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Systematic Review

Physical therapy in Down syndrome: systematic review and meta-analysis

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Abstract

Background Down syndrome is the most common chromosomal abnormality, with a worldwide incidence of around 0.1% in live births. It is related to several conditions in which the physical therapy could take action-preventing co-morbidities. This study aims to evaluate the effectiveness of physical therapy in Down syndrome, to know and compare the effectiveness of different physical therapy interventions in this population.
Methods A systematic review and a meta-analysis of randomised controlled trials were conducted. The search was performed during June 2018 in the following databases: PubMed, Web of Science, Physiotherapy Evidence Database and Scopus. The studies were selected using predefined inclusion and exclusion criteria. The Physiotherapy Evidence Database scale evaluated the quality of the methods used in the studies. Subsequently, the data were extracted, and statistical analysis was performed when possible.
Results A total of 27 articles were included, of which nine contributed information to the meta-analysis. Statistical analysis showed favourable results for the strength of upper and lower limbs [standardised mean difference (SMD) = 1.46; 95% confidence interval (CI): (0.77–2.15); and SMD = 2.04; 95% CI: (1.07–3.01)] and mediolateral oscillations of balance [SMD = −3.30; 95% CI: (−5.34 to −1.26)].
Conclusions The results show the potential benefit of certain types of physical therapy interventions, specifically in strength and balance, in people with Down syndrome. There are still many aspects to clarify and new lines of research.

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Keywords Down syndrome, intellectual disabilities, meta-analysis, physical therapy, physical therapy modalities, systematic review

What this paper adds

- Physical therapy interventions in Down syndrome are different and varied.
- Increase on maximum strength of upper and lower limbs and balance, specifically on mediolateral displacements of the centre of gravity, has been evidenced.

- Inconclusive data for cardiovascular capacity or decrease of the body mass index were found.

Introduction

Down syndrome (DS) is the most common chromosomal abnormality (Megarbane *et al.* 2009; Asim *et al.* 2015; Colvin & Yeager 2017; Kazemi *et al.* 2016). The estimated global incidence of this chromosomopathy is around 0.1% in live births (Mao *et al.* 2003). It is characterised by a variable degree of intellectual disability (ID), some effects on health and development, as well as peculiar physical features (Haydar & Reeves 2012; Asim *et al.* 2015). A wide range of co-morbidities can be present in these people, affecting the respiratory, cardiovascular, sensory, gastrointestinal, haematological, immunological, endocrine, musculoskeletal, renal and genitourinary systems, as well as at the neurological level (Arumugam *et al.* 2016).

The lives of people with DS have changed considerably in the last 50 years (Glasson *et al.* 2002). Despite the many co-morbidities that may coexist in individuals with DS, the survival rate has increased substantially from less than 50% in the mid-1990s to 95% in the early 2000s (Arumugam *et al.* 2016). These data are accompanied by an increase in longevity of this population (Lott & Dierssen 2010; Glasson *et al.* 2014; Holmes 2014; Arumugam *et al.* 2016; Glasson *et al.* 2002), which has a life expectancy of approximately 60 years (Arumugam *et al.* 2016; Holmes 2014).

The improvement in the survival rate can be attributed to factors such as the advancement of medicine in general (Lott & Dierssen 2010). Advances in detection and prenatal diagnosis have enabled early intervention and adequate health care (Arumugam *et al.* 2016; Glasson *et al.* 2002; Lott & Dierssen 2010), as well as changes in attitude in society towards the normalisation of the lives of people with DS (Arumugam *et al.* 2016). These improvements have made it possible to achieve a better state of health, a higher degree of autonomy and integration in the community of this population in the last two decades (Schapira *et al.* 2007).

It should not be forgotten that a comprehensive approach and treatment are required in this group. Therefore, in the care of these people, we must consider medical-health aspects, such as psychological and socio-cultural dimensions (Martínez & García 2008). Within the multidisciplinary team is the figure of the physiotherapist, who begins to intervene in the first days of life (Caballero Blanco *et al.* 2011; Martínez & García 2008). Physical therapy (PT) starts from the movement as the basis of the whole development process, without separating it from the sensory and psychic aspects (Martínez & García 2008). As previously stated in the literature (Henderson *et al.* 2007; Prasher 1995), DS is related to several medical complications, such as congenital heart diseases, type 1 diabetes mellitus, obesity, hypotonia or osteoarthritis. In that way, the co-morbidities derived from these conditions can be improved with specific physical activity programmes.

Nevertheless, it was indicated that the population with proficient motor skills enjoy physical activity and consider it easy to participate. Conversely, those with poor motor skills and lack of coordination show less interest in physical activity (Barr & Shields 2011). Thus, the role of the PT in children is to perform an early intervention programme to develop basic motor skills, such as walking, balance and jumping to prevent future complications (Wang & Ju 2002). Moreover, in the adult population, these skills need to be developed, and the PT intervention is focused on the maintenance and improvement of the cardiopulmonary capacity, muscle strength and weight control (Sugimoto *et al.* 2016).

The limited reviews that study the efficacy of PT (Shields & Dodd 2004; Dodd & Shields 2005; Andriolo *et al.* 2010; Hardee & Fetters 2017; Bertapelli *et al.* 2016; Sugimoto *et al.* 2016) in this population focus on a specific type of intervention. Likewise, there are no known clinical practice guidelines that support the PT interventions in this population. All this requires a reflection on the need for further research in this area of action, the idea from which this article is born. The primary objective of the present paper is to evaluate the effectiveness of PT on the physical outcomes (such as vestibular, cardiovascular and respiratory, weight maintenance and movement-related functions, motor skills, carrying out tasks, mobility and walking indexes) in people with DS. As secondary objectives, we aim to know and compare the effectiveness of different PT interventions, obtain a global view of the current situation of PT in this syndrome and facilitate the creation of new lines of research on this subject.

Methods

The present review was conducted and reported following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines on systematic reviews of randomised controlled trials (Hutton *et al.* 2015).

Search strategy

The search of the literature for the present review was made during June 2018 using the databases and the searches detailed in Table 1. Filters about publication dates or language were not applied. A total of 510 potential articles were found.

Eligibility criteria

Studies included in this review met the following inclusion criteria: (1) the participants were children and adults diagnosed with DS; (2) a physical intervention was performed according to the World Confederation for Physical Therapy statement (WCPT 2011), such as therapeutic exercise, manual therapy techniques, patient-related instructions and orthotic devices; (3) the study design was a randomised controlled trial; and (4) the outcomes were within the measured dimensions of the International Classification of Functioning, Disability and Health (VanSant 2006). Specifically, our targets were the outcomes related to *body functions* (such as vestibular, cardiovascular and respiratory, weight maintenance and movement-related functions) and *activities and participation* (such as motor skills, carrying out tasks, mobility and walking indices). Studies were excluded from this review if (1) the sample included people without DS, but the outcome data were not shown separately for participants with DS, and (2) more than one intervention were compared at the same time. Two reviewers independently assessed the titles and abstracts according to the criteria established earlier.

Assessment of the risk of bias

For the evaluation of the methodological quality of the studies included in this review, the Physiotherapy Evidence Database scale (Maher *et al.* 2003) was used. When the criterion of each category is met, a point is awarded, except for criterion number 1, which is not used for the calculation of the total score of the scale. Therefore, the possible score on the scale ranges from 0 to 10, with a higher score indicating a higher quality in the methods used in the study. A study with a score of 6 or more is considered as evidence level 1 (6–8: good; 9–10: excellent), and a study with a score of 5 or less is considered as evidence level 2 (4–5: fair; <4: poor) (Foley *et al.* 2003).

Data extraction

Two researchers independently reviewed and extracted the data from each study in a systematic way and arriving at a consensus on all the items. The following information was extracted from the studies: author, year of publication, characteristics of the participants (number of participants in both groups, average age, gender, severity of ID, average weight, average height and presence of co-morbidity), in addition to the characteristics of the intervention

Table 1 Search strategy

Databases	Total found articles	Search
PubMed	140	("Down Syndrome"[Mesh]) AND ("Physical Therapy Specialty"[Mesh] OR "Physical Therapy Modalities"[Mesh])
PEDro	97	Down syndrome
WoS	69	TS = ((Physiotherapy OR "physical therapy") AND "Down syndrome")
Scopus	204	TITLE-ABS-KEY (Physiotherapy OR physical therapy) AND "Down syndrome"

PEDro, Physiotherapy Evidence Database; WoS, Web of Science.

carried out (type, frequency, duration of the session, measures of results, measurement instrument and results).

Statistical analysis

A meta-analysis was applied to compare changes in the effect size (post-intervention and pre-intervention) between the intervention group and the control group. For the meta-analysis, the standardised mean difference was calculated along with the 95% confidence interval, with a significance level set to $P < 0.05$. Heterogeneity was determined by the chi-square test and the I^2 statistic. When homogeneity was observed, a fixed-effect model was used. In the case of heterogeneity, a random-effects model was used. The results of all the subgroups included in this meta-analysis were represented in Forest plots. The statistical analyses were carried out with the statistical software REVIEW MANAGER 5.3 (The Cochrane Collaboration) (The Nordic Cochrane Centre 2014).

Study subgroups included in the meta-analysis

For the statistical comparison, the outcome measure, the type of intervention carried out and the measurement instrument were considered. To compare the studies, it was necessary that they measured the same concept with the same instrument, in addition to applying similar interventions. Among the interventions, therapeutic exercise group was divided into three subgroups, according to the classification of interventions proposed by Ryan *et al.* (2017) in their Cochrane review of exercise interventions in cerebral palsy. In this way, therapeutic exercise includes aerobic training (walking/jogging, exercise with an ergometer, treadmill training and treadmill training with partial body weight support), resistance training (progressive resistance training, weight-bearing exercises, strength exercises, learning to ride a bike, conditioning and jumping training and circuit training including plyometric jumps) and mixed training (exercise programmes that include a combination of different types of interventions, e.g. treadmill training + Wii games and training sessions focused on the development of general physical qualities). On the other note, the rest of the groups were based on other interventions, such as balance training, full-body vibration, early intervention techniques (infant massage and neurodevelopmental therapy) and orthotic devices.

Results

As stated in Fig. 1, the search was carried out through the combination of keywords in the databases, retrieving a total of 510 documents.

Risk of bias

Table 2 shows the scores of the Physiotherapy Evidence Database scale for each article included in the review. It was considered that 13 of the studies have a high methodological quality, with results on this scale equal to or higher than 6 (Li *et al.* 2013). Seven studies used a method of concealment of group assignment. Given that the studies analyse physical interventions versus control groups, neither the participants nor the therapists could be blinded in any of the studies. The lowest score reached was 3, obtained by two articles. The maximum score was 8, and a total of four articles obtained this score.

Data extraction

As shown in Table 3, a total of 842 subjects participated in the studies included in this review. The study that used the smallest sample size was Millar *et al.* (1993), with 14 participants. On the other hand, the study with the largest sample size was Lin & Wuang (2012), with a total of 92 participants. Regarding the age of the participants, most of the studies (Harris 1981; Ulrich *et al.* 2001; Rahman & Shaheen 2010) analysed subjects of average age less than 18 years. However, the rest of the studies (Chen *et al.* 2014; Shields *et al.* 2013; Shields *et al.* 2008; Rimmer *et al.* 2004; Carmeli *et al.* 2002; Varela *et al.* 2001; Hernandez-Reif *et al.* 2006; Silva *et al.* 2017; Eid *et al.* 2017; Millar *et al.* 1993) carried out their interventions with participants whose average age exceeded 18 years. Only three studies (Carmeli *et al.* 2002; Rimmer *et al.* 2004; Silva *et al.* 2017) conducted their research with participants over 30 years of age, standing up the study of Carmeli *et al.* (2002) for being the study with older participants. According to the studies detailing the gender of the participants, 60.1% were men and 39.9% were women.

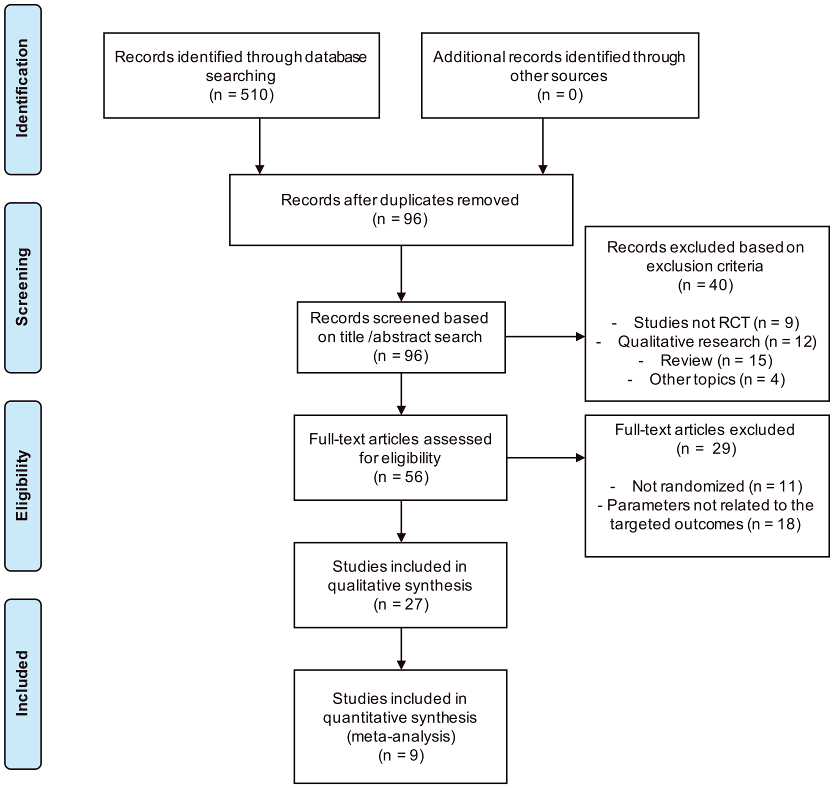

Figure 1 Information flow diagram of the different phases of the systematic review. [Colour figure can be viewed at wileyonlinelibrary.com]

In Table 4, the studies were classified into five groups according to the similarity between the interventions. In this way, the most used was the therapeutic exercise (Shields *et al.* 2013; Shields & Taylor 2010; González-Agüero *et al.* 2012; González-Agüero *et al.* 2014; Rahman & Rahman 2010; Gupta *et al.* 2011; Ferry *et al.* 2014; Ulrich *et al.* 2001; Rahman & Shaheen 2010; Ulrich *et al.* 2011; Shields *et al.* 2008; Eid *et al.* 2017; Millar *et al.* 1993; Chen *et al.* 2014; Carmeli *et al.* 2002; Varela *et al.* 2001; Lin & Wuang 2012; Rimmer *et al.* 2004; Silva *et al.* 2017). This group included aerobic training (Millar *et al.* 1993; Ulrich *et al.* 2001; Chen *et al.* 2014; Carmeli *et al.* 2002; Varela *et al.* 2001), resistance training (Rahman & Shaheen 2010; Shields *et al.* 2013; Shields *et al.* 2008; Shields & Taylor 2010; Ulrich *et al.* 2011; González-Agüero *et al.* 2012; González-Agüero *et al.* 2014; Eid *et al.* 2017) and mixed training (Lin & Wuang 2012; Rimmer *et al.* 2004; Rahman & Rahman 2010; Gupta *et al.* 2011; Ferry *et al.* 2014; Silva *et al.* 2017). Moreover, other interventions were based on balance training (Jankowicz-Szymanska *et al.* 2012; Aly & Abonour 2016), full-body vibration (Eid 2015; Villarroya *et al.* 2013), early intervention techniques, such as infant massage (Hernandez-Reif *et al.* 2006) or neurodevelopment therapy (Harris 1981), and orthotic devices, such as the supramalleolar orthosis (Looper & Ulrich 2010; Looper & Ulrich 2011).

Table 5 shows the main characteristics of the interventions carried out in the different studies of this review. The duration of the interventions ranged from 1 day (Chen *et al.* 2014) to 12 months (Ferry *et al.* 2014). Other interventions did not have a defined duration. That is the case of three studies (Ulrich *et al.* 2001; Looper & Ulrich 2010; Looper & Ulrich 2011) in which the intervention ended when the subject acquired the ability to walk. The frequency of the intervention ranged from only 1 day (Chen *et al.* 2014) to every day (Rahman & Shaheen 2010). Different methods were used to measure outcomes: scales (Ulrich *et al.* 2001; Harris 1981; Looper & Ulrich 2010; Hernandez-Reif *et al.* 2006; González-Agüero *et al.* 2012; González-Agüero *et al.* 2014; Rahman &

Table 2 Physiotherapy Evidence Database scale score for clinical trials included in the review

	PEDro scale												
Study	**Total score**	**Methodological quality**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Harris (1981)	6	Good	–	×		×			×	×		×	×
Millar *et al.* (1993)	3	Poor	–	×								×	×
Varela *et al.* (2001)	5	Fair	–	×		×				×		×	×
Ulrich *et al.* (2001)	5	Fair	–	×		×				×		×	×
Carmeli *et al.* (2002)	6	Good	–	×		×			×	×		×	×
Rimmer *et al.* (2004)	5	Fair	–	×		×				×		×	×
Hernandez-Reif *et al.* (2006)	6	Good	–	×		×			×	×		×	×
Shields *et al.* (2008)	8	Good	–	×	×	×			×	×	×	×	×
Rahman & Shaheen (2010)	4	Fair	–	×		×						×	×
Rahman & Rahman (2010)	4	Fair	–	×		×						×	×
Looper & Ulrich (2010)	4	Fair	–	×		×						×	
Shields & Taylor (2010)	8	Good	–	×	×	×			×	×	×	×	×
Looper & Ulrich (2011)	4	Fair	–	×		×						×	×
Ulrich *et al.* (2011)	4	Fair	–	×		×						×	×
Gupta *et al.* (2011)	6	Good	–	×	×	×				×		×	×
González-Agüero *et al.* (2012)	5	Fair	–	×		×				×		×	×
Jankowicz-Szymanska *et al.* (2012)	3	Poor	–	×								×	×
Lin & Wuang (2012)	7	Good	–	×		×			×	×	×	×	×
Shields *et al.* (2013)	8	Good	–	×	×	×			×	×	×	×	×
Villarroya *et al.* (2013)	4	Fair	–	×		×						×	×
Chen *et al.* (2014)	6	Good	–	×		×				×	×	×	×
González-Agüero *et al.* (2014)	5	Fair	–	×		×				×		×	×
Ferry *et al.* (2014)	4	Fair	–	×		×						×	×
Eid (2015)	8	Good	–	×	×	×			×	×	×	×	×
Aly & Abonour (2016)	6	Good	–	×		×				×	×	×	×
Silva *et al.* (2017)	7	Good	–	×	×	×			×	×		×	×
Eid *et al.* (2017)	7	Good	–	×	×	×			×	×		×	×

The '×' symbol indicates that the item where it is found has been punctuated.

Shaheen 2010; Rahman & Rahman 2010; Gupta *et al.* 2011; Lin & Wuang 2012), dynamometer (Carmeli *et al.* 2002; Rimmer *et al.* 2004; Gupta *et al.* 2011; Lin & Wuang 2012; Chen *et al.* 2014; Ferry *et al.* 2014; Eid 2015; Eid *et al.* 2017), balance platform (Jankowicz-Szymanska *et al.* 2012; Aly & Abonour 2016; Villarroya *et al.* 2013; Eid 2015; Eid *et al.* 2017), anthropometric measurements (Ulrich *et al.* 2001; Ulrich *et al.* 2011; Silva *et al.* 2017), physical and functional tests (Ferry *et al.* 2014; Carmeli *et al.* 2002; Shields & Taylor 2010; Shields *et al.* 2013; Ulrich *et al.* 2011; Shields *et al.* 2008; Millar *et al.* 1993; Varela *et al.* 2001; González-Agüero *et al.* 2014; Rimmer *et al.* 2004; Silva *et al.* 2017), bone densitometry (González-Agüero *et al.* 2012; Ferry *et al.* 2014), video recording (Looper & Ulrich 2011), activity monitors (Ulrich *et al.* 2011; Shields *et al.* 2013), electrocardiogram (Millar *et al.* 1993; Varela *et al.* 2001; Rimmer *et al.* 2004; González-Agüero *et al.* 2014), heart rate monitor (Varela *et al.* 2001) and gas consumption control (Millar *et al.* 1993; Varela *et al.* 2001; Rimmer *et al.* 2004; González-Agüero *et al.* 2014). In the assessment of motor skills, 1-repetition maximum (1RM) test (Rimmer *et al.* 2004; Shields *et al.* 2008; Shields & Taylor 2010; Shields *et al.* 2013) and Bruininks–Oseretsky test of motor proficiency (Rahman & Shaheen 2010; Rahman & Rahman 2010; Lin & Wuang 2012; Silva *et al.* 2017) were the most used.

Study subgroups included in the meta-analysis

Different subgroups have been established according to the measurement of the effect: muscle strength (subgroups 1a and 1b), balance (subgroups 2a and

Table 3 Main characteristics of participants in the studies

Study	Groups	Average age	Females : Males	Severity of intellectual disability	Average weight (kg)	Average height (cm)	Co-morbidity among theparticipants
Harris (1981)	IG (n = 10) CG (n = 10)	10.91 (7.64) 9.45 (6.66) Months	5:5 6:4	ND	ND	ND	Two participants with serious heart defects
Millar *et al.* (1993)	IG (n = 10) CG (n = 4)	18.4 (2.9) 17.0 (2.8) Years	3:11	IQ between 30 and 70 Mild to severe	66.5 (12.5) 58.4 (25.3)	153.7 (7.1) 150.0 (15.8)	ND
Varela *et al.* (2001)	IG (n = 8) CG (n = 8)	22.0 (3.8) 20.8 (2.3) Years	0:8 0:8	IQ = 39.4 (12.2) IQ = 38.4 (7.4) Mild to moderate	62.2 (10.7) 60.1 (7.4)	153.6 (21.5) 157.3 (4.1)	ND
Ulrich *et al.* (2001)	IG (n = 15) CG (n = 15)	302.6 (52.6) 312.1 (66.1) Days	ND	ND	8.2 (0.90) 8.1 (0.92)	69.2 (2.62) 69.6 (2.74)	Nine participants were born with heart disease and required surgery (of which seven were in the intervention group)
Carmeli *et al.* (2002)	IG (n = 16) CG (n = 10)	63.5 (2.0) 63.3 (4.8) Years	10:6 6:4	IQ between 56 and 75 Mild	ND	ND	15% of the participants had heart disease. Other conditions of co-morbidity were depression and possible adverse reactions to the drugs
Rimmer *et al.* (2004)	IG (n = 30) CG (n = 22)	38.6 (6.2) 40.6 (6.5) Years	16:14 13:9	ND	80.5 (20.0) 76.0 (18.2)	151.0 (9.0) 151.0 (4.0)	Four participants were diagnosed with heart disease
Hernandez-Reif *et al.* (2006)	IG (n = 11) CG (n = 10)	24.36 (10.57) 25.1 (7.95) Months	5:6 3:7	ND	ND	ND	ND
Shields *et al.* (2008)	IG (n = 9) CG (n = 11)	25.8 (5.4) 27.6 (9.5) Years	2:7 5:6	Mild to severe (20% mild, 80% moderate to severe)	78.4 (13.5) 61.2 (6.7)	158.8 (7.12) 152.0 (10.0)	ND
Rahman & Shaheen (2010)	IG (n = 13) CG (n = 13)	4.56 (0.44) 3.92 (1.16) Years	8:5 7:6	IQ between 36 to 67 Mild to moderate	ND	ND	ND
Rahman & Rahman (2010)	IG (n = 15) CG (n = 15)	10.92 (1.16) 11.56 (0.44) Years	8:7 9:6	IQ between 36 to 67 Mild to moderate	ND	ND	ND
	IG (n = 10)	642 (121)	ND	ND	10.26 (0.61)	78.67 (2.74)	ND

Table 3. *(Continued)*

Study	Groups	Average age	Females : Males	Severity of intellectual disability	Average weight (kg)	Average height (cm)	Co-morbidity among theparticipants
Looper & Ulrich (2010)	CG (*n* = 7)	578 (188) Days			9.41 (1.39)	75.81 (7.93)	
Shields & Taylor (2010)	IG (*n* = 11) CG (*n* = 12)	15.9 (1.5) 15.3 (1.7) Years	3:8 3:9	Mild to severe (26% mild, 65% moderate, 9% severe)	63 (6) 58 (7)	159 (11) 156 (7)	ND
Looper & Ulrich (2011)	IG (*n* = 10) CG (*n* = 7)	642 (121) 578 (188) Days	ND	ND	10.26 (0.61) 9.41 (1.39)	78.67 (2.74) 75.81 (7.93)	ND
Ulrich *et al.* (2011)	IG (*n* = 19) CG (*n* = 27)	12.0 (1.9) 12.4 (2.2) Years	10:9 16:11	ND	ND	ND	ND
Gupta *et al.* (2011)	IG (*n* = 12) CG (*n* = 11)	13.0 (ND) 13.5 (ND) Years	4:8 5:6	IQ of 36–52 IQ of 38–49 Mild to moderate	28.5 (ND) 23.9 (ND)	132.2 (ND) 137.3 (ND)	ND
González-Agüero *et al.* (2012)	IG (*n* = 13) CG (*n* = 14)	13.8 (2.6) 15.5 (2.6) Years	8:6 5:9	ND	40.1 (9.6) 48.7 (10.7)	141.9 (12.5) 146.8 (10.7)	Seven participants (four from the control group and three from the intervention group) took medication during the study (levothyroxine sodium)
Jankowicz-Szymanska *et al.* (2012)	IG (*n* = 20) CG (*n* = 20)	16.8 (ND) Years	20:20	Moderate	63.69 (7.97) 61.43 (10.6)	170 (0.4) 168 (0.3)	ND
Lin & Wuang (2012)	IG (*n* = 46) CG (*n* = 46)	15.6 (3.6) 14.9 (3.9) Years	25:21 24:22	IQ = 52 (ND) IQ = 53 (ND) Mild to moderate	57.2 (10.2) 58.8 (20.0)	153.0 (8.0) 151.0 (9.0)	ND
Shields *et al.* (2013)	IG (*n* = 34) CG (*n* = 34)	17.7 (2.4) 18.2 (2.8) Years	15:19 15:19	Mild to moderate (50% mild, 50% moderate)	65 (9) 64 (14)	155 (8) 153 (10)	ND
Villarroya *et al.* (2013)	IG (*n* = 16) CG (*n* = 13)	15.93 (2.48) 15.64 (2.93) Years	11:19	ND	48.44 (8.83) 51.93 (14.10)	148.75 (8.2) 147.57 (12.6)	ND
Chen *et al.* (2014)	IG (*n* = 12) CG (*n* = 8)	21.76 (4.79) 17.77 (3.49) Years	0:20	Moderate to severe	80.30 (22.92) 70.96 (24.25)	145.86 (11.6) 151.40 (7.8)	ND
	IG (*n* = 14)	13.7 (2.6)	8:6	ND	40.1 (9.6)	141.9 (12.5)	ND

Table 3. *(Continued)*

Study	Groups	Average age	Females : Males	Severity of intellectual disability	Average weight (kg)	Average height (cm)	Co-morbidity among theparticipants
González-Agüero *et al.* (2014)	CG (*n* = 13)	15.6 (2.5) Years	4:9		47.9 (10.7)	146.7 (11.1)	
Ferry *et al.* (2014)	IG (*n* = 20)	16.0 (1.8)	10:10	ND	59.8 (16.9)	153.9 (8.4)	ND
	CG (*n* = 22)	16.9 (1.5) Years	8:14		65.4 (16.1)	155.3 (8.9)	
Eid (2015)	IG (*n* = 15)	8.93 (0.7)	7:8	IQ = 57.6 (3.08)	29.2 (3.4)	118 (2.27)	ND
	CG (*n* = 15)	9.26 (0.79) Years	6:9	IQ = 57.06 (2.98) Mild	29.53 (3.22)	119.06 (2.81)	
Aly & Abonour (2016)	IG (*n* = 15)	8.11 (1.26)	4:11	IQ = 48.33 (6.38)	21.46 (2.44)	120.46 (5.46)	ND
	CG (*n* = 15)	8.34 (1.07) Years	5:10	IQ = 50.33 (4.70) Mild to moderate	22.06 (2.4)	119.26 (4.35)	
Silva *et al.* (2017)	IG (*n* = 12)	18–60 Years	ND	ND	72.97 (15.12)	ND	ND
	CG (*n* = 13)				70.01 (69.65)		
Eid *et al.* (2017)	IG (*n* = 15)	10.26 (0.79)	7:8	IQ: 56.46 (5.62)	30.53 (3.22)	120.06 (2.81)	ND
	CG (*n* = 16)	10.05 (0.68) Years	7:9	IQ: 57.18 (4.38)	30.2 (3.29)	119.2 (2.19)	

Mean (standard deviation); IG, intervention group; CG, control group; IQ, intellectual quotient; ND, not described.

Table 4 Classification of the studies according to the type of intervention

Intervention group		Number of studies	Examples of the type of therapy
Therapeutic exercise	Aerobic training	5 (Millar *et al.* 1993; Ulrich *et al.* 2001; Chen *et al.* 2014; Carmeli *et al.* 2002; Varela *et al.* 2001)	Walking/jogging, exercise with an ergometer, treadmill training and treadmill training with partial body weight support
	Resistance training	8 (Rahman & Shaheen 2010; Shields *et al.* 2013; Shields *et al.* 2008; Shields & Taylor 2010; Ulrich *et al.* 2011; González-Agüero *et al.* 2012; González-Agüero *et al.* 2014; Eid *et al.* 2017)	Progressive resistance training, weight-bearing exercises, strength exercises, learning to ride a bike, conditioning and jumping training and circuit training including plyometric jumps
	Mixed training	6 (Lin & Wuang 2012; Rimmer *et al.* 2004; Rahman & Rahman 2010; Gupta *et al.* 2011; Ferry *et al.* 2014; Silva *et al.* 2017)	Exercise programmes that include a combination of different types of interventions (e.g. treadmill training + Wii games and training sessions focused on the development of general physical qualities …)
Balance training		2 (Jankowicz-Szymanska *et al.* 2012; Aly & Abonour 2016)	Exercises programmes targeted at improving the quality of balance (e.g. exercises on rehabilitation ball and core-stability exercises)
Vibration		2 (Eid 2015; Villarroya *et al.* 2013)	Full-body vibration
Early stimulation		2 (Harris 1981; Hernandez-Reif *et al.* 2006)	Neurodevelopment therapy and massage therapy
Technical aid		2 (Looper & Ulrich 2010; Looper & Ulrich 2011)	Supramalleolar orthosis

2b), cardiovascular function (subgroups 3a and 3b) and body mass index (BMI) (subgroup 4). The results show that three of the subgroups (1a, 1b and 2a) presented favourable results in a significant way. In contrast, the results were inconclusive for four of the subgroups (2b, 3a, 3b and 4).

Figures 2–8 present the results related to the meta-analyses of the subgroups.

Muscle strength

In the meta-analysis performed in this work, muscle strength was assessed in the different studies through tests for maximum strength generation, such as 1RM. The generation of maximum muscular strength was tested by establishing the amount of weight that each participant could lift in a bench press and a sitting leg press (Shields *et al.* 2008). The meta-analysis for bench and leg press was performed independently in two subgroups.

Three studies (Shields *et al.* 2008; Shields & Taylor 2010; Shields *et al.* 2013) measured bench press in upper limbs and leg press muscle strength in lower limbs valued by 1RM, with resistance training as the intervention. Both the individual results and the overall result obtained show that the interventions performed had a positive effect on the maximum strength bench press and leg press.

The study by Shields *et al.* (2008) had a positive effect on the upper limbs strength, but on the other hand, no significant improvements were obtained on the lower limbs. In another study by Shields *et al.* (2013), the effect of the intervention on muscle strength at week 24, although diminished, is maintained for both the upper and lower extremities, being higher in the lower limbs. Nevertheless, the

Table 5 Main characteristics of the study interventions

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Harris (1981)	IG: Neurodevelopment therapy CG: No additional intervention	Three times/ week	40 min	9 weeks	Motor development	-The Bayley Scales of Infant Development -Peabody Developmental Motor Scales	No statistically significant difference was found between the groups. However, there was a significant difference in favour of IG in achieving individual treatment goals ($P = 0.05$).
Millar *et al.* (1993)	IG: Aerobic training (walking/jogging) CG: No regular physical training	Three times /week	30 min	10 weeks	VO_2 max, VM, HR, RER, time and degree of exhaustion	-Treadmill exercise test with gas consumption control and electrocardiogram	There were no statistically significant differences for any of the parameters of aerobic capacity. However, there was a significant improvement over time (and grade) in the treadmill exercise test after the intervention in the IG ($P < 0.00089$).
Varela *et al.* (2001)	IG: Exercise in an ergometer CG: No regular physical activity	Three times/ week	15–25 min	16 weeks	VO_2 max, VM max, HR max, RER, distance covered, working level, body weight and percentage of body fat	-Stress tests in treadmill and rowing-ergometer with gas consumption control, heart rate monitor and electrocardiogram	Training did not improve the cardiovascular capacity of the participants. However, exercise resistance and work capacity were improved in both tests ($P < 0.01$ for the treadmill and $P < 0.05$ for rowing-ergometer) after the intervention in comparison with the CG.

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Ulrich *et al.* (2001)	IG: Training on a treadmill with partial weight support CG: No training	Five times/ week	8 min	Until the child learned to walk	Motor development and growth	-The Bayley Scales of Infant Development -Battery of 11 anthropometric measurements	The IG learned to walk with help ($P = 0.03$) and to walk independently ($P = 0.02$) significantly faster than the CG. There were no significant differences in any of the anthropometric variables.
Carmeli *et al.* (2002)	IG: Training on a treadmill CG: No training	Three times/ week	10–45 min	6 months	Leg strength and dynamic balance	-Dynamometer -Functional test: 'Time-up and go'	After the intervention, there was a significant improvement in the isokinetic strength of knee flexion and extension (P values < 0.01), as well as in the dynamic equilibrium ($P < 0.05$) in the IG.
Rimmer *et al.* (2004)	IG: Cardiovascular training and strength training CG: No training	Three times/ week	30–45 min aerobic exercise 15–20 min strength exercises	12 weeks	Cardiovascular capacity, strength (upper and lower limbs) and body composition (weight, BMI and skin folds)	-Exercise test on a cycle ergometer with control of gas consumption and electrocardiogram. -1RM bench press and seated leg press machine. Hand grip dynamometer	Results showed that IG significantly improved cardiovascular fitness: VO_2 max ($mL \cdot min^{-1}$); VO_2 max ($mL \cdot kg^{-1} \cdot min^{-1}$); HR max; time of exhaustion; and maximum workload (all values $P < 0.01$). Also the strength of the extremities ($P < 0.0001$) and slightly the body weight ($P < 0.01$).

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Hernandez-Reif *et al.* (2006)	IG: Massage therapy CG: Reading	Two times/week	30 min	2 months	Motor development and muscle tone	-Developmental programming for infants and young children scale -The arms, legs and trunk muscle tone score	Results after the intervention revealed significant improvements in gross and fine motor development (both $P < 0.05$). In addition, the tone of the limbs also improved (less hypotonia) significantly ($P \leq 0.05$).
Shields *et al.* (2008)	IG: Progressive resistance training CG: Continued daily activities	Two times/ week	ND	10 weeks	Strength muscle function and functionality upper and lower extremities	-1RM repetition maximum tests -The number of repetitions complete to 50% of a 1RM -Time up and downstairs test; the grocery shelving task	Results showed that the intervention significantly improved the muscular resistance of the upper extremities ($P < 0.01$) compared with the CG. The rest of the measures did not show significant differences between the groups.
Rahman & Shaheen (2010)	IG: Traditional PT + weight-bearing exercises CG: Traditional PT	Daily	IG: 80 min CG: 60 min	6 weeks	Static, dynamic and total balance	-Sub-scale of the scale The Bruininks–Oseretsky Test of Motor Proficiency	The results showed significant improvements in the static ($P = 0.006$), dynamic ($P = 0.002$) and total ($P = 0.002$) balance in the IG after the intervention.
Rahman & Rahman (2010)	IG: Traditional training + Wii games CG: Traditional PT	Two times/ week	Conventional programme 60 min IG + 30 min Wii-Fit games	6 weeks	Balance	-Sub-scale of the scale The Bruininks–Oseretsky Test of Motor Proficiency	The results revealed a significant improvement on the balance ($P = 0.000$) when the IG was compared with the CG.

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Looper & Ulrich (2010)	IG: Treadmill training + supramalleolar orthosis CG: Treadmill training	Five times/ week	8 h/day use of the orthosis 8 min/day treadmill training	Until the child learned to walk	Gross motor function	-The Gross Motor Function Measure	All children showed significant improvements in the gross motor scores over time ($P < 0.001$). One month after the intervention, the CG had higher scores in total than the IG ($P = 0.01$), as well as the standing sub-scale ($P = 0.01$) and walking, running and jumping sub-scale ($P = 0.02$).
Shields & Taylor (2010)	IG: Progressive resistance training CG: Continued his usual activities	Two times/ weeks	ND	10 weeks	Muscle strength and functionality upper and lower extremities	-1RM repetition maximum tests -Time up and downstairs test -The grocery shelving task	The results showed improvement in muscle strength of the lower extremities compared with the CG. There were no significant differences between the groups for the rest of the measurements.
Looper & Ulrich (2011)	IG: Treadmill training + supramalleolar orthosis CG: Treadmill training	Five times/ weeks	8 h/day use of the orthosis 8 min/day treadmill training	Until the child learned to walk	Support of the child's upper extremities during play in an upright position	-Video recording	Significant group differences were not found in support of the hands during the game in the vertical position. All the children decreased the support on both hands with the passage of time ($P = 0.05$).

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Ulrich *et al.* (2011)	IG: Learning to ride a bicycle -Scale, meter, plicometer	Five consecutive days	75 min	5 days	Lower extremities muscle strength, balance, height, weight, skin folds and physical activity	-Manual muscle tester -Keep the balance on one leg	The participants who learned to ride spent significantly less time in sedentary activity at 7 weeks ($P = 0.035$) and at 12 months ($P = 0.004$) after the intervention and more time in moderate to vigorous physical activity at 12 months ($P = 0.023$) compared with CG participants. Body fat also seemed to be positively influenced over time by the subjects who learned to ride ($P = 0.047$).
-Monitor with accelerometers	CG: No intervention						
Gupta *et al.* (2011)	IG: Strength and physical balance training CG: They continued their normal activities	Three times/ weeks	ND	6 weeks	Lower limb strength and balance	-Dynamometer -Sub-scale of The Bruininks–Oseretsky scale Test of Motor Proficiency	After the training, the IG participants showed a statistically significant improvement ($P < 0.05$) in the strength of the lower limbs of all the muscle groups evaluated. The score on the balance sub-scale also improved in the IG significantly ($P = 0.001$).

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
González-Agüero *et al.* (2012)	IG: Conditioning and jumping training CG: No intervention	Two times/weeks	25 min	21 weeks	Bone mineral density, pubertal development and anthropometric measurements	-Dual-energy X-ray absorptiometry -Five stages by Tanner and Whitehouse	After the intervention, increments were observed in total and hipbone mineral density and total lean mass in the IG (all $P < 0.05$). The interaction between time and exercise was found for total lean mass ($P < 0.05$). The increase of the total lean mass, the height and Tanner's stage represented almost 60% in the increase of mineral bone total density in the group of intervention ($P < 0.05$).
Jankowicz-Szymanska *et al.* (2012)	IG: Sensorimotor training CG: No intervention	Two times/weeks	45 min	12 weeks	Static balance	Balance platform	After the training sessions, the tests improved in the intervention group, but the differences were not statistically significant. Except for the time in the maintenance of the CoG within the circle of 13 mm at the beginning and the end in the intervention subjects ($P = 0.0014$).
Lin & Wuang (2012)	IG: Treadmill training + Wii sports games CG: Everyday activities	Three times/week	25 min	6 weeks	Lower limb strength and agility	-Dynamometer -Subtests of the Bruininks–Oseretsky Test of Motor Proficiency – Second Edition	IG had significant improvements in agility ($P = 0.02$) and muscle strength of all muscle groups evaluated ($P < 0.05$).

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Shields *et al.* (2013)	IG: Progressive resistance training CG: Social activities	IG: 2 times/week CG: 1 time/week	IG: 45–60 min CG: 90 min	10 weeks both groups	Execution of work tasks, muscular strength and physical activity	-Weighted box stacking test and a weighted pail carry test -Tests of maximum force of a repetition (1RM) -Activity monitor	There was no difference between the groups for the execution of work tasks. IG increased muscle strength in the upper and lower limb at week 11 compared with CG. In week 24, only the lower limb muscle strength was increased. Physical activity levels were significantly higher in the IG at week 24 but not at 11 (all values $P < 0.05$).
Villarroya *et al.* (2013)	IG: Vibration CG: No vibration	Three times/week	15–20 min	20 weeks	Static balance	-Pressure platform	Significant decrease in condition 4 (closed eyes surface unstable/open eyes stable surface) of the mid-lateral displacement and average velocity of the CoG in the group of SD who performed the intervention ($P < 0.05$).
Chen *et al.* (2014)	IG: Treadmill exercise CG: Viewing a video	Only one time	20 min	1 session	Gripping strength	-Dynamometer	The post-test between both groups was significantly different. The IG obtained greater strength in the post-test compared with the CG ($P = 0.03$).

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
González-Agüero *et al.* (2014)	IG: Circuit training that includes plyometric jumps CG: No increase in daily activities	Two times/week	20–25 min	21 weeks	Working time, VO_2 max, RER max, HR max, VM max Anthropometric measurements and puberty state	-Test of effort in a treadmill with control of gas consumption and electrocardiogram -Scale of Tanner	After 21 weeks of training, the IG improved its cardiorespiratory parameters (VO_2 max, HR max, RER max, VM max and work time) (all values $P < 0.05$). In addition, improvements in cardiorespiratory parameters (VO_2 max, HR max and VM max) were significantly higher compared with the CG (all values $P < 0.05$).
Ferry *et al.* (2014)	GI: Physical qualities training GC: No intervention	Two times/week	60 min	12 months	Bone mineral density, density, attenuation of ultrasound and speed. Motor skills	-Dual X-ray absorptiometry -QUS device -Physical tests: standing broad jump; sit-and-reach test; sit-ups; manual dynamometry	The year of intervention increased the values of bone mineral density in the lumbar spine ($P < 0.005$) and in the hip ($P < 0.05$). Bone mineral density was only increased in the lumbar spine ($P < 0.05$). The punctuations of the physical tests increased significantly compared with the CG.

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Eid (2015)	IG: PT + vibration programme GC: PT programme	Three times/ week	Both groups 1 h, the GI plus 5–10 min of full-body vibration	6 months	Balance and muscle strength of knee flexors and extensors	-Biodex Stability System -Manual dynamometry	There was a statistically significant improvement in favour of the IG regarding strength: knee flexors ($P = 0.04$) and knee extensors ($P = 0.01$). There were also improvements on the balance of the IG compared with CG: mediolateral stability ($P = 0.001$); anteroposterior ($P = 0.0001$); stability in general ($P = 0.004$).
Aly & Abonour (2016)	GI: Conventional PT programme + core-stability exercises GC: Conventional physical therapy programme	Three times/ weeks	45–60 min	8 weeks	Balance (postural stability)	-Biodex balance system	There was a significant decrease in the anteroposterior ($P = 0.0001$), mediolateral ($P = 0.002$) and general stability ($P = 0.0001$) indices of the IG participants compared with the CG after the intervention. Both groups showed a significant decrease in the three stability indices in the post-treatment compared with the pre-treatment.

Table 5. *(Continued)*

Study	Intervention	Frequency	Session duration	Intervention duration	Outcome measure	Measuring instrument	Results
Silva *et al.* (2017)	IG: Wii-based exercise programme CG: Usual daily activities	Three times/week	1 h	8 weeks	-Body weight -BMI -Body fat % -Visceral fat -Muscle mass -Waist circumference -Test speed of limb movement -Static arm strength -Speed and agility -Balance -Flexibility -Explosive leg power -Trunk strength -Muscular endurance -Aerobic endurance -Right and left hand coordination -Functional mobility	-Segmental body composition analyser -Eurofit Test Battery: plate tapping; handgrip test; shuttle run; flamingo balance test; sit and reach test; standing broad jump; 30-s sit-ups; bent arm hang; 6-min walk; beanbag overhead throw -Bruininks–Oseretsky Response speed subtest -Timed up and go	IG obtained significant improvements on waist circumference ($P = 0.008$), handgrip test ($P = 0.025$), sit and reach test ($P = 0.014$), standing broad jump ($P < 0.001$), 6-min walk ($P = 0.003$) and Bruininks–Oseretsky Response speed subtest ($P = 0.028$). Participants from the control group also experienced improvements in the handgrip test ($P = 0.039$).
Eid *et al.* (2017)	IG: Conventional physical therapy + isokinetic training CG: Conventional physical therapy	Three times/ Week	45 min physical therapy +15 min isokinetic training programme 60 min physical therapy programme	12 weeks	Leg strength and postural balance	-Isokinetic dynamometer -Biodex Stability System	After the intervention, each group showed significant improvements in postural balance and peak torque of knee flexors and extensors ($P < 0.05$). IG obtained greater improvements on outcomes measures compared with CG ($P < 0.05$).

IG, intervention group; CG, control group; ND, not described; VO_2, oxygen consumption; HR, heart rate; RER, respiratory exchange ratio; VM, minute ventilation; BMI, body mass index; RM, repetition maximum; CoG, centre of gravity.

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Shields et al 2008	9	5.1	9	3.6	3.63	11	20.8%	1.19 [0.22, 2.16]	2008
Shields and Taylor 2010	11	6.52	11	4	3.12	12	21.7%	1.34 [0.42, 2.26]	2010
Shields et al. 2013 (11w)	7.7	2.66	34	2	2.23	34	27.6%	2.30 [1.68, 2.92]	2013
Shields et al. 2013 (24w)	7.6	2.91	34	5	2.4	34	29.8%	0.96 [0.46, 1.47]	2013
Total (95% CI)			**88**			**91**	**100.0%**	**1.46 [0.77, 2.15]**	

Heterogeneity: Tau² = 0.35; Chi² = 11.06, df = 3 (P = 0.01); I² = 73%
Test for overall effect: Z = 4.13 (P < 0.0001)

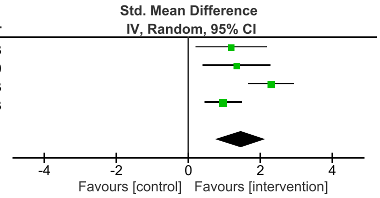

Figure 2 Subgroup 1a: Forest plot for strength (1-repetition maximum) measured by bench press. [Colour figure can be viewed at wileyonlinelibrary.com]

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Shields et al 2008	15.4	9.72	9	11.4	5.99	11	24.4%	0.49 [-0.41, 1.38]	2008
Shields and Taylor 2010	45	14.51	11	8	12.56	12	21.3%	2.64 [1.47, 3.81]	2010
Shields et al. 2013 (11w)	36.1	7.89	34	13	8.38	34	26.8%	2.81 [2.13, 3.49]	2013
Shields et al. 2013 (24w)	41.3	9.23	34	21.8	8.24	34	27.5%	2.20 [1.59, 2.81]	2013
Total (95% CI)			**88**			**91**	**100.0%**	**2.04 [1.07, 3.01]**	

Heterogeneity: Tau² = 0.79; Chi² = 17.47, df = 3 (P = 0.0006); I² = 83%
Test for overall effect: Z = 4.13 (P < 0.0001)

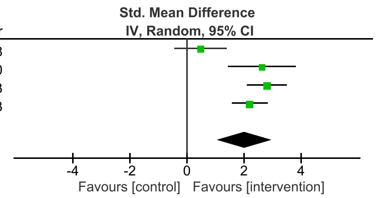

Figure 3 Subgroup 1b: Forest plot for strength (1-repetition maximum) measured by leg press. [Colour figure can be viewed at wileyonlinelibrary.com]

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Villarroya et al. 2013	-0.4	0.49	16	0.61	0.32	13	53.0%	-2.32 [-3.29, -1.35]	2013
Eid 2015	-0.29	0.04	15	-0.13	0.03	15	47.0%	-4.40 [-5.80, -3.01]	2015
Total (95% CI)			**31**			**28**	**100.0%**	**-3.30 [-5.34, -1.26]**	

Heterogeneity: Tau² = 1.79; Chi² = 5.76, df = 1 (P = 0.02); I² = 83%
Test for overall effect: Z = 3.18 (P = 0.001)

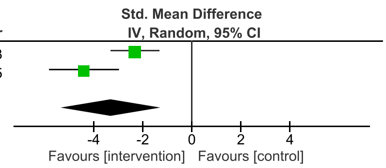

Figure 4 Subgroup 2a: Forest plot for balance (centre of gravity mediolateral displacement). [Colour figure can be viewed at wileyonlinelibrary.com]

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Year
Villarroya et al. 2013	0.02	0.14	16	0.04	0.22	13	51.8%	-0.11 [-0.84, 0.62]	2013
Eid 2015	-0.22	0.19	15	-0.09	0.03	15	48.2%	-0.93 [-1.69, -0.17]	2015
Total (95% CI)			**31**			**28**	**100.0%**	**-0.50 [-1.03, 0.02]**	

Heterogeneity: Chi² = 2.33, df = 1 (P = 0.13); I² = 57%
Test for overall effect: Z = 1.88 (P = 0.06)

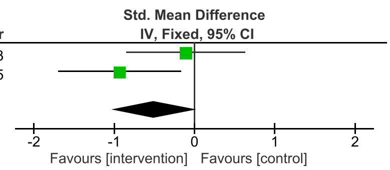

Figure 5 Subgroup 2b: Forest plot for balance (centre of gravity anterolateral displacement). [Colour figure can be viewed at wileyonlinelibrary.com]

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Year
Millar et al. 1993	-1.39	2.49	10	0.02	2.77	4	43.2%	-0.52 [-1.70, 0.67]	1993
Varela et al. 2001	0.3	1.51	8	-1	1.61	8	56.8%	0.79 [-0.24, 1.82]	2001
Total (95% CI)			**18**			**12**	**100.0%**	**0.23 [-0.55, 1.00]**	

Heterogeneity: Chi² = 2.66, df = 1 (P = 0.10); I² = 62%
Test for overall effect: Z = 0.57 (P = 0.57)

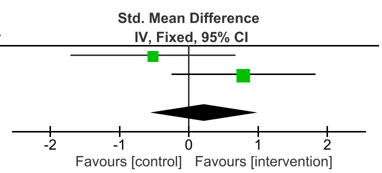

Figure 6 Subgroup 3a: Forest plot for cardiovascular function (oxygen consumption max). [Colour figure can be viewed at wileyonlinelibrary.com]

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Millar et al. 1993	-5.6	4.35	10	4	6.74	4	47.9%	-1.78 [-3.17, -0.38]	1993
Varela et al. 2001	-3	3.24	8	-5	2.89	8	52.1%	0.62 [-0.39, 1.63]	2001
Total (95% CI)			**18**			**12**	**100.0%**	**-0.53 [-2.87, 1.81]**	

Heterogeneity: $Tau^2 = 2.48$; $Chi^2 = 7.42$, df = 1 (P = 0.006); $I^2 = 87\%$
Test for overall effect: Z = 0.44 (P = 0.66)

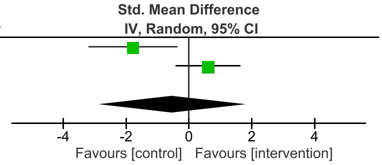

Figure 7 Subgroup 3b: Forest plot for cardiovascular function (heart rate max). [Colour figure can be viewed at wileyonlinelibrary.com]

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Year
Rimmer 2004	-0.5	1.64	30	0.5	1.57	22	66.1%	-0.61 [-1.17, -0.05]	2004
Silva et al. 2017	0.22	1.82	12	-0.15	1.9	13	33.9%	0.19 [-0.59, 0.98]	2017
Total (95% CI)			**42**			**35**	**100.0%**	**-0.34 [-0.80, 0.12]**	

Heterogeneity: $Chi^2 = 2.65$, df = 1 (P = 0.10); $I^2 = 62\%$
Test for overall effect: Z = 1.45 (P = 0.15)

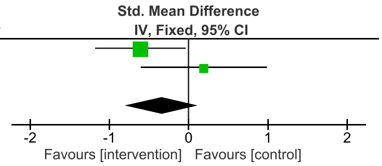

Figure 8 Subgroup 4: Forest plot for body mass index. [Colour figure can be viewed at wileyonlinelibrary.com]

meta-analysis performed in this study shows positive effects in both upper and lower limbs.

Balance

Two studies (Villarroya *et al.* 2013; Eid 2015) analysed the effects of their interventions (based on vibration therapy) on displacements of the centre of gravity in the stabilometric platform. The oscillations in the mediolateral direction were reduced after the intervention in both studies. However, the anteroposterior oscillations were not reduced in the work of Villarroya *et al.* (2013), and in this case, the global effect of the meta-analysis did not provide conclusive data. In this way, the meta-analysis shows positive effects on the improvement of mediolateral oscillations.

Cardiovascular function

The effects of exercise on the maximum absorption of VO_2 (VO_2 max) were studied in two of the reviewed trials (Millar *et al.* 1993; Varela *et al.* 2001). The same researchers that studied VO_2 max measured the maximum heart rate with an intervention based on aerobic training. The maximum heart rate study aimed to determine if there were changes in the effort and intensity of the exercise that the participants could reach after carrying out the intervention. Nonetheless, the two studies (Millar *et al.* 1993; Varela *et al.* 2001) did not have favourable effects on this parameter. Then, the results of the meta-analysis revealed that the data provided by the studies were inconclusive.

Body mass index

In the study by Rimmer *et al.* (2004), a favourable effect on the BMI of the participants of adult age was obtained after the training of cardiovascular exercises and strength (mixed training). By contrast, the study by Silva *et al.* (2017) did not obtain conclusive results on the decrease of the BMI of its participants. In this sense, the meta-analysis shows inconclusive results.

Discussion

First, we would like to note that, to the best of our knowledge, this is the first meta-analysis summarising the findings on PT interventions in the DS population in the literature. Once the analysis of the studies retrieved has been performed, some comments and considerations about the articles included in the meta-analysis and systematic review need to be addressed.

The findings on strength levels highlight the benefits of the resistance training programmes on the improvement of muscle strength in people with DS. Shields *et al.* (2008) stated that the intervention had a positive effect on the upper limbs' strength but no significant improvements on the lower limbs. The authors suggested that people usually exercise the lower limb muscles in their daily life activities more frequently than their upper limb musculature being, therefore, more effective an intervention in these last muscle groups. Furthermore, the same authors in a later study (Shields *et al.* 2013) stated the possibility that the participants trained during the intervention period continued to train voluntarily after the end of the programme.

According to the postural balance analysis, two studies applied to adolescents (Villarroya *et al.* 2013) and children (Eid 2015) evaluated the effects of vibration on the number of the centre of gravity oscillations in the anteroposterior and mediolateral directions in the stabilometric platform. In that way, Eid (2015) research had better results in both directions and Villarroya *et al.* (2013) in mediolateral oscillations. These outcomes suggest that interventions based on vibration therapy are effective in improving balance in children and adolescents with DS.

Besides, the PT influence in cardiovascular function was also analysed. In that way, the effects of aerobic training interventions on the maximum absorption of VO_2 were studied in two of the reviewed trials (Millar *et al.* 1993; Varela *et al.* 2001). None of the studies obtained significative improvements in cardiovascular capacity in people with DS. Millar *et al.* (1993) suggested that the intervention based on walking/jogging may not be sufficiently motivating or may become monotonous, thus affecting performance and effort of some participants.

Finally, according to the meta-analysis, some comments about the effect on BMI need to be stated. As previously addressed, the overweight and obesity prevalence in people with DS is a common problem. Thus, the health promotion through initiatives that encourage greater participation in physical activities can be an essential pillar when working with this population (Bertapelli *et al.* 2016; Rimmer *et al.* 2004; Ulrich *et al.* 2011). In the study by Rimmer *et al.* (2004), a favourable effect on the BMI of the participants of adult age was obtained after the training of cardiovascular exercises and strength. Moreover, Silva *et al.* (2017) incorporated the use of new technologies as a form of therapy in adults. The advantages of the use of videogames include the prevention of monotony and boredom, the increase of motivation and the ability to provide direct feedback and allow the execution of a second task (Bonnechere *et al.* 2016). Nonetheless, no improvements were obtained in the reduction of BMI in adults. In this way, the results of the meta-analysis performed show that interventions based on mixed training are not effective to improve BMI.

From our systematic review, not all the studies were included in the meta-analysis. Therefore, some paragraphs about 'additional evidence', highlighting their findings, are provided.

Accordingly, others studies included in this review have also studied the balance (Gupta *et al.* 2011; Aly & Abonour 2016; Jankowicz-Szymanska *et al.* 2012; Eid *et al.* 2017; Carmeli *et al.* 2002; Rahman & Rahman 2010; Rahman & Shaheen 2010; Silva *et al.* 2017) and strength (Carmeli *et al.* 2002; Rimmer *et al.* 2004; Lin & Wuang 2012; Chen *et al.* 2014; Silva *et al.* 2017; Eid *et al.* 2017) in people with DS. Most studies obtained some improvements in the balance and the strength of their participants after the interventions, strengthening the previously commented idea that the exercise programmes are effective for improving these capacities.

Additionally, previous studies have observed lower levels of bone mineral density in people with DS (González-Agüero *et al.* 2011; González-Agüero *et al.* 2012). In this way, in the present review, two studies (González-Agüero *et al.* 2012; Ferry *et al.* 2014) measured the effect of training programmes on bone mineral density at the lumbar spine level obtaining favourable results.

Furthermore, it is well known that walking is an especially important skill for young children. Its impact is multidimensional, affecting motor, cognitive and social development (Agulló & González 2006; Malak *et al.* 2015; Jung *et al.* 2017; Ulrich *et al.* 2001). Ulrich *et al.* (2001) reveal the opportunity offered by the treadmill intervention on the gait development of children with DS. Subsequently, other studies not included in this review have focused on studying the most optimal intensity of this type of intervention for motor development and gait in these children (Wu *et al.* 2007; Wu *et al.* 2010; Ulrich *et al.* 2008). In this sense, it is also widespread to provide children with SD orthoses to improve the gait functionality (Looper & Ulrich 2011). Looper & Ulrich (2010) showed the effects of supramalleolar orthosis on gait in children with DS, presenting some adverse effects in children who have not yet reached the gait.

Moreover, some studies incorporated the use of new technologies as a form of therapy. This is the case of Lin & Wuang (2012), Rahman & Rahman (2010) and Silva *et al.* (2017), who used Nintendo Wii® games in their interventions. Given the good results obtained in both studies in children and adolescents, the use of new technologies could be a useful tool in the PT treatment of people with DS.

Regarding the interventions, the results of our study show that the most used was therapeutic exercise. In this way, resistance training was effective to improve muscle strength, but aerobic training and mixed training were not effective in improving cardiovascular function and BMI, respectively. Furthermore, interventions based on vibration therapy show benefits on balance. Despite being an extensive revision collecting works of different interventions, other types of PT interventions are not present in the works found, for example, respiratory PT, which may be of potential use if we take into account that respiratory problems have high morbidity and contribute to the reduction of the quality of life of this group (Colvin & Yeager 2017). Another example would be the PT approach to orofacial stimulation and swallowing disorders, with oral problems also being characteristic of this population (Arumugam *et al.* 2016). Besides, further research is needed on essential aspects that, despite having been studied previously, have not been clarified yet. Therefore, all this leads to highlight the clear need for more research in PT in the DS.

Limitations

Some limitations of this study need to be addressed. Despite careful selection of keywords and search strategies, it is possible that potentially useful literature has been excluded from the review. Also, an exhaustive search of unpublished literature could provide interesting articles to consider. Furthermore, the studies were heterogeneous, making comparisons difficult. For this reason, out of the 27 articles included in the review, only nine provided information to the meta-analysis. Additionally, despite evaluating the same parameter, the difference in scales or instruments used for the assessment makes statistical comparison impossible. Another remarkable aspect is the sample size, small in most of the studies, and the lack of long-term follow-up interventions. Finally, because of the small number of studies that composed some subgroups, the data provided by the statistical analysis should be taken with caution.

Conclusions

In the present systematic review and meta-analysis, an overview of the research evidence on PT intervention in DS is provided. Concerning our primary objective, the different modalities of PT interventions seem to be effective in the improvement of different motor outcomes related to DS. In this sense, interventions based on resistance training are effective in the improvement of the strength of upper and lower limbs. Furthermore, interventions based on vibration therapy have a positive effect on balance, specifically in the reduction of mediolateral displacements of the centre of gravity. Moreover, the evidence of improvement of the anteroposterior displacements of the centre of gravity, cardiovascular capacity or decrease of the BMI, was inconclusive. These findings suggest that PT is recommended to improve strength and balance. Finally, the outcomes of the present study suppose an evidence-based framework in which clinical therapists can base their interventions with DS subjects.

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Conflict of Interest

The authors declare no conflict of interest.

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