Respuesta al tapiz rodante y entrenamiento en niños con riesgo de retraso en el desarrollo motor

Marta Valentín Gudiol

Tesis Doctoral

RESPUESTA AL TAPIZ RODANTE Y ENTRENAMIENTO EN NIÑOS CON RIESGO DE RETRASO EN EL DESARROLLO MOTOR

(Treadmill Stepping and Training in Children at Risk for Neuromotor Delay)

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Federico García Lorca una vez dijo:

“Vamos a no llegar, pero vamos a ir.”

Y yo, aquí y ahora, añado: si vamos, llegamos.

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INDICE

RESUMEN

El recién nacido prematuro y los bebés de bajo peso al nacer frecuentemente presentan retrasos/anomalías en el desarrollo motor, cognitivo y emocional[1]. Son una población que será clasificada como niños con riesgo de retraso en el desarrollo psicomotor[2]. Uno de los diagnósticos más frecuentes en esta población es el de parálisis cerebral (PC)[3], que suele establecerse a partir de los 12 meses de edad del niño[4]. El tapiz rodante se ha utilizado en población pediátrica con diferentes diagnósticos para estimular la adquisición de la marcha autónoma, como aspecto clave del desarrollo motriz del niño, dada la relación que tiene con aspectos cognitivos y emocionales[5]. Estudios en niños con PC[6,7] han resultado en una mejora de sus capacidades globales de desarrollo después de recibir la intervención. El impacto del entrenamiento con el tapiz rodante se desconoce en el caso de población clasificada como con riesgo. Esta tesis, que se presenta como compendio de publicaciones, plantea dos objetivos principales en relación a esta población: (1) explorar el estado actual de la evidencia científica respecto a la respuesta al tapiz rodante de los niños con riesgo de retraso en el desarrollo motriz, y (2) estudiar los efectos del entrenamiento de la marcha con el tapiz, en relación al desarrollo motriz y a la adquisición de la marcha autónoma. Para responder al primero de los objetivos, se realizó una revisión sistemática de la literatura publicada sobre las intervenciones con tapiz rodante en niños con riesgo de retraso en el desarrollo motriz, con edades comprendidas de los 0 hasta los 6 años. Las conclusiones principales encontradas en esta revisión fueron que faltaban ensayos clínicos controlados con muestras mayores en población con riesgo, sobre todo en relación al estudio de los efectos del entrenamiento de la marcha con el tapiz. En relación al segundo de los objetivos de esta tesis, se presentan los resultados de un ensayo clínico controlado realizado con una muestra de 28 niños con riesgo de retraso en el desarrollo motriz. Aproximadamente la mitad recibieron un entrenamiento protocolizado de la marcha con el tapiz. Al inicio del estudio los niños tenían edades comprendidas entre los 8 y los 11 meses. En este estudio no se observaron diferencias entre grupos en cuanto a la edad de inicio de la marcha autónoma, pero sí se vio una mejora en la calidad de los pasos en el tapiz, en aquellos sujetos que habían recibido el entrenamiento.

Asimismo, se estableció una relación significativa entre la frecuencia de pasos en el tapiz y la edad de inicio de la marcha autónoma. Finalmente, se hizo un tercer estudio de caso con unas mellizas con antecedentes de prematuridad leve, en el cual se implementó un entrenamiento individualizado a partir de los 8 meses de edad, a la melliza que mostró mayor retraso motriz. Las conclusiones de este estudio fueron que, posiblemente, el entrenamiento con el tapiz tuvo un impacto positivo sobre la velocidad de desarrollo motriz de la melliza entrenada. En relación a aspectos de locomoción y la respuesta al tapiz rodante, se observó una mejora en la calidad de los pasos, y un aumento en la frecuencia de pasos alternos sobre el tapiz. Esto ocurrió en ambas mellizas, pero de una manera más acentuada en la melliza que recibió el entrenamiento.

Como síntesis final, el tapiz rodante es una herramienta en uso creciente en el ámbito de la pediatría para potenciar aspectos relacionados con la locomoción. La evidencia científica disponible hasta la fecha indica que el entrenamiento de la marcha con el tapiz puede tener efectos positivos en niños con riesgo de retraso en el desarrollo motriz, tanto para la detección de retrasos o anomalías en el desarrollo, como para la prevención de retrasos más severos en relación a la adquisición de la marcha autónoma. Conseguir este hito motriz es de gran importancia, ya que conllevará la autonomía del niño, la cual es fundamental dada la relación de la misma con el desarrollo cognitivo y con la calidad de vida de las personas.

ABSTRACT

Low birth-weight and premature infants are considered to be at risk for neuromotor, cognitive and emotional developmental delays[1]. Some of these infants are diagnosed with cerebral palsy (CP), while others with early motor behaviour problems do not develop CP[2]. Locomotor difficulties have been demonstrated in children with CP. Studies in children with CP have used a paediatric treadmill to improve functional gait and ambulation. Treadmill training (TT) has been shown to improve ambulatory capability in children with CP[6,8,9]. However, little is known about the impact of such training in infant populations at risk for neuromotor delay.

This thesis aimed to: (1) assess the current state of scientific evidence regarding treadmill interventions in infants at risk for neuromotor delays (ND), and (2) to study the effects of TT in relation to motor development and the onset of independent walking. First, a systematic review about treadmill interventions in children under 6 years of age at risk of ND was carried out. The findings indicated that task-specific training (TT for independent walking acquisition) might be a useful tool to promote development in children at risk for ND. However, the number of studies found was limited and fairly heterogeneous, especially regarding the type of population studied (different diagnoses), treadmill parameters and training protocols[10]. A controlled clinical trial was then conducted with a sample of 28 infants at risk for ND. The experimental group, which received TT (entry age 8-11 months), demonstrated an improvement in step quality. Although no differences were found between groups regarding age of onset of independent walking, a significant relationship between treadmill step frequency and onset of independent walking was established[11]. Finally, an individualised TT protocol was implemented in a case study of twins with a history of mild prematurity. At 8 months corrected age, the twin who showed greater motor delays started to receive TT. An increase in the rate of gross motor development was shown in the trained twin 2 months after training had started. Improvement in step quality and frequency of alternate treadmill steps occurred in both twins, but was more accentuated on the trained one.

In conclusion, TT may be considered as a useful tool to potentiate aspects related to locomotion in infants with or at risk for ND. Locomotion and

walking acquisition is a key milestone for all children since it is associated with cognitive and emotional development[5], as well as quality of life.

CAPÍTULO 1. Introducción

En la actualidad, los avances en el campo de la medicina han supuesto un aumento en la supervivencia de recién nacidos prematuros y/o con bajo peso al nacer. Sin embargo, prematuridad y bajo peso al nacer son factores que pueden representar riesgos en varios niveles del desarrollo del propio individuo, pudiendo dejar secuelas de carácter físico, emocional o cognitivo. En esta tesis nos centraremos en el estudio del desarrollo de la motricidad gruesa de esta población, concretamente en relación al proceso de adquisición de la marcha autónoma, durante los primeros dos años de vida.

Prematuridad y bajo peso al nacer

Según una revisión sistemática publicada en enero de 2010 por la Organización Mundial de la Salud[12], la prematuridad en Europa tiene una tasa de incidencia del 6.2%, representando la proporción más baja a nivel mundial. En España, en 2010, la tasa de nacimientos prematuros fue del 7.4%[13]. La mayoría de nacimientos prematuros se deben a causas desconocidas. Sin embargo, en la literatura médica, se han descrito algunos factores de riesgo como: desventajas sociales (sobre todo en relación al bajo peso al nacer)[14], estrés durante el embarazo, hábitos tóxicos como alcoholismo y tabaquismo, infecciones genitales, hipertensión arterial, o un índice de masa corporal por debajo de 19 o por encima de 30[15,16]. Desde una perspectiva socio-económica, la prematuridad y el bajo peso al nacer suponen un incremento en los costes sanitarios, que podrían ser reducidos con la implementación de un plan de intervención preventivo[1].

El recién nacido prematuro y el bebé de bajo peso al nacer presenta de manera frecuente retrasos y/o anomalías en el desarrollo motriz, cognitivo y emocional[1]. Las morbilidades o diagnósticos más frecuentes en esta población son la parálisis cerebral (PC), patología obstructiva de las vías respiratorias, disminución de la audición, y problemas oftalmológicos o deficiencias visuales como la ceguera[2]. Sin embargo, diagnósticos como el de PC (que resultará en un repertorio de movimientos reducido, y una dificultad para seleccionar los patrones neurales más eficientes) suele establecerse de forma tardía, después del primer año de vida[4]. Durante el periodo neonatal tiene lugar un rápido crecimiento cerebral. La presencia de morbilidades durante este periodo, que

pueden estar o no asociadas al grado de prematuridad, puede comprometer el desarrollo neuronal[17]. Sin embargo, evidencias físicas de daño en la estructura cerebral se observan solamente en un tercio de niños* con disfunción motriz menor[18,19]. La mayoría de niños diagnosticados de trastorno en el desarrollo de la coordinación (alteración principal del desarrollo motriz, juntamente con la PC) no presentan anormalidades cerebrales visibles a través de técnicas de diagnóstico por imagen. Sin embargo, a nivel microscópico, se pueden detectar anormalidades en el funcionamiento de los neurotransmisores y/o receptores del sistema nervioso[18,19]. En términos generales, se suele observar una relación entre el lugar de la lesión del sistema nervioso central y la sintomatología clínica presentada por el sujeto. Aun así, no siempre existe una correlación exacta con el tipo de disfunción motriz que presenta cada sujeto[18,19].

En la población con antecedentes de prematuridad, independientemente de las causas de retrasos y/o anomalías, una característica común es el retraso en el desarrollo motriz, concretamente en la adquisición de la marcha autónoma. Para poder entender cómo emergen las habilidades motrices en los niños a lo largo de la etapa de desarrollo, es importante revisar las teorías de desarrollo motriz que han ido surgiendo a lo largo de los años.

Teorías del desarrollo motriz en pediatría

Existen diferentes modelos o perspectivas teóricas que buscan explicar el proceso de desarrollo motriz durante la etapa infantil. Entender los fundamentos sobre los que se basan estas teorías es de gran importancia desde la visión terapéutica. El diseño de los planes terapéuticos de intervención se constituirá a partir de los fundamentos que sustente la teoría que se considere referente[18,19]. Según J.E. Clark, que presenta una visión histórica sobre dichas teorías en su artículo publicado en el año 1995[20], inicialmente se establecieron dos perspectivas o paradigmas sobre el funcionamiento del sistema nervioso central. Éstas intentaban explicar cómo este sistema conseguía controlar y coordinar el movimiento del individuo: (1) la

* Con el objetivo de facilitar la lectura, a no ser que se indique lo contrario, se utilizará el término "niños" de manera genérica para referirse a la población infantil. A pesar de que este término se exprese en género masculino, incluye también al femenino.

perspectiva de la **neuro-maduración**, que se centraba principalmente en explicar el proceso de adquisición de habilidades motrices durante la etapa infantil, y (2) la perspectiva del **procesamiento de la información** (*information-processing*) que era la elegida para interpretar la adquisición de habilidades en la etapa adultas. Más tarde, entre los años 1980 y 1993, se desarrollaron dos teorías más: la **Teoría de los Sistemas Dinámicos** y **Teoría de Selección del Grupo Neuronal**. Desde una perspectiva terapéutica, la aportación más relevante de estas dos últimas teorías fue que tenían en cuenta la influencia de las condiciones del entorno del individuo en relación a su desarrollo motriz.

A continuación, se presentan con más detalle las bases sobre las que se fundamentan estos cuatro modelos teóricos, para poder comprender cómo tiene lugar la adquisición de la marcha en el niño.

Teoría de la Neuro-Maduración ("Neural-Maturationist Theory")

La teoría de la neuro-maduración fue propuesta en el año 1943 por Frossberg, Gesell y McGraw, siendo el primer intento de explicar cómo tenían lugar la evolución y los cambios motrices en el neonato desde el inicio de la vida extra-uterina. Esta teoría postula que el desarrollo motriz se debe a un despliegue gradual y progresivo de una serie de patrones de movimiento que se encuentran prediseñados y predeterminados dentro del sistema nervioso central del niño. A medida que este proceso se va estableciendo, la corteza cerebral va ganando terreno en el control de los movimientos del sujeto. De esta manera, las respuestas motrices reflejas que se observaban inicialmente en la conducta motriz del neonato irán disminuyendo progresivamente. Por tanto, según esta teoría, la adquisición de habilidades motrices (y funcionales) es la consecuencia de la *maduración* del sistema nervioso[21]. Bajo este supuesto, una retraso en el desarrollo motriz se podría detectar observando el proceso de adquisición de los hitos motrices del niño a lo largo del tiempo (éstos se encuentran descritos para cada edad, en el que se considera desarrollo normal o "típico"). Para llegar a adquirir la marcha autónoma, los patrones motrices más "inmaduros" y los movimientos empleados por el niño como estrategia inicial de desplazamiento (como pueden ser el rastreo o el gateo en cuadrupedia) acabarían siendo sustituidos por la marcha bípeda. La

detección de anormalidades en el tono muscular y/o la persistencia de reflejos primarios más allá de los límites considerados como dentro de la normalidad, podrían ser signos clínicos de alarma. Una disfunción en estos aspectos podría ser consecuencia de una afectación de origen neurológico, la cual podría implicar dificultades en mayor o menor grado para llegar a adquirir la marcha autónoma. El plan terapéutico de intervención, según los fundamentos teóricos de la teoría de la neuro-maduración, se enfocaría desde la normalización del tono muscular[18,19], ya que una alteración del mismo puede dificultar el desarrollo del comportamiento motriz.

Procesamiento de la Información ("Information-processing")

Concepto teórico introducido por Fitts y Postner en 1967, inspirado en el funcionamiento de los ordenadores y la capacidad de éstos para almacenar información, recuperarla, procesarla y, en ocasiones, perderla. Este modelo teórico posteriormente derivó en dos líneas de pensamiento diferentes, que fueron objeto de disputa entre investigadores[20]. Mientras un grupo de investigadores explicaba que los movimientos surgían de las instrucciones mandadas por un único (y desconocido) "ejecutor", otro grupo hablaba de que existía una compleja relación entre el entorno y el sistema biológico, la cual tenía también un rol importante en relación al comportamiento motriz. Ambas perspectivas podían explicar tanto la adquisición de capacidades o comportamientos motrices sencillos, como la adquisición de habilidades motrices en la edad adulta. Sin embargo, según Clark[20], ninguna de estas visiones teóricas podía explicar la ejecución de actividades motrices de mayor complejidad, ni tampoco argumentar cómo se adquirían habilidades nuevas en el niño, como podría ser la adquisición de la marcha autónoma.

Teoría de los Sistemas Dinámicos ("Dynamic Systems Theory")

La Teoría de los Sistemas Dinámicos (TSD) tiene sus orígenes en las ciencias físicas y en las matemáticas. Fundamentalmente, busca explicar el proceso de cambios que tiene lugar a lo largo del tiempo en cualquier sistema. Esta idea, que surgió hace más de un siglo en base a los avances en

conocimientos científicos, no llegó al campo de las ciencias del movimiento hasta los años 80. Fue entonces cuando los investigadores Kugler, Kelso, Turvey, y posteriormente Thelen, empezaron a difundir la idea de que el desarrollo motriz no se limitaba exclusivamente a un despliegue de patrones innatos, sino que las características del entorno tenían un papel altamente relevante en el desarrollo del niño[20,22-24]. La TSD dice que el movimiento ni está impuesto por nuestros genes, ni resulta de las instrucciones de un único ejecutor, tal y como estipulaban las teorías de la neuro-maduración y del procesamiento de la información, respectivamente. Según la TSD, el proceso de adquisición de habilidades nuevas y la progresión en el desarrollo motriz viene dada por la interacción de varios elementos, los cuales constituyen el *"complejo de los sistemas dinámicos"*. Los elementos de estos sistemas tienen la capacidad de combinarse de diferentes maneras, según el contexto o entorno, dando así respuestas motrices funcionales diferentes. A continuación se definen algunos conceptos básicos de esta teoría:

Limitaciones: "Límites" con los que el sujeto se encuentra a lo largo de su desarrollo, que enmarcarán el desarrollo motriz del propio sistema. Newell (1986), según se cita en el estudio de Clark,[20] categorizó estos límites según se encontraran en el organismo (peso, talla, cognición, aspectos emocionales y/o psicológicos), en el entorno (físico y sociocultural) o en la tarea en cuestión. Estos tres aspectos determinarán el comportamiento final, es decir, el movimiento.

Auto-organización: Proceso que favorece la aparición de movimientos más complejos que serán los que constituirán acciones más organizadas. Este fenómeno surgirá a partir de los *limitaciones* encontradas y de la interacción de factores intrínsecos del sujeto (peso corporal, fuerza muscular, estructuras articulares, estado emocional del niño, condiciones específicas del entorno y/o grado de desarrollo cerebral)[19].

Patrones: Conjunto de movimientos que resultan de una interacción dinámica entre subsistemas (unidades motrices, neuronas y estructuras musculo-esqueléticas), generando un comportamiento o acción motriz de mayor complejidad, como por ejemplo el de la marcha.

Estabilidad: Estado que se define cuando un patrón de movimiento se caracteriza por tener poca variabilidad en el conjunto de movimientos que lo

constituyen. La TSD nombra estos estados de baja variabilidad como de "fuerte atracción" (*attractors*). Sin embargo, puede haber periodos de transición o de cambios en el organismo del sujeto en los que esta variabilidad aumente, dando lugar a una pérdida de estabilidad del patrón de movimiento. Por ejemplo, durante la etapa transitoria entre la fase de gateo y la adquisición de marcha, habrá un aumento de variabilidad en los movimientos y una carencia de la estabilidad en los patrones motrices[20].

Parámetro de control: Límite determinante en el desarrollo motriz, capaz de regular la velocidad de desarrollo del sujeto. Cuando el niño consigue sobrepasar uno de estos límites, su sistema adquiere un cambio en el comportamiento motriz o un comportamiento motriz nuevo[25].

Thelen, en 1986[26], presentó una hipótesis dentro de la TSD, donde definió ocho subsistemas en relación a la adquisición de la marcha autónoma en el niño. Esta hipótesis dice que es necesario que los componentes de los subsistemas, que se citan a continuación, lleguen previamente a cierto nivel de maduración para que el niño pueda adquirir la marcha autónoma. Los subsistemas que define Thelen son los siguientes: (i) la generación de patrones, (ii) la diferenciación articular, (iii) el control postural, (iv) la sensibilidad visual, (v) el control del tono muscular, (vi) la fuerza de la musculatura extensora, (vii) los límites corporales y (viii) la motivación. Si uno de los componentes no llegase a un nivel basal mínimo (no describe cuál sería el nivel mínimo para cada uno de éstos), ése actuaría como *límite*, frenando o inhibiendo la aparición del nuevo comportamiento motriz, y actuando así como *parámetro de control*. Si ponemos el ejemplo de la locomoción, podemos identificar patrones funcionales de movimiento previos a la adquisición de la marcha autónoma, como el gateo o el rastreo. Sin embargo, el desarrollo global del sujeto (si no hay condición médica que físicamente lo impida) lo llevará progresivamente a utilizar la marcha como patrón de desplazamiento habitual. El niño pasará por una etapa exploratoria en la que se irá encontrando con limitaciones (definidos anteriormente, dentro de los complejos de sistemas dinámicos), y aparecerá una variabilidad de movimientos y de estados dinámicos posibles, como pudieran ser la marcha lateral o la marcha con apoyo externo[20].

En resumen, la TSD postula que el proceso de adquisición de una habilidad motriz puede entenderse como una sucesión de eventos que el sujeto experimenta de manera dinámica, antes de encontrar y aprender un estado motriz nuevo. Este estado será aquél que mejor consiga satisfacer las demandas de una tarea o contexto específico, y que además lo haga con la mayor estabilidad y la eficacia posibles. Es decir, que el patrón o el movimiento finalmente adquirido sea resistente a las perturbaciones del entorno, y que sea eficiente en cuanto a consumo energético del organismo.

Las terapias infantiles que se enmarcan dentro las bases de la TSD contemplan la manipulación del entorno del niño como estrategia central en el plan terapéutico de intervención.

Teoría de la Selección del Grupo Neuronal ("Neuronal Group Selection Theory")

Esta teoría, en términos relativos, engloba y une conceptos de la teoría de la neuro-maduración y de la TSD, pues en términos relativos recoge conceptos de ambas perspectivas. La teoría de la selección del grupo neuronal (TSGN) (Sporns y Edelman 1989, 1993)[27] centra la atención en la existencia de circuitos de neuronas, que constituyen la corteza cerebral, y en cómo será el funcionamiento de las estructuras del cerebro en desarrollo. En el niño, durante la etapa inicial de desarrollo motriz, los circuitos neuronales no se encuentran unidos a nivel micro-anatómico. Así, en el cerebro del niño habrá una v*ariabilidad estructural* (la anatomía microscópica no estará estructuralmente definida). Esto, a su vez, implicará que, según qué circuitos de neuronas se activen en un momento determinado, se generen diferentes tipos de movimientos. La TSGN define este fenómeno como *variabilidad dinámica*. Los circuitos neuronales constituyen los llamados *grupos neuronales*. Un *grupo neuronal* es un colectivo local de neuronas (de varios centenares hasta millares) interconectadas con mayor fuerza en comparación con otras neuronas circundantes. Además, estas neuronas tenderán a compartir propiedades funcionales y a activarse de manera correlacionada en el tiempo. Los grupos neuronales se consideran como las *unidades funcionales básicas* o *unidades de selección*[27]. En el córtex cerebral, los grupos neuronales están ordenados en

mapas neuronales, los cuales representan diferentes partes de la superficie corporal. Estos mapas neuronales ocupan áreas bien delimitadas en la corteza cerebral, y están unidos por gran cantidad de conexiones recíprocas, que permitirán que se establezcan señalizaciones de manera constante entre ellos. Este proceso se conoce como *re-entrada* ("*reentry*").

La existencia de alta variabilidad (estructural y dinámica) de grupos neuronales implica que sea necesaria una *selección somática* (que tendrá lugar a lo largo de la vida). Se seleccionarán aquellos grupos de neuronas que resulten en el mejor comportamiento motriz, es decir, el más efectivo y más eficaz dentro de un contexto determinado. En el sistema nervioso, el mecanismo de selección se marcará a través de cambios en las sinapsis, resultando en una amplificación o en una disminución selectiva de las respuestas de los grupos de neuronas. Esta selección de grupos neuronales es de gran importancia en el proceso de desarrollo motriz, ya que permitirá al sujeto discriminar y categorizar la información de entrada, recibida por las vías sensitivas. Igualmente, el niño podrá ir integrando sus habilidades motrices (conjuntamente con la información sensitiva) para producir un *comportamiento adaptativo* dirigido a un objetivo externo.

Para el desarrollo de la coordinación sensitivo-motriz, este proceso de selección es producto de tres pasos convergentes: (i) la *generación espontánea* de una variedad de movimientos, que formarán el llamado *repertorio básico de movimientos*, (ii) desarrollo de la *habilidad para sentir* los efectos que provocan los movimientos ejecutados en un entorno determinado, hecho que eventualmente permitirá que tenga lugar la selección neuronal guiada por el *valor adaptativo* (ver descripción del concepto de *valor* más adelante en el texto), y (iii) la selección de los movimientos finales. A medida que vaya teniendo lugar la selección de grupos neuronales, los repertorios de movimientos existentes en un determinado momento irán igualmente modificándose. Esto llevará a definir la actividad motriz del organismo. Además, cambios en la biomecánica o en las demandas del entorno provocarán la aparición de nuevos repertorios de movimientos, los cuales guiarán el proceso de selección para que tenga lugar una coordinación adaptativa de manera constante.

En la medida en que el sistema de selección trabaja sobre una diversidad de patrones de movimiento pre-existentes (patrones innatos determinados evolutivamente, los cuales imponen límites en los repertorios de movimiento básicos del organismo y el posterior desarrollo motriz), y carece de un programa específico para la mayoría de movimientos refinados, la TSGN introduce un nuevo concepto para explicar cuáles son las restricciones que dan lugar al propio proceso de selección. Según la TSGN, estas restricciones vienen dadas por los llamados *sistemas* o *circuitos de valor*, los cuales están pre-especificados por selección evolutiva y, por tanto, no se ven influenciados por la experiencia previa del organismo. Si nos referimos específicamente al movimiento, estas restricciones se encuentran a nivel neuro-anatómico, en los circuitos de señalización específicos guiados por neurotransmisores concretos. Los *sistemas de valor* implicados en el desarrollo sensitivo-motriz reciben información sensitiva. Gracias a esta información, éstos podrán dar respuesta a las acciones o eventos que ocurran en el entorno inmediato del sujeto, aumentando o disminuyendo el nivel de actividad neuronal. Por ejemplo, el movimiento de alcance implica el establecimiento de contacto táctil entre la mano del sujeto y el objeto que se quiere alcanzar. Los eventos motrices en la secuencia de este gesto pueden dar como resultado un aumento de descarga neuronal en un sistema de valor, estableciendo la señal de adaptación de ese movimiento para poder lograr conseguir el objetivo por el cual se inició dicho movimiento.

El proceso de selección de repertorios de movimientos y la formación de sinergias neuro-motrices requieren de la interacción del organismo con el entorno. Además, es importante que el medio en que el sujeto se encuentre permita captar el valor adaptativo de un movimiento, ya que esto tendrá influencia sobre los movimientos de aparición futura. Inicialmente, los movimientos de los cuales puede disponer el organismo están limitados exclusivamente por la estructura mecánica pre-existente del conjunto motriz, y se encuentran esencialmente libres de restricciones impuestas por la experiencia en el entorno. Por tanto, en términos generales, se puede decir que el repertorio de movimientos primarios carece de estructura pre-establecida. Cuando se inicia la experiencia sensitivo-motriz, el organismo tiene que enfrentarse a las demandas de su entorno, al mismo tiempo que se encuentra

sujeto bajo sus propios sistemas de valores. La selección somática resultará del refuerzo de las conexiones neuronales (sinapsis) involucradas en la generación de comportamientos eficaces y eficientes (en el ejemplo del movimiento de alcance, en aquellos que consigan el contacto táctil con el objeto de la mejor manera). Como resultado de los cambios sinápticos selectivos, los movimientos que ayuden a lograr la tarea encontrada tendrán una mayor probabilidad de volver a aparecer en un futuro, ante una situación similar. El proceso de desarrollo motriz no está determinado exclusivamente por la información genética, ni únicamente a través de la interacción con el medio, sino que es el resultado de un enlazamiento de información proporcionada por los genes y el entorno[21]. Es decir, el desarrollo motriz empieza a través de los llamados *repertorios neuronales primarios*, los cuales están determinados evolutivamente, pero que tienen la capacidad de modificarse y generar variaciones substanciales en sí mismos según la regulación epigenética (selección somática de grupos neuronales en función del entorno). El desarrollo procede de forma selectiva y en base a la información aferente que proviene tanto del comportamiento del individuo como de la propia experiencia adquirida.

En resumen, durante el proceso de desarrollo motriz, la TSGN distingue entre dos fases de variación de movimientos: la fase primaria, donde la actividad motriz no está estrictamente sintonizada con el entorno; y la fase secundaria o de adaptación, que define la creación de repertorios motrices en relación a la función motriz específica de una situación[18]. Para que, a partir de los movimientos del repertorio primario (representados por una gran riqueza y espontaneidad de movimientos), tenga lugar la selección del grupo neuronal más adecuado a las condiciones del individuo dentro de un contexto determinado, es preciso que dicho individuo tenga la capacidad de sentir la variabilidad del entorno. Ésta le servirá de guía para su adaptación y posterior selección del mejor movimiento que responda a las demandas del ambiente en el que se encuentra. La selección de un movimiento o comportamiento concreto supondrá una amplificación de la fuerza de los patrones neuronales que lo representan, mientras que el sistema nervioso ejercerá un sistema de retro-alimentación de la información en cuanto a la satisfacción del patrón elegido en la condición ambiental. Por lo tanto, y según esta teoría, la

adaptación resulta de la interacción dinámica entre el conjunto motriz y el entorno, estando limitada por los patrones evolutivos innatos[27].

En el ámbito de la rehabilitación, según la TSGN, se trabajará desde la manipulación de las condiciones del entorno con el objetivo de reforzar los patrones de movimiento más adecuados/funcionales para cada tarea. Esto facilitará la selección de grupos neuronales que resulten en movimientos favorables para lograr una tarea, de manera que tengan mayor probabilidad de establecerse como patrones preferidos en un futuro.

Valoración y diagnóstico de retraso en el desarrollo motriz

Para la valoración del desarrollo motriz en población pediátrica existe un amplio repertorio de escalas y tests, publicados y validados, la mayoría de los cuales son en lengua inglesa. Entre ellos están el *Bayley Scales of Infant and Toddler Development* (BSID)[28] y el *Alberta Infant Motor Scale* (AIMS)[29], los cuales se utilizarán para la recogida de datos del estudio presentado en el capítulo 4 de esta tesis. Según una revisión sistemática sobre los tests y escalas de valoración del desarrollo motriz en niños prematuros durante el primer año de vida, se concluye que es recomendable el uso de más de una escala o test para obtener toda la información necesaria en diferentes aspectos del desarrollo del niño[30]. En esta revisión, el AIMS demostró tener las mejores propiedades psicométricas y la mayor utilidad clínica, mientras que el BSID (tercera edición) destacó por su elevada validez y fiabilidad, a pesar de ser menos sensible en la detección de cambios cualitativos en el movimiento[30]. Otras escalas de uso frecuente son: el *Gross Motor Function Measure*, el *Griffiths Developmental Scales*, el *Neonatal Behavioral Assessment Score* y el *Peabody Developmental Motor Scales*[31]. La existencia de tal cantidad de escalas de valoración para el desarrollo motriz hace que no pueda haber consenso en cuanto a medidas estandarizadas de puntuación para la clasificación del nivel o grado de desarrollo de un niño. En ocasiones, es dificultoso llegar a conclusiones extrapolables a la población, por no poder comparar los resultados obtenidos entre estudios que han utilizado diferentes instrumentos de medida. Además, en términos generales, la mayoría de tests carecen de la suficiente sensibilidad como para detectar pequeños cambios

motrices que, en ocasiones, pueden llegar a significar mejoras importantes en la capacidad funcional del niño. Otro problema asociado con los resultados obtenidos tras las mediciones es que principalmente se limitan a cuantificar datos, omitiéndose cualquier tipo de observación cualitativa que puede ser de gran importancia a nivel de cambios en el desarrollo motriz[31]. Aun así, a pesar de las limitaciones que presentan estos instrumentos de valoración, son altamente utilizados y, en la mayoría de los casos, se complementan con una exploración cualitativa por parte de un experto.

La intervención temprana para mejorar el desarrollo motriz

El término 'intervención temprana' puede tener dos significaciones: referirse a intervención precoz en la vida del neonato, o precoz en cuanto a la aparición de la condición que causa una disfunción. A nivel clínico y social el significado con mayor uso se refiere a una intervención rápida a partir de la aparición del problema[31]. De esta manera se evita intervenir innecesariamente en niños que están considerados como de riesgo (por sus antecedentes personales e historia clínica), ya que puede que no lleguen a presentar ningún problema a lo largo de su desarrollo. Es de interés evitar lo que podría suponer una carga innecesaria para un niño, además de minimizar la repercusión económica y social que normalmente conlleva cualquier intervención terapéutica. Por el contrario, esta estrategia de no atender a niños considerados de riesgo, independientemente de que muestren o no algún signo clínico de afectación en relación a su desarrollo, puede también demorar la atención al niño en un momento de gran plasticidad cerebral[32]. Si este fuera el caso, una intervención tardía podría comprometer los resultados del tratamiento, especialmente cuando se trata de niños de cortas edades.

Según una revisión sistemática publicada por Riethmuller (2009), hay una cantidad muy limitada de estudios de calidad en cuanto a la eficacia de la intervención temprana y el desarrollo motriz[33]. Los posibles beneficios de la intervención temprana en niños con riesgo biológico de retraso en el desarrollo sigue siendo poco concluyente[31]. Sin embargo, en relación a la promoción del desarrollo motriz, se establece la recomendación de que pediatras y

profesionales de la salud lleven a cabo la promoción de la actividad física durante los años pre-escolares[33].

El tapiz rodante como medio de intervención temprana

En la literatura científica encontramos varios estudios en población pediátrica donde se ha utilizado el tapiz rodante con asistencia del peso corporal[10], con diferentes objetivos: (1) para re-habilitar la marcha después de una lesión adquirida[34-36], (2) para describir trayectorias de patrones de desarrollo[25,37], y (3) para prevenir retrasos en la adquisición de la marcha, a través del entrenamiento de la misma[38]. El tapiz rodante es una actividad centrada en promover específicamente el patrón de la marcha, que es una habilidad motriz que puede verse alterada en los niños con riesgo de retraso en el desarrollo motriz[39,40]. La intervención con tapiz rodante, especialmente cuando se tiene por objetivo la prevención de retrasos en la adquisición de la marcha autónoma, se caracteriza por entrenar el paso sobre el tapiz a base de repeticiones. Éste se considera un precursor de la habilidad motriz que se quiere potenciar: la marcha[41]. Otro atributo que puede reconocerse sobre el uso del tapiz rodante, es que ofrece un entrenamiento *específico a la tarea*. Existe evidencia de que el entrenamiento específico a la tarea es la clave del aprendizaje motriz[42]. Esto, además, tiene gran importancia en relación al planteamiento y diseño de intervenciones terapéuticas para habilitar o re-habilitar un movimiento[43,44]. En cuanto a parámetros o protocolos de entrenamiento, existe evidencia que sugiere que si el entrenamiento es intenso e individualizado al sujeto entrenado, es más efectivo sobre los aspectos del desarrollo motriz relacionados con la locomoción[7,38,45].

Desarrollo de la marcha bípeda e independiente

El objetivo final en el desarrollo de la motricidad gruesa en el niño es la adquisición de la marcha bípeda e independiente. La marcha autónoma se considera establecida a partir del momento en que el niño es capaz de realizar tres pasos de manera autónoma, sin soporte ni asistencia externa de ningún tipo, y sobre una superficie estable[2].

Como ya se ha mencionado en apartados anteriores, para la generación de la locomoción es preciso que el sujeto progresivamente vaya adquiriendo una mayor sincronización y coordinación muscular. Si hablamos de la marcha, la coordinación es un concepto que se puede analizar según dos componentes: la coordinación inter-segmentaria y la coordinación intra-segmentaria. La primera hace referencia a la relación entre ambas piernas durante la secuencia del paso, y puede estudiarse bajo parámetros espacio-temporales. Es decir, se observa qué es lo que pasa entre el ciclo de una pierna (que se inicia en el momento en que un pie contacta con el suelo, y termina cuando aparece de nuevo la pisada con ese mismo pie) y la otra. La segunda se refiere a la relación que se establece entre las articulaciones principales de una misma pierna (articulaciones de la cadera, rodilla y tobillo). Clark[20] menciona un estudio de Raibert realizado en 1986, en el cual se observó que cuando los niños iniciaban la marcha autónoma, mostraban una coordinación inter-segmentaria igual a la de un sujeto adulto: ambas piernas presentaban un desfase del 50%. Cuando una pierna empezaba su ciclo, la otra pierna se encontraba a la mitad anterior de su propio ciclo. Por otra parte, se observó que la variabilidad de movimientos durante la marcha era mayor en el niño, además de que éste presentaba una mayor inestabilidad en el patrón de marcha, en comparación con los adultos. Aun así, se observó cómo a medida que el niño recibía práctica en la acción de dar pasos, dicha variabilidad iba disminuyendo progresivamente a favor de la estabilidad del patrón de marcha. Asimismo, Clark, en un estudio del año 1988[46], observó que al cabo de tres meses después del inicio de la marcha autónoma, a través de la práctica de la misma, ya no se observaban diferencias significativas entre la marcha adulta y la del niño. En términos de coordinación intra-segmentaria, Thelen[25,26] observó que, en los pasos sobre el tapiz, los bebés de 7 meses tenían una coordinación intra-segmentaria muy parecida a la de los pasos de los adultos. Se determinó que las tres articulaciones principales de la extremidad inferior (cadera, rodilla y tobillo) se movían de manera compleja entre ellas, y existía algo más que una simple sincronización articular. Esta misma autora describió la coordinación intra-segmentaria durante el pataleo del bebé en decúbito supino, en estudios previos[26], donde sí habló de sincronización articular simple. En resumen, se podría decir que las diferencias más relevantes entre la marcha del niño y la del

adulto recaen sobre la existencia de una mayor variabilidad de patrones de pasos en el caso de los niños. Esto se podría explicar por la falta de práctica de la acción de caminar, además de tratarse de un periodo inicial de transición dentro del desarrollo motriz del niño[47].

Durante los primeros años de vida del niño, su cuerpo experimentará grandes cambios morfológicos, los cuales hay que tener en cuenta para poder entender el proceso de adquisición de la marcha autónoma. Un recién nacido no puede caminar porque su cabeza y su tronco son proporcionalmente muy grandes en relación a la morfología y tamaño de sus extremidades. Esto hace que, biomecánicamente, no esté capacitado para caminar. Además, su centro de gravedad está muy elevado, y esto hace que tenga grandes dificultades para mantener su equilibrio. En general, para la mayoría de la población que sigue un desarrollo motriz normal, entre los 12 y los 24 meses de edad la estructura corporal y la proporcionalidad del niño se verán suficientemente modificadas de manera que podrá tener lugar la adquisición de la marcha independiente[25]. Para que el niño pueda llegar a este punto, es preciso que previamente haya conseguido una bipedestación estable. Haciendo referencia a los términos de la TSD, lograr la postura erguida estable podría ser un parámetro de control en relación a la adquisición de la marcha autónoma[20]. Además, en relación a este aspecto, se pueden definir tres componentes principales que ayudarán al sujeto en el mantenimiento de su postura. Se trata de los inputs de informaciones visuales, vestibulares y somato-sensitivas. Estos sistemas, sin embargo, no se desarrollan de manera sincronizada, lo cual hace que no se pueda establecer de manera exacta la edad en la que un niño estará suficientemente capacitado como para conseguir una postura erguida estable[25].

El curso del desarrollo motriz no es, por tanto, lineal, y puede aparecer un nuevo comportamiento motriz en cualquier momento. Sin embargo, como se ha explicado anteriormente, en determinados momentos se pueden identificar componentes que juegan el papel de factores limitantes o reguladores de la velocidad del desarrollo[26]. Un ejemplo de éstos podría ser el nivel de control postural o la fuerza muscular. Cuando el niño logre adquirir suficiente fuerza muscular y control de su postura, habrá otros componentes cualitativos y cuantitativos de otras habilidades ya existentes en el sujeto que se combinarán con éstas nuevas. De esta manera, según Thelen, emergerá la locomoción

bípeda. A través de la observación del proceso de adquisición de la marcha en niños con dificultades motrices, se pueden valorar las reacciones motrices de respuesta ante situaciones de inestabilidad percibidas por el sujeto. A su vez, un observador externo o un terapeuta tendrá la posibilidad de adquirir cierto conocimiento teórico sobre las respuestas de re-equilibración del niño[25]. Al entender e identificar estas respuestas, se podría trabajar en el ámbito de la rehabilitación pediátrica para superar los límites que se establecen como parámetros de control en un momento determinado en el desarrollo de un niño.

La ejecución de pasos en el tapiz rodante es pues una acción compleja, que requiere movimientos coordinados entre ambas piernas y entre segmentos de la misma extremidad. En la marcha, el nivel de coordinación necesaria para lograr el patrón funcional es mucho más alto en comparación con los movimientos espontáneos observados en los bebés y, por tanto, nos puede servir de indicador de alteraciones en el sistema nervioso[48]. Bajo el supuesto que los pasos realizados en el tapiz rodante son precursores de los pasos en la marcha independiente, y son además indicadores del nivel de desarrollo del sistema motriz, es de interés revisar la literatura científica que hace uso del tapiz rodante para describir el desarrollo de la motricidad gruesa y la adquisición de la marcha autónoma.

Pasos en el tapiz rodante

Un estudio longitudinal publicado como monográfico valoró la respuesta al tapiz rodante en 9 bebés sanos, nacidos a término, con edades comprendidas entre 1 y 7 meses. Se trata de *Hidden Skills*[25], que presenta un análisis de los pasos en el tapiz rodante durante el primer año de vida en niños con desarrollo normal, y lo explica según los conceptos de la TSD. Busca detectar periodos de transición, que se identificarán cuando se observe un aumento de variabilidad de movimientos y una consecuente pérdida de estabilidad en los patrones motrices. El objetivo está en descubrir cuáles serían los parámetros de control que ejercen de guía en el proceso de la adquisición de la marcha independiente. En este monográfico[25] se observó que, a partir del primer mes de vida, los bebés ya tenían la capacidad de realizar pasos sobre el tapiz rodante. En este punto del texto, es de interés resaltar los hallazgos

presentados en un estudio anterior de la misma autora[26]. Cuando los bebés eran suspendidos en posición bípeda de manera estática, ofreciéndoles un contacto plantar con el suelo, no realizaban pasos de manera espontánea. En cambio, al suspenderlos encima de una base dinámica como era tapiz rodante en marcha, éstos empezaban a dar pasos. El tapiz rodante, al provocar de manera pasiva un desplazamiento de las piernas del sujeto hacia atrás, generaría un estímulo para dar pasos. Esto podría explicarse por una activación refleja inducida por el estiramiento de los flexores de cadera[26]. Este fenómeno se observó en bebés pequeños, mucho tiempo antes del inicio de la marcha autónoma. Estudios posteriores concluyeron que los pasos en el tapiz rodante representaban un componente importante del comportamiento funcional de la marcha, y que están "disponibles" mucho tiempo antes de su uso funcional[47]. Volviendo a la descripción de la evolución de los pasos según el monográfico de Thelen[25], a pesar de que a los 2 meses de edad se observó una regresión en la respuesta al tapiz debido a cambios en el tamaño y estructura corporal[26], fue principalmente a partir de los 4-5 meses de edad cuando todos los bebés mostraron capacidad para realizar pasos alternos sobre el tapiz rodante. A partir de los 6 meses de edad, se observó un aumento en la frecuencia absoluta de pasos, y una mejora en la calidad de éstos. Se observó una disminución en la variabilidad de los tipos de apoyo, estableciéndose una preferencia de apoyos en pie plano versus pie en punta. En cuanto al tipo de pasos, se vio un aumento considerable en el número de pasos alternos en comparación con otro tipo de pasos como podían ser los pasos simples o paralelos[25]. Los resultados de un ensayo clínico controlado corroboraron estos hallazgos, concluyendo que la práctica de la marcha en el tapiz rodante resultaba en un aumento drástico en la frecuencia de pasos entre el mes y los 6 meses de edad en niños con desarrollo normal[49]. Esta descripción general del proceso de adquisición del patrón de marcha ha seguido siendo corroborada en estudios posteriores como el de Angulo-Barroso[2].

Otro aspecto estudiado en relación a los pasos en el tapiz, es la reacción de los sujetos ante cambios de velocidad de la cinta. Se observó que éstos eran capaces de adaptarse satisfactoriamente a los cambios de velocidad, lo cual contribuyó a demostrar que la marcha no era un patrón de acción

automática, como explicaba la teoría de la neuro-maduración. Otras investigaciones con el tapiz rodante han estudiado las respuestas motrices de un sujeto al recibir velocidades diferentes para cada pierna sobre el tapiz[50], y la respuesta motriz del niño al añadirle resistencias externas (con pesos alrededor de los tobillos o aplicando resistencias manuales), de manera que la demanda muscular se viese aumentada[51,52].

Descrita la respuesta al tapiz rodante de los bebés nacidos a término que siguen un desarrollo normal, es de interés revisar a continuación el tipo de respuesta de aquellos sujetos con antecedentes de prematuridad. En 1994, Davis *y col*.[48] realizaron un estudio con bebés prematuros, considerados de bajo riesgo en relación a posibles trastornos en el desarrollo. El objetivo era poder determinar los patrones de desarrollo de la marcha de esta población, utilizando el tapiz rodante y siguiendo las líneas de investigación que otros autores habían llevado a cabo anteriormente con bebés nacidos a término. El objetivo fue, a través del conocimiento de los patrones de desarrollo de estos últimos, poder identificar posibles diferencias en el desarrollo y adquisición de la marcha entre los bebés prematuros y los nacidos a término. De esta manera el tapiz rodante podría servir como herramienta complementaria de diagnóstico de déficits en la locomoción en etapas tempranas. Se valoró la respuesta al tapiz rodante en un total de 12 bebés prematuros (con edades gestacionales inferiores a las 35 semanas). Las valoraciones tuvieron lugar a las edades de 1, 6 y 9 meses de edad corregida. Todos los bebés, excepto uno, fueron capaces de realizar pasos alternos sobre el tapiz rodante a todas las edades valoradas, observándose una clara preferencia por los pasos alternos con el aumento de la edad[48] (patrón que coincide con el explicado previamente en este texto, en investigaciones realizadas con muestras de bebés nacidos a término). Por otra parte, en este estudio, no se encontraron relaciones significativas entre valores antropométricos y frecuencia de pasos alternos. Se observó también que, a pesar de la prematuridad, los bebés que iniciaron la marcha más tempranamente demostraron mayor frecuencia de pasos en el tapiz (previamente al inicio de la marcha) que los bebés nacidos a término de edades equivalentes. Esto podría ser debido a las diferencias que se observan entre bebés nacidos a término y bebés prematuros, en cuanto al tono muscular y a la postura. Los prematuros suelen presentar una postura con mayor

tendencia a la extensión de tronco y de extremidades, y un tono muscular más elevado, lo cual podría facilitarles la acción de dar los pasos sobre el tapiz[48].

Luo *y col.*[37] compararon el proceso y la respuesta al tapiz rodante (sin entrenamiento) que seguían un grupo de bebés prematuros en comparación con un grupo de nacidos a término, hasta adquirir la marcha autónoma. Se observó que los bebés prematuros iniciaban la marcha en edades más tardías (edad media corregida de 12.8 meses versus 11 meses en los nacidos a término). Igualmente, se concluyó que era necesaria la adquisición predominante de pasos alternos en edades de 7 a 9 meses, para la posterior adquisición de la marcha independiente, tanto en el grupo prematuro como en el grupo control. A partir de esta conclusión, el análisis de la respuesta al tapiz rodante podría tenerse en consideración para predecir la posibilidad de que un niño presentara un retraso motriz si, por ejemplo, se observara una predominancia de pasos simples o paralelos en las edades comprendidas entre los 7 y los 9 meses. Angulo *y col*.[2] llevaron a cabo un estudio piloto con un grupo de 15 bebés, considerados con riesgo de retraso en el desarrollo motriz, dados sus antecedentes médicos. Se utilizó el tapiz rodante como herramienta de valoración, testando a los sujetos cada dos meses a partir de los 6 meses de edad, y hasta la adquisición de la marcha independiente o, en su defecto, hasta los 24 meses de edad. Durante el estudio, 6 sujetos recibieron el diagnóstico de parálisis cerebral. Al analizar la respuesta al tapiz rodante del grupo que había sido diagnosticado en comparación con el grupo sin diagnóstico, se observó que igualmente el patrón de desarrollo entre ambos grupos seguía una misma línea de desarrollo. Se vio un aumento de pasos alternos a medida que la edad del sujeto aumentaba, y una predominancia de apoyos en pie plano en sustitución de los apoyos de pie en punta. Sin embargo, la diferencia principal y más significativa desde un punto de vista clínico fue que, en el caso de los sujetos diagnosticados, ese progreso apareció en edades más tardías.

Mattern-Baxter *y col.*[7] recientemente presentaron los resultados de un ensayo clínico quasi-aleatorizado sobre los efectos del entrenamiento intensivo con tapiz rodante, implementado a un grupo de doce niños con diagnóstico de parálisis cerebral. La media de las edades de los participantes incluidos en el estudio fue de 22 meses, y los sujetos tenían un nivel I y II de clasificación

según la *Gross Motor Function Classification System*[53]. El entrenamiento tuvo una duración total de 6 semanas. El protocolo fue individualizado, de manera que se pautó entrenar dos veces al día, 6 días por semana, un mínimo de 5 minutos por sesión con un máximo de 20 minutos, y a velocidad específica y determinada para cada sujeto de manera individual en función de la respuesta al tapiz durante cada sesión. Los resultados de este estudio indicaron que el grupo entrenado adquirió la marcha independiente significativamente antes en el tiempo en comparación con el grupo control. Igualmente en el grupo entrenado se observaron mejorías en relación a la marcha, como un aumento de velocidad de la misma y una disminución de la necesidad de asistencia para caminar.

JUSTIFICACIÓN, ESTRUCTURA, OBJETIVOS E HIPÓTESIS

El tapiz rodante asistido con soporte del peso corporal ha demostrado ser una buena herramienta para el tratamiento de rehabilitación en pacientes adultos, para el reentrenamiento de la marcha tras una lesión neurológica. La evidencia científica existente es abundante, sin embargo, en el caso de la población pediátrica en general, la evidencia disponible es insuficiente. Aún así, varios estudios sugieren un efecto positivo del uso del tapiz rodante para la mejora de la marcha[54].

En rehabilitación pediátrica, el entrenamiento de la marcha con el tapiz rodante se ha llevado a cabo en sujetos con diagnósticos médicos muy variados, destacando parálisis cerebral[8,55,56], síndrome de Down[38,57] y lesiones medulares[34]. La mayoría de estos estudios, que se realizan con soporte manual del peso corporal del sujeto, han demostrado una mejora en las capacidades motrices de estos niños después de recibir la intervención[3,48,58]. Sin embargo, presentan limitaciones que no permiten obtener conclusiones suficientemente fiables como para tomar decisiones de implementación del tapiz rodante dentro de la población pediátrica de manera protocolizada y estandarizada. Las muestras estudiadas han sido pequeñas (en muchos casos encontramos solamente estudios piloto, sin grupo control), y la información proporcionada en los ensayos es insuficiente para realizar una lectura crítica de los mismos. Además, hay gran diversidad de tipos de intervención con el tapiz (por ejemplo: diferencias en frecuencia de entrenamiento, velocidad de la cinta del tapiz, duración de la sesión y duración de la intervención), y de monitorización de las variables de estudio (las escalas de valoración utilizadas para valorar el desarrollo motriz y detectar cambios han sido muy dispares y, por tanto, poco comparables). Igualmente, las edades de los sujetos estudiados han sido de un rango muy amplio, la mayoría centrándose en niños mayores de 6 años y, por tanto, que ya tienen experiencia previa en la marcha (ya sea autónoma o asistida con ayudas técnicas u ortesis).

En términos generales, podemos concluir que se desconoce el impacto del entrenamiento con tapiz rodante en niños no diagnosticados pero clasificados como con riesgo de retraso en el desarrollo psicomotor. De manera más específica, este desconocimiento se encuentra en dos sentidos: (1) en relación a los posibles efectos de mejora sobre los parámetros de la marcha después de recibir entrenamiento con el tapiz rodante, y (2) en relación a la facilitación de la adquisición de la misma, a través del entrenamiento.

Los niños prematuros y/o los de bajo peso al nacer pueden tener un riesgo de retraso en la adquisición de la marcha independiente[2]. Igualmente se ha visto que el entrenamiento con el tapiz rodante promueve un aumento en la frecuencia de los pasos totales por minuto, y esto, a su vez, facilita la transición de un patrón múltiple de marcha (alta variabilidad en los tipos de pasos ejecutados por el sujeto) hacia una preferencia y selección motriz de los pasos alternos[59]. Dada la escasez de evidencia científica disponible en población con riesgo de retraso en el desarrollo motriz en relación al tapiz rodante y la adquisición de la marcha, queda justificado el planteamiento de nuevas investigaciones con bebés prematuros o de bajo peso al nacer para explorar tanto las respuestas al tapiz rodante, como los efectos que tendrá un entrenamiento de la marcha con el uso del tapiz. Así mismo, se justifica el realizar una revisión sistemática para aclarar el estado de la investigación actual en relación a la temática que nos ocupa: describir el estado de la cuestión sobre las intervenciones con tapiz rodante que se hayan realizado en investigación en niños con riesgo de retraso en el desarrollo motriz en relación a la marcha.

Esta tesis se divide en 5 capítulos, el primero de los cuales es esta introducción, seguida de dos artículos publicados (capítulos 2 y 3), y de los resultados de un estudio piloto (capítulo 4). Finalmente se presenta la discusión general con conclusiones finales, y con la reflexión sobre las limitaciones de esta tesis y las futuras líneas de investigación (capítulo 5).

Capítulo 2. ***Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay.***

Revisión sistemática registrada en el grupo *Cochrane Developmental Psychosocial and Learning Problems Group*, sobre las intervenciones con tapiz rodante con soporte del peso corporal en niños de hasta seis años de edad, con riesgo de retraso en el desarrollo motriz.

El objetivo de esta revisión sistemática fue evaluar la efectividad de la intervención con tapiz rodante sobre el desarrollo motriz en población pediátrica de hasta seis años de edad, en niños sin experiencia previa de la marcha (ya fuera marcha autónoma o dependiente de ayudas técnicas). Se incluyeron estudios con niños de edades comprendidas entre cero y seis años, y considerados con riesgo de retraso en el desarrollo motriz, independientemente de su diagnóstico médico, en el caso de que se hubiese establecido.

De esta revisión, siguiendo la guía metodológica que establecen las revisiones sistemáticas Cochrane, se derivaron dos publicaciones. En primer lugar se publicó el protocolo detallado de la revisión y, posteriormente, se llevó a cabo la revisión en sí misma, culminando el proceso con la publicación a texto completo.

Capítulo 3. ***Treadmill training in moderate risk preterm infants promotes stepping quality - Results of a small randomised controlled trial.***

Ensayo clínico controlado aleatorizado compuesto por datos de una muestra de población pediátrica, los cuales fueron recogidos previamente al inicio de esta tesis, en la *University of Michigan* (MI, USA). En este estudio se implementó un protocolo de entrenamiento con parámetros definidos con anterioridad y de acuerdo con la evidencia científica conocida de estudios similares[38]. El grupo experimental recibió entrenamiento de la marcha con el tapiz rodante en su propio domicilio, con la implicación activa de los padres o cuidadores para llevar a cabo dicho entrenamiento. La muestra de estudio tenía edades comprendidas de entre seis y trece meses de edad en el momento de entrada al estudio. Todos los sujetos incluidos fueron niños que habían sido

clasificados como con riesgo de retraso en el desarrollo motriz, bajo criterios médicos.

Los objetivos principales fueron los siguientes: (1) determinar si el entrenamiento con tapiz rodante en niños con riesgo de retraso en el desarrollo motriz conllevaba un aumento en la frecuencia de pasos alternos y una mejor calidad del paso en los niños del grupo de entrenamiento, (2) examinar si el entrenamiento con tapiz rodante adelantaba la edad de inicio de la marcha independiente en el grupo experimental, y (3) estudiar si existía una relación entre la respuesta al tapiz rodante y la edad del inicio de la marcha autónoma en la población con riesgo de retraso.

Las hipótesis de estudio fueron, respectivamente y en relación a cada objetivo: (1) que se observaría una mayor frecuencia de pasos alternos y una mejor calidad de los pasos en el grupo que recibió el entrenamiento, (2) que los niños entrenados iniciarían la marcha independiente más precozmente, en edades más tempranas en comparación con los sujetos del grupo control, y (3) que se encontraría una relación significativa y positiva entre la respuesta al tapiz rodante y la edad de inicio de la marcha autónoma.

Capítulo 4. Entrenamiento de la marcha con tapiz rodante y desarrollo psicomotor en mellizas prematuras

Estudio piloto donde se implementó el entrenamiento con tapiz rodante a una niña prematura tardía con signos objetivables de retraso (moderado) en el desarrollo motriz y cognitivo, en comparación con el patrón de evolución típica del desarrollo. Así mismo, se comparó con su hermana melliza, la cual también presentaba un retraso que, en su caso, se clasificó de muy leve, pudiéndose considerar dentro de los límites de la normalidad según la edad corregida por prematuridad. Ambas mellizas asistieron a un Centro de Desarrollo Infantil y Atención Precoz (CDIAP) en Sant Adrià del Besòs (Barcelona), donde recibieron sesiones semanales de fisioterapia. El protocolo de entrenamiento inicial se planteó según los parámetros de Ulrich *y col.*[38]. A través de un seguimiento semanal de la respuesta al tapiz, los parámetros del entrenamiento se fueron adaptando en función de la evolución del patrón de

marcha y del desarrollo motriz global de la melliza experimental. Por tanto, el entrenamiento fue individualizado.

El objetivo principal de este estudio fue evaluar si la intervención con el tapiz rodante contribuiría a disminuir las diferencias iniciales objetivadas a nivel de desarrollo motriz entre ambas mellizas, especialmente en relación a la motricidad gruesa, y también a la respuesta al tapiz rodante. La hipótesis fue que se observaría una aceleración mayor del desarrollo motriz en la melliza experimental, especialmente en los aspectos relacionados con la locomoción. Además, se consideró la posibilidad de que las diferencias iniciales observadas en comparación con su hermana melliza se verían progresivamente disminuidas.

CAPÍTULO 2.

Treadmill interventions with partial body weight support in children under 6 years of age at risk of neuromotor delay

Cochrane Database of Systematic Reviews

Protocolo de la Revisión

Valentin-Gudiol M, Girabent-Farrés M, Bagur-Calafat C, Mattern-Baxter K, Hadders-Algra M, Angulo-Barroso RM. Treadmill interventions with partial body weight support in children under 6 years of age at risk of neuromotor delay (Protocol). Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No.: CD009242.

Treadmill interventions with partial body weight support in children under 6 years of age at risk of neuromotor delay

Protocol information

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What's new

Date	Event	Description

History

Date	Event	Description

Abstract

Background

Objectives

Search methods

Selection criteria

Data collection and analysis

Main results

Authors' conclusions

Plain language summary

[Summary title]

[Summary text]

Background

Description of the condition

Typical gross motor development

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

Developmental delay

The *International Classification of Functioning, Disability and Health for Children and Youth* (ICFCY) (WHO 2005) describes developmental delay as retardation in the achievement of developmental milestones. The most plausible cause of the motor delay is an alteration in the typical development and function of the central nervous system. Motor delays in locomotor abilities are defined by standards used in clinical paediatric settings. For example, the onset of independent walking should occur prior to 18 months of corrected age, so the presence of a motor delay would not be considered before this age. Developmental delay in infants is usually diagnosed via routine screening (Case-Smith 1998) and/or the use of one or more of the following diagnostic tests: (1) norm-referenced tests; (2) criterion-referenced tests; (3) brain imaging techniques; (4) kinetic and kinematic analysis using force plates and video motion analysis. Although used for both research and clinical purposes, these tests are typically not good predictors for later outcomes and generally lack sensitivity in detecting small changes in motor development (Heineman 2008). In addition, in the paediatric population the reliability of some of these tests may be affected by the child's emotional state, by daily fluctuations in performance or by the experience of the tester. Due to the continuous developmental changes occurring in the young brain, early diagnostic tests are relatively limited in predicting developmental outcomes (de Graaf-Peters 2006) and the high level of variation in motor developmental trajectories in healthy children means that care has to be taken when interpreting results from motor assessments (Roze 2010).

Consequences of motor developmental delay

One of the major tasks in gross motor development is locomotion, the ability to move from one place to another (Bly 1995). The failure to attain walking or the late attainment of walking has consequences for the musculoskeletal system. The anatomy of the hip, for instance, needs weight bearing for proper bone growth and correct orientation of the femoral head, as well as for a correct alignment of the spine (Campbell 2006). As well as its importance for subsequent motor skill development, acquiring the ability to locomote is important for infants because of its impact on cognitive, social and emotional skills. Researchers have demonstrated that for infants with typical development, experience with locomotion is associated with the development of a broad array of cognitive skills, including the onset of wariness of heights; the concept of object permanence (objects hidden from sight still exist); a shift from self-centred to landmark-based spatial coding strategies; the ability to follow the pointing gestures and gaze of another person, and aspects of social referencing and detour reaching (Bertenthal 1984; Kermoian 1988; Campos 1989; Bertenthal 1990).¬This suggests that infants are better able to develop spatial cognition and learn about the world around them as they become able to locomote independently. Children who can walk independently show improved active exploration of their environment, as opposed to children who passively observe the environment when being held or carried through space.¬Rosenbloom 1971 further suggests that the quality of movement may affect subsequent development. He proposes that inefficient locomotion may hamper development by limiting the attention and energy that infants spend on exploration of the environment. Moreover, early locomotor experiences may have a larger impact on the developing brain than similar experiences at a later age due to the brain's high plasticity during the first few postnatal years (Webb 2001; de Graaf-Peters 2006). Earlier achievement of developmental milestones, in particular independent walking, have also been associated with better intellectual performance in adulthood (Murray 2007). In summary, independent locomotion at early age not only facilitates the infant's motor development, but also impacts other developmental domains and affects quality of life for the child and his or her family.

Population affected

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

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

The incidence of preterm birth rate is 6.2% in Europe, 10.6% in North America (excluding Mexico) and 6.4% in Australia

(Beck 2010) and the incidence of CP is 1.5 to 2 per 1000 live births (Surveillance CP Europe). However, more epidemiological studies are needed to reliably assess the incidence for CP as its causes are not fully understood (Lie 2010). Approximately one in 800 children in the USA are born with Down syndrome, while the incidence in the UK is one in 1000 (Down's Syndrome Association).

Description of the intervention

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

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

Locomotor treadmill interventions, with and without partial weight support, have been shown to promote the acquisition of independent walking in children with Down Syndrome (DS). Therefore, it can be used to prevent delay in the onset of walking. Ulrich 2001 found that children with DS who received intensive stepping practice on a treadmill with partial body weight support began walking independently 101 days sooner than their peers who were not exposed to treadmill stepping. In a subsequent study, it was found that children with DS who engaged in high frequency intervention protocols showed better results than children with low frequency intervention protocols (Ulrich 2008).

Locomotor treadmill interventions have also been used for children with cerebral palsy (CP) (Richards 1997; Begnoche 2007; Mattern-Baxter 2009). For both children with DS and children with CP, treadmill interventions not only enhanced the onset of independent walking but also improved the quality of step type (Looper 2006; Cherng 2007).

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

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

How the intervention might work

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

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

Plausible positive outcomes from treadmill interventions via CNS plasticity have been proposed in infants with DS and premature infants. Evidence from studies with children who have Down Syndrome indicate statistically significant

improvements in a variety of outcome measures including obstacle negotiation and onset of walking. For this population, two main benefits from treadmill interventions implemented during early development have been described. Firstly, it promotes the transition to continuous alternating steps in infants (including typically developing infants (Thelen 1986; Thelen 1991)), which is an important precursor to walking (Ulrich 1992; Ulrich 1995; Ulrich 2001). Secondly, it leads to an acceleration of the onset of independent walking and an improvement of the quality of gait (Ulrich 2001).

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

Why it is important to do this review

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

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

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

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

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

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

Objectives

To assess the effectiveness of treadmill interventions in preambulatory infants and children under six years of age who are at risk of neuromotor delay.

Methods

Criteria for considering studies for this review

Types of studies

Randomised controlled trials, quasi-randomised controlled trials (that is, where participants are allocated in a way that is not strictly speaking random, such as by alternation or date of birth) and controlled clinical trials.

Types of participants

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

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

Types of interventions

Treadmill intervention of any type, frequency or intensity, aimed at (1) improving gait parameters such as walking speed, endurance, quality of step (how the foot lands on the floor surface) or (2) facilitating onset of independent walking or walking with assistive devices.

Comparison groups will be no treatment or another treatment. Control group treatments may include physical therapy or another intervention designed to improve gait. We will include studies in which treadmill intervention is an adjunctive treatment. We will also report on studies comparing different types of treadmill interventions.

Types of outcome measures

We will accept five types of outcome measures: standardized measures, questionnaires, self-report data, data from motion analysis systems and coded-video observations. Based on the ICFCY, we will assess the following outcomes.

Primary outcomes

A. Body functions - Neuromusculoskeletal and movement related functions - Gait pattern functions.

1. Step frequency (number of steps per minute).
2. Step quality (foot doing toe versus flat contact during treadmill stepping).

B. Activities and participation functions.

1. Age of onset of independent walking.
2. Age of onset of walking with assistive devices.
3. Gross motor function.
4. Falls and injuries due to falls.

Secondary outcomes

C. Body functions - Neuromusculoskeletal and movement related functions - Gait pattern functions.

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

D. Activities and participation functions.

1. Infant or child quality of life.

If data permit, we will examine outcomes by intervention type (preventive or rehabilitative) and by diagnosis (for example CP, DS and other).
We will include the primary outcomes in a 'Summary of findings' table, if data permit.

Search methods for identification of studies

Electronic searches

We will search the following electronic databases with no language restrictions.

MEDLINE
EMBASE
CINAHL
PsycINFO
LILACS (Latin American and Caribbean Health Sciences Literature)
PEDro
Science Citation Index
Conference Proceedings Citation Index
metaRegister of Controlled Trials
National Research Register Archive (UK)
Center Watch Clinical Trials Listing Service (USA)

We will also search Trials Registers - Clinical Trials.gov and WHO ICTRP.

For dissertations, we will perform a search in WorldCat.

We will use the following search strategy, modified as required for each database.

1 Physical Therapy Modalities/
2 "Physical Therapy (Specialty)"/
3 (physiotherap$ or physio therap$ or physical therap$).tw.
4 Exercise Therapy/
5 tread-mill$.tw.
6 treadmill$.tw.
7 or/1-6
8 Motor Skills/
9 Motor Skills Disorders/
10 Motor Activity/
11 Psychomotor Disorders/
12 Psychomotor Performance/
13 Movement Disorders/
14 Developmental Disabilities/
15 ((motor or neuromotor or neuro-motor or psychomotor or psycho-motor or development$) adj3 (impair$ or skill$ or disorder$ or deficit$ or delay$ or disabilit$)).tw.
16 exp Walking/

17 Gait/
18 Gait Disorders, Neurologic/
19 Gait Ataxia/
20 gait.tw.
21 locomotion/
22 (walk or walking).tw.
23 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory).tw.
24 (locomotor$ or locomotion$).tw.
25 stepping.tw.
26 or/8-25
27 Disabled Children/
28 down syndrome/
29 cerebral palsy/
30 spinal dysraphism/
31 (down$ syndrome or cerebral pals$ or (spin$ adj3 injur$) or spina bifida).tw.
32 exp infant, low birth weight/ or infant, premature/
33 (low birth weight or pre-term$ or preterm$ or prematur$).tw.
34 or/27-33
35 Infant/
36 exp child/
37 (baby or babies or infant$ or child$ or toddler$ or pre-school$ or preschool$ or schoolchild$).tw.
38 35 or 36 or 37
39 randomized controlled trial.pt.
40 controlled clinical trial.pt.
41 randomi#ed.ab.
42 placebo$.ab.
43 drug therapy.fs.
44 randomly.ab.
45 trial.ab.
46 groups.ab.
47 or/39-46
48 exp animals/ not humans.sh.
49 47 not 48
50 7 and 26 and 38
51 7 and 34 and 38
52 50 or 51
53 49 and 52

Searching other resources

1. We will identify studies incorporated in previous systematic reviews and other reviews of the subject to consider them for inclusion.
2. We will also read bibliographies of articles identified through the search strategy for additional sources for inclusion.
3. We will evaluate unpublished abstracts and dissertations for possible inclusion.

Data collection and analysis

Selection of studies

We will divide the titles and abstracts yielded by the search strategy into two blocks. Two authors will independently screen the first block of references (KMB and CB), while two other authors will do so with the second block (RA and MV), using the inclusion criteria described above. RA will be the arbiter for KMB and CB, while KMB will fulfil this role for RA and MV, in case of discrepancies. We will then obtain the selected titles in full text to determine their relevance for the review. We will resolve disagreement about eligibility through discussion, and when disagreements cannot be resolved, by seeking advice from another author (MHA). We will record the reasons for excluding trials.

Data extraction and management

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

Assessment of risk of bias in included studies

Three authors (CB, MV and RA) will independently assess the risk of bias of each included study using the Cochrane Collaboration's tool for assessing risk of bias (Higgins 2008).¬Review authors will independently assess the risk of bias within each included study in relation to the following six domains on the basis of ratings of low risk of bias, high risk of bias and unclear risk of bias: sequence generation; allocation concealment; blinding; incomplete outcome data (including data on attrition and exclusions; differentiating intention-to-treat analyses from per-protocol ("as treated") analyses); selective outcome reporting, and other risks of bias**.** We will enter these judgements into a 'Risk of bias' table in Review Manager 5.1 (Review Manager 2011) with a brief rationale for the judgements.

Details on the possible sources of bias are below.

Sequence generation

We will describe the method used to generate the allocation sequence in detail so as to assess whether it should have produced comparable groups. We will evaluate whether or not the allocation concealment sequence was adequately generated.

Allocation concealment

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

Blinding

We will describe any measures used to blind outcome assessors so as to assess whether knowledge of the allocated intervention was adequately prevented. It is not possible to blind either those who deliver the therapy (treadmill training) or those infants who receive it, due to the nature of the intervention. Our assessment of risk of bias will take into account the likely bias attributable to the inability to blind participants or personnel in such interventions.

Incomplete outcome data

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

Selective reporting

We will make attempts to assess the possibility of selective outcome reporting by investigators. We will evaluate if each study is free from selective outcome reporting by following these judgements:

- low risk of bias, when all collected data seems to be reported;
- unclear risk of bias, when it is not clear whether other data was collected and not reported;
- high risk of bias, when the data from some measures used in the trial are not reported.

Other risks of bias

We will assess the extent to which each study is apparently free of other problems that could put it at high risk of bias, by describing important concerns not addressed in the other domains with the Cochrane Collaboration's 'Risk of bias' tool. We will assess other threats to validity as 'low risk of bias' if the study appears to be free of other sources of bias. Where the risk of bias is unclear from published information, we will attempt to contact the authors for clarification. If that fails, we will then classify that study as at unclear risk of bias.

Measures of treatment effect

We will use the Cochrane Collaboration's Review Manager software (RevMan 5.1) to calculate the adjustments of measures of treatment effects (Review Manager 2011).

Continuous data

We will analyse continuous data if means and standard deviations are reported, can be obtained from primary investigators or can be calculated from the available data. If continuous outcomes are measured identically across studies, we will calculate the mean difference (MD) with 95% confidence interval (CI). If the same continuous outcome (for example, infant's gross motor development level) is measured differently across studies, we will compare standardised mean differences (SMD) with 95% CI across studies (Higgins 2008). Where necessary, we will use formulas to convert F ratios, t-values and chi-square values into SMDs (Lipsey 2001), using Hedges *g* to correct for small sample bias.

Dichotomous data

We will analyse the outcomes of any study reporting binary/dichotomous data by calculation of the risk ratio for the occurrence of an event (rather than a non-event) for its consistency as a summary statistic and ease of interpretation.

Unit of analysis issues

The authors will take into account the unit of analysis to determine whether: (1) individuals were randomised in groups¬(i.e. cluster-randomised trials); (2) results were reported at multiple time points, and (3) individuals simultaneously received multiple interventions.

Cluster-randomised trials

For trials that use clustered randomisation, we will present results with proper controls for clustering (robust standard errors or¬hierarchical linear model). If appropriate controls are not used and it is not possible to obtain the full set of each individual participant's data, we will control the data for clustering using the procedures outlined by Higgins 2008.¬For dichotomous outcome measures, we will divide the number of events and the number of participants per trial arm by the design effect [1 + (1-m)*r], where *m* is the average cluster size and *r* is the intra-cluster correlation coefficient (ICC).¬ For continuous outcome measures, we will divide the number of participants per trial arm by the design effect, with the mean values unchanged.¬To determine the ICC, we will use estimates in the primary trials on a study-by-study basis.¬In the case of these values not

being reported, we will use external estimates of the ICC that are appropriate to the context of each trial and average cluster size. If they were still not available, we will then use statistical procedures outlined by Higgins 2008.

Cross-over trials

We will combine the results from cross-over trials with those of parallel group trials. In cross-over trials, we will only include the first phase before the point of cross-over in the analyses. In case of not having the results for the first phase separated from the rest, we will contact the authors to obtain these data.

Multiple time points

When the results are measured at multiple time points, we will only consider baseline measurements and the last time point measurements.

Multiple interventions per individual

If it is found that participants in some trials receive multiple treatments, we will conduct meta-analysis on those studies separately: the treadmill intervention plus treatment as usual arm will be compared to treatment as usual alone. ¬

Dealing with missing data

We will assess missing data and dropouts in the included studies. We will investigate and report the reasons, numbers and characteristics of dropouts. We will make efforts to contact the authors when further information or data are necessary.

For dichotomous data, we will report the missing data and dropouts for included studies along with the number of participants who are included in the final analyses as a proportion of all participants in each study. We will provide reasons for missing data in a narrative summary. The extent to which the results of the review could be altered by the missing data can be assessed based on consideration of best-case and worst-case scenarios (Gamble 2005). The best-case scenario is the one where all participants with missing outcomes in the experimental condition had good outcomes and all those with the missing outcomes in the control condition had poor outcomes, and the worst-case scenario is vice versa (Higgins 2008). However, the best-case and worst-case scenarios method is too extreme and a more plausible approach is needed. We will use the method suggested by Higgins 2008, which can incorporate specific reasons for missing data and considers plausible event risks among missing participants in relation to risks among those observed.

We will analyse missing continuous data either on an endpoint basis, including only participants with a final assessment, or using last observation carried forward to the final assessment if the¬last observation carried forward data were reported by the trial authors. If SDs are missing, we will make attempts to obtain these data through contacting trial authors. If SDs are not available from trial authors, we will calculate them from t-values, confidence intervals or standard errors, where reported in¬articles (Deeks 1997a; Deeks 1997b). If these additional figures are still not available or obtainable, we will not include the study data in the comparison of interest.

Assessment of heterogeneity

We anticipate finding considerable heterogeneity across studies that might be included in this review. We will assess clinical heterogeneity by comparing the distribution of important participant factors among trials (for example, age, diagnosis), and trial factors (for example, randomisation concealment, blinding of outcome assessment, form of treadmill training, losses to follow-up). We will describe statistical heterogeneity using I^2 (Higgins 2002), a quantity that describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error). In addition, we will employ a chi^2 test of homogeneity to determine the strength of evidence that heterogeneity is genuine.

If an individual study appears to be an outlier, we may carry out sensitivity analysis with and without the study. If the primary studies are judged to be substantially heterogeneous even within these sub-groupings, we will only give a descriptive analysis, particularly if there is variation in direction of effect.

Assessment of reporting biases

In order to investigate the relationship between effect size and standard error, we will draw funnel plots if sufficient studies are available (i.e., ten or more individuals studies).¬Asymmetry could be attributable to publication bias, but might also reflect a real relationship between trial size and effect size. if we find such a relationship, we will examine clinical variation of the studies (Higgins 2008, Section 10.4). As a direct test for publication bias, we will compare results extracted from published journal reports with results obtained from other sources, including correspondence.

Data synthesis

We will synthesise the data using RevMan 5.1, the latest version of the Cochrane Collaboration's meta-analysis software (Review Manager 2011).¬We anticipate finding small trials, with sparse amounts of data. We propose to use the Mantel-Haenszel method, the default fixed-effect method in RevMan 5.1 (Higgins 2008, section 9.4.4.1). This method can pool odds ratios, risk ratios and risk differences.

For continuous variables, we will apply the mean difference approach where data allow.

For dichotomous outcomes, we will also calculate the number needed to treat for an additional beneficial outcome.

When meta-analysis is inappropriate, we will provide a narrative description of the study results.

Subgroup analysis and investigation of heterogeneity

We will undertake subgroup analysis if clinically different interventions are identified or there are clinically relevant differences between participant groups. We will thus investigate any subgroup differences in order to establish whether there is a single

intervention effect, specifically:

- treadmill 'dose' (total number of training sessions, frequency of training per week or duration of each training session);
- type of intervention (preventive or rehabilitative);
- diagnosis (cerebral palsy, Down's syndrome etc.);
- conditions affecting the neuro-musculoskeletal system (hypo- or hypertonia, spasticity, posture etc.).

Sensitivity analysis

We will conduct sensitivity analysis, where data permit, to determine whether findings are sensitive to restricting inclusion to studies judged to be at low risk of bias. In these analyses, we will re-evaluate the findings, limiting the inclusion to published studies or to those studies that have a low risk of:

- selection bias (associated with allocation concealment and sequence generation);
- performance bias (associated with blinding);
- attrition bias (associated with completeness of data).

Results

Description of studies

Results of the search

Included studies

Excluded studies

Risk of bias in included studies

Allocation (selection bias)

Blinding (performance bias and detection bias)

Incomplete outcome data (attrition bias)

Selective reporting (reporting bias)

Other potential sources of bias

Effects of interventions

Discussion

Summary of main results

Overall completeness and applicability of evidence

Quality of the evidence

Potential biases in the review process

Agreements and disagreements with other studies or reviews

Authors' conclusions

Implications for practice

Implications for research

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Contributions of authors

MV and RA wrote this protocol. MG contributed by developing the methods section, while KMB, MHA and CB helped revising the final draft.

Declarations of interest

- Marta Valentin Gudiol - None known.
- Rosa Maria Angulo-Barroso - Participated in the design and publication of some articles that are referenced in this protocol and may be included in the review.
- Caritat Bagur Calafat - None known.
- Mijna Hadders-Algra - None known.
- Montserat Girabent Farrés - None known.

- Katrin Mattern-Baxter - Participated in the design and publication of some articles that are referenced in this protocol and may be included in the review.

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Excluded studies

Studies awaiting classification

Ongoing studies

Other references

Additional references

Adolph 1998

Adolph KE, Vereijken B, Denny MA. Learning to crawl. Child Development 1998;69(5):1299-312.

Angulo-Barroso 2010

Angulo-Barroso RM, Tiernan CW, Chen LC, Ulrich D, Neary H. Treadmill responses and physical activity levels of infants at risk for neuromotor delay. Pediatric Physical Therapy 2010;22(1):61.

Barbeau 1987

Barbeau H, Rossignol S. Recovery of locomotion after chronic spinalization in the adult cat. Brain Research 1987; 412(1):84-95.

Beck 2010

Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bulletin of the World Health Organization 2010;88(1):31-8.

Begnoche 2007

Begnoche DM, Pitetti KH. Effects of traditional treatment and partial body weight treadmill training on the motor skills of children with spastic cerebral palsy: a pilot study. Pediatric Physical Therapy 2007;19(1):11-9.

Bernitsky-Beddingfield 2007

Bernitsky-Beddingfield A, Burtner PA, Caprihan A, Phillips JP, Provost B, Sullivan KJ. Ankle dorsiflexion fMRI in children with cerebral palsy undergoing intensive body-weight supported treadmill training: a pilot study. Developmental Medicine and Child Neurology 2007;49(1):39.

Bertenthal 1984

Bertenthal BI, Campos JJ, Barrett KC. Self-produced locomotion: an organizer of emotional, cognitive, and social development in infancy. In: Emde RHarmon R, editors(s). Continuities and Discontinuities in Development. New York: Plenum, 1984:175–210.

Bertenthal 1990

Bertenthal BI, Campos JJ. A systems approach to the organizing effects of self-produced locomotion during infancy. Advances in Infancy Research 1990;6:1-60.

Blackman 2002

Blackman JA. Early intervention: a global perspective. Infants and Young Children 2002;15(2):11-9.

Bly 1995

Bly L, Ariz TN. Motor skills acquisition in the first year, an illustrated guide to normal development. Pediatric Physical Therapy 1995;7(2):86.

Bodkin 2003

Bodkin AW, Baxter RS, Heriza CB. Treadmill training for an infant born preterm with a grade III intraventricular hemorrhage. Physical Therapy 2003;83(12):1107.

Campbell 2006

Campbell SK, Palisano RJ, Vander Linden DW. Physical Therapy for Children. St Louis, Missouri: Elsevier Saunders, 2006.

Campos 1989

Campos JJ, Bertenthal BI. Locomotion and psychological development in infancy. Applied Developmental Psychology 1989; 2:230–58.

Case-Smith 1998

Case-Smith J, Heaphy T, Marr D, Galvin B, Koch V, Ellis MG et al. Fine motor and functional performance outcomes in preschool children. American Journal of Occupational Therapy 1998;52:10.

Cernak 2008

Cernak K, Stevens V, Price R, Shumway-Cook A. Locomotor training using body-weight support on a treadmill in conjunction with ongoing physical therapy in a child with severe cerebellar ataxia. Physical Therapy 2008;88(1):88.

Cherng 2007

Cherng R, Liu C, Lau T, Hong R. Effects of treadmill training with body weight support on gait and gross motor function in children with spastic cerebral palsy. American Journal of Physical Medicine and Rehabilitation 2007;86(7):548-55.

Cotman 2002

Cotman CW, Berchtold NC. Exercise: a behavioral intervention to enhance brain health and plasticity. Trends in Neurosciences 2002;25(6):295-301.

Cotman 2002a

Cotman CW, Engesser-Cesar C. Exercise enhances and protects brain function. Exercise and Sport Sciences Reviews 2002;30(2):75.

Damiano 2006

Damiano DL. Activity, activity, activity: rethinking our physical therapy approach to cerebral palsy. Physical Therapy 2006; 86(11):1534.

Damiano 2009

Damiano DL, de Jong SL. A systematic review of the effectiveness of treadmill training and body weight support in paediatric rehabilitation. Journal of Neurologic Physical Therapy 2009;33(1):27-44.

Davis 1994

Davis DW, Thelen E, Keck J. Treadmill stepping in infants born prematurely. Early Human Development 1994;39(3):211-23.

Day 2004

Day JA, Fox EJ, Lowe J, Swales HB, Behrman AL. Locomotor training with partial body weight support on a treadmill in a nonambulatory child with spastic tetraplegic cerebral palsy: a case report. Pediatric Physical Therapy 2004;16(2):106.

de Bode 2007

de Bode S, Mathern GW, Bookheimer S, Dobkin B. Locomotor training remodels fMRI sensorimotor cortical activations in children after cerebral hemispherectomy. Neurorehabilitation and Neural Repair 2007;21(6):497.

de Graaf-Peters 2006

de Graaf-Peters VB, Hadders-Algra M. Ontogeny of the human central nervous system: what is happening when? Early Human Development 2006;82(4):257-66.

de Graaf-Peters 2007

de Graaf-Peters VB, Blauw-Hospers CH, Dirks T, Bakker H, Bos AF, Hadders-Algra M. Development of postural control in typically developing children and children with cerebral palsy: possibilities for intervention? Neuroscience and Biobehavioral Reviews 2007;31(8):1191-200.

Deeks 1997a

Deeks J. Are you sure that's a standard deviation? (part 1). Cochrane News 1997;10:11-2.

Deeks 1997b

Deeks J. Are you sure that's a standard deviation? (part 2). Cochrane News 1997;11:11-2.

Dodd 2007

Dodd KJ, Foley S. Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: a clinical controlled trial. Developmental Medicine and Child Neurology 2007;49(2):101-5.

Down's Syndrome Association

What is the incidence of Down's Syndrome? http://www.downs-syndrome.org.uk/component/content/article/35-general/159-3-what-is-the-incidence-of-downs-syndrome.html (accessed 19 April 2011).

Edgerton 1997

Edgerton VR, de Leon RD, Tillakaratne N, Recktenwald MR, Hodgson JA, Roy RR. Use-dependent plasticity in spinal stepping and standing. Advances in Neurology 1997;72:233-47.

Eidelberg 1980

Eidelberg E, Story JL, Meyer BL, Nystel J. Stepping by chronic spinal cats. Experimental Brain Research 1980;40(3):241-6.

Eng 2007

Eng JJ, Tang PF. Gait training strategies to optimize walking ability in people with stroke: a synthesis of the evidence. Expert Review of Neurotherapeutics 2007;7(10):1417-36.

Eyre 2003

Eyre JA. Development and plasticity of the corticospinal system in man. Neural Plasticity 2003;10(1-2):93-106.

Formiga 2011

Formiga CKMR, Linhares MBM. Motor development curve from 0 to 12 months in infants born preterm. Acta Paediatrica 2011;100(3):379-84.

Gamble 2005

Gamble C, Hollis S. Uncertainty method improved on best-worst case analysis in a binary meta-analysis. Journal of Clinical Epidemiology 2005;58(6):579-88.

Goyen 2002

Goyen TA. Longitudinal motor development of apparently normal high-risk infants at 18 months, 3 and 5 years. Early Human Development 2002;70(1-2):103-15.

Hadders-Algra 1996

Hadders-Algra M, Brogren E, Forssberg H. Training affects the development of postural adjustments in sitting infants. The Journal of Physiology 1996;493(Pt 1):289-98.

Harbourne 2003

Harbourne RT, Stergiou N. Nonlinear analysis of the development of sitting postural control. Developmental Psychobiology 2003;42(4):368-377.

Heineman 2008

Heineman KR, Hadders-Algra M. Evaluation of neuromotor function in infancy -¬ a systematic review of available methods. Journal of Developmental and Behavioral Pediatrics 2008;29(4):315-23.

Higgins 2002

Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in Medicine 2002;21(11):1539-58.

Higgins 2008

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 [Updated February 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

Hodgson 1994

Hodgson JA, Roy RR, de Leon R, Dobkin B, Edgerton VR. Can the mammalian lumbar spinal cord learn a motor task? Medicine and Science in Sports and Exercise 1994;26(12):1491-7.

Jones 1999

Jones TA, Chu CJ, Grande LA, Gregory AD. Motor skills training enhances lesion-induced structural plasticity in the motor cortex of adult rats. Journal of Neuroscience 1999;19(22):10153-63.

Kermoian 1988

Kermoian R, Campos JJ. Locomotor experience: a facilitator of spatial cognitive development. Child Development 1988;

59(4):908-17.

Kleim 2008

Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. Journal of Speech, Language, and Hearing Research 2008;51(1):S225-39.

Lie 2010

Lie KK, Grøholt EK, Eskild A. Association of cerebral palsy with Apgar score in low and normal birthweight infants: population based cohort study. BMJ 2010;341:c4990.

Lipsey 2001

Lipsey MW, Wilson DB. Practical meta-analysis. Sage Publications, Inc., 2001.

Looper 2006

Looper J, Wu J, Angulo-Barroso R, Ulrich D, Ulrich B. Changes is step variability of new walkers with typical development and with Down Syndrome. Journal of Motor Behavior 2006;38(5):367-72.

Luo 2009

Luo H, Chen P, Hsieh W, Lin K, Lu T, Chen WJ et al. Associations of supported treadmill stepping with walking attainment in preterm and full-term infants. Physical Therapy 2009;89(11):1215-25.

Mattern-Baxter 2009

Mattern-Baxter K, Bellamy S, Mansoor J. Effects of intensive locomotor treadmill training on young children with cerebral palsy. Pediatric Physical Therapy 2009;21(4):308-18.

Mattern-Baxter 2009a

Mattern-Baxter K. Effects of partial body weight supported treadmill training on children with cerebral palsy. Pediatric Physical Therapy 2009;21(1):12-22.

Meyer-Heim 2007

Meyer-Heim A, Borggraefe I, Ammann-Reiffer C, Berweck S, Sennhauser FH, Colombo G et al. Feasibility of robotic-assisted locomotor training in children with central gait impairment. Developmental Medicine and Child Neurology 2007; 49(12):900-6.

Molina-Rueda 2010

Molina-Rueda F, Aguila-Maturana AM, Molina-Rueda MJ, Miangolarra-Page JC. Treadmill training with or without partial body weight support in children with cerebral palsy: systematic review and meta-analysis [Pasarela rodante con o sin sistema de suspensión del peso corporal en niños con parálisis cerebral infantil: revisión sistemática y metaanálisis]. Revista de Neurologia 2010;51(3):135-45.

Murray 2007

Murray GK, Jones PB, Kuh D, Richards M. Infant developmental milestones and subsequent cognitive function. Annals of Neurology 2007;62(2):128-36.

Mutlu 2009

Mutlu A, Krosschell K, Spira DG. Treadmill training with partial body-weight support in children with cerebral palsy: a systematic review. Developmental Medicine and Child Neurology 2009;51(4):268-75.

Nelson 2000

Nelson CA. Neural plasticity and human development: the role of early experience in sculpting memory systems. Developmental Science 2000;3(2):115-36.

Newell 1991

Newell KM. Motor skill acquisition. Annual Review of Psychology 1991;42:213-37.

Pin 2010

Pin TW, Eldridge B, Galea MP. Motor trajectories from 4 to 18 months corrected age in infants born at less than 30 weeks of gestation. Early Human Development 2010;86(9):573-80.

Prins 2010

Prins SA, von Lindern JS, van Dijk S, Versteegh FGA. Motor development of premature Infants born between 32 and 34 weeks. International Journal of Pediatrics 2010 Sept 7 [Epub ahead of print]:4 pages.

Prosser 2007

Prosser LA. Locomotor training within an inpatient rehabilitation program after pediatric incomplete spinal cord injury. Physical Therapy 2007;87(9):1224-32.

Provost 2007

Provost B, Dieruf K, Burtner PA, Phillips JP, Bernitsky-Beddingfield A, Sullivan K et al. Endurance and gait in children with cerebral palsy after intensive body weight-supported treadmill training. Pediatric Physical Therapy 2007;19(1):2-10.

Review Manager 2011

Review Manager (RevMan) [Computer program]. Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Richards 1997

Richards CL, Malouin F, Dumas F, Marcoux S, Lepage C, Menier C. Early and intensive treadmill locomotor training for young children with cerebral palsy: a feasibility study. Pediatric Physical Therapy 1997;9(4):158-65.

Riethmuller 2009

Riethmuller AM, Jones RA, Okely AD. Efficacy of interventions to improve motor development in young children: a systematic review. Pediatrics 2009;124(4):e782-92.

Rosenbloom 1971

Rosenbloom L. The contribution of motor behaviour to child development. Physiotherapy 1971;57(4):159-62.

Roze 2010

Roze E, Meijer L, Van Braeckel KNJA, Ruiter SAJ, Bruggink JLM, Bos AF. Developmental trajectories from birth to school age in healthy term-born children. Pediatrics 2010;126(5):e1134-42.

Schindl 2000

Schindl MR, Forstner C, Kern H, Hesse S. Treadmill training with partial body weight support in nonambulatory patients with cerebral palsy. Archives of Physical Medicine and Rehabilitation 2000;81(3):301-6.

Stiles 2000

Stiles J. Neural plasticity and cognitive development. Developmental Neuropsychology 2000;18(2):237-72.

Stiles 2005

Stiles J, Reilly J, Paul B, Moses P. Cognitive development following early brain injury: evidence for neural adaptation. Trends in Cognitive Sciences 2005;9(3):136-43.

Sullivan 2007

Sullivan K, Brown D, Klasses T, Mulroy S, Ge T, Azen S et al. Effects of task-specific locomotor and strength training in adults who were ambulatory after stroke: Results of the STEPS randomized clinical trial. Physical Therapy 2007; 87(12):1580-602.

Surveillance CP Europe

Surveillance of Cerebral Palsy in Europe. http://www-rheop.ujf-grenoble.fr/scpe2/site_scpe/index.php (accessed 5 March 2011).

Sveistrup 1997

Sveistrup H, Woollacott MH. Practice modifies the developing automatic postural response. Experimental Brain Research 1997;114(1):33-43.

Thelen 1986

Thelen E. Treadmill-elicited stepping in 7-month-old infants. Child Development 1986;57(6):1498-506.

Thelen 1991

Thelen E, Ulrich BD. Hidden skills: a dynamic systems analysis of treadmill stepping during the first year. Monographs of the Society for Research in Child Development 1991;56(1):1-98.

Ulrich 1992

Ulrich BD, Ulrich DA, Collier DH. Alternating stepping patterns - hidden abilities of 11-month-old infants with Down Syndrome. Developmental Medicine and Child Neurology 1992;34(3):233-9.

Ulrich 1995

Ulrich BD, Ulrich DA, Collier DH, Cole EL. Developmental shifts in the ability of infants with Down Syndrome to produce treadmill steps. Physical Therapy 1995;75(1):14-23.

Ulrich 2001

Ulrich DA, Ulrich BD, Angulo-Kinzler RM, Yun J. Treadmill training of infants with Down Syndrome: evidence-based developmental outcomes. Pediatrics 2001;108(5):e84.

Ulrich 2008

Ulrich DA, Lloyd MC, Tiernan CW, Looper JE, Angulo-Barroso RM. Effects of intensity of treadmill training on developmental outcomes and stepping in infants with Down Syndrome: a randomized trial. Physical Therapy 2008;88(1):114-22.

Verschuren 2008

Verschuren O, Ketelaar M, Takken T, Helders PJM, Gorter JW. Exercise programs for children with cerebral palsy: a systematic review of the literature. American Journal of Physical Medicine and Rehabilitation 2008;87(5):404-17.

Webb 2001

Webb SJ, Monk CS, Nelson CA. Mechanisms of postnatal neurobiological development: implications for human development. Developmental Neuropsychology 2001;19(2):147-71.

WHO 2005

International classification of functioning, disability and health for children and youth. http://www3.who.int/icf/onlinebrowser/icf.cfm?undefined&version = 7 (accessed 10 February 2011).

WHO 2006

WHO Multicentre Growth Reference Study Group. Motor Development Study: windows of achievement for six gross motor development milestones. Acta Paediatrica 2006;Suppl 450:86-95.

Willoughby 2009

Willoughby KL, Dodd KJ, Shields N. A systematic review of the effectiveness of treadmill training for children with cerebral palsy. Disability and Rehabilitation 2009;31(24):1971-9.

Ziviani 2010

Ziviani J, Feeney R, Rodger S, Watter P. Systematic review of early intervention programmes for children from birth to nine years who have a physical disability. Australian Occupational Therapy Journal 2010;57(4):210-23.

Other published versions of this review

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Data and analyses

Figures

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Feedback

Appendices

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Valentin-Gudiol M, Mattern-Baxter K, Girabent-Farrés M, Bagur-Calafat C, Hadders-Algra M, Angulo-Barroso RM. Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay. Cochrane Database of Systematic Reviews 2011;12 [Art. No.: CD009242].

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

Valentin-Gudiol M, Mattern-Baxter K, Girabent-Farrés M, Bagur-Calafat C, Hadders-Algra M, Angulo-Barroso RM

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TABLE OF CONTENTS

[Intervention Review]

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

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ABSTRACT

Background

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

Objectives

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

Search methods

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

Selection criteria

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

Data collection and analysis

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

Main results

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

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

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

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

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

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

Authors' conclusions

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

PLAIN LANGUAGE SUMMARY

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

Children who have a diagnosis of Down syndrome or cerebral palsy, or who are born pre-term, may be delayed in their motor development. Delays in motor development limit children's ability to move and achieve motor milestones such as walking, running and jumping. Helping children to walk is often the focus of therapeutic intervention. There is a body of literature to suggest that the best

way to do this is by getting the child to practice stepping with appropriate support. Treadmill training, in which the child is supported by a harness, provides an opportunity for children to walk with support for long enough periods of time to acquire the necessary motor abilities for independent walking.

This review included five trials involving children under six years of age with, or at risk for, neuromotor delay. The findings suggest that treadmill training may help children with Down syndrome to walk earlier than they would without the intervention. However, for children with cerebral palsy and for pre-term infants, the evidence is not clear due to a lack of studies and differences in their design and focus. This makes it difficult to draw conclusions about treadmill interventions. Further investigation of the effects of treadmill training on children under six years of age, particularly pre-term infants and children with cerebral palsy, is essential in order to determine whether it can accelerate the onset of walking and improve motor development.

BACKGROUND

Description of the condition

Typical gross motor development

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

Developmental delay

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

Consequences of motor developmental delay

One of the major tasks in gross motor development is locomotion, the ability to move from one place to another (Bly 1995). The failure to attain walking or the late attainment of walking has consequences for the musculoskeletal system. The anatomy of the hip, for instance, needs weight bearing for proper bone growth and correct orientation of the femoral head, as well as for a correct alignment of the spine (Campbell 2006). As well as its importance for subsequent motor skill development, acquiring the ability to locomote is important for infants because of its impact on cognitive, social and emotional skills. Researchers have demonstrated that for infants with typical development, experience with locomotion is associated with the development of a broad array of cognitive skills, including the onset of wariness of heights; the concept of object permanence (objects hidden from sight still exist); a shift from self-centred to landmark-based spatial coding strategies; the ability to follow the pointing gestures and gaze of another person,

and aspects of social referencing and detour reaching (Bertenthal 1984; Kermoian 1988; Campos 1989; Bertenthal 1990). This suggests that infants are better able to develop spatial cognition and learn about the world around them as they become able to locomote independently. Children who can walk independently show improved active exploration of their environment, as opposed to children who passively observe the environment when being held or carried through space. Rosenbloom 1971 further suggests that the quality of movement may affect subsequent development. He proposes that inefficient locomotion may hamper development by limiting the attention and energy that infants spend on exploration of the environment. Moreover, early locomotor experiences may have a larger impact on the developing brain than similar experiences at a later age due to the brain's high plasticity during the first few postnatal years (Webb 2001; de Graaf-Peters 2006). Earlier achievement of developmental milestones, in particular independent walking, have also been associated with better intellectual performance in adulthood (Murray 2007). In summary, independent locomotion at early age not only facilitates the infant's motor development, but also impacts other developmental domains and affects quality of life for the child and his or her family (Lepage 1998).

Population affected

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

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

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

Description of the intervention

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

Although the optimal window of intervention within the motor domain is not clear (Nelson 2000), it is reasonable to think of independent walking as a motor task that needs to be achieved by six years of age if long-term negative effects are to be minimised. Locomotor treadmill interventions, with or without partial weight support, have been used to promote the acquisition of independent walking in children with Down Syndrome (Looper 2006; Cherng 2007) and cerebral palsy (Richards 1997; Begnoche 2007; Mattern-Baxter 2009).

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

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

How the intervention might work

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

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

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

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

Why it is important to do this review

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

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

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

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

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

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

OBJECTIVES

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

METHODS

Criteria for considering studies for this review

Types of studies

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

Types of participants

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

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

Types of interventions

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

Types of outcome measures

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

Primary outcomes

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

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

Activities and participation functions

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

Secondary outcomes

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

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

Activities and participation functions

- Infant or child quality of life.

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

Search methods for identification of studies

Electronic searches

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

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

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

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

CINAHL (1937 to current), searched 21 March 2011

PsycINFO (1887 to current), searched 21 March 2011

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

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

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

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

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

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

Searching other resources

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

Data collection and analysis

Selection of studies

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

Data extraction and management

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

Assessment of risk of bias in included studies

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

Sequence generation

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

Allocation concealment

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

Blinding of participants and personnel

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

Blinding of outcome assessment

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

Incomplete outcome data

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

Selective reporting

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

Other risks of bias

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

Measures of treatment effect

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

Continuous data

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

Dichotomous data

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

Unit of analysis issues

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

Dealing with missing data

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

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

Assessment of heterogeneity

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

Assessment of reporting biases

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

Data synthesis

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

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

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

Subgroup analysis and investigation of heterogeneity

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

Sensitivity analysis

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

RESULTS

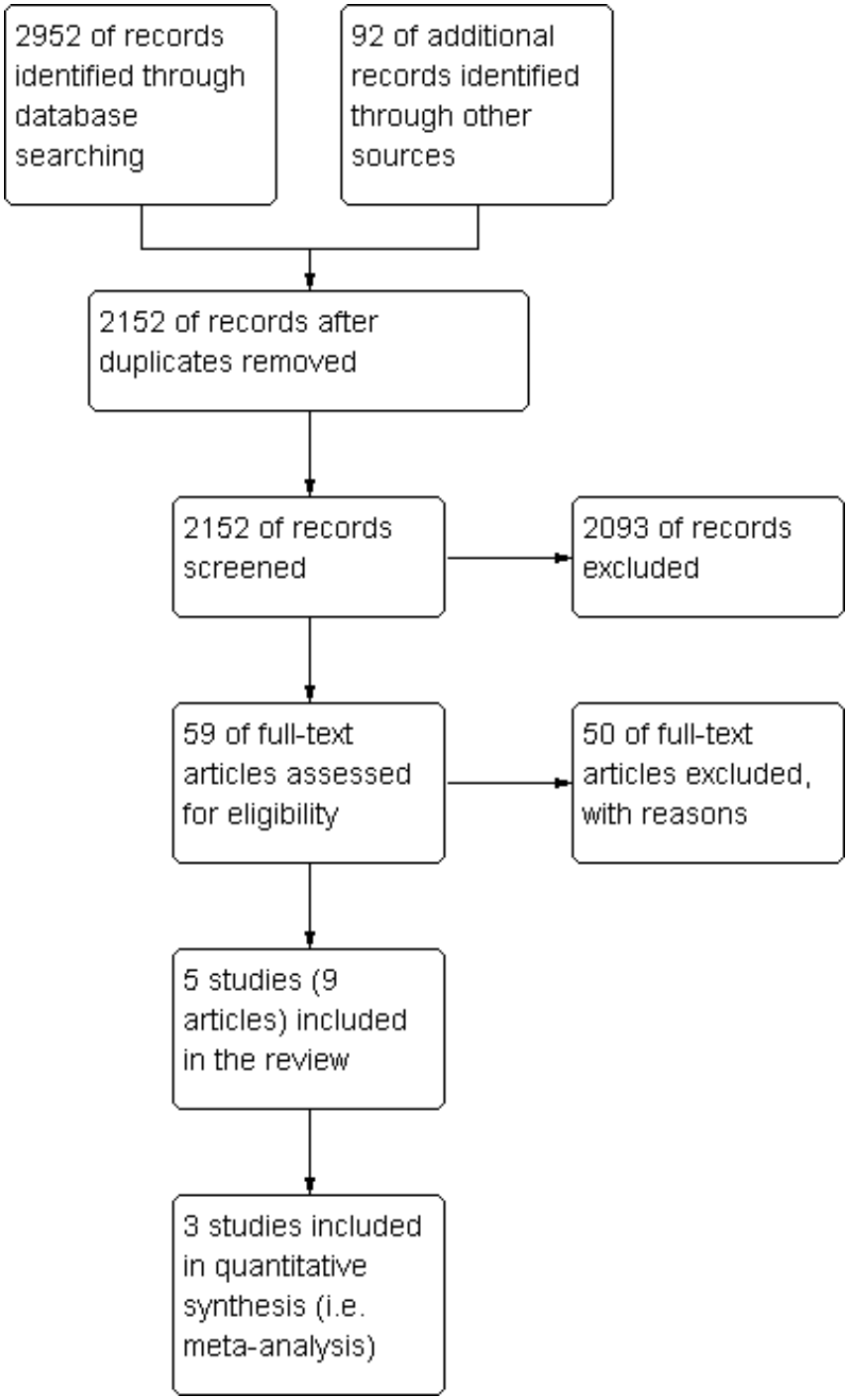
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

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

Figure 1. Study flow diagram.



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

Included studies

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

Location

All studies were conducted in USA.

Design

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

Sample sizes

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

Participants

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

Intervention and comparisons

Treadmill intervention versus no treadmill intervention

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

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

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

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

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

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

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

Outcomes

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

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

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

Infants at risk for developmental delay

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

Cerebral palsy

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

Down syndrome

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

Excluded studies

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

Risk of bias in included studies

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

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

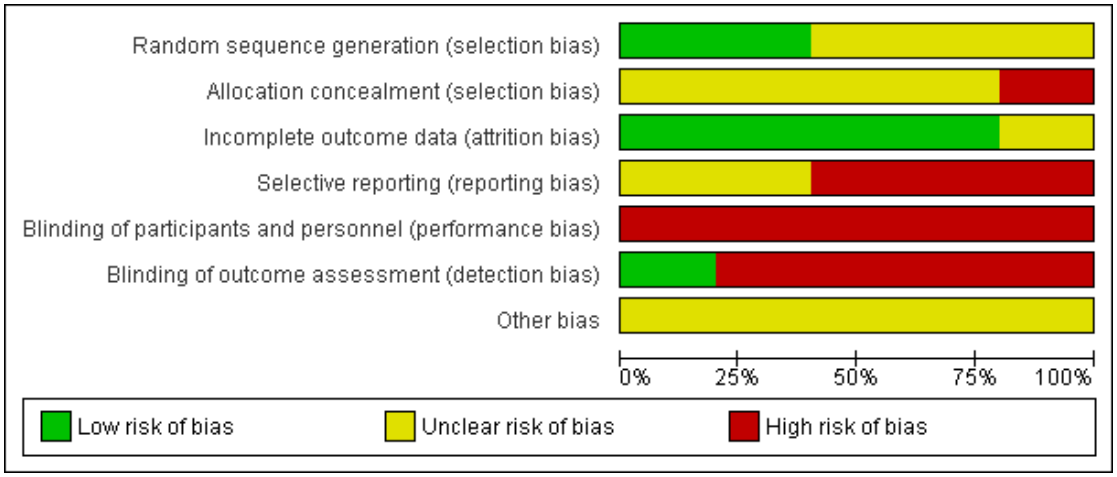
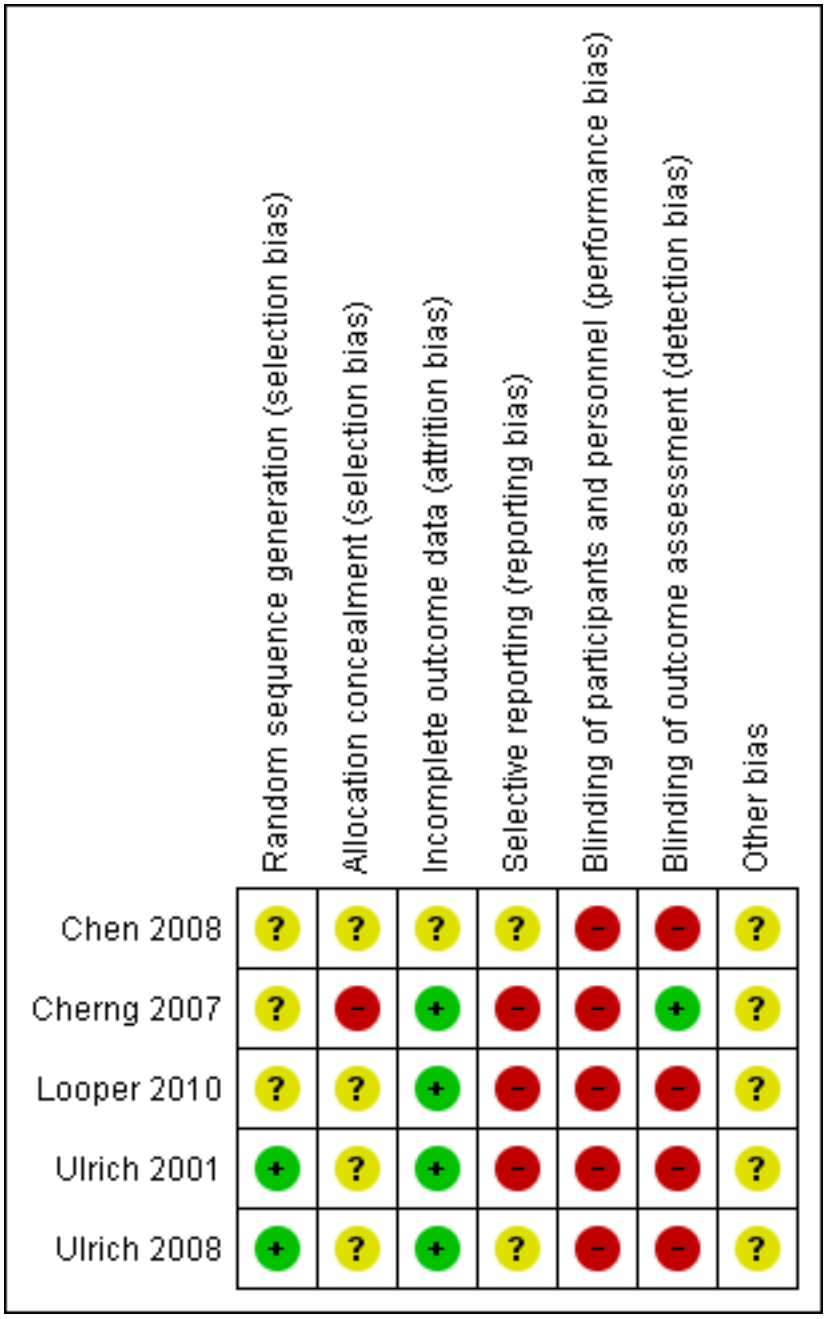


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. + = low risk, - = high risk, ? = unclear risk



Allocation

Random sequence generation

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

Allocation concealment

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

Blinding

Blinding of participants and personnel

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

Blinding of outcome assessment

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

Incomplete outcome data

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

Selective reporting

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

Other potential sources of bias

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

Effects of interventions

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

Treadmill intervention versus no treadmill intervention

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

Primary outcomes

Step frequency (treadmill alternating steps)

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

Step quality

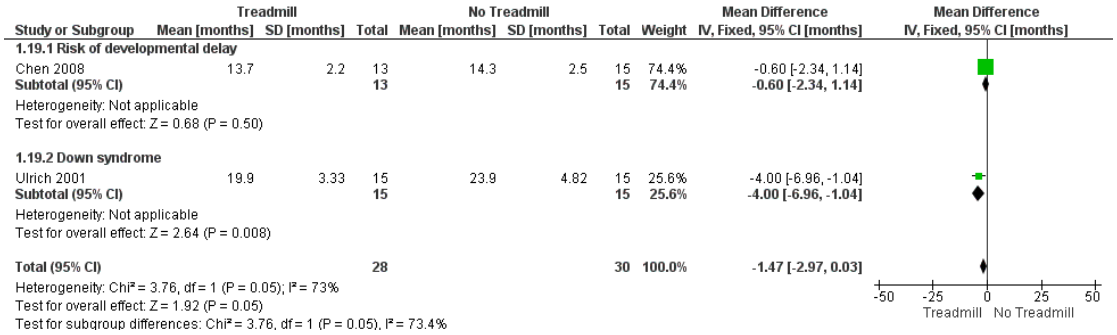
Chen 2008 found that treadmill training helped improve step quality for children at risk of neuromotor disabilities. In the experimental group, from 11 to 16 months of age, there was a significant decrease of foot toe contact during treadmill stepping (effect estimate at 11 months of age: -20.98; 95%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

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

Age of onset of independent walking

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

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



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

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

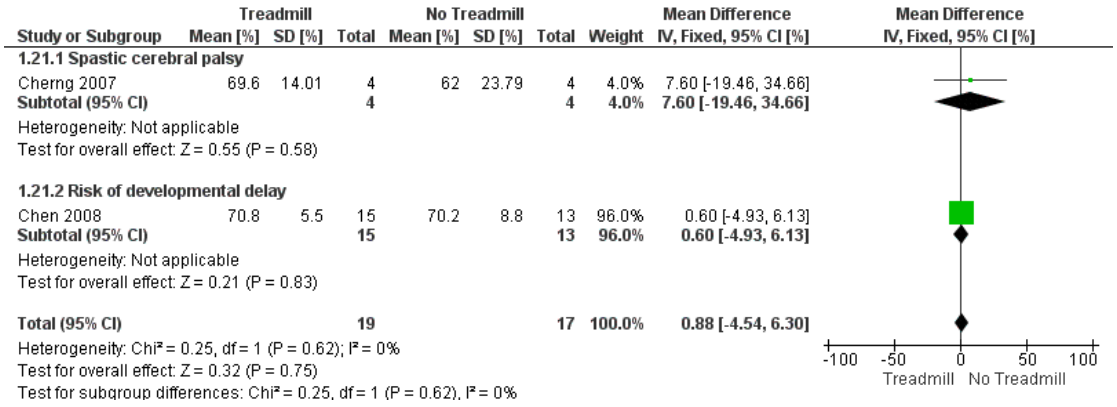
Age of onset of walking with assistance

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

Gross motor function (GMFM)

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

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



Falls and injuries due to falls.

These were not measured.

Secondary outcomes

Inter- and intra-limb co-ordination.

These were not measured.

Other gait parameters

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

Infant or child quality of life

This was not measured.

Treadmill intervention without orthotics versus treadmill intervention with orthotics

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

Age of onset of independent walking

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

Gross motor function

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

High-intensity treadmill intervention versus low-intensity treadmill intervention

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

Step frequency (treadmill alternating steps)

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

Age of onset of independent walking or walking with assistance

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

Other gait parameters

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

DISCUSSION

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

Summary of main results

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

Body functions

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

Activity and participation functions

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

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

Overall completeness and applicability of evidence

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

Quality of the evidence

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

Potential biases in the review process

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

Agreements and disagreements with other studies or reviews

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

AUTHORS' CONCLUSIONS

Implications for practice

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

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

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

Implications for research

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

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

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REFERENCES

References to studies included in this review

Chen 2008 ***{unpublished data only}***

Chen L, Looper J, Neary H, Ulrich D, Angulo-Barosso R. Walking patterns in infants at moderate risk for neuromotor disabilities with or without treadmill training. University of Michigan 2008.

Cherng 2007 ***{published data only}***

Cherng R, Liu C, Lau T, Hong R. Effects of treadmill training with body weight support on gait and gross motor function in children with spastic cerebral palsy. *American Journal of Physical Medicine and Rehabilitation* 2007;**86**(7): 548–55.

Looper 2010 ***{published data only}***

Looper J, Ulrich DA. Effect of treadmill training and supramalleolar orthosis use on motor skill development in infants with Down syndrome: a randomized clinical trial. *Physical Therapy* 2010;**90**:382–90.

Ulrich 2001 ***{published data only}***

Ulrich DA, Ulrich BD, Angulo-Kinzler RM, Yun J. Treadmill training of infants with Down syndrome: evidence-based developmental outcomes. *Pediatrics* 2001; **108**(5):e84.

Ulrich 2008 ***{published data only}***

Angulo-Barroso RM, Wu J, Ulrich DA. Long-term effects of different treadmill interventions on gait development in new walkers with Down syndrome. *Gait and Posture* 2008; **27**:231–8.

* Ulrich DA, Lloyd MC, Tiernan CW, Looper JE, Angulo-Barroso RM. Effects of intensity of treadmill training on developmental outcomes and stepping in infants with Down syndrome: a randomized trial. *Physical Therapy* 2008;**88**(1):114–22.

Wu J, Looper J, Ulrich BD, Ulrich DA, Angulo-Barroso RM. Exploring effects of different treadmill interventions on walking onset and gait patterns in infants with Down syndrome. *Developmental Medicine and Child Neurology* 2007;**49**:839-45.

Wu J, Looper J, Ulrich DA, Angulo-Barroso RM. Effects of various treadmill interventions on the development of joint kinematics in infants with Down syndrome. *Physical Therapy* 2010;**90**:1265–76.

Wu J, Ulrich DA, Looper J, Tiernan CW, Angulo-Barroso RM. Strategy adoption and locomotor adjustment in obstacle clearance of newly walking toddlers with down syndrome after different treadmill interventions. *Experimental Brain Research* 2008;**186**:261–72.

References to studies excluded from this review

Borggraefe 2007 ***{published data only}***

Borggraefe I, Kumar A, Schaefer JS, Berweck S, Meyer-Heim A, Hufschmidt A, et al. Robotic assisted treadmill therapy for children with a central gait impairment. *Monatsschrift Kinderheilkunde* 2007;**155**(6):529–34.

Borggraefe 2010 ***{published data only}***

Borggraefe I, Kiwull L, Schaefer JS, Koerte I, Blaschek A, Meyer-Heim A, et al. Sustainability of motor performance after robotic-assisted treadmill therapy in children: an open,

non-randomized baseline-treatment study. *European Journal of Physical and Rehabilitation Medicine* 2010;**46**(2):125–31.

Dodd 2007 ***{published data only}***
Dodd KJ, Foley S. Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: a clinical controlled trial. *Developmental Medicine and Child Neurology* 2007;**49**(2):101–5.

Maltais 2003 ***{published data only}***
Maltais D, Bar-Or O, Pierrynowski M, Galea V. Repeated treadmill walks affect physiologic responses in children with cerebral palsy. *Medicine & Science in Sports & Exercise* 2003; **35**(10):1653–61.

Matsuno 2010 ***{published data only}***
Matsuno VM, Camargo MR, Palma GC, Alveno D, Barela AMF. Analysis of partial body weight support during treadmill and overground walking of children with cerebral palsy. *Revista Brasileira De Fisioterapia* 2010;**14**(5):404–10.

Meyer-Heim 2007 ***{published data only}***
Meyer-Heim A, Borggraefe I, Ammann-Reiffer C, Berweck S, Sennhauser FH, Colombo G, et al. Feasibility of robotic-assisted locomotor training in children with central gait impairment. *Developmental Medicine and Child Neurology* 2007;**49**(12):900–6.

Mussleman 2007 ***{published data only}***
Musselman KE, Yang JF. Loading the limb during rhythmic leg movements lengthens the duration of both flexion and extension in human infants. *Journal of Neurophysiology* 2007;**97**(2):1247–57.

Pang 2003 ***{published data only}***
Pang MY, Lam T, Yang JF. Infants adapt their stepping to repeated trip-inducing stimuli. *Journal of Neurophisiology* 2003;**90**(4):2731–40.

Phillips 2007 ***{published data only}***
Phillips JP, Sullivan KJ, Burtner PA, Caprihan A, Provost B, Bernitsky-Beddingfield A. Ankle dorsiflexion fMRI in children with cerebral palsy undergoing intensive body-weight-supported treadmill training: a pilot study. *Developmental Medicine and Child Neurology* 2007;**49**(1): 39–44.

Schindl 2000 ***{published data only}***
Schindl MR, Forstner C, Kern H, Hesse S. Treadmill training with partial body weight support in nonambulatory patients with cerebral palsy. *Archives of Physical Medicine and Rehabilitation* 2000;**81**(3):301–6.

Schlittler 2011 ***{published data only}***
Schlittler CX, Lopes TF, Raniero EP, Barela JA. Treadmill training effects on walking acquisition and motor development in infants at risk of developmental delay. *Revista Paulista de Pediatria* 2011;**29**:91–9.

Smania 2011 ***{published data only}***
Smania N, Bonetti P, Gandolfi M, Cosentino A, Waldner A, Hesse S, Werner C, Bisoffi G, Geroin C, Munari D. Improved gait after repetitive locomotor training in children with cerebral palsy. *American Journal of Physical Therapy and Rehabilitation* 2011;**90**(2):137–49.

Teulier 2009 ***{published data only}***
Teulier C, Smith BA, Kubo M, Chang C, Moerchen V, Murazko K, et al. Stepping responses of infants with myelomeningocele when supported on a motorized treadmill. *Physical Therapy* 2009;**89**(1):60–72.

Additional references

Adolph 1998
Adolph KE, Vereijken B, Denny MA. Learning to crawl. *Child Development* 1998;**69**(5):1299–312.

Angulo-Barroso 2010
Angulo-Barroso RM, Tiernan CW, Chen LC, Ulrich D, Neary H. Treadmill responses and physical activity levels of infants at risk for neuromotor delay. *Pediatric Physical Therapy* 2010;**22**(1):61.

Barbeau 1987
Barbeau H, Rossignol S. Recovery of locomotion after chronic spinalization in the adult cat. *Brain Research* 1987; **412**(1):84–95.

Bayley 1993
Bayley N. *Bayley Scales of Infant Development*. 2nd Edition. The Psychological Corporation, 1993.

Beck 2010
Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bulletin of the World Health Organization* 2010;**88**(1):31–8.

Begnoche 2007
Begnoche DM, Pitetti KH. Effects of traditional treatment and partial body weight treadmill training on the motor skills of children with spastic cerebral palsy: a pilot study. *Pediatric Physical Therapy* 2007;**19**(1):11–9.

Bertenthal 1984
Bertenthal BI, Campos JJ, Barrett KC. Self-produced locomotion: an organizer of emotional, cognitive, and social development in infancy. In: Emde RHarmon R editor(s). *Continuities and Discontinuities in Development*. New York: Plenum, 1984:175-210.

Bertenthal 1990
Bertenthal BI, Campos JJ. A systems approach to the organizing effects of self-produced locomotion during infancy. *Advances in Infancy Research* 1990;**6**:1–60.

Blackman 2002
Blackman JA. Early intervention: a global perspective. *Infants and Young Children* 2002;**15**(2):11–9.

Bly 1995
Bly L, Ariz TN. Motor skills acquisition in the first year, an illustrated guide to normal development. *Pediatric Physical Therapy* 1995;**7**(2):86.

Bodkin 2003
Bodkin AW, Baxter RS, Heriza CB. Treadmill training for an infant born preterm with a grade III intraventricular hemorrhage. *Physical Therapy* 2003;**83**(12):1107.

Butler 2001
Butler C, Darrah J. Effects of neurodevelopmental treatment (NDT) for cerebral palsy: an AAcerebral palsyDM evidence report. *Developmental Medicine & Child Neurology* 2001; **43**:778–790.

Campbell 2006
Campbell SK, Palisano RJ, Vander Linden DW. *Physical Therapy for Children*. St Louis, Missouri: Elsevier Saunders, 2006.

Campos 1989
Campos JJ, Bertenthal BI. Locomotion and psychological development in infancy. *Applied Developmental Psychology* 1989;**2**:230-58.

Case-Smith 1998
Case-Smith J, Heaphy T, Marr D, Galvin B, Koch V, Ellis MG, et al. Fine motor and functional performance outcomes in preschool children. *American Journal of Occupational Therapy* 1998;**52**:10.

Cernak 2008
Cernak K, Stevens V, Price R, Shumway-Cook A. Locomotor training using body-weight support on a treadmill in conjunction with ongoing physical therapy in a child with severe cerebellar ataxia. *Physical Therapy* 2008;**88** (1):88.

Cotman 2002
Cotman CW, Berchtold NC. Exercise: a behavioral intervention to enhance brain health and plasticity. *Trends in Neurosciences* 2002;**25**(6):295–301.

Cotman 2002a
Cotman CW, Engesser-Cesar C. Exercise enhances and protects brain function. *Exercise and Sport Sciences Reviews* 2002;**30**(2):75.

Damiano 2006
Damiano DL. Activity, activity, activity: rethinking our physical therapy approach to cerebral palsy. *Physical Therapy* 2006;**86**(11):1534.

Damiano 2009
Damiano DL, de Jong SL. A systematic review of the effectiveness of treadmill training and body weight support in paediatric rehabilitation. *Journal of Neurologic Physical Therapy* 2009;**33**(1):27–44.

Davis 1994
Davis DW, Thelen E, Keck J. Treadmill stepping in infants born prematurely. *Early Human Development* 1994;**39**(3): 211–23.

Day 2004
Day JA, Fox EJ, Lowe J, Swales HB, Behrman AL. Locomotor training with partial body weight support on a treadmill in a nonambulatory child with spastic tetraplegic cerebral palsy: a case report. *Pediatric Physical Therapy* 2004;**16**(2):106.

de Bode 2007
de Bode S, Mathern GW, Bookheimer S, Dobkin B. Locomotor training remodels fMRI sensorimotor cortical activations in children after cerebral hemispherectomy. *Neurorehabilitation and Neural Repair* 2007;**21**(6):497.

de Graaf-Peters 2006
de Graaf-Peters VB, Hadders-Algra M. Ontogeny of the human central nervous system: what is happening when?. *Early Human Development* 2006;**82**(4):257–66.

de Graaf-Peters 2007
de Graaf-Peters VB, Blauw-Hospers CH, Dirks T, Bakker H, Bos AF, Hadders-Algra M. Development of postural control in typically developing children and children with cerebral palsy: possibilities for intervention?. *Neuroscience and Biobehavioral Reviews* 2007;**31**(8):1191–200.

Down's Syndrome Association
What is the incidence of Down's Syndrome?. http://www.downs-syndrome.org.uk/component/content/article/35-general/159-3-what-is-the-incidence-of-downs-syndrome.html (accessed 19 April 2011).

Edgerton 1997
Edgerton VR, de Leon RD, Tillakaratne N, Recktenwald MR, Hodgson JA, Roy RR. Use-dependent plasticity in spinal stepping and standing. *Advances in Neurology* 1997; **72**:233–47.

Eidelberg 1980
Eidelberg E, Story JL, Meyer BL, Nystel J. Stepping by chronic spinal cats. *Experimental Brain Research* 1980;**40** (3):241–6.

Eng 2007
Eng JJ, Tang PF. Gait training strategies to optimize walking ability in people with stroke: a synthesis of the evidence. *Expert Review of Neurotherapeutics* 2007;**7**(10):1417–36.

Eyre 2003
Eyre JA. Development and plasticity of the corticospinal system in man. *Neural Plasticity* 2003;**10**(1-2):93–106.

Formiga 2011
Formiga CKMR, Linhares MBM. Motor development curve from 0 to 12 months in infants born preterm. *Acta Paediatrica* 2011;**100**(3):379–84.

Gordon
Gordon AM. To constrain or not to constrain and other stories of intensive upper extremity training for children with unilateral cerebral palsy. Developmental Medicine and Child Neurology. In press.

Goyen 2002
Goyen TA. Longitudinal motor development of apparently normal high-risk infants at 18 months, 3 and 5 years. *Early Human Development* 2002;**70**(1-2):103–15.

Hadders-Algra 1996
Hadders-Algra M, Brogren E, Forssberg H. Training affects the development of postural adjustments in sitting infants. *The Journal of Physiology* 1996;**493**(Pt 1):289–98.

Harbourne 2003
Harbourne RT, Stergiou N. Nonlinear analysis of the development of sitting postural control. *Developmental Psychobiology* 2003;**42**(4):368–377.

Heineman 2008
Heineman KR, Hadders-Algra M. Evaluation of neuromotor function in infancy - a systematic review of

available methods. *Journal of Developmental and Behavioral Pediatrics* 2008;**29**(4):315–23.

Higgins 2008
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 [Updated February 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

Hodgson 1994
Hodgson JA, Roy RR, de Leon R, Dobkin B, Edgerton VR. Can the mammalian lumbar spinal cord learn a motor task? . *Medicine and Science in Sports and Exercise* 1994;**26**(12): 1491–7.

Jones 1999
Jones TA, Chu CJ, Grande LA, Gregory AD. Motor skills training enhances lesion-induced structural plasticity in the motor cortex of adult rats. *Journal of Neuroscience* 1999;**19** (22):10153–63.

Kermoian 1988
Kermoian R, Campos JJ. Locomotor experience: a facilitator of spatial cognitive development. *Child Development* 1988; **59**(4):908–17.

Kleim 2008
Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *Journal of Speech, Language, and Hearing Research* 2008;**51**(1):S225–39.

Lepage 1998
Lepage C, Noreau L, Bernard P. Association between characteristics of locomotion and accomplishment of life habits in children with cerebral palsy. *Physical Therapy* 1998;**78**:458–469.

Lie 2010
Lie KK, Grøholt EK, Eskild A. Association of cerebral palsy with Apgar score in low and normal birthweight infants: population based cohort study. *BMJ* 2010;**341**:c4990.

Looper 2006
Looper J, Wu J, Angulo-Barroso R, Ulrich D, Ulrich B. Changes is step variability of new walkers with typical development and with Down syndrome. *Journal of Motor Behavior* 2006;**38**(5):367–72.

Luo 2009
Luo H, Chen P, Hsieh W, Lin K, Lu T, Chen WJ, et al. Associations of supported treadmill stepping with walking attainment in preterm and full-term infants. *Physical Therapy* 2009;**89**(11):1215–25.

Mattern-Baxter 2009
Mattern-Baxter K, Bellamy S, Mansoor J. Effects of intensive locomotor treadmill training on young children with cerebral palsy. *Pediatric Physical Therapy* 2009;**21**(4): 308–18.

Mattern-Baxter 2009a
Mattern-Baxter K. Effects of partial body weight supported treadmill training on children with cerebral palsy. *Pediatric Physical Therapy* 2009;**21**(1):12–22.

Molina-Rueda 2010
Molina-Rueda F, Aguila-Maturana AM, Molina-Rueda MJ, Miangolarra-Page JC. Treadmill training with or without partial body weight support in children with cerebral palsy: systematic review and meta-analysis [Pasarela rodante con o sin sistema de suspensión del peso corporal en niños con parálisis cerebral infantil: revisión sistemática y metaanálisis]. *Revista de Neurologia* 2010;**51**(3):135–45.

Murray 2007
Murray GK, Jones PB, Kuh D, Richards M. Infant developmental milestones and subsequent cognitive function. *Annals of Neurology* 2007;**62**(2):128–36.

Mutlu 2009
Mutlu A, Krosschell K, Spira DG. Treadmill training with partial body-weight support in children with cerebral palsy: a systematic review. *Developmental Medicine and Child Neurology* 2009;**51**(4):268–75.

Nelson 2000
Nelson CA. Neural plasticity and human development: the role of early experience in sculpting memory systems. *Developmental Science* 2000;**3**(2):115–36.

Newell 1991
Newell KM. Motor skill acquisition. *Annual Review of Psychology* 1991;**42**:213–37.

Pin 2010
Pin TW, Eldridge B, Galea MP. Motor trajectories from 4 to 18 months corrected age in infants born at less than 30 weeks of gestation. *Early Human Development* 2010;**86**(9): 573–80.

Prins 2010
Prins SA, von Lindern JS, van Dijk S, Versteegh FGA. Motor development of premature Infants born between 32 and 34 weeks. International Journal of Pediatrics 2010 Sept 7 [Epub ahead of print]:4 pages.

Prosser 2007
Prosser LA. Locomotor training within an inpatient rehabilitation program after pediatric incomplete spinal cord injury. *Physical Therapy* 2007;**87**(9):1224–32.

Provost 2007
Provost B, Dieruf K, Burtner PA, Phillips JP, Bernitsky-Beddingfield A, Sullivan K, et al. Endurance and gait in children with cerebral palsy after intensive body weight-supported treadmill training. *Pediatric Physical Therapy* 2007;**19**(1):2–10.

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

Richards 1997
Richards CL, Malouin F, Dumas F, Marcoux S, Lepage C, Menier C. Early and intensive treadmill locomotor training for young children with cerebral palsy: a feasibility study. *Pediatric Physical Therapy* 1997;**9**(4):158–65.

Riethmuller 2009
Riethmuller AM, Jones RA, Okely AD. Efficacy of interventions to improve motor development in young children: a systematic review. *Pediatrics* 2009;**124**(4): e782–92.

Rosenbloom 1971
Rosenbloom L. The contribution of motor behaviour to child development. *Physiotherapy* 1971;**57**(4):159–62.

Roze 2010
Roze E, Meijer L, Van Braeckel KNJA, Ruiter SAJ, Bruggink JLM, Bos AF. Developmental trajectories from birth to school age in healthy term-born children. *Pediatrics* 2010; **126**(5):e1134–42.

Russell 2002
Russell DJ, Rosenbaum PL, Avery LM, Lane M. *Gross Motor Function Measure (GMFM 66 & GMFM 88): User's Manual*. London: McKeith Press, 2002.

Sackett 1996
Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *British Medical Journal* 1996;**312(7023)**: 71–72.

Sherrington 1910
Sherrington CS. Flexion-reflex of the limb, crossed extension-reflex, and reflex stepping and standing. *Journal of Physiology* 1910;**40**:28–121.

Stiles 2000
Stiles J. Neural plasticity and cognitive development. *Developmental Neuropsychology* 2000;**18**(2):237–72.

Stiles 2005
Stiles J, Reilly J, Paul B, Moses P. Cognitive development following early brain injury: evidence for neural adaptation. *Trends in Cognitive Sciences* 2005;**9**(3):136–43.

Sullivan 2007
Sullivan K, Brown D, Klasses T, Mulroy S, Ge T, Azen S, et al. Effects of task-specific locomotor and strength training in adults who were ambulatory after stroke: Results of the STEPS randomized clinical trial. *Physical Therapy* 2007;**87** (12):1580–602.

Surveillance CP Europe
Surveillance of Cerebral Palsy in Europe. http://www-rheop.ujf-grenoble.fr/scpe2/site˙scpe/index.php (accessed 5 March 2011).

Sveistrup 1997
Sveistrup H, Woollacott MH. Practice modifies the developing automatic postural response. *Experimental Brain Research* 1997;**114**(1):33–43.

Thelen 1986
Thelen E. Treadmill-elicited stepping in 7-month-old infants. *Child Development* 1986;**57**(6):1498–506.

Thelen 1991
Thelen E, Ulrich BD. Hidden skills: a dynamic systems analysis of treadmill stepping during the first year. *Monographs of the Society for Research in Child Development* 1991;**56**(1):1–98.

Ulrich 1992
Ulrich BD, Ulrich DA, Collier DH. Alternating stepping patterns - hidden abilities of 11-month-old infants with Down syndrome. *Developmental Medicine and Child Neurology* 1992;**34**(3):233–9.

Ulrich 1995
Ulrich BD, Ulrich DA, Collier DH, Cole EL. Developmental shifts in the ability of infants with Down syndrome to produce treadmill steps. *Physical Therapy* 1995;**75**(1):14–23.

Verschuren 2008
Verschuren O, Ketelaar M, Takken T, Helders PJM, Gorter JW. Exercise programs for children with cerebral palsy: a systematic review of the literature. *American Journal of Physical Medicine and Rehabilitation* 2008;**87**(5):404–17.

Volpe 2009
Volpe JJ. The encephalopathy of prematurity--brain injury and impaired brain development inextricably intertwined. *Seminars in Pediatric Neurology* 2009;**16**:167–78.

Webb 2001
Webb SJ, Monk CS, Nelson CA. Mechanisms of postnatal neurobiological development: implications for human development. *Developmental Neuropsychology* 2001;**19**(2): 147–71.

WHO 2005
International Classification of Functioning, Disability and Health for Children and Youth. http://www3.who.int/icf/onlinebrowser/icf.cfm?undefined&version = 7 (accessed 10 February 2011).

WHO 2006
WHO Multicentre Growth Reference Study Group. Motor Development Study: windows of achievement for six gross motor development milestones. *Acta Paediatrica* 2006; **Suppl 450**:86–95.

Willoughby 2009
Willoughby KL, Dodd KJ, Shields N. A systematic review of the effectiveness of treadmill training for children with cerebral palsy. *Disability and Rehabilitation* 2009;**31**(24): 1971–9.

Ziviani 2010
Ziviani J, Feeney R, Rodger S, Watter P. Systematic review of early intervention programmes for children from birth to nine years who have a physical disability. *Australian Occupational Therapy Journal* 2010;**57**(4):210–23.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Chen 2008

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

Risk of bias

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

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

Cherng 2007

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

Cherng 2007 (*Continued*)

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

Looper 2010

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

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

Risk of bias

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

Looper 2010 (*Continued*)

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

Ulrich 2001

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

Ulrich 2001 (*Continued*)

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

Ulrich 2008

Methods	Randomised controlled trial.
Participants	36 infants with Down syndrome were randomised into two groups: low-intensity and high-intensity. They were included when they were able to take 6 steps per minute on a treadmill while being supported 30 children were analysed in the final sample (16 experimental group: high-intensity training 12 males / 4 female, 14 control group: low-intensity training 6 males / 8 females) ; (28 with trisomy 21; two with mosaic type) 6 infants discontinued the intervention, 4 in the low-intensity and 2 in the high-intensity group. An additional 5 infants were lost to gait follow-up (2 in the low-intensity and 3 in the high-intensity group). Any discrepancies in the paper were resolved through personal discussion with RA who was one of the authors involved in both Ulrich 2001 and this study, and who is also a review author Corrected age at entry: 9.65 (SD 1.61) months for the higher-intensity group; and 10.40 (SD 2.14) months for the lower-intensity group 2 African American, 2 biracial, and remaining infants were white
Interventions	Experimental group (high-intensity treadmill training): 5days/week, with two treadmill parameters (minutes/day, treadmill belt speed) individualised, as well as an ankle weight being added as the infant progressed in frequency of alternating steps; co-interventions: early intervention services and any other activities that were prescribed by their health care providers Control group (low-intensity treadmill training): 5 days/week, 6min/session, belt speed 0.18m/s; co-interventions: early intervention services and any other activities that were prescribed by their health care providers The training stopped when infants could take 3 independent steps overground Four additional publications (Wu 2007; Angulo-Barroso 2008; Wu 2008; Wu 2010) dealt with the follow-up from this intervention including assessments from 1 to 15 months post walking onset (i.e. after termination of the intervention)
Outcomes	The study reported frequency of alternating TM steps and onset of assisted and independent walking. The follow-up publications reported on spatio-temporal variables, joint kinematics, and gait adaptation parameters, In addition, Wu 2007 presented follow-up spatio-temporal gait variables including a historical control group from Ulrich 2001, which we did not use this data as it was not randomised) **Publication Wu 2007** Gait follow-up assessment, between 1 and 3 months after walking onset (training groups) and 1 month after walking onset (control group) Age at walking onset (decreased when any training, with further decreases in high-intensity group = positive effects of training at higher intensities) Elapsed time from entry to walking onset. Gait speed. Gait stride length. Gait stride width. **Publication Angulo-Barroso 2008** Measured after the onset of independent walking during 4 home-visits scheduled at the following infant's age (low-intensity group: 24.9 mo SD 5.1; 28.4 mo SD 4.6; 30.5 SD 5.1; 36.5 SD 4.9 - high-intensity group: 21.3 mo SD 2.4, 24.4 mo SD 2.4, 27.3 SD 2.3, 33.7 SD 2.5). The walking experience prior to visit one had been 3.3 mo (SD 1.2

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

Risk of bias

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

Ulrich 2008 (*Continued*)

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

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

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

DATA AND ANALYSES

Comparison 1. Treadmill vs No Treadmill

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

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

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

Comparison 2. Treadmill without orthoses vs Treadmill with orthoses

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

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

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

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

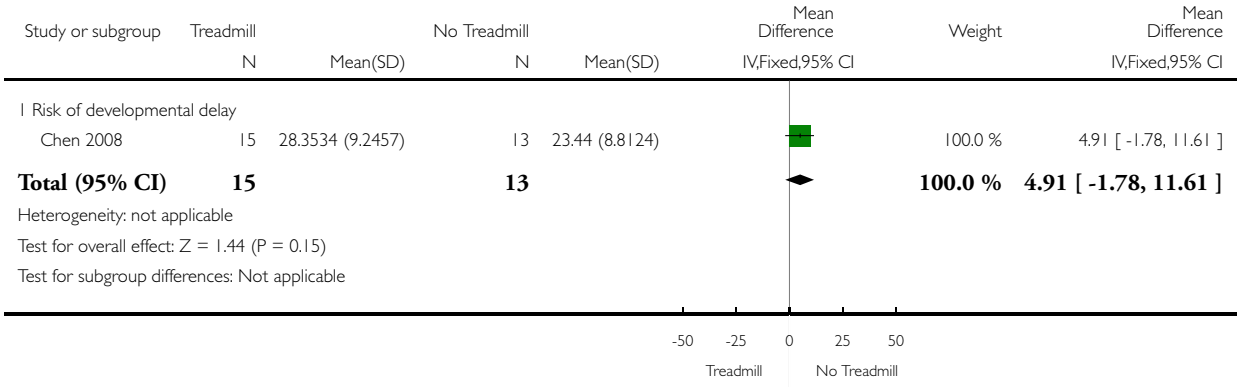
30.1 Down syndrome	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-2.69, 2.49]
31 Other gait parameters:gait ankle dorsiflexion. Follow-up (Visit 4)	1	25	Mean Difference (IV, Fixed, 95% CI)	-2.80 [-5.96, 0.36]
31.1 Down syndrome	1	25	Mean Difference (IV, Fixed, 95% CI)	-2.80 [-5.96, 0.36]
32 Other gait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

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 1 Step frequency (8 months)

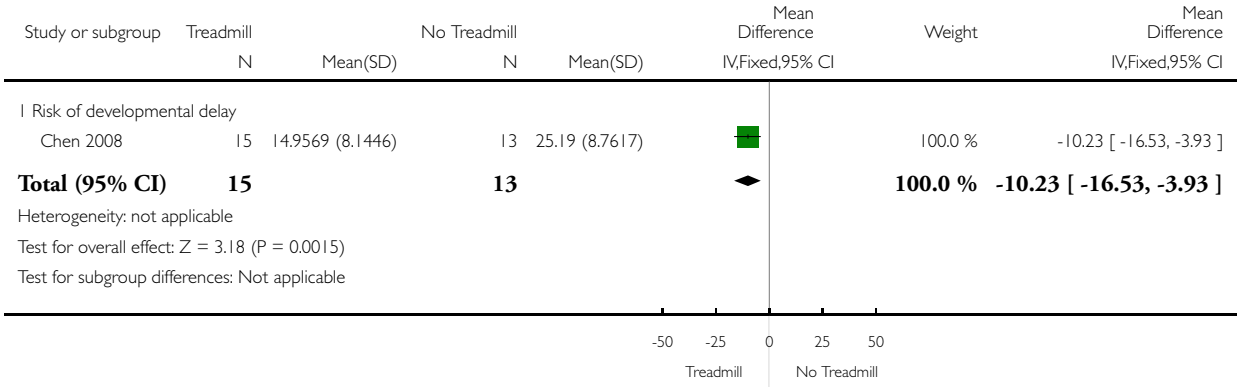


Analysis 1.2. Comparison 1 Treadmill vs No Treadmill, Outcome 2 Step frequency (9 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 2 Step frequency (9 months)

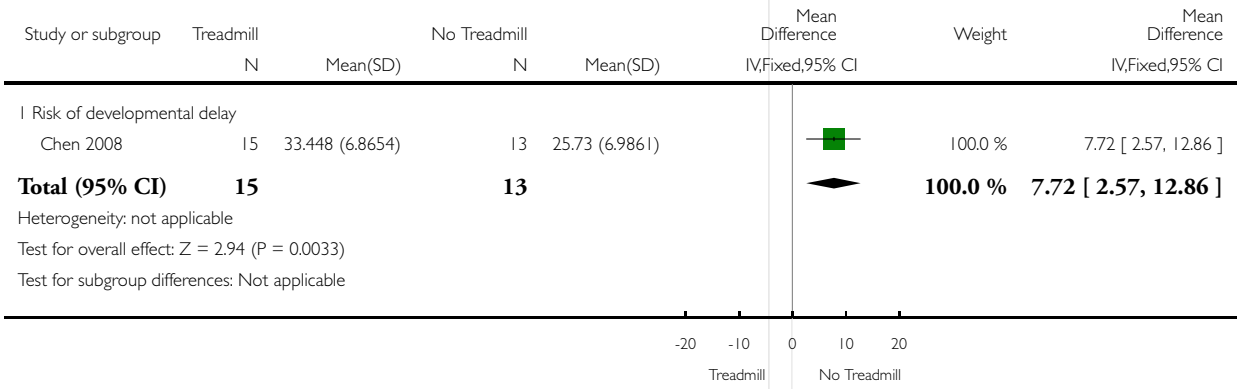


Analysis 1.3. Comparison 1 Treadmill vs No Treadmill, Outcome 3 Step frequency (10 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 3 Step frequency (10 months)

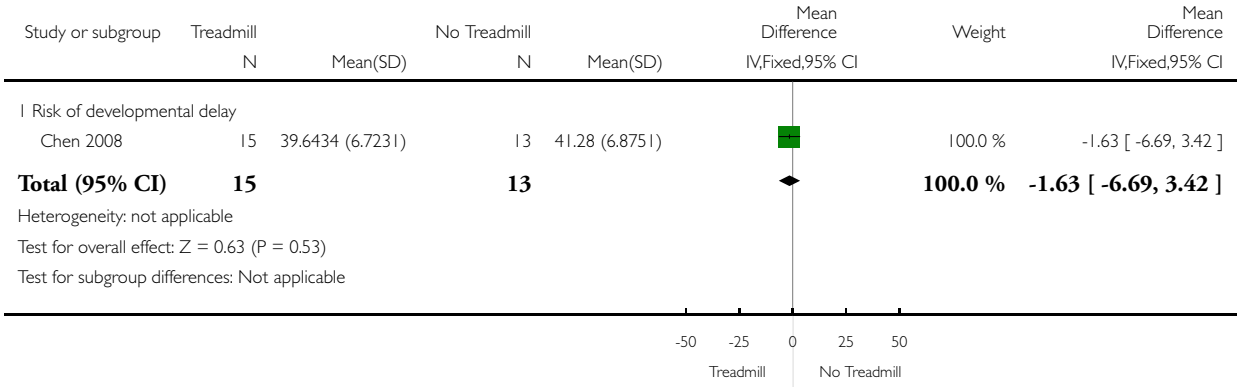


Analysis 1.4. Comparison 1 Treadmill vs No Treadmill, Outcome 4 Step frequency (11 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 4 Step frequency (11 months)

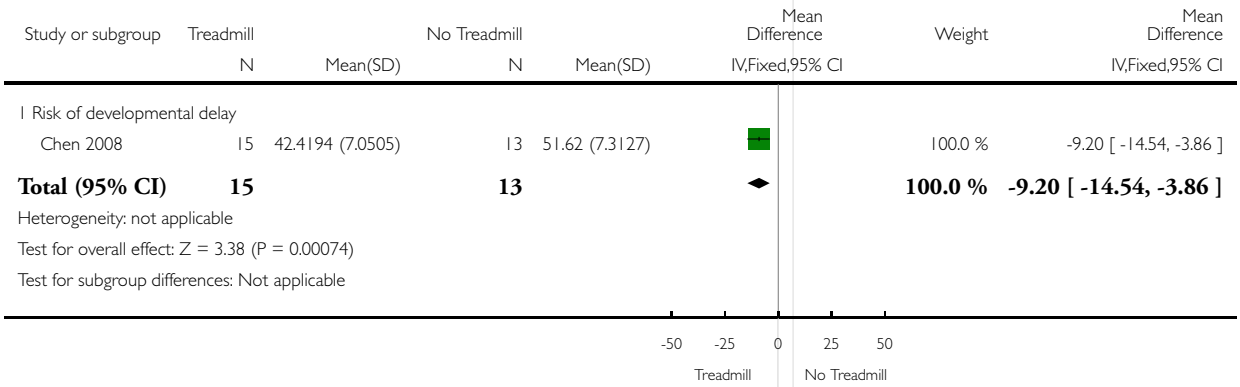


Analysis 1.5. Comparison 1 Treadmill vs No Treadmill, Outcome 5 Step frequency (12 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 5 Step frequency (12 months)

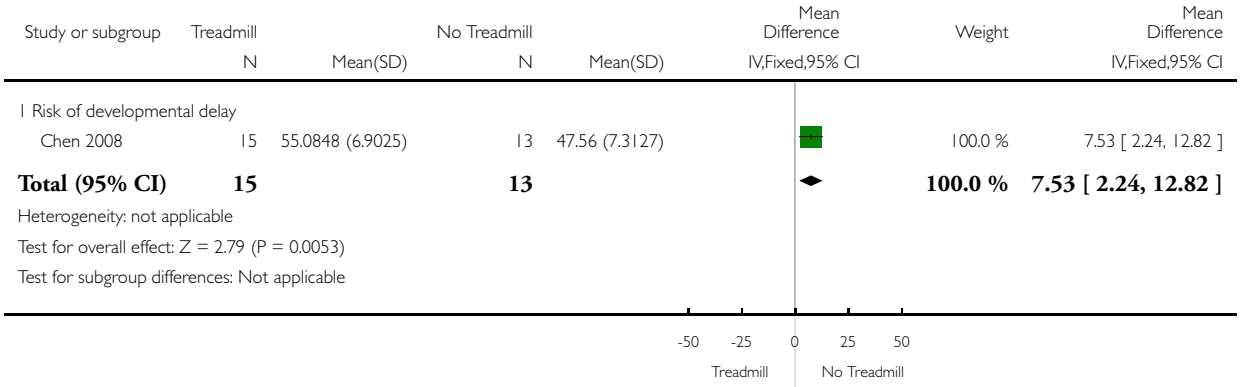


Analysis 1.6. Comparison 1 Treadmill vs No Treadmill, Outcome 6 Step frequency (13 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 6 Step frequency (13 months)

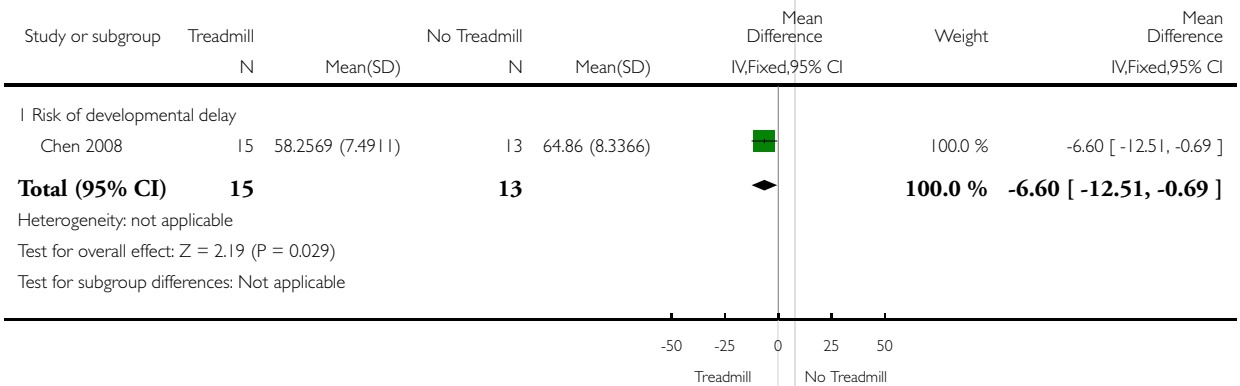


Analysis 1.7. Comparison 1 Treadmill vs No Treadmill, Outcome 7 Step frequency (14 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 7 Step frequency (14 months)

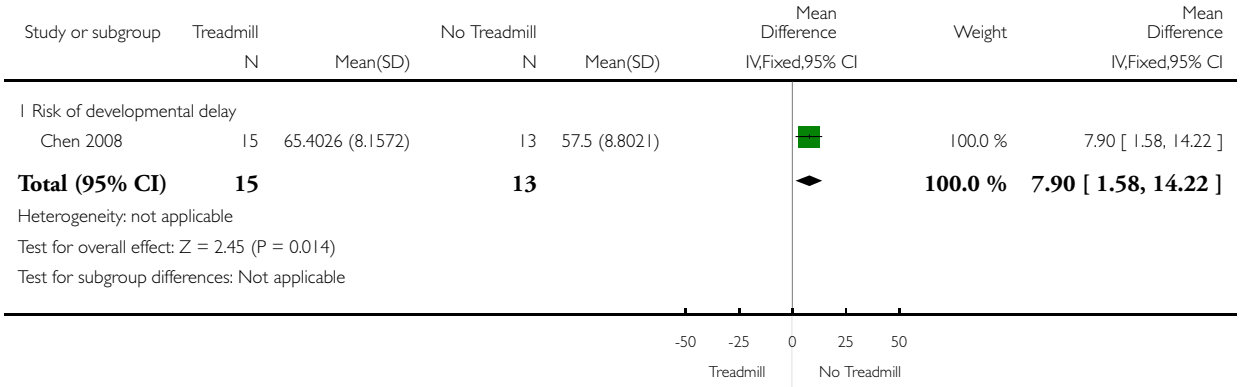


Analysis 1.8. Comparison 1 Treadmill vs No Treadmill, Outcome 8 Step frequency (15 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 8 Step frequency (15 months)

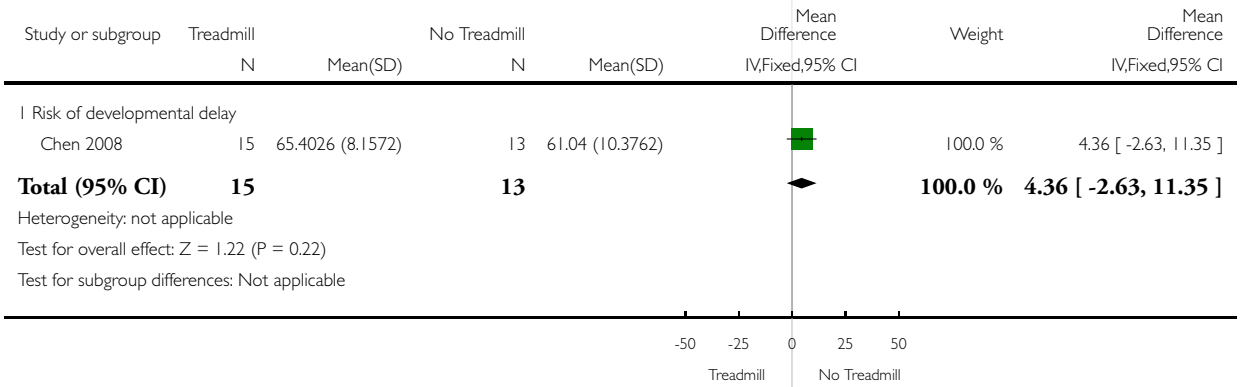


Analysis 1.9. Comparison 1 Treadmill vs No Treadmill, Outcome 9 Step frequency (16 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 9 Step frequency (16 months)

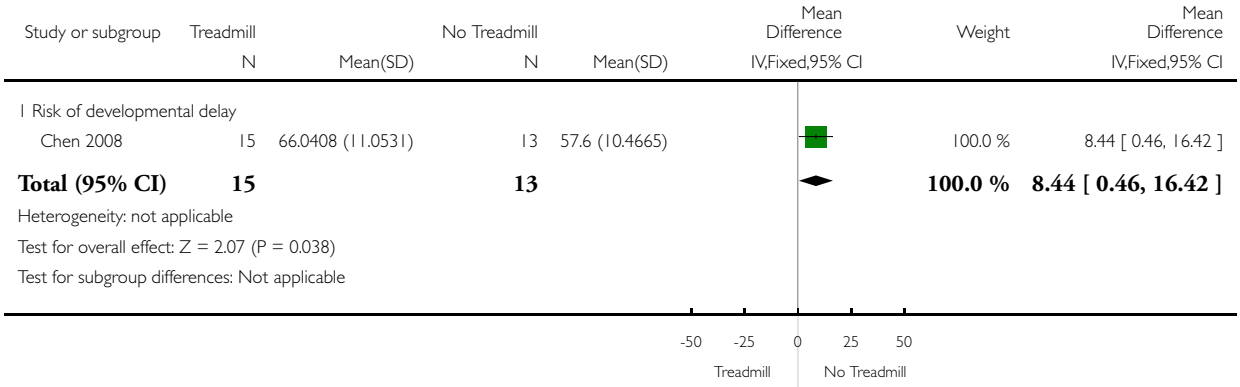


Analysis 1.10. Comparison 1 Treadmill vs No Treadmill, Outcome 10 Step quality (8 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 10 Step quality (8 months)

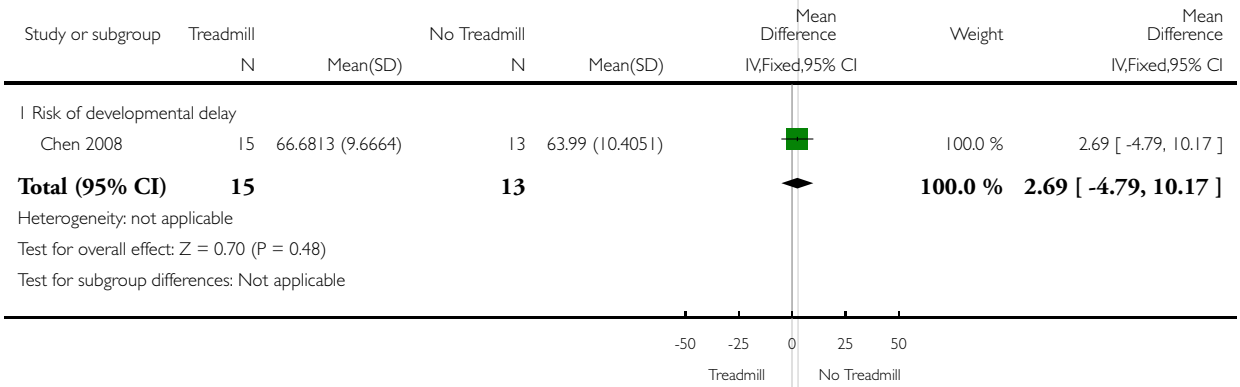


Analysis 1.11. Comparison 1 Treadmill vs No Treadmill, Outcome 11 Step quality (9 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 11 Step quality (9 months)



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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 12 Step quality (10 months)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 13 Step quality (11 months)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 14 Step quality (12 months)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 15 Step quality (13 months)

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

Heterogeneity: not applicable

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

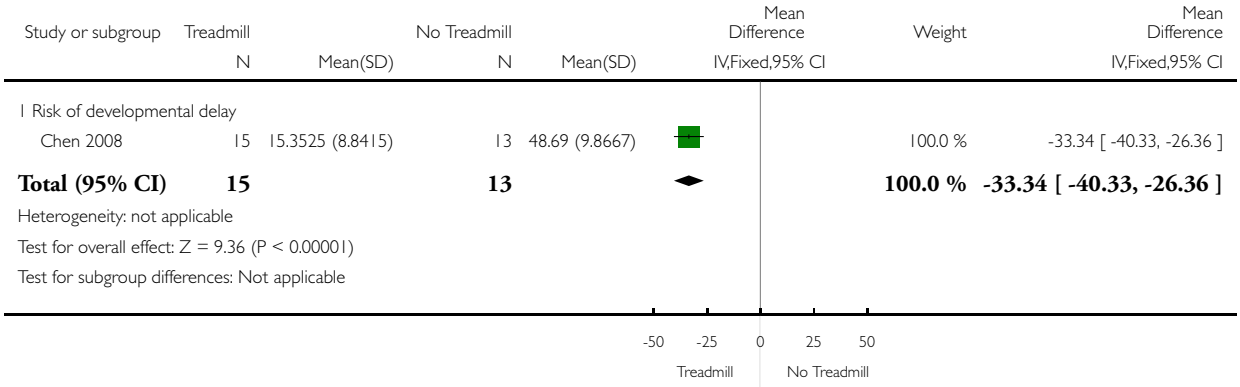
Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 16 Step quality (14 months)

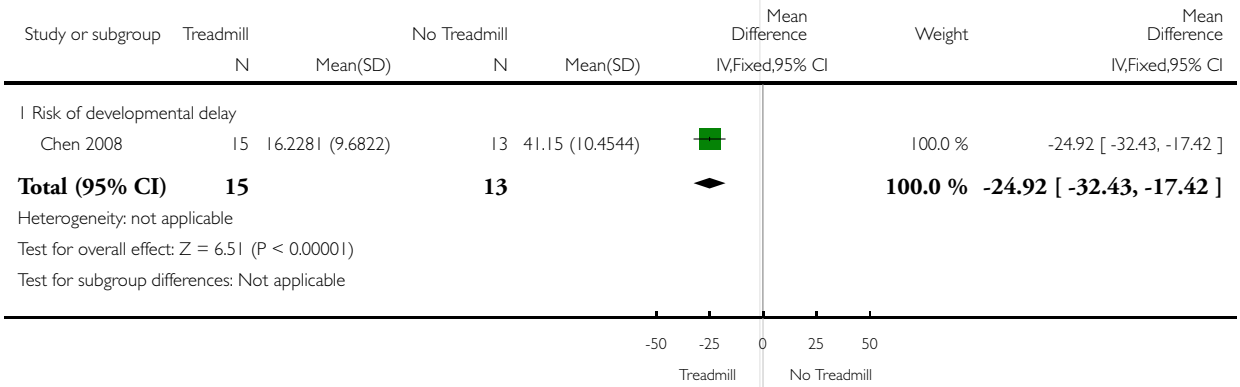


Analysis 1.17. Comparison 1 Treadmill vs No Treadmill, Outcome 17 Step quality (15 months).

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 17 Step quality (15 months)



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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 18 Step quality (16 months)

Study or subgroup	Treadmill N	Mean(SD)	No Treadmill N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Risk of developmental delay							
Chen 2008	15	14.2113 (9.6822)	13	29.82 (12.4323)		100.0 %	-15.61 [-23.96, -7.27]
Total (95% CI)	**15**		**13**			**100.0 %**	**-15.61 [-23.96, -7.27]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.67 (P = 0.00025)

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 19 Age of onset of independent walking

Study or subgroup	Treadmill N	Mean(SD)[months]	No Treadmill N	Mean(SD)[months]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Risk of developmental delay							
Chen 2008	13	13.7 (2.2)	15	14.3 (2.5)		74.4 %	-0.60 [-2.34, 1.14]
Subtotal (95% CI)	**13**		**15**			**74.4 %**	**-0.60 [-2.34, 1.14]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.68 (P = 0.50)

2 Down syndrome							
Ulrich 2001	15	19.9 (3.33)	15	23.9 (4.82)		25.6 %	-4.00 [-6.96, -1.04]
Subtotal (95% CI)	**15**		**15**			**25.6 %**	**-4.00 [-6.96, -1.04]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.64 (P = 0.0082)

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Treadmill N	Mean(SD)[months]	No Treadmill N	Mean(SD)[months]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Total (95% CI)	**28**		**30**			**100.0 %**	**-1.47 [-2.97, 0.03]**

Heterogeneity: Chi² = 3.76, df = 1 (P = 0.05); I² =73%

Test for overall effect: Z = 1.92 (P = 0.055)

Test for subgroup differences: Chi² = 3.76, df = 1 (P = 0.05), I² =73%

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

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

Comparison: 1 Treadmill vs No Treadmill

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 21 Gross motor function: GMFM

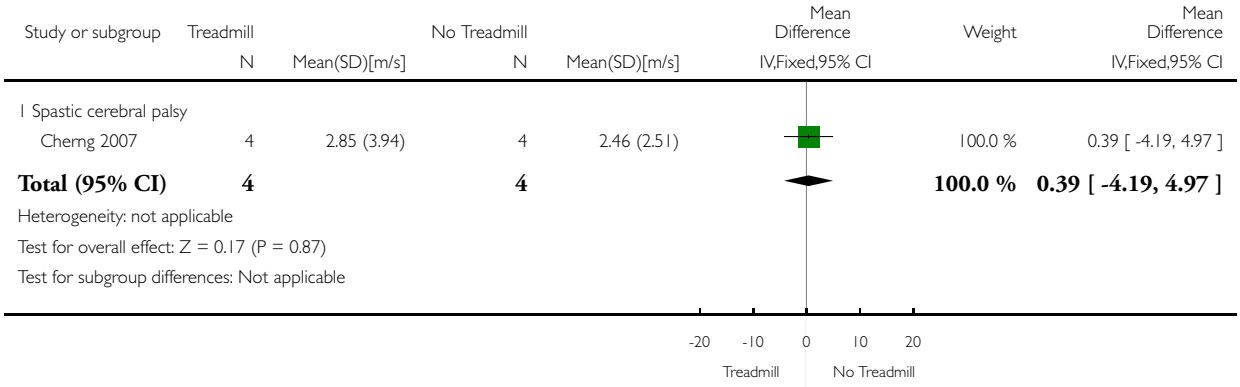
Study or subgroup	Treadmill N	Mean(SD)[%]	No Treadmill N	Mean(SD)[%]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Spastic cerebral palsy							
Cherng 2007	4	69.6 (14.01)	4	62 (23.79)		4.0 %	7.60 [-19.46, 34.66]
Subtotal (95% CI)	**4**		**4**			**4.0 %**	**7.60 [-19.46, 34.66]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.55 (P = 0.58)							
2 Risk of developmental delay							
Chen 2008	15	70.8 (5.5)	13	70.2 (8.8)		96.0 %	0.60 [-4.93, 6.13]
Subtotal (95% CI)	**15**		**13**			**96.0 %**	**0.60 [-4.93, 6.13]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.21 (P = 0.83)							
Total (95% CI)	**19**		**17**			**100.0 %**	**0.88 [-4.54, 6.30]**
Heterogeneity: Chi^2 = 0.25, df = 1 (P = 0.62); I^2 =0.0%							
Test for overall effect: Z = 0.32 (P = 0.75)							
Test for subgroup differences: Chi^2 = 0.25, df = 1 (P = 0.62), I^2 =0.0%							

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 22 Other gait parameters: velocity

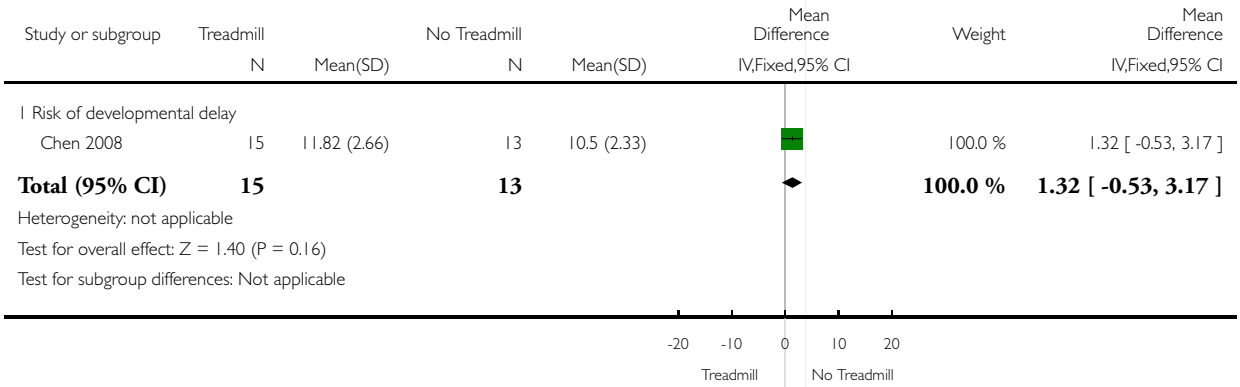


Analysis 1.23. Comparison 1 Treadmill vs No Treadmill, Outcome 23 Other gait parameters: velocity (follow-up when walking independently).

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

Comparison: 1 Treadmill vs No Treadmill

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



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

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

Comparison: 1 Treadmill vs No Treadmill

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

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

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

Heterogeneity: not applicable

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

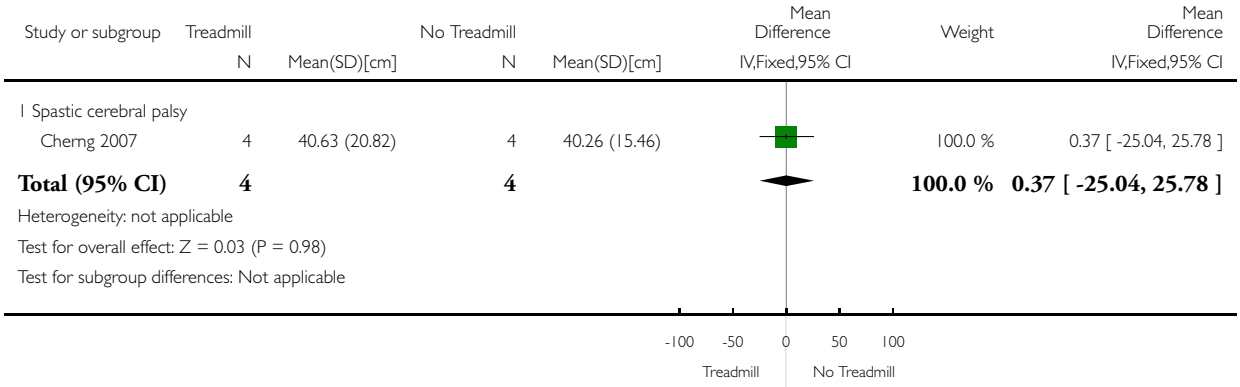
Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

Outcome: 26 Other gait parameters: step length

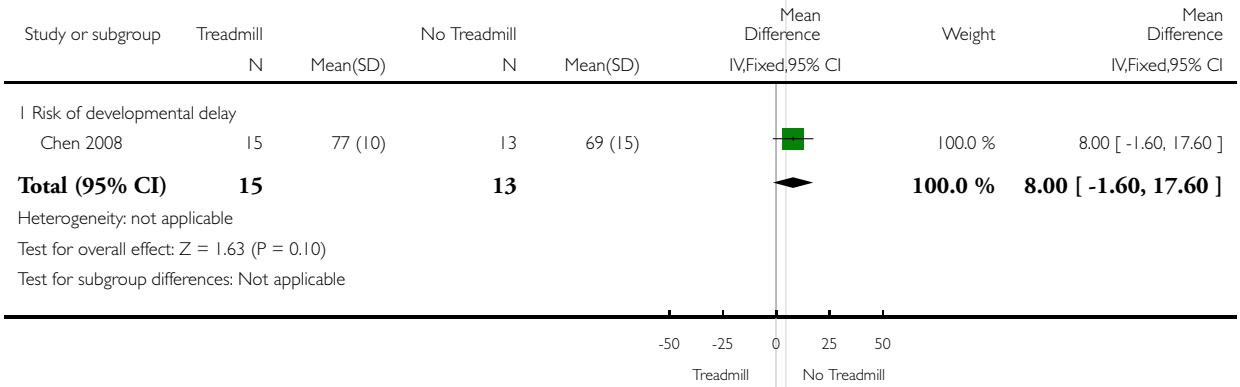


Analysis 1.27. Comparison 1 Treadmill vs No Treadmill, Outcome 27 Other gait parameters: step length (follow-up when walking independently).

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

Comparison: 1 Treadmill vs No Treadmill

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

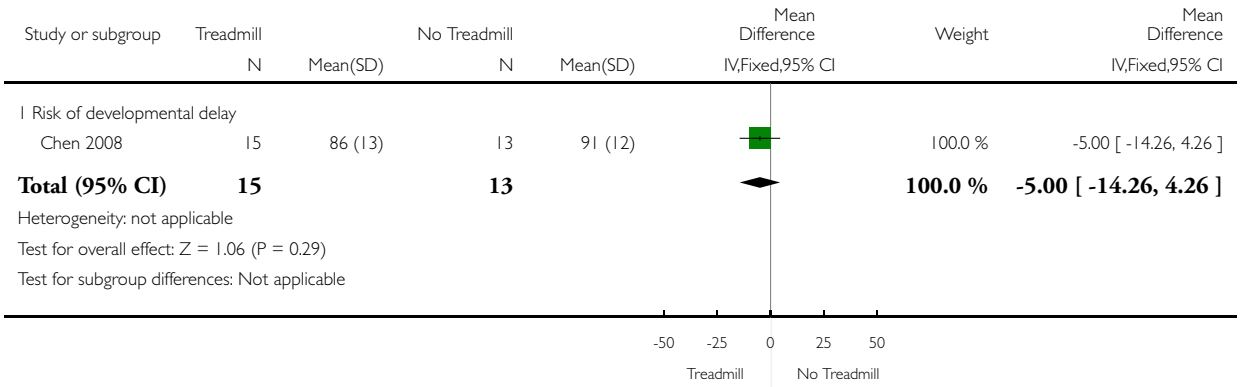


Analysis 1.28. Comparison 1 Treadmill vs No Treadmill, Outcome 28 Other gait parameters: step length (follow-up 3 months later).

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

Comparison: 1 Treadmill vs No Treadmill

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

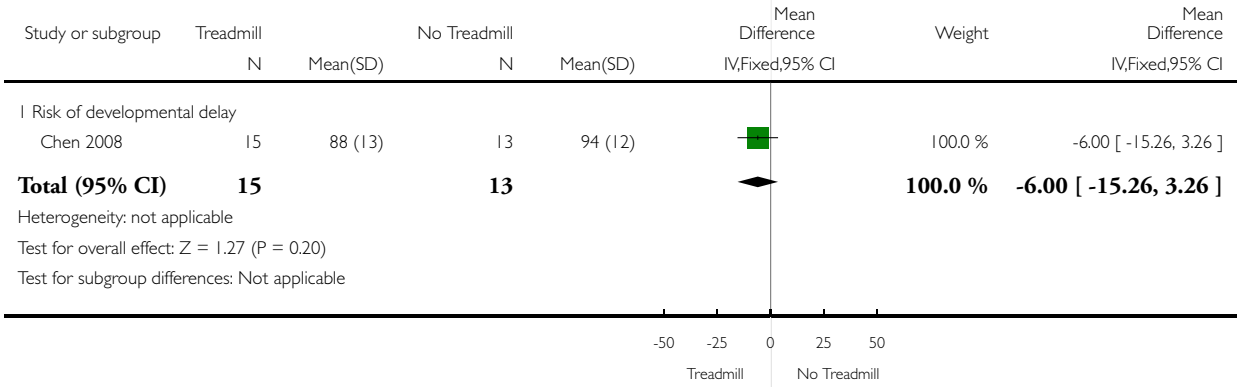


Analysis 1.29. Comparison 1 Treadmill vs No Treadmill, Outcome 29 Other gait parameters: step length (follow-up 6 months later).

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

Comparison: 1 Treadmill vs No Treadmill

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

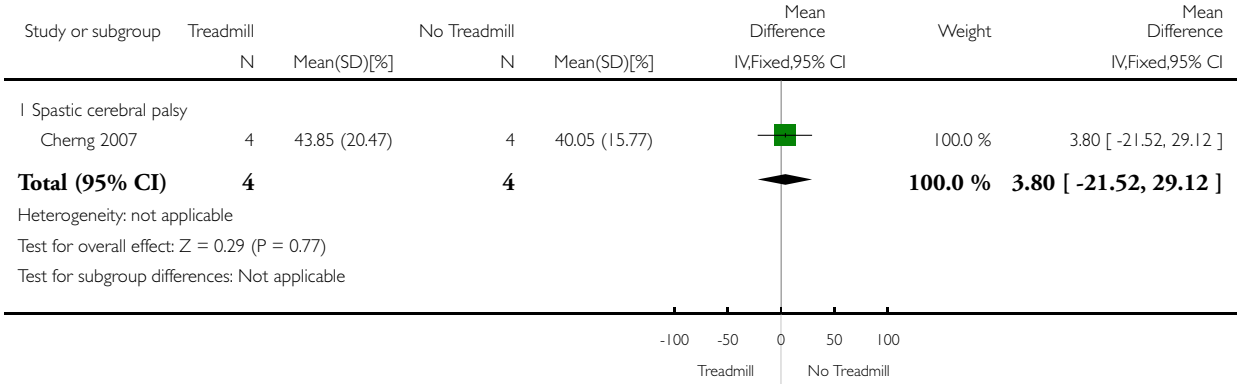


Analysis 1.30. Comparison 1 Treadmill vs No Treadmill, Outcome 30 Other gait parameters: gait double-limb support.

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

Comparison: 1 Treadmill vs No Treadmill

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

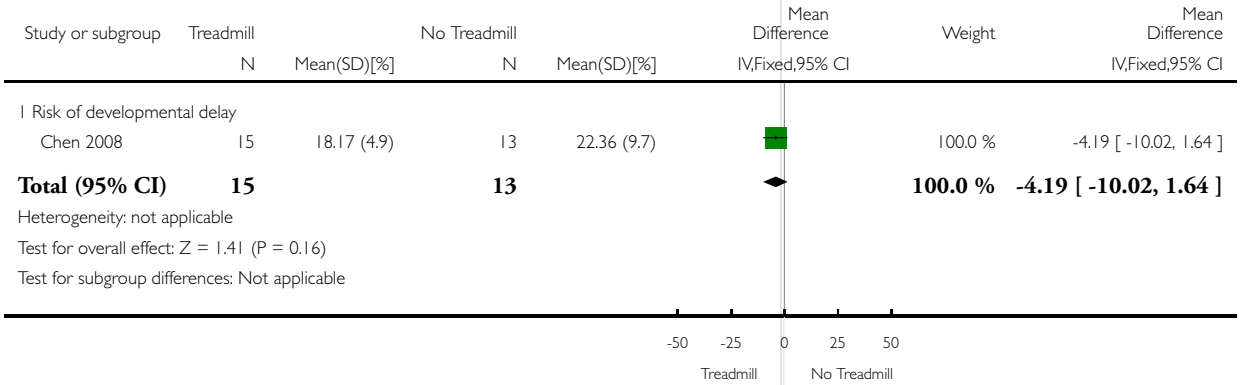


Analysis 1.31. Comparison 1 Treadmill vs No Treadmill, Outcome 31 Other gait parameters: gait double-limb support (follow-up when walking independently).

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

Comparison: 1 Treadmill vs No Treadmill

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



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

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

Comparison: 1 Treadmill vs No Treadmill

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Treadmill vs No Treadmill

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

Comparison: 2 Treadmill without orthoses vs Treadmill with orthoses

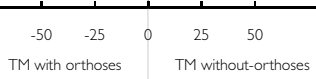
Outcome: 1 Walking independently (1 month follow-up)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

Comparison: 2 Treadmill without orthoses vs Treadmill with orthoses

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

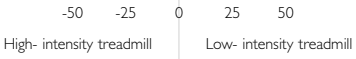
Outcome: 1 Step frequency

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

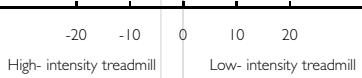
Outcome: 2 Age of onset of independent walking

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

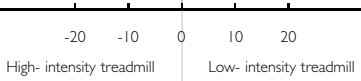
Outcome: 3 Onset of walking with assistance

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

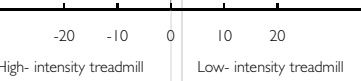
Outcome: 4 Chronological Age. Follow-up (visit 1)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

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

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

Heterogeneity: not applicable

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

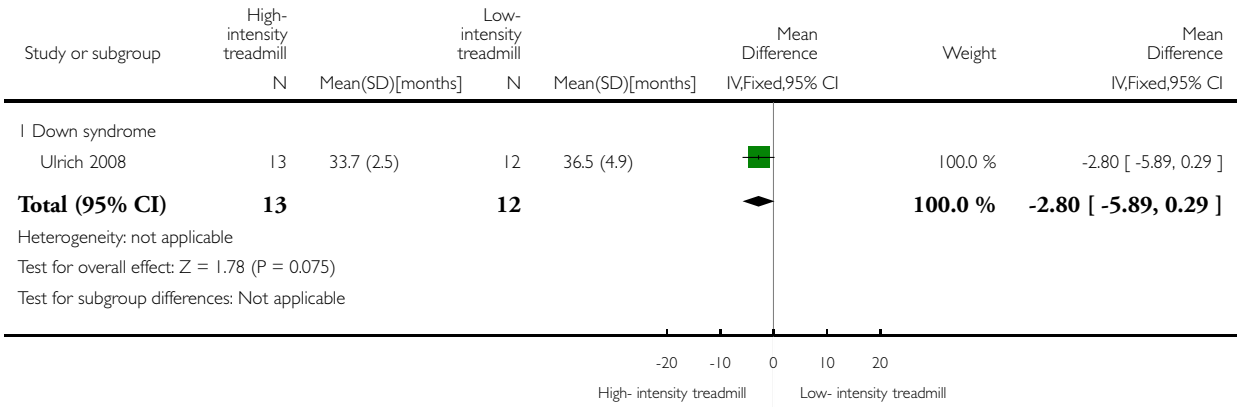
Test for subgroup differences: Not applicable

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

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

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

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

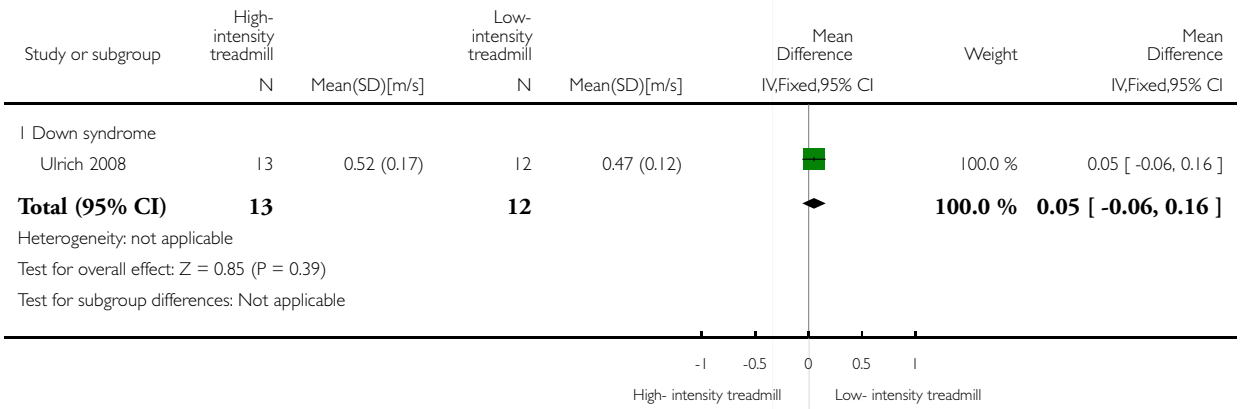


Analysis 3.8. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 8 Other gait parameters: velocity follow-up (visit1).

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

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

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



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

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

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

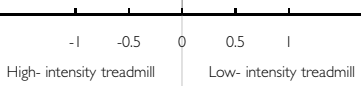
Outcome: 9 Other gait parameters: velocity follow-up (visit 2)

Study or subgroup	High-intensity treadmill N	Mean(SD)[m/s]	Low-intensity treadmill N	Mean(SD)[m/s]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Down syndrome							
Ulrich 2008	13	0.84 (0.2)	12	0.68 (0.18)		100.0 %	0.16 [0.01, 0.31]
Total (95% CI)	**13**		**12**			**100.0 %**	**0.16 [0.01, 0.31]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.11 (P = 0.035)

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

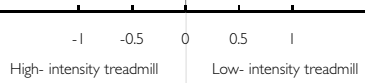
Outcome: 11 Other gait parameters: velocity follow-up (visit 4)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

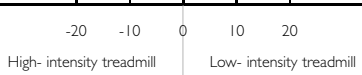
Outcome: 14 Other gait parameters: step length follow-up (visit 3)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

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

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

Heterogeneity: not applicable

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

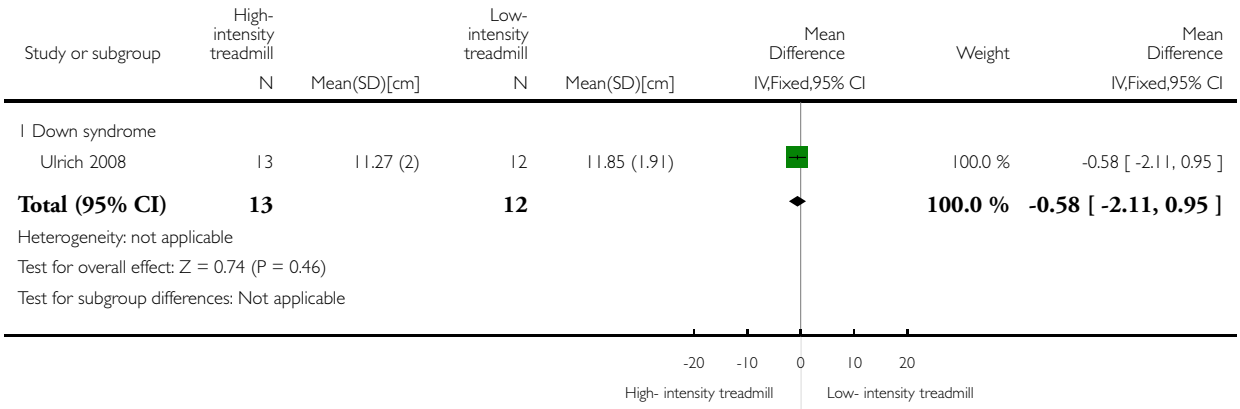
Test for subgroup differences: Not applicable

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

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

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

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

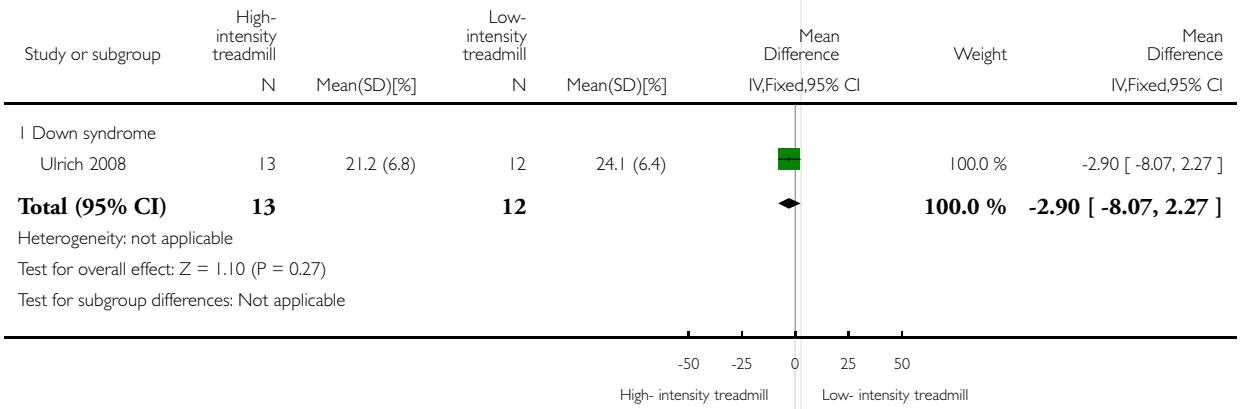


Analysis 3.20. Comparison 3 High-intensity treadmill vs Low-intensity treadmill, Outcome 20 Other gait parameters: gait double-limb support follow-up (visit 1).

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

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

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



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

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

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

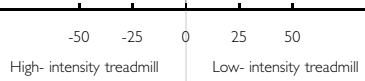
Outcome: 21 Other gait parameters: gait double-limb support follow-up (visit 2)

Study or subgroup	High-intensity treadmill N	Mean(SD)[%]	Low-intensity treadmill N	Mean(SD)[%]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Down syndrome							
Ulrich 2008	13	12.8 (2.7)	12	16.8 (6.4)		100.0 %	-4.00 [-7.91, -0.09]
Total (95% CI)	**13**		**12**			**100.0 %**	**-4.00 [-7.91, -0.09]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.01 (P = 0.045)

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

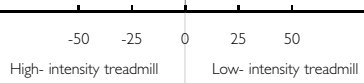
Outcome: 23 Other gait parameters: gait double-limb support follow-up (visit 4)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

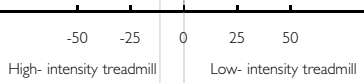
Outcome: 24 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 1)

Study or subgroup	High-intensity treadmill N	Mean(SD)[% cycle]	Low-intensity treadmill N	Mean(SD)[% cycle]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Down syndrome							
Ulrich 2008	13	66.2 (6.6)	12	69.3 (4)		100.0 %	-3.10 [-7.34, 1.14]
Total (95% CI)	**13**		**12**			**100.0 %**	**-3.10 [-7.34, 1.14]**

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

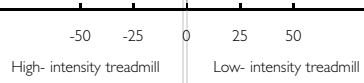
Outcome: 26 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 3)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

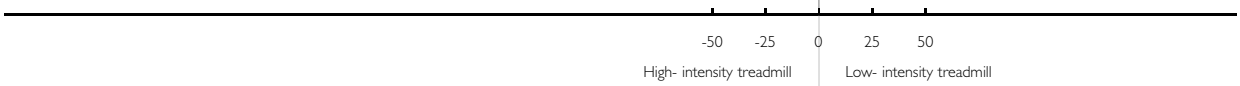
Outcome: 27 Other gait parameters: gait ankle plantar flexion. Follow-up (Visit 4)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

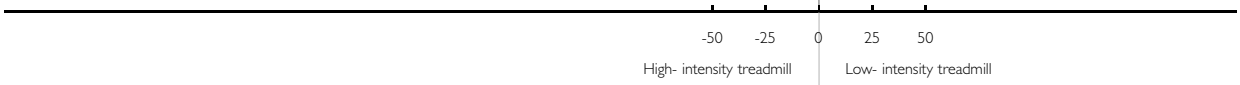
Outcome: 28 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 1)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

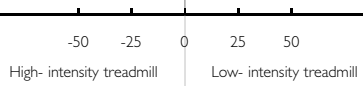
Outcome: 29 Other gait parameters: gait ankle dorsiflexion. Follow-up (Visit 2)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

Study or subgroup	High-intensity treadmill N	Mean(SD)[% cycle]	Low-intensity treadmill N	Mean(SD)[% cycle]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Down syndrome							
Ulrich 2008	13	83.6 (3.3)	12	83.7 (3.3)		100.0 %	-0.10 [-2.69, 2.49]
Total (95% CI)	**13**		**12**			**100.0 %**	**-0.10 [-2.69, 2.49]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.08 (P = 0.94)

Test for subgroup differences: Not applicable

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

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

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

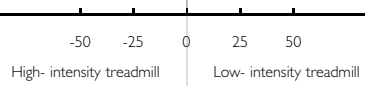
Outcome: 31 Other gait parameters:gait ankle dorsiflexion. Follow-up (Visit 4)

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

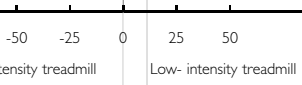
Outcome: 32 Other gait parameters: toe-off follow-up visit 1

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

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

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

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

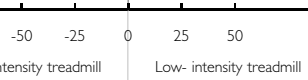
Outcome: 34 Other gait parameters: toe-off; follow-up visit 3

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

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable



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

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

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

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

Study or subgroup	High-intensity treadmill N	Mean(SD)[%]	Low-intensity treadmill N	Mean(SD)[%]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Down syndrome							
Ulrich 2008	13	59 (5.2)	12	59.9 (6.4)		100.0 %	-0.90 [-5.49, 3.69]
Total (95% CI)	**13**		**12**			**100.0 %**	**-0.90 [-5.49, 3.69]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.38 (P = 0.70)							
Test for subgroup differences: Not applicable							

APPENDICES

Appendix 1. Search strategies

Cochrane CENTRAL Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor Physical Therapy Modalities, this term only
#2 MeSH descriptor Physical Therapy (Specialty), this term only
#3 physiotherap* or physio NEXT therap* or physical NEXT therap*
#4 MeSH descriptor Exercise Therapy, this term only
#5 treadmill* or tread-mill*
#6 (#1 OR #2 OR #3 OR #4 OR #5)
#7 MeSH descriptor Motor Skills, this term only
#8 MeSH descriptor Motor Skills Disorders, this term only
#9 MeSH descriptor Psychomotor Disorders, this term only
#10 MeSH descriptor Psychomotor Performance, this term only
#11 MeSH descriptor Movement Disorders, this term only
#12 MeSH descriptor Developmental Disabilities, this term only
#13 ((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) NEAR/3 (impair* or skill* or disorder* or deficit* or delay* or disabilit* or dysfunc*))
#14 MeSH descriptor Walking explode tree 1
#15 MeSH descriptor Gait, this term only
#16 MeSH descriptor Gait Disorders, Neurologic, this term only
#17 MeSH descriptor Gait Ataxia, this term only
#18 gait*
#19 walk or walking

#20 MeSH descriptor Locomotion, this term only
#21 locomotor* or locomotion*
#22 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory)
#23 stepping
#24 (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25 MeSH descriptor Disabled Children, this term only
#26 MeSH descriptor Down syndrome, this term only
#27 MeSH descriptor Cerebral Palsy, this term only
#28 MeSH descriptor Spinal Dysraphism, this term only
#29 (down* NEXT syndrome or cerebral NEXT pals* or (spin* NEAR/3 injur*) or spina NEXT bifida)
#30 MeSH descriptor Infant, Low Birth Weight explode all trees
#31 MeSH descriptor Infant, Premature, this term only
#32 low NEXT birth NEXT weight
#33 preterm* or pre NEXT term* or prematur*
#34 (#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 or #33)
#35 baby or babies or infant* or toddler* or child* or preschool* or pre-school* or schoolchild*
#36 MeSH descriptor Child explode all trees
#37 MeSH descriptor Infant, this term only
#38 (#35 OR #36 OR #37)
#39 (#24 OR #34)
#40 (#6 AND #38 AND #39)

MEDLINE (OVID)

1 Physical Therapy Modalities/
2 "Physical Therapy (Specialty)"/
3 (physiotherap$ or physio therap$ or physical therap$).tw.
4 Exercise Therapy/
5 tread-mill$.tw.
6 treadmill$.tw.
7 or/1-6
8 Motor Skills/
9 Motor Skills Disorders/
10 Psychomotor Disorders/
11 Psychomotor Performance/
12 Movement Disorders/
13 Developmental Disabilities/
14 ((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development$) adj3 (impair$ or skill$ or disorder$ or deficit$ or delay$ or disabilit$ or dysfunc$)).tw.
15 exp Walking/
16 Gait/
17 Gait Disorders, Neurologic/
18 Gait Ataxia/
19 gait.tw.
20 locomotion/
21 (walk or walking).tw.
22 (locomotor$ or locomotion$).tw.
23 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory).tw.
24 stepping.tw.
25 or/8-24
26 Disabled Children/
27 down syndrome/
28 cerebral palsy/

29 spinal dysraphism/
30 (down$ syndrome or cerebral pals$ or (spin$ adj3 injur$) or spina bifida).tw.
31 exp infant, low birth weight/ or infant, premature/
32 (low birth weight or pre-term$ or preterm$ or prematur$).tw.
33 or/26-32
34 Infant/
35 exp child/
36 (baby or babies or infant$ or child$ or toddler$ or pre-school$ or preschool$ or schoolchild$).tw.
37 34 or 35 or 36
38 randomized controlled trial.pt.
39 controlled clinical trial.pt.
40 randomi#ed.ab.
41 placebo$.ab.
42 drug therapy.fs.
43 randomly.ab.
44 trial.ab.
45 groups.ab.
46 or/38-45
47 exp animals/ not humans.sh.
48 46 not 47
49 25 or 33
50 7 and 37 and 48 and 49

EMBASE (OVID)

1 physiotherapy/
2 pediatric physiotherapy/
3 (physiotherap$ or physio therap$ or physical therap$).tw.
4 treadmill/
5 tread-mill$.tw.
6 treadmill.tw.
7 kinesiotherapy/
8 or/1-7
9 motor performance/
10 psychomotor performance/
11 motor dysfunction/
12 developmental disorder/
13 motor development/
14 ((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development$) adj3 (impair$ or skill$ or disorder$ or deficit$ or delay$ or disabilit$ or dysfunc$)).tw.
15 locomotion/
16 walking/
17 gait/
18 GAIT DISORDER/
19 ataxia/
20 gait.tw.
21 (walk or walking).tw.
22 (ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory).tw.
23 (locomotor$ or locomotion$).tw.
24 stepping.tw.
25 handicapped child/
26 Down syndrome/ (21539)
27 cerebral palsy/ (18656)
28 spina bifida/ (4734)

29 (down$ syndrome or cerebral pals$ or (spin$ adj3 injur$) or spina bifida).tw.
30 prematurity/
31 exp low birth weight/
32 (low birth weight or pre-term$ or preterm$ or prematur$).tw.
33 or/9-24
34 or/25-32
35 or/33-34
36 exp child/
37 infant/
38 (baby or babies or infant$ or child$ or toddler$ or pre-school$ or preschool$ or schoolchild$).tw.
39 or/36-38
40 Clinical trial/
41 Randomized controlled trial/
42 Randomization/
43 Single blind procedure/
44 Double blind procedure/
45 Crossover procedure/
46 Placebo/
47 Randomi#ed.tw.
48 RCT.tw.
49 (random$ adj3 (allocat$ or assign$)).tw.
50 randomly.ab.
51 groups.ab.
52 trial.ab.
53 ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
54 Placebo$.tw.
55 Prospective study/
56 (crossover or cross-over).tw.
57 prospective.tw.
58 or/40-57
59 8 and 35 and 39 and 58

CINAHLPlus (EBSCOhost)

S50 S31 and S34 and S49
S49 S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or
S45 or S46 or S47 or S48
S48 TI (evaluat* study or evaluat* research) or AB (evaluate* study or evaluat* research) or TI (effectiv* study or effectiv* research) or AB(effectiv* study or effectiv* research) OR TI (prospectiv* study or prospectiv* research) or AB(prospectiv* study or prospectiv* research) orTI (follow-up study or follow-up research) or AB (follow-up study or follow-up research)
S47 "cross over*"
S46 crossover*
S45 (MH "Crossover Design")
S44 (tripl* N3 mask*) or (tripl* N3 blind*)
S43 (trebl* N3 mask*) or (trebl* N3 blind
S42 (doubl* N3 mask*) or (doubl* N3 blind
S41 (singl* N3 mask*) or (singl* N3 blind
S40 (clinic* N3 trial*) or (control* N3 trial*)
S39 (random* N3 allocat*) or (random* N3 assign*)
S38 randomis* or randomiz*
S37 (MH "Meta Analysis")
S36 (MH "Clinical Trials+")
S35 MH random assignment
S34 S32 or S33

S33 TI(baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*) or AB(baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*)
S32 (MH "Child") OR (MH "Infant") OR (MH "Child, Preschool
S31 S29 or S30
S30 S6 and S28
S29 S6 and S19
S28 S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27
S27 TI(low birth weight or pre-term* or preterm* or prematur*) or AB(low birth weight or pre-term* or preterm* or prematur*)
S26 (MH "Infant, Low Birth Weight+")
S25 (MH "Infant, Premature")
S24 TI (down* syndrome or cerebral pals* or (spin* N3 injur*) or spina bifida) or AB (down* syndrome or cerebral pals* or (spin* N3 injur*) or
spina bifida)
S23 (MH "Down syndrome")
S22 (MH "Spina Bifida")
S21 (MH "Cerebral Palsy")
S20 (MH "Child, Disabled")
S19 S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18
S18 AB((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) and (impair* or skill* or disorder* or deficit* or delay*
or disabilit* or dysfunc*))
S17 TI((motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) and (impair* or skill* or disorder* or deficit* or delay*
or disabilit* or dysfunc*))
S16 TI(ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory) or AB(ambulation or ambulatory or
nonambulation or nonambulatory or non-ambulation or non-ambulatory)
S15 TI(gait* or locomotor* or locomotion* or step or stepping or walk* or walking) or AB(gait* or locomotor* or locomotion* or step or stepping or
walk* or walking)
S14 (MH "Locomotion")
S13 (MH "Gait") OR (MH "Gait Disorders, Neurologic") OR (MH "Gait Apraxia") OR (MH "Step")
S12 (MH "Walking")
S11 (MH "Infant Development Disorders")
S10 (MH "Child Development Disorders")
S9 (MH "Developmental Disabilities
S8 (MH "Psychomotor Disorders")
S7 (MH "Motor Skills") OR (MH "Motor Skills Disorders") OR (MH "Psychomotor Performance")
S6 S1 or S2 or S3 or S4 or S5
S5 TI(physiotherap* or physio therap* or physical therap*) or AB(physiotherap* or physio therap* or physical therap*)
S4 TI (treadmill* or tread-mill*) or AB(treadmill* or tread-mill*)
S3 TI (treadmill* or tread-mill*) or AB(treadmill* or tread-mill*)
S2 (MH "Treadmills")
S1 (MH "Physical Therapy") OR (MH "Gait Training") OR (MH "Pediatric Physical Therapy") OR (MH "Therapeutic Exercise")

PsycINFO (EBSCOhost)

S43 S4 and S25 and S28 and S42
S42 S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or
S39 or S40 or S41
S41 (evaluation N3 stud* or evaluation N3 research*)
S40 (effectiveness N3 stud* or effectiveness N3 research*)

S39 DE “Placebo” or DE “Evaluation” or DE “Program Evaluation” OR DE “Educational Program Evaluation” OR DE “Mental Health Program Evaluation”
S38 (DE “Random Sampling” or DE “Clinical Trials”) or (DE “Experiment Controls”)
S37 “cross over*”
S36 crossover*
S35 (tripl* N3 mask*) or (tripl* N3 blind*)
S34 (trebl* N3 mask*) or (trebl* N3 blind*)
S33 (doubl* N3 mask*) or (doubl* N3 blind*)
S32 (singl* N3 mask*) or (singl* N3 blind*)
S31 (clinic* N3 trial*) or (control* N3 trial*)
S30 (random* N3 allocat*) or (random* N3 assign*)
S29 randomis* or randomiz*
S28 S26 or S27
S27 (ZG “infancy (2-23 mo)”) or (ZG “preschool age (2-5 yrs)”)
S26 baby or babies or infant* or child* or toddler* or pre-school* or preschool* or schoolchild*
S25 S16 or S24
S24 S17 or S18 or S19 or S20 or S21 or S22 or S23
S23 low birth weight or pre-term* or preterm* or prematur*
S22 DE “Birth Weight”
S21 DE “Premature Birth”
S20 (down* syndrome or cerebral pals* or (spin* N3 injur*) or spina bifida)
S19 DE “Spina Bifida”
S18 DE “Cerebral Palsy”
S17 DE “Down’s Syndrome”
S16 S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15
S15 DE “Developmental Disabilities”
S14 (motor or neuromotor or neuro-motor or psychomotor or psycho motor or development*) and (impair* or skill* or disorder* or deficit* or delay* or
disabilit* or dysfunct*)
S13 ambulation or ambulatory or nonambulation or nonambulatory or non-ambulation or non-ambulatory
S12 gait* or locomotor* or locomotion* or step or stepping or walk* or walking
S11 DE “Locomotion”
S10 DE “Motor Skills”
S9 DE “Walking”
S8 DE “Motor Coordination”
S7 DE “Motor Performance”
S6 DE “Motor Development”
S5 DE “Psychomotor Development”
S4 S1 or S2 or S3
S3 treadmill* or tread-mill*
S2 physiotherap* or physio therap* or physical therap*
S1 DE “Physical Therapy”

LILACS

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

Science Citation Index and Conference Proceedings Citation Index - Science

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

PED*ro*
Using Simple search : treadmill* child*

metaRegister of Controlled Trials
treadmill and children

CenterWatch
treadmill **limited to** Clinical trial Listings

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

Clinicaltrials.gov
treadmill | Interventional Studies | Child

Appendix 2. Table of unused methods

Continuous data	If the same continuous outcome (for example, infant's gross motor development level) is measured differently across studies, we will compare standardised mean differences (SMD) with 95% CI across studies (Higgins 2008). Where necessary, we will use formulas to convert F ratios, t-values and Chi ^{2} values into SMDs (Lipsey 2001), using Hedges *g* to correct for small sample bias.
Dichotomous data	We will analyse the outcomes of any study reporting binary/dichotomous data by calculation of the risk ratio for the occurrence of an event (rather than a non-event) for its consistency as a summary statistic and ease of interpretation
Unit of analysis issues	*Cluster-randomised trials* For trials that use clustered randomisation, we will present results with proper controls for clustering (robust standard errors or hierarchical linear model). If appropriate controls are not used and it is not possible to obtain the full set of each individual participant's data, we will control the data for clustering using the procedures outlined by Higgins 2008. For dichotomous outcome measures, we will divide the number of events and the number of participants per trial arm by the design effect [1 + (1-m)*r], where *m* is the average cluster size and *r* is the intra-cluster correlation coefficient (ICC)

(*Continued*)

	. For continuous outcome measures, we will divide the number of participants per trial arm by the design effect, with the mean values unchanged. To determine the ICC, we will use estimates in the primary trials on a study-by-study basis. In the case of these values not being reported, we will use external estimates of the ICC that are appropriate to the context of each trial and average cluster size. If they were still not available, we will then use statistical procedures outlined by Higgins 2008. *Multiple time points* When the results are measured at multiple time points, we will only consider baseline measurements and the last time point measurements *Multiple interventions per individual* If it is found that participants in some trials receive multiple treatments, we will conduct meta-analysis on those studies separately
Dealing with missing data	For dichotomous data, we will report the missing data and dropouts for included studies along with the number of participants who are included in the final analyses as a proportion of all participants in each study. We will provide reasons for missing data in a narrative summary. The extent to which the results of the review could be altered by the missing data can be assessed based on consideration of best-case and worst-case scenarios (Gamble 2005). The best-case scenario is the one where all participants with missing outcomes in the experimental condition had good outcomes and all those with the missing outcomes in the control condition had poor outcomes, and the worst-case scenario is vice versa (Higgins 2008). However, the best-case and worst-case scenarios method is too extreme and a more plausible approach is needed. We will use the method suggested by Higgins 2008, which can incorporate specific reasons for missing data and considers plausible event risks among missing participants in relation to risks among those observed We will analyse missing continuous data either on an endpoint basis, including only participants with a final assessment, or using last observation carried forward to the final assessment if the last observation carried forward data were reported by the trial authors. If SDs are missing, we will make attempts to obtain these data through contacting trial authors. If SDs are not available from trial authors, we will calculate them from t-values, confidence intervals or standard errors, where reported in articles (Deeks 1997a; Deeks 1997b). If these additional figures are still not available or obtainable, we will not include the study data in the comparison of interest
Assessment of heterogeneity	We will describe statistical heterogeneity using I^2 (Higgins 2002), a quantity that describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error). In addition, we will employ a chi^2 test of homogeneity to determine the strength of evidence that heterogeneity is genuine. If an individual study appears to be an outlier, we may carry out sensitivity analysis with and without the study. If the primary studies are judged to be substantially heterogeneous even within these sub-groupings, we will only give a descriptive analysis, particularly if there is variation in direction of effect
Assessment of reporting biases	In order to investigate the relationship between effect size and standard error, we will draw funnel plots if sufficient studies are available (i.e., ten or more individuals studies). Asymmetry could be attributable to publication bias, but might also reflect a real relationship between trial size and effect size. If we find such a relationship, we will examine clinical variation of the studies (Higgins 2008, Section 10.4). As a direct test for publication bias, we will compare results extracted from published journal reports with results obtained from other sources, including correspondence
Data synthesis	For dichotomous outcomes, we will also calculate the number needed to treat for an additional beneficial outcome

(*Continued*)

Subgroup analysis	We will undertake subgroup analysis if clinically different interventions are identified or there are clinically relevant differences between participant groups. We will thus investigate any subgroup differences in order to establish whether there is a single intervention effect, specifically: · treadmill 'dose' (total number of training sessions, frequency of training per week or duration of each training session); · type of intervention (preventive or rehabilitative); · diagnosis (cerebral palsy, Down's syndrome etc.); · conditions affecting the neuro-musculoskeletal system (hypo- or hypertonia, spasticity, posture etc.)
Sensitivity analysis	We will conduct sensitivity analysis, where data permit, to determine whether findings are sensitive to restricting inclusion to studies judged to be at low risk of bias. In these analyses, we will re-evaluate the findings, limiting the inclusion to published studies or to those studies that have a low risk of: · selection bias (associated with allocation concealment and sequence generation); · performance bias (associated with blinding); · attrition bias (associated with completeness of data)

HISTORY

Protocol first published: Issue 7, 2011

Review first published: Issue 12, 2011

CONTRIBUTIONS OF AUTHORS

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

DECLARATIONS OF INTEREST

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

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- National Institute for Health Research, UK.

Cochrane Incentive Award

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. Background - minor modifications.

2. Primary outcomes - for clarity, defined 'step frequency' and replaced 'walking with assistive devices' with 'walking with assistance'.

3. Secondary outcomes - 'gait parameters' was added as we had assumed this under 'gait pattern functions' but not explicitly expressed it.

4. Electronic searches - we did not search for dissertations in WorldCat.

5. Other risk of bias - individual authors of each included study were contacted when RoB was unclear. We have kept the classification as 'unclear' where relevant.

6. See Appendix 2 for methods not used due to type or amount of data.

CAPÍTULO 3.

Treadmill training in moderate risk preterm infants promotes stepping quality—Results of a small randomised controlled trial

Research Developmental Disabilities

Angulo-Barroso, R., Tiernan, C., Chen, L., Valentin-Gudiol, M. & Ulrich, D. 2013, "Treadmill training in moderate risk preterm infants promotes stepping quality—Results of a small randomised controlled trial", Research in developmental disabilities, vol. 34, no. 11, pp. 3629-3638.

Research in Developmental Disabilities 34 (2013) 3629–3638

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Research in Developmental Disabilities

Treadmill training in moderate risk preterm infants promotes stepping quality—Results of a small randomised controlled trial

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ABSTRACT

Infants at risk for neuromotor delay (NMD) are associated with premature birth and low birth weight. These infants frequently exhibit tone, posture, and movement abnormalities. Therefore, it is important to identify potential interventions to facilitate early motor development within this population. The purpose of this study was to examine the potential benefits of treadmill (TM) training in infants at risk for NMD. Furthermore, relationships between TM stepping performance and onset of walking have been suggested, and therefore, were also explored. Twenty-eight infants at moderate risk for NMD were randomly assigned to one of two groups: (1) TM training (experimental) ($N = 15$) or (2) control ($N = 13$). Infants in the experimental group were trained for 8 min/day, five days/week from study entry until walking onset. Monthly, 5 min of TM stepping performance were videotaped and analysed for infants in both groups to obtain frequency and quality of TM stepping. Groups were different in terms of TM stepping performance with experimental group displaying better stepping. However, they did not differ in age of walking onset (experimental = 15.1 months, control = 14.6 months). In both groups, frequency of TM stepping was significantly related to onset of walking. Findings suggest that TM training as implemented impact the quality of TM stepping, but did not significantly improve walking onset. Given the significant relationship between stepping and walking onset, the moderate affection of the population, the relative low intensity and lack of individualisation of the training, we suggest future research should further explore the impact of TM training on gait-related variables and include individualised, more intense, and prolonged training.

1. Introduction

Infants at risk for neuromotor delay (NMD) of non-genetic origin often display perinatal histories significant for prematurity and other related factors, such as low birth weight, brain abnormalities, respiratory difficulties, and multiparity (Spittle, Orton, Anderson, Boyd, & Doyle, 2012; Sutcliffe & Derom, 2006). From a motor perspective, these individuals may

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demonstrate abnormalities related to tone, movement, and posture (Molnar, 1985). Recent reports estimate the incidence of cerebral palsy (CP) amongst infants who were born prematurely or with low birth weight at five to fifteen percent (Spittle et al., 2012; Tin, Wariyar, & Hey, 1997; Vohr, Wright, Poole, & McDonald, 2005). Such rates suggest that a large proportion of infants, i.e. 85–95%, with perinatal risk factors experience deficits that are transient in nature or consistent with other developmental disabilities, such as Developmental Coordination Disorder (Davis, Ford, Anderson, & Doyle, 2007; Holsti, Grunau, & Whitfield, 2002).

Regardless of whether they receive a diagnosis, most of these infants will require early intervention to manage their deficits and promote motor development. Reviews of the literature surrounding the impact of early intervention on motor development in infants at risk for NMD have provided inconclusive results (Blauw-Hospers & Hadders-Algra, 2005; Brown & Burns, 2001; Spittle et al., 2012). However, programmes that are highly structured and have substantial parent involvement seem to have more favourable results (Hauser-Cram et al., 2001). Furthermore, ample evidence supports the value of task-specific training in therapeutic interventions (Alloway & Warner, 2008; Hubbard, Parsons, Neilson, & Carey, 2009). One intervention that meets these criteria is parent-implemented, task-specific treadmill (TM) training. This may be an attractive intervention tool because it specifically targets walking, a skill that is often delayed in infants at risk for NMD (Jeng, Chen, Tsou, Chen, & Luo, 2004; Jeng, Yau, Liao, Chen, & Chen, 2000). Further, the TM is believed to facilitate practice of functional leg movements (i.e. alternating steps) that are necessary for independent walking. Vereijken and Thelen (1997) found that daily TM training caused infants with typical development to increase their alternate stepping to the point where it was a dominant pattern despite being initially non-preferred.

To date, there is limited knowledge surrounding TM training in infants at risk for NMD (Valentin-Gudiol et al., 2011). However, the importance of alternating step practice provided by the TM has been documented in infants with certain paediatric disabilities. For instance, several studies have shown that TM training facilitates walking onset (Ulrich, Lloyd, Tiernan, Looper, & Angulo-Barroso, 2008; Ulrich, Ulrich, Angulo-Kinzler, & Yun, 2001) and improves quality of gait in infants with Down syndrome (DS) (Angulo-Barroso, Wu, & Ulrich, 2008; Wu, Looper, Ulrich, Ulrich, & Angulo-Barroso, 2007). It is widely known that infants with DS are typically characterised as having hypotonia and heightened ligamentous laxity. Whether the favourable results observed in DS can be replicated in infants with different neuromotor characteristics (ex. spasticity, hypertonia) of non-genetic origin remains unclear. Nevertheless, past studies concerning TM training in infants who are at risk for NMD have provided generally positive results. Davis and colleagues (Davis, Thelen, & Keck, 1994) demonstrated that premature low risk infants can produce alternating steps on a TM at 1, 6, and 9 months of age. Since then, Bodkin, Baxter, and Heriza (2003) have conducted a case study where they trained a premature infant with a grade III IVH on a TM. While they concluded that training may facilitate proper foot placement during stepping, it is important to note that the authors terminated TM training prior to the infant achieving independent walking. The latter two studies suggest that infants at risk for NMD are capable of producing TM steps and that TM training appears to be feasible in this population of infants. To our knowledge there is only one study that implemented a 6-week intensive TM training in infants with early diagnosis of mild CP at an average age of 22 months (Mattern-Baxter, McNeil, & Mansoor, 2013). This study found improvements in walking skills such as walking onset and increased speed in infants who received the TM intervention.

Further examination of the effects of TM training in infants at risk for NMD is warranted in order to determine if prolonged stepping practice up to the point of walking onset can both facilitate attainment of this skill and improve stepping performance. Given the limited evidence regarding the effects of TM training in infants at risk for NMD and the probably unfounded yet real clinical concern that this type of motor training could worsen spasticity, the target population for this trial was limited to less involved infants excluding high risk infants.

The research questions were:

1. Do infants at moderate risk for neuromotor delays who receive TM training demonstrate more alternating steps and superior quality of stepping on the TM relative to infants in the control group?
2. Will independent walking occur earlier in the TM training group than in the control group?
3. Is there a relationship between pre-walking onset TM performance and walking onset?

2. Material and methods

2.1. Participants

Participants were recruited via high-risk clinics of local hospital doctors who referred potential subjects. Each subject was checked against the inclusion and exclusion criteria, prior to the initial assessment. Forty-five infants were referred from the University Medical Centre's Neonatal Follow-up/Developmental Assessment Clinic (see Fig. 1 for flow of participants through the study). These infants were admitted to the clinic because of low birth weight (<1500 g), prolonged ventilator use, or neonatal neurological insults including intraventricular haemorrhage, periventricular leukomalacia, hypoxic-ischaemic encephalopathy, neonatal seizures, and other intracranial haemorrhage. The inclusion criteria for our study were: (1) moderate hypo/hypertonia or developmental delay when examined by their paediatrician; and (2) corrected age between 6 and 13 months; 6 months was considered the minimum age to produce 10 steps on the TM (see below), and 13 months the maximum age to warranty a minimum length of TM training. Exclusion criteria were congenital musculoskeletal deficits, or other neurological or genetic disorders (e.g. Down syndrome, spina bifida). Study procedures were approved by the Institutional

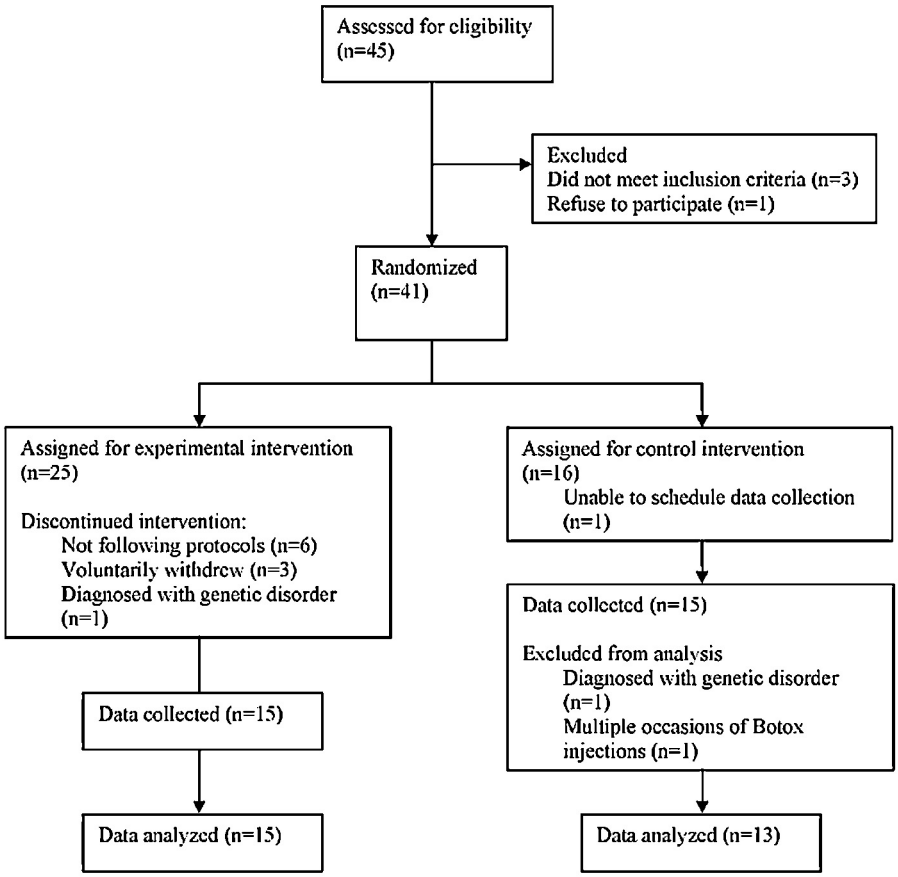

Fig. 1. Flowchart of participants' recruitment through the study.

Review Board at the University and all parents gave written informed consent before entering the study. In order to enter into the study and based on our previous experience, the infant was required to produce 10 supported steps on a TM (belt speed = 0.2 m/s) within a 1 min trial before turning 13 months corrected age. In the event that the infant was not able to produce 10 supported steps during the initial visit, the next observation was scheduled approximately one month later. This process continued until the infant was able to display the entry criterion. Four infants (8.9%) were excluded from the study: three of them (6.7%) because they did not meet the 10-step minimum prior to reaching a corrected age of 13 months, and one infant who's collaboration on the TM could not be achieved. Once enrolled, the infant was randomly assigned to either the experimental or control group. Data was not collected in 11 (26.8%) infants because of impossibility to schedule data collection ($n = 1$), noncompliance with the research protocol ($n = 6$, 14.6%), voluntary withdrawal ($n = 3$, 7.3%), and a diagnosis of genetic disorder ($n = 1$, 2.4%). An additional two infants were not included in the data analysis due to a later diagnosis of genetic disorder ($n = 1$, 6.7%) and multiple occasions of receiving Botox injections to the legs ($n = 1$, 6.7%). Therefore, a final study sample of 28 infants (15 experimental, 13 control) was included in the analysis (see Fig. 1). Table 1 presents the participant characteristics' at study entry. All diagnoses of CP were given at two years corrected age by the neuropaediatrician in charge.

2.2. Design

A randomised, controlled clinical trial was performed to examine the potential benefits of TM training in infants at risk for neuromotor delay. Eligible participants were randomised to either TM training group or the control group by a statistician using a computer programme for group allocation, considering 3 stratification factors: age, gender, birth weight. All participants were assigned an ID, which was entered into the computer by the statistician to conduct the subject's allocation. This information was provided to the project coordinator and home assessment personnel but maintaining the laboratory assessors blind to group allocation. Therefore, only outcomes from video coding came from a blinded process.

2.3. Intervention

The entry age ranges for the experimental and control groups were 8.3–12.7 and 6.3–11.0 months, respectively. Infants randomly assigned to the control group did not receive TM training but continued with the standard physical therapy

Table 1
Perinatal, social and developmental characteristics of experimental and control group.

	All ($N = 28$)		CP ($N = 5$)	
	Experimental	Control	Experimental	Control
Birth				
N	15	13	2	3
Gender	6F, 9M	4F, 9M	1F, 1M	1F, 2M
Birth weight (g)	1596 (944)	1465 (1012)	822 (401)	1441 (1014)
Gestational age (weeks)	30.8 (4.8)	29.0 (4.8)	27.7 (1.2)	26.2 (3.3)
Maternal education (%)				
Level 1	50	41.67	100	66.67
Level 2	50	41.67	0	0
Level 3	0	16.66	0	33.33
Low birth wt. (<1500 g)	8/15	10/13	2/2	2/3
Low gest. age (<32 weeks)	10/15	11/13	2/2	3/3
Brain insult				
IVH I–II	4/15	5/13	1/2	2/3
IVH III–IV	3/15	0/13	0/2	0/3
HIE	0/15	1/13	0/2	0/3
Neonatal seizures	0/15	3/13	0/2	0/3
Other intracranial HL	4/15	2/13	0/2	0/3
Prolonged ventilator use	8/15	7/13	0/1[a]	0/3
Multiple births	5/15	6/13	0/2	1/3
Status at study entry				
Corrected age (months)	9.7 (1.3)	9.0 (1.4)	9.1 (0.9)	10.2 (0.6)
Weight (kg)	8.1 (1.1)	8.6 (1.2)	7.5 (2.4)	9.2 (1.0)
Head circumference (cm)	44.3 (2.0)	45.4 (1.5)	41.9 (3.0)	46.7 (0.8)
Bayley motor (PDI)	69.1 (16.8)	69.6 (14.8)	56.5 (0.7)	71.7 (15.0)
Bayley mental (MDI)	68.9 (13.3)	67.6 (12.0)	70.0 (8.5)	72.3 (13.0)
GMFM	41.2 (13.1)	35.2 (11.5)	33.8 (4.2)	45.7 (11.1)
Ashworth_{LE}*	2.2 (2.0)	4.9 (2.9)	4.0 (2.8)	4.0 (2.6)
Exit				
Walking onset (months)	15.1 (3.0)	14.6 (2.3)	19.1 (3.0)	14.6 (2.8)
Weight	9.4 (1.2)	10.0 (1.0)	9.0 (2.4)	10.1 (0.3)
Head circumference	46.1 (1.9)	46.5 (1.7)	45.2 (3.7)	48.1 (0.1)
Bayley motor	71.9 (14.8)	72.5 (12.0)	61.5 (17.7)	79.0 (3.5)
Bayley mental	78.7 (16.4)	82.1 (17.1)	88.0 (14.1)	91.0 (20.2)
GMFM	70.8 (5.5)	70.2 (8.8)	67.9 (3.1)	77.4 (5.2)
Ashworth_{LE}	2.2 (3.8)	2.5 (1.4)	9.0 (7.1)	2.0 (0)[b]
Study duration (days)	161.5 (80.2)	166.5 (73.9)	301.5 (61.5)	131.0 (81.3)

Values presented as means (SD), percentage, or ratios of infants. Levels 1–3 in maternal education correspond to high school, some college or bachelor's degree, and graduate level degree, respectively IVH (intraventricular haemorrhage grades), HIE (hypoxic-ischaemic encephalopathy). Other intracranial haemorrhage or lesion (HL). GMFM (Gross Motor Function Measure). GMFM and Bayley's values represent total scores and index scores, respectively. Ashworth_{LE} = sum of lower extremity (LE) scores. Prolonged ventilator use = 4 days or longer than predicted by gestational age 37. All five participants with CP were diagnosed with spastic diplegia.

[a] Data available for only 1 of the 2 participants.

[b] Data available for only 2 of the 3 participants.

* Denotes significant group difference ($p < .05$) between experimental and control for $N = 28$.

intervention prescribed by the local Early Intervention programme, as did infants in the experimental group. Families assigned to the experimental group received an infant sized TM (Carlin's Creations, MI) for the duration of the study. They also received training on how to position and support their infant on the TM for 8 min of training per day, five days each week, beginning with 1 min training intervals and then taking a brief rest before continuing the training until 8 min were completed. As the child's supported TM stepping increased over time, parents were encouraged to gradually increase the training beyond 1-min intervals before resting. The belt speed used in the intervention was 0.2 m/s. All these TM training parameters were the same than those used in a previous paediatric TM training study (Ulrich et al., 2001). TM training continued until the infant was observed walking 3 independent steps over ground, at which time the TM was removed from the home. During the monthly visit to the infants in the experimental group, we recorded the amount of TM use in minutes from the small gauge attached to the side of the TM. When caregivers did not meet the desired monthly training times (8 min per day, 5 days per week for 4 weeks), staff reminded them of the required intervention protocols and provided feedback on the infant's progress on TM stepping and other developmental milestones. If caregivers consistently failed to achieve the required training protocol, they were dropped from the study and the TM was removed from the home.

2.4. Data collection

Frequency and quality of stepping were assessed monthly from entry into the study until the onset of independent walking for all participants, despite group membership. Two staff members visited all families monthly to monitor

adherence to the TM training protocol (experimental group), answer any questions from the caregivers, videotape five 1-min trials of the infants stepping while being supported on the TM (both groups: a TM was taken to the home when the infant was in the control group), measure body length and weight, head circumference, and administer the modified Ashworth scale (Bohannon & Smith, 1987) which employs a 6 point ordinal scale (0–5) to evaluate muscle tone. Muscle groups tested included the hip adductors, knee flexors and extensors, and the ankle plantar-flexors for each leg. All the scores for each leg were summed. The Modified Ashworth Scale is an often-used tool to measure muscle tone (Damiano, Dodd, & Taylor, 2002; Damiano & Quinlivan, 2002). At the entry to the study, Motor and Mental Subscales (PDI and MDI, respectively) of the Bayley Scales of Infant Development II (Bayley, 1993) were assessed to determine the presence of any initial group differences. During each monthly home visit, we updated the achievement of any new items on the subscales. We also administered the Gross Motor Function Measure (Palisano et al., 1997; Russell et al., 1989) at entry and at walking onset. Evaluators of these two tests were trained to achieve at least 85% reliability with the first author before they were able to assess infants in the study. Five additional infants were used to determine the final reliability Person coefficient values, which ranged from 0.77 to 1.0, with an average reliability value of 0.95.

2.5. Data reduction and analysis

The sample size utilised in this study was extrapolated from the TM RCT conducted in infants with DS (Ulrich et al., 2001), which resulted in a sample of 15 subjects per group for 80% power. No other power analysis was conducted given the lack of previous studies with the population of interest and the difficulty of enrolling subject with the required criteria. The videotapes of the five 1 min trials of the TM stepping performance were coded by trained kinesiologists researchers blind to group membership. Each TM step was coded as alternating, single, or parallel following the definitions provided by Thelen, Ulrich, and Wolff (1991). An alternating step was coded when the flexion and extension of one leg overlaps the flexion and extension of the opposite leg in an alternating pattern. A single step was defined as when there was no overlap between the flexion and extension of the legs. A parallel step was defined as both legs flexed and extended synchronously. Foot placement at the initiation of the stance phase in the step was scored as either toe or flat contact. Toe contact meant that the forefront of the foot was predominantly in contact with the surface, with over half of the posterior of the foot being off the surface of the TM. Flat contact implied that over half of the foot was in contact with the belt surface. The assessors had to reach a minimum of 90% accuracy in independent coding of a training videotape of infant TM stepping (first author used as a gold standard) before they were permitted to code any research tapes used in this study. Based on a five percent of the total steps identified at the beginning, mid, and close to final point of the study, a mean inter-assessor reliability coefficient (Kappa) of 0.92 (range = 0.90–0.93) and 0.98 (range = 0.95–1.0) were obtained for alternating steps and toe contacts, respectively, for the three assessors. The mean intra-assessor stability across the study for the assessors was 0.94 (range = 0.89–0.98).

The differences between the two groups in perinatal, social and developmental characteristics (Table 1) were analysed using *t*-tests and non-parametric tests when appropriate. Frequency of alternating steps per minute (AltStp), percentage of alternating steps (%AltStp), and percentage of toe contacts (%Toe) were analysed with a two-way (group × age) repeated measure ANCOVA to examine group, age and group by age interaction effects, with $\text{Ashworth}_{\text{LE}}$ score at entry as the covariate since group differences existed for this variable despite randomisation. To assess developmental change and group differences in TM response as a whole, a composite score was formed by averaging the *Z*-scores of the two percentage TM variables (%AltStp and %Toe). The previous statistical design was also utilised in the TM composite variable and in the $\text{Ashworth}_{\text{LE}}$ score to address potential group, age, or group by age interaction effects. These analyses were limited to the corrected age range of 8–16 months because insufficient sample existed outside this range. Appropriate post hoc comparisons with Bonferroni adjustment were performed on any significant age effect or group × age interaction. Finally, Pearson's correlations were employed, at each individual corrected age level and each group, to examine the relationship of walking onset age with infants' stepping performance on the TM across the age range of 8–14 months. Because the average age of walking onset was between 14 and 15 months in both groups, these analyses were limited up to 14 months. A p value of less than .05 was defined as statistically significant.

3. Results

3.1. Intervention compliance and duration

Six infants were eliminated from the study due to noncompliance with the research protocol (14.6%) due to lack of time or family complications. Compliance to the TM training protocol in the analysed experimental group was on average $X = 79.29\%$

Table 2
Treadmill training duration in the experimental group.

Age	8	9	10	11	12	13	14	15	16
Mean	1.0	1.3	2.0	2.9	3.5	4.2	5.0	5.5	6.5
Range	1–1	1–2	1–3	1–4	1–5	1–6	2–7	3–8	4–9

All data are in months.

(SD = 22.51), range = 35.42–101.97 of the total requested minutes. These results indicate that infants on average trained only 4 days per week instead of five. There were no reported adverse effects to the intervention. The experimental group received an average of 5.2 (range 2–9) months of TM training from 8 to 16 months of age. Table 2 shows the average and range of TM training per age in the experimental group.

3.2. Infants' characteristics: birth and entry

Except for $\text{Ashworth}_{\text{LE}}$ scores at entry (higher scores representing greater spasticity), none of the infants' characteristics at birth or entry were different between the experimental and control groups. Infants in the control group had an average $\text{Ashworth}_{\text{LE}}$ score of $X = 4.9$ (SD = 2.9) compared to $X = 2.1$ (SD = 2.0) in the experimental group (Chi-square = 7.18, $p = .007$, 95%CI (−4.78, −0.75)) (see Table 1). To control for this initial difference, $\text{Ashworth}_{\text{LE}}$ score at entry was considered as a covariate in subsequent analyses. Descriptive values of birth and entry variables are also provided for the infants who received a diagnosis of CP in each group in Table 1.

3.3. Effect of intervention

3.3.1. Treadmill responses

When examining individual variables of TM performance, infants at risk for NMD increased AltStp (see Fig. 2a), improved the %AltStp (Fig. 2b), and decreased the %Toe contacts with age (Fig. 2c). All three variables had significant age main effects with $p < .0001$, with $\eta^2 p$ of 0.51, 0.54, and 0.35, respectively.

The TM composite scores improved with time from 8 to 16 months of corrected age (significant age main effect, $F(8,93) = 16.5$, $p < .0001$, $\eta^2 p$ 0.59) (Fig. 2e). However, infants in the experimental group improved TM performance at a higher level across age compared to infant in the control group (group by age interaction, $F(8,93) = 2.26$, $p = .03$, $\eta^2 p$ 0.16). By 16 months, infants in the experimental group averaged a composite Z-score of $X = 1.12$ (SD = 0.25) compared to $X = 0.68$ (SD = 0.29) in the control group for the TM performance. Post hoc analyses revealed group differences at 13 ($p = .02$, Cohen's $d = 0.51$) and 15 ($p = .05$, Cohen's $d = 0.41$) months corrected age. The covariate, $\text{Ashworth}_{\text{LE}}$ score and group main effect were not significant.

3.3.2. Total lower extremity Ashworth score

$\text{Ashworth}_{\text{LE}}$ scores did not change significantly over time, were not different by group except at the entry point, and they did not show a group by age interaction (Fig. 2d). The only significance in the statistical model was the covariate, i.e. the initial $\text{Ashworth}_{\text{LE}}$ score at entry. As shown in Table 1, the control group showed higher levels of LE spasticity than the experimental group at entry. Similar results were observed at 8 months of age ($X = 5.20$, SD = 4.6 versus $X = 2.25$, SD = 1.2 between the control and experimental groups), although the values at 8 months were different from entry since infants entered at different corrected ages. With time, the $\text{Ashworth}_{\text{LE}}$ scores remained constant and similar between the two groups.

3.3.3. Outcomes at exit

As shown in Table 1, none of the functional outcomes measured in this study were different by group. Infants in the experimental group had similar age at onset of independent walking (effect size Cohen's $d = 0.2$) and similar global GMFM and Bayley scores. Although the duration of days in the study was shorter for the experimental group, the variability among the infants was large enough for this difference not to be significant.

3.4. Relationship between TM response and onset of independent walking

Utilising the whole sample, Pearson correlation analyses to examine the relationship between walking onset and AltStp were conducted at each corrected age between 8 and 14 months in each group. These analyses resulted in significant or suggestive relationships at 8, 10, and 11 months for the experimental group ($p = .04$, $p = .014$, and $p = .002$, respectively) and at 10 and 11 months for the control group ($p = .012$ and $p = .078$, respectively) (see Fig. 3a and c).

When examining the relationship between %AltStp and onset of walking, suggestive or significant correlations were found at 9, 10, 11, and 12 months in the control group ($p = .038$, $p = .004$, $p = .007$, and $p = .018$, respectively), while in the experimental group this relationship was suggestive or significant at 10, and 11 months of age ($p = .013$ and $p = .048$, respectively) (see Fig. 3b and d). Correlations between %Toe and onset of walking failed to bring any significant results.

4. Discussion

Because this study was an initial attempt to systematically examine the impact of TM intervention in infants at risk, we were cautious with the selection of the population and the implementation of the intervention. Infants were at a moderate risk, and our TM programme could best be described as "moderate" in intensity (compared to previous studies in infants with Down syndrome (Ulrich et al., 2008), with constant and generalised training parameters. We were primarily concerned with training effects on task-specific outcome variables, such as those related to TM stepping and precursors to walking

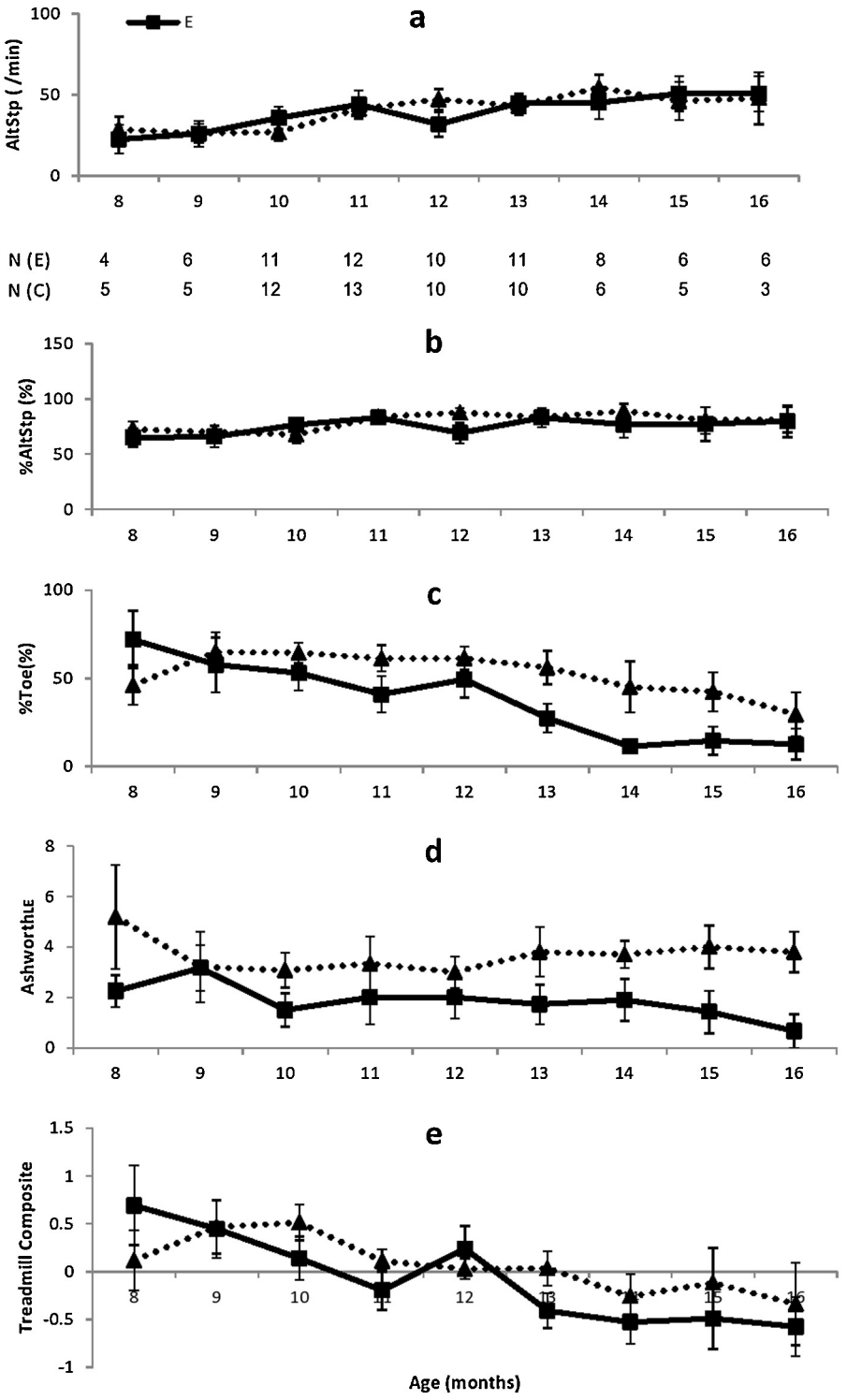

Fig. 2. Average values for infants in the experimental (E) and control (C) groups across age in months: (a) frequency of alternating steps, AltStp (steps/min), (b) percentage of alternating steps, %AltStp, (c) percentage of toe contacts, %Toe (%), (d) total sum of Ashworth scores in the lower extremity, $Ashworth_{LE}$, and (e) TM composite (*Z*-scores average of %AltStp and %Toe). In (a) bottom, *N* (E) and *N* (C) represent the number of infants at each age per group.

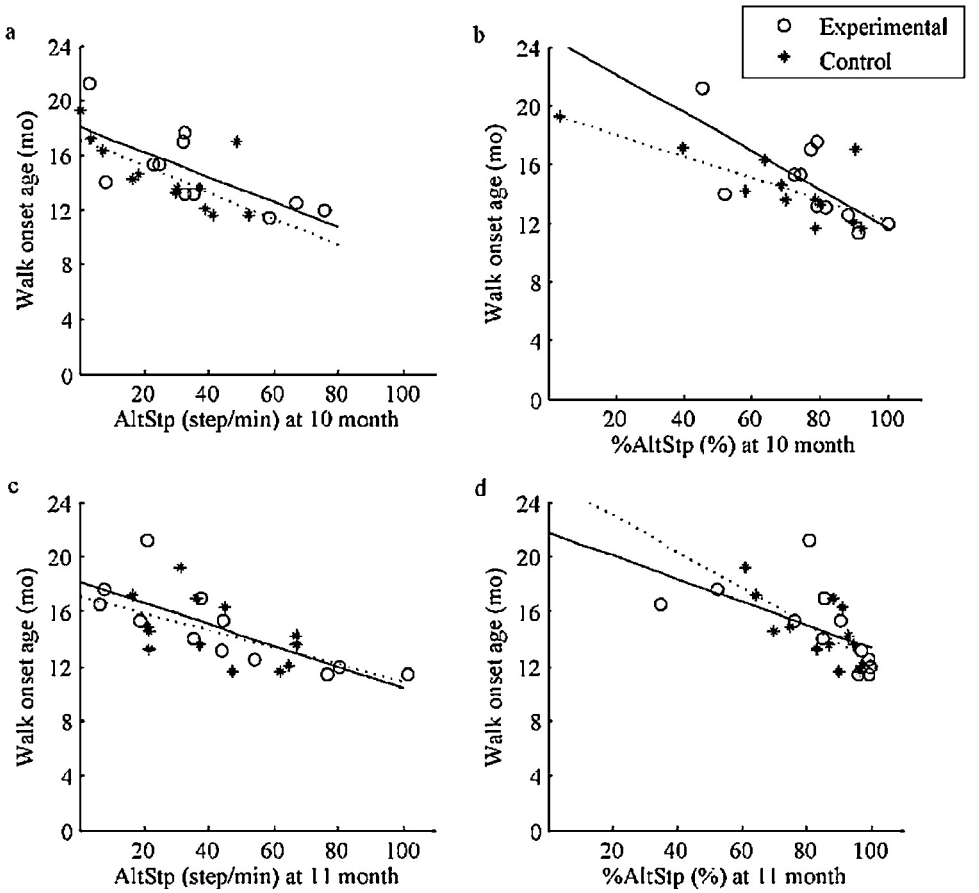

Fig. 3. Correlation between infants' age of walking onset and their stepping performance per group: frequency of alternating steps, AltStp (a and c) and percent of alternating steps, %AltStp (b and d) at 10 (a and b) and 11 (c and d) months of age.

onset. However, we also wanted to explore whether or not TM performance variables might be related to developmental outcomes such as walking onset.

While our findings failed to support the proposal that TM training in infants at risk for NMD would lead to earlier onset of walking relative to an untrained control group, group differences in TM composite scores (particularly at 13 and 15 months) suggest that training may have had a combined effect on TM performance that was not detected in any single TM variable. However, significant age effects were found for all three of our individual TM variables. This last finding, in conjunction with the observation that Ashworth scores did not increase over time, reinforces the ability to safely implement TM training in this population. Nevertheless, Ashworth scores should be taken with caution given that this scale has not been validated in infants. The notion of feasibility of TM training has previously been demonstrated in a slightly older population of individuals with characteristics similar to those in the current study (Richards et al., 1997).

We believe that several factors may have led to our limited findings regarding our outcome variables. First of all, we recruited subjects who were deemed to be at "moderate" risk for NMD. As we previously stated, at the time of this study little evidence existed regarding how infants at risk for NMD might respond to longitudinal TM training. Our conversations with paediatric physicians resulted in the decision to be cautious in this first study. As a consequence of this determination, many of the infants that met our inclusion criteria ended up "catching up" developmentally and walking within typical range. Other researchers have acknowledged the difficulty with early intervention in an at-risk population. For example, Blauw-Hospers and Hadders-Algra (2005) discussed how many infants initially classified as being at-risk may not develop a disorder, making the intervention relatively unhelpful in these children.

In addition to difficulties with our sample, our results were likely influenced by the implementation and design of our TM training programme. We recommended training five days per week with 8 min per day. However, several factors (busy schedule, illness, vacation, and perhaps lack of a definite diagnosis) limited families' ability to implement the training with the suggested frequency. In fact, infants received one less day per week on average than we had programmed and many infants received significantly less. On a similar note, it is also plausible that we started the intervention too late. We began training when infants could take ten supported steps on a TM within a minute. This resulted in an average entry corrected

age of nine to ten months. Perhaps we should have started earlier when there was a greater degree of plasticity in the system. It has been reported that high levels of plasticity exist six to eight months after term age (Hadders-Algra, 2001).

A final issue regarding our training strategy that warrants discussion is the concept of generalised versus individualised training. In the current study, we chose to use a standardised protocol similar to clinical trials involving infants with DS (Ulrich et al., 2001). While this generalised protocol was successful in the DS population, it did not appear to be as effective in the current study. Individualising training would allow one to continually "push" the system as the infant progresses. Previous research has already observed additional benefits of individualised training in infants with DS when compared to a generalised programme (Angulo-Barroso et al., 2008; Mattern-Baxter et al., 2013; Ulrich et al., 2008). Several parameters, such as TM speed, session duration, and ankle weights were incremented or added on the basis of individualised frequency of TM steps. One challenge for future researchers is to determine the optimal training parameters to benefit infants at risk for NMD. In a review of the early intervention literature, Ramey and Ramey (1998) concluded that larger positive outcomes occur as a result of higher intensity interventions. However, most early interventions are implemented at a relatively low level of intensity (Shonkoff, Hauser-Cram, Krauss, & Upshur, 1992). We suggest that individualised, higher intensity TM training, as compared to generalised-low intensity, could provide further benefits to infants at risk for NMD. In fact, a recent RCT showed that a home-based, parent implemented high intensity and individualised TM training programme in very young infants with a diagnosis of CP accelerated their walking skills (Mattern-Baxter et al., 2013). Whether the same results could be obtained in infants at moderate risk for NMD is still to be determined.

Our results exploring the relationship between stepping performance and walking onset were much more encouraging. Our results suggested that (a) infants who produced more alternating steps during the ages of 10 and 11 months also were inclined to walk independently at an earlier age, and (b) the intervention did not drastically modify this relationship since significant correlations were found for both groups. Our observation of a stepping-walking relationship is consistent with previous studies (Luo, Jeng, Lu, & Lin, 2004; Yang, Stephens, & Vishram, 1998; Zelazo, Zelazo, Cohen, & Zelazo, 1993; Zelazo, Zelazo, & Kolb, 1972). Overall, we are hopeful that the observed relationship between TM stepping and walking onset may have clinical importance. In medical evaluations of high-risk infants, best predictions are achieved when multiple, complementary clinical tools are used, including achieved milestones, physical and neurological examination with neuroimaging, and specific assessment of the quality of motor behaviours (Heineman & Hadders-Algra, 2008). Stepping performance on the TM could be one specific assessment used as complementary tool available to clinicians. This issue requires further exploration.

Our study is not free from limitations. First, we recognised the limited sample necessitating further controlled randomised trials to evidence the effect of a TM intervention in this population. Second, the fact that evaluators of the Motor and Mental Subscales of the Bayley Scales of Infant Development, the Gross Motor Function Measure, and Modified Ashworth Scale were not blind to group assignment may have introduced some bias. Yet the coders of the TM steps remained blind eliminating such bias from these data. Another limitation included the limited applicability of the Modified Ashworth Scale since this scales has not been validated in our population.

5. Conclusions

We started this study with the concern raised by many clinicians that perhaps the TM intervention would increase muscle tone in this population. The results suggest this is not the case. Although the benefits of the TM intervention were limited, we are encouraged by our findings. Information of great value was gained from this initial clinical trial. The results suggest that TM training in infants at risk for NMD may still be a viable method of early intervention. Additional research on appropriate participant selection (refining inclusion/exclusion criteria), training compliance/design (individualised, entry/endpoint), and clinical relevance (diagnostic aid) should be examined through large, multi-centre studies.

Ethics approval

The University of Michigan Medical School Institutional Review Board for Human Subject Research approved this study. All participants gave written informed consent before data collection began.

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References

Alloway, T. P., & Warner, C. (2008). Task-specific training, learning, and memory for children with developmental coordination disorder: A pilot study. *Perceptual and Motor Skills, 107*(2), 473–480.

Angulo-Barroso, R. M., Wu, J., & Ulrich, D. A. (2008). Long-term effect of different treadmill interventions on gait development in new walkers with Down syndrome. *Gait and Posture, 27*(2), 231–238.

Bayley, N. (1993). *Bayley scales of infant development*. San Antonio, TX: Harcourt Brace & Company.

Blauw-Hospers, C. H., & Hadders-Algra, M. (2005). A systematic review of the effects of early intervention on motor development. *Developmental Medicine and Child Neurology, 47*(6), 421–432.

Bodkin, A. W., Baxter, R. S., & Heriza, C. B. (2003). Treadmill training for an infant born preterm with a grade III intraventricular hemorrhage. *Physical Therapy, 83*(12), 1107–1118.

Bohannon, R. W., & Smith, M. B. (1987). Interrater reliability of a modified Ashworth scale of muscle spasticity. *Physical Therapy, 67*(2), 206–207.

Brown, G. T., & Burns, S. A. (2001). The efficacy of neurodevelopmental treatment in paediatrics: A systematic review. *The British Journal of Occupational Therapy, 64*(5), 235–244.

Damiano, D. L., Dodd, K., & Taylor, N. F. (2002). Should we be testing and training muscle strength in cerebral palsy? *Developmental Medicine and Child Neurology, 44*(1), 68–72.

Damiano, D. L., Quinlivan, J. M., Owen, B. F., Payne, P., Nelson, K. C., & Abel, M. F. (2002). What does the Ashworth scale really measure and are instrumented measures more valid and precise? *Developmental Medicine and Child Neurology, 44*(2), 112–118.

Davis, D. W., Thelen, E., & Keck, J. (1994). Treadmill stepping in infants born prematurely. *Early Human Development, 39*(3), 211–223.

Davis, N. M., Ford, G. W., Anderson, P. J., & Doyle, L. W. (2007). Developmental coordination disorder at 8 years of age in a regional cohort of extremely-low-birthweight or very preterm infants. *Developmental Medicine and Child Neurology, 49*(5), 325–330.

Hadders-Algra, M. (2001). Early brain damage and the development of motor behavior in children: Clues for therapeutic intervention? *Neural Plasticity, 8*(1–2), 31–49.

Hauser-Cram, P., Warfield, M. E., Shonkoff, J. P., Krauss, M. W., Sayer, A., Upshur, C. C., et al. (2001). Children with disabilities: A longitudinal study of child development and parent well-being. *Monographs of the Society for Research in Child Development, 66*(3), 1–131.

Heineman, K. R., & Hadders-Algra, M. (2008). Evaluation of neuromotor function in infancy – A systematic review of available methods. *Journal of Developmental and Behavioral Pediatrics, 29*(4), 315–323.

Holsti, L., Grunau, R. V., & Whitfield, M. F. (2002). Developmental coordination disorder in extremely low birth weight children at nine years. *Journal of Developmental and Behavioral Pediatrics, 23*(1), 9–15.

Hubbard, I. J., Parsons, M. W., Neilson, C., & Carey, L. M. (2009). Task-specific training: Evidence for and translation to clinical practice. *Occupational Therapy International, 16*(3–4), 175–189.

Jeng, S. F., Chen, L. C., Tsou, K. I., Chen, W. J., & Luo, H. J. (2004). Relationship between spontaneous kicking and age of walking attainment in preterm infants with very low birth weight and full-term infants. *Physical Therapy, 84*(2), 159–172.

Jeng, S. F., Yau, K. T., Liao, H., Chen, L., & Chen, P. (2000). Prognostic factors for walking attainment in very low-birthweight preterm infants. *Early Human Development, 59*(3), 159–173.

Luo, H. J., Jeng, S. F., Lu, T. W., & Lin, K. H. (2004). Relationship between stepping movements and age of walking attainment in full-term infants without known impairment or pathology. *Formosan Journal of Physical Therapy, 29*(2), 67–78.

Mattern-Baxter, K., McNeil, S., & Mansoor, J. K. (2013). Effects of home-based locomotor treadmill training on gross motor function in young children with cerebral palsy: A quasi-randomized controlled trial. *Archives of Physical Medicine and Rehabilitation* [available online 05.06.13].

Molnar, G. E. (1985). Pediatric rehabilitation. In Molnar, G. E. (Ed.). *Cerebral palsy*. (pp.481–533). .

Palisano, R., Rosenbaum, P., Walter, S., Russell, D., Wood, E., & Galuppi, B. (1997). Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Developmental Medicine and Child Neurology, 39*(4), 214–223.

Ramey, C. T., & Ramey, S. L. (1998). Early intervention and early experience. *American Psychologist, 53*(2), 109–120.

Richards, C. L., Malouin, F., Dumas, F., Marcoux, S., Lepage, C., & Menier, C. (1997). Early and intensive treadmill locomotor training for young children with cerebral palsy: A feasibility study. *Pediatric Physical Therapy, 9*(4), 158–165.

Russell, D. J., Rosenbaum, P. L., Cadman, D. T., Gowland, C., Hardy, S., & Jarvis, S. (1989). The gross motor function measure: A means to evaluate the effects of physical therapy. *Developmental Medicine and Child Neurology, 31*(3), 341–352.

Shonkoff, J. P., Hauser-Cram, P., Krauss, M. W., & Upshur, C. C. (1992). Development of infants with disabilities and their families: Implications for theory and service delivery. *Monographs of the Society for Research in Child Development, 57*(6), 1–163.

Spittle, A. J., Orton, J., Anderson, P., Boyd, R., & Doyle, L. W. (2012). Early developmental intervention programs post hospital discharge to prevent motor and cognitive impairments in preterm infants. *Cochrane Database of Systematic Reviews*, *12* [Art. No.: CD005495].

Sutcliffe, A. G., & Derom, C. (2006). Follow-up of twins: Health, behaviour, speech, language outcomes and implications for parents. *Early Human Development, 82*(2), 379–386.

Thelen, E., Ulrich, B. D., & Wolff, P. H. (1991). Hidden skills: A dynamic systems analysis of treadmill stepping during the first year. *Monographs of the Society for Research in Child Development, 56*(1), 1–103.

Tin, W., Wariyar, U., & Hey, E. (1997). Changing prognosis for babies of less than 28 weeks' gestation in the north of england between 1983 and 1994. Northern neonatal network. *British Medical Journal, 314*(7074), 107–111.

Ulrich, D. A., Ulrich, B. D., Angulo-Kinzler, R. M., & Yun, J. (2001). Treadmill training of infants with Down syndrome: Evidence-based developmental outcomes. *Pediatrics, 108*(5), 84–90.

Ulrich, D. A., Lloyd, M. C., Tiernan, C. W., Looper, J. E., & Angulo-Barroso, R. M. (2008). Effects of intensity of treadmill training on developmental outcomes and stepping in infants with Down syndrome: A randomized trial. *Physical Therapy, 88*(1), 114–122.

Valentin-Gudiol, M., Mattern-Baxter, K., Girabent-Farrés, M., Bagur-Calafat, C., Hadders-Algra, M., & Angulo-Barroso, R. M. (2011). Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay. *Cochrane Database of Systematic Reviews*, *12* [Art. No.: CD009242].

Vereijken, B., & Thelen, E. (1997). Training infant treadmill stepping: The role of individual pattern stability. *Developmental Psychobiology, 30*(2), 89–102.

Vohr, B. R., Wright, L. L., Poole, W. K., & McDonald, S. A. (2005). Neurodevelopmental outcomes of extremely low birth weight infants <32 weeks' gestation between 1993 and 1998. *Pediatrics, 116*(3), 635–643.

Wu, J., Looper, J., Ulrich, B. D., Ulrich, D. A., & Angulo-Barroso, R. M. (2007). Exploring effects of different treadmill interventions on walking onset and gait patterns in infants with Down syndrome. *Developmental Medicine and Child Neurology, 49*(11), 839–945.

Yang, J. F., Stephens, M. J., & Vishram, R. (1998). Infant stepping: A method to study the sensory control of human walking. *Journal of Physiology, 507*(Pt 3), 927L 937.

Zelazo, N. A., Zelazo, P. R., Cohen, K. M., & Zelazo, P. D. (1993). Specificity of practice effects on elementary neuromotor patterns. *Developmental Psychology, 29*(4), 686–691.

Zelazo, P. R., Zelazo, N. A., & Kolb, S. (1972). "Walking" in the newborn. *Science, 176*(4032), 314–315.

CAPÍTULO 4.

Entrenamiento de la marcha con tapiz rodante y desarrollo psicomotor en mellizas prematuras

Estudio Piloto en CDIAP

Antecedentes

Los bebés prematuros o nacidos con bajo peso, y la presencia de anormalidades cerebrales suelen inducir a la clasificación de dicha población como niños con riesgo de retraso en el desarrollo psicomotor, independientemente de si reciben o no a posteriori un diagnóstico como parálisis cerebral, trastorno del desarrollo de la coordinación o trastorno del espectro autista, entre otros[1]. Estas anormalidades motrices, que suelen aparecer tempranamente, pueden tener un impacto negativo en la adquisición de funciones y habilidades motrices durante el proceso de crecimiento y maduración, y en el desarrollo de la actividad motriz global del niño[2].

Hay estudios que han utilizado el tapiz rodante para describir el patrón de desarrollo de los pasos hasta el momento en que el niño inicia la marcha autónoma. Estos estudios han descrito cómo, a medida que se acerca el inicio de la marcha autónoma, la respuesta al tapiz se caracteriza por un aumento en la frecuencia de pasos por minuto y una disminución en la variabilidad de éstos con predominancia de los pasos alternos sobre los otros tipos de pasos. Esto se cumple tanto en niños con desarrollo típico[3], como en niños con síndrome de Down[4] o con riesgo de retraso en el desarrollo motriz[2].

Una revisión sistemática reciente sobre las intervenciones con tapiz rodante en niños menores de seis años de edad con riesgo de retraso en el desarrollo motriz concluye que, en el casos de niños con síndrome de Down, el entrenamiento de la marcha con el tapiz acelera la adquisición de la marcha autónoma de manera significativa[5]. Hay estudios publicados sobre la viabilidad del entrenamiento de la marcha con el tapiz rodante (con soporte manual del peso corporal del sujeto) en niños con parálisis cerebral[6], que demuestran una mejora en las capacidades de estos niños después de recibir la intervención[7-12]. Sin embargo, se desconoce el impacto de este tipo de entrenamiento en niños no diagnosticados pero clasificados como grupo con riesgo de retraso en el desarrollo psicomotor[5]. A fecha de hoy, en la literatura científica, sólo se encuentra un estudio de una intervención de entrenamiento con tapiz rodante en niños con riesgo moderado de retraso en el desarrollo motriz[13]. Al final de dicho estudio se concluye que los parámetros de la marcha estudiados en los niños entrenados fueron diferentes en cuanto a su magnitud, pero parecidos en

cuanto a su evolución en el tiempo a los de los niños con desarrollo normal. Los beneficios de la intervención con tapiz rodante en los niños con riesgo fueron menores a los demostrados en población con síndrome de Down[5]. En el estudio citado sobre entrenamiento en niños con riesgo[13], el entrenamiento realizado fue de corta duración y sin ajuste o individualización de los parámetros de entrenamiento en el tapiz. En cambio, estos ajustes sí se hicieron en la intervención en niños con síndrome de Down[14].

Es necesario poder implementar un entrenamiento individualizado de la marcha con el tapiz rodante en niños con riesgo de retraso en el desarrollo motriz, siguiendo las pautas del protocolo realizado en estudios previos por Angulo *y col.*[15]. El objetivo principal de este planteamiento sería poder valorar si, en esa situación, habría beneficios significativos en relación al desarrollo de la motricidad gruesa, y especialmente en relación a la locomoción y al patrón de la marcha.

En este proyecto se plantea realizar la intervención individualizada con el tapiz rodante en un caso de mellizas con prematuridad leve, donde se implementará el entrenamiento a la melliza que presenta el mayor retraso motriz, según los resultados obtenidos al pasar escalas de valoración del desarrollo psicomotor.

Objetivos

El objetivo principal de este estudio fue implementar un entrenamiento individualizado de la marcha en un caso de mellizas prematuras, para determinar el efecto del mismo sobre la melliza experimental, que presentaba signos clínicos de retraso moderado en el desarrollo motriz. Se pretendió evaluar si la intervención con el tapiz tenía efectos positivos sobre la reducción de las diferencias basales existentes entre ambas mellizas en el momento de entrada al estudio, sobre todo en relación a los aspectos de motricidad gruesa. Igualmente fue de interés describir las trayectorias de desarrollo motriz a través de las escalas de valoración y estudiar la respuesta al tapiz rodante.

Hipótesis

La hipótesis principal de estudio fue que se observaría una aceleración en el desarrollo motriz de la melliza entrenada con el tapiz rodante. Se esperó que las diferencias existentes encontradas en el momento de entrada al estudio entre nivel de desarrollo de la motricidad gruesa, y especialmente sobre aspectos relacionados con la locomoción, se verían disminuidas por efectos positivos del entrenamiento de la marcha. Igualmente se esperó que las diferencias basales obtenidas entre ambas mellizas en la puntuación de las escalas de desarrollo motriz irían disminuyendo de manera progresiva.

Instituciones participantes y equipo investigador

La Fundación Roger Torné financió una parte de este estudio en relación a la adquisición de material de valoración para las mellizas. Se utilizó el laboratorio de investigación del Institut Nacional d'Educació Física de Catalunya (INEFC Barcelona), Universitat de Barcelona, para llevar a cabo el entrenamiento del equipo investigador en cuanto a la metodología de intervención. El Centre de Desenvolupament Infantil i Atenció Precoç (CDIAP) de Sant Adrià de Besòs fue el lugar donde se recogieron los datos iniciales de ambas mellizas, y donde se realizaron algunas de las sesiones de seguimiento.

La investigadora principal de este proyecto fue la Dra. Rosa Angulo-Barroso, profesora de Biomecánica en INEFC e investigadora en CHGD, University of Michigan (MI, USA). Marta Valentín Gudiol, fisioterapeuta y doctoranda de esta tesis, coordinó el proyecto y llevó a cabo toda la recogida de datos. Sergi Nogués Orte, fisioterapeuta pediátrico, colaboró en la codificación de los pasos.

Diseño del Estudio

Estudio experimental longitudinal de un caso, con manipulación del entrenamiento según la respuesta de la melliza entrenada en el tapiz rodante. La evolución y desarrollo de melliza experimental se comparó con la melliza control, que no recibió entrenamiento.

Descripción de los Casos

Mellizas de un embarazo espontáneo de una pareja sana. Parto distócito por cesárea de urgencia a las 36 semanas de gestación porque la melliza control (MC) llevaba 2 vueltas de cordón. Antecedentes de anemia maternal severa e hipotensión durante el último trimestre de gestación. En ambas mellizas se realizó un tratamiento preventivo con cortisona para estimulación de la maduración pulmonar. Ambas recibieron diez días de lactancia materna y lactancia artificial a continuación.

Melliza experimental (ME):

Peso al nacer: 2220g, talla: 47cm, perímetro craneal: 31cm, Apgar: 9/10. Detección precoz de metabolopatías congénitas: normal. Crecimiento de acuerdo con los percentiles. A los 36 días de edad corregida fue derivada al centro de desarrollo infantil y atención precoz para iniciar sesiones de fisioterapia. A la edad corregida de 4 meses presentaba hipotonía axial e hipertonía en aductores, y la mano izquierda frecuentemente cerrada en puño. El ojo izquierdo estaba más cerrado que el derecho, y había una sonrisa asimétrica con una desviación del maxilar inferior bastante evidente.

Melliza control (MC):

Peso al nacer: 2700g, talla: 49.5cm, perímetro craneal: 34cm, Apgar: 9/10. Llevaba dos vueltas de cordón al nacer, sin distrés respiratorio. Detección precoz de metabolopatías congénitas: normal. Crecimiento de acuerdo con los percentiles. A los 36 días de edad corregida fue derivada al centro de desarrollo infantil y atención precoz para iniciar una valoración de fisioterapia.

Intervención

Para definir el tipo de intervención a utilizar en este estudio de caso, se revisó la literatura científica sobre el entrenamiento con tapiz rodante en población pediátrica. Según los estudios de referencia sobre este tema, podría iniciarse el entrenamiento a partir del momento en el que el niño fuese capaz de realizar un mínimo de 6 pasos por minuto sobre el tapiz rodante[2]. Los parámetros de inicio del entrenamiento serían los siguientes: 5 días a la semana, 8 minutos al día, y con la cinta del tapiz a una velocidad de 0.15m/s[14].

El protocolo de entrenamiento se planteó siguiendo los parámetros utilizados en el ensayo clínico de Ulrich *y col.*[14](tabla 1). Consistía en ir aumentando progresivamente la intensidad del entrenamiento en función del número de pasos por minuto que la ME realizaba sobre el tapiz rodante, que se valoraba semanalmente por medio de una grabación en videocámara en el CDIAP, al inicio la sesión de fisioterapia. Según el protocolo, se consideró la manipulación de los siguientes parámetros, para individualizar el entrenamiento: (1) velocidad del tapiz, (2) minutos de duración total del entrenamiento diario y (3) fuerza-resistencia añadiendo pesos en los tobillos de la melliza durante la sesión de entrenamiento. Por ejemplo, si la melliza realizaba entre 20 y 29 pasos por minuto, se aumentaría la velocidad del tapiz de 0.20 a 0.25m/s, y la duración de la sesión de 8 a 10 minutos. A partir de que la niña fuera capaz de hacer 30 pasos, la velocidad aumentaría a 0.30m/s, así como la duración de la sesión pasaría entonces a ser de 12 minutos totales. En la tabla 1 queda igualmente detallada la progresión de los pesos que se añadirían en los tobillos. La cantidad de peso añadido se calcularía como porcentaje en función de la masa del segmento de la pierna baja de la ME[16]. En el caso de que al añadir el peso en el tobillo disminuyera la frecuencia de pasos por minuto por debajo del mínimo requerido según el protocolo, se mantendría el peso utilizado anteriormente hasta que dicha frecuencia se mantuviera estable. La fase de entrenamiento se daría por terminada cuando la melliza iniciase la marcha autónoma, definida como el momento en que ésta fuese capaz de dar tres pasos en el suelo de manera independiente[2].

A lo largo del transcurso de cada sesión se iría observando el estado de la melliza y su respuesta al tapiz para determinar cuándo ésta necesitara una pausa.

Tabla 1. Protocolo de entrenamiento según Ulrich *y col.*[14]

Pasos/min	Velocidad TM (m/s)	Peso tobillo (% masa pierna baja)	Duración sesión (min/día)
<10	0.15	0	8
10-19	0.20	50	8
20-29	0.25	75	10
30-39	0.30	100	12
> o = 40	0.30	123	12

Procedimiento

Se realizó una evaluación inicial a las dos mellizas en la cual se tomaron las mediciones antropométricas de peso, talla y el perímetro craneal. Se pasaron dos escalas para valorar el nivel de desarrollo psicomotor: *Alberta Infant Motor Scale* (AIMS)[17] y *Bayley Scales of Infant and Toddler Development (third edition)* (BSID, sub-escalas de motricidad fina, gruesa, y cognitiva)[18].

La respuesta al tapiz rodante se grabó desde un plano sagital con una videocámara (SONY Handycam HDR-SR12E), y el soporte manual del peso fue realizado por una persona entrenada para la tarea. Se utilizó un tapiz rodante pediátrico (Carlin's Creations, MI, USA). En la sesión inicial de valoración se estableció una velocidad de la cinta del tapiz rodante de 0.15m/s. Para que la familia pudiera llevar a cabo los entrenamientos de la melliza experimental siguiendo el protocolo pautado, se facilitó un tapiz rodante, que se instaló en el domicilio familiar. Los padres fueron entrenados sobre cómo debían realizarse las presas de soporte parcial del peso corporal, y sobre el funcionamiento técnico del tapiz. Durante los cinco primeros días de intervención, la coordinadora del proyecto se desplazó al domicilio familiar en el momento del entrenamiento con el tapiz, para verificar que la ejecución era correcta y para poder modificar cualquier aspecto del entrenamiento o de la técnica de soporte manual, en caso de necesidad. La familia colaboró en la recogida de datos registrando en una libreta los minutos totales realizados por

la ME en cada sesión de entrenamiento. En las visitas mensuales de recogida de datos de seguimiento, que tenían lugar en el domicilio familiar, la coordinadora del proyecto grabó con la videocámara 5 minutos totales de marcha en el tapiz con soporte parcial del peso, tanto de la ME como de la MC. Dicho soporte del peso corporal se realizó de la misma manera como se asistía a la ME durante el entrenamiento, con presas a nivel axilar (ver figura 1). Los parámetros del tapiz para cada sesión mensual de valoración-seguimiento fueron los mismos que se habían establecido durante el entrenamiento previo. Asimismo, se pasaban las escalas de desarrollo psicomotor BSID III (sub-escalas de motricidad fina, gruesa y cognitiva) y AIMS a ambas mellizas en cada visita de seguimiento mensual. Las sesiones de seguimiento mensual se dieron por terminadas, de manera individual, en el momento de inicio de la marcha autónoma de cada melliza.

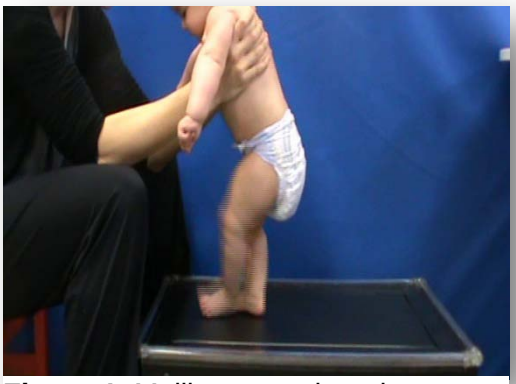

Figura 1. Melliza en tapiz rodante con soporte parcial del peso corporal, realizado por la investigadora.

A lo largo de todo el estudio ambas mellizas continuaron asistiendo a sesiones semanales de fisioterapia en su centro de atención precoz de referencia para estimular el desarrollo psicomotor de manera global con el objetivo de tratar y prevenir posibles retrasos.

Reducción de datos y variables

El análisis de la respuesta al tapiz rodante se realizó visualizando imagen por imagen los vídeos obtenidos de cada grabación mensual, con el software Adobe Premiere Pro. La descripción de los pasos, simple o alterno, se estableció de acuerdo con las siguientes definiciones del patrón de marcha: un paso se consideró cuando la pierna que realizaba la acción sobrepasaba la mitad del pie estacionario, considerándose alterno si venía seguido de otro paso con la pierna contraria y cumplía con los criterios definidos anteriormente. Un tercer tipo de pasos descrito y observado en la marcha sobre el tapiz rodante con soporte parcial del peso corporal, fue el paso paralelo. Este fue definido como un paso en el que la niña activamente realizaba una flexión bilateral de caderas, de manera que las dos piernas avanzaban simultáneamente hacia adelante[3]. La calidad del paso se definió mediante la determinación del porcentaje de contacto con los dedos del pie en la fase de apoyo, considerándose un apoyo en pie plano cuando más de la mitad del pie estaba en contacto con el tapiz rodante un mínimo de 200mseg (5 imágenes por segundo). Todos aquellos pasos que no cumplieran los requisitos de pie plano, fueron definidos como pie en punta[2]. La codificación de cada vídeo la realizaron de manera independiente la coordinadora del proyecto y otro miembro del equipo investigador, conocedor de los términos de codificación de pasos e igualmente entrenado para la tarea. La fiabilidad entre ambos codificadores fue del 99% ICC (97.0%, 99.7%).

Las variables principales del estudio en relación a los pasos alternos, fueron su frecuencia y su calidad.

Se recogió mensualmente la frecuencia de pasos que realizó cada melliza en cada sesión de seguimiento en el tapiz rodante (número de pasos por minuto, tanto alternos como de otro tipo). Igualmente se registró la calidad de los pasos, analizando qué porcentaje de éstos se realizaron con contacto de pie en punta con el tapiz (ver definición en párrafo anterior) en relación a la frecuencia total de pasos por minuto. Además, se registraron las variables antropométricas de talla, peso y perímetro craneal, y los resultados del BSID III (sub-escalas de motricidad fina, gruesa y cognitivo) y del AIMS, también mensualmente.

Resultados y Discusión

Al inicio del entrenamiento de la ME, las mellizas tenían 8 meses de edad corregida (9 meses de edad cronológica).

Adherencia a la intervención

En la tabla 2 se presenta el volumen de entrenamiento real que recibió la ME, en comparación con el propuesto inicialmente (tabla 1).

Tabla 2. Volumen de entrenamiento realizado vs. propuesta inicial.

		Entrenamiento	Intención
Días/semana		**4**	**5**
Min/semana	**Velocidad TR** *(m/s)*		
	0,15	29	40
	0,20	30	40
	0,25	33	50
	0,30	27	60
Min totales entrenados		**119**	**190**

Velocidad TR: velocidad tapiz rodante, expresada en metros por segundo (m/s). Minutos totales entrenados, independientemente de las velocidades del tapiz rodante.

El volumen de entrenamiento recibido por la ME, en días de entrenamiento por semana, fue de un día por debajo del pautado por protocolo: entrenó como media cuatro días en lugar de cinco días a la semana. Los minutos totales de entrenamiento por semana fueron también inferiores. Tampoco se pudo llevar a cabo el aumento de tiempo por sesión individual ni añadir las cargas con pesos en los tobillos. El parámetro que sí se aumentó de acuerdo con el protocolo fue la velocidad de la cinta del tapiz. Según el análisis de la respuesta al tapiz rodante de la ME en la sesión de valoración (‘entrada’), y siguiendo el protocolo descrito en la tabla 1, la velocidad inicial de entrenamiento tendría que haber sido de 0.25m/s (puesto que la niña podía realizar una media de 27 pasos por minuto sobre el tapiz, ver tabla 4). Sin embargo, cuando empezaron los entrenamientos implementados por los padres, la ME no colaboró satisfactoriamente, razón por la cual se decidió

disminuir la velocidad inicial del tapiz a 0.15m/s, e ir aumentándola progresivamente según colaboración y evolución en la respuesta. Por motivos de logística familiar, los padres (jóvenes, primerizos y ambos con trabajos a jornada completa), solamente podían implementar el entrenamiento a la ME a última hora del día, momento en que la niña estaba menos colaboradora y más cansada. A pesar de que se intentó modificar este aspecto del entorno del entrenamiento, no fue posible. Se optó por continuar con la individualización de los parámetros en función de la situación familiar y del estado de la melliza durante las sesiones de entrenamiento, evitando en todo momento el malestar de la niña o el llanto durante el entrenamiento en el tapiz.

En términos generales, el volumen de entrenamiento que recibió la ME se mantuvo constante a lo largo de la intervención. Por calendario real, desde la fecha de inicio del entrenamiento hasta el momento en que se dio por finalizada la intervención, pasaron un total de 19 semanas y 2 días. La intención de entrenamiento para ese periodo hubiese sido que la ME recibiera 97 días de entreno de la marcha sobre el tapiz. Por el contrario, el total de días recibidos de entrenamiento fueron 80 días. El motivo principal de esta falta de cumplimiento fue por coincidencia con periodo vacacional familiar.

Variables de desarrollo

En la tabla 3 se presentan los resultados de las valoraciones iniciales, finales y en edades iguales para todos las variables de estudio excepto las variables relacionadas con los pasos en el tapiz rodante. Tanto para describir la respuesta al tapiz rodante de cada melliza, como para describir el desarrollo motriz, se consideraron los valores obtenidos en el momento de ‘salida’ (inicio de la marcha autónoma) del estudio, el cual fue diferente para cada niña. Por definición en el diseño de este estudio, se planteó el seguimiento de los casos hasta el inicio de la marcha autónoma, que tuvo lugar con un mes de diferencia entre ambas niñas. En total se realizaron cuatro sesiones de seguimiento en cuatro meses consecutivos para cada niña, y una valoración adicional en el último mes sólo para la ME. Las valoraciones presentadas en edades iguales en la tabla 3 pertenecen a la sesión de seguimiento 4 (equivalente a sesión de 'salida' de la MC).

Tabla 3. Variables de entrada y en inicio de la marcha autónoma de cada melliza.

		ME	MC
	Género	femenino	femenino
	Peso al nacer *(kg)*	2.2	2.7
	Edad gestacional *(semanas)*	36.0	36.0
Entrada	Edad corregida *(m.d)*	8.8	8.8
	Peso *(kg)*	8.1	8.1
	Talla *(cm)*	69.5	70.5
	Perímetro craneal *(cm)*	43.0	46.0
	BSID Cog	28	32
	BSID MG	28	34
	BSID MF	19	19
	AIMS	24	36
Misma edad	Edad corregida *(m.d)*	12.2	12.2
	Peso *(kg)*	8.7	9.1
	Talla *(cm)*	74.0	73.5
	Perímetro craneal *(cm)*	45.0	48.1
	BSID Cog	42	45
	BSID MG	38	42
	BSID MF	25	28
	AIMS	50	57
Salida*	Edad corregida - inicio marcha *(m.d)*	13.9	12.2
	Peso *(kg)*	8.8	9.1
	Talla *(cm)*	75.0	73.5
	Perímetro craneal *(cm)*	45.0	48.1
	BSID Cog	47	45
	BSID MG	41	42
	BSID MF	27	28
	AIMS	54	57
	Duración estudio *(días)*	154	115

* Edades de salida distintas por corresponder al momento de inicio de la marcha autónoma de cada niña. BSID (Bayley Scales Infant and Toddler Development) puntuación 'cruda'; Cog (sub-escala cognitiva); MG (sub-escala motricidad gruesa); MF (sub-escala motricidad fina); AIMS (Alberta Infant Motor Scale) puntuación total

En cuanto a valores obtenidos en las escalas de medición de desarrollo de la motricidad gruesa (BSID sub-escala de motricidad gruesa y AIMS), no se observaron cambios significativos en el ritmo de desarrollo de la ME respecto la MC (figura 2). Ambas demostraron un aumento lineal y progresivo en las dos escalas, aunque la ME obtuvo siempre puntuaciones inferiores en su desarrollo en comparación con la MC. A partir de los 10 meses de edad corregida, a los dos meses de entrenamiento de la ME y según los resultados de las puntuaciones de las escalas, ésta mostró un aumento en la velocidad de

desarrollo. Según BSID (sub-escala de motricidad gruesa) este aumento en la velocidad de desarrollo se objetivó hasta los 11 meses, mientras que para AIMS perduró hasta los 12 meses. Aun así, estas escalas parecieron no resaltar la evidencia de los cambios observados en los patrones relacionados con la locomoción, en cambio sí objetivados en el análisis de la respuesta al tapiz rodante de la ME.

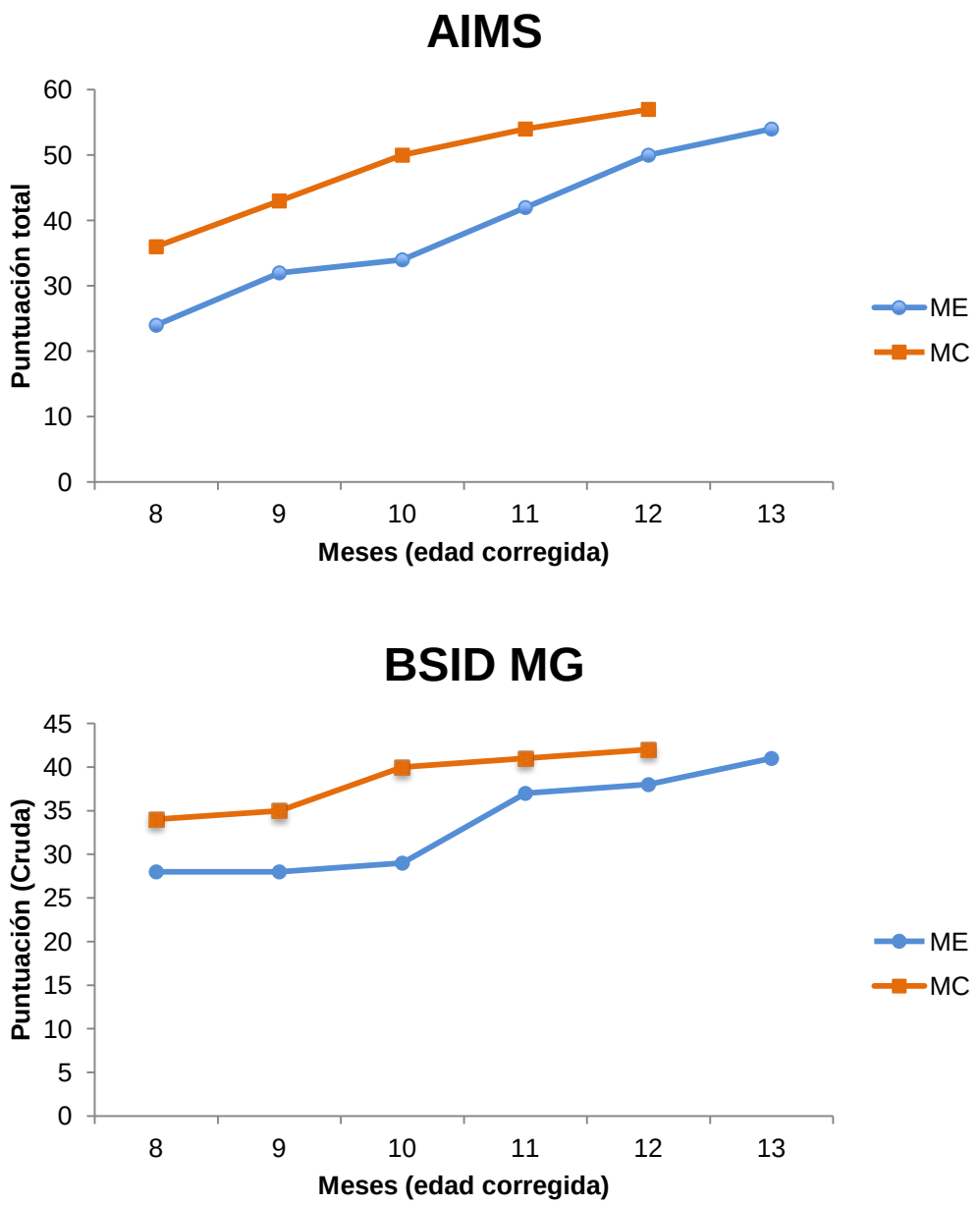

Figura 2. Evolución del desarrollo motriz según la escala Alberta Infant Motor Scale (AIMS) y la sub-escala Bayley Scale of Infant and Toddler Development, motricidad gruesa (BSID MG).

Variables del tapiz rodante

En la tabla 4 se presentan, para el primer minuto codificado, los resultados de la evolución de los tipos de pasos a lo largo de los seguimientos mensuales, tanto para el tipo de pasos y sus frecuencias como para tipo de apoyo de los pasos, para cada melliza.

Tabla 4. Evolución de la respuesta al tapiz a lo largo del estudio.

		Melliza Estudio						Melliza Control					
		Pasos			Punta			Pasos			Punta		
	EC (m.d)	A	S	P	A	S	P	A	S	P	A	S	P
Entrada	8.8	9	18	0	8	11	0	40	15	0	26	8	0
S. 1	9.8	14	8	1	2	1	0	31	11	5	8	4	0
S. 2	10.10	66	8	0	0	0	0	54	11	0	4	1	0
S. 3	11.8	57	7	1	0	0	0	70	6	0	9	1	0
S. 4	12.2	72	3	0	0	0	0	82	4	0	6	0	0
S. 5	13.9	84	3	0	1	0	0	-	-	-	-	-	-

EC: edad corregida (meses.días); S. x: sesión de seguimiento; A: alterno; S: simple; P: paralelo; Pasos: frecuencia de pasos por minuto; Punta: número de apoyos de pie en punta.

De los valores detallados en la tabla 4, fue de especial interés estudiar la evolución de pasos alternos como variable principal, juntamente con el estudio de la calidad del paso. En la figura 3 se presenta la respuesta al tapiz rodante de cada melliza a través de la variable pasos alternos, expresada como porcentaje del total de pasos obtenidos en el primer minuto de codificación.

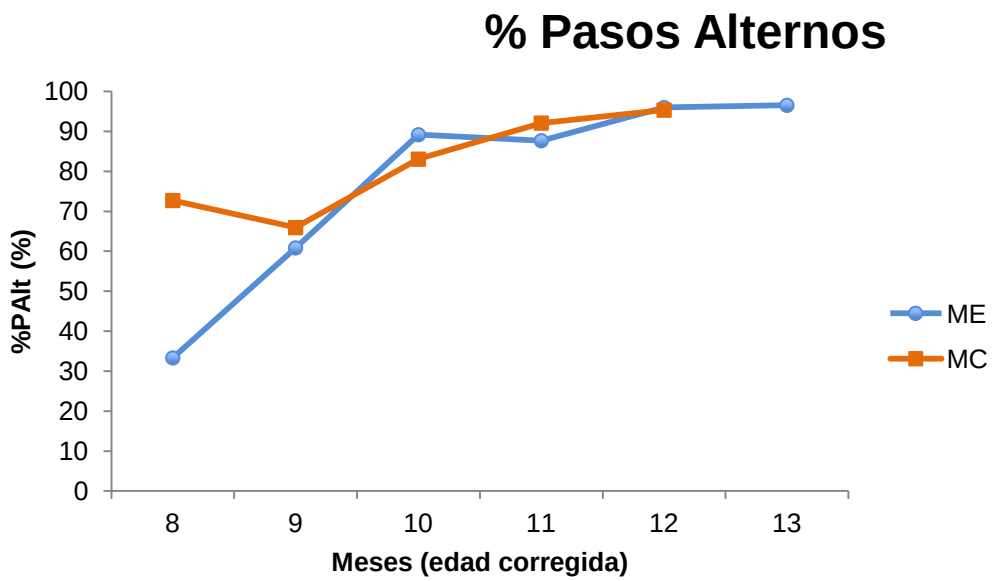

Figura 3. Porcentaje de pasos alternos (%PAlt) en minuto 1 de melliza experimental (ME) y melliza control (MC) a lo largo de los seguimientos mensuales.

Se observaron diferencias iniciales en el porcentaje de pasos alternos a la edad de 8 meses de edad corregida, que fueron los valores obtenidos en el momento de entrada al estudio, antes de iniciar el entrenamiento de la ME. Para ambas mellizas, con el aumento de la edad, aumentó progresivamente el porcentaje de pasos alternos, a la vez que disminuyeron los pasos simples y los pasos paralelos (tabla 4). En el caso de la ME, este aumento se acentuó a partir del inicio del entrenamiento con el tapiz rodante. En la gráfica se puede ver cómo, durante los dos primeros meses de entrenamiento, el porcentaje de pasos alternos de la ME aumentó exponencialmente hasta alcanzar los valores de la MC a la edad corregida de 10 meses. A partir de ese momento el porcentaje de pasos alternos siguió en aumento con un patrón más lineal y en paralelo con valores muy similares entre ambas niñas, hasta el inicio de la marcha autónoma.

En la figura 4 podemos ver la evolución de la calidad del paso, medida como porcentaje de pasos con apoyo en pie en punta.

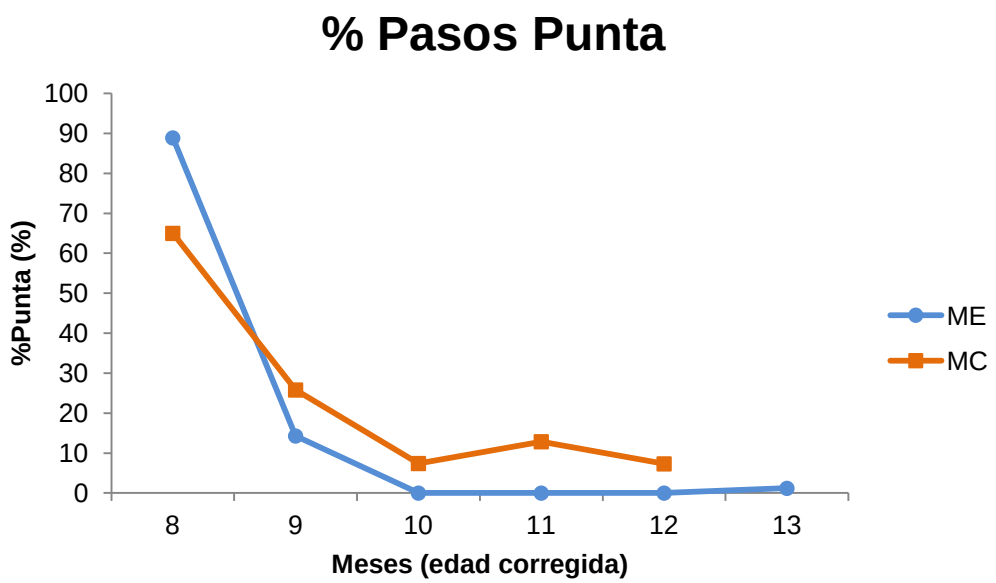

Figura 4. Porcentaje de pie en punta, %Punta (%), de melliza experimental (ME) y melliza control (MC) a lo largo de los seguimientos mensuales.

Se puede observar como ambas mellizas mostraron una disminución progresiva de los apoyos de pie en punta con el aumento de la edad, patrón que coincidió con el descrito por Thelen sobre el desarrollo de la marcha sobre el tapiz en niños con desarrollo típico[3].

En el momento de entrada al estudio, el porcentaje de apoyos de pie en punta fue mayor en la ME. Después de un mes de entrenamiento con el tapiz (ME) este porcentaje disminuyó drásticamente y lo hizo de manera ligeramente más acentuada y en mayor medida en el caso de la melliza experimental. A partir del tercer mes de entrenamiento, la ME no mostró más pasos de pie en punta (tabla 4) mientras que la MC continuó realizando algún apoyo de pie en punta hasta el inicio de la marcha autónoma.

Conclusiones y Limitaciones

El entrenamiento con tapiz rodante implementado de manera individualizada a una niña con antecedentes de prematuridad leve y con retraso moderado en el desarrollo motriz, posiblemente contribuyó positivamente en la velocidad de su desarrollo motriz según las escalas utilizadas. A través del análisis de la respuesta al tapiz rodante se pudieron objetivar efectos positivos en aspectos del desarrollo relacionados con la locomoción. Se observó una mejora en la calidad de los pasos, juntamente con un aumento rápido en la frecuencia de pasos alternos por minuto sobre el tapiz. Especialmente estos efectos fueron más pronunciados en la melliza experimental. Este aumento en frecuencia, además de la predominancia de pasos alternos sobre los otros tipos de pasos descritos sobre el tapiz, fueron un requisito previo para la adquisición posterior de la marcha autónoma, en este caso y de acuerdo con los hallazgos de otros estudios publicados[19]. Los efectos globales de la intervención con el tapiz se podrían considerar como beneficiosos ya que, además, e igualmente como se evidenció en el estudio de Mattern-Baxter *y col.*[12], no se observaron efectos adversos del entrenamiento con el tapiz rodante. El volumen de entrenamiento implementado se adaptó a la viabilidad e implicación familiar y a la respuesta de la ME. Se desconoce si el efecto de la intervención habría sido mayor de haberse cumplido el protocolo de entrenamiento pautado en el momento de entrada al estudio, más intensivo que el que se pudo llevar a cabo realmente. Un aspecto a destacar en relación a la respuesta al tapiz fue que la ME, a lo largo de los entrenamientos, necesitó progresivamente menos pausas durante las sesiones individuales de entrenamiento sobre el tapiz.

En términos generales, se puede concluir que el entrenamiento con el tapiz rodante, analizado como actividad tarea-específica, contribuyó positivamente sobre los aspectos del desarrollo relacionados con la actividad entrenada, la marcha. Los resultados presentados en este estudio deberían ser corroborados con ensayos clínicos controlados con grupos de niños con riesgo de retraso en el desarrollo motriz. Sería de interés verificar los efectos encontrados en este estudio de caso, en relación la respuesta al tapiz rodante y al desarrollo motriz y de la locomoción. Las dificultades encontradas a nivel de logística familiar en la implementación del protocolo de entrenamiento

planteado inicialmente sugieren la necesidad de valorar detenidamente los tipos de niños y familias a las que se les podría plantear una intervención de este tipo. Quizás sería necesario poder pensar en una figura de becario/a (que podría ser un estudiante de kinesiología o fisioterapia pediátrica) que colaborase con el equipo investigador y que pudiera desplazarse al domicilio familiar para hacer un seguimiento más cercano del desarrollo de las sesiones semanales, con el objetivo de garantizar al máximo la adherencia al entrenamiento pautado. Finalmente, la objetividad que ha ofrecido el estudiar el patrón de locomoción a través de la marcha, analizando la respuesta al tapiz rodante, plantea la posibilidad de hacer uso del tapiz rodante como herramienta complementaria de valoración del desarrollo motriz de los niños con riesgo de retraso en el desarrollo u otras condiciones.

Referencias capítulo 4

1. Álvarez Mingorance P. *Morbilidad y secuelas de los niños prematuros en edad escolar.* Directores: Elena Burón y Alfredo Blanco. Universidad de Valladolid. Facultad de Medicina. Departamento de Pediatría. 2009.

2. Angulo-Barroso R, Tiernan CW, Chen L, Ulrich D, Neary H. Treadmill responses and physical activity levels of infants at risk for neuromotor delay. *Pediatr Phys Ther*. 2010;22(1):61-68.

3. Thelen E, Ulrich BD. Hidden skills: A dynamic systems analysis of treadmill stepping during the first year. *Monogr Soc Res Child Dev*. 1991;56(1):1-98; discussion 99-104.

4. Ulrich BD, Ulrich DA, Collier DH, Cole EL. Developmental shifts in the ability of infants with down-syndrome to produce treadmill steps. *Phys Ther*. 1995;75(1):14-23.

5. Valentin-Gudiol M, Mattern-Baxter K, Girabent-Farres M, Bagur-Calafat C, Hadders-Algra M, Angulo-Barroso RM. Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay. *Cochrane Database Syst Rev*. 2011;(12):CD009242.

6. Richards CL, Malouin F, Dumas F, Marcoux S, Lepage C, Menier C. Early and intensive treadmill locomotor training for young children with cerebral palsy: A feasibility study. *Pediatr Phys Ther*. 1997;9(4):158-165.

7. Begnoche DM, Pitetti KH. Effects of traditional treatment and partial body weight treadmill training on the motor skills of children with spastic cerebral palsy. A pilot study. *Pediatr Phys Ther*. 2007;19(1):11-19.

8. Dodd KJ, Foley S. Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: A clinical controlled trial. *Dev Med Child Neurol*. 2007;49(2):101-105.

9. Provost B, Dieruf K, Burtner PA, et al. Endurance and gait in children with cerebral palsy after intensive body weight-supported treadmill training. *Pediatr Phys Ther*. 2007;19(1):2-10.

10. Schindl MR, Forstner C, Kern H, Hesse S. Treadmill training with partial body weight support in nonambulatory patients with cerebral palsy. *Arch Phys Med Rehabil*. 2000;81(3):301-306.

11. Day JA, Fox EJ, Lowe J, Swales HB, Behrman AL. Locomotor training with partial body weight support on a treadmill in a nonambulatory child with spastic tetraplegic cerebral palsy: A case report. *Pediatr Phys Ther*. 2004;16(2):106-113.

12. Mattern-Baxter K, McNeil S, Mansoor JK. Effects of home-based locomotor treadmill training on gross motor function in young children with cerebral palsy: A quasi-randomized controlled trial. *Arch Phys Med Rehabil*. 2013;94(11):2061-2067.

13. Angulo-Barroso RM, Tiernan C, Chen LC, Valentin-Gudiol M, Ulrich D. Treadmill training in moderate risk preterm infants promotes stepping quality--results of a small randomised controlled trial. *Res Dev Disabil*. 2013;34(11):3629-3638.

14. Ulrich DA, Lloyd MC, Tiernan CW, Looper JE, Angulo-Barroso RM. Effects of intensity of treadmill training on developmental outcomes and stepping in infants with down syndrome: A randomized trial. *Phys Ther*. 2008;88(1):114-122.

15. Angulo-Barroso RM, Wu J, Ulrich DA. Long-term effect of different treadmill interventions on gait development in new walkers with down syndrome. *Gait Posture*. 2008;27(2):231-238.

16. Schneider K, Zernicke RF. Mass, center of mass, and moment of inertia estimates for infant limb segments. *J Biomech*. 1992;25(2):145-148.

17. Piper MC, Pinnell LE, Darrah J, Maguire T, Byrne PJ. Construction and validation of the alberta infant motor scale (AIMS). *Can J Public Health*. 1992;83 Suppl 2:S46-50.

18. Bayley. N. *Bayley scales of infant and toddler development. technical manual.* 1st ed. USA: Pearson; 2006.

19. Luo H, Chen P, Hsieh W, et al. Associations of supported treadmill stepping with walking attainment in preterm and full-term infants. *Phys Ther*. 2009;89(11):1215-1225.

CAPÍTULO 5. Discusión, Conclusiones y Limitaciones Generales

La adquisición de la marcha independiente es un hito motriz importante en el desarrollo del niño. Una forma de promover el inicio y la calidad de la marcha sería el entrenamiento del paso en un tapiz rodante. Al analizar la evidencia científica sobre el uso del tapiz rodante en población con riesgo de retraso en el desarrollo motriz, encontramos que el tapiz rodante se ha utilizado en estudios observacionales y en estudios experimentales. La revisión sistemática que forma parte de esta tesis (capítulo 2) demuestra que hay poca evidencia de los efectos del tapiz rodante en población con este tipo de riesgo[10].

Los estudios con diseño observacional han utilizado el tapiz rodante para describir y estudiar la trayectoria de desarrollo y adquisición de la marcha autónoma en los niños con riesgo de retraso en el desarrollo motriz[2,37]. Las conclusiones principales de estos estudios han sido que los niños prematuros y/o de bajo peso al nacer se desarrollan siguiendo un patrón similar, aunque retrasado en el tiempo, al de los niños considerados que siguen un desarrollo normal[25].

Los estudios experimentales en niños con riesgo han sido principalmente ensayos clínicos controlados, donde se ha implementado un entrenamiento sobre el tapiz rodante a un grupo de sujetos, de manera protocolizada[11,60] o individualizada (estudio capítulo 4). Los únicos resultados estadísticamente significativos que se han encontrado han sido aquellos relacionados con la variable que define la calidad del paso en el tapiz rodante. Los sujetos del grupo entrenado han demostrado una disminución más acentuada y más precoz en el tiempo de los apoyos de pie en punta a favor de apoyos en pie plano, lo cual confiere al paso una mayor calidad y lo aproxima a un patrón evolutivamente más maduro. Es de interés destacar un estudio publicado recientemente por Mattern-Baxter *y col.*[7], en el cual la población de estudio ya había recibido diagnóstico de parálisis cerebral, a pesar de que los sujetos eran de muy corta edad (edad media de 21.8 meses). Los sujetos de estudio fueron clasificados de afectación leve según el sistema de clasificación de la funcionalidad motriz global (niveles I y II según la GMFCS[53]), con lo cual podría considerarse que las características de estos niños son comparables a las de los niños clasificados con riesgo pero sin diagnóstico, como es el caso de la población de estudio de esta tesis. Mattern-Baxter *y col.*[7] implementaron un

entrenamiento intensivo con el tapiz rodante, obteniendo resultados positivos en el grupo entrenado en relación a la velocidad de la marcha y en aspectos como la puntuación de ítems motrices en la escala GMFM, que fue más acelerada en el tiempo en comparación con el grupo control. Igualmente, el grupo entrenado obtuvo mejores puntuaciones en la escala *Peabody Developmental Motor Scales-2* (sub-escala de locomoción, PDMS-2[61]). Sin embargo, cabe resaltar que las diferencias significativas encontradas en las puntuaciones de las escalas en el estudio de Mattern.Baxter *y col.*[7] se observaron en las valoraciones de seguimiento, una vez se dio por terminada la intervención. Este tipo de información de seguimiento post-intervención no se encuentra disponible en los estudios citados previamente en niños con síndrome de Down o con riesgo de retraso en el desarrollo motriz. Por tanto, exceptuando la información presentada en el estudio individual de población con PC[7], se desconoce el impacto de los efectos del entrenamiento con el tapiz rodante a corto y medio plazo una vez se da por finalizada la fase de entrenamiento.

Centrándonos en los estudios experimentales mencionados, las variables de análisis de resultado comunes escogidas por los diferentes autores y en relación a la respuesta al tapiz rodante, han sido: la frecuencia de pasos alternos (expresada como frecuencia de pasos por minuto y como porcentaje de pasos alternos respecto al número total de pasos por minuto), y la calidad de los pasos (definida según el tipo de contacto del pie con la cinta del tapiz, si es en punta o en pie plano). Dichas variables han servido para hacer una descripción básica y funcional de los pasos en el tapiz rodante. Además de estas variables, se han utilizado diferentes escalas estandarizadas de valoración del desarrollo motriz, como la *Gross Motor Function Measure* (GMFM)[62], la *Bayley Scales of Infant and Toddler Development* (BSID)[28], o la *Alberta Infant Motor Scale* (AIMS)[29]. El hecho de que, en general, no se utilicen escalas de valoración comunes, dificulta el poder comparar con facilidad el nivel de desarrollo entre los grupos de niños de cada estudio. Aun así, pueden relacionarse las puntuaciones obtenidas en cada escala con la respuesta al tapiz rodante dentro de un mismo estudio y establecer las conclusiones correspondientes. En términos generales para todos los estudios experimentales, no se han encontrado diferencias significativas entre el grupo

entrenado y el grupo control, en cuanto a puntuaciones de las escalas utilizadas en población de niños con riesgo. Las escalas utilizadas fueron GMFM[11,60], BSID[11], y AIMS (esta última solamente en el estudio del capítulo 4, conjuntamente con el BSID). La variable de interés de carácter más funcional y en relación a las escalas que valoran adquisición de ítems motrices, es la edad del inicio de la marcha autónoma. Ninguno de los estudios realizados en niños con riesgo de retraso en el desarrollo motriz han encontrado diferencias significativas sobre esta variable, aunque sí que se ha visto una relación significativa entre la frecuencia de pasos y la edad de inicio de la marcha[2,11] (estudio capítulo 4). Es importante destacar que esta correlación se ha observado en cualquier caso, independientemente de la intervención con el tapiz rodante. Debida la falta de conocimiento suficiente previo sobre posibles efectos adversos del entrenamiento en niños con riesgo de retraso en el desarrollo motriz, los investigadores han pautado protocoles genéricos y de baja intensidad. Puede que esto explique el motivo por el cual, hasta la fecha, no se hayan encontrado efectos del tapiz rodante en esta población. No se ha llegado a implementar un entrenamiento individualizado y progresivo, como sí se ha hecho en otras poblaciones.

Plasticidad cerebral, el tapiz rodante como entrenamiento tarea-específico y las teorías del desarrollo motriz

La plasticidad cerebral se define como la capacidad que tiene el cerebro de cambiar estructural y funcionalmente en respuesta a influencias endógenas (recibidas por el propio cuerpo) y exógenas (recibidas desde el entorno)[63-65]. Según los conocimientos en neurociencia, se sabe que a lo largo de la vida del ser humano existe plasticidad cerebral y capacidad de aprendizaje[44]. Sin embargo, es durante las etapas tempranas del desarrollo cuando mayor margen de cambios estructurales se pueden imprimir a nivel de las células neuronales del cerebro, con los consiguientes resultados funcionales que esto puede representar[66].

El tapiz rodante es una herramienta que facilita la generación de una serie de estímulos sensitivos y motrices, que serán procesados a nivel cerebral. Por ejemplo, el hecho de que la cinta del tapiz lleve de manera pasiva las

extremidades inferiores hacia la extensión de cadera, el gesto en sí implica un estiramiento de los flexores de cadera, los cuales de manera refleja (reflejo miotático) se contraerán facilitando la ejecución de los pasos. Consecuentemente, se estimula una coordinación intra-segmentaria de las articulaciones implicadas en la ejecución del paso (articulaciones del pie, tobillo, rodilla y cadera), y entre ambas extremidades inferiores (coordinación inter-segmentaria). En este sentido, se podría decir que con el tapiz rodante se consigue entrenar un patrón de movimiento que implica varias articulaciones del cuerpo. Dada la alta plasticidad cerebral en edades tempranas, la implementación de un entrenamiento con tapiz rodante en dichas edades podría potenciar el desarrollo de la marcha a través de mecanismos neuronales. Recordemos que la adquisición de la marcha es funcionalmente importante dado que da independencia y autonomía a los seres humanos. Además, en población pediátrica se ha demostrado la estrecha relación que existe entre la adquisición de la marcha independiente y el desarrollo perceptual y cognitivo[5].

Según Hubbard *y col.*[44], en el contexto de la rehabilitación, el entrenamiento tarea-específico se centra en mejorar la funcionalidad a través de la práctica y la repetición de acciones motrices concretas. Esto, a su vez, cobra mayor sentido si se explica desde las bases de la teoría más reciente sobre el desarrollo motriz: la teoría de selección de grupo neuronal (TSGN)[27], que explica también el concepto de plasticidad cerebral. El entrenamiento con el tapiz rodante se podría considerar como un modo de ofrecer los aspectos de práctica funcional y de repetición, siendo además una acción específica a la tarea en relación a cuál es el objetivo de la práctica: mejorar el patrón de la marcha y adquirir la marcha autónoma. Visto esto, cabe aclarar que en la población de interés de esta tesis, estaríamos hablando de *habilitación* y no de *re-habilitación*, puesto que la población de estudio son niños sin experiencia previa en la marcha. Según la TSGN[27], se podría considerar que a través del estímulo sensorio-motriz que se produce durante la actividad de caminar sobre el tapiz rodante, se estarán activando unos determinados grupos de neuronas, las cuales estarán a su vez imprimiendo una variabilidad de movimientos que generarán el repertorio motriz básico. A partir de ese repertorio de movimientos, se irán reforzando aquellas conexiones neuronales que sean más

efectivas y más eficaces en función de la adecuación entre respuesta motriz y entorno (si el movimiento realizado satisface o resuelve la situación del contexto). Así pues, se establecerán uniones anatómicas entre neuronas a nivel de la corteza cerebral, formando los llamados grupos neuronales.

La TSGN proponía dos fases para el desarrollo motriz: una primera fase de generación de variabilidad, y una segunda de selección de los patrones más eficientes. A través del entrenamiento con el tapiz rodante se pretende ofrecer al niño un entorno que le permita generar suficiente variabilidad de movimientos (diferentes tipos de pasos), y suficiente variabilidad en las características de los mismos (diferente velocidad, amplitud o coordinación), lo cual irá constituyendo su variabilidad dinámica. El objetivo de favorecer la generación de estos movimientos es que se pueda ir estableciendo lo que la TSGN define como *repertorio motriz básico* en relación al patrón de marcha. Además de esta generación intrínseca de variabilidad, los investigadores han utilizado dos estrategias principales para aumentarla aún más: (1) la manipulación de los parámetros de entrenamiento, como la velocidad o la resistencia externa (pesos en el tobillo de los sujetos), y (2) una estimulación independiente aplicada a cada pierna del niño mientras se encuentra en el tapiz, al utilizar dos cintas a diferentes velocidades[50-52]. De esta manera se consigue reforzar la capacidad de adaptación al entorno, a pesar de que se trabaje en un patrón inicialmente simétrico y estable. El objetivo final es el de promover la selección del grupo neuronal más estable y más eficiente posible para la marcha.

En la literatura científica encontramos estudios que han descrito cómo el patrón de la marcha de los niños es muy similar al de los adultos, con la diferencia principal que los primeros tienen mayor variabilidad en los movimientos, y la hipótesis es que se trata de una falta de práctica de dicha habilidad[25,26,47]. Por tanto, el entrenamiento con el tapiz rodante podría colaborar en disminuir la variabilidad inicial, y en reforzar un patrón motriz más estable para, a posteriori y cuando el nivel de desarrollo del sujeto lo permitiera, se pudiera dar la variabilidad necesaria para permitir suficiente adaptación al entorno. En su globalidad, todo este proceso implicaría todavía una fase más. En ésta, después de haber reducido la variabilidad inicial, el patrón

seleccionado volvería a aumentar su variabilidad para adaptarse a un entorno real, dinámico y cambiante.

Bajo los conceptos de otra de las teorías del desarrollo motriz, la teoría de sistemas dinámicos (TSD)[22-24] también se podría explicar y justificar la utilización del tapiz rodante para el entrenamiento de la marcha en niños. En el caso de los niños con antecedentes de prematuridad, y en relación a esta teoría, podría considerarse que éstos pueden presentar diferentes tipos de limitaciones: (1) físicas o emocionales (debido a las experiencias previas vividas a nivel hospitalario inmediatamente después de nacer), (2) en su entrono físico (muchas veces suele haber una falta de estimulación global por sobreprotección familiar), y (3) en ejercer una tarea en cuestión (por ejemplo la locomoción a través de la marcha). Estos tres aspectos (características del individuo, el entorno, y la tarea) deben tenerse en cuenta al implementar un entrenamiento con tapiz rodante.

Relacionando las hipótesis y conceptos de Thelen en la TSD[24,26], donde se proponen ocho subsistemas que tienen que llegar a cierto nivel de desarrollo o maduración antes de que el niño logre la marcha bípeda independiente, podríamos considerar que el tapiz: (1) ofrece la generación de un patrón de movimiento, (2) permite una diferenciación articular de las articulaciones de las extremidades inferiores, (3) favorece el control postural al dar estímulos diferentes sobre el equilibrio en función de la cantidad de soporte del peso ejercido sobre el niño manualmente, (4) favorece el desarrollo de la visión al proporcionar la posición bípeda y con cierto dinamismo, (5) estimula el control del tono muscular por el hecho de tener que ajustarse a la velocidad de la cinta del tapiz y de soportar parcialmente el peso de su cuerpo, (6) se trabaja la musculatura extensora en relación a la posición bípeda, (7) favorece el esquema corporal, y (8) se incorpora la motivación del niño. Considerando el trabajo realizado en esta tesis doctoral, y con el resto de evidencia disponible sobre el uso del tapiz rodante y los conocimientos de neurociencia, se podría considerar el tapiz rodante como una herramienta que incide directamente sobre la mayoría de los componentes previos a la adquisición de la marcha. Por tanto, el concepto de entrenamiento de la marcha con el tapiz rodante quedaría justificadamente explicado según las bases de las dos teorías más recientes que intentan explicar el desarrollo motriz.

Limitaciones y futuras líneas de investigación

Los estudios presentados en esta tesis no están libres de limitaciones. En primer lugar, la efectividad del entrenamiento de la marcha con un tapiz rodante en el domicilio familiar, supervisada por un terapeuta, ha sido comprobado en niños con síndrome de Down[10] y, recientemente, en niños con parálisis cerebral[7]. Sin embargo, no se ha podido establecer en el caso de niños con riesgo de retraso en el desarrollo motriz. Faltan ensayos clínicos controlados con muestras mayores, que implementen un entrenamiento de la marcha con el tapiz rodante, para poder corroborar los resultados encontrados hasta la fecha. Investigaciones futuras deberían también estudiar el impacto del entrenamiento con tapiz rodante en población de mayor riesgo de retraso en el desarrollo motriz. Una vez demostrado que el entrenamiento con el tapiz no hizo aumentar ni la espasticidad ni el tono muscular en niños que tenían el tono muscular alterado o espasticidad previamente al entrenamiento[11], se podría empezar a estudiar población más afectada o con antecedentes médicos más graves que pudieran implicar un mayor grado de riesgo de retraso global. Se cree que la población de mayor riesgo es la que más beneficio podría obtener de una intervención de entrenamiento de la marcha con el tapiz rodante, sobre todo en el caso de que se consiguiera adelantar la edad del inicio de la marcha autónoma.

El nivel de intensidad necesaria de entrenamiento en el tapiz rodante en niños con riesgo está aún por determinar. Los estudios realizados en esta población han implementado protocolos genéricos y de baja intensidad, por precaución, ante el desconocimiento de la respuesta al tapiz de esta población. Además, los niños considerados con riesgo de retraso en el desarrollo motriz son una población que puede presentar diversidad de características físicas, según antecedentes médicos y/o condiciones de su entorno. Por tanto, quizás el entrenamiento debería considerarse con mayor individualización y con un seguimiento más cercano que el que se planteó para niños con síndrome de Down, población que, por ejemplo a nivel de tono muscular, se caracteriza por hipotonía generalizada.

Otro aspecto a revisar sería la adherencia al entrenamiento. Puede que la falta de adherencia al protocolo pautado se debiera a una insuficiente

información ofrecida a los padres y/o cuidadores. Sería necesario hacer mayor hincapié tanto sobre los beneficios potenciales del entrenamiento, como sobre la utilidad del tapiz para la detección temprana de retrasos o anomalías físicas o funcionales en el desarrollo motriz de los niños clasificados como con riesgo de retraso en el desarrollo motriz. Si se diera mayor información sobre estos aspectos y sobre la importancia de la detección y de la intervención precoz (si fuera necesario), la adherencia al protocolo quizás sería mayor.

En cuanto a aspectos de metodología de estudio, el tipo de intervención realizada (entrenamiento con el tapiz) y la logística que requiere la propia intervención, hizo imposible un diseño de estudio con cegamiento de las personas implicadas (niño y familia). Para mejorar la calidad metodológica en futuros estudios deberían considerarse diseños de estudios donde los codificadores fueran desconocedores del grupo al que perteneciera el niño que se evaluara, así como del diagnóstico del niño (si lo hubiese). Además, las escalas de desarrollo motriz utilizadas en la mayoría de estudios, como hemos visto, no detectaron cambios sí objetivados en el análisis de la respuesta al tapiz de los sujetos entrenados. Por lo tanto, podría considerarse el uso del tapiz rodante como herramienta de valoración complementaria para poder determinar objetivamente el nivel de desarrollo en relación a la adquisición de la marcha. Un retraso motriz en este aspecto podría igualmente ir acompañado de un retraso en otras habilidades o hitos motrices, y hasta conllevar un retraso cognitivo.

Líneas de investigación futuras podrían dirigirse a estudiar la coordinación inter-segmentaria e intra-segmentaria de las extremidades inferiores durante la marcha en el tapiz rodante. Hay investigaciones que han estudiado variables relacionadas con los movimientos articulares en tobillos, rodillas y caderas de una misma pierna durante el paso, y la relación que se establece entre las articulaciones de ambas piernas durante la marcha en el tapiz[50,52]. Sin embargo, esto solamente se ha estudiado en niños con desarrollo típico, y por tanto sería de interés estudiar estas relaciones articulares durante la marcha de niños con riesgo.

Implicaciones para la práctica clínica

Como se ha discutido a lo largo de los apartados anteriores, los estudios experimentales realizados en niños con riesgo de retraso en el desarrollo motriz han observado y destacado cambios en la calidad del paso de los niños que habían recibido el entrenamiento. Sin embargo, estos cambios objetivados en el tapiz rodante, no han sido captados a nivel de puntuaciones de las escalas que valoran el desarrollo motriz. Se ha visto que una mayor calidad del paso no tiene por qué tener relación directa con la edad de inicio de la marcha autónoma y, por consiguiente, con el nivel de desarrollo motriz. Sin embargo, es importante tener presente que, dado que tanto a través de la TSGN como de la TSD se han podido explicar los posibles efectos del entrenamiento con el tapiz en relación al desarrollo motriz, debería considerarse el hecho de incluir el entrenamiento de la marcha en niños con riesgo de retraso en el desarrollo motriz. Además, es de importancia recordar que es posible que, a medio plazo, algunos de estos niños puedan recibir un diagnóstico como el de parálisis cerebral, especialmente si han sido grandes prematuros o han tenido antecedentes de complicaciones neurológicas pre-, peri- o post-natales.

A nivel clínico, el tapiz rodante podría tener relevancia en dos aspectos. En primer lugar, podría ser útil como herramienta objetivable de anormalidades motrices de aparición temprana que estuvieran relacionadas con la calidad del movimiento. Este tipo de anormalidades a menudo no son detectables médicamente (las estructuras del sistema nervioso central pueden parecer intactas), y además las escalas de valoración del desarrollo o los tests de screening mayoritariamente puntúan de manera cuantitativa, lo cual implica que a menudo tampoco detectan cambios, retrasos ni anormalidades sobre todo relacionadas con la calidad del movimiento. En segundo lugar, y como hemos visto, el tapiz tendría relevancia clínica a nivel de entrenamiento de la marcha en niños con riesgo de retraso leve-moderado, ya que además se ha visto que puede aplicarse sin efectos secundarios negativos al entrenamiento.

Según la clasificación internacional de la funcionalidad (*International Classification of Funtioning, Disability and Health for Children and Youth, ICF*)[67], un retraso en la adquisición de la marcha autónoma podría implicar limitaciones funcionales al niño, de manera que podría dificultar su participación en la

sociedad y en las actividades que podría realizar. Todo esto, a su vez, disminuiría su calidad de vida. Si se corrobora que con el entrenamiento con el tapiz se puede influir positivamente sobre el desarrollo de la actividad funcional que representa la marcha, estaríamos realizando un trabajo preventivo a todos estos niveles citados anteriormente.

REFERENCIAS RESUMEN (ABSTRACT) Y CAPÍTULOS 1 Y 5

1. Almond D, Chay KY, Lee DS. The costs of low birth weight. *Q J Econ*. 2005;120(3):1031-1083.

2. Angulo-Barroso R, Tiernan CW, Chen L, Ulrich D, Neary H. Treadmill responses and physical activity levels of infants at risk for neuromotor delay. *Pediatr Phys Ther*. 2010;22(1):61-68.

3. Korvenranta E, Lehtonen L, Peltola M, et al. Morbidities and hospital resource use during the first 3 years of life among very preterm infants. *Pediatrics*. 2009;124(1):128-134.

4. Wood E. The child with cerebral palsy: Diagnosis and beyond. *Semin Pediatr Neurol*. 2006;13(4):286-296.

5. Campos JJ, Anderson DI, Barbu-Roth MA, Hubbard EM, Hertenstein MJ, Witherington D. Travel broadens the mind. *Infancy*. 2000;1(2):149-219.

6. Richards CL, Malouin F, Dumas F, Marcoux S, Lepage C, Menier C. Early and intensive treadmill locomotor training for young children with cerebral palsy: A feasibility study. *Pediatr Phys Ther*. 1997;9(4):158-165.

7. Mattern-Baxter K, McNeil S, Mansoor JK. Effects of home-based locomotor treadmill training on gross motor function in young children with cerebral palsy: A quasi-randomized controlled trial. *Arch Phys Med Rehabil*. 2013;94(11):2061-2067.

8. Begnoche DM, Pitetti KH. Effects of traditional treatment and partial body weight treadmill training on the motor skills of children with spastic cerebral palsy. A pilot study. *Pediatr Phys Ther*. 2007;19(1):11-19.

9. Day JA, Fox EJ, Lowe J, Swales HB, Behrman AL. Locomotor training with partial body weight support on a treadmill in a nonambulatory child with spastic tetraplegic cerebral palsy: A case report. *Pediatr Phys Ther*. 2004;16(2):106-113.

10. Valentin-Gudiol M, Mattern-Baxter K, Girabent-Farres M, Bagur-Calafat C, Hadders-Algra M, Angulo-Barroso RM. Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay. *Cochrane Database Syst Rev*. 2011;(12):CD009242.

11. Angulo-Barroso RM, Tiernan C, Chen LC, Valentin-Gudiol M, Ulrich D. Treadmill training in moderate risk preterm infants promotes stepping quality--results of a small randomised controlled trial. *Res Dev Disabil*. 2013;34(11):3629-3638.

12. Beck S, Wojdyla D, Say L, et al. The worldwide incidence of preterm birth: A systematic review of maternal mortality and morbidity. *Bull World Health Organ*. 2010;88:31-38.

13. World Health Organization. Tasa de nacimientos prematuros por 100 nacimientos. http://www.who.int/pmnch/media/news/2012/preterm_birth_report/es/index.html. Updated 2010. Accessed 11/12, 2013.

14. Hodnett ED FS. Apoyo durante el embarazo a mujeres con mayor riesgo de recién nacidos de bajo peso al nacer. (Revisión Cochrane traducida). En: *La Biblioteca Cochrane Plus*, 2008 Número 4. Oxford: Update Software Ltd. Disponible en: http://www.update-software.com. (Traducida de *The Cochrane Library*, 2008 Issue 3. Chichester, UK: John Wiley & Sons, Ltd.). *Cochrane Database Syst Rev*. 2007;4

15. Silva AM, de Almeida MF, Matsuo T, Soares DA. Risk factors for pre-term birth in londrina, parana state, brazil. *Cad Saude Publica*. 2009;25(10):2125-2138.

16. van Batenburg-Eddes T, de Groot L, Huizink AC, et al. Maternal symptoms of anxiety during pregnancy affect infant neuromotor development: The generation R study. *Dev Neuropsychol*. 2009;34(4):476-493.

17. Kalia JL, Visintainer P, Brumberg HL, Pici M, Kase J. Comparison of enrollment in interventional therapies between late-preterm and very preterm infants at 12 months' corrected age. *Pediatrics*. 2009;123(3):804-809.

18. Hadders-Algra M. The neuronal group selection theory: Promising principles for understanding and treating developmental motor disorders. *Dev Med Child Neurol*. 2000;42(10):707-715.

19. Hadders-Algra M. The neuronal group selection theory: A framework to explain variation in normal motor development. *Dev Med Child Neurol*. 2000;42(8):566-572.

20. Clark JE. On becoming skillful: Patterns and constraints. *Res Q Exerc Sport*. 1995;66(3):173-183.

21. Kalverboer A. GA. *Handbook of brain and behaviour in human development.* The Netherlands: Kluwer Academic Publishers; 2001.

22. Kugler P, Kelso JS, Turvey M. On the control and coordination of naturally developing systems. *The development of movement control and coordination*. 1982:5-78.

23. Kugler PN, Kelso JS, Turvey M. On the concept of coordinative structures as dissipative structures: I. theoretical lines of convergence. *Tutorials in motor behavior*. 1980;3:47.

24. Thelen E. SLB. *A dynamic systems approach to the development of cognition and action.* First ed. England: MIT Press; 1994:376.

25. Thelen E, Ulrich BD. Hidden skills: A dynamic systems analysis of treadmill stepping during the first year. *Monogr Soc Res Child Dev*. 1991;56(1):1-98; discussion 99-104.

26. Thelen E. Treadmill-elicited stepping in seven-month-old infants. *Child Dev*. 1986;57(6):1498-1506.

27. Sporns O, Edelman GM. Solving bernstein's problem: A proposal for the development of coordinated movement by selection. *Child Dev*. 1993;64(4):960-981.

28. Bayley. N. *Bayley scales of infant and toddler development. technical manual.* 1st ed. USA: Pearson; 2006.

29. Piper MC, Pinnell LE, Darrah J, Maguire T, Byrne PJ. Construction and validation of the alberta infant motor scale (AIMS). *Can J Public Health*. 1992;83 Suppl 2:S46-50.

30. Spittle AJ, Doyle LW, Boyd RN. A systematic review of the clinimetric properties of neuromotor assessments for preterm infants during the first year of life. *Dev Med Child Neurol*. 2008;50(4):254-266.

31. Blauw-Hospers CH, Hadders-Algra M. A systematic review of the effects of early intervention on motor development. *Dev Med Child Neurol*. 2005;47(6):421-432.

32. Vaccarino FM, Ment LR. Injury and repair in developing brain. *Arch Dis Child Fetal Neonatal Ed*. 2004;89(3):F190-2.

33. Riethmuller AM, Jones R, Okely AD. Efficacy of interventions to improve motor development in young children: A systematic review. *Pediatrics*. 2009;124(4):e782-92.

34. Behrman AL, Harkema SJ. Locomotor training after human spinal cord injury: A series of case studies. *Phys Ther*. 2000;80(7):688-700.

35. Behrman AL, Nair PM, Bowden MG, et al. Locomotor training restores walking in a nonambulatory child with chronic, severe, incomplete cervical spinal cord injury. *Phys Ther*. 2008;88(5):580-590.

36. Prosser LA. Locomotor training within an inpatient rehabilitation program after pediatric incomplete spinal cord injury. *Phys Ther*. 2007;87(9):1224-1232.

37. Luo H, Chen P, Hsieh W, et al. Associations of supported treadmill stepping with walking attainment in preterm and full-term infants. *Phys Ther*. 2009;89(11):1215-1225.

38. Ulrich DA, Lloyd MC, Tiernan CW, Looper JE, Angulo-Barroso RM. Effects of intensity of treadmill training on developmental outcomes and stepping in infants with down syndrome: A randomized trial. *Phys Ther*. 2008;88(1):114-122.

39. Jeng SF, Yau KT, Liao H, Chen L, Chen P. Prognostic factors for walking attainment in very low-birthweight preterm infants. *Early Human Development*. 2000;59(3):159-173.

40. Jeng SF, Chen LC, Tsou KI, Chen WJ, Luo HJ. Relationship between spontaneous kicking and age of walking attainment in preterm infants with very low birth weight and full-term infants. *Physical Therapy*. 2004;84(2):159-172.

41. Jensen JL, Schneider K, Ulrich BD, Zernicke RF, Thelen E. Adaptive dynamics of the leg movement patterns of human infants .1. the effects of posture on spontaneous kicking. *J Mot Behav*. 1994;26(4):303-312.

42. Schmidt R, Lee T. *Motor learning and performance, 5E with web study guide: From principles to application.* Human Kinetics; 2013.

43. Alloway TP, Warn C. Task-specific training, learning, and memory for children with developmental coordination disorder: A pilot study. *Percept Mot Skills*. 2008;107(2):473-480.

44. Hubbard IJ, Parsons MW, Neilson C, Carey LM. Task-specific training: Evidence for and translation to clinical practice. *Occup Ther Int*. 2009;16(3-4):175-189.

45. Angulo-Barroso RM, Wu J, Ulrich DA. Long-term effect of different treadmill interventions on gait development in new walkers with down syndrome. *Gait Posture*. 2008;27(2):231-238.

46. Clark JE, Whitall J, Phillips SJ. Human interlimb coordination: The first 6 months of independent walking. *Dev Psychobiol*. 1988;21(5):445-456.

47. Ulrich BD, Schneider K, Jensen JL, Zernicke RF, Thelen E. Adaptive dynamics of the leg movement patterns of human infants .2. treadmill stepping in infants and adults. *J Mot Behav*. 1994;26(4):313-324.

48. Davis DW, Thelen E, Keck J. Treadmill stepping in infants born prematurely. *Early Hum Dev*. 1994;39(3):211-223.

49. Yang JF, Stephens MJ, Vishram R. Infant stepping: A method to study the sensory control of human walking. *J Physiol*. 1998;507 (Pt 3)(Pt 3):927-937.

50. Yang JF, Lamont EV, Pang MY. Split-belt treadmill stepping in infants suggests autonomous pattern generators for the left and right leg in humans. *J Neurosci*. 2005;25(29):6869-6876.

51. Pang MY, Yang JF. The initiation of the swing phase in human infant stepping: Importance of hip position and leg loading. *J Physiol*. 2000;528 Pt 2:389-404.

52. Pang MY, Yang JF. Interlimb co-ordination in human infant stepping. *J Physiol*. 2001;533:617-625.

53. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev Med Child Neurol*. 1997;39(4):214-223.

54. Damiano DL, de Jong SL. A systematic review of the effectiveness of treadmill training and body weight support in pediatric rehabilitation. *J Neurol Phys Ther*. 2009;33(1):27-44.

55. Damiano DL. Activity, activity, activity: Rethinking our physical therapy approach to cerebral palsy. *Phys Ther*. 2006;86(11):1534-1540.

56. Mutlu A, Krosschell K, Gaebler Spira D. Treadmill training with partial body-weight support in children with cerebral palsy: A systematic review. 2009;51(4):268-275.

57. Wu J, Ulrich DA, Looper J, Tiernan CW, Angulo-Barroso RM. Strategy adoption and locomotor adjustment in obstacle clearance of newly walking toddlers with down syndrome after different treadmill interventions. *Exp Brain Res*. 2008;186(2):261-272.

58. Hadders-Algra M. Early brain damage and the development of motor behavior in children: Clues for therapeutic intervention? *Neural Plasticity*. 2001;8(1-2):31-49.

59. Vereijken B, Thelen E. Training infant treadmill stepping: The role of individual pattern stability. *Dev Psychobiol*. 1997;30(2):89-102.

60. Chen L, Looper J, Neary H, Ulrich D, Angulo-Barroso R. Walking patterns in infants at moderate risk for neuromotor disabilities with or without treadmill training. *J Sport Exerc Psychol*. 2008;30:S40-S41.

61. van Hartingsveldt MJ, Cup EH, Oostendorp RA. Reliability and validity of the fine motor scale of the peabody developmental motor scales-2. *Occup Ther Int*. 2005;12(1):1-13.

62. Russell DJ, Rosenbaum PL, Cadman DT, Gowland C, Hardy S, Jarvis S. The gross motor function measure: A means to evaluate the effects of physical therapy. *Developmental medicine and child neurology*. 1989;31(3):341-52.

63. Chen R, Cohen LG, Hallett M. Nervous system reorganization following injury. *Neuroscience*. 2002;111(4):761-773.

64. Ziemann U, Muellbacher W, Hallett M, Cohen LG. Modulation of practice-dependent plasticity in human motor cortex. *Brain*. 2001;124(Pt 6):1171-1181.

65. Hebb DO. The mammal and his environment. *Am J Psychiatry*. 1955;111(11):826-831.

66. Johnson MH. Functional brain development in humans. *Nat Rev Neurosci*. 2001;2(7):475-483.

67. World Health Organization. *International classification of functioning, disability and health for children and youth*. http://apps.who.int/classifications/icfbrowser/. Updated 2005. Accessed February/10, 2011.

ANEXOS

A - Documento de aprobación del Comité de Ética e Investigación Científica de la University of Michigan

University of Michigan Medical School

The University of Michigan Medical School
Institutional Review Board for Human Subject Research (IRBMED)
Argus I Building, 517 W. William Street; Ann Arbor, Michigan 48103-4943
Telephone: 734 763 4768 • *Telefacsimile:* 734 763 9603 •
Electronic Mail: irbmed@umich.edu • *Internet Web Location:* http://www.med.umich.edu/irbmed

NOTICE OF OUTCOME OF REVIEW OF HUMAN SUBJECT RESEARCH

FAX TO: 6-1925

Angulo-Barroso,Rosa (Principal Investigator) •• IRBMED #: 2004-0537
Project Title: Treadmill Training in Infants at Risk for Cerebral Palsy
Sponsor & Identifier Code: U.S. Dept. of Education-Office of Special Education & Rehabilitative Services
Local Identifier Code: Other 888880
Submit Date: Jan 17, 2008 •• **Receipt Date:** Jan 17, 2008
Project Type: Direct involvement of human subjects (prospective): Research solely using surveys, interviews, focus groups, observations, or other similar methods.
Supporting Documents: Updated Current Consent with New Template, Cover Letter (dated 01/17/2008) •• **Adverse Event Reports:** Initial Report: Z, 5/15/2007 (no separate supporting report received)
Application Type: Adverse Event, Amendment: Study Protocol, Scheduled-Continuation Review
FDA-Regulated Test Articles: No test articles used.
Vulnerable Subjects: Children and Minors
Informed Consent Process: Comprehensive written, Waiver/alteration of consent
HIPAA Compliant: Yes (PHI as described in application or protocol) •• **Review Type:** Convened Board
Risk Level: No More Than Minimal
Outcome: Approved/Acknowledgement •• **Decision Date:** Jan 31, 2008
Approval Date of Most Recent Version of Consent Document: Jan 31, 2008
Expiration Date of Project Approval: Jan 30, 2009

Information on the project and the outcome of the review by the IRBMED appear in the descriptive paragraph above. The content of the submitted material conforms to relevant regulations of the United States Government and the University of Michigan. If the descriptive paragraph indicates that a "Comprehensive Written" informed consent process is to be implemented, all copies of the consent document are required to display the following information in the descriptive paragraph: [1] IRBMED Archive Number. [2] Approval Date of Most Recent Version of Consent Document. [3] Expiration Date of Project Approval. If the descriptive paragraph acknowledges that the project has been terminated, all activity involving human subjects will have come to an end, and will not resume unless reviewed and approved by the IRBMED as a new or extension project.

The investigators are required to report to the IRBMED [1] planned changes in any aspect of the study, and do not implement any change without receiving approval, except to eliminate immediate hazard to subjects, [2] any serious or unexpected adverse events, and [3] any new information on the project that may adversely influence the risk/benefit ratio.

The investigators are responsible for applying to the IRBMED to receive Scheduled-Continuation Review and Approval of the project about eight weeks prior to the "Expiration Date of Project Approval" shown in the descriptive paragraph. In case IRBMED approval is not secured prior to Expiration Date, subject recruitment activity will cease, and no research interventions will be administered to the research subjects except to eliminate immediate hazard.

In accordance with 45 CFR 46.111 and IRBMED practice, consent document(s) and process are considered as part of Continuing Review to ensure accuracy and completeness. The approval and expiration dates of the consent document have been updated to reflect the date of Continuing Review approval.

A list of IRBMED members is available at the IRBMED Internet web site ("Membership Roster (IRBMED)"). This Notice of Outcome document and the membership roster may be submitted to sponsors of the research.

Note: If this research study will take place in the General Clinical Research Center (GCRC) please remember to send the GCRC a copy of all IRBMED approval letters and approved consent forms. Send to: GCRC, A7119 UH, Box 0108 or fax to 936-4024. GCRC phone: 936-9090. CGRC Website: http://www.med.umich.edu/gcrc/

John G. Weg, M.D.

Copies to:
Principal Investigator
Medical School Assoc. Dean for Research & Graduate Studies
Division of Research & Development Administration

John G. Weg, M.D.
Professor Emeritus, Internal Medicine
Co-Chair, IRBMED

IMPORTANT CHANGE TO IRBMED PRACTICES

STUDIES RECEIVING RENEWAL OF IRBMED APPROVAL (SCR Approval) MUST UPDATE THE CONSENT APPROVAL DATE IN ADDTION TO THE STUDY EXPIRATION DATE ON INFORMED CONSENT DOCUMENTS

In accordance with 45 CFR 46.111, federal guidance, and IRBMED practice, the consent process is reviewed as part of Scheduled Continuing Review (SCR) in order to ensure the document is still accurate and complete. If your submission was for the SCR of a previously approved project the approval date on the informed consent document (ICD) must be updated to reflect the dates on the Notice of Outcome (approval notice).

Study Team Actions Required at SCR Approval In Legacy (Paper Application System)

1. Change the expiration date on the ICD to match the study's new expiration (same practice as in the past).
2. Change the consent approval date to match the SCR approval date (new practice).

If no revisions to the consent were made at the time of continuing review, it is not required for you to modify the version number or version date of the consent document (but it is allowed if required by a sponsor).

For studies in the eResearch system the IRBMED will update the informed consent documents. We will place the 'water-marked' electronic copy in eResearch, in the Approved Application Workspace ('Parent' workspace) under the 'Currently Approved Documents' header in the 'Documents' tab.

B - Documento de aprobación del Comité de Ética e Investigación Científica del Consell Català de l'Esport

Generalitat de Catalunya
Comitè d'Ètica d'Investigacions Clíniques
de l'Administració Esportiva de Catalunya

CARLES TRULLOLS I CLEMENTE, RESPONSABLE DE SUPORT JURÍDIC I TÈCNIC DEL CONSELL CATALÀ DE L'ESPORT, ACTUANT COM A SECRETARI DEL COMITÈ D'ÈTICA D'INVESTIGACIONS CLÍNIQUES DE L'ADMINISTRACIÓ ESPORTIVA DE CATALUNYA

CERTIFICO

Que en la reunió duta a terme el dia 24 de maig de 2013, aquest Comitè d'Ètica va acordar avaluar favorablement el projecte presentat per les senyores Rosa Angulo-Barroso i Marta Valentín Gudiol, titulat **"Entrenamiento de la marcha con tapíz rodante y desarrollo psicomotor en mellizas prematures".**

La qual cosa faig constar als efectes oportuns

Esplugues de Llobregat, 24 de maig de 2013

C - Consentimiento Informado Entrenamiento de la Marcha con Tapiz Rodante y Desarrollo Psicomotor en Mellizas Prematuras

INFORMACIÓN DEL PROYECTO

ESTUDIO DE CASO DEL ENTRENAMIENTO CON TAPIZ RODANTE Y DESARROLLO PSICOMOTOR EN MELLIZA PREMATURA Y DE BAJO PESO

Esponsors:
Fundación Roger Torné, Universitat Internacional de Catalunya, Institut Nacional d'Educació Física de Catalunya (Universitat de Barcelona), Centre de Desenvolupament Infantil i Atenció Precoç Sant Adrià de Besòs

Investigador Principal:
Rosa M. Angulo-Barroso, PhD Profesora Biomecánica INEFC, Investigadora CHGD, University of Michigan.

Introducción:
Se ha solicitado de la participación de sus hijas en un estudio de investigación en el ámbito de la pediatría. Antes de tomar la decisión de ofrecer sus hijas como voluntarias, quisiéramos informarle detalladamente sobre qué consistirá dicho estudio. La ley requiere de nuestra parte la presentación de un documento de consentimiento informado que se le pedirá firmar en caso de aceptar participar en el estudio. Usted es libre de hablar con sus familiares o médicos antes de firmar dicho documento.

Las investigaciones en seres humanos se llevan a cabo bajo los principios siguientes:

1. Formar parte del estudio es completamente voluntario. Esto significa que no tiene por qué participar si no lo desea.
2. Si decide participar y en un futuro cambia de opinión, tiene el derecho de dejar el estudio sin penalización alguna.
3. Sus hijas pueden o no mejorar su estado físico por el hecho de haber tomado parte en este estudio. Sin embargo podremos aumentar los conocimientos sobre la condición de sus hijas con su participación, lo cual podrá ayudar a otros casos en un futuro.

En este estudio hay dos instituciones participantes: el Centro de Desarrollo Infantil y Atención Precoz de Sant Adrià de Besòs y el Institut Nacional d'Educació Física de Catalunya - Universitat de Barcelona La Fundación Roger Torné ha financiado parcialmente este proyecto de investigación a través de la Universitat Internacional de Catalunya.

Este estudio ha sido aprobado por un comité de ética de la investigación?

Sí. Este estudio ha sido revisado y aprobado por el Comité Ético del Consell Català de l'Esport. Los hospitales de Sant Joan de Déu i Hospital General de Catalunya revisaron y aprobaron igualmente el proyecto planteado inicialmente con una muestra de 120 sujetos. Los miembros de los comités son médicos y otros profesionales de la salud.

Por qué se ha escogido a mis hijas para que participen en el estudio?
Se ha pedido la participación de sus hijas en este estudio por tener la edad adecuada, y por ser usuarias de los servicios de atención precoz en el CDIAP Sant Adrià. Sus hijas son de especial interés para este estudio por ser mellizas. Es de interés poder implementar la intervención de estudio en una de ellas mientras que la otra nos será de referencia de control para comparar los resultados de la intervención.

Cuáles son los objetivos del estudio?
Los objetivos principales de este estudio son examinar las diferencias en la respuesta al tapiz rodante entre las dos mellizas, y evaluar si la intervención de entrenamiento con el tapiz puede acelerar la adquisición de la marcha y el desarrollo motriz de la melliza que presenta retraso en el desarrollo.
Este estudio se realizará para conocer la viabilidad de aplicar un entrenamiento individualizado con tapiz rodante dentro del ámbito familiar. Igualmente es de interés observar la respuesta al tapiz como factor predictivo de diagnóstico final del caso.

Qué es lo que tiene que hacer mi hija en este estudio?
Si usted accede a participar, se realizará una evaluación inicial a sus hijas en la cual se tomarán mediciones antropométricas (peso, talla y el perímetro craneal) y pasarán dos tests (Alberta Infant Motos Scale (AIMS) y Bayley III, componentes motriz y cognitivo) para la valoración del desarrollo neurológico y psicomotor de sus hijas. A continuación se realizará una prueba de 5 minutos totales de medición de la frecuencia y la calidad de los pasos que sus hijas realicen en un tapiz rodante pediátrico con soporte manual del peso (realizado por la terapeuta). La prueba en el tapiz se grabará con una videocámara (omitiendo cualquier tipo de imagen que pueda revelar la identidad del sujeto participante), respetando en todo momento las leyes de protección de datos, de imagen y de confidencialidad.
A continuación el equipo investigador pautará el entrenamiento a la melliza de estudio, el cual será implementado por los padres en su propio domicilio con un tapiz rodante que se les facilitará para la tarea. Previamente una terapeuta habrá entrenado a los padres sobre cómo realizar la intervención. Durante los cinco primeros días de intervención, ésta será supervisada por la misma terapeuta para modificar cualquier aspecto, en caso de que fuera necesario. Mensualmente una terapeuta visitará el domicilio familiar para realizar una grabación con videocámara de la sesión de entrenamiento en el tapiz, y para hacer un seguimiento del desarrollo psicomotor con el test Bayley III. En la misma visita, la melliza no entrenada será grabada 5 minutos en el tapiz rodante y se evaluará igualmente su desarrollo con el Bayley III y AIMS.

Cuánto tiempo será necesario que mis hijas estén en el estudio?

La duración y seguimiento del estudio será hasta el inicio de la marcha independiente de la melliza de estudio.
La duración total de las sesiones de evaluación será de 90 minutos.

Cuáles son los riesgos o incomodidades que pueden tener mis hijas si participan en el estudio?
Nosotros tomamos las precauciones máximas para asegurar la seguridad de sus hijas. Los procedimientos y el equipamiento se verificarán regularmente cada mes. El equipamiento eléctrico está homologado, es resistente al agua y es revisado regularmente por personal experto. El tapiz rodante ha sido usado exitosamente en estudios pediátricos por una variedad de investigadores, incluyéndonos a nosotros. Normalmente los niños/as se divierten en este tipo de intervención, sin embargo si su hija se muestra inquieta o molesta, o por alguna razón está intranquila con la situación, se concluirá la sesión inmediatamente. Le invitamos a estar presente durante todas la sesiones de evaluación y seguimiento, cerca de sus hijas para ver en todo momento el procedimiento del estudio. Cualquier duda o pregunta que usted tenga será bienvenida en todo momento.

Adicionalmente siempre existen posibles efectos adversos previamente desconocidos que muy raramente pueden resultar en complicaciones de salud.

Esta información no tiene como objetivo causar alarma sino más bien tomar conciencia de los posibles riesgos existentes en toda intervención. Ante cualquier duda que usted pueda tener puede ponerse en contacto con la investigadora principal del estudio (su nombre y detalles de contacto aparecen al final de este documento). Es también importante que usted notifique a su médico cualquier síntoma que pueda aparecer.

Cuáles son los beneficios de la participación en este estudio?
Desconocemos si el procedimiento realizado en este estudio podrá ayudar a su hija. Sin embargo la información obtenida podrá ser beneficiosa para otros en el futuro.

Cuáles son mis derechos y mis responsabilidades?
Si usted permite que sus hijas participen en el estudio, tiene derecho a cambiar de opinión sin necesidad de dar ninguna explicación al respecto, aun habiendo firmado este documento.

Quién tendrá acceso a los resultados de la valoración de mis hijas y cómo se mantiene la confidencialidad?
Las historias clínicas, las mediciones y los vídeos de la pruebas en el tapiz rodante de sus hijas se guardarán en una carpeta confidencial en el Institut Nacional d'Educació Física de Catalunya. Las grabaciones en vídeo se conservarán indefinidamente para futuras revisiones en investigación. Solamente las personas integrantes en el estudio (el equipo investigador) tendrán acceso a información que le identifique a usted y/o a sus hijas. Dichas personas podrán obtener (total o parcialmente) datos de las valoraciones y de las pruebas realizadas a su hijas, con propósitos de investigación.

Al final del estudio, toda la información recogida se combinará para ser revisada. Su nombre, el nombre de sus hijas y cualquier tipo de información de identidad no serán usados en ninguna publicación ni presentación pública.

Cuáles son mis responsabilidades financieras?
La participación en este estudio no supondrá ningún gasto económico. Será la terapeuta del equipo investigador quien se desplace al domicilio familiar para realizar el seguimiento y adherencia a la intervención

Si mis hijas participan en este estudio, ¿pueden también participar en otros estudios?
La participación simultánea de sus hijas en dos estudios similares puede afectar los resultados de las mediciones. Sus hijas no deberían participar en más de un estudio de forma simultánea sin haber obtenido el acuerdo de los investigadores participantes en cada estudio.

¿Podría ser que mis hijas fuesen excluidas de participar en el estudio aunque yo quisiera que participase?
Sí. Existen algunas razones que podrían hacer que aun habiendo cumplido inicialmente los criterios de inclusión, apareciese algún motivo que hiciera excluirlo del estudio. Algunos ejemplos se listan a continuación:

- Si el investigador cree que no sería beneficioso para sus hijas participar en el estudio.
- Si la condición de sus hijas cambiase y necesitara un tratamiento que no se permite bajo los criterios de selección de los participantes en el estudio.
- Si se suspendiera o cancelara el estudio por cualquier motivo.

¿Con quién puedo contactar si necesito más información sobre este estudio?
Los nombres y la información de contacto del investigador principal se detallan más abajo. Usted puede contactarlo si:

- Tiene dudas o preguntas.
- Quiere obtener más información sobre el estudio.
- Decide no participar en el estudio después de haber accedido a ello firmando este documento.

Investigador principal: Rosa M. Angulo-Barroso, PhD. 93-4255445 ext 246

Coordinador del Proyecto: Marta Valentín-Gudiol, Fisioterapeuta. 630573247

CONSENTIMIENTO INFORMADO

Entiendo que al consentir en participar en este estudio yo soy responsable de seguir las instrucciones e informar al personal investigador sobre cualquier efecto secundario, lesión o complicación que mis hijas puedan tener antes, durante y después de su participación en el estudio.

También voy a expresar cualquier preocupación o duda que pueda tener acerca de participar en este estudio. Entiendo que seré informado acerca de cualquier nueva información sobre el estudio que podrían afectar a mi disposición a seguir participando.

He tenido la oportunidad de hacer preguntas sobre el estudio y se me ha brindado suficiente tiempo para considerar la participación de mis hijas en este estudio. He hablado con todas las personas que he necesitado para ayudarme a tomar mi decisión. Entiendo que la participación de mis hijas es totalmente voluntaria. He recibido una copia de este formulario y estoy de acuerdo y permito que mis hijas participen en este estudio de investigación.

Doy mi consentimiento a que se realicen las grabaciones necesarias para el estudio, proporciono mi información de contacto para continuar con el seguimiento de las niñas y para recibir feedback de los resultados del estudio.

Sujeto de investigación (niño/a) Nombre _____

Correo electrónico _____

Teléfono de contacto _____

_____ _____

Firma del padre, madre o responsable legal Fecha

DNI del padre, madre o responsable legal: _____

_____ _____

Firma del investigador Fecha

REVOCACIÓNDE PARTICIPACIÓN EN EL ESTUDIO

Yo, _____, con DNI _____, revoco el consentimiento subscrito en fecha _____ y declaro no desear continuar en el estudio titulado _____ _____, dando por finalizada la participación en él de mi hija menor de edad _____ _____.

_____ _____

Firma del padre, madre o responsable legal Fecha

D - Publicación European Journal of Physical and Rehabilitation Medicine

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Treadmill interventions with partial body weight support in children under six years of age at risk of neuromotor delay: a report of a Cochrane systematic review and meta-analysis

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

***Aim*. The aim of this paper was to assess the effectiveness of treadmill intervention on locomotor motor development in pre-ambulatory infants and children under six years of age who are at risk for neuromotor delay.**

***Design*. A Cochrane systematic review with meta-analysis.**

***Methods*. We employed a comprehensive search strategy. We included randomised, quasi-randomised and controlled clinical trials that evaluated the effect of treadmill intervention in children up to six years of age with delays in gait development or the attainment of independent walking or who were at risk of neuromotor delay. We searched CENTRAL, MEDLINE, EMBASE, PsycINFO, CINAHL, Science Citation Index, PEDro, CPCI-S and LILACS; and also ICTRP, ClinicalTrials.gov, mRCT and CenterWatch. Four authors independently extracted the data using standardized forms.**

***Results*. We included five studies, which reported on treadmill intervention in 139 children. Of the 139 children, 73 were allocated to treadmill intervention groups. The studies varied in the type of population studied, the type of comparison, the time of evaluation and the parameters assessed. Due to the diversity of the studies, we were only able to use data from three studies in meta-analyses and these were limited to two outcomes: age of onset of independent walking and gross motor function. Evidence suggested that treadmill intervention could lead to earlier onset of independent walking when compared to no treadmill intervention (effect estimate -1.47; 95% CI: -2.97, 0.03), though these trials studied two different populations: Down syndrome and children at risk of neuromotor disabilities. Children with Down syndrome seemed to benefit while it was not clear if this was the case for children at high risk of neuromotor disabilities. Two other studies, both in children with Down syndrome, compared different types of treadmill intervention (high versus low intensity training). Both were inconclusive regarding the impact of these different protocols on the age at which children started to walk. There is insufficient evidence to determine whether treadmill intervention improves gross motor function (effect estimate 0.88; 95% CI: -4.54, 6.30).**

***Conclusion*. The current review provided only limited evidence of the efficacy of treadmill intervention in children up to six years of age. Few studies have assessed treadmill interventions in young children using an appropriate control group. The available evidence**

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indicates that treadmill intervention may accelerate the development of independent walking in children with Down syndrome. Further research is needed to confirm this and should also address whether intensive treadmill intervention can accelerate walking onset in young children with cerebral palsy and high risk infants, and whether treadmill intervention has a general effect on gross motor development in the various subgroups of young children at risk for developmental delay.

KEY WORDS: Exercise therapy - Psychomotor disorders - Infant - Child - Gait - Physical therapy modalities.

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

Description of the condition

Typical gross motor development

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

Developmental delay

The International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) [2] describes developmental delay as retardation in the achievement of developmental milestones. The most plausible cause of the motor delay is an alteration in the typical development and function of the central nervous system. Motor delays in locomotor abilities are defined by standards used in clinical pediatric settings. For example, the onset of independent walking should occur prior to 18 months of corrected age, so the presence of a motor delay would not be considered before this age. Developmental delay in infants is usually diagnosed via routine screening [3] and/or the use of norm-referenced tests and/or criterion-referenced tests. Kinetic and kinematic analysis using force plates and video motion analysis may be used to further specify the delay; brain imaging techniques may be used to elucidate the etiology of the delay. Although used for both research and clinical purposes, the tests are typically not good predictors for later outcomes and generally lack sensitivity in detecting small changes in motor development.[4] In addition, in the paediatric population the reliability of some of these tests may be affected by the child's emotional state, by daily fluctuations in performance or by the experience of the tester. Due to the continuous developmental changes occurring in the young brain, early diagnostic tests are relatively limited in predicting developmental outcomes [5] and the high level of variation in motor developmental trajectories in healthy children means that care has to be taken when interpreting results from motor assessments.[6]

Consequences of motor developmental delay

One of the major tasks in gross motor development is locomotion, the ability to move from one place to another.[7] The failure to attain walking or the late attainment of walking has consequences for the musculoskeletal system. The anatomy of the hip, for instance, needs weight bearing for proper bone growth and correct orientation of the femoral head, as well as for a correct alignment of the spine.[8] As well as its importance for subsequent motor skill development, acquiring the ability to locomote is important for infants because of its impact on cognitive, social and emotional skills. Researchers have demonstrated that for infants with typical development, experience with locomotion is associated with the development of a broad array of cognitive

skills, including the onset of wariness of heights; the concept of object permanence (objects hidden from sight still exist); a shift from self-centered to landmark-based spatial coding strategies; the ability to follow the pointing gestures and gaze of another person, and aspects of social referencing and detour reaching.[9-12] This suggests that infants are better able to develop spatial cognition and learn about the world around them as they become able to locomote independently. Children who can walk independently show improved active exploration of their environment, as opposed to children who passively observe the environment when being held or carried through space [13] further suggests that the quality of movement may affect subsequent development. He proposes that inefficient locomotion may hamper development by limiting the attention and energy that infants spend on exploration of the environment. Moreover, early locomotor experiences may have a larger impact on the developing brain than similar experiences at a later age due to the brain's high plasticity during the first few postnatal years.[5, 14] Earlier achievement of developmental milestones, in particular independent walking, have also been associated with better intellectual performance in adulthood[15]. In summary, independent locomotion at early age not only facilitates the infant's motor development, but also impacts other developmental domains and affects quality of life for the child and his or her family.[16]

Population affected

There are various reasons for delays in typical motor development. Disorders affecting motor development during infancy include Down syndrome, cerebral palsy, spina bifida and a broad range of other neuromuscular disorders.[8]

In addition, preterm birth, defined as childbirth occurring at less than 37 weeks or 259 days gestation,[17] is associated with a series of risk factors that make children vulnerable to delays in their developmental process.[18] For instance, children who are born prematurely have higher rates of cerebral palsy, sensory deficits and learning disabilities compared with children born at term.[17]

The incidence of preterm birth rate is 6.2% in Europe, 6.4% in Australia and 10.6% in North America (excluding Mexico) [17] and the incidence of cerebral palsy is 1.5 to 2 per 1000 live births[19]. However, more epidemiological studies are needed to reliably assess the incidence for cerebral palsy as its causes are not fully understood.[20] Approximately one in 800 children in the USA are born with Down syndrome, while the incidence in the UK is one in 1000.[21]

Description of the intervention

According to some authors, high levels of motor activity are the key to motor development.[22, 23] In order to best influence neural plasticity, it is important that any training is performed early in development and that it is specific to the task the child needs to master.[24, 25] Intervention studies examining infants developing in a typical and atypical way show that task-specific training may best facilitate the development of postural control.[26-28] This concept of task-specificity can be considered an evidence-based concept based on neuroscientific principles.[24]

Although the optimal window of intervention within the motor domain is not clear,[29] it is reasonable to think of independent walking as a motor task that needs to be achieved by six years of age if long-term negative effects are to be minimized. Locomotor treadmill interventions, with or without partial weight support, have been used to promote the acquisition of independent walking in children with Down Syndrome [30, 31] and cerebral palsy.[32-34]

Protocols of treadmill interventions described in the literature vary with regard to training speeds, support provided, manual assistance with stepping, and frequency and duration of the intervention. In studies of infants, the majority had training speeds ranging from 0.1 m/s to 0.22 m/s;[35] whereas, older children were trained at higher speeds of 1.8 m/s.[32] The percentage of body weight used as partial weight support varied across studies and was provided either manually (the infant is supported under the arms, with the feet resting on the treadmill surface, bearing as much weight as comfortable),[36] or with a commercially available pelvic harness or trunk harness, or both.[37, 38] Only a few studies quantified the amount of body weight support provided during training.[34, 38-40] Training duration ranged between two weeks [38, 41, 42] and 57 weeks,[36] with some studies including breaks during the training programme.[43-45] Frequency of the training sessions

varied between studies from two to six training sessions per week.[23, 34] Manual facilitation of gait varied from no assistance with leg advancement to assistance from up to three physical therapists.[34]

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

How the intervention might work

It is well established that brain plasticity exists and is particularly pronounced in the young nervous system (NS).[46, 47] Experience-dependent and/or activity-dependent plasticity has been demonstrated in the human nervous system [48, 49] and postural control intervention studies.[50] The capacity for the nervous system to reorganize is one of the fundamental mechanisms by which therapeutic interventions may be effective.

The treadmill is one form of intervention used in physical therapy to enhance the locomotor capabilities of patients[51, 52]; however, most of the scientific knowledge related to this topic comes from animal models (already since the pioneering work of Sir Charles Scott Sherrington) [53] or interventions in adult human populations.[54] In fact, the use of treadmill interventions for people with neurological disorders has its roots in animal studies [55, 56] where adult cats were able to regain stepping skills after a complete lesion of the spinal cord. The underlying mechanism by which this technique is effective is thought to reside in the regenerating capacity (plasticity) of the central nervous system when task-specific motor practice is provided. Voluntary exercise and treadmill interventions specifically have been utilised in humans and in animal models to promote central nervous system (including spinal cord) plasticity and functional change.[57-59] The underlying neuronal mechanisms responsible for such change are thought to be up-regulation of trophic factors, neurogenesis, synaptogenesis, pre- and postsynaptic modulation and angiogenesis, among others. These plasticity mechanisms are particularly active during early development. These neuroscience principles are the basis of the current motor learning theories.[60, 61]

Plausible positive outcomes from treadmill interventions via central nervous system plasticity have been proposed in infants with Down syndrome and premature infants. Evidence from studies with children who have Down syndrome indicate statistically significant improvements in a variety of outcome measures including obstacle negotiation and onset of walking. For this population, two main benefits from treadmill interventions implemented during early development have been described. Firstly, it promotes the transition to continuous alternating steps in infants (including typically developing infants,[62, 63] which is an important precursor to walking.[36, 64, 65] Secondly, it leads to an acceleration of the onset of independent walking and an improvement of the quality of gait.[36]

Observational studies suggest that infants born prematurely follow similar developmental trajectories to their full-term peers, although frequently with some delay.[66, 67] The neonatal period of preterm infants is stressful as the immaturity of vital physiological functions, such as respiration, blood pressure control, and autoregulation of cerebral blood flow, makes it difficult for the infant to adapt to the extrauterine situation. This results in vulnerability to delay in motor development and to developmental disorders,[18, 68-70] a vulnerability which in part is mediated by detectable lesions of the brain.[71] The evidence available on the effect of treadmill interventions for this population is almost non-existent. A case study of a premature infant showed an increase in the number of steps, of which almost 100% were exclusively alternating steps, during the post-training phase.[72] However, encouraging as these results may seem, evidence of the effectiveness of treadmill interventions remains inconclusive.

Why it is important to do this review

The importance of children attaining independent walking has been well documented. A range of interventions to improve motor development in children is currently used in practice.[73] However, research on early interventions for children with phys-

ical disabilities is very limited and most studies have methodological limitations.[74]

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

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

There are several existing systematic reviews on treadmill interventions in paediatric populations,[23, 34, 75-77] However, these reviews evaluated published reports from 1980 to 2008 on treadmill training for children aged up to 21 years. In addition to their reliance on published reports in English, their search strategy did not include terms of specific diagnoses that are known to cause gross motor delay in childhood, and some were limited to children with cerebral palsy.

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

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

Objectives

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

Methods

Criteria for considering studies for this review

Types of studies

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

Types of participants

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

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

Types of interventions

Treadmill intervention of any type, frequency or intensity aimed at 1) improving gait parameters such as walking speed, endurance, quality of step (how the foot lands on the floor surface) or 2) facilitating onset of independent walking or walking with assistance.

Comparison groups received no treatment or another treatment. Control group treatments could include physical therapy or another intervention designed to improve gait. We included studies with treadmill intervention as an adjunctive treatment. We also reported on studies comparing different types of treadmill interventions, for example, low versus high intensity.

Types of outcome measures

We accepted five types of outcome measures: standardized measures, questionnaires, self-report data, data from motion analysis systems and cod-

ed-video observations. We assessed the following outcomes, which are based on the International Classification of Functioning, Disability and Health, Children & Youth version.[2]

PRIMARY OUTCOMES

Body functions (neuromusculoskeletal and movement related functions - gait pattern functions):
— step frequency (number of alternating treadmill steps per minute, cadence during independent walking);
— step quality (foot doing toe versus flat contact during treadmill stepping);
Activities and participation functions:
— age of onset of independent walking;
— age of onset of walking with assistance;
— gross motor function;
— falls and injuries due to falls.

SECONDARY OUTCOMES

Body functions (neuromusculoskeletal and movement related functions - gait pattern functions):
— inter- and intra-limb co-ordination;
— other gait parameters, for example, speed, step width etc.
Activities and participation functions:
— Infant or child quality of life.
There were insufficient data to examine outcomes by intervention type (preventive or rehabilitative). When data permitted, we examined outcomes by diagnosis (cerebral palsy, Down syndrome and other).

Search methods for identification of studies

Electronic searches

We searched the following databases. No date or language restrictions were applied.
— The Cochrane Central Register of Controlled Trials (CENTRAL) 2011 (1), part of the Cochrane Library, searched 21 March 2011;
— MEDLINE (1948 to March Week 2, 2011), searched 21 March 2011;
— EMBASE (1980 to 2011, Week 11), searched 21 March 2011;
— CINAHL (1937 to current), searched 21 March 2011;
— PsycINFO (1887 to current), searched 21 March 2011;
— Science Citation Index (1970 to 19 March 2011), searched 21 March 2011;
— PEDro (last updated 7 March 2011), searched 21 March 2011;
— Conference Proceedings Citation Index -Science (1990 to 19 March 2011), searched 21 March 2011;
— LILACS (Latin American and Caribbean Health Sciences Literature) until March 2011, searched 22 March 2011.
We also searched ClinicalTrials.gov, WHO ICTRP, CenterWatch and metaRegister of Controlled Trials on 22 March 2011.

Searching other resources

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

Data collection and analysis

Selection of studies

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

Data extraction and management

Four authors (MV, RA, CB and MG) independently extracted data for each trial using a data extraction form to collect information about the population,

intervention, randomisation methods, blinding, sample size, outcome measures, follow-up duration, attrition and handling of missing data, and methods of analysis.

Assessment of risk of bias in included studies

Three authors (CB, MV and RA) independently assessed the risk of bias of each included study using the Cochrane Collaboration's tool for assessing risk of bias.[78] Review authors independently assessed each included study as low risk of bias, high risk of bias or unclear risk of bias in relation to the following six domains: sequence generation; allocation concealment; blinding; incomplete outcome data (including data on attrition and exclusions); selective outcome reporting, and other risks of bias. Details on the possible sources of bias are described below.

Sequence generation

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

Allocation concealment

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

Blinding of participants and personnel

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

Blinding of outcome assessment

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

Incomplete outcome data

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

Selective reporting

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

Other risks of bias

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

Measures of treatment effect

We used Review Manager 5.1 software to calculate the adjustments of measures of treatment effects.

Continuous data

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

Dichotomous data

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

Unit of analysis issues

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

Dealing with missing data

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

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

Assessment of heterogeneity

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

Assessment of reporting biases

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

Data synthesis

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

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

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

Subgroup analysis and investigation of heterogeneity

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

Sensitivity analysis

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

Results

Description of studies

Results of the search

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

Of the remaining 10 records, six were original studies, with four being additional publications relating to one of the studies. One of these was excluded after consulting a trials registry as it was a nonrandomised trial with participants choosing whether to be in the intervention or control group.[79]

TABLE I.—*Characteristics of included studies.*

Chen 2008	
Methods	Randomized controlled trial.
Participants	Information provided through a personal communication with the author. 41 infants with moderate risk for neuromotor disabilities were initially randomised (25 on the experimental group and 16 on the control group), but only 28 finally analyzed (13 control group: 9 male / 4 female vs. 15 treadmill-experimental group 9 male / 6 female). They entered the study when they were able to take 10 steps on the treadmill in 1 minute. Infants at risk include: low-birth-weight (<1250g), low gestational-age (<32weeks), brain insult, prolonged ventilator use or multiple births. Mean age: 9.0 mo (SD 1.4) control group; 9.7 (SD 1.3) experimental group. No information on ethnicity available.
Interventions	Experimental group: home-based treadmill training: 8min/day, 5days/week until onset of independent walking, defined as the ability to take 8-10 continuous steps without support. They were followed monthly to assess stepping performance on the treadmill until the onset of independent walking. Gait was re-examined 3 and 6 months later. Control group: twice weekly physical therapy without treadmill intervention.
Outcomes	Treadmill step frequency Treadmill step quality (type of foot contact) Age at onset of independent walking Step length Step velocity Cadence Step width
Notes	Country: USA. Unpublished trial, only data and abstract available from authors.
Cherng 2007	
Methods	Randomized controlled trial (crossed design: AAB, ABA)
Participants	8 children with spastic cerebral palsy Age range: 3.5 - 6.3 years old Ethnicity not reported.
Interventions	Experimental (B): Treadmill treatment (TBWS); 20 min/session, 2–3 sessions/wk, for a total of 12 weeks. Control (A): Regular therapeutic treatment (NDT, mat exercises of range of motion, stretching, strengthening, and motor function activities. Gross motor activities included changing positions, lie to sit, sit to stand, and standing); 2–3 times/wk, 30 min/session.
Outcomes	GMFM total score Gait speed Gait stride length Gait double-limb support
Notes	Country: Taiwan This study was supported by NSC 92-2218-E-006-003 and through a collaboration of National Cheng Kung University and Chi Mei Medical Center
Looper 2010	
Methods	Quasi-randomized controlled trial, according to a personal communication with the author.
Participants	22 infants with Down syndrome were randomized (10 to the experimental group; 12 to the control group). Five infants discontinued the intervention in the control group. Mean age: 21.4 mo (SD 4.0). Ethnicity not reported.
Interventions	Experimental group: use of orthosis; cointerventions of treadmill training and regular physical therapy. Orthoses (SMOs, Surestep. 17530 Dugdale Dr, South Bend. IN 46635). 8 hrs/wk, 5 days/wk, from entry to end of follow-up. Treadmill terminated at the onset of independent walking. Control group: treadmill training (5 days/week, 8 min/day, belt speed 0.2m/s; co-interventions of regular physical therapy).
Outcomes	Average time in study until the infants achieved independent walking. GMFM after one-month follow-up.
Notes	Country: USA Funds provided by the Foundation for Physical Therapy PO Down syndrome II awards to Dr Looper, a grant from the Michigan Physical Therapy Association, and a grant from the Rackham Graduate School, University of Michigan.

TABLE I.—*Continues from previous page.*

Ulrich 2001	
Methods	Randomised controlled trial.
Participants	32 infants with Down syndrome, randomized into 2 groups (16 experimental; 16 control). Enrolled when able to sit for 30 seconds. 2 infants discontinued the intervention (one in each group) and 2 more were lost to gait follow-up (one in each group), as reported in Wu 2007. Any discrepancies in the paper were resolved through personal discussion with RA who was one of the authors involved in both this study and in Ulrich 2008, and who is also a review author. Average age at entry: 10.1 months (SD 1.94). The 15 analyzed infants in the control group who did not receive treadmill intervention (8 male, 7 female), had a mean age: 10.2 months (SD 2.2). The experimental group (15 infants) has a mean age of 9.9 months (SD 1.7) (no breakdown by sex is provided for this group). 2 mixed raced; remaining were white.
Interventions	Experimental: parents were trained in the treadmill intervention and delivered it 5days/week; 8min/session; belt speed 0.2 m/s. It stopped when infants achieved independent walking (*i.e.* took 3 independent steps on the ground). They also received traditional physical therapy as well as any activity that was prescribed by their health care provider and early intervention team. Control: traditional physical therapy as well as any activity that was prescribed by their health care provider and early intervention team. Researchers visited biweekly to measure growth and assess child. Parents kept a log book of the intervention and infant's response, which was shared with researcher.
Outcomes	Length of time from entry into study until the raising up to stand, the onset of walking with help or independent walking (*i.e.* taking 3 steps), which are items from the Bayley Scales of Infant Development.
Notes	Country: USA (Indiana, Tennesse, Ohio). Founding sources: grants from the National Institute for Disability and Rehabilitation Research and from the March of Dimes Birth Defects Foundation. The control group from this study is also used in another paper (Wu 2007) that relates to Ulrich 2008.
Ulrich 2008	
Methods	Randomized controlled trial.
Participants	36 infants with Down syndrome were randomized into two groups: low-intensity and high-intensity. They were included when they were able to take 6 steps per minute on a treadmill while being supported. 30 children were analyzed in the final sample (16 experimental group: high-intensity training 12 males / 4 female, 14 control group: low-intensity training 6 males / 8 females); (28 with trisomy 21; two with mosaic type). 6 infants discontinued the intervention, 4 in the low-intensity and 2 in the high-intensity group. An additional 5 infants were lost to gait follow-up (2 in the low-intensity and 3 in the high-intensity group). Any discrepancies in the paper were resolved through personal discussion with RA who was one of the authors involved in both Ulrich 2001 and this study, and who is also a review author. Corrected age at entry: 9.65 (SD 1.61) months for the higher-intensity group; and 10.40 (SD 2.14) months for the lower-intensity group. 2 African American, 2 biracial, and remaining infants were white.
Interventions	Experimental group (high-intensity treadmill training): 5days/week, with two treadmill parameters (minutes/day, treadmill belt speed) individualized, as well as an ankle weight being added as the infant progressed in frequency of alternating steps; co-interventions: early intervention services and any other activities that were prescribed by their health care providers. Control group (low-intensity treadmill training): 5 days/week, 6min/session, belt speed 0.18m/s; co-interventions: early intervention services and any other activities that were prescribed by their health care providers. The training stopped when infants could take 3 independent steps overground. Four additional publications (Wu 2007; Angulo-Barroso 2008; Wu 2008; Wu 2010) dealt with the follow-up from this intervention including assessments from 1 to 15 months post walking onset (i.e. after termination of the intervention).
Outcomes	The study reported frequency of alternating TM steps and onset of assisted and independent walking. The follow-up publications reported on spatio-temporal variables, joint kinematics, and gait adaptation parameters, In addition, Wu 2007 presented follow-up spatio-temporal gait variables including a historical control group from Ulrich 2001, which we did not use this data as it was not randomised). Publication Wu 2007 Gait follow-up assessment, between 1 and 3 months after walking onset (training groups) and 1 month after walking onset (control group). Age at walking onset (decreased when any training, with further decreases in high-intensity group = positive effects of training at higher intensities).

TABLE I.—*Contniues from previous page.*

	Elapsed time from entry to walking onset. Gait speed. Gait stride length. Gait stride width. Publication Angulo-Barroso 2008 Measured after the onset of independent walking during 4 home-visits scheduled at the following infant's age (low-intensity group: 24.9 mo SD 5.1; 28.4 mo SD 4.6; 30.5 SD 5.1; 36.5 SD 4.9 - high-intensity group: 21.3 mo SD 2.4, 24.4 mo SD 2.4, 27.3 SD 2.3, 33.7 SD 2.5). The walking experience prior to visit one had been 3.3 mo (SD 1.2 mo) for the low-intensity group and 2.6 mo (SD 0.9 mo) for the high-intensity group. Velocity (increased after hi-intensity training = positive effect) Cadence (increased after hi-intensity training = positive effect) Step length (increased after hi-intensity training = positive effect) Step width (decreased after hi-intensity training = positive effect) Gait double-limb support. Publication Wu 2008 Age at onset of independent walking Publication Wu 2010 Toe-off as % of gait cycle Joint angle (ankle: plantar flexion and dorsiflexion; hip: extension and flexion and abduction and adduction; knee: extension and flexion).
Notes	Country: USA (Michigan, Ohio, Indiana). Funding sources: research grant from the US Office of Special Education and Rehabilitative Services (H324C010067), a US Office of Special Education Programs Leadership Training Grant (H325D020028), and the Steelcase Foundation in Michigan.

One of the included studies [80] is unpublished and the data were obtained from personal communication with the author, who was also one of the review authors (RA).

Included studies

We included five studies of treadmill intervention with partial body weight support in children under six years of age at risk for neurodevelopmental delay[30, 31, 36, 80, 81] Data from the Ulrich 2008[81] study were also presented in four further publications, Angulo-Barroso 2008; Wu 2007; Wu 2008; Wu 2010[52, 82-85]; therefore this review considers the information reported from a total of nine articles.

Location

All studies were conducted in USA.

Design

One study had a cross-over design,[31] one was a quasi-randomized controlled trial (personal communication[30]) and the other three were reported as randomized controlled trials without additional information about the randomization process.

Sample sizes

The five studies included 139 children. Sample sizes ranged from eight [31] to 41 children,[80] with the remaining three studies comprising 22, 32 and 36 participants.[30, 36, 81]

According to diagnosis, there were 41 infants at risk of developmental delay; (in Chen *et al.* 2008);[80] 8 with cerebral palsy (in Cherng *et al.* 2007) [31] and 90 children with Down syndrome (22 in Looper *et al.* 2010;[30] 32 in Ulrich *et al.* 2001;[36] 36 in Ulrich *et al.* 2008).[81]

Participants

Further details of participant characteristics can be found in the Characteristics of included studies Table I.

Chen *et al.* 2008[80] examined the effects of treadmill intervention on children at high risk for neuromotor disabilities. The children ranged from corrected age 6.2 months to 11.4 months at study onset as an inclusion criteria, infants entered into the study when they were able to take 10 steps on the treadmill in one minute. No information on ethnicity was reported.

Cherng *et al.* 2007 [31] focused on children diag-

nosed with cerebral palsy. Participants were between 42 and 75.6 months old at study onset and were diagnosed with spastic diplegic cerebral palsy. Two of the children were ambulatory without assistive devices; the remaining six children ambulated with assistive devices at study onset. No information on ethnicity was reported.

Three studies examined the effects of treadmill intervention on nonambulatory children with Down syndrome.[30, 36, 81] Participants in Ulrich *et al.* 2001,[36] were children with Down syndrome who had a mean age of 10.1 months (SD 1.94) at study onset. Participants were admitted into the study when they were able to sit for 30 seconds. Two infants were of mixed race with the remaining infants being white. Nine of the 32 infants (28.1%) had received surgery for congenital heart disease.

Ulrich *et al.* 2008 [81] examined a different group of children with Down syndrome with mean age ranging from 9.6 to 10.4 months. Two of the children were African-American, two were biracial and the remaining were white. Fourteen of the 36 (38.9%) children had congenital heart defects. An eligibility criterion for commencing treadmill intervention was the ability to take a minimum of six steps in one minute on a moving treadmill while supported under the arms by a parent.[81] Looper *et al.* 2010 [30] examined children with Down syndrome with mean ages from 18.9 to 21.1 months old at study onset. There was no information on ethnicity or medical conditions. Children entered the study when they were able to pull to stand but unable to cruise.

Intervention and comparisons

Treadmill intervention versus no treadmill intervention

This comparison was examined in a total of 81 children across three diagnoses: children at risk for neuromotor disabilities,[80] children with cerebral palsy [31] and children with Down syndrome.[36]

Chen *et al.* 2008 [80] randomly allocated high risk infants to a control group (N.=16) or a treadmill intervention group (N.=25). Infants in the treadmill intervention group engaged in home-based intervention for eight minutes a day, five days a week at an unspecified speed, whereas children in the control group received twice weekly physical therapy without treadmill intervention. Treadmill intervention was discontinued once the children could walk for eight to 10 continuous steps.[80]

Cherng *et al.* 2007 [31] randomized eight children with cerebral palsy into two groups, each of whom received three 12-week blocks of intervention with varying intervention schedules. Intervention A in the cross-over design was a regular therapeutic intervention without use of a treadmill, while intervention B consisted of treadmill intervention in addition to a traditional therapeutic intervention. Interventions were carried out in 12-week blocks for two to three sessions per week and for 30 minutes per session, with one group receiving intervention schedule AAB and the other group receiving intervention schedule ABA. Assessments were conducted at study entry and subsequently in 12 week increments.

Ulrich *et al.* 2001 [36] randomized 32 children with Down syndrome to a a treadmill training intervention (N.=16) or a control group (N.=16). The intervention group received treadmill intervention five days per week at a speed of 0.2 meters/second for up to eight minutes as tolerated. The intervention was carried out in the children's homes by the children's families on portable treadmills. Children were held under the arms over the moving treadmill by a parent. The control group received physical therapy intervention without treadmill intervention at least every other week.

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

Looper *et al.* 2010 [30] allocated 22 children with Down syndrome to a treadmill intervention, with and without use of orthotics. Both the intervention and control groups engaged in home-based treadmill intervention at a speed of 0.2 m/s for up to eight minutes a day, five days a week. This was carried out by the parents and the children were held over the moving treadmill. Treadmill intervention was discontinued when the children could take three independent steps. The difference in the intervention group was the use of orthotics. The children were measured for these on the first visit and received them on their second, thereafter wearing them for eight hours a day five days a week for the study duration. The control group received orthotics after the end of the intervention and wore them prior to the final developmental assessment.

HIGH-INTENSITY TREADMILL INTERVENTION VERSUS A LOW-INTENSITY TREADMILL INTERVENTION

Ulrich *et al.* 2008 [81] randomized 36 children with Down syndrome to two groups to compare the effects of high-intensity versus low-intensity treadmill intervention. The low-intensity group (N.=18) received home-based treadmill intervention for five days a week, eight minutes per day at a speed of 0.15 meters/second until walking onset. The high-intensity group (N.=18) received an individualised treadmill intervention protocol in which the speed of the treadmill was increased depending on the child's performance and additional ankle weights were added during treadmill intervention. Treadmill intervention was terminated in both groups when the children achieved independent walking for three steps. In addition to the information provided in Ulrich *et al.* 2008,[81] information about this study came from four other publications: Wu 2007, Angulo-Barroso 2008, Wu, 2008 and Wu, 2010.[82-85]. Wu *et al.* 2007 [82] also included comparisons of the high intensity and low intensity group data to no treatment using an historical control group from another included study.[36] We did not use data from these comparisons due to their being non-randomized.

Outcomes

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

Ulrich *et al.* 2001,[36] Ulrich *et al.* 2008 [81] and Chen *et al.* 2008 [80] used the standard assessment batteries BSID-II (Bayley Scales of Infant Development) [86] to assess onset of assisted and independent walking. Cherng *et al.* 2007 [31] and Chen *et al.* 2008 [80] used GMFM (Gross Motor Function Measure) [87] to assess gross motor function. Video coding was used to count frequency of alternating steps.[80, 81] An instrumented gait mat (GaitRite mat, CIR systems) was used to compute the spatial-temporal gait parameters in both gait with and without an obstacle,[36, 80, 81] and a 3D motion analysis system (VICON Peak) was used to obtain the gait kinematics variables.[81]

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

Infants at risk for developmental delay

Chen *et al.* 2008 [80] examined children each month during the intervention period and at three and six months post intervention. During the treadmill period, they examined frequency of alternating steps on the treadmill, type of foot contact (step quality) and Gross Motor Function Measure (GMFM).[87] After independent walking onset, spatiotemporal gait parameters measured by the GAITRite system, in addition to gait speed, were measured during the follow-up.

Cerebral palsy

Cherng *et al.* 2007 [31] used all dimensions of the GMFM, muscle tone, selective motor control and gait velocity and gait parameters, such as stride length and double limb support, as outcome measures.

Down syndrome

Ulrich *et al.* 2001 [36] assessed effectiveness using the number of days lapsed between entry into the study and the attainment of three developmental milestones as outcome measures: raising to stand, walking with help and walking independently for three steps.

In addition, follow-up data for gait spatiotemporal parameters were measured in the control and experimental groups but were not reported.

Looper *et al.* 2010 [30] examined the average time in study until the infants achieved independent walking and the infant's motor skill development after one-month follow-up (GMFM).

Ulrich *et al.* 2008 [81] compared high intensity with low intensity treadmill intervention and examined the onset of several gross motor milestones from the Bayley Scales of Infant Development motor subscale, *i.e.* moving forward using pre-walking methods (item 43), raising self to sitting position (item 47), raising self to standing position (item 52), walking sideways/cruising (item 54), walking with help

(item 60), standing alone (item 61), walking alone (item 62) and walking alone with good coordination (item 63). In addition, videotape analysis was performed on the frequency of alternating steps per minute on the treadmill every two months until onset of independent walking.

Additional data from this study were reported in four other publications,[82-85] some of which contained follow-up data for this group of children with Down syndrome.

Wu *et al.* 2007 [82] presented data for age of walking onset, average velocity, stride length, step width, stride time, stance time and dynamic base. In a follow-up article, Wu *et al.* 2008 [83] examined the ability and methods of obstacle clearance at walking onset, and at three, six, and 12 months after walking onset in 26 of the 30 children from the original high intensity versus low intensity treadmill intervention by Ulrich *et al.* 2008.[81] The ability to clear an obstacle was categorised as "refusal, crawl, fall, and walk." The five steps taken by the children leading up to the obstacle were analysed with the GAITRite system.

The long-term effects of high intensity treadmill and low intensity treadmill intervention in the same group of children with Down syndrome at three, six, nine and 12 months post intervention were reported in an article by Angulo-Barroso *et al.* 2008.[85] Six basic gait parameters were examined in a principal component analysis (normalised velocity, cadence, step length, step width, double support percentage and dynamic base).

Additionally, gait laboratory analysis was conducted during the one-year follow-up in these children with Down syndrome after walking onset following high intensity and low intensity treadmill intervention on 26 of the 30 analyzed children with Down syndrome.[84] Timing and magnitude of peak extension and flexion at the hip, knee, and ankle joints, as well as peak adduction and abduction at the hip joint, were compared in the high intensity and low intensity intervention groups.

Excluded studies

Thirteen studies appeared eligible to be included in this review when examining the full articles. All but four studies were excluded on the basis of the age of the participants, i.e. the participants were older than six years. Three studies [88-90] were excluded because they did not evaluate treadmill intervention but used the treadmill for other investigations. Lastly, one study was excluded because participants were not randomly assigned to the groups.[79]

Risk of bias in included studies

A comprehensive description of the risk of bias for each study can be found in the Characteristics of included studies table 1. This information is summarised in Figure 1.

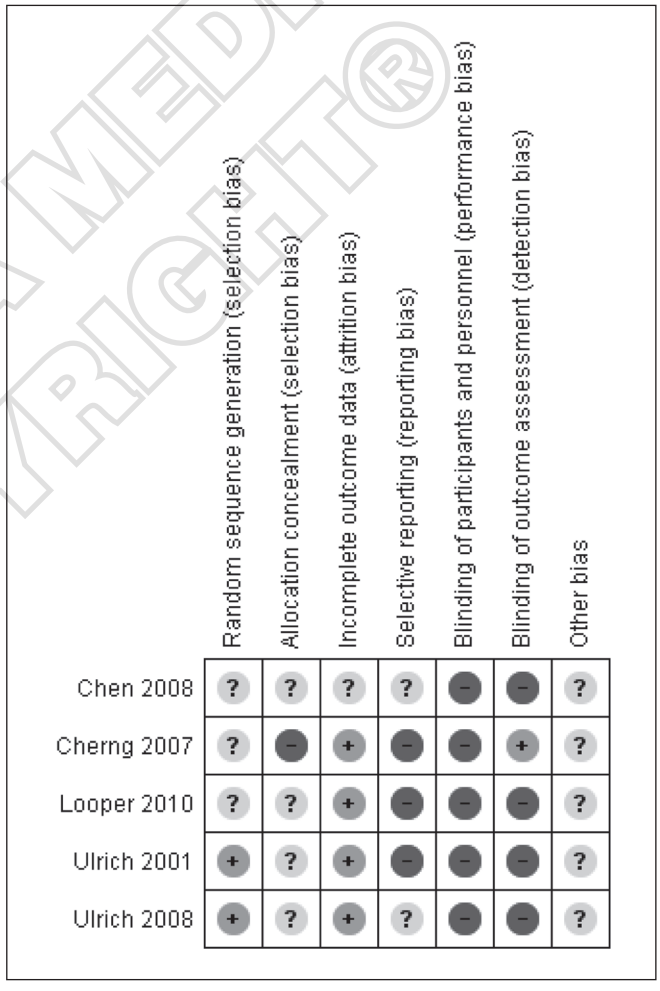

Figure 1.—Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

Allocation (selection bias)

Random sequence generation

Ulrich *et al.* 2001 [36] and Ulrich *et al.* 2008 [81] were judged to be at low risk of bias as a table of random numbers was used to assign participants to the intervention or control group. Information on how the random sequence was generated was lacking in the other studies, which we therefore assessed as at unclear risk of bias for this domain.

Allocation concealment

In Ulrich *et al.* 2001 [36] and Ulrich *et al.* 2008,[81] one of the investigators used a table of random numbers to assign allocation, but this is not an acceptable method to ensure allocation concealment.[78] In the absence of other information, we assessed this as unclear risk of bias. All other studies were also at unclear risk of bias as they did not report how the allocation process took place.

Blinding (performance bias and detection bias)

Blinding of participants and personnel

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

Blinding of outcome assessment

Most studies suffered from a high risk of detection bias as the assessors usually were aware of group allocation. In one study[31] the risk of bias was low as there was one independent therapist who took gait parameter measurements and who was unaware of the therapy the children had received.

Incomplete outcome data (attrition bias)

Attrition was related to the duration of follow-up after treadmill intervention. In the four studies that assessed outcome during and/or immediately after the intervention, attrition and bias due to attrition was low.[14, 30, 31, 36, 81] The remaining study had an unclear risk related to intervention attrition and bias.[80]

Selective reporting (reporting bias)

In three studies reporting bias was high as not all data were reported.[30, 31, 36] It was unclear whether all data had been reported in Ulrich *et al.* 2008 [81] and the unpublished study Chen *et al.* 2008.[80]

Other potential sources of bias

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

Effects of interventions

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

Treadmill intervention *versus* no treadmill intervention

This comparison was evaluated by three studies.[31, 36, 80]

Primary outcomes

STEP FREQUENCY (TREADMILL ALTERNATING STEPS)

In children at risk for motor delays, Chen *et al.* 2008 [80] found an increase of step frequency for both experimental and control groups, especially from 10 to 16 months of age. However, the differences between the two groups were not significant. There is no evidence that suggests that TM training helps to increase step frequency in children at risk for motor delays (effect estimate at 16 months of age: 4.36; 95% CI: -2.63, 11.35) (Table II).

STEP QUALITY

Chen *et al.* 2008 [80] found that treadmill training helped improve step quality for children at risk of neuromotor disabilities. In the experimental group, from 11 to 16 months of age, there was a significant decrease of foot toe contact during treadmill stepping (effect estimate at 11 months of age: -20.98; 95% CI: -26.87, -15.08 (Table II); effect estimate at 16 months of age: -15.61; 95% CI: -23.96, -7.27 (Table II), thus an increase of flat foot contact steps occurred.

AGE OF ONSET OF INDEPENDENT WALKING

The onset of independent walking was characterized across studies as the ability to take three to 10 independent steps. Meta-analysis of two studies, Ulrich *et al.* 2001 and Chen *et al.* 2008 [36, 80] was conducted on a total of 58 children who had Down syndrome or were high-risk infants with an effect estimate of -1.47 (95% CI: -2.97, 0.03) (Figure 2), which suggests that the treadmill intervention was effective in promoting earlier independent walking; however, it must be noted that the studies examined children with different diagnoses.

Chen *et al.* 2008[80] found that children both in the control and the experimental group attained independent walking at similar corrected ages and did not find support for an effect of treadmill intervention on the age of onset of independent walking in children at risk of motor delays (effect estimate -0.60, 95% CI -2.34, 1.14) (Table II).

For children with Down syndrome, those in the treadmill intervention group learned to walk independently significantly faster (effect estimate -4.00; 95% CI: -6.96, -1.04) than the control group (Table II).[36]

AGE OF ONSET OF WALKING WITH ASSISTANCE

Ulrich *et al.* 2001 [36] found a significant effect of treadmill intervention on the onset of supported walking in a study of 30 children with Down syndrome (effect estimate -74.00; 95% CI: -135.40, -12.60) (Table II).

GROSS MOTOR FUNCTION (GMFM)

Meta-analysis of two studies [31, 80] on the effects of treadmill versus no treadmill intervention for the GMFM percentage change suggested that treadmill intervention did not affect GMFM scores (effect estimate 0.88; 95% CI: -4.54, 6.30) (Table II). The two studies were conducted on infants with different diagnoses (cerebral palsy and high-risk infants). The absence of evidence of an effect of treadmill intervention on GMFM scores was reported in both groups of infants: cerebral palsy (in Cherng *et al.* 2007:[80] effect estimate 7.60; 95% CI: -19.46, 34.66) and high risk (in Chen *et al.* 2008:[80] effect estimate 0.60; 95% CI: -4.93, 6.13) (Figure 3).

FALLS AND INJURIES DUE TO FALLS.

These were not measured.

Secondary outcomes

INTER- AND INTRA-LIMB CO-ORDINATION.

These were not measured.

OTHER GAIT PARAMETERS

Gait velocity, step length and double limb support were measured in two studies that examined treadmill versus no treadmill intervention in children with cerebral palsy and high-risk infants.[31, 80] There was no effect across studies with respect to velocity (for children with cerebral palsy: effect estimate 0.39; 95% CI: -4.19, 4.97; Table II, Analysis 1.22; for high-risk infants: effect estimate 1.32; 95%CI: -0.53, 3.17; Table II, Analysis 1.23); step length (for cerebral palsy: effect estimate 0.37; 95% CI: -25.04, 25.75; Table II, Analysis 1.26; for high-risk: effect estimate

TABLE II.—*Data analysis.*

Outcome or Subgroup	Disorder	Studies		N[a].	Comparsion groups (G1 *vs.* G2)	Sample size (G1 /G2)	Effect estimate	Results
		N.º	Ref					
1.1. Step frequency 8 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	4.91 [-1.78, 11.61]	G1=G2
1.2. Step frequency 9 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-10.23 [-16.53, -3.93]	G1<G2
1.3. Step frequency 10 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	7.72 [2.57, 12.86]	G1>G2
1.4. Step frequency 11 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-1.63 [-6.69, 3.42]	G1=G2
1.5. Step frequency 12 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-9.20 [-14.54, -3.86]	G1<G2
1.6 Step frequency 13 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	7.53 [2.24, 12.82]	G1>G2
1.7. Step frequency 14 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-6.60 [-12.51, -0.69]	G1<G2
1.8. Step frequency 15 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	7.90 [1.58, 14.22]	G1>G2
1.9. Step frequency 16 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	4.36 [-2.63, 11.35]	G1=G2
1.10. Step quality 8 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	8.44 [0.46, 16.42]	G1>G2
1.11. Step quality 9 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	2.69 [-4.79, 10.17]	G1=G2
1.12. Step quality 10 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-15.67 [-21.69, -9.66]	G1<G2
1.13. Step quality 11 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-20.98 [-26.87, -15.08]	G1<G2
1.14. Step quality 12 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-14.30 [-20.57, -8.04]	G1<G2
1.15. Step quality 13 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-34.67 [-40.87, -28.47]	G1<G2
1.16. Step quality 14 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-33.34 [-40.33, -26.36]	G1<G2
1.17. Step quality 15 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-24.92 [-32.43, -17.42]	G1<G2
1.18. Step quality 16 months	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-15.61 [-23.96, -7.27]	G1<G2
1.19. Age of onset of independent walking [months]	DS/Risk	2		58	NTM *vs.* TM	30/28	-1.47 [-2.97, 0.03]	G1<G2
1.19.1. Age of onset of independent walking [months]	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-0.60 [-2.34,1.14]	G1=G2
1.19.2. Age of onset of independent walking [months]	DS	1	Ulrich 2001	30	NTM *vs.* TM	15/15	-4.00 [-6.96,-1.04]	G1<G2
1.20. Onset of walking with assistance [days in study]	DS	1	Ulrich 2001	30	NTM *vs.* TM	15/15	-74.00 [-135.40, -12.60]	G1<G2
1.21. GMFM total score [%]	CP/Risk	2		36	NTM *vs.* TM	19/17	0.88 [-4.54, 6.30]	G1=G2
1.21.1. GMFM total score [%]	SCP		Cherng 2007	8	NTM *vs.* TM	4/4	7.60 [-19.46,34.66]	G1=G2
1.21.2. GMFM total score [%]	Risk		Chen 2008	28	NTM *vs.* TM	15/13	0.60 [-4.93,6.13]	G1=G2
1.22. Other gait parameters: velocity [m/s]	CP	1	Cherng 2007	8	NTM *vs.* TM	4/4	0.39 [-4.19, 4.97]	G1=G2
1.23. Other gait parameters: velocity (Follow-up when walking independent)	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	1.32 [-0.53, 3.17]	G1=G2
1.24. Other gait parameters: velocity. (Follow-up 3 months later)	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-1.92 [-4.72, 0.88]	G1=G2
1.25. Other gait parameters: velocity. (Follow-up 6 months later)	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-3.35 [-7.44, 0.74]	G1=G2
1.26. Other gait parameters: step length [cm]	CP	1	Cherng 2007	8	NTM *vs.* TM	4/4	0.37 [-25.04, 25.78]	G1=G2
1.27. Other gait parameters: step length. (follow-up when walking independent)	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	8 [-1.60, 17.60]	G1=G2
1.28. Other gait parameters: step length. (follow-up 3 months later)	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-5 [-14.29, 4.29]	G1=G2
1.29. Other gait parameters: step length. Follow-up (Follow-up 6 months later)	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-6 [-15.26, 3.26]	G1=G2
1.30. Other gait parameters: gait double-limb support [%]	CP	1	Cherng 2007	8	NTM *vs.* TM	4/4	3.80 [-21.52, 29.12]	G1=G2
1.31. Other gait parameters: gait double-limb support. (Follow-up when walking independent) [%]	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	-4.19 [-10.02, 1.64]	G1=G2
1.32. Other gait parameters: gait double-limb support. (Follow-up 3 months later) [%]	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	3.16 [-0.22, 6.54]	G1>G2
1.33. Other gait parameters: gait double-limb support. (Follow-up 6 months later) [%]	Risk	1	Chen 2008	28	NTM *vs.* TM	15/13	3.17 [-0.10, 6.44]	G1>G2

TABLE II.—*Continues from previous page.*

Outcome or Subgroup	Disorder	Studies		N[a].	Comparsion groups (G1 *vs.* G2)	Sample size (G1 /G2)	Effect estimate	Results
		N.º	Ref					
2.1. Walking independent (1 month follow-up) months]	DS	1	Looper 2010	17	TM&O *vs.* TM	10/7	0.10 [-5.96, 6.16]	G1=G2
2.2. GMFM (1month follow-up) [%]	DS	1	Looper 2010	17	TM&O *vs.* TM	10/7	-8.40 [-14.55, -2.25]	G1>G2
3.1. Step frequency [steps/min]	DS	1	Ulrich 2008	30	HI TM *vs.* LG TM	16/14	-11.00 [-15.90, -6.10]	G1>G2
3.2. Age of onset of independent walking [months]	DS	1	Wu 2007	30	HI TM *vs.* LG TM	16/14	-2.13 [-4.96, 0.70]	G1=G2
3.3. Onset of walking with assistance [months]	DS	1	Ulrich 2008	30	HI TM *vs.* LG TM	16/14	-1.86 [-4.09, 0.37]	G1=G2
3.4. Chronological age. (Follow-up visit 1) [months]	DS	1	Wu 2008	25	HI TM *vs.* LG TM	13/12	-3.60 [-6.77, -0.43]	G1>G2
3.5. Chronological age. (Follow-up visit 2) [months]	DS	1	Wu 2008	25	HI TM *vs.* LG TM	13/12	-4.00 [-6.86, -1.14]	G1>G2
3.6. Chronological age. (Follow-up visit 3) [months]	DS	1	Wu 2008	25	HI TM *vs.* LG TM	13/12	-3.20 [-6.34, -0.06]	G1>G2
3.7. Chronological age. (Follow-up visit 4) [months]	DS	1	Wu 2008	25	HI TM *vs.* LG TM	13/12	-2.80 [-5.89, 0.29]	G1>G2
3.8. Other gait parameters: velocity. (Follow-up visit1) [m/s]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	0.05 [-0.06, 0.16]	G1=G2
3.9. Other gait parameters: velocity. (Follow-up visit 2) [m/s]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	0.16 [0.01, 0.31]	G1<G2
3.10. Other gait parameters: velocity. (Follow-up visit 3) [m/s]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	0.10 [-0.07, 0.27]	G1=G2
3.11. Other gait parameters: velocity. (Follow-up visit 4) [m/s]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	0.16 [-0.07, 0.39]	G1=G2
3.12. Other gait parameters: step length. (Follow-up visit 1) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	1.83 [-0.89, 4.55]	G1=G2
3.13. Other gait parameters: step length. (Follow-up visit 2) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	2.55 [-0.67, 5.77]	G1=G2
3.14. Other gait parameters: step length. (Follow-up visit 3) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	0.68 [-1.96, 3.32]	G1=G2
3.15. Other gait parameters: step length. (Follow-up visit 4) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	2.68 [-0.99, 6.35]	G1=G2
3.16. Other gait parameters: step width. (Follow-up visit 1) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	0.12 [-2.37, 2.61]	G1=G2
3.17. Other gait parameters: step width. (Follow-up visit 2) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	-1.23 [-3.69, 1.23]	G1=G2
3.18. Other gait parameters: step width. (Follow-up visit 3) [cm]	DS	1	Angulo 2008	24	HI TM *vs.* LG TM	13/12	-0.54 [-2.52, 1.44]	G1=G2
3.19. Other gait parameters: step width. (Follow-up visit 4) [cm]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	-0.58 [-2.11, 0.95]	G1=G2
3.20. Other gait parameters: gait double-limb support. (Follow-up visit 1) [%]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	-2.90 [-8.07, 2.27]	G1=G2
3.21. Other gait parameters: gait double-limb support. (Follow-up visit 2) [%]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	-4.00 [-0.09, -7.91]	G1>G2
3.22. Other gait parameters: gait double-limb support. (Follow-up visit 3) [%]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	-2.00 [-6.29, 2.29]	G1=G2
3.23. Other gait parameters: gait double-limb support. (Follow-up visit 4) [%]	DS	1	Angulo 2008	25	HI TM *vs.* LG TM	13/12	-0.80 [-3.27,1.67]	G1=G2
3.24. Other gait parameters: gait ankle plantar flexion. (Follow-up visit 1) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-3.10 [-7.34, 1.14]	G1=G2
3.25. Other gait parameters: gait ankle plantar flexion. (Follow-up visit 2) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-4.80 [-8.77, -0.83]	G1>G2
3.26. Other gait parameters: gait ankle plantar flexion. (Follow-up visit 3) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-2.90 [-6.28,0.480]	G1=G2
3.27. Other gait parameters: gait ankle plantar flexion. (Follow-up visit 4) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-3.40 [-8.98, 2.18]	G1=G2

TABLE II.—*Continues from previous page.*

Outcome or Subgroup	Disorder	Studies N.º	Studies Ref	N[a].	Comparsion groups (G1 *vs.* G2)	Sample size (G1 /G2)	Effect estimate	Results
3.28. Other gait parameters: gait ankle dorsiflexion. (Follow-up visit 1) [%]	DS	1	Wu 2010	26	HI TM *vs.* LG TM	13/12	-0.40 [-3.47,2.67]	G1=G2
3.29. Other gait parameters: gait ankle dorsiflexion. (Follow-up visit 2) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-1.50 [-5.08,2.08]	G1=G2
3.30. Other gait parameters: gait ankle dorsiflexion. (Follow-up visit 3) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-0.10 [-2.69, 2.49]	G1=G2
3.31. Other gait parameters: gait ankle dorsiflexion. (Follow-up visit 4) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-2.80 [-5.96, 0.36]	G1>G2
3.32. Other gait parameters: toe-off. (Follow-up visit 1) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-2.20 [-6.17,1.77]	G1=G2
3.33. Other gait parameters: toe-off. (Follow-up visit 2) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-2.30 [-5.50, 0.90]	G1=G2
3.34. Other gait parameters: toe-off. (Follow-up visit 3) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-1.20 [-3.95, 1.55]	G1=G2
3.35. Other gait parameters: toe-off. (Follow-up visit 4) [%]	DS	1	Wu 2010	25	HI TM *vs.* LG TM	13/12	-0.90 [-5.49, 3.69]	G1=G2

N.: number of studies included; N[a]: total participants: number of analysed subjects, TM: treadmill; NTM: no treadmill; TM&O: treadmill and orthoses; HI TM: treadmill high-intensity; LG TM: treadmill low-intensity; CP: cerebral palsy; Risk: risk of developmental delay; DS= Down Syndrome

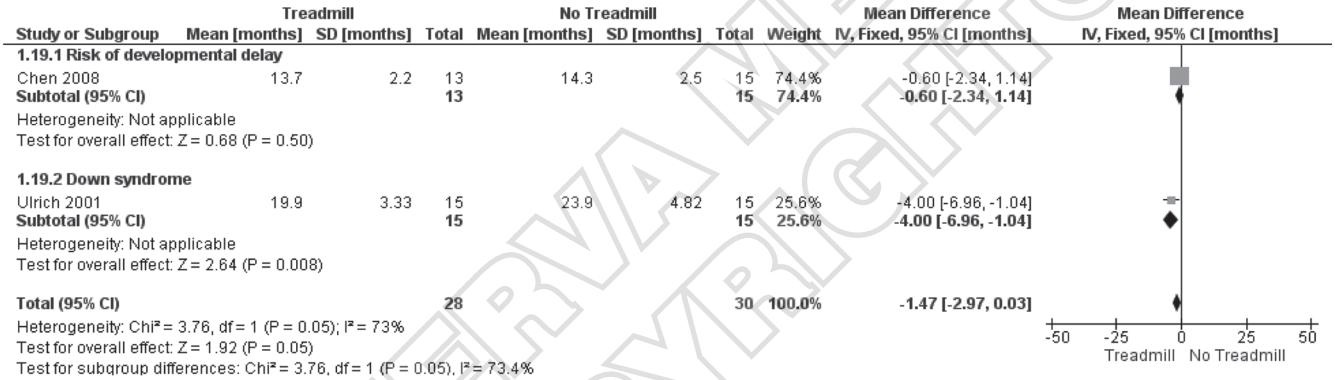

Figure 2.—Forest plot of comparison: 1 No Treadmill vs. Treadmill: Walking independently (months).

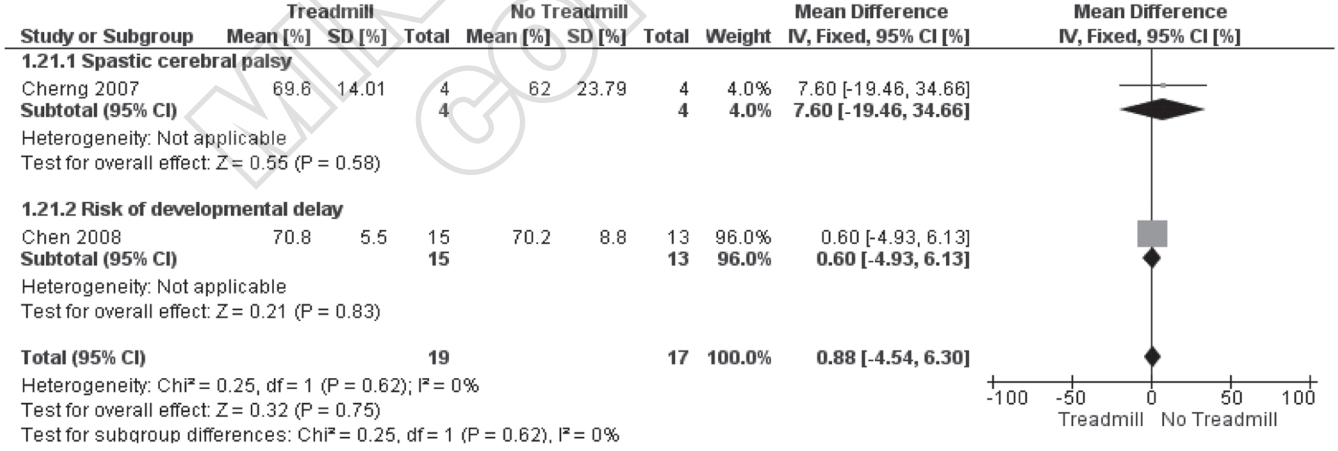

Figure 3.—Forest plot of comparison: 1 No Treadmill vs. Treadmill: Gross motor function (GMFM as %).

0.08; 95% CI: -0.02, 0.18; Table II, Analysis 1.27) or double limb support (for cerebral palsy: effect estimate 3.80; 95% CI: -21.52, 29.12; Table II, Analysis 1.30; for high-risk: effect estimate -4.19; 95%CI: -10.02, 1.64; Table II, Analysis 1.31) at time of walking onset.

INFANT OR CHILD QUALITY OF LIFE

This was not measured.

Treadmill intervention without orthotics *versus* treadmill intervention with orthotics

Only one study [30] evaluated this comparison. In this study of children with Down syndrome, only two of our outcomes were measured: age of onset of independent walking and gross motor function. These were both primary outcomes.

Age of onset of independent walking

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

GMFM

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

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

Ulrich *et al.* 2008 [81] was the only study to evaluate this comparison in their study of children with Down syndrome. Three of our primary outcomes were measured in this study: step frequency, age of onset of independent walking and age of onset of walking with assistance; and one of our secondary outcomes: other gait parameters.

Step frequency (treadmill alternating steps)

Ulrich *et al.* 2008 [81] calculated the values for frequency of alternating steps in both the high intensity and the low intensity groups. No differences in frequency of stepping were found prior to the training. After the intervention, those infants who received the high-intensity training protocol took a greater number of steps than those who belonged to the low-intensity group: effect estimate 11.00 (95%CI: 6.03, 15.97) (Table II, Analysis 3.1).

Age of onset of independent walking or walking with assistance

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

Other gait parameters

Various gait parameters were examined in Ulrich *et al.* 2008 [81] and three additional publications of the same sample of children with Down syndrome at three, six, nine and 12 months after walking onset.[83-85] There was a positive effect of high intensity treadmill intervention on children with Down syndrome on the ability to clear obstacles in the upright position compared to children who received low intensity treadmill intervention at follow-up visits after the onset of independent walking (effect estimate: -3.60, 95% CI: -6.77, -0.43 (Table II, Analysis 3.4) at three months; -4.00, 95% CI: -6.86, -1.14 (Analysis 3.5) at six months; -3.20, 95% CI: -6.34, -0.06 (Table II, Analysis 3.6) at nine months; -2.80, 95% CI: -5.89, 0.29 at 12 months (Table II, Analysis 3.7)). At follow-up visit two, there was a positive effect of high intensity treadmill intervention compared to low intensity treadmill intervention on gait velocity of 0.16, 95% CI: 0.01, 0.31 (Table II, Analysis 3.9) and on decreased double-limb support of -4.00, 95% CI: -7.91, -0.09 (Table II, Analysis 3.21); however, at follow-up visits one, three and four there was no clear difference in the effect of the two interventions on these two outcomes. Similarly, the high intensity treadmill intervention resulted in better timing of maximum ankle plantar flexion during gait compared to the low intensity group at the second follow-up visit

(-4.80, 95% CI: -8.76, -0.84; Table II, Analysis 3.25), but not at follow-up visits one, three and four. There was no difference between the high intensity and low intensity treadmill intervention groups on other gait parameters, such as step length (effect estimate at follow-up visit four: 2.68, 95% CI -0.99, 6.35; Table II, Analysis 3.15), step width (effect estimate at follow-up visit four: -0.58, 95% CI -2.11, 0.95; Table II, Analysis 3.19), gait ankle dorsiflexion (effect estimate at follow-up visit four: 2.80, 95% CI: -5.96, 0.36; Table II, Analysis 3.31) and toe-off (effect estimate at follow-up visit four: -0.90, -5.49, 3.69; Table II, Analysis 3.35).

Discussion

We have included data from four randomised and one quasi-randomized controlled trials in which 139 children (73 of whom engaged in treadmill with the remainder acting as controls) below the age of six years participated. One trial [83] was reported in multiple publications.

Summary of main results

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

Body functions

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

Activity and participation functions

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

Treadmill intervention in children with cerebral palsy and children at risk for developmental delay was not associated with improved gross motor development measured with the GMFM. However, only two randomized controlled trials, one of which is unpublished to date, have been conducted on this population.[31, 80]

Overall completeness and applicability of evidence

Overall, there were few studies assessing the effect of treadmill intervention in young children with or at high risk for motor developmental delay. Three of the five studies examined treadmill intervention in children with Down syndrome.[30, 36, 81] One study [80] assessed treadmill intervention in infants at high risk for developmental delay and one in children with cerebral palsy.[31] Two of the five studies did not evaluate the effect of treadmill intervention versus no treadmill intervention, but assessed two modifications of treadmill intervention (high versus low intensity, with orthosis versus without orthosis)[30, 81].

This means that the evidence on the effect of treadmill intervention itself is limited. The effect has been most extensively studied in children with Down syndrome.

Quality of the evidence

Most studies were designed as RCTs, a design which is associated with a high standard of evidence, all things being equal.[91, 92] However, the studies in this review suffered from methodological limitations, in particular from a high risk of bias due to the absence of blinding. Performance bias is inevitable in studies on treadmill intervention, but detection bias, from which most studies suffered, may be prevented. Another important methodological limitation was the risk of attrition bias. Attrition occurred in particular during follow-up after treadmill intervention. In general the extent of attrition was moderate, but it was unclear whether attrition was selective or not.

Potential biases in the review process

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

Agreements and disagreements with other studies or reviews

The effects of treadmill intervention have been examined in previous reviews in children of all ages with or at risk of a motor developmental disorder, but most of the these reviews dealt with school-aged children and adolescents with cerebral palsy.

These reviews concluded that 1) treadmill intervention in children with Down syndrome accelerates development of walking [23] and 2) limited evidence on the effect of treadmill intervention in children with cerebral palsy is available, even though many studies in the reviews note some positive effect.[23, 34, 75-77] These conclusions are similar to the findings of the present review, which focuses on the effect of treadmill intervention on children with or at risk for developmental delay in a specific age group (six years or younger) and uses only high quality evidence, i.e. randomised controlled trials and controlled clinical trials, rather than including nonrandomised trials and single case studies.

Conclusions

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

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

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

levels of muscle tone and frequently hypertonicity. An intervention with more variability of movement in individuals with less compliant neuromuscular system would perhaps be more appropriate.

Regarding possible implications for research, both neurophysiologic and early intervention literature suggest that task-specific training facilitates motor development. Treadmill intervention is a good example of task-specific training. The current study highlights the need for RCTs on the effect of treadmill intervention. Given the limited evidence on the effect of treadmill intervention, it is ethically justified to assess the effect of treadmill intervention versus no treadmill intervention (and not only of its intensity). Well-controlled RCT studies are needed, of sufficient power, and enrolling children with a variety of diagnoses, such as Down syndrome, cerebral palsy and high risk infants Given the results in Down syndrome, and because the literature suggests that high intensity intervention has a larger effect on motor development than low intensity intervention in children with cerebral palsy[93], it would be worthwhile to investigate the effect of treadmill intervention applied at higher dosages than applied in the studies reviewed, for instance increasing progressively minutes of training. Additionally, the effects of home-based treadmill intervention carried out by the parent or caregiver should be examined in young children with diagnoses other than Down syndrome. Important for future studies is to avoid bias through lack of blinding. Although blinding of parents, children and personnel applying treadmill intervention is impossible, masking of persons assessing outcomes is perfectly feasible.

References

1. WHO. WHO motor development study: Windows of achivement for six gross motor development milestones. Acta Paediatr 2006;86-95.
2. World Health Organization International classification of functioning, disability and health for children and youth 2005 [Internet]. Available from: http://apps.who.int/classifications/icfbrowser/ [cited 2011, Feb 10].
3. Case-Smith J, Heaphy T, Marr D, *et al.* Fine motor and functional performance outcomes in preschool children. Am J Occup Ther 1998;10.
4. Heineman KR, Hadders-Algra M. Evaluation of neuromotor function in infancy-A systematic review of available methods. J Dev Behav Pediatr 2008;29:315-23.
5. de Graaf-Peters VB, Hadders-Algra M. Ontogeny of the human central nervous system: What is happening when? Early Hum Dev 2006;82:257-66.
6. Roze E, Meijer L, Van Braeckel KNJA, Ruiter SAJ, Bruggink JLM, Bos AF. Developmental trajectories from birth to school age in healthy term-born children. Pediatrics 2010;126:e1134-1142.
7. Bly L, Ariz TN. Motor skills acquisition in the first year, an illustrated guide to normal development. Pediatr Phys Ther 1995;7(2):86.
8. Campbell SK, Palisano RJ, Vander Linden DW. Physical Therapy for Children. Elsevier Saunders, 2006.
9. Bertenthal B, Campos J, Barrett K. Self-produced locomotion: An organizer of emotional, cognitive, and social development in infancy. Continuities and discontinuities in development 1984; p. 175-210.
10. Kermoian R, Campos JJ. Locomotor experience: A facilitator of spatial cognitive development. Child Dev 1988;59:908-17.
11. Campos JJ, Bertenthal B. Locomotion and psychological development in infancy. Applied developmental psychology 1989;2:230-58.
12. Bertenthal BI, Campos JJ. A systems approach to the organizing effects of self-produced locomotion during infancy. Advances in infancy research 1990;6:1-60.
13. Rosenbloom L. The contribution of motor behaviour to child development. Physiotherapy 1971;57:159-62.
14. Webb SJ, Monk CS, Nelson CA. Mechanisms of postnatal neurobiological development: Implications for human development. Dev Neuropsychol 2001;19:147-71.
15. Murray GK, Jones PB, Kuh D, Richards M. Infant developmental milestones and subsequent cognitive function. Ann Neurol 2007;62:128-36.
16. Lepage C, Noreau L, Bernard PM. Association between characteristics of locomotion and accomplishment of life habits in children with cerebral palsy. Phys Ther 1998;78:458-69.
17. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH *et al.* The worldwide incidence of preterm birth: A systematic review of maternal mortality and morbidity. Bull World Health Organ 2010;88:31-8.
18. Formiga CKMR, Linhares MBM. Motor development curve from 0 to 12 months in infants born preterm. Acta Pædiatrica 2011;100:379-84.
19. Surveillance CP Europe. [Internet]. Surveillance of Cerebral Palsy in Europe [Internet]. Available from: http://www.rheop.ujf-grenoble.fr/scpe2/site'scpe/index.php [cited 2011, Mar 5].
20. Lie KK, Groholt EK, Eskild A. Association of cerebral palsy with apgar score in low and normal birthweight infants: Population based cohort study. BMJ 2010;341:c4990.
21. Down's Syndrome Association. What is the incidence of Down's Syndrome? [Internet]. Available from: http://www.down-syndrome.org.uk/component/content/article/35-general/159-3-what-is-the-incidence-of-down-syndrome.html [cited 2011, Apr 19].
22. Adolph KE, Vereijken B, Denny MA. Learning to crawl. Child Dev 1998;69:1299-312.
23. Damiano DL, de Jong SL. A systematic review of the effectiveness of treadmill training and body weight support in pediatric rehabilitation. J Neurol Phys Ther 2009;33:27-44.
24. Hodgson JA, Roy RR, de Leon R, Dobkin B, Edgerton VR. Can the mammalian lumbar spinal cord learn a motor task? Med Sci Sports Exerc 1994;26:1491-7.
25. Blackman JA. Early intervention: a global perspective. Inf Young Children 2002;15:11-19.
26. de Graaf-Peters VB, Blauw-Hospers CH, Dirks T, Bakker H, Bos AF, Hadders-Algra M. Development of postural control in typically developing children and children with cerebral palsy: Possibilities for intervention? Neurosci Biobehav Rev 2007;31:1191-200.
27. Hadders-Algra M, Brogren E, Forssberg H. Training affects the development of postural adjustments in sitting infants. J Physiol (Lond) 1996;493(Pt 1):289-98.

28. Sveistrup H, Woollacott MH. Practice modifies the developing automatic postural response. Exp Brain Res 1997;114(1):33-43.
29. Nelson CA. Neural plasticity and human development: The role of early experience in sculpting memory systems. Develop Sci 2000;3:115-36.
30. Looper J, Ulrich DA. Effect of treadmill training and supramalleolar orthosis use on motor skill development in infants with down syndrome: A randomized clinical trial. Phys Ther 2010;90:382-90.
31. Cherng RJ, Liu CF, Lau TW, Hong RB. Effect of treadmill training with body weight support on gait and gross motor function in children with spastic cerebral palsy. Am J Phys Med Rehabil 2007;86:548-55.
32. Begnoche DM, Pitetti KH. Effects of traditional treatment and partial body weight treadmill training on the motor skills of children with spastic cerebral palsy: A pilot study. Pediatr Phys Ther 2007;19:11-9.
33. Richards CL, Malouin F, Dumas F, Marcoux S, Lepage C, Menier C. Early and intensive treadmill locomotor training for young children with cerebral palsy: A feasibility study. Pediatr Phys Ther 1997;9:158-65.
34. Mattern-Baxter K. Effects of partial body weight supported treadmill training on children with cerebral palsy. Pediatr Phys Ther 2009;21:12-22.
35. Davis D, Thelen E, Keck J. Treadmill stepping in infants born prematurely. Early Hum Dev 1994;39:211-23.
36. Ulrich DA, Ulrich BD, Angulo-Kinzler RM, Yun J. Treadmill training of infants with down syndrome: Evidence-based developmental outcomes. Pediatrics 2001;108:E84.
37. Dodd KJ, Foley S. Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: A clinical controlled trial. Dev Med Child Neurol 2007;49:101-5.
38. Provost B, Dieruf K, Burtner PA, Phillips JP, Bernitsky-Beddingfield A *et al.* Endurance and gait in children with cerebral palsy after intensive body weight-supported treadmill training. Pediatr Phys Ther 2007;19:2-10.
39. Schindl MR, Forstner C, Kern H, Hesse S. Treadmill training with partial body weight support in nonambulatory patients with cerebral palsy. Arch Phys Med Rehabil 2000;81:301-6.
40. Meyer-Heim A, Borggraefe I, Ammann-Reiffer C, Berweck S, Sennhauser FH, Colombo G *et al.* Feasibility of robotic-assisted locomotor training in children with central gait impairment. Dev Med Child Neurol 2007;49:900-6.
41. Phillips JP, Sullivan KJ, Burtner PA, Caprihan A, Provost B, Bernitsky-Beddingfield A. Ankle dorsiflexion fMRI in children with cerebral palsy undergoing intensive body-weight-supported treadmill training: A pilot study. Dev Med Child Neurol 2007;49:39-44.
42. de Bode S, Mathern GW, Bookheimer S, Dobkin B. Locomotor training remodels fMRI sensorimotor cortical activations in children after cerebral hemispherectomy. Neurorehabil Neural Repair 2007;21:497.
43. Day JA, Fox EJ, Lowe J, Swales HB, Behrman AL. Locomotor training with partial body weight support on a treadmill in a nonambulatory child with spastic tetraplegic cerebral palsy: A case report. Pediatr Phys Ther 2004;16:106.
44. Cernak K, Stevens V, Price R, Shumway-Cook A. Locomotor training using body-weight support on a treadmill in conjunction with ongoing physical therapy in a child with severe cerebellar ataxia. Phys Ther 2008;88:88.
45. Prosser LA. Locomotor training within an inpatient rehabilitation program after pediatric incomplete spinal cord injury. Phys Ther 2007;87:1224-32.
46. Stiles J. Neural plasticity and cognitive development. Dev Neuropsychol 2000;18:237-72.
47. Stiles J, Reilly J, Paul B, Moses P. Cognitive development following early brain injury: Evidence for neural adaptation. Trends Cogn Sci (Regul Ed) 2005;9(3):136-43.
48. Edgerton V, DE L. Use-dependent plasticity in spinal stepping and standing. Adv Neurol 1997;72:233-47.
49. Eyre J. Development and plasticity of the corticospinal system in man. Neural Plast 2003;10:93-106.
50. Harbourne RT, Stergiou N. Nonlinear analysis of the development of sitting postural control. Dev Psychobiol 2003;42:368-77.
51. Eng JJ, Tang PF. Gait training strategies to optimize walking ability in people with stroke: A synthesis of the evidence. Exp Rev Neurotherapeut 2007;7:1417-36.
52. Verschuren O, Ketelaar M, Takken T, Helders PJM, Gorter JW. Exercise programs for children with cerebral palsy: A systematic review of the literature. Am J Phys Med Rehabil 2008;87:404-17.
53. Sherrington CS. Flexion-reflex of the limb, crossed extension-reflex, and reflex stepping and standing. J Physiol 1910;40:28-121.
54. Sullivan KJ, Brown DA, Klassen T, Mulroy S, Ge T, Azen SP *et al.* Effects of task-specific locomotor and strength training in adults who were ambulatory after stroke: Results of the STEPS randomized clinical trial. Phys Ther 2007;87:1580-602.
55. Barbeau H, Rossignol S. Recovery of locomotion after chronic spinalization in the adult cat. Brain Res 1987;412:84-95.
56. Eidelberg E, Story J, Meyer B, Nystel J. Stepping by chronic spinal cats. Exp Brain Res 1980;40:241-6.
57. Jones TA, Chu CJ, Grande LA, Gregory AD. Motor skills training enhances lesion-induced structural plasticity in the motor cortex of adult rats. J Neurosci 1999;19:10153-63.
58. Cotman CW, Berchtold NC. Exercise: A behavioral intervention to enhance brain health and plasticity. Trends Neurosci 2002;25:295-301.
59. Cotman CW, Engesser-Cesar C. Exercise enhances and protects brain function. Exerc Sport Sci Rev 2002;30:75.
60. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: Implications for rehabilitation after brain damage. Journal of Speech, Language, and Hearing Research 2008;51:S225-S239.
61. Newell KM. Motor skill acquisition. Annu Rev Psychol 1991;42:213-37.
62. Thelen E. Treadmill-elicited stepping in 7-month-old infants. Child Dev 1986;57:1498-506.
63. Thelen E, Ulrich BD. Hidden skills: A dynamic systems analysis of treadmill stepping during the first year. Monogr Soc Res Child Dev 1991;56:1-98.
64. Ulrich BD, Ulrich DA, Collier DH. Alternating stepping patterns - hidden abilities of 11-month-old infants with down-syndrome. Dev Med Child Neurol 1992;34:233-9.
65. Ulrich BD, Ulrich DA, Collier DH, Cole EL. Developmental shifts in the ability of infants with down-syndrome to produce treadmill steps. Phys Ther 1995;75:14-23.
66. Luo H, Chen P, Hsieh W, Lin KH, Lu TW, Chen WJ *et al.* Associations of supported treadmill stepping with walking attainment in preterm and full-term infants. Phys Ther 2009;89:1215-25.
67. Angulo-Barroso RM, Tiernan CW, Chen LC, Ulrich D, Neary H. Treadmill responses and physical activity levels of infants at risk for neuromotor delay. Pediatr Phys Ther 2010;22:61.
68. Goyen TA. Longitudinal motor development of apparently normal high-risk infants at 18 months, 3 and 5 years. Early Hum Dev 2002;70:103-15.
69. Pin TW, Eldridge B, Galea MP. Motor trajectories from 4 to 18months corrected age in infants born at less than 30weeks of gestation. Early Hum Dev 2010;86:573-80.
70. Prins SA, von Lindern J, van Dijk S, Versteegh F. Motor development of premature infants born between 32 and 34 weeks. Int J Pediatr 2010[Internet]. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2946567/ [cited 2011, Mar 5].

71. Volpe JJ. The encephalopathy of prematurity--brain injury and impaired brain development inextricably intertwined. Semin Pediatr Neurol 2009;16:167-78.
72. Bodkin AW, Baxter RS, Heriza CB. Treadmill training for an infant born preterm with a grade III intraventricular hemorrhage. Phys Ther 2003;83:1107.
73. Riethmuller AM, Jones RA, Okely AD. Efficacy of interventions to improve motor development in young children: A systematic review. Pediatrics 2009;124:e782-e792.
74. Ziviani J, Feeney R, Rodger S, Watter P. Systematic review of early intervention programmes for children from birth to nine years who have a physical disability. Aust Occup Ther J 2010;57:210-23.
75. Mutlu A, Krosschell K, Gaebler Spira D. Treadmill training with partial body-weight support in children with cerebral palsy: A systematic review. Dev Med Child Neurol 2009;51:268-75.
76. Molina-Rueda F, Águila-Maturana A, Molina-Rueda M, Miangolarra-Page J. Pasarela rodante con o sin sistema de suspensión del peso corporal en niños con parálisis cerebral infantil: Revisión sistemática y metaanálisis. Revista de Neurología 2010;51:135-45.
77. Willoughby KL, Dodd KJ, Shields N. A systematic review of the effectiveness of treadmill training for children with cerebral palsy. Disabil Rehabil 2009;31:1971-9.
78. Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.0. Chichester (UK): John Wiley & Sons; 2008.
79. Schlittler DXC, Lopes TF, Raniero EP, Barela JA. Treadmill training effects on walking acquisition and motor development in infants at risk of developmental delay. Revista Paulista de Pediatria 2011;29:91-9.
80. Chen L, Looper J, Neary H, Ulrich D, Angulo-Barroso R. Walking patterns in infants at moderate risk for neuromotor disabilities with or without treadmill training. J Sport Exerc Psychol 2008;30:S40-S41.
81. Ulrich DA, Lloyd MC, Tiernan CW, Looper JE, Angulo-Barroso RM. Effects of intensity of treadmill training on developmental outcomes and stepping in infants with down syndrome: A randomized trial. Phys Ther 2008;88:114-22.
82. Wu J, Looper J, Ulrich BD, Ulrich DA, Angulo-Barroso RM. Exploring effects of different treadmill interventions on walking onset and gait patterns in infants with down syndrome. Dev Med Child Neurol 2007;49:839-45.
83. Wu J, Ulrich DA, Looper J, Tiernan CW, Angulo-Barroso RM. Strategy adoption and locomotor adjustment in obstacle clearance of newly walking toddlers with down syndrome after different treadmill interventions. Exp Brain Res 2008;186:261-72.
84. Wu J, Looper J, Ulrich DA, Angulo-Barroso RM. Effects of various treadmill interventions on the development of joint kinematics in infants with down syndrome. Phys Ther 2010;90:1265-76.
85. Angulo-Barroso RM, Wu J, Ulrich DA. Long-term effect of different treadmill interventions on gait development in new walkers with down syndrome. Gait Posture 2008;27:231-8.
86. Bayley N. Bayley Scales Infant Development (2nd Ed). USA: The Psychological Corporation; 1993.
87. Russell DJ, Rosenbaum PL, Avery LM, Lane M. Gross Motor Function Measure (GMFM 66 & GMFM 88);User's Manual. London: McKeith Press; 2002.
88. Pang MY, Lam T, Yang JF. Infants adapt their stepping to repeated trip-inducing stimuli. J Neurophysiol 2003;90:2731-40.
89. Musselman KE, Yang JF. Loading the limb during rhythmic leg movements lengthens the duration of both flexion and extension in human infants. J Neurophysiol 2007;97:1247-57.
90. Teulier C, Smith BA, Kubo M, Chang CL, Moerchen V, Murazko K *et al*. Stepping responses of infants with myelomeningocele when supported on a motorized treadmill. Phys Ther 2009;89:60-72.
91. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: What it is and what it isn't 1996. Br Med J 1996;312:71-2.
92. Butler C, Darrah J. Effects of neurodevelopmental treatment (NDT) for cerebral palsy: An AACPDM evidence report. Dev Med Child Neurol 2001;43:778-90.
93. Gordon AM. To constrain or not to constrain, and other stories of intensive upper extremity training for children with unilateral cerebral palsy. Dev Med Child Neurol 2011;53(Suppl 4):56-61.

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