Locomotor training for walking after spinal cord injury (Review)

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[Intervention Review]

Locomotor training for walking after spinal cord injury

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ABSTRACT

Background

A traumatic spinal cord injury (SCI) is a lesion of neural elements of the spinal cord that can result in any degree of sensory and motor deficit, autonomic or bowel dysfunction. Improvement of locomotor function is one of the primary goals for people with SCI. Locomotor training for walking is therefore used in rehabilitation after SCI and might help to improve a person's ability to walk. However, a systematic review of the evidence is required to assess the effects and acceptability of locomotor training after SCI.

Objectives

To assess the effects of locomotor training on improvement in walking for people with traumatic SCI.

Search methods

We searched the Cochrane Injuries Group's Specialised Register (searched November 2011); the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 4); MEDLINE (Ovid) (1966 to November 2011); EMBASE (Ovid) (1980 to November 2011); CINAHL (1982 to November 2011); AMED (Allied and Complementary Medicine Database) (1985 to November 2011); SPORTDiscus (1949 to November 2011); PEDro (the Physiotherapy Evidence database) (searched November 2011); COMPENDEX (engineering databases) (1972 to November 2011); and INSPEC (1969 to November 2011). We also searched the online trials databases Current Controlled Trials (www.controlled-trials.com/isrctn) and Clinical Trials (www.clinicaltrials.gov). We handsearched relevant conference proceedings, checked reference lists of relevant published papers and contacted study authors in an effort to identify published, unpublished and ongoing trials.

Selection criteria

We included randomised controlled trials (RCTs) involving people with SCI that compared locomotor training to a control of any other exercise or no treatment.

Data collection and analysis

Two review authors independently selected trials for inclusion, assessed trial quality and extracted data. The primary outcomes were the speed of walking and walking capacity at final follow-up.

Main results

Five RCTs involving 309 people are included in this review. Overall, the results were inconclusive. There was no statistically significant superior effect of any locomotor training approach on walking function after SCI compared with any other kind of physical rehabilitation. The use of bodyweight supported treadmill training as locomotor training for people after SCI did not significantly increase walking velocity (0.03 m/sec with a 95% confidence interval (CI) -0.05 to 0.11; P = 0.52; I^2 = 22%) nor did it increase walking capacity (-1.3 metres (95% CI -41 to 40); P = 0.95; I^2 = 62%). However, in one study involving 74 people the group receiving robotic-assisted locomotor training had reduced walking capacity compared with people receiving any other intervention, a finding which needs further investigation. In all five studies there were no differences in adverse events or drop-outs between study groups.

Authors' conclusions

There is insufficient evidence from RCTs to conclude that any one locomotor training strategy improves walking function more than another for people with SCI. The effects especially of robotic-assisted locomotor training are not clear, therefore research in the form of large RCTs, particularly for robotic training, is needed. Specific questions about which type of locomotor training might be most effective in improving walking function for people with SCI need to be explored.

PLAIN LANGUAGE SUMMARY

Providing locomotor training to people with spinal cord injury to improve walking ability

A traumatic spinal cord injury (SCI) is a lesion of neural elements of the spinal cord that can result in any degree of sensory and motor deficit, autonomic or bowel dysfunction. Locomotor training for walking is used in rehabilitation after spinal cord injury (SCI) and might help to improve a person's ability to walk. However, many strategies exist to improve this function, such as treadmill training with and without bodyweight support, robotic-assisted gait training and electrical stimulation.

Five randomised controlled trials were identified involving 309 people with spinal cord injury. None of the locomotor interventions had a beneficial or harmful effect on the people taking part. In all five studies there were no differences in adverse events or drop-outs between study groups. There is not enough evidence to conclude which locomotor training strategy is most effective in improving walking ability in people with spinal cord injury, or that locomotor training benefits a person's ability to walk over other kinds of rehabilitation.

BACKGROUND

A traumatic spinal cord injury (SCI) is a lesion of neural elements of the spinal cord that can result in any degree of sensory and motor deficit, autonomic or bowel dysfunction. The annual incidence of traumatic SCI in industrialised nations is approximately 15 to 40 cases per million population (Albert 2005; Pickett 2006; Sekhon 2001). The extent of disability resulting from SCI varies greatly and depends on the severity of the injury, the segment of the spinal cord at which the injury occurs and which nerve fibres are damaged (NINDS 2006). The neurologic deficit or dysfunction can be temporary or permanent, complete or incomplete (ONF 2006). Over 50% of people with SCI have incomplete motor lesions. Most motor recovery occurs within the first two months of inpatient rehabilitation after the injury (Waters 1993; Wirz 2005).

The American Spinal Injury Association's (ASIA) International Classification of Spinal Cord Injury is often used as a measure of recovery as well as for describing the neurological level of the damage and completeness of injury (ASIA 2002; Marino 2003; SCIRE 2006). SCI is classified as follows.

- A: complete, no sensory or motor function is preserved in the sacral segments S4 to S5.
- B: incomplete, sensory but not motor function is preserved below the neurological level and includes the sacral segments S4 to S5.
- C: incomplete, motor function is preserved below the neurological level and more than half of the key muscles below the neurological level have a muscle grade less than 3.
- D: incomplete, motor function is preserved below the

neurological level and at least half of the key muscles below the neurological level have a muscle grade greater than or equal to 3.

- E: normal, sensory and motor function is normal.

A significant proportion of patients improve one grade on the AIS (ASIA Impairment Scale) in the first few months post injury, particularly those initially assessed as AIS grades B and C (SCIRE 2006). One of the primary goals for people with SCI is improvement of locomotor function (Kirshblum 2007). The prognosis for ambulation after SCI depends on the type of syndrome and on the lesion. Based on neurological assessment at the first week after injury, 80% to 90% of complete lesions (AIS: A) remain complete (Kim 2004a; Maynard 1979; Waters 1994); for patients with sensory-incomplete lesions (AIS: B), with preserved sacral pin sensation, often more than 50% become ambulatory; and for patients with motor-incomplete lesions (AIS: C) 75% will recover community ambulation (Burns 1997; Crozier 1991; Kim 2004a; Maynard 1979; Waters 1994).

Although there is general consensus that inpatient rehabilitation programmes initiated soon after SCI may improve locomotor function, approximately 25% of people with initially incomplete SCI do not become independent ambulators (Waters 1993; Wirz 2005).

The rehabilitation of persons with SCI should involve multiple health professions, be initiated in the acute phase and be continued with specialised inpatient services. Inpatient rehabilitation after SCI incorporates different therapeutic approaches. One of the most important rehabilitation approaches, especially for regaining locomotor function, is physiotherapy. The main limitations of overground locomotion ability for patients with SCI are reduced co-ordination, leg paresis and impaired balance (Dietz 1995). Physiotherapists work on these limitations and provide support in standing (for example, through use of braces and tilt tables). If leg strength improves, the therapist may employ braces, parallel bars or other walking aids to work on balance and weight bearing. Physiotherapeutic strategies for people with SCI to regain ambulatory function include using repetitive and intensive practice of gait. This can be done either with or without treadmill training. To enhance the use of weight-bearing muscles, partial bodyweight support (BWS) can be provided with an overhead harness. Leg movements are assisted by therapists who can use orthoses combined with treadmill training. Other strategies are to use functional electrical stimulation (FES) with one or several channels or bracing (single or multi-joint braces) and walking aids (for example, crutches) when practising walking. Combinations of these therapies, such as combining FES, bracing and walking aids, are often used. A very comprehensive overview of existing forms of therapy used to regain ambulatory function can be found in SCIRE 2006.

Many studies have suggested that locomotion may improve after SCI due to mechanisms of neuroplasticity (Barbeau 2002; Barbeau 2006). These mechanisms are commonly thought to be influenced by sensorimotor training, for example, during physiotherapy sessions (Dobkin 2003).

Although compensation-based strategies (for example, brace walking) may facilitate walking, such strategies do not result in the recovery of previous (pre-injury) walking ability. For example, a patient who walks with braces will probably not be able to walk if the braces are removed. To facilitate and enhance the recovery of locomotor function, new therapeutic strategies and treatment options have been developed. They have been introduced in recent years for locomotor rehabilitation in people with motor-incomplete spinal cord injury (that is, people with some motor function). Such specific locomotor treatment options combine massed, repetitive practice of complex gait cycles during treadmill-based training with BWS and bodyweight support systems involving manual trainers or robotics (Barbeau 1987; Colombo 2000; Hesse 2004; Hornby 2005). These treatments are built upon an entirely different premise and aim to achieve restoration and recovery of walking using the intrinsic capacities of the nervous system. The aim is for the skills to persist once the person leaves the training environment. Historically, clinicians have compensated for post-SCI deficits to achieve mobility (that is, by providing wheeled mobility, brace walking or reciprocating gait orthosis) instead of tapping into the nervous system's intrinsic capability to restore itself.

Despite early reports of very promising results (Visintin 1989; Wernig 1992), the evidence for the effectiveness of treadmill-based training is mostly restricted to case reports (Behrman 2000; Gardner 1998; Protas 2001) and cohort studies (Dietz 1995; Hesse 2004; Wernig 1998; Wernig 1999; Wernig 1995; Wirz 2001).

In recent years, more sophisticated automated electromechanical gait machines have been developed. These consist of either a robot-driven exoskeleton orthosis (Colombo 2000; Hornby 2005) or an electromechanical device with two driven foot plates that simulate the phases of gait (Hesse 1998; Schmidt 2003). Evidence for these new locomotor treatment options is limited to case reports and single cohort studies.

Why it is important to do this review

A systematic review of the evidence is required to assess the effects and acceptability of locomotor training (defined as the repetitive practice of complex gait cycles, for example, treadmill-based walking) after SCI.

OBJECTIVES

To assess the effects of locomotor training on the improvement in walking speed and walking capacity for people with traumatic spinal cord injury (SCI).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) of parallel-group or cross-over design. Where randomised controlled cross-over trials were identified, we analysed only the first period (pre-cross-over).

Types of participants

We included studies with participants, of any age and gender, with a traumatic spinal cord injury.
We included people with any level of traumatic incomplete lesion (with an AIS Impairment of B, C or D) regardless of the duration of illness (acute or chronic SCI) or level of initial walking ability.

Types of interventions

We included all trials that compared locomotor training (over-ground gait training, hybrid strategies using BWS and functional electrical stimulation) to any other exercise or to a no treatment control group.
In light of ongoing developments with automated electromechanical devices or robots, we also included any newly developed devices for locomotor training after SCI.
We also included studies comparing different forms of locomotor training.
We excluded studies which only tested specific components of treatment. Therefore we excluded studies on electrical stimulation and continuous passive motion treatment.

Types of outcome measures

Primary outcomes

- Speed of walking: measured by the 10-metre or 15-metre walking speed (either fastest or casual walking speed (Dobkin 2006a; Miller 2006)) or any other scale. Physical assistance from another person was allowed. A speed of zero metres/second was allocated to people who could not walk even with assistance.
- Walking capacity: defined as the capacity to cover a distance in a defined time (for example, distance walked in six minutes) (Dobkin 2006a). A walking capacity of zero metres was allocated to people who could not walk even with assistance.

Secondary outcomes

- Level of independence in walking: measured by the Functional Independence Measure (FIM) (Hamilton 1994), where people who scored five or less on the walking item were classified as dependent walkers; Spinal Cord Independence Measure (SCIM) (Catz 2001), where people scoring three or less on items 12 to 14 of the SCIM were classified as dependent walkers; or Walking Index for Spinal Cord Index (WISCI or WISCI II) (Dittuno 2001; Morganti 2005), where the total score of the WISCI II was used as a continuous outcome for dependency in walking.
- Safety of exercises: determined by the incidence of adverse effects during the study period, such as thrombosis, major cardiovascular events, injuries (for example, injurious falls or other injuries), pain or any other reported adverse events.
- Rate of dropouts or withdrawals for any reason during the study period: used as an indicator of the acceptance of locomotor training.

Depending on the above-stated categories, and the availability of variables used in the included trials, all review authors discussed and reached consensus on which outcome measures should be included in the analysis.

Search methods for identification of studies

The searches were not restricted by language, date or publication status (published or unpublished).

Electronic searches

We searched the following electronic databases:
- Cochrane Injuries Group Specialised Register (searched 02 Nov 2011);
- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 4);
- MEDLINE (Ovid) 1948 to 2011;
- EMBASE (Ovid) 1980 to 2011;
- CINAHL (1982 to Nov 2011);
- ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) 1970 to Nov 2011;
- ISI Web of Science: Social Sciences Citation Index (SSCI) 1970 to Nov 2011;
- ISI Web of Science: Conference Proceedings Citation Index - Science (CPCI-S) 1990 to Nov 2011;
- ISI Web of Science: Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI-SSH) 1990 to Nov 2011;
- PubMed (www.ncbi.nlm.nih.gov/sites/entrez/);
- AMED (Allied and Complementary Medicine Database) (1985 to November 2011);
- SPORTDiscus (1949 to November 2011);

- PEDro (the Physiotherapy Evidence database) (searched November 2011);
- COMPENDEX (engineering databases) (1972 to November 2011);
- INSPEC (1969 to November 2011);

Search strategies are reported in full in Appendix 1. All the other database searches were based on the strategies reported.
We also searched the following online trials registers:

- International Standard Randomised Controlled Trial Number Register (ISRCTN) (www.controlled-trials.com/isrctn) (searched November 2011);
- www.clinicaltrials.gov (searched November 2011).

Searching other resources

We screened the reference lists of all relevant articles and reviews. We also contacted trial authors, experts and researchers in the field. In an effort to identify published, unpublished and ongoing trials that were not available in the major databases, we handsearched the following relevant conference proceedings:

- World Congress of NeuroRehabilitation (2002, 2006 and 2010);
- World Congress of Physical Medicine and Rehabilitation (2001, 2003, 2005, 2007, 2009 and 2011);
- World Congress of Physical Therapy (2003, 2007 and 2011);
- Deutsche Gesellschaft für Neurotraumatologie und Klinische Neurorehabilitation (2001 to 2010);
- Deutsche Gesellschaft für Neurologie (2000 to 2011);
- Deutsche Gesellschaft für Neurorehabilitation (1999 to 2011).

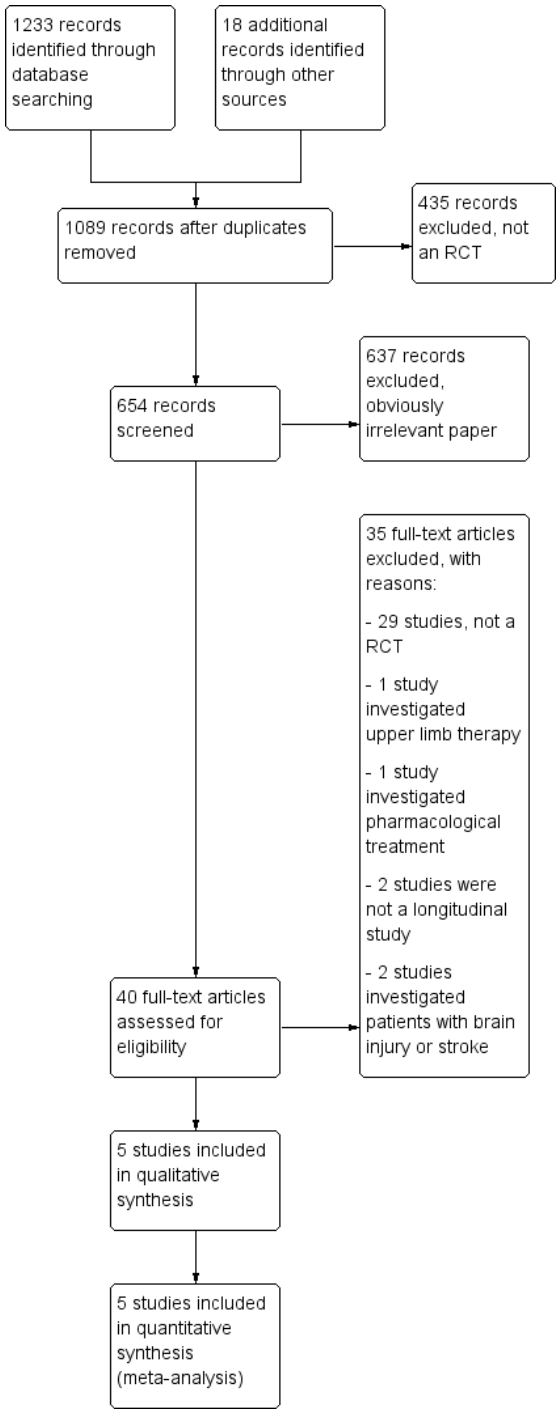
Data collection and analysis

We ran searches with the help of the Injuries Group Trials Search Co-ordinator who collated results and sent them to the authors (JM and MP) for screening.

Selection of studies

Two authors (JM and MP) independently examined titles and abstracts of citations identified by the electronic searches to identify potentially relevant studies. We then obtained the full text of all relevant studies for those selected and two authors (JM and MP) independently assessed the studies for inclusion against the predefined criteria. See Figure 1 for the study identification and selection process. Disagreement was resolved through discussion with all three review authors. If further trial information was needed, we tried to contact the trial authors in an effort to obtain missing data.

Figure 1. Study identification and selection process.



Data extraction and management

Two authors (JM and MP) independently extracted data from the included trials. We established the characteristics of unpublished trials through correspondence with the trial co-ordinator or principal investigator.

We used a data extraction form to record the following details for each study:

- method of generating randomisation schedule;
- method of concealment of allocation;
- blinding of assessors;
- use of an intention-to-treat analysis (all patients initially randomised included in the analyses in their allocated groups);
- adverse events and dropouts, for all reasons;
- any important imbalance in prognostic factors;
- participants (country, number of participants, age, gender, type of SCI, time from SCI to entry to the study, inclusion and exclusion criteria);
- comparison (details of intervention in treatment and control groups, details of co-intervention(s) in both groups, duration of treatment);
- outcomes and time points of measures (with number of participants in each group and outcome, regardless of compliance).

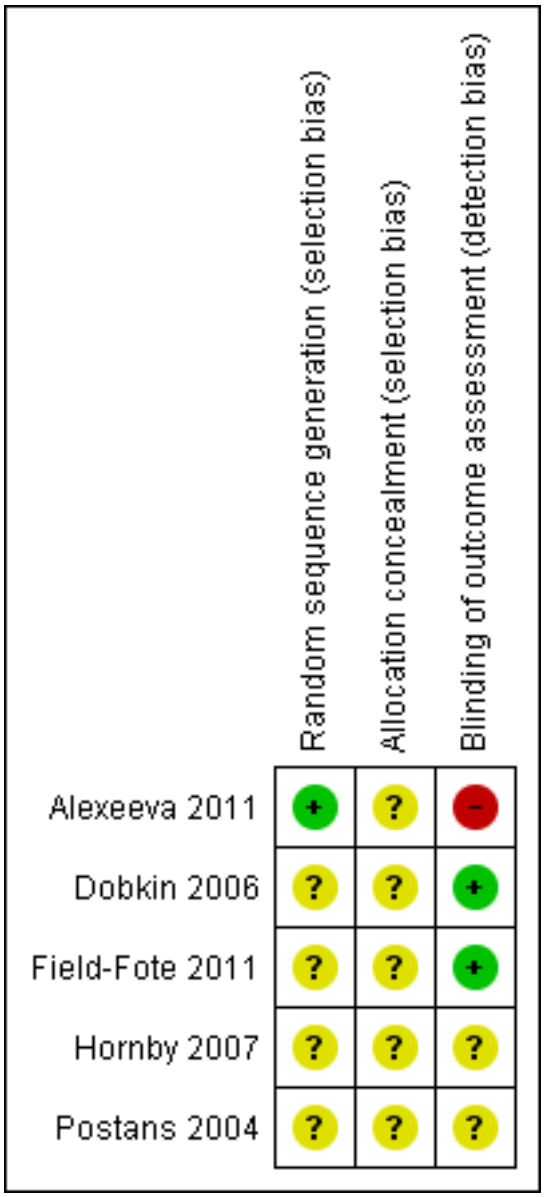
We checked all extracted data for agreement between authors, with a third author (JK) arbitrating for when consensus was not reached. If any of the review authors were involved in any of the selected studies another member of the review team extracted the data from that study.

We contacted all trial authors of the included studies for further information when needed or for missing data and clarification.

Assessment of risk of bias in included studies

All authors assessed the methodological quality of included trials independently according to the PEDro Scale (Maher 2003; PEDro 2006). The results of quality ratings are presented in Figure 2 and additional Table 1. The items of the PEDro Scale are as follows (Herbert 1998):

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



- specification of eligibility criteria;
- random allocation to groups;
- concealed allocation;
- groups similar at baseline;
- blinding of participants;
- blinding of therapists and assessors;
- outcome measurements obtained from more than 85% of participants;
- presence of an intention-to-treat analysis;
- reporting of results of between-group statistical comparisons;
- reporting of point measures and measures of variability.

The maximum achievable PEDro sum score is 10 points (PEDro 2006).

We checked all methodological quality assessments for agreement between authors. We resolved disagreements by discussion.

Assessment of heterogeneity

We examined statistical heterogeneity using the I^2 statistic. The I^2 statistic describes the percentage of total variation across studies due to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity and larger values show increasing heterogeneity; substantial heterogeneity is considered to exist when $I^2 > 50\%$ (Higgins 2005). Where there was statistically significant heterogeneity we calculated the overall effect using a random-effects model instead of a fixed-effect model. Variability in participants, interventions and the outcomes studied (clinical diversity) are described in Table 2.

Data synthesis

We calculated the mean difference (MD) for all outcomes of interest which were interval scaled (for example, walking velocity). If appropriate, we calculated a pooled estimate of the MD using either the fixed-effect or the random-effects model (depending on heterogeneity), with 95% confidence intervals (CI).

For all binary outcomes (such as walking dependency) we calculated relative risks (RRs). Where trials (or groups within a trial) had zero adverse events or no dropouts we calculated risk differences (RDs) with 95% CI.

For all statistical analyses we used The Cochrane Collaboration's Review Manager 5 software (RevMan 2011).

In our protocol we stated that we would carry out separate analyses with respect to the timing of outcome assessment (at the end of the training period and after a follow-up period) but these could not be undertaken due to the limited number of trials.

Sensitivity analysis

Although initially planned, we did not identify a sufficient number of studies to do a sensitivity analysis. Such an analysis compares the results when all studies are included and when studies assessed to have lower or ambiguous methodological quality are excluded. This leaves studies with adequately concealed allocation of participants, blinded outcome assessors and an intention-to-treat analysis.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies.

The search identified 1089 unique records, and 40 full-text articles were assessed for eligibility (see Appendix 1).

Two new study reports met the inclusion criteria for the review (Alexeeva 2011; Field-Fote 2011). One of the new reports (Field-Fote 2011) replaces and completes preliminary study results (Field-Fote 2005) already included in the review.

Included studies

A total of five RCTs involving 309 patients met our inclusion criteria and were included in the analysis (Alexeeva 2011; Dobkin 2006; Field-Fote 2011; Hornby 2007; Postans 2004).

In the last version of this review (2008) we used the published preliminary data of Field-Fote 2005. In the updated review we are now able to use the results from the completed study (Field-Fote 2011). The study Field-Fote 2005 was therefore excluded and substituted by Field-Fote 2011 to avoid duplication of data. Another included study is still unpublished (Hornby 2007); the trial's principal investigator provided us with sufficient information to enable the trial's inclusion (see Additional Table 3). There were no disagreement between the authors in the selection of studies.

Details of included studies are presented in the table 'Characteristics of included studies' and in Table 1; Table 2; Table 3 and Table 4. The following is a brief overview.

Study types

Four studies were conducted in the USA (Alexeeva 2011; Dobkin 2006; Field-Fote 2011; Hornby 2007) and one in the United Kingdom (Postans 2004).

One study used a cross-over design (Postans 2004) and we only used the first trial period (pre-cross-over) for our analyses. All

other included studies used a parallel-group design (Alexeeva 2011; Dobkin 2006; Field-Fote 2011; Hornby 2007).
The duration of the training interventions ranged from four weeks (Postans 2004) to eight weeks (Hornby 2007) and 12 weeks (Dobkin 2006; Field-Fote 2011) and the maximum length of follow-up was six months (Dobkin 2006).

Participants

The number of participants in each study ranged from 14 participants (Postans 2004) to 146 participants (Dobkin 2006).
The age of the participants ranged from 18 years (Hornby 2007) to 68 years (Dobkin 2006); where stated, more men participated than women. Two trials did not include data on the male to female ratio. However, the other studies had a ratio of 2.6 men to one woman (89 male participants and 34 female).
All included studies provided information on the level of spinal cord injury (C3 to L4) and baseline severity (AIS grades A to D). A detailed description of patient characteristics can be found in the table 'Patient characteristics in studies (demographic)' (Table 2).

Interventions

Two studies investigated the robotic-assisted device 'Lokomat' as one of the experimental interventions (Field-Fote 2011; Hornby 2007) and all four studies investigated bodyweight supported treadmill training with manual guidance without any robotic device. One study investigated bodyweight supported treadmill training with manual guidance in combination with functional electrical stimulation (Postans 2004).
The frequency of treatment ranged from two to three times a week (Hornby 2007) to five times a week (Dobkin 2006; Field-Fote 2011; Postans 2004). The duration of treatment was four weeks (Postans 2004), eight weeks (Hornby 2007) or 12 weeks (Dobkin 2006; Field-Fote 2011).
The intensity of treatment (in terms of the length of an experimental therapy session) ranged from 30 to 45 minutes (Hornby 2007) to 60 minutes (Dobkin 2006; Field-Fote 2011). The gait training time did not differ between control and experimental groups.

Outcomes

The follow-up assessment was at four weeks in Postans 2004, after eight weeks in Hornby 2007 and after 12 weeks in Dobkin 2006 and Field-Fote 2011. One of the included trials had additional follow-up at six and 12 months (Dobkin 2006).
All included studies investigated the improvement in walking function, measured as speed of walking, as their primary outcome. Other frequently investigated outcomes were: walking function gait capacity (metres walked in six minutes) (Dobkin 2006; Hornby 2007) and Functional Independence Measure - Lokomotion (FIM-L) (Dobkin 2006; Hornby 2007).
A more detailed description of the primary outcomes for each trial can be found in 'Characteristics of included studies'.

Ongoing studies

Four ongoing studies were also identified (Behrman NCT00127439; Calancie NCT00061295; Popovic NCT00201968; Wirz 2011). Further details are presented in the table 'Characteristics of ongoing studies'.

Risk of bias in included studies

Details of the methodological quality for each included study are provided in the table 'Characteristics of included studies', Figure 2 and in Table 1 'PEDro scores'.
We contacted the trial authors of all the included studies to request clarification on study design or missing information in order to complete the quality ratings. The correspondence was via email and letter. We wrote reminders every month if no answer was received. All trial authors of included studies provided at least some of the requested data and information. No further information could be reached for ongoing studies (Characteristics of ongoing studies).
Using the PEDro scale, two review authors (JM and MP) independently assessed the methodological quality of all the included trials.
The assessors disagreed on only one of a total of 10 PEDro test items. The item where disagreement occurred was on the use of an intention-to-treat analysis (Dobkin 2006; Field-Fote 2011; Hornby 2007). However, the disagreement was discussed and finally arbitrated by another author (JC). The ratings for each of the PEDro items and the total PEDro score (that is, the score derived from adding all PEDro scale items) are listed in Table 1.
The maximum total PEDro score possible for the studies included in this review was eight (out of 10) as it was considered impossible to blind the participants or the physiotherapists to the intervention. Three studies attained a total PEDro score of five (Hornby 2007; Postans 2004), one study reached a score of six (Field-Fote 2011) and one study reached a total PEDro score of seven (Dobkin 2006) (Table 1).
One trial (Postans 2004) used a cross-over design with random allocation to the order of treatment sequences. Only the first period was analysed, as a parallel-group trial, in this review. Four studies used a parallel-group design with true randomisation of participants to groups (Alexeeva 2011; Dobkin 2006; Field-Fote 2011; Hornby 2007). Three studies used concealed allocation of participants (Dobkin 2006; Hornby 2007; Postans 2004).
One of the included studies described outcome assessors as blinded to group allocation (Dobkin 2006).
Four of the included studies achieved a dropout rate of less than 15% (Alexeeva 2011; Field-Fote 2011; Hornby 2007; Postans 2004), however the largest of the included studies had a dropout

rate of 20% (29 dropouts out of 146 randomised participants) (Dobkin 2006).

Follow-up assessments after the end of the study were reported for two studies (Dobkin 2006; Hornby 2007).

Additional functional electrical stimulation of leg muscles during gait training was applied in one of the treatment groups in two trials (Field-Fote 2011; Postans 2004).

We combined the results of the intervention groups bodyweight supported treadmill training (BWSTT), robotic-assisted locomotor training and FES in combination with BWSTT from two trials (Alexeeva 2011; Hornby 2007) into one group to compare with the control group - other locomotor training approaches.

Effects of interventions

1. Bodyweight supported treadmill training versus all other training approaches

Speed of walking at the end of intervention phase

Analysis 1.1

Four trials involving a total of 274 participants (Alexeeva 2011; Dobkin 2006; Field-Fote 2011; Postans 2004) measured speed of walking in metres per second (m/sec). The use of bodyweight supported treadmill training as locomotor training for people after spinal cord injury (SCI) did not increase walking velocity. The pooled mean difference (fixed-effect model) was 0.03 m/sec (95% confidence interval (CI) -0.05 to 0.11; P = 0.52; I^2 = 22%).

Walking capacity at the end of intervention phase

Analysis 1.2

Three trials involving a total of 234 participants (Dobkin 2006; Field-Fote 2011; Postans 2004) measured walking capacity as metres walked in six minutes. The use of bodyweight supported treadmill training as locomotor training for people after SCI did not significantly increase their walking capacity. The pooled mean difference (random-effects model) was -1.25 metres (95% CI -41.26 to 3.77; P = 0.95; I^2 = 62%).

Independence in walking at the end of intervention phase

Analysis 1.3

One trial involving 146 participants (Dobkin 2006) measured recovery of independent walking. The use of bodyweight supported treadmill training as locomotor training for people after SCI did not increase the chances of walking independently (risk difference (RD) 0.07, 95% CI -0.08 to 0.23, P = 0.36).

Safety of exercise - incidence of adverse events during the trial

Analysis 1.4

Five trials involving a total of 309 participants provided information about adverse events during the trial period. The rates of adverse events were between 0% (3 studies) and 4%. The use of bodyweight supported treadmill training as locomotor training for people after SCI did not significantly increase the risk of participants having an adverse event during training (RD 0.03 (fixed-effect model), 95% CI -0.02 to 0.07; P = 0.21; I^2 = 0%). All adverse events for each trial are described in detail in Table 4.

Dropouts for any reason during the trial

Analysis 1.5

Five trials involving a total of 309 participants provided data on the rate of participants dropping out during the trial period from any cause. The dropout rates were between 0% and 20%. The use of bodyweight supported treadmill training as locomotor training for people after SCI did not significantly increase the risk of participants dropping out (RD -0.05 (fixed-effect model), 95% CI -0.13 to 0.04; P = 0.29; I^2 = 0%). The reasons for dropout for each trial are described in detail in Table 4.

2. Robotic-assisted locomotor training versus all other training approaches

Walking speed at the end of intervention phase

One study (Hornby 2007) provided median and range values for speed of walking which could not be pooled. A description of the results of this study is given in Table 3.

One trial involving 74 participants (Field-Fote 2011) measured speed of walking in metres per second (m/sec) at the end of the study. The use of robotic-assisted locomotor training as locomotor training for people after SCI did not significantly increase the walking velocity. The mean difference was 0.06 m/sec (95% CI -0.01 to 0.13; P = 0.11). Analysis 2.1

Walking capacity at the end of intervention phase

One study (Hornby 2007) provided median and range values for walking capacity which could not be pooled. A description of the results of this study is given in Table 3.

One trial involving 74 participants (Field-Fote 2011) measured walking capacity as metres walked in six minutes. People with SCI who used robotic-assisted locomotor training had reduced walking capacity at final follow-up. The pooled mean difference (fixed-effect model) was 10.29 metres less ability to walk compared with the control group (95% CI 0.15 to 20.43; P = 0.05). Analysis 2.2

Independent walking at the end of intervention phase

None of the included studies investigated independence in walking when comparing robotic-assisted locomotor training with all other locomotor training approaches. One trial (Hornby 2007) provided median and range values for independence in walking which could not be pooled. A description of the results of this study is given in Table 3.

Safety - incidence of adverse events during the trial

Analysis 2.3

Two trials involving a total of 109 participants (Field-Fote 2011; Hornby 2007) provided information about adverse events during the trial period. The rate of adverse events was 0%. The use of robotic-assisted locomotor training as locomotor training for people after SCI did not significantly increase the risk of participants having an adverse event during training (RD 0.00 (fixed-effect model), 95% CI -0.07 to 0.07; P = 1.0; I^2 = 0%). All adverse events are described in detail for each trial in Table 4.

Dropouts during the trial

Analysis 2.4

Two trials involving a total of 109 participants (Field-Fote 2011; Hornby 2007) provided information on the rate of participant dropouts during the trial period, from any cause. The dropout rates were between 0% and 23%. The use of robotic-assisted locomotor training for people after SCI did not significantly increase the risk of participants dropping out (RD 0.01 (fixed-effect model), 95% CI -0.13 to 0.15; P = 0.94; I^2 = 58%). The reasons for dropouts are described in detail for each trial in Table 4.

3. Functional electrical stimulation (FES) AND bodyweight supported treadmill training (BWSTT) versus all other training approaches

Walking speed at the end of the intervention phase

Analysis 3.1

Two trials involving a total of 88 participants (Field-Fote 2011; Postans 2004) measured speed of walking (m/sec) at the end of the study. The use of bodyweight supported treadmill training in combination with functional electrical stimulation as locomotor training for people after SCI did not significantly increase walking velocity. The pooled mean difference (fixed-effect model) was -0.03 m/sec (95% CI -0.11 to 0.06; P = 0.53; I^2 = 50%).

Walking capacity at the end of intervention phase

One study involving 14 participants (Postans 2004) investigated walking capacity when comparing bodyweight supported treadmill training in combination with functional electrical stimulation versus all other locomotor training approaches. The data were not comparable at baseline (the groups differed significantly) and we did not analyse the results of this trial for this comparison.

One trial involving 74 participants (Field-Fote 2011) measured walking capacity as metres walked in six minutes. People with SCI who used functional electrical stimulation did not significantly increase their walking capacity compared with all other approaches. The pooled mean difference (fixed-effect model) was 2.43 metres (95% CI -10.82 to 15.67; P = 0.72). Analysis 3.2

Independent walking at the end of intervention phase

None of the included studies investigated independence in walking when comparing bodyweight supported treadmill training in combination with functional electrical stimulation versus all other locomotor training approaches.

Safety - incidence of adverse events during the trial

Analysis 3.3

Two trials involving a total of 88 participants (Field-Fote 2011; Postans 2004) provided information on adverse events during the trial period. The rate of adverse events was between 0% and 14%. The use of bodyweight supported treadmill training in combination with functional electrical stimulation as locomotor training for people after SCI did not significantly increase the risk of participants having an adverse event during training (RD 0.00 (fixed-effect model), 95% CI -0.09 to 0.09; P = 1.0; I^2 = 0%). All adverse events are described in detail for each trial in Table 4.

Dropouts during the trial

Analysis 3.4

Two trials involving a total of 88 participants (Field-Fote 2011; Postans 2004) provided information about the rate of participants dropping out during the trial period, from all causes. The dropout rate was in both trials 14%. The use of bodyweight supported treadmill training in combination with functional electrical stimulation as locomotor training after SCI did not significantly increase the risk of participants dropping out (RD 0.05 (fixed-effect model), 95% CI -0.11 to 0.22; P = 0.52; I^2 = 0%). The reasons for dropping out from each trial are described in detail in Table 4.

Subgroup and sensitivity analyses

Although planned for this review and stated in the protocol, we did not perform subgroup or sensitivity analyses (for example, a separate analysis for participants with acute or chronic SCI) due to the low number of included studies.

DISCUSSION

Principal findings

The aim of this review was to evaluate the effects of locomotor training on walking function in people with spinal cord injury (SCI). The search for studies through November 2011 identified five studies involving a total of 309 participants. We found no significant differences between the different forms of locomotor training for improving walking function in people with SCI, with one exception. We found a statistically significant effect in that robotic-assisted locomotor training might result in a reduced walking capacity when compared with all other interventions, but this is based on only one published study with 74 participants and needs further investigation. Adverse events and dropouts were no more frequent for participants who received bodyweight supported treadmill training with or without functional electrical stimulation or robotic-assisted locomotor training. This indicates that for most of the participants in the trials included in this review, different types of locomotor training did not differ with respect to safety and acceptability.

Methodological issues

There was heterogeneity between the trials in terms of trial design (two, three and four arms; parallel-group or cross-over trials; duration of study and selection criteria for participants), characteristics of the therapy interventions and participant characteristics (duration of SCI, age). There were also methodological differences in the mechanism of randomisation and allocation concealment methods used, blinding of primary outcomes and the use of intention-to-treat analysis. There were not enough studies to conduct sensitivity analyses according to methodological quality.

Limitations of the review

There is a risk of publication bias in all systematic reviews. In an effort to minimise this we searched extensively for relevant literature in databases, handsearched conference abstracts and contacted trial authors and experts in the field for unpublished and ongoing trials. We are confident that our detailed search strategy combined with handsearching identified all relevant trials. However, it may be possible that there is some 'grey literature' that we did not identify. It would be unlikely, however, that this would have a significant impact on our results. No statistical or graphical evidence for publication bias was detected.

A limitation of this review is that only five relevant randomised trials were identified. Another limitation is that some of these studies had methodological shortcomings including lack of concealed allocation and only one of five studies had blinded outcome assessors (Dobkin 2006). The use of a rigorous study design is very important to minimise bias. Therefore, the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2005) states that randomised controlled trials are to be considered when addressing questions regarding therapeutic efficacy in order to reduce bias. A recent systematic review included non-randomised trials (Lam 2007). However, this review did not include all the randomised trials that we have located and did not pool any data to determine effects of locomotor training for people with SCI.

The biggest study included in this review, with 146 participants and the highest methodological quality (Dobkin 2006), showed no difference between the intervention groups. However, both groups in this trial demonstrated walking speeds that exceeded those previously achieved at these clinical sites (Dobkin 2003). All participants received one additional hour of walking training therapy, regardless of the group. One explanation could therefore be that the amount of therapy and thus intensity of treatment may have played a role in both groups achieving unprecedented successes.

We used the data from people with either Lower Motor Neuron (LMN) or Upper Motor Neuron (UMN) lesions in the study by Dobkin et al. One could criticise this because the majority of included outcomes are more relevant for persons with UMN lesions. However, we decided to include all participants in this clinical study as a further analysis for differences between UMNL and LMN was not delineated in our protocol and would, therefore, be beyond the scope of our review.

It can also be argued that the grouping of participants into categories based on the ASIA Impairment Scale (AIS) evaluation or lesion level, or both, may not provide the most sensitive measure associated with walking recovery.

The inconclusive results of our analysis may, therefore, come from our lack of ability to characterise our population beyond the AIS and lesion level. There may be other relevant, meaningful groups that would help to understand differences. It may also be that the population of people with SCI is so heterogeneous that we are missing the critical group that would benefit; and that we should look for sub-populations who benefit most from different locomotor training approaches.

Another problem is that different methods are applicable for people with minimal voluntary activity and high degrees of flexor activity or tone to people with low activity and tone and those with voluntary activity and extensor activity or spasticity. Furthermore, the role of the various treatments may differ at different times after injury. Different approaches are therefore likely to be needed, for example, different rehabilitation efforts to address acute and chronic injuries.

The interventions described in the included trials delineate the modality used in the study. The means of progression, the role of the therapist, the role of or instructions to the patient or other distinguishing factors that may be the critical components in the intervention were not well described.

One should also discuss the meaningfulness of gains in gait speed critically under the premise of clinical and statistical significance. A 100% change in gait speed may at first appear important, but when gait speed improves from 0.04 m/sec to 0.08 m/sec it is unlikely to be a meaningful change. Such gain could also be within

the realm of measurement error or participant variability. In this review no pooled comparison of walking speed reached statistical significance.

Another further limitation of this review is that not all of the trial authors provided us with the information we required.

This review provides a template for the inclusion of future trials and could be used, in addition to recent guidelines (such as SCIRE 2006; Tuszynski 2007), to guide further research. There is a clear need for well-designed, large, multicentre randomised controlled trials to evaluate the effects of locomotor training for people with SCI. However, such clinical trials involving people with incomplete SCI are costly and may be difficult. Further research should, therefore, predefine certain subgroups (for example, patients in either the acute or chronic phase after injury) to show which participants may benefit from which training approaches and the intensities to use in the short and long term. Future trials should use relevant walking variables such as walking speed, capacity and independence in walking (Steeves 2007).

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to conclude that any one approach to locomotor training is more effective than another for improving walking function in people with spinal cord injury (SCI).

Implications for research

Insufficient evidence is mostly due to the small number of trials and small sample sizes of the trials. The trials and participants were also very heterogenous. We therefore recommend that further multicentre randomised controlled trials with larger sample sizes be undertaken to evaluate the efficacy of different locomotor training approaches, and especially robotic-locomotor training, for people with SCI. Further research should define sub-populations of people with SCI to find out who is benefiting most from which locomotor training approaches and at which stage of recovery. Furthermore, it is important that further research describes the complete intervention strategy rather than just the modality of treatment, progression of therapy and the role of the therapist.

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REFERENCES

References to studies included in this review

Alexeeva 2011 *{published data only}*
Alexeeva N, Sames C, Jacobs PL, Hobday L, DiStasio M, Mitchell SA, et al.Comparison of training methods to improve walking in persons with chronic spinal cord injury: a randomized clinical trial. *Journal of Spinal Cord Medicine* 2011;**34**(4):362–79.

Dobkin 2006 *{published data only}*
Dobkin B, Apple D, Barbeau H, Basso M, Behrman A, Deforge D, et al.Weight-supported treadmill vs over-ground training for walking after acute incomplete SCI. *Neurology* 2006;**66**(4):484–93. [: CN–00555430]

Field-Fote 2011 *{published data only}*
* Field-Fote E, Roach K. Influence of a locomotor training approach on walking speed and distance in people with chronic spinal cord injury: a randomized clinical trial. *Physical Therapy* 2011;**91**(1):48–60.
Field-Fote EC, Lindley SD, Sherman AL. Locomotor training approaches for individuals with spinal cord injury: a preliminary report of walking-related outcomes. *Journal of Neurological Physical Therapy* 2005;**29**(3):127–38.

Hornby 2007 *{unpublished data only}*
Hornby TG, Campbell DD, Zemon DH, Kahn JH, Moore J, Roth H. Assessment of robotic-assisted locomotor training in individuals with subacute, motor incomplete SCI: a randomized, controlled pilot study. Archives of Physical Medicine and Rehabilitation.

Postans 2004 *{published data only}*
Postans NJ, Hasler JP, Granat MH, Maxwell DJ. Functional electric stimulation to augment partial weight-bearing supported treadmill training for patients with acute incomplete spinal cord injury: a pilot study. *Archives of Physical Medicine and Rehabilitation* 2004;**85**(4):604–10. [: CN–00470560]

References to studies excluded from this review

Adams 2011 *{published data only}*
Adams MM, Hicks AL. Comparison of the effects of body-weight-supported treadmill training and tilt-table standing on spasticity in individuals with chronic spinal cord injury. *Journal of Spinal Cord Medicine* 2011;**34**(5):488–94.

Behrmann 2005 *{published data only}*
Behrman AL, Lawless-Dixon AR, Davis SB, Bowden MG, Nair P, Phadke C, et al.Locomotor training progression and

outcomes after incomplete spinal cord injury. Physical Therapy. United States: American Physical Therapy Association, 2005; Vol. 85, issue 12:1356–71.

Effing 2006 *{published data only}*
Effing TW, van Meeteren NL, van Asbeck FW, Prevo AJ. Body weight-supported treadmill training in chronic incomplete spinal cord injury: a pilot study evaluating functional health status and quality of life. *Spinal Cord* 2006;**44**(5):287–96.

Field-Fote 2001 *{published data only}*
Field-Fote E. Combined use of body weight support, functional electric stimulation, and treadmill training to improve walking ability in individuals with chronic incomplete spinal cord injury. *Archives of Physical Medicine and Rehabilitation* 2001;**82**(6):818–24.

Field-Fote 2002 *{published data only}*
Field-Fote EC, Tepavac D. Improved intralimb coordination in people with incomplete spinal cord injury following training with body weight support and electrical stimulation. *Physical Therapy* 2002;**82**(7):707–15.

Granat 1993 *{published data only}*
Granat MH, Ferguson AC, Andrews BJ, Delargy M. The role of functional electrical stimulation in the rehabilitation of patients with incomplete spinal cord injury - observed benefits during gait studies. *Paraplegia* 1993;**31**(4):207-15.

Hardin 2006 *{published data only}*
Hardin EC, Kobetic R, Murray L, Corado-Ahmed M, Pinault G, Nogan S, et al.Walking mechanics after training with an implanted functional electrical stimulation system for incomplete spinal cord injury. *Journal of Biomechanics* 2006;**39**(Suppl 1):112.

Hesse 2004 *{published data only}*
Hesse S, Werner C, Bardeleben A. Electromechanical gait training with functional electrical stimulation: case studies in spinal cord injury. *Spinal Cord* 2004;**42**(6):346–52.

Hicks 2005 *{published data only}*
Hicks AL, Adams MM, Martin Ginis K, Giangregorio L, Latimer A, Phillips SM, et al.Long-term body-weight-supported treadmill training and subsequent follow-up in persons with chronic SCI: effects on functional walking ability and measures of subjective well-being. *Spinal Cord* 2005;**43**(5):291–8.

Hornby 2005 *{published data only}*
Hornby TG, Zemon DH, Campbell D. Robotic-assisted, body-weight-supported treadmill training in individuals following motor incomplete spinal cord injury. *Physical Therapy* 2005;**85**(1):52–66.

Jezernik 2003 *{published data only}*
Jezernik S, Schärer R, Colombo G, Morari M. Adaptive robotic rehabilitation of locomotion: a clinical study in spinally injured individuals. *Spinal Cord* 2003;**41**(12): 657–66. [: CN–00559373]

Johnston 2003 *{published data only}*
Johnston TE, Finson RL, Smith BT, Bonaroti DM, Betz RR, Mulcahey MJ. Functional electrical stimulation for augmented walking in adolescents with incomplete spinal cord injury. *Journal of Spinal Cord Medicine* 2003;**26**(4): 390-400.

Kim 2004a *{published data only}*
Kim CM, Eng JJ, Whittaker MW. Level walking and ambulatory capacity in persons with incomplete spinal cord injury: relationship with muscle strength. *Spinal Cord* 2004;**42**(3):156–62.

Kim 2004b *{published data only}*
Kim CM, Eng JJ, Whittaker MW. Effects of a simple functional electric system and/or a hinged ankle-foot orthosis on walking in persons with incomplete spinal cord injury. *Archives of Physical Medicine and Rehabilitation* 2004;**85**(10):1718–23.

Klose 1990 *{published data only}*
Klose KJ, Schmidt DL, Needham BM, Brucker B, Green BA, Ayyar DR. Rehabilitation therapy for patients with long-term spinal cord injuries. *Archives of Physical Medicine and Rehabilitation* 1990;**71**:659–62.

Klose 1997 *{published data only}*
Klose KJ, Jacobs PL, Broton JG, Guest RS, Needham-Shropshire BM, Lebwohl N, et al.Evaluation of a training program for persons with SCI paraplegia using the Parastep 1 ambulation system: part 1. Ambulation performance and anthropometric measures. *Archives of Physical Medicine and Rehabilitation* 1997;**78**(8):789–93.

Ladoceur 2000 *{published data only}*
Ladouceur M, Barbeau H. Functional electrical stimulation-assisted walking for persons with incomplete spinal injuries: longitudinal changes in maximal overground walking speed. *Scandinavian Journal of Rehabilitation Medicine* 2000;**32**(1): 28–36. [: 0036–5505]

Nair 2004 *{published data only}*
Nair P, Phadke C, Bowden MG, Davis S, Lawless A, Behrman A. Poster 14: Clinical gait outcomes after locomotor training in persons with chronic, incomplete spinal cord injury. *Archives of Physical Medicine and Rehabilitation* 2004;**85**(8):e8.

Protas 2001 *{published data only}*
Protas EJ, Holmes SA, Qureshy H, Johnson A, Lee D, Sherwood AM. Supported treadmill ambulation training after spinal cord injury: a pilot study. *Archives of Physical Medicine and Rehabilitation* 2001;**82**(6):825–31.

Rastelli 2010 *{published data only}*
* Rastelli TF, Caserio M, Milia P. Robotic orthosis Lokomat: its use in the rehabilitation of locomotion for neuromotor outcomes of patients with brain injury. Presentation of a pilot study. 8th World Congress on Brain Injury of the International Brain Injury Association, Washington. *Brain Injury* 2010;**24**(3):115–463.

Stein 1993 *{published data only}*
Stein RB, Belanger M, Wheeler G, Wieler M. Electrical systems for improving locomotion after incomplete spinal cord injury: an assessment. *Archives of Physical Medicine and Rehabilitation* 1993;**74**(9):954.

Swinnen 2010 *{published data only}*
Swinnen E, Duerinck S, Baeyens J, Meeusen R, Kerckhofs E. Effectiveness of robot-assisted gait training in persons with spinal cord injury: a systematic review. *Journal of Rehabilitation Medicine* 2010;**42**(6):520–6.

Tefertiller 2011 *{published data only}*
Tefertiller C, Pharo B, Evans N, Winchester P. Efficacy of rehabilitation robotics for walking training in neurological disorders: a review. *Journal of Rehabilitation Research & Development* 2011;**48**(4):387–416.

Thomas 2005 *{published data only}*
Thomas SL, Gorassini MA. Increases in corticospinal tract function by treadmill training after incomplete spinal cord injury. *Journal of Neurophysiology* 2005;**94**(4):2844–55.

Thoumie 1995a *{published data only}*
Thoumie P, Perrouin-Verbe B, Le Claire G, Bedoiseau M, Busnel M, Cormerais A, et al.Restoration of functional gait in paraplegic patients with the RGO-II hybrid orthosis. A multicentre controlled study. I. Clinical evaluation. *Paraplegia* 1995;**33**(11):647–53.

Thoumie 1995b *{published data only}*
Thoumie P, Le Claire G, Beillot J, Dassonville J, Chevalier T, Perrouin-Verbe B, et al.Restoration of functional gait in paraplegic patients with the RGO-II hybrid orthosis. A multicenter controlled study. II: Physiological evaluation. *Paraplegia* 1995;**33**(11):654–9.

Walker 1993 *{published data only}*
Walker J, Harris M. GM-1 ganglioside administration combined with physical therapy restores ambulation in humans with chronic spinal cord injury. *Neuroscience Letters* 1993;**161**(2):174–8. [: CN–00097955]

Wernig 1995 *{published data only}*
Wernig A, Muller S, Nanassy A, Cagol E. Laufband therapy based on 'rules of spinal locomotion' is effective in spinal cord injured persons. *European Journal of Neuroscience* 1995;**7**(4):823–9.

Wernig 1998 *{published data only}*
Wernig A, Nanassy A, Muller S. Maintenance of locomotor abilities following Laufband (treadmill) therapy in para- and tetraplegic persons: follow-up studies. *Spinal Cord* 1998;**36**(11):744–9.

Wernig 2000 *{published data only}*
Wernig A, Nanassy A, Muller S. Laufband (LB) therapy in spinal cord lesioned persons. *Progress in Brain Research* 2000;**128**:89–97.

Wessels 2010 *{published data only}*
Wessels M, Lucas C, Eriks I, de Groot S. Body weight-supported gait training for restoration of walking in people with an incomplete spinal cord injury: a systematic review. *Journal of Rehabilitation Medicine* 2010;**42**(6):513–9.

Wieler 1999 *{published data only}*
Wieler M, Stein RB, Ladouceur M, Whittaker M, Smith AW, Naaman S, et al.Multicenter evaluation of electrical stimulation systems for walking. *Archives of Physical Medicine and Rehabilitation* 1999;**80**(5):495–500. [: 0003–9993]

Winchester 2005 *{published data only}*
Winchester P, McColl R, Querry R, Foreman N, Mosby J, Tansey K, et al.Changes in supraspinal activation patterns following robotic locomotor therapy in motor-incomplete spinal cord injury. *Neurorehabilitation and Neural Repair* 2005;**19**(4):313–24.

Wirz 2005 *{published data only}*
Wirz M, Zemon DH, Rupp R, Scheel A, Colombo G, Dietz V, et al.Effectiveness of automated locomotor training in patients with chronic incomplete spinal cord injury: a multicenter trial. *Archives of Physical Medicine and Rehabilitation* 2005;**86**(4):672–80.

Zhu 2004 *{published data only}*
Zhu HX, Dou ZL, Li K, Lan Y, Hu XQ. A preliminary investigation on the correlation of partial body weight support training with hemiplegic gait and ambulation function after brain injury [Chinese]. *Zhongguo Linchuang Kangfu [Chinese Medical Journal]* 2004;**8**(25):5205–7. [: 1671–5926]

References to studies awaiting assessment

Alcobendas-Maestro 2012 *{published data only}*
* Alcobendas-Maestro M, Esclarin-Ruz A, Casado-Lopez RM, Munoz-Gonzalez A, Perez-Mateos G, Gonzalez-Valdizan E, et al.Lokomat Robotic-Assisted Versus Overground Training Within 3 to 6 Months of Incomplete Spinal Cord Lesion: Randomized Controlled Trial. *Neurorehabil Neural Repair* 2012;**epub ahead**.

Wirz 2011 *{published data only}*
Wirz M, Bastiaenen C, de Bie R, Dietz V. Effectiveness of automated locomotor training in patients with acute incomplete spinal cord injury: a randomized controlled multicenter trial. *BMC Neurology* 2011;**11**:60.

Wu 2012 *{published data only}*
* Wu M, Landry JM, Schmit BD, Hornby TG, Yen SC. Robotic resistance treadmill training improves locomotor function in human spinal cord injury: a pilot study. *Arch Phys Med Rehabil* 2012;**93**(5):782–9.

References to ongoing studies

Behrman NCT00127439 *{published data only}*
Differential effects of robotic vs. manually-assisted locomotor training. Ongoing study Record first received: 3 August 2005.

Calancie NCT00061295 *{published data only}*
Body weight supported ambulation training after spinal cord injury. Ongoing study Record first received: 23 May 2003.

Popovic NCT00201968 *{published data only}*
Functional electrical stimulation-assisted walking: reduction of secondary complications due to spinal cord injury. Ongoing study Record first received: 12 September 2005.

Additional references

Albert 2005

Albert T, Ravaud JF. Rehabilitation of spinal cord injury in France: a nationwide multicentre study of incidence and regional disparities. *Spinal Cord* 2005;**43**(6):357–65.

ASIA 2002

American Spinal Injury Association. Reference manual for international standards for neurological and functional classification of spinal cord injury patients. American Spinal Injury Association 2002.

Barbeau 1987

Barbeau H, Wainberg M, Finch L. Description and application of a system for locomotor rehabilitation. *Medical & Biological Engineering & Computing* 1987;**25**(3): 341–4.

Barbeau 2002

Barbeau H, Fung J, Leroux A, Ladouceur M. A review of the adaptability and recovery of locomotion after spinal cord injury. *Progress in Brain Research* 2002;**137**:9–25.

Barbeau 2006

Barbeau H, Nadeau S, Garneau C. Physical determinants, emerging concepts, and training approaches in gait of individuals with spinal cord injury. *Journal of Neurotrauma* 2006;**23**(3-4):571–85.

Behrman 2000

Behrman AL, Harkema SJ. Locomotor training after human spinal cord injury: a series of case studies. *Physical Therapy* 2000;**80**(7):688–700.

Burns 1997

Burns SP, Golding DG, Rolle WA Jr, Graziani V, Ditunno JF Jr. Recovery of ambulation in motor-incomplete tetraplegia. *Archives of Physical Medicine and Rehabilitation* 1997;**78**(11):1169–72.

Catz 2001

Catz A, Itzkovich M, Steinberg F, Philo O, Ring H, Ronen J, et al.The Catz-Itzkovich SCIM: a revised version of the Spinal Cord Independence Measure. *Disability and Rehabilitation* 2001;**23**(6):263–8.

Colombo 2000

Colombo G, Joerg M, Schreier R, Dietz V. Treadmill training of paraplegic patients using a robotic orthosis. *Journal of Rehabilitation Research and Development* 2000;**37** (6):693–700.

Crozier 1991

Crozier KS, Graziani V, Ditunno JF Jr, Herbison GJ. Spinal cord injury: prognosis for ambulation based on sensory examination in patients who are initially motor complete. *Archives of Physical Medicine and Rehabilitation* 1991;**72**(2): 119–21.

Dietz 1995

Dietz V, Colombo G, Jensen L, Baumgartner L. Locomotor capacity of spinal cord in paraplegic patients. *Annals of Neurology* 1995;**37**(5):574–82.

Dittuno 2001

Dittuno PL, Dittuno JF Jr. Walking index for spinal cord injury (WISCI II): scale revision. *Spinal Cord* 2001;**39**(12): 654–6.

Dobkin 2003

Dobkin BH, Apple D, Barbeau H, Basso M, Behrman A, Deforge D, et al.Methods for a randomized trial of weight-supported treadmill training versus conventional training for walking during inpatient rehabilitation after incomplete traumatic spinal cord injury. *Neurorehabilitation and Neural Repair* 2003;**17**(3):153–67.

Dobkin 2006a

Dobkin BH. Short-distance walking speed and timed walking distance: redundant measures for clinical trials?. *Neurology* 2006;**66**(4):584–6.

Gardner 1998

Gardner MB, Holden MK, Leikauskas JM, Richard RL. Partial body weight support with treadmill locomotion to improve gait after incomplete spinal cord injury: a single-subject experimental design. *Physical Therapy* 1998;**78**(4): 361–74.

Hamilton 1994

Hamilton BB, Laughlin JA, Fiedler RC, Granger CV. Interrater reliability of the 7-level functional independence measure (FIM). *Scandinavian Journal of Rehabilitation Medicine* 1994;**26**(3):115–9.

Herbert 1998

Herbert R, Moseley A, Sherrington C. PEDro: a database of randomised controlled trials in physiotherapy. *Health Information Management: Journal of the Health Information Management Association of Australia* 1998;**28**(4):186–8.

Hesse 1998

Hesse S, Malezic M, Lucke D, Mauritz KH. Value of functional electrostimulation in patients with paraplegia. *Nervenarzt* 1998;**69**(4):300–5.

Higgins 2005

Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 [updated May 2005]. In: The Cochrane Library Issue 3, 2005*. Chichester, UK: John Wiley & Sons, Ltd., 2005.

Kirshblum 2007

Kirshblum SC, Priebe MM, Ho CH, Scelza WM, Chiodo AE, Wuermser LA. Spinal cord injury medicine. 3. Rehabilitation phase after acute spinal cord injury. *Archives of Physical Medicine and Rehabilitation* 2007;**88**(3 (Suppl 1)):62–70.

Lam 2007

Lam T, Eng JJ, Wolfe DL, Hsieh JTC, Whittaker M, SCIRE Research Team. A systematic review of the efficacy of gait rehabilitation strategies for spinal cord injury. *Topics in Spinal Cord Injury Rehabilitation* 2007;**13**(1):32-57.

Maher 2003

Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Physical Therapy* 2003;**83** (8):713–21.

Marino 2003
Marino RJ, Barros T, Biering-Sorensen F, Burns SP, Donovan WH, Graves DE, et al.International standards for neurological classification of spinal cord injury. *Journal of Spinal Cord Medicine* 2003;**26**(Suppl 1):50–6.

Maynard 1979
Maynard FM, Reynolds GG, Fountain S, Wilmot C, Hamilton R. Neurological prognosis after traumatic quadriplegia. Three-year experience of California Regional Spinal Cord Injury Care System. *Journal of Neurosurgery* 1979;**50**(5):611–6.

Miller 2006
Miller WC, Curt A, Elliott S, Hsieh JTC, Mortenson WB, Noonan V, et al.Outcome measures. In: Eng JJ, Teasell RW, Miller WC, Wolfe DL, Townson AF, Aubut J, et al. editor (s). *Spinal Cord Injury Rehabilitation Evidence*. Vancouver: Spinal Cord Injury Rehabilitation Evidence (SCIRE), 2006: 22.1–22.89.

Morganti 2005
Morganti B, Scivoletto G, Ditunno P, Ditunno JF, Molinari M. Walking index for spinal cord injury (WISCI): criterion validation. *Spinal Cord* 2005;**43**(1):27–33.

NINDS 2006
National Institute of Neurological Disorders and Stroke. Spinal Cord Injury: Emerging Concepts. www.ninds.nih.gov/news˙and˙events/proceedings/sci˙report.htm#Spinal (accessed November 2006).

ONF 2006
Ontario Neurotrauma Foundation (ONF). Glossary of terms. www.onf.org/knowledge/glossary.htm accessed on 10.06.2008.

PEDro 2006
Centre for Evidence-Based Physiotherapy (CEBP). Physiotherapy evidence database (PEDro). www.pedro.fhs.usyd.edu.au/index.html (accessed 28 February 2006).

Pickett 2006
Pickett GE, Campos-Benitez M, Keller JL, Duggal N. Epidemiology of traumatic spinal cord injury in Canada. *Spine* 2006;**31**(7):799–805.

RevMan 2011
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Schmidt 2003
Schmidt H, Sorowka D, Hesse S, Bernhardt R. Development of a robotic walking simulator for gait rehabilitation. *Biomedizinische Technik. Biomedical Engineering* 2003;**48** (10):281–6.

SCIRE 2006
Eng J, Teasell R, Miller W, Wolfe D, Townson A, Aubut JA, et al.Spinal Cord Injury Rehabilitation Evidence (SCIRE). www.icord.org/scire/pdf/SCIRE˙COMPLETE.pdf 2006.

Sekhon 2001
Sekhon LH, Fehlings MG. Epidemiology, demographics, and pathophysiology of acute spinal cord injury. *Spine* 2001;**26 (24 Suppl)**:2–12.

Steeves 2007
Steeves JD, Lammertse D, Curt A, Fawcett JW, Tuszynski MH, Ditunno JF, et al.Guidelines for the conduct of clinical trials for spinal cord injury (SCI) as developed by the ICCP panel: clinical trial outcome measures. *Spinal Cord* 2007; **45**(3):206–21.

Tuszynski 2007
Tuszynski MH, Steeves JD, Fawcett JW, Lammertse D, Kalichman M, Rask C, et al.Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP Panel: clinical trial inclusion/exclusion criteria and ethics. *Spinal Cord* 2007;**45**(3):222–31.

Visintin 1989
Visintin M, Barbeau H. The effects of body weight support on the locomotor pattern of spastic paretic patients. *Canadian Journal of Neurological Sciences* 1989;**16**(3): 315–25.

Waters 1993
Waters RL, Adkins RH, Yakura J, Sie I. Motor and sensory recovery following complete tetraplegia recovery following complete tetraplegia. *Archives of Physical Medicine and Rehabilitation* 1993;**74**:242–7.

Waters 1994
Waters RL, Adkins R, Yakura J, Vigil D. Prediction of ambulatory performance based on motor scores derived from standards of the American Spinal Injury Association. *Archives of Physical Medicine and Rehabilitation* 1994;**75**(7): 756–60.

Wernig 1992
Wernig A, Muller S. Laufband locomotion with body weight support improved walking in persons with severe spinal cord injuries. *Paraplegia* 1992;**30**(4):229–38.

Wernig 1999
Wernig A, Nanassy A, Muller S. Laufband (treadmill) therapy in incomplete paraplegia and tetraplegia. *Journal of Neurotrauma* 1999;**16**(8):719–26.

Wirz 2001
Wirz M, Colombo G, Dietz V. Long term effects of locomotor training in spinal humans. *Journal of Neurology, Neurosurgery and Psychiatry* 2001;**71**(1):93–6.

References to other published versions of this review

Mehrholz 2008
Mehrholz J, Kugler J, Pohl M. Locomotor training for walking after spinal cord injury. *Cochrane Database of Systematic Reviews* 2008, Issue 2. [DOI: 10.1002/14651858.CD006676.pub2]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Alexeeva 2011

Methods	3-arm, parallel-group, multicentre randomised controlled trial
Participants	Country: USA Sample size: 40 participants (13 in the first group, 14 in the second group and 13 in the third group) Inclusion criteria - 16 to 70 years old - Had sustained injury to the spinal cord at or rostral to the T10 (vertebral) level - Were injured at least 1 year prior to enrolment - Had voluntary movement in at least 1 leg - Were able to rise to standing from a seated position with no more than moderate assistance, and independently advance at least 1 leg - Agreed to maintain their current routine of medications and activity levels while training - Received medical clearance from the study physician (assessment of general health and bilateral hip/knee radiographs to rule out significant pathology, e.g. significant osteoarthritis; heterotopic ossification; joint subluxation) Exclusion criteria - Degenerative myelopathy, neoplasm or congenital spinal cord anomalies - Prior gait training with BWS - The need for bilateral knee-ankle-foot orthoses for standing - The ability to jog or run
Interventions	- First group received individual physiotherapy - Second group received bodyweight supported (BWS) gait training using an overhead monorail track and trolley apparatus - Third group received bodyweight supported treadmill training (BWSTT) Training was delivered for all groups 3 days/week for 13 weeks (39 sessions)
Outcomes	- Maximum walking speed - Balance (Tinetti test) - Fitness (VO2 peak) - Muscle strength - Functional independence - Quality of life
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly assigned to training groups; assignment was done by a staff member not associated with the study, who drew printed

Alexeeva 2011 (*Continued*)

		labels from a box
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not described

Dobkin 2006

Methods	Multicentre randomised controlled trial - Parallel-group design
Participants	Inclusion criteria - Age 16 to 70 years - Traumatic SCI within 56 days of injury -Incomplete lesion (ASIA B, C or D at time of randomisation) from below C4 on at least one side of the body to no lower than L3 on either side of the body - Unable to ambulate over ground at randomisation without at least moderate assistance - Mini-Mental State Examination score more or equal to 26 Exclusion criteria - Symptomatic orthostatic hypotension or > 30 mm Hg drop when upright in the BWS apparatus - Subject with a spine-stabilising device whose treating surgeon states that BWSTT is contraindicated - Contraindication to weight bearing on lower extremities (pelvic or leg fracture, chronic joint pain) - Pressure sore stage 2 or higher, located where a harness or treadmill training or standing could affect healing - A debilitating disease prior to SCI that caused exercise intolerance and limited mobility-related self care and instrumental activities of daily living - Must use anti-spasticity medication at entry (initial use to prevent spasms that interfere with sleep allowed) - Premorbid major depression or psychosis; suicide attempt caused the SCI - Unlikely to complete the intervention or return for follow-up - Participation in another research study
Interventions	- One group received BWSTT - One group received overground walking
Outcomes	- Speed of walking - Walking distance - Walking Index for Spinal Cord Injury (WISCI) - Functional Independence Measure - Lokomotion (FIM-L)
Notes	

Risk of bias

Dobkin 2006 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Trained blinded observer at site

Field-Fote 2011

Methods	4-arm, parallel-group randomised controlled trial
Participants	Country: USA Sample size: 74 participants (19 in the first group, 22 in the second group, 18 in the third group and 15 in the fourth group) Inclusion criteria - Sustained spinal cord injury > 1 year - Injury level above T10 - Able to take at least 1 step with 1 leg - Able to rise from sitting to standing with at most moderate assistance (less than 50% effort) from 1 person Exclusion criteria - Orthopaedic problems - History of cardiac condition - Presence of active hip pathology (e.g. arthritis, ossification)
Interventions	- Group TM (Treadmill) Bodyweight supported (BWS) treadmill training with manual assistance - Group TS (Treadmill and Stimulation) BWS treadmill training with peroneal nerve stimulation (FES) - Group OG (Overground) BWS overground training with FES - Group LR (Locomotion by Robot) BWS treadmill training with robotic assistance
Outcomes	- Speed of walking (m/s) - Step length (m) - Lower extremity motor score - Step symmetry (step length ratio)
Notes	This study contains the final results of the project, and contains preliminary data from the study Field-Fote 2005. The last study results from 2005 where therefore excluded from all analysis
Risk of bias	

Field-Fote 2011 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information of sequence generation
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	People who captured and analysed the (video) data where unaware of group assignments

Hornby 2007

Methods	3-arm, parallel-group randomised controlled trial
Participants	Inclusion criteria - Age between 12 to 65 years - A recent (< 6 months) history of traumatic or non-traumatic, non-progressive SCI - Incomplete lesion (ASIA C or D) - Neurological lesion level between C1 and T10 - No history of anatomical injury to the spinal column below T10 - No history of other concurrent or previous neurological disorders - Participants walked independently prior to SCI but required physical assistance from at least 1 therapist to walk at study entry - Lower extremity range of motion within normal limits - Absence of unhealed decubiti - No history of osteoporosis or recurrent fractures - No history of orthopaedic injury that may limit walking ability - Lack of metabolic or cardiopulmonary instability - No other medical complications that limit exercise participation Exclusion criteria - Bodyweight > 120 kg - Femur length < 35 cm or > 47 cm - Extensive bracing of the spinal column
Interventions	- 1 group received BWSTT - 1 group received robotic-assisted treadmill walking - 1 group received overground walking
Outcomes	Speed of walking Walking distance WISCI FIM
Notes	Unpublished study (in peer review) Data provided by the first author

Hornby 2007 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information

Postans 2004

Methods	Randomised controlled cross-over trial
Participants	Inclusion criteria - Incomplete SCI (defined as ASIA classes C and D) - Nonambulatory or significant walking dysfunction Exclusion criteria - Medically unstable - Not be able to stand up safely
Interventions	Group AB Overground walking Group BA Bodyweight supported treadmill training with functional (peroneal) nerve stimulation
Outcomes	Speed of walking Walking distance
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information

ASIA: American Spinal Injury Association; BWS: bodyweight support; BWSTT: bodyweight supported treadmill training; FES: functional electrical stimulation; FIM: Functional Independence Measure; OG: overground; RCT: randomised controlled trial; SCI: spinal cord injury; TM: treadmill training; WISCI: Walking Index for Spinal Cord Injury

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

Study	Reason for exclusion
Adams 2011	Not a randomised controlled trial
Behrmann 2005	Not a randomised controlled trial; single case description
Effing 2006	Not a randomised controlled trial; single case series
Field-Fote 2001	Not a randomised controlled trial; pre-post comparison of 19 persons
Field-Fote 2002	Not a randomised controlled trial; pre-post comparison of 14 persons
Granat 1993	Not a randomised controlled trial; pre-post comparison of 6 persons
Hardin 2006	Not a randomised controlled trial; single case description
Hesse 2004	Not a randomised controlled trial; pre-post comparison of 4 persons
Hicks 2005	Not a randomised controlled trial; pre-post comparison of 14 persons
Hornby 2005	Not a randomised controlled trial; pre-post comparison of 2 persons
Jezernik 2003	Not a randomised controlled trial
Johnston 2003	Not a randomised controlled trial; pre-post comparison of 3 persons
Kim 2004a	Not a longitudinal locomotor training study
Kim 2004b	Not a longitudinal locomotor training study
Klose 1990	Randomised controlled cross-over trial which investigated upper limb impairment in 39 people
Klose 1997	Not a randomised controlled trial; pre-post comparison of 16 persons
Ladoceur 2000	Not a randomised controlled trial; pre-post comparison of 14 persons
Nair 2004	Not a randomised controlled trial; controlled trial of 10 persons with SCI; random allocation to groups was not described
Protas 2001	Not a randomised controlled trial; pre-post comparison of 3 persons

(*Continued*)

Rastelli 2010	Investigated patients with brain injury
Stein 1993	Not a randomised controlled trial; pre-post comparison of 10 persons
Swinnen 2010	Not a randomised controlled trial; review
Tefertiller 2011	Not a randomised controlled trial
Thomas 2005	Not a randomised controlled trial; pre-post comparison of 10 persons
Thoumie 1995a	Not a randomised controlled trial; pre-post comparison of 26 persons
Thoumie 1995b	Not a randomised controlled trial; pre-post comparison of 21 persons
Walker 1993	A pharmacological agent was tested
Wernig 1995	Not a randomised controlled trial, description of one cohort with 29 persons compared to an historical cohort of 24 persons
Wernig 1998	Not a randomised controlled trial; pre-post comparison of 35 persons
Wernig 2000	Not a randomised controlled trial; review
Wessels 2010	Not a randomised controlled trial
Wieler 1999	Not a randomised controlled trial; pre-post comparison of 31 persons
Winchester 2005	Not a randomised controlled trial; pre-post comparison of 2 persons
Wirz 2005	Not a randomised controlled trial; pre-post comparison of 20 persons
Zhu 2004	Investigated treadmill training in patients after stroke

SCI: spinal cord injury

Characteristics of studies awaiting assessment *[ordered by study ID]*

Alcobendas-Maestro 2012

Methods	randomized trial
Participants	80 participants from 3 to 6 months after onset
Interventions	all patients received 40 walking sessions using either a Lokomat program with overground practice or overground mobility therapy alone (of equal therapy time)

Alcobendas-Maestro 2012 (*Continued*)

Outcomes	Primary measurements of outcome included walking speed and the Walking Index for Spinal Cord Injury (WISCI II) Secondary outcomes included the 6-minute walk test, locomotor section of the Functional Independence Measure, Lower Extremity Motor Score (LEMS), the Ashworth Scale, and a Visual Analog Scale for pain
Notes	

Wirz 2011

Methods	RCT
Participants	Patients from multiple sites with a subacute incomplete SCI and who are not able to walk independently
Interventions	Either standard training (3 to 5 sessions per week, session duration maximum 25 minutes) or an intensive training (3 to 5 sessions per week, session duration minimum 50 minutes) After 8 weeks of training and 4 months later the walking ability, the occurrence of adverse events and the perceived rate of exertion as well as the patients' impression of change will be compared between groups
Outcomes	Primary outcome measures: • 10-metre walking test (at start of training, at weeks 2, 4, 6, 8, 6 and 24). Self selected walking speed over a distance of 10 m Secondary outcome measures: • Walking Index for Spinal Cord Injury (WISCI) (at start of training, at weeks 2, 4, 6, 8, 6 and 24). Classification of walking ability on a rank ordered scale with 21 categories. • Spasticity (at start of training, at weeks 2, 4, 6, 8, 6 and 24). Muscle tone is rated using the modified Ashworth and the Pess spasm frequency tests. • Perceived exertion (after every training) • Spinal Cord Independence Measure (at start of training, at weeks 2, 4, 6, 8, 6 and 24) • Spinal cord injury classification (at weeks 2, 4, 6, 8, 6 and 24). Classification according to the standards by the American Spinal Cord Injury Association (ASIA) • Patients' Global Impression of Change Scale (at week 8)
Notes	Information provided by Wirz et al. BMC Neurology 2011, 11:60 and by clinicaltrials.gov, identifier: NCT01147185

Wu 2012

Methods	randomized crossover trial
Participants	ten patients with chronic incomplete SCI
Interventions	one group received four weeks assistance training followed by four weeks of resistance training the other group received four weeks resistance training followed by four weeks assistance training (locomotor training was provided by using a cable-driven robotic locomotor training system in combination with body weight supported treadmill training
Outcomes	Primary outcome measures included self-selected and fast overground walking velocity and 6-minute walking distance Secondary measures included clinical assessments of balance, muscle tone, and strength (at baseline and after 4 and

	8 weeks of training)
Notes	

Characteristics of ongoing studies *[ordered by study ID]*

Behrman NCT00127439

Trial name or title	Differential effects of robotic vs. manually-assisted locomotor training
Methods	
Participants	Inclusion criteria: * Adults age 18 to 65 years * SCI within 6 months to 5 years * Motor I-SCI, upper motor neuron lesion only at cervical or thoracic levels * A diagnosis of first time SCI including aetiology from trauma, vascular or orthopaedic pathology * SCI as defined by the American ASIA Impairment Scale categories C or D * Medically stable condition that is asymptomatic for bladder infection, decubiti, osteoporosis, cardiopulmonary disease, pain, contractures or other significant medical complications that would prohibit or interfere with testing of walking function and training or alter compliance with the training protocol * Documented medical approval from the participant's personal physician verifying the participant's medical status at time of enrolment * Ability to walk a minimum of 30 feet with or without an assistive device, independently or with minimal assistance * Over ground gait speed < 0.8 m/s * Persons using anti-spasticity medication must maintain stable medication dosage during the study * Able to give informed consent Exclusion criteria: * Current participation in a rehabilitation programme/research protocol that could interfere or influence the outcome measures of the current study * History of congenital SCI (e.g. myelomeningocele, intraspinal neoplasm, Friedreich's ataxia) or other degenerative spinal disorders (e.g. spinocerebellar degeneration, syringomyelia) that may complicate the protocol * Inappropriate or unsafe fit of the harness or robotic trainer due to the participant's body size and/or joint contractures or severe spasticity that would prohibit the safe provision of either training modality
Interventions	The primary objective of this project is to assess and compare the effects of robotic-assisted versus manually-assisted locomotor training using the bodyweight support (BWS) on sub-tasks of walking. Specifically, we believe that at least 4 subtasks of walking are differentially affected by the robotic-assisted training when compared to manually-assisted training (propulsion, transition from stance to step, stepping, and equilibrium) The investigators hypothesise that robotic-assisted training will have a greater effect on generating improved stepping compared to manually assisted training, whereas manually assisted training will have a greater effect on improving propulsion, transition and equilibrium Participants will be randomised to one of 2 training groups: robotic-assisted or manually assisted, and evaluated for performance on sub-tasks of walking

Behrman NCT00127439 (*Continued*)

Outcomes	Primary outcome measures: * Participants will undergo a series of pre-training evaluations, followed by 9 weeks of training, and repeat the evaluations at the completion of training * 4 primary outcome measures: propulsion, transition, stepping and equilibrium represent critical sub-tasks to the control of walking. These measures will be based on biomechanical testing and analyses (i.e. treadmill designed to record bilateral ground reaction forces * Motion analysis * Dynamic equilibrium during bodyweight supported walking) Secondary outcome measures: * Additional outcome measures for participants will also be performed the week before and the week following completion of the 9 weeks of training. These evaluations will include: American Spinal Injury Association (ASIA) classification of impairment
Starting date	Record first received: 3 August 2005
Contact information	Jeff Fox jfox@phhp.ufl.edu Lisa Demanuel lisa.demanuel@med.va.gov Malcom Randall VA Medical Center, Gainesville, Florida, 32608, United States Andrea Behrman, Principal Investigator VA RR&D Brain rehabilitation Research Center of Excellence United States, Florida
Notes	

Calancie NCT00061295

Trial name or title	Body weight supported ambulation training after spinal cord injury
Methods	
Participants	Inclusion criteria for patients with chronic injury: * Spinal cord injury at or above the T10 spine * 1 year post injury * Some volitional movement in one or both limbs (i.e. motor incomplete) * Ability to stand with limited bracing * Ability to rise from sit to stand with no more that moderate assistance Inclusion criteria for patients with subacute injury: * Spinal cord injury at or above the T10 spine * 2 to 8 months post injury * Volitional movement in at least one lower limb muscle (i.e. motor incomplete), although may not be capable of unsupported standing or moving from sit-to-stand without maximal assistance Exclusion criteria: * Fractures at or below T11 * Neoplastic, degenerative or vascular disorders of the spine or spinal cord * Significant orthopaedic conditions that would interfere with regular exercise or rehabilitation therapy * Decubitus ulcer

Calancie NCT00061295 (*Continued*)

	* Advanced urinary tract infection * Medical conditions that increase the probability of having a seizure in response to single pulse transcranial magnetic stimulation
Interventions	This study will evaluate whether BWS gait training is more effective than conventional rehabilitation therapy in improving functional gait in patients with neurologically incomplete spinal cord injury. The study will also compare treadmill-based training to overground-based training. Treadmill-based training has the inherent advantage of providing highly rhythmic input to the participant's legs; overground-based training has the inherent advantage of allowing use of assistive devices and thereby replicating a more 'natural' training condition
Outcomes	All patients will be evaluated with a battery of functional, metabolic and neurophysiologic measures prior to the onset of training and during the week after training has been completed. The primary outcome measure will be average maximum overground walking velocity without bodyweight support but with the use of passive assistive devices. Secondary measures will concentrate on function (balance, mobility), fitness (work capacity, strength, gait efficiency), and spinal cord neurophysiology (motor conduction, reflex excitability)
Starting date	Record first received: 23 May 2003
Contact information	Blair M. Calancie 305-585-8347 bcalancie@miamiproj.med.miami.edu USA
Notes	

Popovic NCT00201968

Trial name or title	Functional electrical stimulation-assisted walking: reduction of secondary complications due to spinal cord injury
Methods	
Participants	Inclusion criteria: * Incomplete spinal cord lesion of sudden onset between C6 and T12 that is motor incomplete (grade C or D on the ASIA neurological impairment scale). The injury must have occurred at least 2 years prior to recruitment Exclusion criteria: * Contraindications for FES, such as cardiac pacemakers, skin lesions or rush at potential electrode sites, or denervation of targeted muscles * Pressure ulcers anywhere on the lower extremities * Hypertension that is uncontrolled. * Symptoms of orthostatic hypotension when standing for 15 minutes * Susceptibility to autonomic dysreflexia, requiring medication * If there is a history of cardiovascular disease, participants must obtain medical clearance from their physician before inclusion

Popovic NCT00201968 (*Continued*)

Interventions	The purpose of this study is to evaluate whether an aerobic and resistance training programme or a functional electrical stimulation-assisted walking programme is more effective for reducing health complications related to spinal cord injury, for example, the occurrence of bladder infections, pressure sores and/or frequency of spasms. It is hypothesised that the functional electrical stimulation-assisted walking will have a greater impact on secondary complications than the aerobic and resistance training programme
Outcomes	Primary outcome measures: * All of the measures below at 4 months: * Whole body muscle mass via dual-energy x-ray absorptiometry including * Bone density at hip, spine, proximal tibia and distal femur using dual-energy x-ray absorptiometry * Bone density, bone geometry and muscle area via computed tomography * Spasticity via Ashworth Scale and Pendulum Test * Factor analysis of electromyography and kinematics of gait Secondary outcome measures: * All of the measures above at 6 months and 12 months, as well as the measures below at 4 months, 6 months and 12 months: * Incidence of urinary tract infections * Spinal cord independence measure * Urinary N-telopeptide and serum osteocalcin * Timed up and go and 2-minute walk test (functional mobility) * Incidence of pressure sores * Reintegration to normal living index * Satisfaction with life scale * Instrumental Activities of Daily Living SubScale * Craig Handicap assessment and reporting technique * Client perception of treatment (qualitative)
Starting date	Record first received: 12 September 2005
Contact information	Kieva Richards 416 597 3422 Ext. 6310 richards.kieva@torontorehab.on.ca Lora Giangregorio 519 362 5672 giangregorio.lora@torontorehab.on.ca Lyndhurst Centre, Toronto Rehabilitation Institute, Toronto, Ontario, M4G 3V9, CANADA
Notes	

ASIA: American Spinal Injury Association; BWS: bodyweight support; FES: functional electrical stimulation; RCT: randomised controlled trial; SCI: spinal cord injury; WISCI: Walking Index for Spinal Cord Injury

DATA AND ANALYSES

Comparison 1. Bodyweight supported treadmill training versus all other

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Speed of walking (in metres/second)	4	274	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.05, 0.11]
2 Walking capacity (in metres walked in 6 minutes)	3	234	Mean Difference (IV, Random, 95% CI)	-1.25 [-41.26, 38.77]
3 Independence in walking (at the end of the intervention)	1		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
4 Safety of exercises - incidences of adverse events during the trial	5	309	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.02, 0.07]
5 Dropouts for any reason	5	309	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.13, 0.04]

Comparison 2. Robotic-assisted training versus all other

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Speed of walking (at final follow-up in metres/second)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Walking capacity (metres walked in 6 minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Safety of exercises	2	109	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.07, 0.07]
4 Dropouts for any reason	2	109	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.13, 0.15]

Comparison 3. FES AND BWSTT versus all other

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Speed of walking (at final follow-up in metres/second)	2	88	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.11, 0.06]
2 Walking capacity (metres walked in 6 minutes)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Safety of exercises	2	88	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.09, 0.09]
4 Dropouts for any reason	2	88	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.11, 0.22]

Analysis 1.1. Comparison 1 Bodyweight supported treadmill training versus all other, Outcome 1 Speed of walking (in metres/second).

Review: Locomotor training for walking after spinal cord injury

Comparison: 1 Bodyweight supported treadmill training versus all other

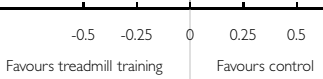
Outcome: 1 Speed of walking (in metres/second)

Study or subgroup	Control (all other) N	Mean(SD)	Treatment (BWSTT) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Alexeeva 2011	30	0.48 (0.34)	10	0.47 (0.39)		9.0 %	0.01 [-0.26, 0.28]
Dobkin 2006	71	0.45 (0.4)	75	0.39 (0.38)		41.1 %	0.06 [-0.07, 0.19]
Field-Fote 2011	18	0.28 (0.28)	56	0.21 (0.16)		35.7 %	0.07 [-0.07, 0.21]
Postans 2004	7	0.21 (0.15)	7	0.38 (0.25)		14.2 %	-0.17 [-0.39, 0.05]
Total (95% CI)	**126**		**148**			**100.0 %**	**0.03 [-0.05, 0.11]**

Heterogeneity: $Chi^2 = 3.86$, df = 3 (P = 0.28); $I^2 = 22\%$

Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable

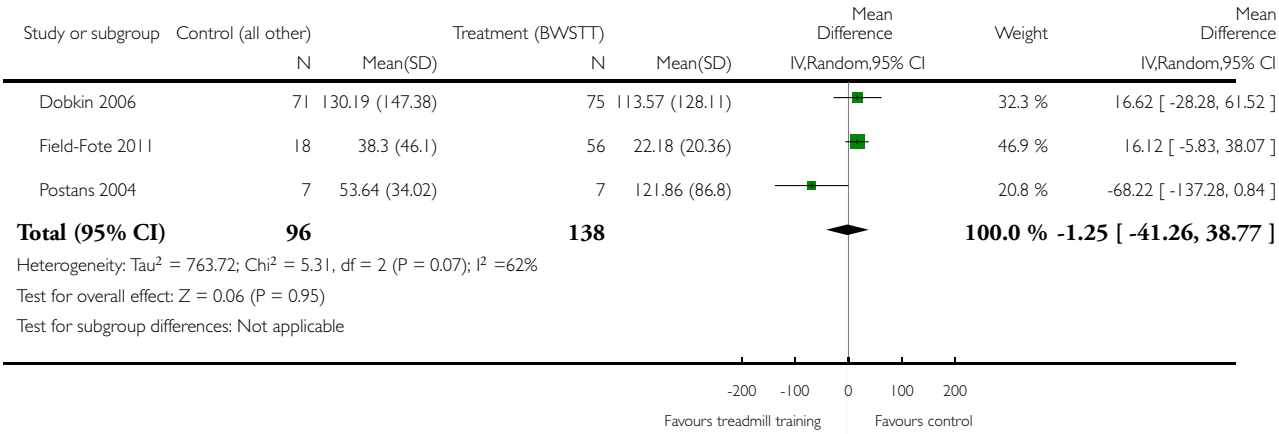


Analysis 1.2. Comparison 1 Bodyweight supported treadmill training versus all other, Outcome 2 Walking capacity (in metres walked in 6 minutes).

Review: Locomotor training for walking after spinal cord injury

Comparison: 1 Bodyweight supported treadmill training versus all other

Outcome: 2 Walking capacity (in metres walked in 6 minutes)



Analysis 1.3. Comparison 1 Bodyweight supported treadmill training versus all other, Outcome 3 Independence in walking (at the end of the intervention).

Review: Locomotor training for walking after spinal cord injury

Comparison: 1 Bodyweight supported treadmill training versus all other

Outcome: 3 Independence in walking (at the end of the intervention)

Analysis 1.4. Comparison 1 Bodyweight supported treadmill training versus all other, Outcome 4 Safety of exercises - incidences of adverse events during the trial.

Review: Locomotor training for walking after spinal cord injury

Comparison: 1 Bodyweight supported treadmill training versus all other

Outcome: 4 Safety of exercises - incidences of adverse events during the trial

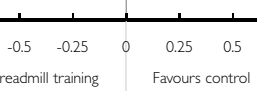
Study or subgroup	Treatment (BWSTT) n/N	Control (all other) n/N	Risk Difference M-H,Fixed,95% CI	Weight	Risk Difference M-H,Fixed,95% CI
Alexeeva 2011	0/30	0/10		11.0 %	0.0 [-0.13, 0.13]
Dobkin 2006	4/75	0/71		53.4 %	0.05 [0.00, 0.11]
Field-Fote 2011	0/56	0/18		20.0 %	0.0 [-0.08, 0.08]
Hornby 2007	0/25	0/10		10.5 %	0.0 [-0.13, 0.13]
Postans 2004	1/7	1/7		5.1 %	0.0 [-0.37, 0.37]
Total (95% CI)	**193**	**116**		**100.0 %**	**0.03 [-0.02, 0.07]**

Total events: 5 (Treatment (BWSTT)), 1 (Control (all other))

Heterogeneity: $Chi^2 = 1.66$, $df = 4$ ($P = 0.80$); $I^2 = 0.0\%$

Test for overall effect: $Z = 1.25$ ($P = 0.21$)

Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1 Bodyweight supported treadmill training versus all other, Outcome 5 Dropouts for any reason.

Review: Locomotor training for walking after spinal cord injury

Comparison: 1 Bodyweight supported treadmill training versus all other

Outcome: 5 Dropouts for any reason

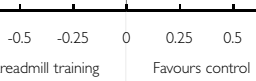
Study or subgroup	Control (all other) n/N	Treatment (BWSTT) n/N	Risk Difference M-H,Fixed,95% CI	Weight	Risk Difference M-H,Fixed,95% CI
Alexeeva 2011	1/10	4/30		11.0 %	-0.03 [-0.26, 0.19]
Dobkin 2006	12/71	17/75		53.4 %	-0.06 [-0.19, 0.07]
Field-Fote 2011	3/18	7/56		20.0 %	0.04 [-0.15, 0.23]
Hornby 2007	0/10	5/25		10.5 %	-0.20 [-0.40, 0.00]
Postans 2004	1/7	1/7		5.1 %	0.0 [-0.37, 0.37]
Total (95% CI)	**116**	**193**		**100.0 %**	**-0.05 [-0.13, 0.04]**

Total events: 17 (Control (all other)), 34 (Treatment (BWSTT))

Heterogeneity: $Chi^2 = 3.18$, df = 4 (P = 0.53); $I^2 = 0.0\%$

Test for overall effect: Z = 1.05 (P = 0.29)

Test for subgroup differences: Not applicable



Analysis 2.1. Comparison 2 Robotic-assisted training versus all other, Outcome 1 Speed of walking (at final follow-up in metres/second).

Review: Locomotor training for walking after spinal cord injury

Comparison: 2 Robotic-assisted training versus all other

Outcome: 1 Speed of walking (at final follow-up in metres/second)

Study or subgroup	Control (all other) N	Mean(SD)	Treatment (robotic) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Field-Fote 2011	59	0.24 (0.21)	15	0.18 (0.1)		0.06 [-0.01, 0.13]
Subtotal (95% CI)	**0**		**0**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 2.2. Comparison 2 Robotic-assisted training versus all other, Outcome 2 Walking capacity (metres walked in 6 minutes).

Review: Locomotor training for walking after spinal cord injury

Comparison: 2 Robotic-assisted training versus all other

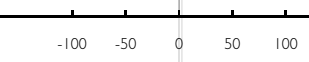
Outcome: 2 Walking capacity (metres walked in 6 minutes)

Study or subgroup	Control (all other) N	Mean(SD)	Treatment (robotic) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Field-Fote 2011	59	28.19 (31.951)	15	17.9 (11.9)		10.29 [0.15, 20.43]
Subtotal (95% CI)	**0**		**0**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable

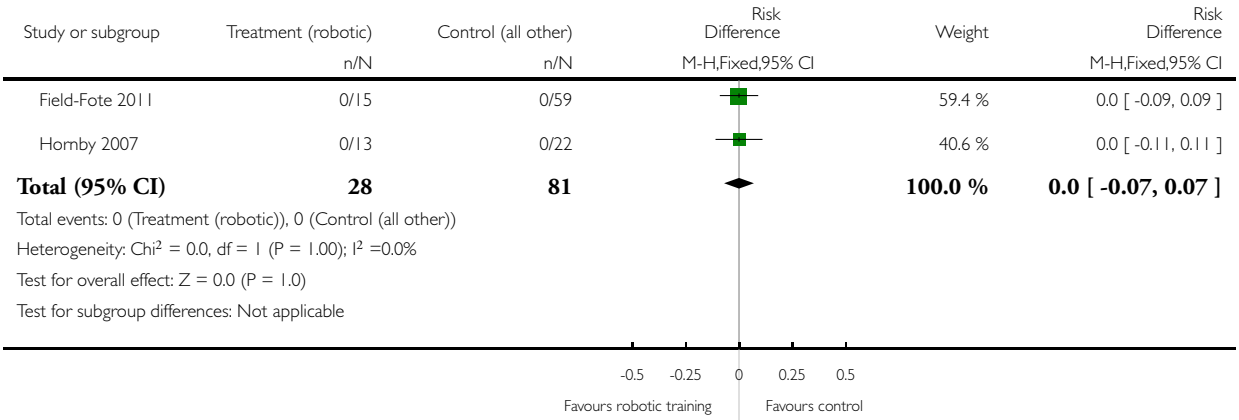


Analysis 2.3. Comparison 2 Robotic-assisted training versus all other, Outcome 3 Safety of exercises.

Review: Locomotor training for walking after spinal cord injury

Comparison: 2 Robotic-assisted training versus all other

Outcome: 3 Safety of exercises

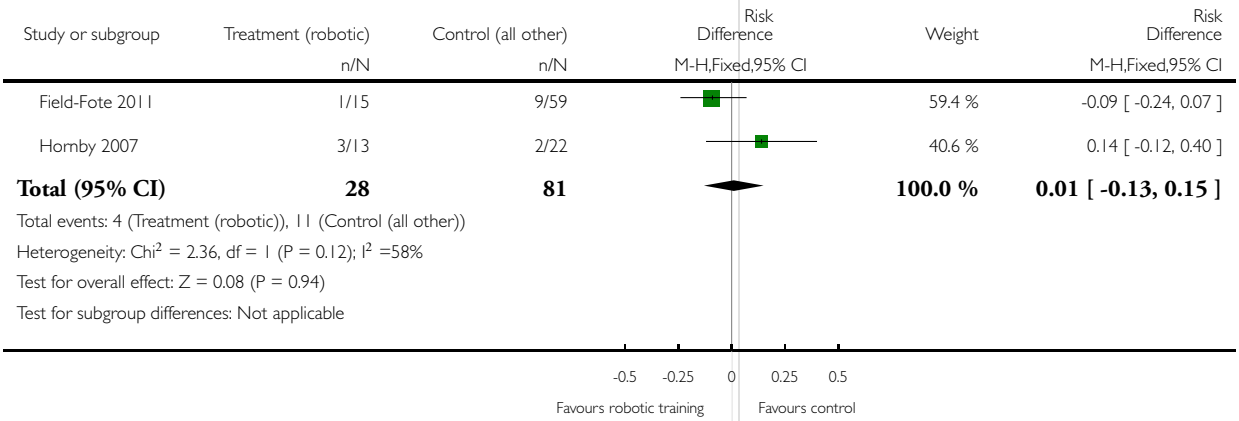


Analysis 2.4. Comparison 2 Robotic-assisted training versus all other, Outcome 4 Dropouts for any reason.

Review: Locomotor training for walking after spinal cord injury

Comparison: 2 Robotic-assisted training versus all other

Outcome: 4 Dropouts for any reason



Analysis 3.1. Comparison 3 FES AND BWSTT versus all other, Outcome 1 Speed of walking (at final follow-up in metres/second).

Review: Locomotor training for walking after spinal cord injury

Comparison: 3 FES AND BWSTT versus all other

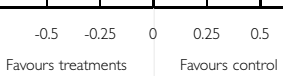
Outcome: 1 Speed of walking (at final follow-up in metres/second)

Study or subgroup	Control (all other) N	Mean(SD)	Treatment (FES + BWSTT) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Field-Fote 2011	52	0.2292 (0.2018)	22	0.23 (0.18)		84.3 %	0.00 [-0.09, 0.09]
Postans 2004	7	0.21 (0.15)	7	0.38 (0.25)		15.7 %	-0.17 [-0.39, 0.05]
Total (95% CI)	**59**		**29**			**100.0 %**	**-0.03 [-0.11, 0.06]**

Heterogeneity: Chi^2 = 1.99, df = 1 (P = 0.16); I^2 =50%

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

Test for subgroup differences: Not applicable



Analysis 3.2. Comparison 3 FES AND BWSTT versus all other, Outcome 2 Walking capacity (metres walked in 6 minutes).

Review: Locomotor training for walking after spinal cord injury

Comparison: 3 FES AND BWSTT versus all other

Outcome: 2 Walking capacity (metres walked in 6 minutes)

Study or subgroup	Control (all other) N	Mean(SD)	Treatment (FES + BWSTT) N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Field-Fote 2011	52	26.825 (31.3012)	22	24.4 (24.3)		2.43 [-10.82, 15.67]
Subtotal (95% CI)	**0**		**0**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 3.3. Comparison 3 FES AND BWSTT versus all other, Outcome 3 Safety of exercises.

Review: Locomotor training for walking after spinal cord injury

Comparison: 3 FES AND BWSTT versus all other

Outcome: 3 Safety of exercises

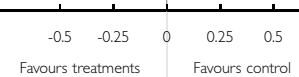
Study or subgroup	Treatment (FES + BWSTT) n/N	Control (all other) n/N	Risk Difference M-H,Fixed,95% CI	Weight	Risk Difference M-H,Fixed,95% CI
Field-Fote 2011	0/22	0/52		81.5 %	0.0 [-0.07, 0.07]
Postans 2004	1/7	1/7		18.5 %	0.0 [-0.37, 0.37]
Total (95% CI)	**29**	**59**		**100.0 %**	**0.0 [-0.09, 0.09]**

Total events: 1 (Treatment (FES + BWSTT)), 1 (Control (all other))

Heterogeneity: Chi^2 = 0.0, df = 1 (P = 1.00); I^2 =0.0%

Test for overall effect: Z = 0.0 (P = 1.0)

Test for subgroup differences: Not applicable

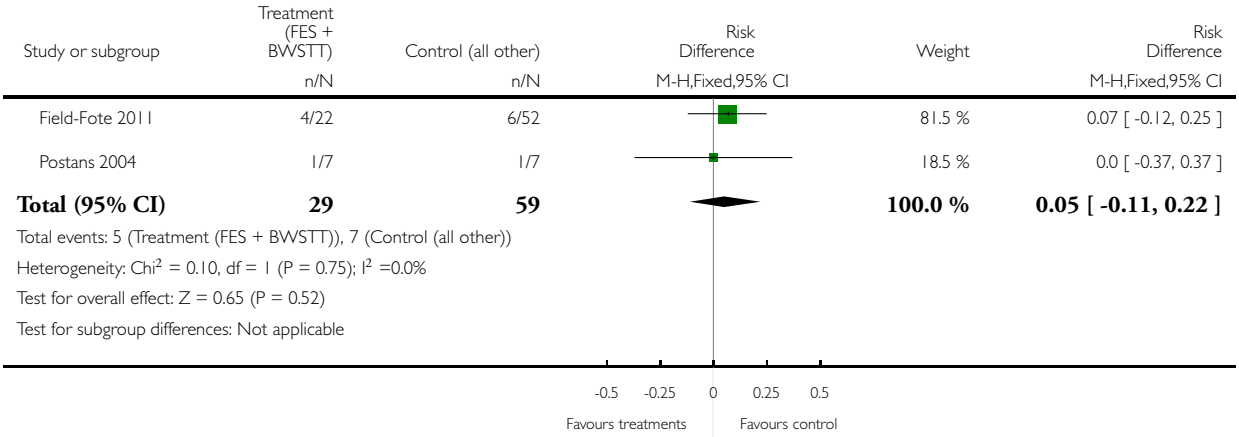


Analysis 3.4. Comparison 3 FES AND BWSTT versus all other, Outcome 4 Dropouts for any reason.

Review: Locomotor training for walking after spinal cord injury

Comparison: 3 FES AND BWSTT versus all other

Outcome: 4 Dropouts for any reason



ADDITIONAL TABLES

Table 1. PEDro scores

PEDro score	Dobkin 2006	Field-Fote 2011	Postans 2004	Hornby 2007	Alexeeva 2011
Random allocation	yes	yes	yes	yes	yes
Concealed allocation	yes	unclear	yes	unclear	unclear
Baseline comparability	yes	yes	no	yes	yes
Blind participants	no	no	no	no	no
Blind therapists	no	no	no	no	no

Table 1. PEDro scores (*Continued*)

Blind assessors	yes	no	no	no	no
Adequate follow-up* (dropout rate)	no (20%)	yes (13%)	yes (14%)	yes (14%)	yes (13%)
Intention-to-treat analysis	yes	yes	no	no	no
Between-group comparisons	yes	yes	yes	yes	yes
Point estimates and variability	yes	yes	yes	yes	yes
Total PEDro score	7 (10)	6 (10)	5 (10)	5 (10)	5 (10)
*Defined as less than 15% dropouts					

Table 2. Patient characteristics in studies (demographics)

Study ID	Age, mean (SD) EXP	Age, mean (SD) CON	Duration of SCI EXP	Duration of SCI CON	Female/male ratio	Number of patients
Alexeeva 2011#	40 (14)	37 (13)	6 (7) years	8 (7) years	3/27 (EXP) 2/13 CON	40
Dobkin 2006#	26 (16 to 68)*	24 (16 to 61)*	30 (7 to 56) weeks*	29 (10 to 56) weeks*	45/7 (EXP) 42/15 (CON)	146
Field-Fote 2011#	41 (12)	42 (16)	More than 1 year	More than 1 year	82% (EXP) 73% (CON)	74
Postans 2004	42 (17)	41 (14)	12 (7) weeks	12 (5) weeks	1/6 (EXP) 1/6 (CON)	14
Hornby 2007*+	EXP1: 24.5 (22 to 26)* EXP2: 32,5 (19 to 45) *	24 (18-43)	EXP1: 55 (21 to 86) days EXP2: 51 (28 to 81) days	52.5 (35-96) days	Not provided by the authors	35
* Median (range)						
# EXP defined as all groups containing treadmill training as inter-						

Table 2. Patient characteristics in studies (demographics) (*Continued*)

vention (pooled results)						
+ EXP 2 groups served as experimental groups (EXP1 robotic and treadmill)						

CON: control group; EXP: experimental group; SCI: spinal cord injury; SD: standard deviation

Table 3. Other data (data from the unpublished trial of Hornby et al 2007)

Outcome measures	Group 1 (Robotic)	Group 2 (Treadmill)	Group 3 (Overground)
Ashworth	B: 0 (0 to 1); FU: 0.5 (0 to 1)	B: 0 (0 to 1); FU: 0.5 (0 to 1)	B: 0 (0 to 1); FU: 0.5 (0 to 1)
FIM > 4	FU: 4 of 13 (31%)	FU: 3 of 12 (25%)	FU: 5 of 10 (50%)
WISCI	FU: 4.5 (0 to 13)	FU: 3.5 (0 to 13)	FU: 10.5 (0 to 15)
Walking speed (m/s)	FU: 0.35 (0.22 to 0.97)	FU: 0.75 (0.28 to 0.81)	FU: 0.86 (0.51 to 1.1)
Walking distance (m)	FU: 234 (107 to 394)	FU: 237 (84 to 257)	FU: 336 (197 to 393)
B = baseline; FU = follow-up at study end			
All data as median (IQR)			
Unpublished data as provided by the author			

FIM: Functional Independence Measure; IQR: interquartile range; WISCI: Walking Index for Spinal Cord Injury

Table 4. Safety and acceptance of interventions: adverse events and drop-out rates

Study ID	Alexeeva 2011	Dobkin 2006	Field-Fote 2011	Postans 2004	Hornby 2007
Percentage of drop-outs	13%	20%	13%	14%	14%
Dropouts	5/40 (4 TM, 1 PT)	29/146 (17 EXP; 12 CON)	10/74 (3 PT, 2 TM, 4 TM + FES, 1 ROB)	2/14	5/35 (5 EXP; 0 CON)

Table 4. Safety and acceptance of interventions: adverse events and drop-out rates (*Continued*)

Reasons for dropout and adverse events in EXP	Reasons for all groups: 1 not meeting inclusion criteria, 1 declined, 3 other reasons	8 people were inadequately entered and 10 dropped prior to completing 6 weeks of intervention (2 felt too taxing and 2 had tendon or joint injury)	Reasons for all groups: PT: 2 family issues, 1 medical issues TM: 2 non adherence to protocol TM + FES: 1 non adherence, 1 back pain, 1 death in family, 1 increased spasticity ROB: 1 transportation problem	1 dropped due to knee pain	3 dropped out due to travel limitations, 1 due to poor attendance and 1 due to excessive fatigue
Reasons for dropout and adverse events in CON	n/a	8 people were inadequately entered and 3 dropped prior to completing 6 weeks of intervention	n/a	1 dropped due to mental problems	n/a
Source of information	As published by the authors	As published by the authors	As published by the authors	As provided by the authors	As provided by the author

CON: control group; EXP: experimental group; FES: functional electrical stimulation; PT: physical therapy (overground training); ROB: robotic-assisted training; TM: treadmill training

APPENDICES

Appendix 1. Search strategy

Cochrane Injuries Group Specialised Register (searched 02 Nov 2011)
((spine or spinal) and (damag* or trauma* or injur* or broke* or break or fracture)) and (exercise or train* or walk* or locomotor or "physical therapy" or physiotherapy or kinesiotherapy or exercise or train* or therapy or rehabilitat* or re-educat* or strengthen* or robot* or orthos* or orthotic or automat* or "computer aided" or "computer assisted" or BWS or harness or treadmill or Lokomat or Locomat or GaiTrainer or Kinetron or autoambulator* or electromechanical or electro-mechanical or mechanical or mechanised or mechanized or driven or "functional electrical stimulation" or "electric stimulation")

Cochrane Central Register of Controlled Trials 2011, Issue 4 (*The Cochrane Library):*
#1 MeSH descriptor Spinal Cord Injuries explode all trees
#2 MeSH descriptor Spinal Fractures explode all trees
#3 MeSH descriptor Trauma, Nervous System explode all trees

(*Continued*)

#4 (spine or spinal) near (damag* or trauma* or injur* or broke* or break or fracture*)
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Gait explode all trees
#7 MeSH descriptor Gait Disorders, Neurologic explode all trees
#8 MeSH descriptor Walking explode all trees
#9 MeSH descriptor Dependent Ambulation explode all trees
#10 locomotion near walking
#11 MeSH descriptor Locomotion explode all trees
#12 walk* or gait* or ambulat* or mobil* or locomot* or stride*
#13 (#6 OR #7 OR #8 OR #8 OR #10 OR #11 OR #12)
#14 (#5 AND #13)

MEDLINE (Ovid) 1948 to 2011

1. exp Spinal Cord Injuries/
2. exp Spinal Fractures/
3. exp Trauma, Nervous System/
4. ((spine or spinal) adj3 (damag* or trauma* or injur* or broke* or break or fracture*)).ti,ab
5. or/1-4
6. exp Gait/
7. exp Gait Disorders, Neurologic/
8. exp Walking/
9. (locomotion and walking).ti,ab.
10. *Locomotion/
11. locomotor?training.ab,ti.
12. *Dependent Ambulation/
13. (walk* or gait* or ambulat* or mobil* or locomot* or stride*).ti,ab
14. or/6-13
15. 5 and 14
16. exp Physical Therapy Modalities/
17. exp Electric Stimulation Therapy/
18. *Electric Stimulation/
19. exp Exercise/
20. exp Exercise Test/
21. exp Exercise Movement Techniques/
22. exp Automation/
23. exp Robotics/
24. exp Orthotic Devices/
25. exp Weight-Bearing/
26. ("continuous passive therapy" or CPM).ab,ti.
27. (weight?bearing or load?bearing).ab,ti.
28. (body?weight adj3 (support* or relief)).ab,ti.
29. (electromechanical or electro-mechanical or mechanical or mechanised or mechanized or driven or functional electrical stimulation or electric stimulation).ti,ab
30. (robot* or orthos* or orthotic* or automat* or computer?aided or computer?assisted or BWS or harness* or treadmill* or Lokomat or Locomat or GaiTrainer or Kinetron or autoambulator*).ab,ti
31. ("physical therapy" or physiotherapy or kinesiotherapy or exercis* or train* or therap* or rehabilitat* or re?educat* or strengthen*).ab,ti
32. ((gait or walk* or ambulatory) adj3 (recover* or test* or abilit* or function or speed*)).ab,ti
33. or/16-32

(*Continued*)

34. 15 and 33
35. randomi?ed.ab,ti.
36. randomized controlled trial.pt.
37. controlled clinical trial.pt.
38. placebo.ab.
39. clinical trials as topic.sh.
40. randomly.ab.
41. trial.ti.
42. 35 or 36 or 37 or 38 or 39 or 40 or 41
43. (animals not (humans and animals)).sh.
44. 42 not 43
45. (rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*).ti
46. 44 not 45
47. 34 and 46

EMBASE (Ovid) 1980 to 2011

1. exp Spinal Cord Injury/
2. Spinal Fractures/
3. exp NERVOUS SYSTEM INJURY/
4. ((spine or spinal) adj3 (damag* or trauma* or injur* or broke* or break or fracture*)).ti,ab
5. or/1-4
6. exp GAIT/
7. exp Gait Disorder/
8. exp WALKING/
9. exp MOBILIZATION/
10. (locomotion and walking).ti,ab.
11. exp LOCOMOTION/
12. Locomotor?training.ab,ti.
13. (walk* or gait* or ambulat* or mobil* or locomot* or stride*).ti,ab
14. or/6-13
15. 5 and 14
16. exp PHYSIOTHERAPY/
17. exp Electrostimulation Therapy/
18. exp ELECTROSTIMULATION/
19. exp EXERCISE/
20. exp Exercise Test/
21. exp kinesiotherapy/
22. (Exercise adj3 (Movement* or therap* or Treatment*)).ab,ti
23. exp AUTOMATION/
24. exp ROBOTICS/
25. exp orthotics/
26. exp weight bearing/
27. (continuous passive therapy or CPM).ab,ti.
28. (weight?bearing or load?bearing).ab,ti.
29. (body?weight adj3 (support* or relief)).ab,ti.
30. (electromechanical or electro-mechanical or mechanical or mechanised or mechanized or driven or functional electrical stimulation or electric stimulation).ti,ab
31. (robot* or orthos* or orthotic* or automat* or computer?aided or computer?assisted or BWS or harness* or treadmill* or Lokomat

(*Continued*)

or Locomat or GaiTrainer or Kinetron or autoambulator*).ab,ti
32. ("physical therapy" or physiotherapy or kinesiotherapy or exercis* or train* or therap* or rehabilitat* or re?educat* or strengthen*) .ab,ti
33. ((gait or walk* or ambulatory) adj3 (recover* or test* or abilit* or function or speed*)).ab,ti
34. or/16-33
35. 15 and 34
36. exp Randomized Controlled Trial/
37. exp controlled clinical trial/
38. randomi?ed.ab,ti.
39. placebo.ab.
40. *Clinical Trial/
41. randomly.ab.
42. trial.ti.
43. 36 or 37 or 38 or 39 or 40 or 41 or 42
44. exp animal/ not (exp human/ and exp animal/)
45. 43 not 44
46. (rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*).ti
47. 45 not 46
48. 35 and 47

PubMed (www.ncbi.nlm.nih.gov/sites/entrez/) (searched 02 Nov 2011)
#1 "Spinal Cord Injuries"[Mesh] OR "Spinal Fractures"[Mesh] OR "Trauma, Nervous System"[Mesh]
#2 ((spine OR spinal) AND (damag* OR trauma* OR injur* OR broke* OR break OR fracture*)))
#3 #1 OR #2
#4 "Gait"[Mesh] OR "Gait Disorders, Neurologic"[Mesh] OR "Walking"[Mesh] OR "Locomotion"[Mesh] OR "Dependent Ambulation"[Mesh]
#5 (locomotion and walking) OR (locomotor and training)
#6 (walk* OR gait* OR ambulat* OR mobil* OR locomot* OR stride*)
#7 #4 or #5 or #6
#8 #3 AND #7
#9 (randomized controlled trial[pt] OR controlled clinical trial[pt]) OR (randomized OR randomised OR randomly OR placebo[tiab]) OR (trial[ti]) OR ("Clinical Trials as Topic"[MeSH Major Topic]))
#10 ("Animals"[Mesh]) NOT ("Humans"[Mesh] AND "Animals"[Mesh])
#11 (rat OR rats OR rodent* OR mouse OR mice OR murine OR dog OR dogs OR canine* OR cat OR cats OR feline* OR rabbit OR rabbits OR pig OR pigs OR porcine OR swine OR sheep OR ovine* OR guinea pig*[ti])
#12 #10 OR #11
#13 #9 NOT #12
#14 #8 AND #13

CINAHL (EBSCO) 1982 to Nov 2011
1. exp Spinal Cord Injuries/
2. exp Spinal Fractures/
3. exp Trauma, Nervous System/
4. ((spine or spinal) adj3 (damag* or trauma* or injur* or broke* or break or fracture*)).ti,ab
5. or/1-4
6. exp Gait/
7. exp Gait Disorders, Neurologic/
8. exp Walking/
9. (locomotion and walking).ti,ab.

(*Continued*)

10. *Locomotion/
11. locomotor?training.ab,ti.
12. *Dependent Ambulation/
13. (walk* or gait* or ambulat* or mobil* or locomot* or stride*).ti,ab
14. or/6-13
15. 5 and 14

ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) 1970 to Nov 2011
ISI Web of Science: Social Sciences Citation Index (SSCI) 1970 to Nov 2011, ISI Web of Science: Conference Proceedings Citation Index- Science (CPCI-S) 1990 to Nov 2011
ISI Web of Science: Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI-SSH) 1990 to Nov 2011 (limit: publication date 2007 to Nov 2011)
#1 Topic=((spine or spinal) near/3 (damag* or trauma* or injur* or broke* or break or fracture*)) AND Topic=(walk* or gait* or ambulat* or mobil* or locomot* or stride*)
#2 Topic=((singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)) OR Topic=((clinical OR control* OR placebo OR random*) NEAR/3 (trial* or group* or study or studies or placebo or controlled)) NOT Title=(Animal* or rat or rats or rodent* or mouse or mice or murine or dog or dogs or canine* or cat or cats or feline* or rabbit or rabbits or pig or pigs or porcine or swine or sheep or ovine* or guinea pig*)
#3 #1 and #2

WHAT'S NEW

Last assessed as up-to-date: 15 November 2011.

Date	Event	Description
17 January 2012	New citation required but conclusions have not changed	The search for studies was updated to 15 November 2011. One new study has been included (Alexeeva 2011). The final results from Field-Fote 2011 have been included, and replace preliminary results (Field-Fote 2005) which were included in the previous version of this review The manuscript has been updated.
11 January 2012	New search has been performed	The search for studies has been updated to November 2011.

HISTORY

Protocol first published: Issue 3, 2007

Review first published: Issue 2, 2008

Date	Event	Description
11 July 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Jan Mehrholz (JM) contributed to the conception and design of the protocol and approved the final manuscript. He searched electronic databases and conference proceedings, screened titles and abstracts of references identified by the search, selected and assessed trials, extracted trial and outcome data, guided the analysis and the interpretation of data, and contributed to and approved the final manuscript of the review.

Joachim Kugler (JK) screened titles and abstracts of references identified by the search, located, selected and assessed trials, extracted trial and outcome data, assessed the methodological quality of selected trials, and contributed to and approved the final manuscript of the review.

Marcus Pohl (MP) contributed to the conception and design of the review, drafted the protocol, and assessed the methodological quality of selected trials. He, together with JM, contacted trial authors about unpublished data and also entered the data into statistical software, carried out statistical analysis, helped with the interpretation of data, drafted the review, and approved the final manuscript of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Klinik Bavaria Kreischa, Germany.
- Technical University Dresden, Germany.
- SRH FH für Gesundheit Gera, Germany.
- ZVK Stiftung, Germany.
- Wissenschaftliches Institut der Privaten Europäischen Medizinischen Akademie für Rehabilitation der Klinik BAVARIA, Kreischa, Germany.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In our protocol we stated that we will for all binary outcomes (such as walking dependency) calculate relative risks (RRs). Addtionally we stated that we will where trials (or groups within a trial) have no adverse events or drop-outs we will calculate risk differences (RDs) with 95% CI instead of RRs.

In this review we have used consistently RDs for all binary outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

*Locomotion; *Walking; Randomized Controlled Trials as Topic; Spinal Cord Injuries [*rehabilitation]

MeSH check words

Humans