11 Step quality (9 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 2.69 [-4.79, 10.17] |
| 11.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 2.69 [-4.79, 10.17] |
| 12 Step quality (10 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -15.67 [-21.69, -9.66] |
| 12.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -15.67 [-21.69, -9.66] |
| 13 Step quality (11 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -20.98 [-26.87, -15.08] |
| 13.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -20.98 [-26.87, -15.08] |

| | | | | |
|---|---|---|---|---|
| 14 Step quality (12 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -14.30 [-20.57, -8.04] |
| 14.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -14.30 [-20.57, -8.04] |
| 15 Step quality (13 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -34.67 [-40.87, -28.47] |
| 15.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -34.67 [-40.87, -28.47] |
| 16 Step quality (14 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -33.34 [-40.33, -26.36] |
| 16.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -33.34 [-40.33, -26.36] |
| 17 Step quality (15 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -24.92 [-32.43, -17.42] |
| 17.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -24.92 [-32.43, -17.42] |
| 18 Step quality (16 months) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -15.61 [-23.96, -7.27] |
| 18.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -15.61 [-23.96, -7.27] |
| 19 Age of onset of independent walking | 2 | 58 | Mean Difference (IV, Fixed, 95% CI) | -1.47 [-2.97, 0.03] |
| 19.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -0.60 [-2.34, 1.14] |
| 19.2 Down syndrome | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -4.0 [-6.96, -1.04] |
| 20 Onset of walking with assistance [days in study] | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -74.0 [-135.40, -12.60] |
| 20.1 Down syndrome | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -74.0 [-135.40, -12.60] |
| 21 Gross motor function: GMFM | 2 | 36 | Mean Difference (IV, Fixed, 95% CI) | 0.88 [-4.54, 6.30] |
| 21.1 Spastic cerebral palsy | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 7.60 [-19.46, 34.66] |
| 21.2 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 0.60 [-4.93, 6.13] |
| 22 Other gait parameters: velocity | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 0.39 [-4.19, 4.97] |
| 22.1 Spastic cerebral palsy | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 0.39 [-4.19, 4.97] |
| 23 Other gait parameters: velocity (follow-up when walking independently) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 1.32 [-0.53, 3.17] |
| 23.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 1.32 [-0.53, 3.17] |
| 24 Other gait parameters: velocity (follow-up 3 months later) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -1.92 [-4.72, 0.88] |
| 24.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -1.92 [-4.72, 0.88] |
| 25 Other gait parameters: velocity (follow-up 6 months later) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -3.35 [-7.44, 0.74] |
| 25.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -3.35 [-7.44, 0.74] |
| 26 Other gait parameters: step length | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 0.37 [-25.04, 25.78] |
| 26.1 Spastic cerebral palsy | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 0.37 [-25.04, 25.78] |

| | | | | |
|---|---|---|---|---|
| 27 Other gait parameters: step length (follow-up when walking independently) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 8.0 [-1.60, 17.60] |
| 27.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 8.0 [-1.60, 17.60] |
| 28 Other gait parameters: step length (follow-up 3 months later) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -5.0 [-14.26, 4.26] |
| 28.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -5.0 [-14.26, 4.26] |
| 29 Other gait parameters: step length (follow-up 6 months later) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -6.0 [-15.26, 3.26] |
| 29.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -6.0 [-15.26, 3.26] |
| 30 Other gait parameters: gait double-limb support | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 3.80 [-21.52, 29.12] |
| 30.1 Spastic cerebral palsy | 1 | 8 | Mean Difference (IV, Fixed, 95% CI) | 3.80 [-21.52, 29.12] |
| 31 Other gait parameters: gait double-limb support (follow-up when walking independently) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -4.19 [-10.02, 1.64] |
| 31.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | -4.19 [-10.02, 1.64] |
| 32 Other gait parameters: gait double-limb support (follow-up 3 months later) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 3.16 [-0.22, 6.54] |
| 32.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 3.16 [-0.22, 6.54] |
| 33 Other gait parameters: gait double-limb support (follow-up 6 months later) | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 3.17 [-0.10, 6.44] |
| 33.1 Risk of developmental delay | 1 | 28 | Mean Difference (IV, Fixed, 95% CI) | 3.17 [-0.10, 6.44] |

**Comparison 2. Treadmill without orthoses vs Treadmill with orthoses**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Walking independently (1 month follow-up) | 1 | 17 | Mean Difference (IV, Fixed, 95% CI) | 0.10 [-5.96, 6.16] |
| 1.1 Down syndrome | 1 | 17 | Mean Difference (IV, Fixed, 95% CI) | 0.10 [-5.96, 6.16] |
| 2 Gross motor function (GMFM 1 month follow-up) | 1 | 17 | Mean Difference (IV, Fixed, 95% CI) | -8.40 [-14.55, -2.25] |
| 2.1 Down syndrome | 1 | 17 | Mean Difference (IV, Fixed, 95% CI) | -8.40 [-14.55, -2.25] |

**Comparison 3. High-intensity treadmill vs Low-intensity treadmill**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Step frequency | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -11.0 [-15.90, -6.10] |
| 1.1 Down syndrome | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -11.0 [-15.90, -6.10] |
| 2 Age of onset of independent walking | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -2.13 [-4.96, 0.70] |
| 2.1 Down syndrome | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -2.13 [-4.96, 0.70] |
| 3 Onset of walking with assistance | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -1.86 [-4.09, 0.37] |
| 3.1 Down syndrome | 1 | 30 | Mean Difference (IV, Fixed, 95% CI) | -1.86 [-4.09, 0.37] |
| 4 Chronological Age. Follow-up (visit 1) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.60 [-6.77, -0.43] |
| 4.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.60 [-6.77, -0.43] |
| 5 Chronological Age. Follow-up (visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -4.0 [-6.86, -1.14] |
| 5.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -4.0 [-6.86, -1.14] |
| 6 Chronological Age. Follow-up (visit 3) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.20 [-6.34, -0.06] |
| 6.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.20 [-6.34, -0.06] |
| 7 Chronological Age. Follow-up (visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.80 [-5.89, 0.29] |
| 7.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.80 [-5.89, 0.29] |
| 8 Other gait parameters: velocity follow-up (visit1) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.06, 0.16] |
| 8.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.05 [-0.06, 0.16] |
| 9 Other gait parameters: velocity follow-up (visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.16 [0.01, 0.31] |
| 9.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.16 [0.01, 0.31] |
| 10 Other gait parameters: velocity follow-up (visit 3) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.07, 0.27] |
| 10.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.10 [-0.07, 0.27] |
| 11 Other gait parameters: velocity follow-up (visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.16 [-0.07, 0.39] |
| 11.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.16 [-0.07, 0.39] |
| 12 Other gait parameters: step length follow-up (visit 1) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 1.83 [-0.89, 4.55] |
| 12.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 1.83 [-0.89, 4.55] |
| 13 Other gait parameters: step length follow-up (visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 2.55 [-0.67, 5.77] |
| 13.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 2.55 [-0.67, 5.77] |
| 14 Other gait parameters: step length follow-up (visit 3) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.68 [-1.96, 3.32] |
| 14.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.68 [-1.96, 3.32] |
| 15 Other gait parameters: step length follow-up (visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 2.68 [-0.99, 6.35] |
| 15.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 2.68 [-0.99, 6.35] |
| 16 Other gait parameters: step width follow-up (visit 1) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.12 [-2.37, 2.61] |
| 16.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | 0.12 [-2.37, 2.61] |

| | | | | |
|---|---|---|---|---|
| 17 Other gait parameters: step width follow-up (visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -1.23 [-3.69, 1.23] |
| 17.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -1.23 [-3.69, 1.23] |
| 18 Other gait parameters: step width follow-up (visit 3) | 1 | 24 | Mean Difference (IV, Fixed, 95% CI) | -0.54 [-2.52, 1.44] |
| 18.1 Down syndrome | 1 | 24 | Mean Difference (IV, Fixed, 95% CI) | -0.54 [-2.52, 1.44] |
| 19 Other gait parameters: step width follow-up (visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.58 [-2.11, 0.95] |
| 19.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.58 [-2.11, 0.95] |
| 20 Other gait parameters: gait double-limb support follow-up (visit 1) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.90 [-8.07, 2.27] |
| 20.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.90 [-8.07, 2.27] |
| 21 Other gait parameters: gait double-limb support follow-up (visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -4.0 [-7.91, -0.09] |
| 21.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -4.0 [-7.91, -0.09] |
| 22 Other gait parameters: gait double-limb support follow-up (visit 3) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.0 [-6.29, 2.29] |
| 22.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.0 [-6.29, 2.29] |
| 23 Other gait parameters: gait double-limb support follow-up (visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.80 [-3.27, 1.67] |
| 23.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.80 [-3.27, 1.67] |
| 24 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 1) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.10 [-7.34, 1.14] |
| 24.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.10 [-7.34, 1.14] |
| 25 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -4.80 [-8.76, -0.84] |
| 25.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -4.80 [-8.76, -0.84] |
| 26 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 3) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.90 [-6.28, 0.48] |
| 26.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.90 [-6.28, 0.48] |
| 27 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.40 [-8.98, 2.18] |
| 27.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -3.40 [-8.98, 2.18] |
| 28 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 1) | 1 | 26 | Mean Difference (IV, Fixed, 95% CI) | -0.40 [-3.47, 2.67] |
| 28.1 Down syndrome | 1 | 26 | Mean Difference (IV, Fixed, 95% CI) | -0.40 [-3.47, 2.67] |
| 29 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 2) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -1.5 [-5.08, 2.08] |
| 29.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -1.5 [-5.08, 2.08] |
| 30 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 3) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.10 [-2.69, 2.49] |

| | | | | |
|---|---|---|---|---|
| 30.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.10 [-2.69, 2.49] |
| 31 Other gait parameters:gait ankle dorsiflexion. Follow-up (Visit 4) | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.80 [-5.96, 0.36] |
| 31.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.80 [-5.96, 0.36] |
| 32 Other gait parameters: toe-off follow-up visit 1 | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.20 [-6.17, 1.77] |
| 32.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.20 [-6.17, 1.77] |
| 33 Other gait parameters: toe-off; follow-up visit 2 | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.30 [-5.50, 0.90] |
| 33.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -2.30 [-5.50, 0.90] |
| 34 Other gait parameters: toe-off; follow-up visit 3 | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -1.20 [-3.95, 1.55] |
| 34.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -1.20 [-3.95, 1.55] |
| 35 Other gait parameters: toe-off follow-up visit 4 | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.90 [-5.49, 3.69] |
| 35.1 Down syndrome | 1 | 25 | Mean Difference (IV, Fixed, 95% CI) | -0.90 [-5.49, 3.69] |

### Analysis 1.1. Comparison 1 Treadmill vs No Treadmill, Outcome 1 Step frequency (8 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 1 Step frequency (8 months)

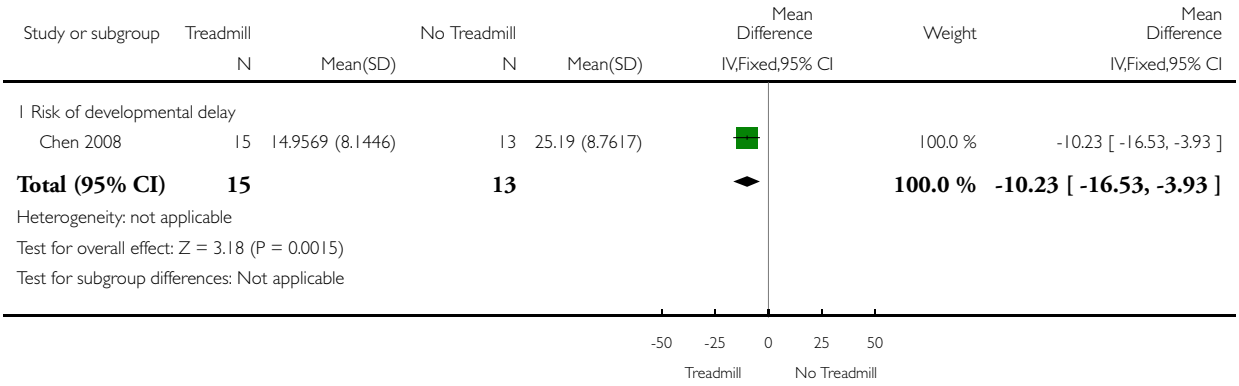
| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 28.3534 (9.2457) | 13 | 23.44 (8.8124) | | 100.0 % | 4.91 [ -1.78, 11.61 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **4.91 [ -1.78, 11.61 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 1.44 (P = 0.15) | | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | | |

### Analysis 1.2. Comparison 1 Treadmill vs No Treadmill, Outcome 2 Step frequency (9 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 2 Step frequency (9 months)

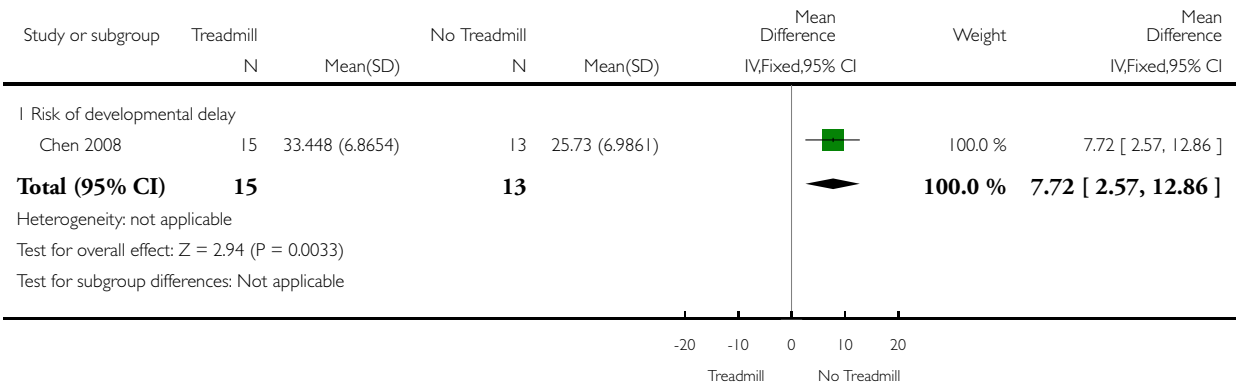



### Analysis 1.3. Comparison 1 Treadmill vs No Treadmill, Outcome 3 Step frequency (10 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 3 Step frequency (10 months)

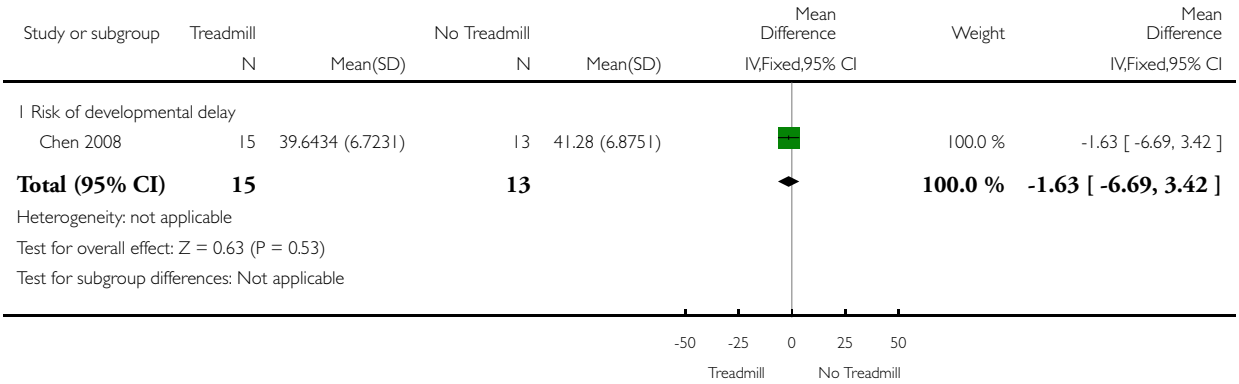


### Analysis 1.4. Comparison 1 Treadmill vs No Treadmill, Outcome 4 Step frequency (11 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 4 Step frequency (11 months)

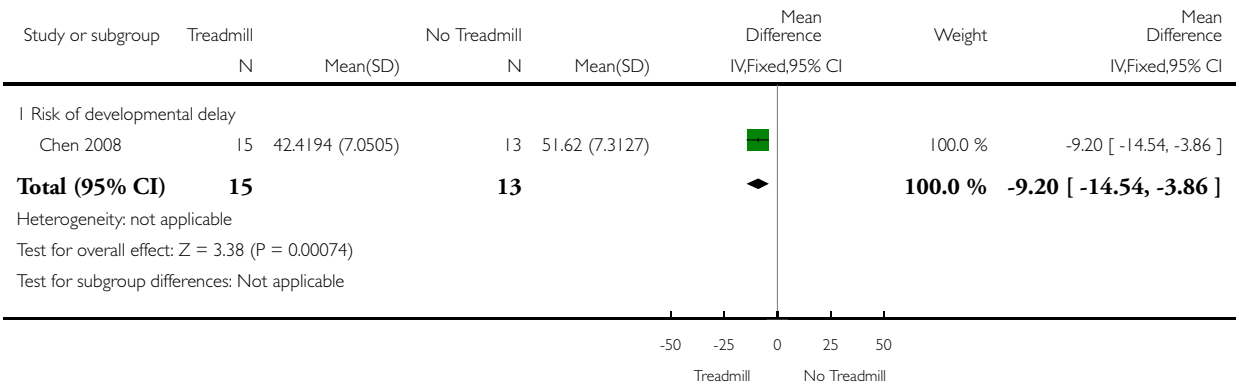



### Analysis 1.5. Comparison 1 Treadmill vs No Treadmill, Outcome 5 Step frequency (12 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 5 Step frequency (12 months)

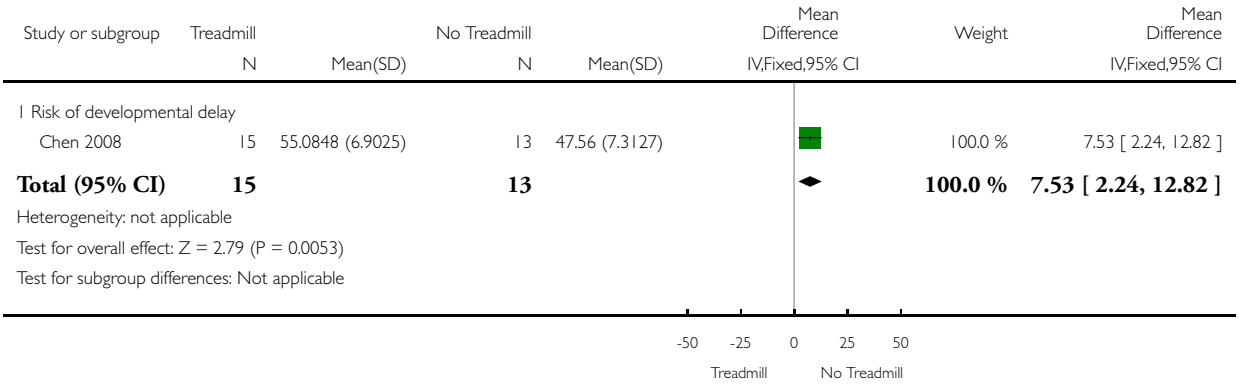


### Analysis 1.6. Comparison 1 Treadmill vs No Treadmill, Outcome 6 Step frequency (13 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 6 Step frequency (13 months)

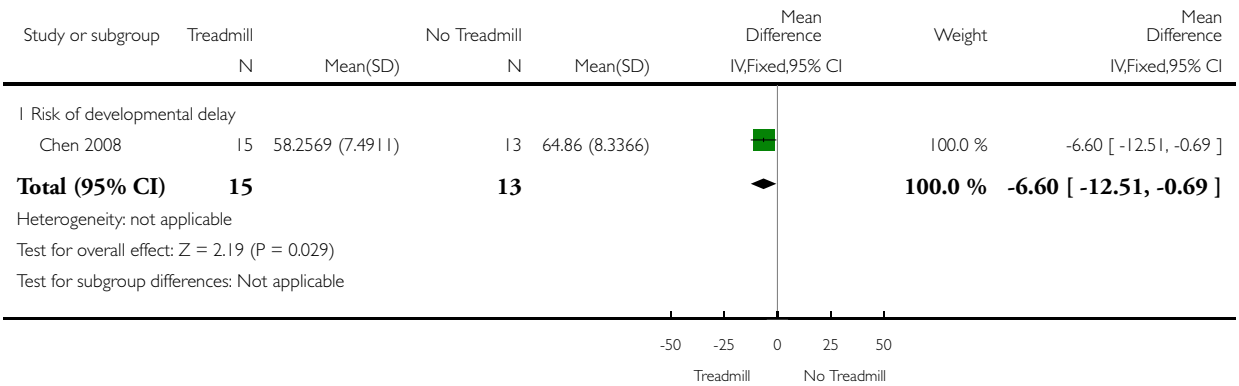



### Analysis 1.7. Comparison 1 Treadmill vs No Treadmill, Outcome 7 Step frequency (14 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 7 Step frequency (14 months)

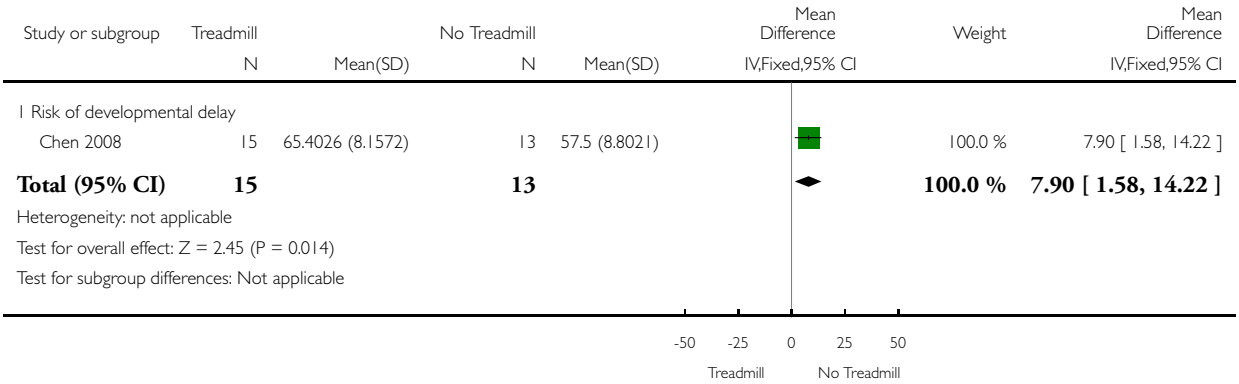


### Analysis 1.8. Comparison 1 Treadmill vs No Treadmill, Outcome 8 Step frequency (15 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 8 Step frequency (15 months)

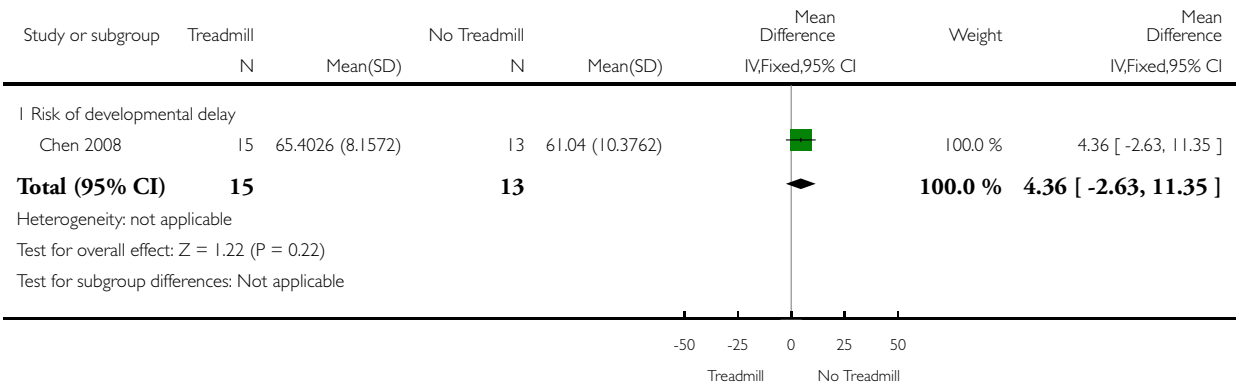



### Analysis 1.9. Comparison 1 Treadmill vs No Treadmill, Outcome 9 Step frequency (16 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 9 Step frequency (16 months)

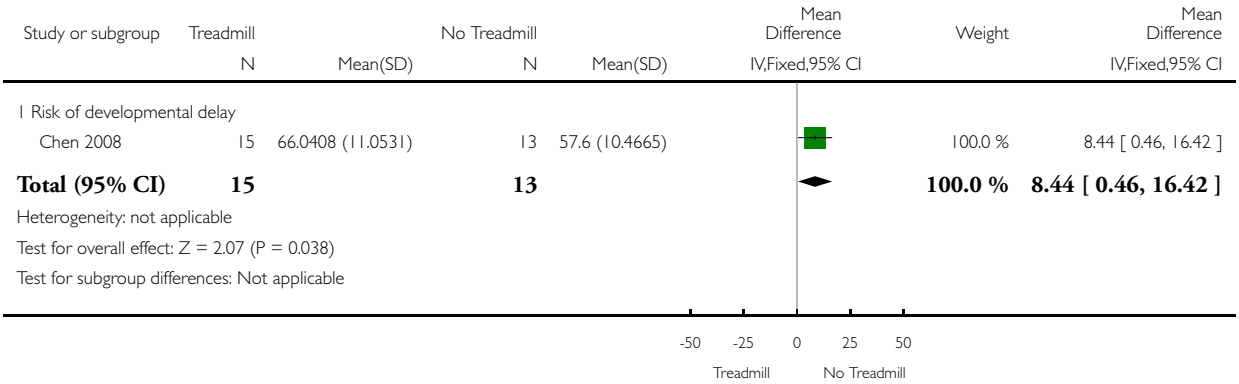


### Analysis 1.10. Comparison 1 Treadmill vs No Treadmill, Outcome 10 Step quality (8 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 10 Step quality (8 months)

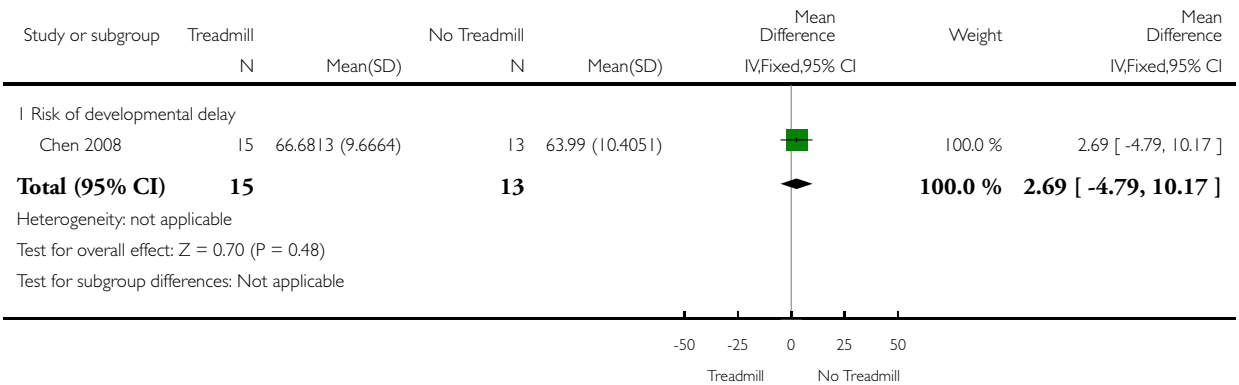



### Analysis 1.11. Comparison 1 Treadmill vs No Treadmill, Outcome 11 Step quality (9 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 11 Step quality (9 months)



### Analysis 1.12. Comparison 1 Treadmill vs No Treadmill, Outcome 12 Step quality (10 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 12 Step quality (10 months)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 48.1682 (8.0483) | 13 | 63.84 (8.1494) | | 100.0 % | -15.67 [ -21.69, -9.66 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-15.67 [ -21.69, -9.66 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 5.11 (P < 0.00001)

Test for subgroup differences: Not applicable


### Analysis 1.13. Comparison 1 Treadmill vs No Treadmill, Outcome 13 Step quality (11 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 13 Step quality (11 months)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 40.2846 (7.8669) | 13 | 61.26 (8.0069) | | 100.0 % | -20.98 [ -26.87, -15.08 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-20.98 [ -26.87, -15.08 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 6.97 (P < 0.00001)

Test for subgroup differences: Not applicable

### Analysis 1.14. Comparison 1 Treadmill vs No Treadmill, Outcome 14 Step quality (12 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 14 Step quality (12 months)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 44.6005 (8.2827) | 13 | 58.9 (8.5653) | | 100.0 % | -14.30 [ -20.57, -8.04 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-14.30 [ -20.57, -8.04 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 4.47 (P < 0.00001)

Test for subgroup differences: Not applicable


### Analysis 1.15. Comparison 1 Treadmill vs No Treadmill, Outcome 15 Step quality (13 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

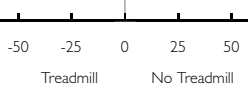
Outcome: 15 Step quality (13 months)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 24.2325 (8.0935) | 13 | 58.9 (8.5653) | | 100.0 % | -34.67 [ -40.87, -28.47 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-34.67 [ -40.87, -28.47 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 10.96 (P < 0.00001)

Test for subgroup differences: Not applicable

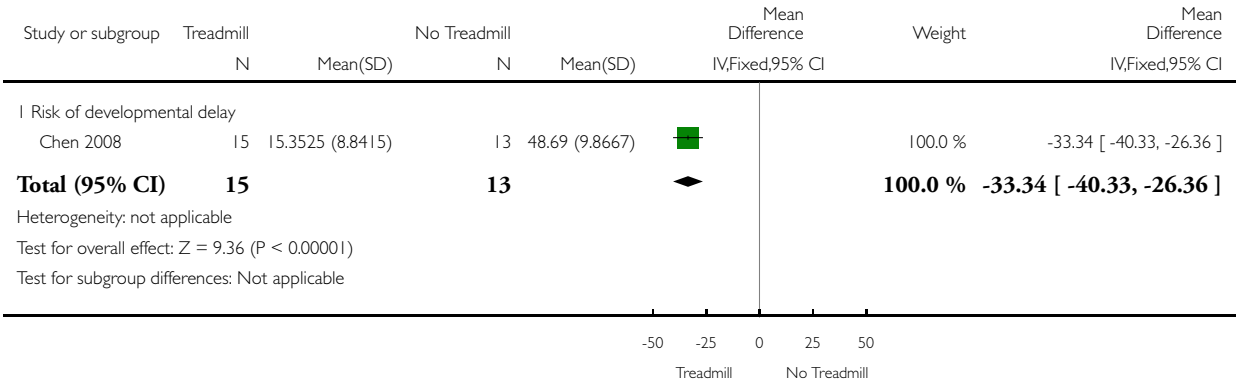


### Analysis 1.16. Comparison 1 Treadmill vs No Treadmill, Outcome 16 Step quality (14 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 16 Step quality (14 months)

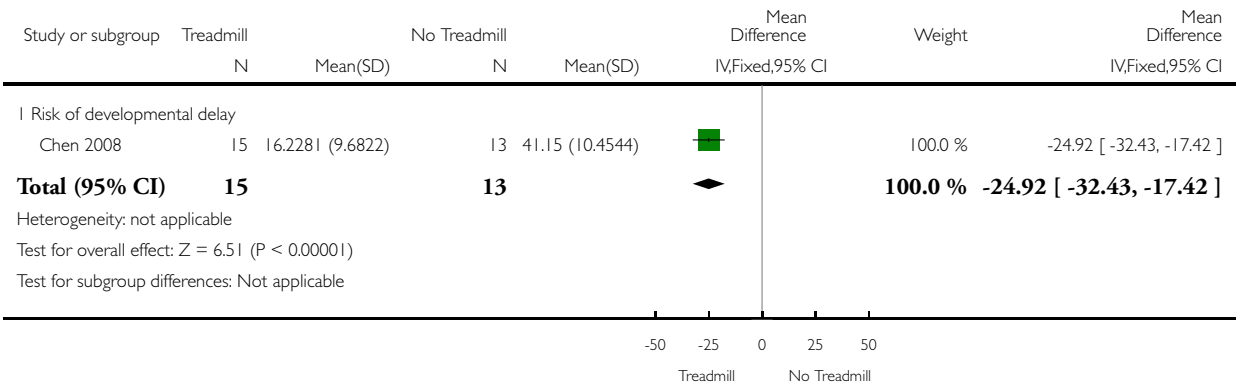



### Analysis 1.17. Comparison 1 Treadmill vs No Treadmill, Outcome 17 Step quality (15 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 17 Step quality (15 months)

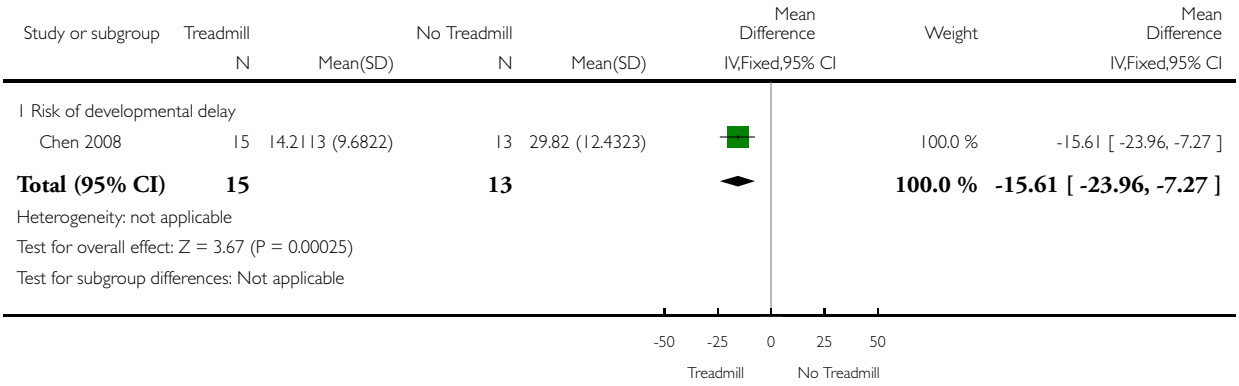


### Analysis 1.18. Comparison 1 Treadmill vs No Treadmill, Outcome 18 Step quality (16 months).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 18 Step quality (16 months)



### Analysis 1.19. Comparison 1 Treadmill vs No Treadmill, Outcome 19 Age of onset of independent walking.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 19 Age of onset of independent walking

| Study or subgroup | Treadmill N | Mean(SD)[months] | No Treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 13 | 13.7 (2.2) | 15 | 14.3 (2.5) | | 74.4 % | -0.60 [ -2.34, 1.14 ] |
| **Subtotal (95% CI)** | **13** | | **15** | | | **74.4 %** | **-0.60 [ -2.34, 1.14 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 0.68 (P = 0.50) | | | | | | | |
| 2 Down syndrome | | | | | | | |
| Ulrich 2001 | 15 | 19.9 (3.33) | 15 | 23.9 (4.82) | | 25.6 % | -4.00 [ -6.96, -1.04 ] |
| **Subtotal (95% CI)** | **15** | | **15** | | | **25.6 %** | **-4.00 [ -6.96, -1.04 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 2.64 (P = 0.0082) | | | | | | | |
| **Total (95% CI)** | **28** | | **30** | | | **100.0 %** | **-1.47 [ -2.97, 0.03 ]** |
| Heterogeneity: $Chi^2$ = 3.76, df = 1 (P = 0.05); $I^2$ =73% | | | | | | | |
| Test for overall effect: Z = 1.92 (P = 0.055) | | | | | | | |
| Test for subgroup differences: $Chi^2$ = 3.76, df = 1 (P = 0.05), $I^2$ =73% | | | | | | | |

## Analysis 1.20. Comparison 1 Treadmill vs No Treadmill, Outcome 20 Onset of walking with assistance [days in study].

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

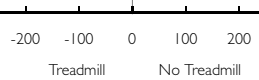
Outcome: 20 Onset of walking with assistance [days in study]

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2001 | 15 | 166 (64.6) | 15 | 240 (102.7) | | 100.0 % | -74.00 [ -135.40, -12.60 ] |
| **Total (95% CI)** | **15** | | **15** | | | **100.0 %** | **-74.00 [ -135.40, -12.60 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 2.36 (P = 0.018)

Test for subgroup differences: Not applicable

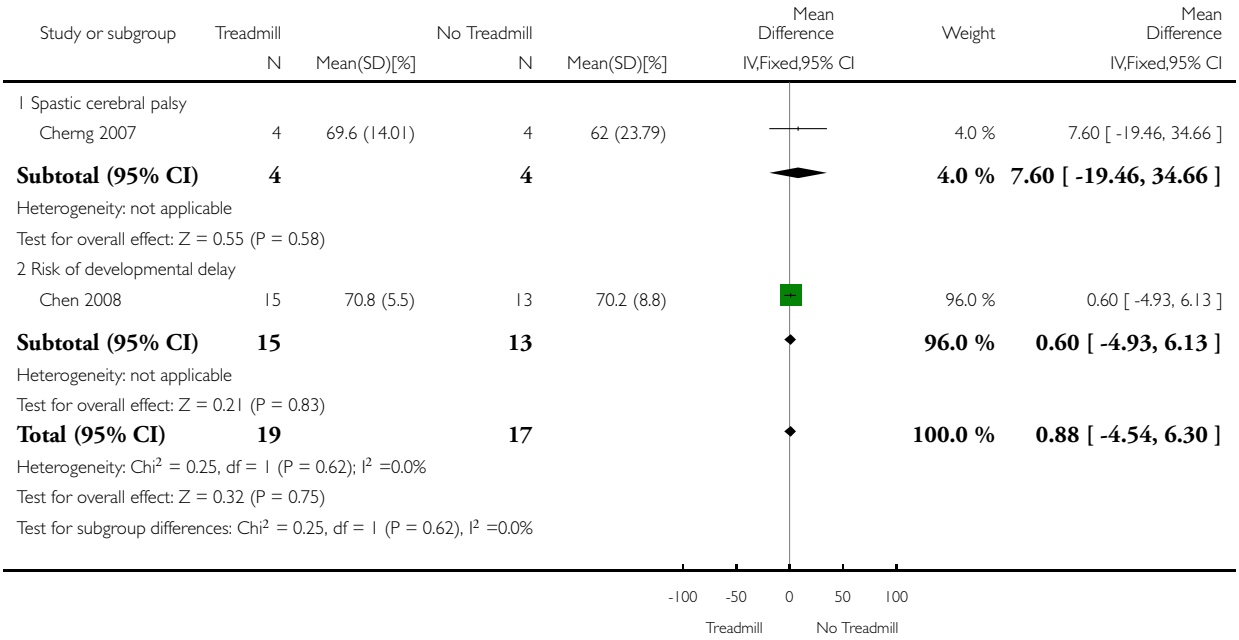


### Analysis 1.21. Comparison 1 Treadmill vs No Treadmill, Outcome 21 Gross motor function: GMFM.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 21 Gross motor function: GMFM



### Analysis 1.22. Comparison 1 Treadmill vs No Treadmill, Outcome 22 Other gait parameters: velocity.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 22 Other gait parameters: velocity

| Study or subgroup | Treadmill N | Mean(SD)[m/s] | No Treadmill N | Mean(SD)[m/s] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Spastic cerebral palsy | | | | | | | |
| Cherng 2007 | 4 | 2.85 (3.94) | 4 | 2.46 (2.51) | | 100.0 % | 0.39 [ -4.19, 4.97 ] |
| **Total (95% CI)** | **4** | | **4** | | | **100.0 %** | **0.39 [ -4.19, 4.97 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.87)

Test for subgroup differences: Not applicable


### Analysis 1.23. Comparison 1 Treadmill vs No Treadmill, Outcome 23 Other gait parameters: velocity (follow-up when walking independently).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 23 Other gait parameters: velocity (follow-up when walking independently)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 11.82 (2.66) | 13 | 10.5 (2.33) | | 100.0 % | 1.32 [ -0.53, 3.17 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **1.32 [ -0.53, 3.17 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.40 (P = 0.16)

Test for subgroup differences: Not applicable

### Analysis 1.24. Comparison 1 Treadmill vs No Treadmill, Outcome 24 Other gait parameters: velocity (follow-up 3 months later).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

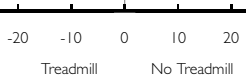
Outcome: 24 Other gait parameters: velocity (follow-up 3 months later)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 15.77 (4.08) | 13 | 17.69 (3.48) | | 100.0 % | -1.92 [ -4.72, 0.88 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-1.92 [ -4.72, 0.88 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.34 (P = 0.18)

Test for subgroup differences: Not applicable




### Analysis 1.25. Comparison 1 Treadmill vs No Treadmill, Outcome 25 Other gait parameters: velocity (follow-up 6 months later).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

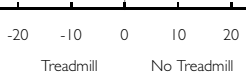
Outcome: 25 Other gait parameters: velocity (follow-up 6 months later)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 16.48 (5.49) | 13 | 19.83 (5.52) | | 100.0 % | -3.35 [ -7.44, 0.74 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-3.35 [ -7.44, 0.74 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.61 (P = 0.11)

Test for subgroup differences: Not applicable

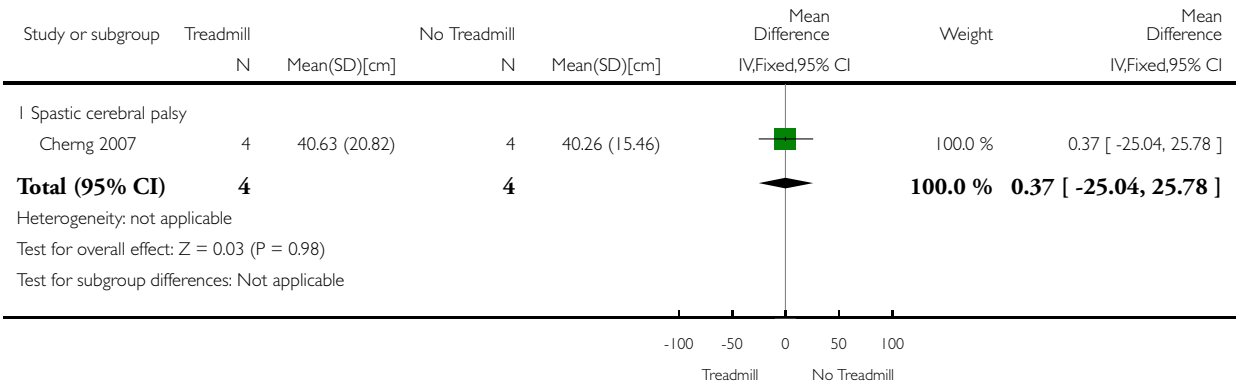


### Analysis 1.26. Comparison 1 Treadmill vs No Treadmill, Outcome 26 Other gait parameters: step length.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 26 Other gait parameters: step length

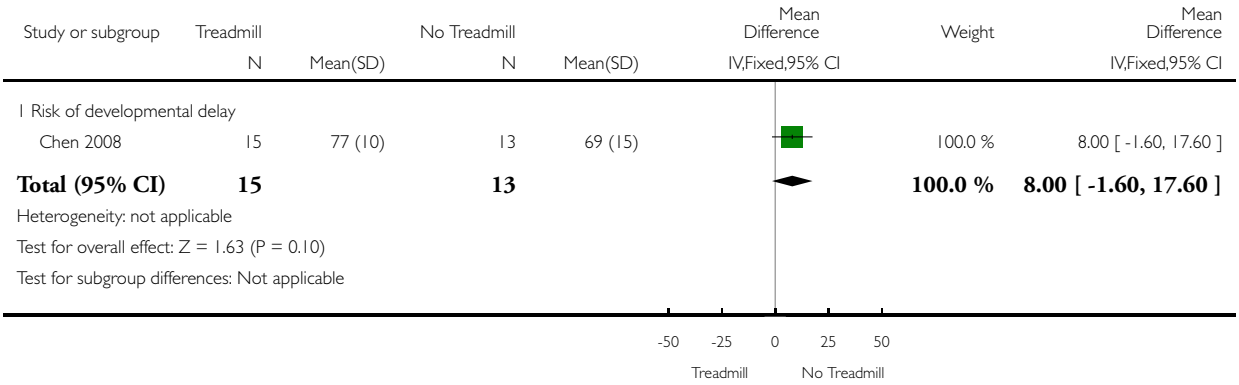


### Analysis 1.27. Comparison 1 Treadmill vs No Treadmill, Outcome 27 Other gait parameters: step length (follow-up when walking independently).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 27 Other gait parameters: step length (follow-up when walking independently)

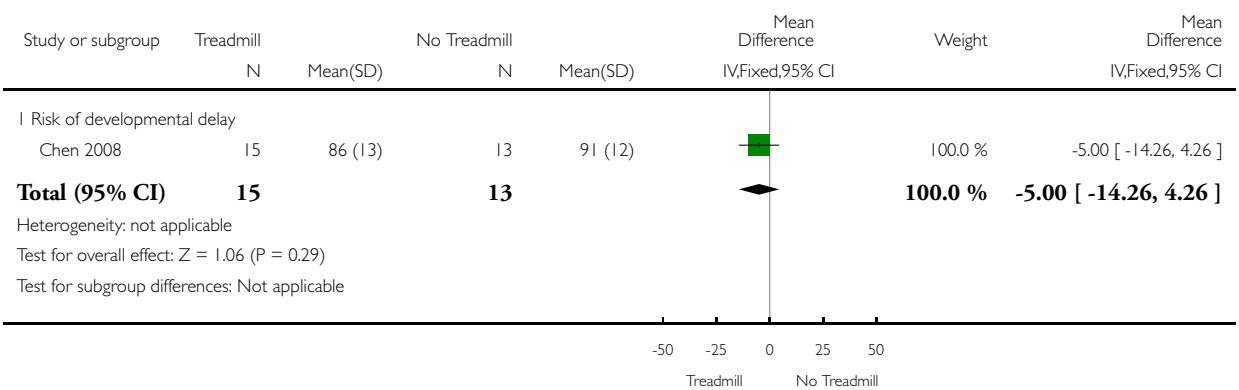



### Analysis 1.28. Comparison 1 Treadmill vs No Treadmill, Outcome 28 Other gait parameters: step length (follow-up 3 months later).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 28 Other gait parameters: step length (follow-up 3 months later)



### Analysis 1.29. Comparison 1 Treadmill vs No Treadmill, Outcome 29 Other gait parameters: step length (follow-up 6 months later).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 29 Other gait parameters: step length (follow-up 6 months later)

| Study or subgroup | Treadmill N | Mean(SD) | No Treadmill N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 88 (13) | 13 | 94 (12) | | 100.0 % | -6.00 [ -15.26, 3.26 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **-6.00 [ -15.26, 3.26 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.27 (P = 0.20)

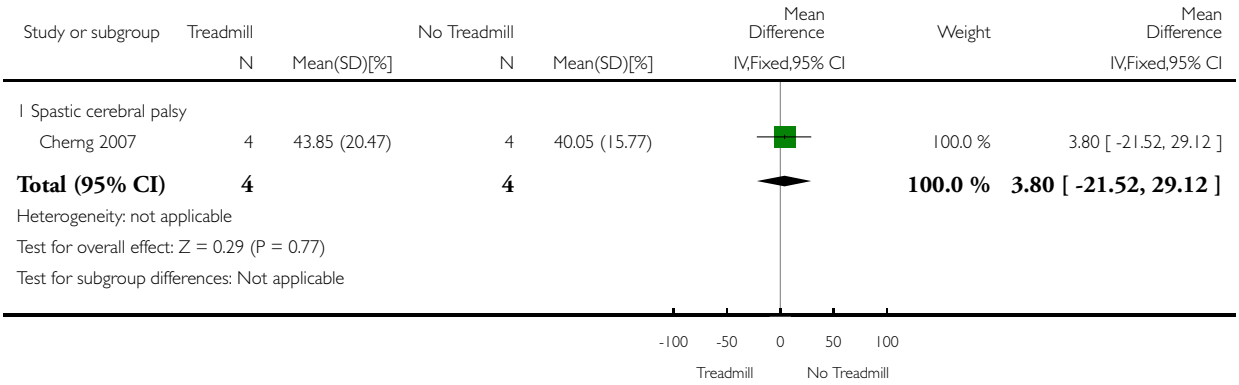
Test for subgroup differences: Not applicable

### Analysis 1.30. Comparison 1 Treadmill vs No Treadmill, Outcome 30 Other gait parameters: gait double-limb support.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 30 Other gait parameters: gait double-limb support

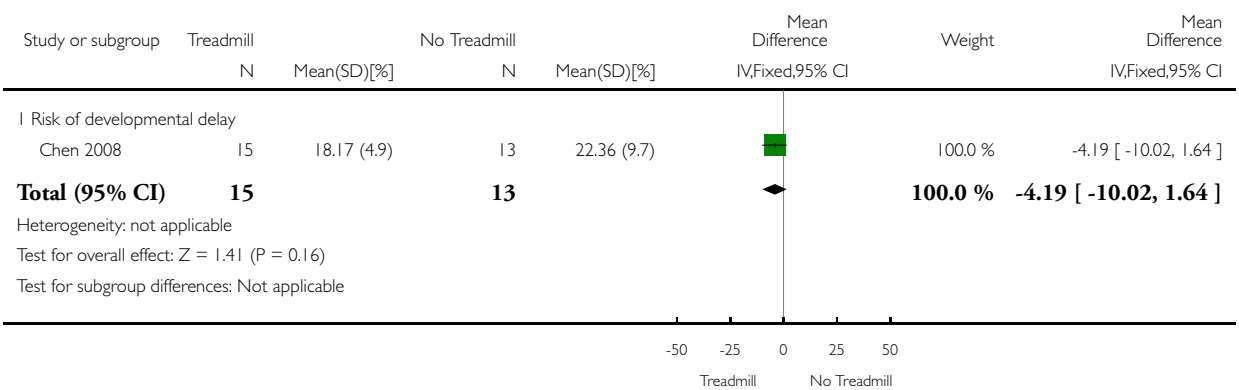



### Analysis 1.31. Comparison 1 Treadmill vs No Treadmill, Outcome 31 Other gait parameters: gait double-limb support (follow-up when walking independently).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 31 Other gait parameters: gait double-limb support (follow-up when walking independently)



### Analysis 1.32. Comparison 1 Treadmill vs No Treadmill, Outcome 32 Other gait parameters: gait double-limb support (follow-up 3 months later).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 32 Other gait parameters: gait double-limb support (follow-up 3 months later)

| Study or subgroup | Treadmill N | Mean(SD)[%] | No Treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 15.46 (5.22) | 13 | 12.3 (3.89) | | 100.0 % | 3.16 [ -0.22, 6.54 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **3.16 [ -0.22, 6.54 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.83 (P = 0.067)

Test for subgroup differences: Not applicable

### Analysis 1.33. Comparison 1 Treadmill vs No Treadmill, Outcome 33 Other gait parameters: gait double-limb support (follow-up 6 months later).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 1 Treadmill vs No Treadmill

Outcome: 33 Other gait parameters: gait double-limb support (follow-up 6 months later)

| Study or subgroup | Treadmill N | Mean(SD)[%] | No Treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Risk of developmental delay | | | | | | | |
| Chen 2008 | 15 | 16.18 (5.05) | 13 | 13.01 (3.75) | | 100.0 % | 3.17 [ -0.10, 6.44 ] |
| **Total (95% CI)** | **15** | | **13** | | | **100.0 %** | **3.17 [ -0.10, 6.44 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.90 (P = 0.057)

Test for subgroup differences: Not applicable


### Analysis 2.1. Comparison 2 Treadmill without orthoses vs Treadmill with orthoses, Outcome 1 Walking independently (1 month follow-up).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 2 Treadmill without orthoses vs Treadmill with orthoses

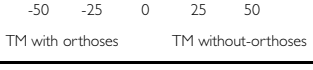
Outcome: 1 Walking independently (1 month follow-up)

| Study or subgroup | TM with orthoses N | Mean(SD)[months] | TM without orthoses N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Looper 2010 | 10 | 27.99 (5.36) | 7 | 27.89 (6.84) | | 100.0 % | 0.10 [ -5.96, 6.16 ] |
| **Total (95% CI)** | **10** | | **7** | | | **100.0 %** | **0.10 [ -5.96, 6.16 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.03 (P = 0.97)

Test for subgroup differences: Not applicable



### Analysis 2.2. Comparison 2 Treadmill without orthoses vs Treadmill with orthoses, Outcome 2 Gross motor function (GMFM 1 month follow-up).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 2 Treadmill without orthoses vs Treadmill with orthoses

Outcome: 2 Gross motor function (GMFM 1 month follow-up)

| Study or subgroup | TM with orthoses | | TM without orthoses | | Mean Difference | Weight | Mean Difference |
|---|---|---|---|---|---|---|---|
| | N | Mean(SD)[%] | N | Mean(SD)[%] | IV,Fixed,95% CI | | IV,Fixed,95% CI |
| 1 Down syndrome | | | | | | | |
| Looper 2010 | 10 | 53.8 (6.6) | 7 | 62.2 (6.2) | | 100.0 % | -8.40 [ -14.55, -2.25 ] |
| **Total (95% CI)** | **10** | | **7** | | | **100.0 %** | **-8.40 [ -14.55, -2.25 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 2.68 (P = 0.0074)

Test for subgroup differences: Not applicable

### Analysis 3.1. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 1 Step frequency.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

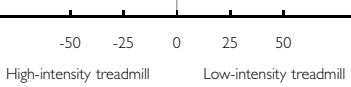
Outcome: 1 Step frequency

| Study or subgroup | High-intensity treadmill N | Mean(SD)[steps/min] | Low-intensity treadmill N | Mean(SD)[steps/min] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 16 | 42.5 (7.5) | 14 | 53.5 (6.2) | | 100.0 % | -11.00 [ -15.90, -6.10 ] |
| **Total (95% CI)** | **16** | | **14** | | | **100.0 %** | **-11.00 [ -15.90, -6.10 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 4.40 (P = 0.000011)

Test for subgroup differences: Not applicable




### Analysis 3.2. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 2 Age of onset of independent walking.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

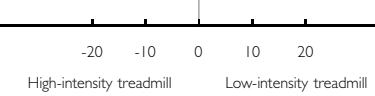
Outcome: 2 Age of onset of independent walking

| Study or subgroup | High-intensity treadmill N | Mean(SD)[months] | Low-intensity treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 16 | 19.23 (2.8) | 14 | 21.36 (4.72) | | 100.0 % | -2.13 [ -4.96, 0.70 ] |
| **Total (95% CI)** | **16** | | **14** | | | **100.0 %** | **-2.13 [ -4.96, 0.70 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.48 (P = 0.14)

Test for subgroup differences: Not applicable



### Analysis 3.3. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 3 Onset of walking with assistance.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

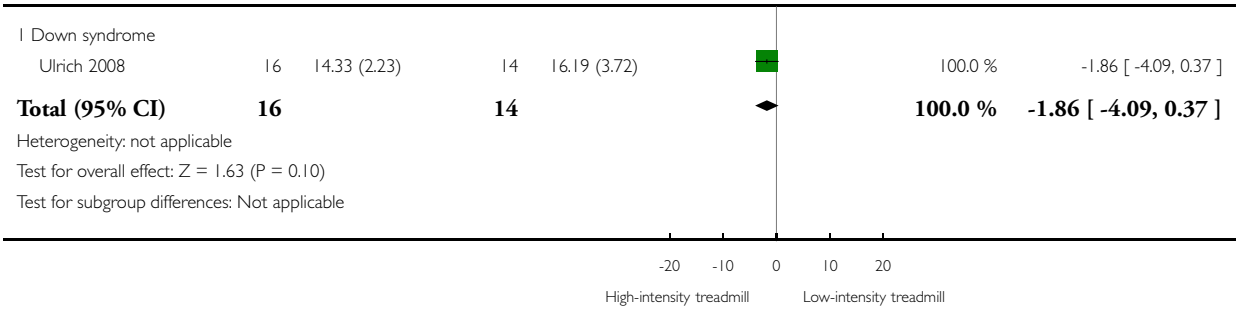
Outcome: 3 Onset of walking with assistance

| Study or subgroup | High-intensity treadmill N | Mean(SD)[months] | Low-intensity treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 16 | 14.33 (2.23) | 14 | 16.19 (3.72) | | 100.0 % | -1.86 [ -4.09, 0.37 ] |
| **Total (95% CI)** | **16** | | **14** | | | **100.0 %** | **-1.86 [ -4.09, 0.37 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.63 (P = 0.10)

Test for subgroup differences: Not applicable



### Analysis 3.4. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 4 Chronological Age. Follow-up (visit 1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 4 Chronological Age. Follow-up (visit 1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[months] | Low-intensity treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 21.3 (2.4) | 12 | 24.9 (5.1) | | 100.0 % | -3.60 [ -6.77, -0.43 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-3.60 [ -6.77, -0.43 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 2.23 (P = 0.026)

Test for subgroup differences: Not applicable


### Analysis 3.5. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 5 Chronological Age. Follow-up (visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 5 Chronological Age. Follow-up (visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[months] | Low-intensity treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 24.4 (2.4) | 12 | 28.4 (4.5) | | 100.0 % | -4.00 [ -6.86, -1.14 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-4.00 [ -6.86, -1.14 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 2.74 (P = 0.0061)

Test for subgroup differences: Not applicable

## Analysis 3.6. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 6 Chronological Age. Follow-up (visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 6 Chronological Age. Follow-up (visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[months] | Low-intensity treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 27.3 (2.3) | 12 | 30.5 (5.1) | | 100.0 % | -3.20 [ -6.34, -0.06 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-3.20 [ -6.34, -0.06 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.99 (P = 0.046)

Test for subgroup differences: Not applicable

### Analysis 3.7. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 7 Chronological Age. Follow-up (visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

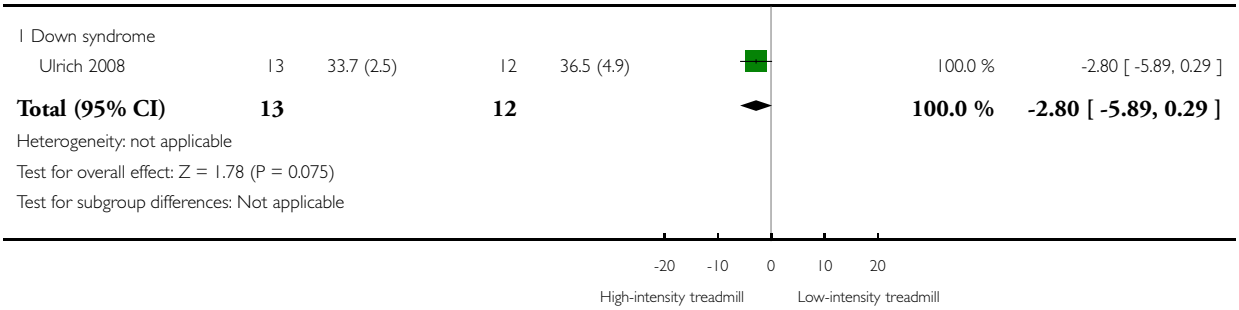
Outcome: 7 Chronological Age. Follow-up (visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[months] | Low-intensity treadmill N | Mean(SD)[months] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 33.7 (2.5) | 12 | 36.5 (4.9) | | 100.0 % | -2.80 [ -5.89, 0.29 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.80 [ -5.89, 0.29 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.78 (P = 0.075)

Test for subgroup differences: Not applicable




### Analysis 3.8. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 8 Other gait parameters: velocity follow-up (visit1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

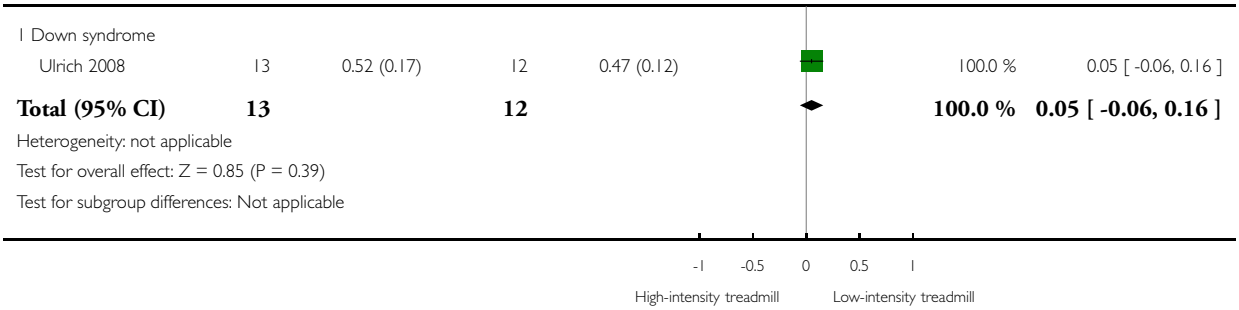
Outcome: 8 Other gait parameters: velocity follow-up (visit1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[m/s] | Low-intensity treadmill N | Mean(SD)[m/s] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 0.52 (0.17) | 12 | 0.47 (0.12) | | 100.0 % | 0.05 [ -0.06, 0.16 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **0.05 [ -0.06, 0.16 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.85 (P = 0.39)

Test for subgroup differences: Not applicable



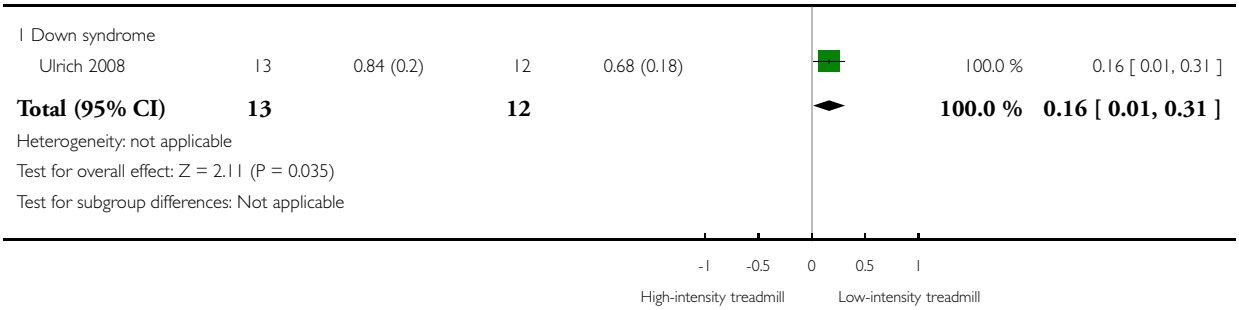
### Analysis 3.9. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 9 Other gait parameters: velocity follow-up (visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 9 Other gait parameters: velocity follow-up (visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[m/s] | Low-intensity treadmill N | Mean(SD)[m/s] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 0.84 (0.2) | 12 | 0.68 (0.18) | | 100.0 % | 0.16 [ 0.01, 0.31 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **0.16 [ 0.01, 0.31 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 2.11 (P = 0.035) | | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | | |



### Analysis 3.10. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 10 Other gait parameters: velocity follow-up (visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 10 Other gait parameters: velocity follow-up (visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[m/s] | Low-intensity treadmill N | Mean(SD)[m/s] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 1.04 (0.23) | 12 | 0.94 (0.21) | | 100.0 % | 0.10 [ -0.07, 0.27 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **0.10 [ -0.07, 0.27 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.14 (P = 0.26)

Test for subgroup differences: Not applicable


### Analysis 3.11. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 11 Other gait parameters: velocity follow-up (visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 11 Other gait parameters: velocity follow-up (visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[m/s] | Low-intensity treadmill N | Mean(SD)[m/s] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 1.3 (0.3) | 12 | 1.14 (0.28) | | 100.0 % | 0.16 [ -0.07, 0.39 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **0.16 [ -0.07, 0.39 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.38 (P = 0.17)

Test for subgroup differences: Not applicable

### Analysis 3.12. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 12 Other gait parameters: step length follow-up (visit 1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

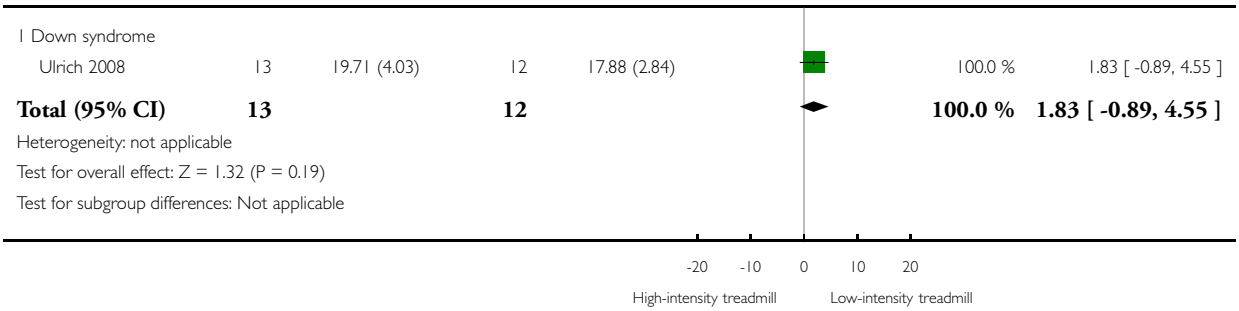
Outcome: 12 Other gait parameters: step length follow-up (visit 1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 19.71 (4.03) | 12 | 17.88 (2.84) | | 100.0 % | 1.83 [ -0.89, 4.55 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **1.83 [ -0.89, 4.55 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.32 (P = 0.19)

Test for subgroup differences: Not applicable



### Analysis 3.13. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 13 Other gait parameters: step length follow-up (visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 13 Other gait parameters: step length follow-up (visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 26.13 (3.71) | 12 | 23.58 (4.44) | | 100.0 % | 2.55 [ -0.67, 5.77 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **2.55 [ -0.67, 5.77 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.55 (P = 0.12)

Test for subgroup differences: Not applicable


### Analysis 3.14. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 14 Other gait parameters: step length follow-up (visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 14 Other gait parameters: step length follow-up (visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 28.86 (2.27) | 12 | 28.18 (4.13) | | 100.0 % | 0.68 [ -1.96, 3.32 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **0.68 [ -1.96, 3.32 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.50 (P = 0.61)

Test for subgroup differences: Not applicable

### Analysis 3.15. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 15 Other gait parameters: step length follow-up (visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 15 Other gait parameters: step length follow-up (visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 33.31 (4.69) | 12 | 30.63 (4.67) | | 100.0 % | 2.68 [ -0.99, 6.35 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **2.68 [ -0.99, 6.35 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.43 (P = 0.15)

Test for subgroup differences: Not applicable

### Analysis 3.16. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 16 Other gait parameters: step width follow-up (visit 1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 16 Other gait parameters: step width follow-up (visit 1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 20.21 (2.89) | 12 | 20.09 (3.41) | | 100.0 % | 0.12 [ -2.37, 2.61 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **0.12 [ -2.37, 2.61 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.09 (P = 0.92)

Test for subgroup differences: Not applicable


### Analysis 3.17. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 17 Other gait parameters: step width follow-up (visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 17 Other gait parameters: step width follow-up (visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 15.39 (2.6) | 12 | 16.62 (3.55) | | 100.0 % | -1.23 [ -3.69, 1.23 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-1.23 [ -3.69, 1.23 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.98 (P = 0.33)

Test for subgroup differences: Not applicable

## Analysis 3.18. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 18 Other gait parameters: step width follow-up (visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

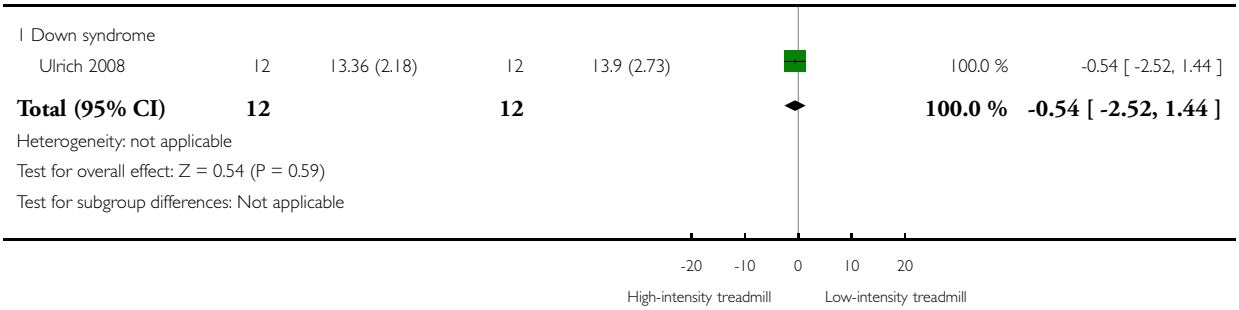
Outcome: 18 Other gait parameters: step width follow-up (visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 12 | 13.36 (2.18) | 12 | 13.9 (2.73) | | 100.0 % | -0.54 [ -2.52, 1.44 ] |
| **Total (95% CI)** | **12** | | **12** | | | **100.0 %** | **-0.54 [ -2.52, 1.44 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.54 (P = 0.59)

Test for subgroup differences: Not applicable



### Analysis 3.19. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 19 Other gait parameters: step width follow-up (visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 19 Other gait parameters: step width follow-up (visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[cm] | Low-intensity treadmill N | Mean(SD)[cm] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 11.27 (2) | 12 | 11.85 (1.91) | | 100.0 % | -0.58 [ -2.11, 0.95 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-0.58 [ -2.11, 0.95 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.74 (P = 0.46)

Test for subgroup differences: Not applicable


### Analysis 3.20. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 20 Other gait parameters: gait double-limb support follow-up (visit 1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

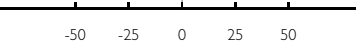
Outcome: 20 Other gait parameters: gait double-limb support follow-up (visit 1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 21.2 (6.8) | 12 | 24.1 (6.4) | | 100.0 % | -2.90 [ -8.07, 2.27 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.90 [ -8.07, 2.27 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.10 (P = 0.27)

Test for subgroup differences: Not applicable



### Analysis 3.21. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 21 Other gait parameters: gait double-limb support follow-up (visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 21 Other gait parameters: gait double-limb support follow-up (visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 12.8 (2.7) | 12 | 16.8 (6.4) | | 100.0 % | -4.00 [ -7.91, -0.09 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-4.00 [ -7.91, -0.09 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 2.01 (P = 0.045) | | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | | |

### Analysis 3.22. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 22 Other gait parameters: gait double-limb support follow-up (visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

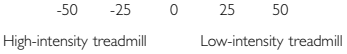
Outcome: 22 Other gait parameters: gait double-limb support follow-up (visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 9.9 (3.9) | 12 | 11.9 (6.6) | | 100.0 % | -2.00 [ -6.29, 2.29 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.00 [ -6.29, 2.29 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Not applicable




### Analysis 3.23. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 23 Other gait parameters: gait double-limb support follow-up (visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 23 Other gait parameters: gait double-limb support follow-up (visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 8.7 (3.1) | 12 | 9.5 (3.2) | | 100.0 % | -0.80 [ -3.27, 1.67 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-0.80 [ -3.27, 1.67 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.63 (P = 0.53)

Test for subgroup differences: Not applicable

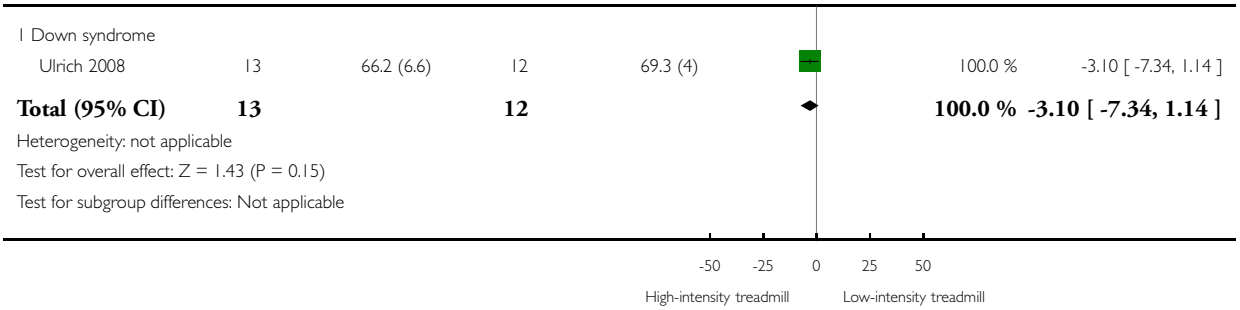
### Analysis 3.24. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 24 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 24 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 66.2 (6.6) | 12 | 69.3 (4) | | 100.0 % | -3.10 [ -7.34, 1.14 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-3.10 [ -7.34, 1.14 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 1.43 (P = 0.15) | | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | | |



### Analysis 3.25. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 25 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 25 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 64.9 (5.3) | 12 | 69.7 (4.8) | | 100.0 % | -4.80 [ -8.76, -0.84 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-4.80 [ -8.76, -0.84 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 2.38 (P = 0.017)

Test for subgroup differences: Not applicable


### Analysis 3.26. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 26 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

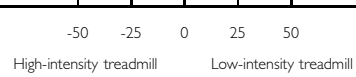
Outcome: 26 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 61.4 (6) | 12 | 64.3 (1.6) | | 100.0 % | -2.90 [ -6.28, 0.48 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.90 [ -6.28, 0.48 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.68 (P = 0.093)

Test for subgroup differences: Not applicable



### Analysis 3.27. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 27 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

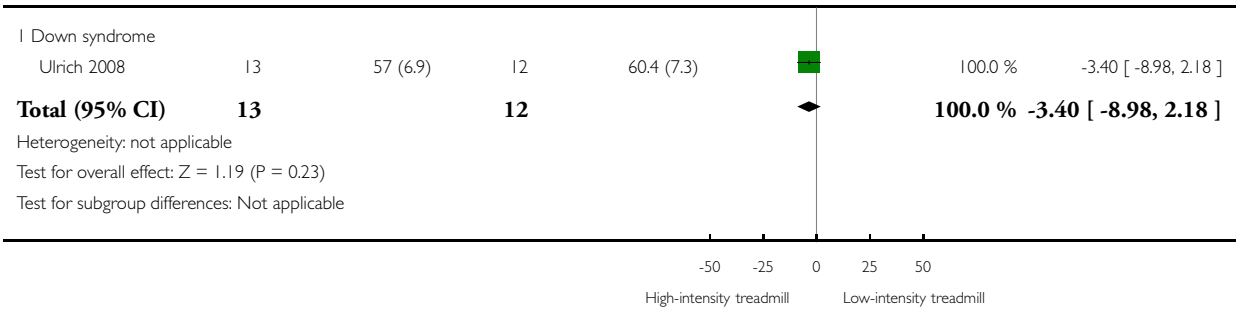
Outcome: 27 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 57 (6.9) | 12 | 60.4 (7.3) | | 100.0 % | -3.40 [ -8.98, 2.18 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-3.40 [ -8.98, 2.18 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.19 (P = 0.23)

Test for subgroup differences: Not applicable



### Analysis 3.28. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 28 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 1).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

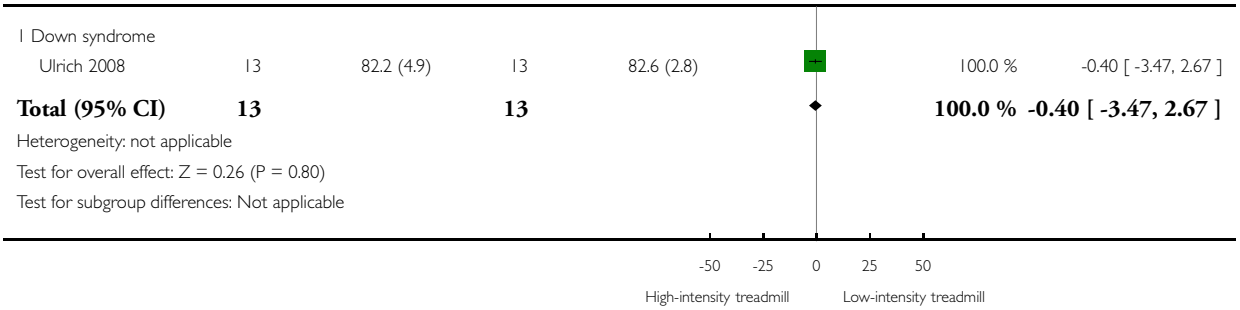
Outcome: 28 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 1)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 82.2 (4.9) | 13 | 82.6 (2.8) | | 100.0 % | -0.40 [ -3.47, 2.67 ] |
| **Total (95% CI)** | **13** | | **13** | | | **100.0 %** | **-0.40 [ -3.47, 2.67 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.26 (P = 0.80)

Test for subgroup differences: Not applicable




### Analysis 3.29. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 29 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 2).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

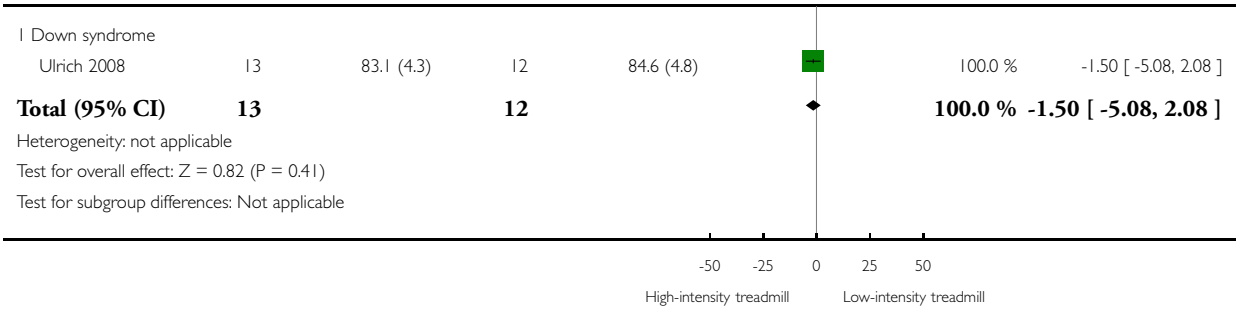
Outcome: 29 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 2)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 83.1 (4.3) | 12 | 84.6 (4.8) | | 100.0 % | -1.50 [ -5.08, 2.08 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-1.50 [ -5.08, 2.08 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.82 (P = 0.41)

Test for subgroup differences: Not applicable



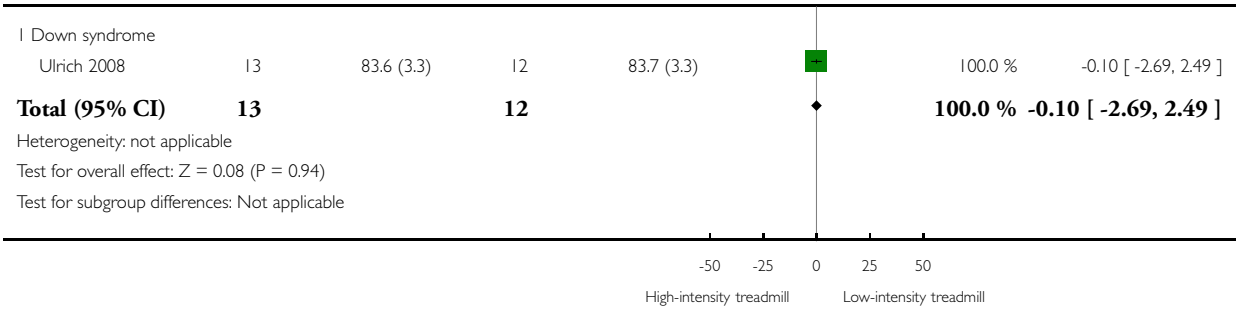
### Analysis 3.30. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 30 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 3).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 30 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 3)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 83.6 (3.3) | 12 | 83.7 (3.3) | | 100.0 % | -0.10 [ -2.69, 2.49 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-0.10 [ -2.69, 2.49 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 0.08 (P = 0.94) | | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | | |



### Analysis 3.31. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 31 Other gait parameters:gait ankle dorsiflexion. Follow-up (Visit 4).

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 31 Other gait parameters:gait ankle dorsiflexion. Follow-up (Visit 4)

| Study or subgroup | High-intensity treadmill N | Mean(SD)[% cycle] | Low-intensity treadmill N | Mean(SD)[% cycle] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 82 (3.3) | 12 | 84.8 (4.6) | | 100.0 % | -2.80 [ -5.96, 0.36 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.80 [ -5.96, 0.36 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.74 (P = 0.083)

Test for subgroup differences: Not applicable


### Analysis 3.32. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 32 Other gait parameters: toe-off follow-up visit 1.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

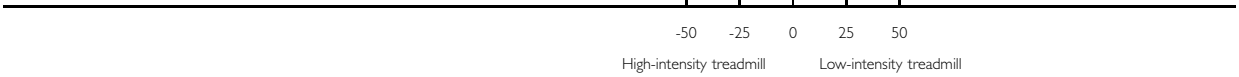
Outcome: 32 Other gait parameters: toe-off follow-up visit 1

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 66.3 (5.7) | 12 | 68.5 (4.4) | | 100.0 % | -2.20 [ -6.17, 1.77 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.20 [ -6.17, 1.77 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.08 (P = 0.28)

Test for subgroup differences: Not applicable



### Analysis 3.33. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 33 Other gait parameters: toe-off; follow-up visit 2.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

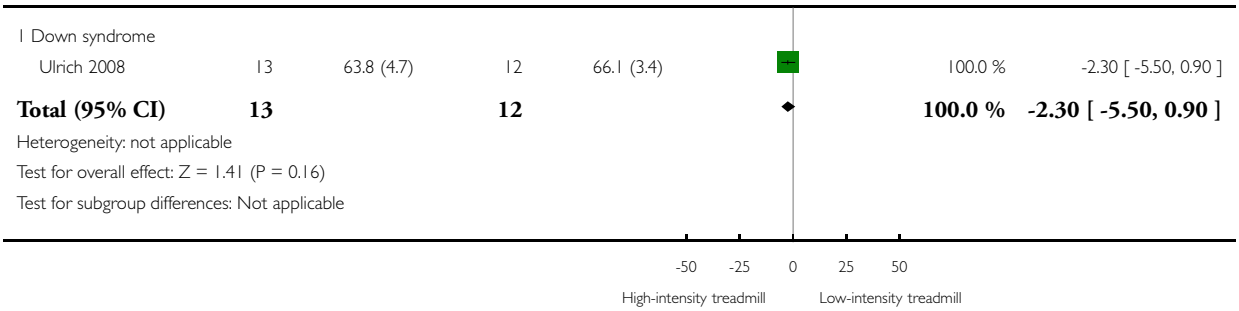
Outcome: 33 Other gait parameters: toe-off; follow-up visit 2

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 63.8 (4.7) | 12 | 66.1 (3.4) | | 100.0 % | -2.30 [ -5.50, 0.90 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-2.30 [ -5.50, 0.90 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 1.41 (P = 0.16)

Test for subgroup differences: Not applicable



### Analysis 3.34. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 34 Other gait parameters: toe-off; follow-up visit 3.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

Outcome: 34 Other gait parameters: toe-off; follow-up visit 3

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 61.6 (4.2) | 12 | 62.8 (2.7) | | 100.0 % | -1.20 [ -3.95, 1.55 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-1.20 [ -3.95, 1.55 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.86 (P = 0.39)

Test for subgroup differences: Not applicable


### Analysis 3.35. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 35 Other gait parameters: toe-off follow-up visit 4.

Review: Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay

Comparison: 3 High-intensity treadmill vs Low-intensity treadmill

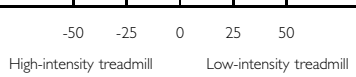
Outcome: 35 Other gait parameters: toe-off follow-up visit 4

| Study or subgroup | High-intensity treadmill N | Mean(SD)[%] | Low-intensity treadmill N | Mean(SD)[%] | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| 1 Down syndrome | | | | | | | |
| Ulrich 2008 | 13 | 59 (5.2) | 12 | 59.9 (6.4) | | 100.0 % | -0.90 [ -5.49, 3.69 ] |
| **Total (95% CI)** | **13** | | **12** | | | **100.0 %** | **-0.90 [ -5.49, 3.69 ]** |

Heterogeneity: not applicable

Test for overall effect: Z = 0.38 (P = 0.70)

Test for subgroup differences: Not applicable



# APPENDICES

## Appendix 1. Search strategies

**Cochrane CENTRAL Register of Controlled Trials (CENTRAL)**

#1 MeSH descriptor Physical Therapy Modalities, this term only
#2 MeSH descriptor Physical Therapy (Specialty), this term only
#3 physiotherap* or physio NEXT therap* or physical NEXT therap*
#4 MeSH descriptor Exercise Therapy, this term only
#5 treadmill* or tread-mill*
#6 (#1 OR #2 OR #3 OR #4 OR #5)
#7 MeSH descriptor Motor Skills, this term only
#8 MeSH descriptor Motor Skills Disorders, this term only
#9 MeSH descriptor Psychomotor Disorders, this term only
#10 MeSH descriptor Psychomotor Performance, this term only
#11 MeSH descriptor Movement Disorders, this term only
#12 MeSH descriptor Developmental Disabilities, this term only
#13 ((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) NEAR/3 (impair* or skill* or disorder* or deficit* or delay* or disabilit* or dysfunc*))
#14 MeSH descriptor Walking explode tree 1
#15 MeSH descriptor Gait, this term only
#16 MeSH descriptor Gait Disorders, Neurologic, this term only
#17 MeSH descriptor Gait Ataxia, this term only
#18 gait*
#19 walk or walking
#20 MeSH descriptor Locomotion, this term only
#21 locomotor* or locomotion*
#22 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory)
#23 stepping
#24 (#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)
#25 MeSH descriptor Disabled Children, this term only
#26 MeSH descriptor Down syndrome, this term only
#27 MeSH descriptor Cerebral Palsy, this term only
#28 MeSH descriptor Spinal Dysraphism, this term only
#29 (down* NEXT syndrome or cerebral NEXT pals* or (spin* NEAR/3 injur*) or spina NEXT bifida)
#30 MeSH descriptor Infant, Low Birth Weight explode all trees
#31 MeSH descriptor Infant, Premature, this term only
#32 low NEXT birth NEXT weight
#33 preterm* or pre NEXT term* or prematur*
#34 (#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 or #33)
#35 baby or babies or infant* or toddler* or child* or preschool* or pre-school* or schoolchild*
#36 MeSH descriptor Child explode all trees
#37 MeSH descriptor Infant, this term only
#38 (#35 OR #36 OR #37)

#39 (#24 OR #34)
#40 (#6 AND #38 AND #39)

**MEDLINE (OVID)**

1 Physical Therapy Modalities/
2 "Physical Therapy (Specialty)"/
3 (physiotherap$ or physio therap$ or physical therap$).tw.
4 Exercise Therapy/
5 tread-mill$.tw.
6 treadmill$.tw.
7 or/1-6
8 Motor Skills/
9 Motor Skills Disorders/
10 Psychomotor Disorders/
11 Psychomotor Performance/
12 Movement Disorders/
13 Developmental Disabilities/
14 ((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development$) adj3 (impair$ or skill$ or disorder$ or deficit$ or delay$ or disabilit$ or dysfunc$)).tw.
15 exp Walking/
16 Gait/
17 Gait Disorders, Neurologic/
18 Gait Ataxia/
19 gait.tw.
20 locomotion/
21 (walk or walking).tw.
22 (locomotor$ or locomotion$).tw.
23 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory).tw.
24 stepping.tw.
25 or/8-24
26 Disabled Children/
27 down syndrome/
28 cerebral palsy/
29 spinal dysraphism/
30 (down$ syndrome or cerebral pals$ or (spin$ adj3 injur$) or spina bifida).tw.
31 exp infant, low birth weight/ or infant, premature/
32 (low birth weight or pre-term$ or preterm$ or prematur$).tw.
33 or/26-32
34 Infant/
35 exp child/
36 (baby or babies or infant$ or child$ or toddler$ or pre-school$ or preschool$ or schoolchild$).tw.
37 34 or 35 or 36
38 randomized controlled trial.pt.
39 controlled clinical trial.pt.
40 randomi#ed.ab.
41 placebo$.ab.
42 drug therapy.fs.
43 randomly.ab.
44 trial.ab.
45 groups.ab.
46 or/38-45
47 exp animals/ not humans.sh.
48 46 not 47

49 25 or 33
50 7 and 37 and 48 and 49

**EMBASE (OVID)**

1 physiotherapy/
2 pediatric physiotherapy/
3 (physiotherap$ or physio therap$ or physical therap$).tw.
4 treadmill/
5 tread-mill$.tw.
6 treadmill.tw.
7 kinesiotherapy/
8 or/1-7
9 motor performance/
10 psychomotor performance/
11 motor dysfunction/
12 developmental disorder/
13 motor development/
14 ((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development$) adj3 (impair$ or skill$ or disorder$ or deficit$ or delay$ or disabilit$ or dysfunc$)).tw.
15 locomotion/
16 walking/
17 gait/
18 GAIT DISORDER/
19 ataxia/
20 gait.tw.
21 (walk or walking).tw.
22 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory).tw.
23 (locomotor$ or locomotion$).tw.
24 stepping.tw.
25 handicapped child/
26 Down syndrome/ (21539)
27 cerebral palsy/ (18656)
28 spina bifida/ (4734)
29 (down$ syndrome or cerebral pals$ or (spin$ adj3 injur$) or spina bifida).tw.
30 prematurity/
31 exp low birth weight/
32 (low birth weight or pre-term$ or preterm$ or prematur$).tw.
33 or/9-24
34 or/25-32
35 or/33-34
36 exp child/
37 infant/
38 (baby or babies or infant$ or child$ or toddler$ or pre-school$ or preschool$ or schoolchild$).tw.
39 or/36-38
40 Clinical trial/
41 Randomized controlled trial/
42 Randomization/
43 Single blind procedure/
44 Double blind procedure/
45 Crossover procedure/
46 Placebo/
47 Randomi#ed.tw.
48 RCT.tw.

49 (random$ adj3 (allocat$ or assign$)).tw.
50 randomly.ab.
51 groups.ab.
52 trial.ab.
53 ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
54 Placebo$.tw.
55 Prospective study/
56 (crossover or cross-over).tw.
57 prospective.tw.
58 or/40-57
59 8 and 35 and 39 and 58

**CINAHLPlus (EBSCOhost)**
S50 S31 and S34 and S49
S49 S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or
S45 or S46 or S47 or S48
S48 TI (evaluat* study or evaluat* research) or AB (evaluate* study or evaluat* research) or TI (effectiv* study or effectiv* research) or AB(effectiv* study or effectiv* research) OR TI (prospectiv* study or prospectiv* research) or AB(prospectiv* study or prospectiv* research) orTI (follow-up study or follow-up research) or AB (follow-up study or follow-up research)
S47 "cross over*"
S46 crossover*
S45 (MH "Crossover Design")
S44 (tripl* N3 mask*) or (tripl* N3 blind*)
S43 (trebl* N3 mask*) or (trebl* N3 blind
S42 (doubl* N3 mask*) or (doubl* N3 blind
S41 (singl* N3 mask*) or (singl* N3 blind
S40 (clinic* N3 trial*) or (control* N3 trial*)
S39 (random* N3 allocat* ) or (random* N3 assign*)
S38 randomis* or randomiz*
S37 (MH "Meta Analysis")
S36 (MH "Clinical Trials+")
S35 MH random assignment
S34 S32 or S33
S33 TI(baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*) or AB(baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*)
S32 (MH "Child") OR (MH "Infant") OR (MH "Child, Preschool
S31 S29 or S30
S30 S6 and S28
S29 S6 and S19
S28 S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27
S27 TI(low birth weight or pre-term* or preterm* or prematur*) or AB(low birth weight or pre-term* or preterm* or prematur*)
S26 (MH "Infant, Low Birth Weight+")
S25 (MH "Infant, Premature")
S24 TI (down* syndrome or cerebral pals* or (spin* N3 injur*) or spina bifida) or AB (down* syndrome or cerebral pals* or (spin* N3 injur*) or
spina bifida)
S23 (MH "Down syndrome")
S22 (MH "Spina Bifida")
S21 (MH "Cerebral Palsy")
S20 (MH "Child, Disabled")
S19 S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18
S18 AB((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) and (impair* or skill* or disorder* or deficit* or delay*

or disabilit* or dysfunc*) )
S17 TI((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) and (impair* or skill* or disorder* or deficit* or delay*
or disabilit* or dysfunc*) )
S16 TI(ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory) or AB(ambulation or ambulatory or
nonambulation or nonambulatory or non-ambulation or non-ambulatory)
S15 TI(gait* or locomotor* or locomotion* or step or stepping or walk* or walking) or AB(gait* or locomotor* or locomotion* or step or stepping or
walk* or walking)
S14 (MH "Locomotion")
S13 (MH "Gait") OR (MH "Gait Disorders, Neurologic") OR (MH "Gait Apraxia") OR (MH "Step")
S12 (MH "Walking")
S11 (MH "Infant Development Disorders")
S10 (MH "Child Development Disorders")
S9 (MH "Developmental Disabilities
S8 (MH "Psychomotor Disorders")
S7 (MH "Motor Skills") OR (MH "Motor Skills Disorders") OR (MH "Psychomotor Performance")
S6 S1 or S2 or S3 or S4 or S5
S5 TI(physiotherap* or physio therap* or physical therap*) or AB(physiotherap* or physio therap* or physical therap*)
S4 TI (treadmill* or tread-mill*) or AB(treadmill* or tread-mill*)
S3 TI (treadmill* or tread-mill*) or AB(treadmill* or tread-mill*)
S2 (MH "Treadmills")
S1 (MH "Physical Therapy") OR (MH "Gait Training") OR (MH "Pediatric Physical Therapy") OR (MH "Therapeutic Exercise")

**PsycINFO (EBSCOhost)**

S43 S4 and S25 and S28 and S42
S42 S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or
S39 or S40 or S41
S41 (evaluation N3 stud* or evaluation N3 research*)
S40 (effectiveness N3 stud* or effectiveness N3 research*)
S39 DE "Placebo" or DE "Evaluation" or DE "Program Evaluation" OR DE "Educational Program Evaluation" OR DE "Mental Health Program Evaluation"
S38 (DE "Random Sampling" or DE "Clinical Trials") or (DE "Experiment Controls")
S37 "cross over*"
S36 crossover*
S35 (tripl* N3 mask*) or (tripl* N3 blind*)
S34 (trebl* N3 mask*) or (trebl* N3 blind*)
S33 (doubl* N3 mask*) or (doubl* N3 blind*)
S32 (singl* N3 mask*) or (singl* N3 blind*)
S31 (clinic* N3 trial*) or (control* N3 trial*)
S30 (random* N3 allocat* ) or (random* N3 assign*)
S29 randomis* or randomiz*
S28 S26 or S27
S27 (ZG "infancy (2-23 mo)") or (ZG "preschool age (2-5 yrs)")
S26 baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*
S25 S16 or S24
S24 S17 or S18 or S19 or S20 or S21 or S22 or S23
S23 low birth weight or pre-term* or preterm* or prematur*
S22 DE "Birth Weight"
S21 DE "Premature Birth"
S20 (down* syndrome or cerebral pals* or (spin* N3 injur*) or spina bifida)

S19 DE “Spina Bifida”
S18 DE “Cerebral Palsy”
S17 DE “Down’s Syndrome”
S16 S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15
S15 DE “Developmental Disabilities”
S14 (motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) and (impair* or skill* or disorder* or deficit* or delay* or
disabilit* or dysfunct* )
S13 ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory
S12 gait* or locomotor* or locomotion* or step or stepping or walk* or walking
S11 DE “Locomotion”
S10 DE “Motor Skills”
S9 DE “Walking”
S8 DE “Motor Coordination”
S7 DE “Motor Performance”
S6 DE “Motor Development”
S5 DE “Psychomotor Development”
S4 S1 or S2 or S3
S3 treadmill* or tread-mill*
S2 physiotherap* or physio therap* or physical therap*
S1 DE “Physical Therapy”

**LILACS**

(“WALKing” or “GAIT” or “GAIT ataxia” or “GAIT disorders, neurologic” or gait$ or walk or walking or “DOWN SYNDROME” or “CEREBRAL PALSY” or “SPINA BIFIDA” or “infant, LOW BIRTH WEIGHT” or “infant, extremely LOW BIRTH WEIGHT” or “infant, very LOW BIRTH WEIGHT” or “infant, PREMATURE” or “MOTOR SKILLS” or “MOTOR SKILLS disorders” or “PSYCHOMOTOR disorders” or “PSYCHOMOTOR performance” or “LOCOMOTION” or step or stepping or ambulation or ambulatory or neuromotor or neuro-motor [Words] ) and ( “PHYSIOTHERAPY (specialty)” OR “PHYSIOTHERAPY (techniques)” or “PHYSICAL THERAPY (specialty)” or “PHYSICAL THERAPY modalities” or physiotherap$ or treadmill$ or tread-mill$ [Words] ) and (baby or babies or toddler$ or infant$ or child$ or preschool$ or pre-school$ or schoolchild$ or “INFANT” or “CHILD, preschool” or “CHILD” [Words] )

**Science Citation Index and Conference Proceedings Citation Index - Science**

#13 #12 AND #11
#12 TS=(random* or trial* or intervention* )
#11 #10 AND #9 AND #3
#10 TS=(baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*)
#9 #8 OR #7 OR #6 OR #5 OR #4
#8 TS=(low birth weight or pre-term* or preterm* or prematur*)
#7 TS=(down* syndrome or cerebral pals* or spin* injur* or spina bifida)
#6 TS=((motor or neuromotor or neuro-motor or psychomotor or psycho-motor or development*) SAME (impair* or skill* or disorder* or deficit* or delay* or disabilit* or dysfunc*) )
#5 TS=(ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory)
#4 TS=(gait* or locomotor* or locomotion* or step or stepping or walk* or walking)
#3 #2 OR #1
#2 TS=(treadmill* or tread mill*)
#1 TS=(physical therap* or physiotherap* or physio therap*)

**PED*ro***

Using Simple search : treadmill* child*

**metaRegister of Controlled Trials**

treadmill and children

**CenterWatch**
treadmill **limited to** Clinical trial Listings

**International Clinical Trials Registry Platform (ICTRP)**
Using Advanced search : Intervention| Treadmill AND limit by Search for clinical trials in children AND Recruitment status = all

**Clinicaltrials.gov**
treadmill | Interventional Studies | Child

## Appendix 2. Table of unused methods

| | |
|---|---|
| Continuous data | If the same continuous outcome (for example, infant's gross motor development level) is measured differently across studies, we will compare standardised mean differences (SMD) with 95% CI across studies (Higgins 2008). Where necessary, we will use formulas to convert F ratios, t-values and Chi $^2$ values into SMDs (Lipsey 2001), using Hedges *g* to correct for small sample bias. |
| Dichotomous data | We will analyse the outcomes of any study reporting binary/dichotomous data by calculation of the risk ratio for the occurrence of an event (rather than a non-event) for its consistency as a summary statistic and ease of interpretation |
| Unit of analysis issues | *Cluster-randomised trials*<br>For trials that use clustered randomisation, we will present results with proper controls for clustering (robust standard errors or hierarchical linear model). If appropriate controls are not used and it is not possible to obtain the full set of each individual participant's data, we will control the data for clustering using the procedures outlined by Higgins 2008. For dichotomous outcome measures, we will divide the number of events and the number of participants per trial arm by the design effect [1 + (1-m)*r], where *m* is the average cluster size and *r* is the intra-cluster correlation coefficient (ICC) . For continuous outcome measures, we will divide the number of participants per trial arm by the design effect, with the mean values unchanged. To determine the ICC, we will use estimates in the primary trials on a study-by-study basis. In the case of these values not being reported, we will use external estimates of the ICC that are appropriate to the context of each trial and average cluster size. If they were still not available, we will then use statistical procedures outlined by Higgins 2008.<br>*Multiple time points*<br>When the results are measured at multiple time points, we will only consider baseline measurements and the last time point measurements<br>*Multiple interventions per individual*<br>If it is found that participants in some trials receive multiple treatments, we will conduct meta-analysis on those studies separately |
| Dealing with missing data | For dichotomous data, we will report the missing data and dropouts for included studies along with the number of participants who are included in the final analyses as a proportion of all participants in each study. We will provide reasons for missing data in a narrative summary. The extent to which the results of the review could be altered by the missing data can be assessed based on consideration of best-case and worst-case scenarios (Gamble 2005). The best-case scenario is the one where all participants with missing outcomes in the experimental condition had good outcomes and all those with the missing outcomes in the control condition had poor outcomes, and the worst-case scenario is vice versa (Higgins 2008). However, the best-case and worst-case scenarios method is too extreme and a more plausible approach is needed. We will use the method suggested by Higgins 2008, which |

(*Continued*)

| | |
|---|---|
| | can incorporate specific reasons for missing data and considers plausible event risks among missing participants in relation to risks among those observed<br>We will analyse missing continuous data either on an endpoint basis, including only participants with a final assessment, or using last observation carried forward to the final assessment if the last observation carried forward data were reported by the trial authors. If SDs are missing, we will make attempts to obtain these data through contacting trial authors. If SDs are not available from trial authors, we will calculate them from t-values, confidence intervals or standard errors, where reported in articles (Deeks 1997a; Deeks 1997b). If these additional figures are still not available or obtainable, we will not include the study data in the comparison of interest |
| Assessment of heterogeneity | We will describe statistical heterogeneity using $I^2$ (Higgins 2002), a quantity that describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error). In addition, we will employ a $chi^2$ test of homogeneity to determine the strength of evidence that heterogeneity is genuine. If an individual study appears to be an outlier, we may carry out sensitivity analysis with and without the study. If the primary studies are judged to be substantially heterogeneous even within these sub-groupings, we will only give a descriptive analysis, particularly if there is variation in direction of effect |
| Assessment of reporting biases | In order to investigate the relationship between effect size and standard error, we will draw funnel plots if sufficient studies are available (i.e., ten or more individuals studies). Asymmetry could be attributable to publication bias, but might also reflect a real relationship between trial size and effect size. If we find such a relationship, we will examine clinical variation of the studies (Higgins 2008, Section 10.4). As a direct test for publication bias, we will compare results extracted from published journal reports with results obtained from other sources, including correspondence |
| Data synthesis | For dichotomous outcomes, we will also calculate the number needed to treat for an additional beneficial outcome |
| Subgroup analysis | We will undertake subgroup analysis if clinically different interventions are identified or there are clinically relevant differences between participant groups. We will thus investigate any subgroup differences in order to establish whether there is a single intervention effect, specifically:<br>· treadmill 'dose' (total number of training sessions, frequency of training per week or duration of each training session);<br>· type of intervention (preventive or rehabilitative);<br>· diagnosis (cerebral palsy, Down's syndrome etc.);<br>· conditions affecting the neuro-musculoskeletal system (hypo- or hypertonia, spasticity, posture etc.) |
| Sensitivity analysis | We will conduct sensitivity analysis, where data permit, to determine whether findings are sensitive to restricting inclusion to studies judged to be at low risk of bias. In these analyses, we will re-evaluate the findings, limiting the inclusion to published studies or to those studies that have a low risk of:<br>· selection bias (associated with allocation concealment and sequence generation);<br>· performance bias (associated with blinding);<br>· attrition bias (associated with completeness of data) |

## CONTRIBUTIONS OF AUTHORS

CB, KMB, MV,and RA screened all results obtained and selected studies to be included. CB, MG, MV and RA extracted data from the trials. MV entered data into RevMan. MG carried out data analysis. KMB, MG and MHA interpreted the analysis. KMB and MHA wrote the results, discussion, conclusions and abstracts with inputs from MV and RA. CB and MG also edited the final document.

## DECLARATIONS OF INTEREST

- Marta Valentin Gudiol - none known.
- Rosa Maria Angulo-Barroso - participated in the design and publication of several articles that are referenced and/or included in this review.
- Caritat Bagur Calafat - none known.
- Mijna Hadders-Algra - none known.
- Montserat Girabent Farrés - none known.
- Katrin Mattern-Baxter - participated in the design and publication of two articles that are referenced in this review.

## SOURCES OF SUPPORT


### Internal sources

- No sources of support supplied

### External sources

- National Institute for Health Research, UK.

Cochrane Incentive Award


## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. Background - minor modifications.
2. Primary outcomes - for clarity, defined 'step frequency' and replaced 'walking with assistive devices' with 'walking with assistance'.
3. Secondary outcomes - 'gait parameters' was added as we had assumed this under 'gait pattern functions' but not explicitly expressed it.
4. Electronic searches - we did not search for dissertations in WorldCat.
5. Other risk of bias - individual authors of each included study were contacted when RoB was unclear. We have kept the classification as 'unclear' where relevant.
6. See Appendix 2 for methods not used due to type or amount of data.

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Body Weight; Cerebral Palsy [complications; rehabilitation]; Child Development [physiology]; Down Syndrome [complications; rehabilitation]; Exercise Movement Techniques [instrumentation; *methods]; Locomotion [physiology]; Motor Skills [*physiology]; Motor Skills Disorders [prevention & control; *rehabilitation]; Randomized Controlled Trials as Topic

### MeSH check words

Child, Preschool; Humans; Infant