Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome (Review)

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[Intervention Review]

Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

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ABSTRACT

Background

Although physical fitness has been suggested to improve physical and psychosocial health for a variety of population profiles, there is a lack of information about the safety and effectiveness of aerobic exercise for adults with Down syndrome.

Objectives

To evaluate the effectiveness and safety of aerobic exercise training programmes for physiological and psychosocial outcomes in adults with Down syndrome.

Search methods

The following electronic databases were searched: The Cochrane Central Register of Controlled Trials (CENTRAL) (2009, Issue 1); MEDLINE (1966 to August 2009); EMBASE (1980 to August 2009); CINAHL (1982 to August 2009); LILACS (1982 to August 2009); PsycINFO (1887 to August 2009); ERIC (1966 to August 2009); Current Controlled Trials (August 2009); and Campbell Collaboration's Social, Psychological, Educational and Criminological Register (C2-SPECTR) (to August 2009). Information about ongoing clinical trials was sought by searching ClinicalTrials.gov (http://clinicaltrials.gov) (accessed August 2009), and the National Research Register (NRR) (2009 Issue 1).

Selection criteria

Randomised or quasi-randomised controlled trials using supervised aerobic exercise training programmes with behavioral components accepted as co-interventions.

Data collection and analysis

Two reviewers selected relevant trials, assessed methodological quality and extracted data. Where appropriate, data were pooled using meta-analysis with a random-effects model. Positive values favour the intervention group, while negative values favour the control group.

Main results

Three studies included in this systematic review used different kinds of aerobic activity: walking/jogging and rowing training for participants from 17 to 65 years old (from USA, Portugal and Israel). In the meta-analyses, only maximal treadmill grade was improved after aerobic exercise training programmes (4.26 grades (%) [95% CI 2.06, 6.45]). Other variables relative to work performance that could not be combined in a meta-analysis were also improved in the intervention group: maximal test time (*P*=0.0003), total turns of fan wheel (*P*=0.02), resistance of ergometer (p=0.003), power knee extension and flexion (p<0.00001), and timed up and go test (p= 0.008). Thirty other outcomes including, oxidative stress and body composition, could not be combined in the meta-analysis. Apart from work performance, trials reported no statistically significant improvements.

Authors' conclusions

There is insufficient evidence to demonstrate that aerobic exercise in adults with Down syndrome improves physical or psychosocial outcomes . Although evidence exists to support improvements in physiological and psychological aspects from strategies using mixed physical activity programmes, well-conducted research examining long-term physical outcomes, adverse effects, psychosocial outcomes and costs is required before informed practice decisions can be made.

PLAIN LANGUAGE SUMMARY

Aerobic exercise training programmes for adults with Down syndrome

Many people with Down syndrome have poor strength, poor muscle mass, and high body fat percentage and so are disposed to cardiovascular health problems. Although physical fitness has been suggested to improve physical and psychosocial health for a variety of healthy patient populations, information about the safety and effectiveness of aerobic exercise for adults with Down syndrome is lacking. This review identified only three small randomized trials. The results showed that only aspects of work performance (for example, maximal test time, maximal distance at the end of the exercise test) were improved after aerobic exercise training programs. Further well-designed research on larger population samples is required to evaluate potential benefits for psychosocial aspects in adults with Down syndrome.

BACKGROUND

Description of the condition

Down syndrome is caused by the presence of the whole or part of an extra copy of chromosome 21 (Hernandez 1996). The disorder can be diagnosed in utero by screening or karotyping, or early after birth by muscle hypotonia (poor muscle tone) and other symptoms and confirmed by karyotype analysis of a blood sample (Saenz 1999). Global estimation of the incidence of Down syndrome is 1 in 1,000 to 1 in 1,200 live births (Irving 2008; WHO 2009).

Recent biomedical and molecular studies have suggested that the chromosomal anomaly in Down syndrome determines several alterations in protein expression patterns (Cabelof 2009) which result in particular biochemical, physiological, anatomical, and behavioural characteristics such as imbalance of the oxidative metabolism (Pastore 2003; Roat 2007), impaired nervous system (Nadel 2003), musculoskeletal disorders (Merrick 2002), congenital problems of the heart (Vilas Boas 2009), narrowed airways (Schloo 1991; Uong 2001), reduced dynamic lung function (Khalili 2009) obesity (Melville 2005), poor sinus drainage (Saenz 1999), immunological abnormalities (Nespoli 1993), premature ageing (Cairney 2009), poor sleep quality (Dyken 2003; Resta 2003), and high risk of psychopathologies, dementia and behavioral problems (Coppus 2009; Nicham 2003; Urv 2008).

Among the characteristics specifically of interest for this systematic review, several authors have been reporting lower cardio-respiratory capacity among people with Down syndrome when compared with other populations, including people with learning disabilities who do not have Down syndrome (Climstein 1993; Fernhall 1996; Fernhall 2001; Guerra 2003; Pitetti 1992; Pitetti 1995), poor muscular strength and mass and high body fat percentage (Baptista 2005; Bronks 1985; Carmeli 2002; Godoy 2005).

All of the above mentioned characteristics have clear repercussions on the health status and social context of people with Down syn-

drome and their families (Handerson 2007).

Description of the intervention

It is well established that physical activity is directly related to perceived quality of life (Conn 2009). Stewart et al, identified positive relationships between quality of life and aerobic capacity in older men and women in a cross-sectional study (Stewart 2003). Likewise, it has been recognised that an active lifestyle is associated with longevity. Physical capacity can be a predictor of mortality as showed in a study involving more than 6000 men followed up over six years (Myers 2002).

Aerobic or sub-maximal exercises are defined as any physical activity where the predominant means of ATP (adenosine triphosphate) resynthesis is by aerobic metabolism provided by dynamic and continuous activities with large muscle groups. Common examples are swimming, running/jogging and hiking (Haskell 2007). Aerobic exercise is distinct from anaerobic exercise in that the energy substrates (mainly fatty acids) are metabolised with oxygen (Spurway 1992; Ahmaidi 1993). Aerobic exercise training programmes are considered the best way to improve cardio-respiratory capacity and achieve maximal fatty acid oxidation (Roberts 1996; Leijssen 2002; Achten 2003; Haskell 2007). To ensure aerobic activity, exercise sessions are performed at an intensity slightly below the anaerobic threshold (Wasserman 1973; Spurway 1992), with working heart rates maintained at around 55 to 90% of the maximal heart rate (Ahmaidi 1993; Swain 1994). The most reliable way to ensure someone is exercising within aerobic range is to conduct ergospirometric tests because predictive methods tend to distort data (Franklin 1986).

Besides particular physiological differences between aerobic and anaerobic exercise training programmes, prospective studies carried out with diverse populations show benefits associated with both aerobic and anaerobic exercise training programs. For example, Norris 1990 showed advantages of aerobic over anaerobic exercise training program for well-being in police officers. In a randomized study, Lee 2008 observed that only aerobic exercise training improved cardiorespiratory aspects, while anaerobic exercise training was associated with higher improvements of some functional aspects in patients after stroke. Among obese adults, only aerobic exercise training was associated with decreased body weight and diastolic blood pressure, but both physical exercises improved cardiorespiratory aspects (Schjerve 2008). Finaly, according to the *American College of Sports Medicine and the American Heart Association*, regular aerobic physical activities have been recommended as an effective strategy for general population to promote and maintain a good health status (Haskell 2007).

How the intervention might work

The stresses obtained through regular aerobic exercise sessions (at least three times weekly) can improve physical and psychological outcomes, including quality of life, skeletal muscle mass, body fat mass, balance and agility, and mood state (Blake 2009, DiLorenzo 1999; Haskell 2007, Mead 2009, USDHHS 2002).

Why it is important to do this review

For adults with Down syndrome, both life expectancy and potential for active functioning in society are increasing (Coppus 2009b). However, there is a lack of consistent information about the safety and effectiveness of aerobic exercise training for this population. A systematic review of the evidence that addresses psychosocial and physiological outcomes is required.

OBJECTIVES

To evaluate the effectiveness of aerobic exercise training programmes for physiological and psychosocial outcomes in adults with Down syndrome.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised or *quasi*-randomised controlled trials.

Types of participants

Adults, aged 18 or above, diagnosed with Down syndrome who are physically capable of undergoing an aerobic exercise training programme.

Types of interventions

Intervention group: supervised exercise training programme, defined as aerobic exercise (dynamic activities using large muscle groups, below the anaerobic threshold). Duration of exercise sessions may vary, but must have occurred at least three times each week for a minimum period of four weeks. Co-interventions could include the addition of instruction in health education or health awareness, but these may be analysed separately.

Control group: non-exercising group with unchanged life-styles, including activities such as physical education classes, ordinary walking, leisure activities; any non-aerobic exercise programme.

Types of outcome measures

Only standardised/validated scales or instruments (for example, the SF-36 (Ware 1992)) were considered in this review. For future versions of this review, exceptions will be made for methods tested for their internal validity (for example, concordance inter- and intra-observer or comparison with an acceptable reference standard).

Primary outcomes

1. Quality of life

2. Safety measures

- falls, exacerbation of chronic or pre-existing illness, injury or death during exercise sessions

Secondary outcomes

1. Professional/scholastic measures

- Daily tasks
- Self-esteem
- Family satisfaction
- Sleep quality
- Teacher-assessed marks
- Communication skills

2. Exercise Physiological data

- maximal heart rate;
- VO_2 max/peak (maximal or peak oxygen consumption);
- RER (respiratory exchange ratio);
- VE (pulmonary ventilation);
- AT (anaerobic threshold);
- other physiological measures (analysis of blood, urine, sweat, biopsy, any other)

3. Measures of performance

- level of activity during physical test;
- strength perception;
- agility;
- balance;
- force;
- other performance measures

4. Biometric and body composition data

- Weight;
- Body fat;
- fat mass;
- lean mass;
- other biometric measures

5. Cost data

Search methods for identification of studies

Electronic searches

The following electronic databases were searched: The Cochrane Central Register of Controlled Trials (CENTRAL) (2009, Issue 1); MEDLINE (1966 to August 2009); EMBASE (1980 to August 2009); CINAHL (1982 to August 2009); LILACS (1982 to August 2009); PsycINFO (1887 to August 2009); ERIC (1966 to August 2009); Current Controlled Trials (August 2009); and Campbell Collaboration's Social, Psychological, Educational and Criminological Register (C2- SPECTR) (to August 2009). Information about ongoing clinical trials was sought by searching ClinicalTrials.gov (http://clinicaltrials.gov) (accessed March 2007), and the National Research Register (NRR) (2009 Issue 1). No language restrictions were applied to potential trials identified for inclusion within this review. Finally, a reference manager was used to exclude duplicates (EndNote Program).

A general search strategy with descriptors and synonyms for "aerobic exercise" and "down syndrome" was adapted for each one of the databases (Appendix 1). Additionally, specialized filters for randomized controlled trials involving human beings were used in different databases (Appendix 2, Appendix 3 and Appendix 4). For the search strategy run in The Cochrane Library, there was no filter for randomized controlled trial (Appendix 5).

Searching other resources

1. Reference lists: references of the identified studies were checked for additional citations.
2. Personal contact: study authors and experts were contacted by email to request any unpublished data.
3. Supplements of the journal *Medicine and Science in Sports and Exercise* were searched.

Data collection and analysis

Selection of studies

Reviewers (RA and RED) independently screened the titles and abstracts of publications obtained by the search strategy.

Data extraction and management

Studies which fulfilled the inclusion criteria were obtained for data extraction by two reviewers (RA and RED) using a standard extraction form. Reviewers were not blinded to the names of the authors, institutions or journal of publication. All disagreements were resolved by consensus amongst the reviewers and planned referral to the editorial base of the Cochrane Developmental, Psychosocial and Learning Problems Group for arbitration was not necessary. Further information was requested from one trialist (Millar 2004).

Assessment of risk of bias in included studies

Included trials were assessed by two independent reviewers (RA and EMKS) for risk of bias based on criteria described in the Cochrane Handbook (Higgins 2008).
The following domains were assessed as 'Yes' (i.e. low risk of bias), 'Unclear' (uncertain risk of bias) or 'No' (i.e. high risk of bias).
(1) Was the sequence generation adequate?
(2) Was allocation adequately concealed?
(3) Were incomplete outcome data adequately addressed?
(4) Are reports of the study free of suggestion of selective outcome reporting?
(5) Was the study apparently free of other problems that could put it at a high risk of bias?

Measures of treatment effect

Dichotomous data

For dichotomous data, we planned to use relative risks (RR) as the effect measures with the respective 95% confidence intervals. We also planned to calculate the NNT (number need to treat, obtained from the inverse of the risk difference) for statistically significant estimate effects ($p<0.05$).

Continuous data

We planned to report continuous data as the difference between average results of intervention and control groups for all outcomes measured in the included studies (end-point and change from baseline) with respective 95% confidence intervals. Positive values favour the intervention group, while negative values favour the control group.

Synthesis of quantitative data

Where continuous and dichotomous data were reported in more than one study we planned to pool the results by using the random-effects meta-analysis model, since it is expected that estimate effects across different studies are not identical. This is the result of expected clinical and methodological differences between included studies. Specifically we planned to pool continuous data by using the weighted average of the differences between comparison groups where outcomes were published for more than one study and in the same scales. Where data are reported on different scales which cannot be adjusted to a uniform scale, we will analyse these data using the standardised mean difference (SMD).

Dichotomous and continuous data without sufficient information to insert in the forest plot.

Estimate effects reported without sufficient information to insert in the forest plot, such as number of patients, number of events, mean, standard deviation and standard error as well as estimate effects for non-parametric data (for example, range, median, percentiles) were planned to be included in the "Additional Tables".

Dealing with missing data

Authors were contacted to supply any data missing from included studies. The percentage of participants lost to follow-up is shown in '**Notes'** in the Characteristics of included studies. Reviewers planned to carry out both available case analysis and intention-to-treat analysis and to compare the results. For continuous data in which it is not possible to acquire the last observation, reviewers planned to perform available data analysis. For dichotomous data, the imputation of data will be invariably used, by assuming all of them as poor outcomes, in future updates of this systematic review. The authors of this review are aware that the insertion of unavailable data does not correspond to the reality, since the strategies for imputation of data are a matter of judgement (Higgins 2008).

Assessment of heterogeneity

The meta-analysis used random-effects models to better account for between study variation. Consistency of results were assessed visually and by calculating I^2 (Higgins 2002), a quantity which describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error.

Assessment of reporting biases

Funnel plots (trial effect versus standard error) could not be drawn as there were insufficient trials, though they may be drawn in future if sufficient data exist (Egger 1997). Clinical and methodological diversity were examined as a possible cause of bias.

Subgroup analysis and investigation of heterogeneity

The authors planned to perform subgroup analyses for gender, age, type aerobic exercise and co-interventions (for example, health education elements).

Sensitivity analysis

Impact of study quality on treatment effect will be analysed using sensitivity analysis. Intention-to-treat analysis versus available data analysis will also be investigated in future versions of this systematic review, because in the current review there are insufficient data to enable any sensitivity analysis.

RESULTS

Description of studies

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

Results of the search

The search strategy retrieved a total of 1,954 titles (without duplicates). The evolution of publications retrieved with the sensitive search strategy is shown in Figure 1. Eight articles derived from three trials were found that met criteria for inclusion in the review (Millar 1993, Varela 2001, Carmelli 2002). Fifty-five articles derived from 35 studies were excluded for reasons of study designs, and/or clinical condition out of interest, and/or intervention not of interest for this review (see Figure 2). No study was excluded by reasons of non-validated/standardized outcomes measures.

Figure 1. Cumulative relative frequency of studies retrieved with a sensitive search strategy used across all databases (from their inception to August/2009). The oldest study observed was published in 1930 (Travis 1930).

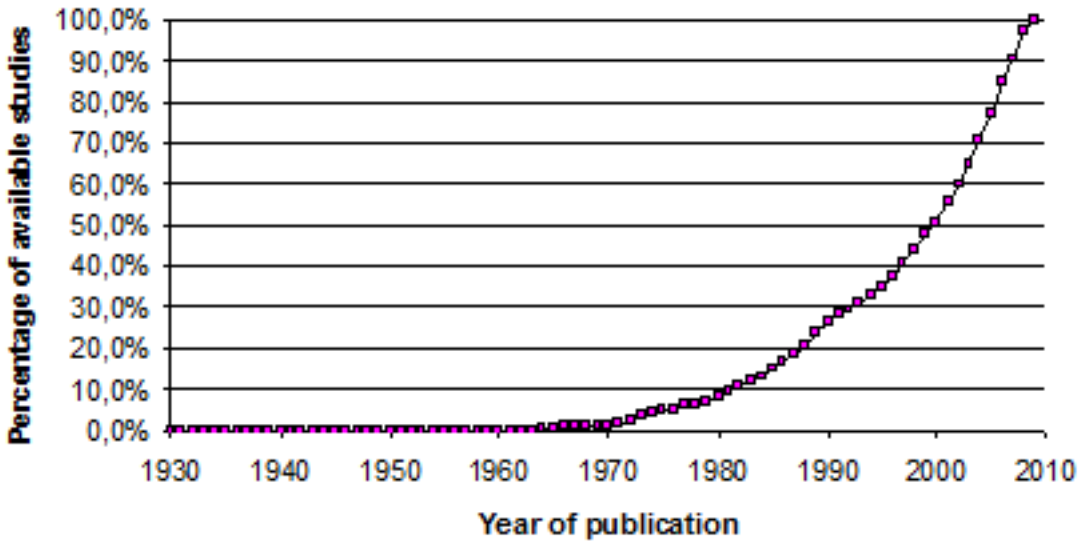
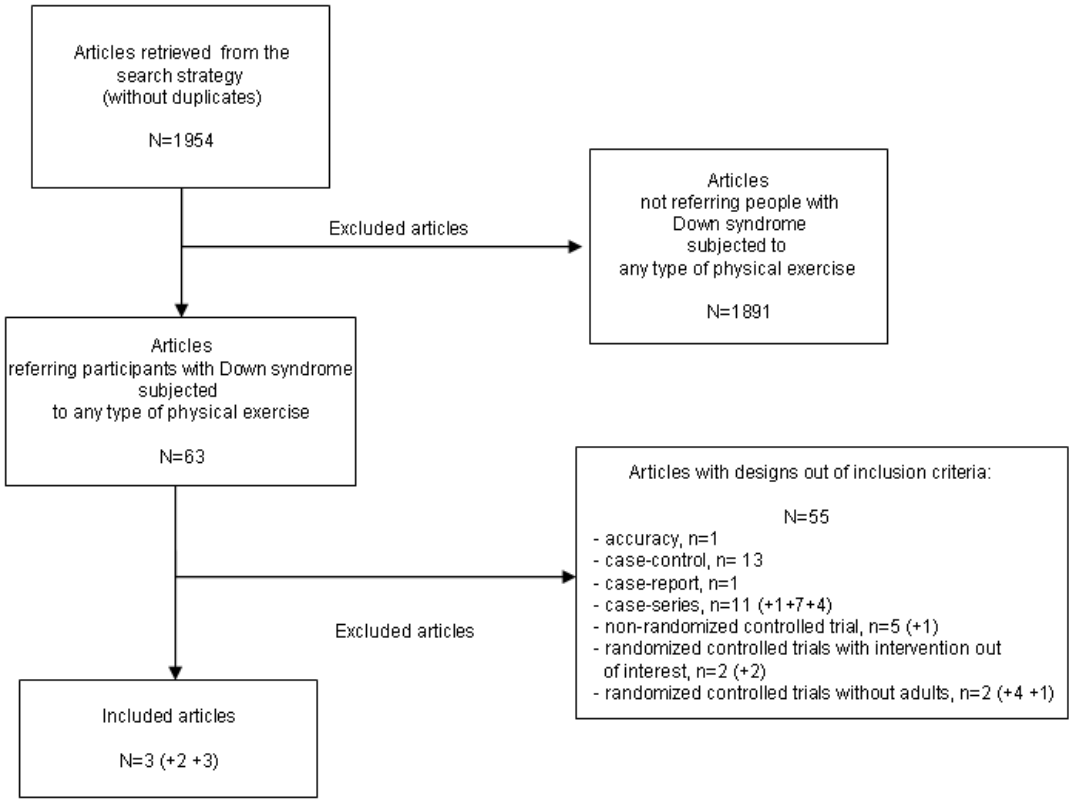


Figure 2. Flow chart of studies retrieved by the sensitive search strategy. Numbers in parentheses indicate secondary references and how many times they are repeated.



Included studies

Comparability of included studies

Three studies were included in this review and they were published in peer-reviewed publications. Millar 1993 (n=14) was carried out in USA. Varela 2001 (n=16) in Portugal and Carmelli 2002 (n= 26) in Israel. Millar 1993 and Varela 2001 had similar aged participants (mean age 19 years), but Carmelli 2002 included participants mean aged 63 years. Only Carmelli 2002 and Millar 1993 included females in the sample (n=16 and 3, respectively). Duration of interventions ranged from 10 to 25 weeks with activity bouts lasting 25 to 45 minutes, with an additional 5 to 10 minutes warm-up in two studies (Millar 1993 and Varela 2001) or active stretching exercises for five minutes (Carmelli 2002). Exercise programmes consisted of walking/jogging and rowing activities, with aerobic character guaranteed by monitoring heart rate (65 to 89% of maximal heart rate) in two studies (Millar 1993 and Varela 2001) or walking at a speed below the threshold of breathlessness (Carmelli 2002). Participants in the three trials were involved in light physical activity, three days per week. In two studies (Millar 1993 and Varela 2001) authors reported that participants usually used the bus as a means of transport to school, while Carmelli 2002 reported that all participants were resident in the foster home. With regard to cognitive status, two studies measured IQ by the Stanford Binet Intelligence Scale Carmelli 2002 (range from 56 to 75) and Varela 2001 (mean 39.4), while Millar 1993 classified the cognitive status of participants as "trainable or educable".

Comparison of outcome measures

Millar 1993 and Varela 2001 measured the following outcomes by ergoespirometric analysis: VO_2 peak ($mL \cdot Kg \cdot min^{-1}$), peak heart rate, respiratory exchange ratio (RER, $VCO_2 \cdot VO_2^{-1}$), pulmonary ventilation (VE, $L \cdot min^{-1}$) and maximal treadmill grade (%). The other outcome measures carried out on the rowing ergometer as well as those outcomes collected at rest were conduced exclusively

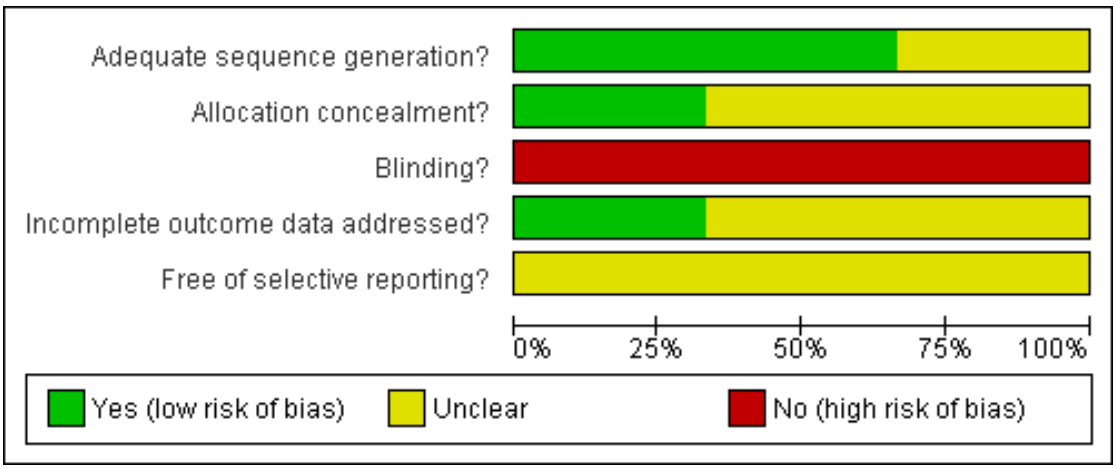
by Varela 2001. Additionally, Carmelli 2002 measured data on average power related to knee flexion and extension (watts/Kg), as well as functional capacity by means of timed-up and go test. See Characteristics of included studies.

None of the studies included in this review sought information on psychological or social outcomes for participants or their families, nor were safety measures considered as outcomes. Costs for individuals, families or service providers were not reported by authors.

Risk of bias in included studies

Please, see Risk of Bias Tables in Characteristics of included studies and Figure 3.

Figure 3. Methodological quality graph: review authors' judgements about each item of risk of bias presented as percentages across all included studies.



Randomisation and allocation concealment (Selection bias)

Method of randomisation and allocation concealment were not reported in Varela 2001. Millar 1993 did not report the method of randomisation in the paper, but described the use of random assignment, using slips pulled by another person (2:1 ratio) (Millar 2004), and upcoming random allocations were concealed from the investigators enrolling participants. A validated method of randomisation, coin toss, was used by Carmelli 2002 thus this item of internal validity was rated as of low risk of bias, but the authors did not report any method to guarantee the allocation concealment (unclear, moderate risk of bias).

Blinding (performance bias and detection bias)

Millar 1993 did not blind outcome assessors to the treatment allocation (Millar 2004, unpublished data). It was not possible to determine whether or not Carmelli 2002 and Varela 2001 did blind at least outcome assessors. The characteristic of the intervention group (supervised physical exercise training) and control group (absence of supervised physical exercise training), would prevent participants and coaches from being blinded. Thus, all studies were considered as high risk of systematic error regarding performance and detection bias (blinding).

Incomplete outcomes data addressed (Attrition bias)

Millar 1993 reported one withdrawal after randomisation, citing

the participant's abnormal electrocardiogram (Millar 2004, unpublished data). Therefore, from 10 patients randomized to the intervention group, nine accomplished the follow-up (10 weeks). Unfortunately, missing data could not be acquired because information concerning such matters was kept confidential on ethical grounds (Millar 2004, unpublished data), and authors did not carry out intent-to-treat analysis. Carmelli 2002 and Varela 2001 did not make available a flow-chart of participants through the study or make available any information about eventual withdrawals (thus, they were considered as of moderate risk of bias).

Selective reporting bias

For the three included studies (Carmelli 2002, Millar 1993 and Varela 2001), there was no suspected selection of outcomes which could reflect manipulation of data.

Methodological aspects of exercise programmes

The studies clearly described the importance of external motivation offered by the instructors during physical activities as well as familiarisation strategy with environment, procedures and evaluators, before true data collection. Moreover, Varela 2001 offered an adaptation period to the training program by dividing it in three phases based on duration of exercise bouts: phase 1, 15 minutes, three times per week for six weeks; phase 2, increasing by five more minutes per two weeks for four weeks; and phase 3, maintaining 25 minutes per session, three times a week. Carmelli 2002 offered treadmill training, three times/week, for 25 weeks, starting with 10 to 15 minutes as tolerated and then gradually increasing to 45 minutes, according to endurance improvements. Millar 1993 reported attendance at the exercise sessions as 85%, however such information is not a reliable source of information about adverse outcomes or the possibility of attrition bias due to unfortunate events such as falls, mechanical injury or feeling unwell during aerobic exercise training sessions. Carmelli 2002 reported that participants were allowed to grab the handrails for walking balance adjustments. Information concerning these aspects (safety, adaptation and attendance) were absent in Varela 2001.

Millar 1993 may have adversely affected the treatment effect by reducing exercise intensity. In this trial, monitoring of participants took place by data collectors interrupting selected participants while exercising to record their pulse. This may have changed participants' energy metabolism and affected their involvement with the activity (concentration). Moreover, this method makes it impossible to assess the intensity of the other (non-assessed) participants. Varela 2001, on the other hand, opted to monitor the intensity of training bouts by using heart rate monitors, guaranteeing that all participants were in the aerobic range during the training. Carmelli 2002 asked the participants to walk at a speed below the threshold of breathlessness but as fast as they could comfortably tolerate.

Neither author followed-up the patients after the conclusion of the physical exercise programs aiming to look for the adherence of the participants to an active lifestyle and associated outcomes.

Effects of interventions

Outcomes combined in a meta-analysis

Two studies included in this systematic review used different kinds of aerobic interventions (walking/jogging in Millar 1993 and rowing training in Varela 2001), but the aerobic character of both activities and the similarities in descriptive data regarding age, weight, height and intellectual levels between included studies were sufficiently similar to enable meta-analyses of results of maximal treadmill tests. Both studies evaluated peak VO_2 ($mL \cdot Kg^{-1} \cdot min^{-1}$), maximal heart rate (HR, beats per minute), expiratory exchange ratio (VCO_2/VO_2), pulmonary ventilation (VE, $L \cdot min^{-1}$) and maximal treadmill grade (%), all of which were measured in maximal treadmill exercise test.

Results of meta-analyses showed statistically significant difference favouring the intervention group only for maximal treadmill grade, a work performance variable [WMD 4.26 (95% CI 2.06, 6.45)% grade, P= 0.0001) (Analysis 1.5).

No statistically significant differences between intervention and control groups were found in the meta-analyses of VO_2 peak, [0.30 (95% CI 3.17, 3.77) $mL \cdot Kg \cdot min^{-1}$, P=0.87] (Analysis 1.1); peak heart rate [2.84 (95% CI 5.05, 10.73) beats per minute, P= 0.48] (Analysis 1.2); respiratory exchange ratio (RER) [-0.01(95% CI -0.06, 0.04) $VCO_2 \cdot VO_2^{-1}$, P=0.70] (Analysis 1.3); and pulmonary ventilation [5.86 (95%CI , -4.34, 16.06) $L \cdot min^{-1}$, P= 0.26] (Analysis 1.4).

Despite methodological diversity regarding type of intervention (rowing vs walking), duration (10 vs 16 weeks) and methods of monitoring intensity, there was no heterogeneity that could be indicated by statistical tests (indicated by $P<0.01$ and I^2 >50% or chi^2<df) for any of the outcomes analysed.

Because of the existence of one withdrawal in one of the included studies (Millar 1993), intention-to-treat analysis would have been feasible had raw data been available (Millar 2004, unpublished data). Informal analysis showed no statistically significant differences between available case versus intention-to-treat analysis when missing data were assumed to be the same value as average baseline data.

Outcomes that could not be combined in a meta-analysis

Varela 2001 reported seven variables obtained from maximal rowing ergometer test, besides those seven measured in the treadmill test. The following aspects of work performance showed statistically significant differences in favour of the intervention as com-

pared to the control group: maximal test time (*P*=0.0003, Analysis 2.5), total turns of fan wheel (*P*=0.02, Analysis 2.6) and resistance of rowing ergometer (*P*=0.003). Maximal test time and maximal distance-also measured on a treadmill, but not available in the Millar 1993 study reported statistically significant results favouring the intervention group (*P*=0.005 and *P*=0.001, respectively). No statistically significant differences in variables collected in rowing ergometer test between intervention and control groups for the cardiorespiratory variables were observed (VO_2 peak, HR, RER and VE).

In Varela 2001, statistically significant differences favouring the intervention group (rowing) as compared to the control group in some variables collected at rest were observed: red blood cell oxidized glutathione (*P*=0.00001, Analysis 3.16), a molecule thought to be an indicator of oxidative stress (a condition associated with ageing process); and plasma reduced glutathione, a molecule that is thought to be an indicator of antioxidant status (Uhlig 1992) (*P*= 0.0001, Analysis 3.17). However, the statistically significant difference observed for plasma zinc, a chemical element related with important antioxidant role (Berg 1996) favoured the control group (*P*=0.02, Analysis 3.13). No statistically significant difference between comparison groups was observed for all of the other outcomes measured in this trial (Varela 2001): oxidative profile (red blood cell magnesium, selenium, copper, zinc, superoxide dismutase and reduced glutathione, plasma magnesium, selenium, copper, oxidized glutathione) and body composition (weight, body fat, lean mass, fat mass and bone mineral content). There was a difference favouring the control group as compared to the intervention group for thiobarbituric acid reactive substances (MD -2.28). This variable is assumed to be one of the indicators of probable oxidative stress (Hartman 1983). However, the difference was not statistically significant (CI 95% -4.56, 0.00, P=0.05) (Analysis 3.19).

Neither outcomes relative to oxidative stress nor body fat, lean mass, fat mass and mineral content mentioned above were measured by Millar 1993.

Only one study (Carmelli 2002) which included older participants (57 to 65 years) has reported improvements on average power for knee extension [MD 17.72 (95% CI 15.91, 19.53), p<0.00001, Analysis 4.1] (watts/Kg-angular velocity at 60/°s) in the intervention group as compared to the control group. The subgroup composed by men showed higher effects as compared to women, probably explaining the I^2 (heterogeneity test) of 72%. Improvements in the intervention group as compared to the control group were also observed for average power for Knee flexion (watts/Kg-angular velocity at 60/°s) [MD 20.57 (16.56, 24.58), p=0.0001, Analysis 4.2]. Again, the subgroup composed by men showed better estimate effects as compared to women. Thus, gender was assumed as the probable reason for the I^2 (heterogeneity test) of 72%. The timed-up and go test (seconds), the other outcome measured by Carmelli 2002 showed results favouring the intervention group as compared to the control group [MD 3.20 (95% CI 0.83, 5.57), p=0.08, Analysis 5.1]. The authors did not make available separate data for men and women for the timed-up and go test.

Authors of included studies did not look for outcomes closely related to the quality of life, including mood state, professional or familial satisfaction, or other psychosocial aspects, measured in a systematic way.

DISCUSSION

Only three trials were obtained, despite an extensive literature search (Carmelli 2002, Millar 1993, Varela 2001). While it is possible that some unpublished trials exist, it is most likely that the inherent difficulties of carrying out trials of physical interventions for people with learning disabilities is the reason only a small number of potentially relevant studies were identified. It is also likely that assumptions about positive effects of physical activities for this population have been made based on evidence from the general population.

The fact that only three studies relevant to this review could be identified, and that they were very small (total number of participants equalled only 56) and gender-biased (37 males to 19 females) indicates that very little published evidence of high quality has been produced in this area. Furthermore, the large confidence interval around the point estimates for the majority of variables analysed and the diversity of data (for which meta-analysis was largely inappropriate) limit the external validity of the results obtained.

The only well-supported evidence of improvement in physiological outcomes besides work performance (Rimmer 2004), and for improvements in psychological outcomes (Heller 2004) comes from other controlled trials which focus on mixed physical activities, not purpose-designed aerobic exercise training programmes. Rimmer 2004 sought to demystify outdated and inconsistent claims made by cross-sectional studies (Eberhard 1989, Pitetti 1992, Fernhall 1996) and *in vitro* studies (Ogawa 2002) which presented physiological impairments as indicators of the supposed unresponsiveness of people with Down syndrome to aerobic exercise training. Moreover, we have found an uncontrolled study in adolescents which used a case-series design and which reported favourable results on fat mass and two physiological parameters (Ordoñez 2006).

Caution must be exercised when making decisions based on the results of this review. A systematic review in this area (Dodd 2005) has reported superior estimate effects for VO_2 peak, minute ventilation and work performance variables in a non-randomised study (Tsimaras 2004, cited in our systematic review as a secondary reference: Tsimaras 2003) as compared to the other randomised studies included by them (Rimmer 2004, Tsimaras 2004, Millar

1993 and Varela 2001). It is fundamental to remember that non-randomised studies tend to overestimate the effects of treatments (Kunz 2006). Moreover Dodd 2005 employed inclusion criteria which were wide, taking in all types of exercise training programmes (for example, aerobic, resistive, jumping and plyometric exercises), allowing therefore the inclusion of Rimmer 2004 in its meta-analysis (Dodd 2005).

Because studies do not currently formally measure occurrence of falls, injuries or adverse events at all during exercise sessions, it is not yet possible to recommend a physical exercise training program as an invariably safe intervention for adults with Down syndrome. However, Carmelli 2002, a study which included older Down syndrome participants (mean age 63 years old), reported no undesired event during a six-month exercise training program.

There is a rich literature on the optimum duration of exercise for adults without learning disabilities (Carr 2003, Haskell 2007, Moreira 1999, Seggar 1998); however, less is published concerning exercise for those with learning disabilities and the duration of exercise training used by the authors here (10 weeks in Millar 1993 and 16 weeks in Varela 2001) could provoke discussion about benefits. Possible differences caused by dose-response effects of an aerobic exercise training programme for Down syndrome remain uncertain.

Besides the paucity of evidence regarding outcomes concerned with psychosocial health as well as safety and cost aspects of an aerobic exercise as an option for health of adults with Down syndrome, the reviewers also have detected a lack of information about long-term potential benefits. We would advise future trialists to emphasise strategies which follow up how well participants continue to adhere to an active lifestyle and measure its consequences, including maintenance of body composition, psychosocial health and independence.

AUTHORS' CONCLUSIONS

Implications for practice

In spite of the fact that moderate and regular physical exercise is popular and established as a sound lifestyle decision both for health and as an intervention to improve quality of life in the general population, current evidence from published studies suggest that in adults with Down syndrome work performance outcomes may be improved by aerobic exercise training programmes, regardless of age range within adulthood. However, cardiorespiratory measures may not be improved. Aspects of quality of life like psychosocial outcomes, safety, and dose-response await systematic evaluation. Overall, the effectiveness of aerobic exercise training programmes in improving the health of adults with Down syndrome remains uncertain.

Implications for research

In light of increasing popular demand for physical fitness, the importance of well-conducted trials involving physical training for people with learning disabilities should be recognised, particularly for those people with conditions like Down syndrome which put special stresses on their physiology. There is a paucity of published studies investigating the effects of aerobic exercise for adults with Down syndrome and an even smaller number of trials of sufficient methodological rigour to determine the effectiveness of such intervention.

Future trials should ensure that interventions are appropriate to this population, with regard to physiological and behavioural aspects. Methodological procedures should guarantee precision for a range of intensities and motivation levels. Standardised methods and outcome assessment is required to facilitate future data syntheses, particularly where sample sizes are small. Formal quantifying of adverse events such as mechanical injuries, falls or feeling unwell during exercise sessions is essential. Cost-benefit analyses of aerobic interventions should be conducted. Finally, attention to long-term maintenance of any improvements caused by aerobic exercise training programmes, adherence of participants to an active lifestyle, and issues of dose-response are all important to the design of future research.

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REFERENCES

References to studies included in this review

Carmelli 2002 *{published data only}*

* Carmeli E, Kessel S, Coleman R, Ayalon M. Effects of a treadmill walking program on muscle strength and balance in elderly people with Down syndrome. *Journals of Gerontology Series A: Biological Sciences & Medical Sciences* 2002;**57**(2):M106–10. [PUBMED: 11818429]

Millar 1993 *{published data only}*

Millar AL, Fernhall B, Burkett LN. Effects of aerobic training for individuals with down syndrome. *Palaestra* 1995;**11**(4):10.

* Millar AL, Fernhall B, Burkett LN. Effects of aerobic training in adolescents with Down syndrome. *Medicine and Science in Sports and Exercise* 1993;**25**(2):270–4. [MEDLINE: 8450732]

Millar AL, Fernhall B, Burkett LN, Tymeson G. Effects of training on maximal oxygen uptake of mentally retarded adolescents and adults. *Medicine and Science in Sports and Exercise* 1988;**20**:S28.

Varela 2001 *{published data only}*

Baptista F, Varela A, Teixeira P, Sardinha LB. The effects of aerobic exercise training program in body composition on Down syndrome subjects (Abstract no. 183). *Medicine and Science in Sports and Exercise* 1996;**28**(5 [Supplement: Annual Meeting Abstracts]):31.

Monteiro CP, Varela A, Pinto M, Neves J, Felisberto GM, Vaz C, et al.Effect of an aerobic training on magnesium, trace elements and antioxidant systems in a Down syndrome population. *Magnesium Research* 1997;**10**(1):65–71. [MEDLINE: 9339840]

Varela A, Sardinha LB, Pitetti KH. Effects of aerobic rowing training in adults with Down syndrome. *Medicine and Science in Sports and Exercise* 1997;**29**(Suppl):S244 [Abstract].

* Varela A, Sardinha LB, Pitetti KH. Effects of an aerobic rowing training regimen in young adults with Down syndrome. *American Journal of Mental Retardation* 2001; **106**(2):135. [MEDLINE: 11321604]

References to studies excluded from this review

Agiovlasitis 2009 *{published data only}*

Agiovlasitis S, McCubbin JA, Pavol MJ, Widrick JJ. Economy and preferred speed of walking in adults with and without down syndrome. *Adapted Physical Activity Quarterly* 2009;**26**(2):118–30. [: 2010242967]

Aguiar 2008 *{published data only}*

Aguiar AS Jr, Tuon T, Albuquerque MM, Rocha GS, Speck AE, Araujo JC, et al.The exercise redox paradigm in the Down's syndrome: improvements in motor function and increases in blood oxidative status in young adults. *Journal of Neural Transmission* 2008;**115**(12):1643–50. [PUBMED: 18795225]

Angulo-Barroso 2008 *{published data only}*

* Angulo-Barroso R, Burghardt AR, Lloyd M, Ulrich DA. Physical activity in infants with Down syndrome receiving a treadmill intervention. *Infant Behavior & Development* 2008;**31**(2):255–69. [PUBMED: 2008–03374–010]

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):231–8. [PUBMED: 17940103]

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. [PUBMED: 17940103]

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 & Child Neurology* 2007;**49**(11):839–45. [PUBMED: 2007–18585–010]

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**(2):261–72. [PUBMED: 2008–06239–007]

Black 2007 *{published data only}*

Black DP, Smith BA, Wu J, Ulrich BD. Uncontrolled manifold analysis of segmental angle variability during walking: Preadolescents with and without Down syndrome. *Experimental Brain Research* 2007;**183**(4):511–21. [: 2008–01182–009]

Black 2009 *{published data only}*

Black D, Chang CL, Kubo M, Holt K, Ulrich B. Developmental trajectory of dynamic resource utilization during walking: toddlers with and without Down syndrome. *Human Movement Science* 2009;**28**(1):141–54. [PUBMED: 18977548]

Bricout 2008 *{published data only}*

Bricout VA, Guinot M, Faure P, Flore P, Eberhard Y, Garnier P, et al.Are hormonal responses to exercise in young men with Down's syndrome related to reduced endurance performance?. *Journal of Neuroendocrinology* 2008;**20**(5): 558–65. [: 2008–04912–003]

Carmeli 2004 *{published data only}*

Carmeli E, Barchad S, Masharawi Y, Coleman R. Impact of a walking program in people with Down syndrome. *Journal of Strength & Conditioning Research* 2004;**18**(1):180–4. [MEDLINE: 14971963]

Chang 2009 *{published data only}*

Chang CL, Kubo M, Ulrich BD. Emergence of neuromuscular patterns during walking in toddlers with typical development and with Down syndrome. *Human Movement Science* 2009;**28**(2):283–96. [PUBMED: 19272665]

Dupont 1987 *{published data only}*

Dupont BB, Schulmann D. Dance therapy with physical therapy for children with Down syndrome. Education Resources Information Center 1987:19. [: ED300960]

Dyer 1994 *{published data only}*

Dyer SM. *The effects of a health related fitness program on the physical, cognitive, social and affective development of Down syndrome subjects aged eight to seventeen (PhD thesis)*. Cairns/Townsville, Australia: James Cook University of North Queensland, 1992.

* Dyer SM. Physiological effects of a 13-week physical fitness program on Down syndrome subjects. *Pediatric Exercise Science* 1994;**6**:88–100.

Eberhard 1989 *{published data only}*

Eberhard Y, Eterradossi J, Rapacchi B. Physical aptitudes to exertion in children with Down's syndrome. *Journal of Mental Deficiency Research* 1989;**33**(Pt 2):167–74. [PUBMED: 2524596]

Eberhard 1990 *{published data only}*

* Eberhard Y, Eterradossi J. Effects of physical exercise in adolescents with Down's syndrome. In: Springer-Verlag, Berlin Heidelberg editor(s). *Adapted Physical Activity - an interdisciplinary approach*. Vol. **16**, New York: Doll-Tepper/Dahms/Döll/von Selzam C., 1990:281–287.

Eberhard 1993 *{published data only}*

Eberhard Y, Eterradossi J, Foulon T, Groslambert P. Changes in plasma lipoproteins in adolescents with trisomy 21 in response to a physical endurance test [Variations des lipoprotéines plasmatiques chez des adolescents trisomiques 21 en réponse à un test déndurance physique]. *Pathologie Biologie (Paris)* 1993;**41**(5):482–6. [MEDLINE: 8414682]

Eberhard 1997 *{published data only}*

* Eberhard Y, Eterradossi J, Debû B. Biological changes induced by physical activity in individuals with Down syndrome. *Adapted Physical Activity Quaterly* 1997;**14**(2):166–75.

Flore 2008 *{published data only}*

Flore P, Bricout VA, van Biesen D, Guinot M, Laporte F, Pepin JL, et al.Oxidative stress and metabolism at rest and during exercise in persons with Down syndrome. *European Journal of Cardiovascular Prevention and Rehabilitation* 2008;**15**(1):35–42. [PUBMED: 18277183]

Galli 2008 *{published data only}*

Galli M, Rigoldi C, Brunner R, Virji-Babul N, Giorgio A. Joint stiffness and gait pattern evaluation in children with Down syndrome. *Gait Posture* 2008;**28**(3):502–6. [PUBMED: 18455922]

Guerra 2009 *{published data only}*

Guerra M, Gine-Garriga M, Fernhall B. Reliability of Wingate testing in adolescents with Down syndrome. *Pediatric Exercise Science* 2009;**21**(1):47–54. [PUBMED: 19411710]

Heffernan 2009 *{published data only}*

Heffernan KS, Sosnoff JJ, Ofori E, Jae SY, Baynard T, Collier SR, et al.Complexity of force output during static exercise in individuals with Down syndrome. *Journal of Applied Physiology* 2009;**106**(4):1227–33. [PUBMED: 19164775]

Lafferty 2005 *{published data only}*

* Lafferty ME. A stair-walking intervention strategy for children with Down's syndrome. *Journal of Bodywork and Movement Therapies* 2005;**9**(1):65–74.

LaForme 2007 *{published data only}*

LaForme Fiss AC, B. Effect of increased practice time using sensorimotor groups on gross motor skill acquisition for children with Down syndrome. ProQuest Information & Learning: US [Thesis] 2007.

LaForme 2009 *{published data only}*

LaForme Fiss AC, Effgen SK, Page J, Shasby S. Effect of sensorimotor groups on gross motor acquisition for young children with Down syndrome. *Pediatric Physical Therapy* 2009;**21**(2):158–66. [PUBMED: 19440]

Lewis 2005 *{published data only}*

Lewis CL, Fragala-Pinkham MA. Effects of aerobic conditioning and strength training on a child with Down syndrome: a case study. *Pediatric Physical Therapy* 2005;**17**(1):30–6.

Lloyd 2008 *{published data only}*

Lloyd MC. Physical activity of preschool age children with and without Down syndrome (Thesis). University of Michigan 2008. [: 2010060819]

Mendonça 2009 *{published data only}*

Mendonça GV, Pereira FD, Fernhall B. Walking economy in male adults with Down syndrome. *European Journal of Applied Physiology* 2009;**105**(1):153–7. [PUBMED: 18850109]

Mendonça 2009a *{published data only}*

Mendonça GV, Pereira FD. Influence of long-term exercise training on submaximal and peak aerobic capacity and locomotor economy in adult males with Down's syndrome. *Medical Science Monitor* 2009;**15**(2):CR33–9. [PUBMED: 19179964]

Ordoñez 2006 *{published data only}*

* Ordoñez FJ, Rosety M, Rosety-Rodriguez M. Influence of 12-week exercise training on fat mass percentage in adolescents with Down syndrome. *Medical Science Monitor* 2006;**12**(10):CR416–9.

Ordoñez FJ, Rosety M, Rosety-Rodriguez M. Regular exercise did not modify significantly superoxide dismutase activity in adolescents with Down's syndrome. *British Journal of Sports Medicine* 2006;**40**(8):717–8.

Ordoñez FJ, Rosety M, Rosety-Rodriguez M. Regular physical activity increases glutathione peroxidase activity in adolescents with Down syndrome Regular physical activity increases glutathione peroxidase activity in adolescents with Down syndrome. *Clinical Journal of Sport Medicine* 2006;**16**(4):355–6.

Ordoñez FJ, Rosety-Rodriguez M. Correlation between glutathione peroxidase activity and anthropometrical

parameters in adolescents with Down syndrome. *Research in Developmental Disabilities* 2006;**28**(1):105–8. [: 16563697]
Ordoñez FJ, Rosety-Rodriguez M. Regular exercise attenuated lipid peroxidation in adolescents with Down's syndrome. *Clinical Biochemistry* 2007;**40**(1-2):141–2. [PUBMED: 17123499]
Ordoñez FJ, Rosety-Rodriguez M, Rosety M. A 12-week physical activity program increases glucose-6-phosphate-dehydrogenase activity in Down syndrome adolescents [Portuguese]. *Medicina (Buenos Aires)* 2005;**65**(6):518–20.
Rosety-Rodriguez M, Rosety I, Fornieles-Gonzalez G, Diaz A, Rosety M, Ordoñez FJ. A 12-week aerobic training program reduced plasmatic allantoin in adolescents with Down syndrome. *British Journal of Sports Medicine* 2008; **[Epub ahead of print]**.
Rosety-Rodriguez M, Rosety M, Ordoñez FJ. Influence of regular exercise on erythrocyte catalase activity in adolescents with Down syndrome. *Medicina Clínica (Barcelona)* 2006;**127**(14):533–4.

Perán 1997 ***{published data only}***
Perán S, Gil JL. The contribution of the practice of athletics in the promotion of health, recuperation and rehabilitation in people with Down syndrome [Contribución a la práctica del atletismo a la promoción de la salud, recuperación y rehabilitación de personas con síndrome de Down]. *Revista Síndrome de Down* 1995;**12**(1):103–6.
Perán S, Gil JL, Ruiz F. Athleticism and sporting activities in people with Down syndrome [Atletismo y deporte en personas con síndrome de Down: Research de un proyecto]. *Revista Síndrome de Down* 1996;**13**(1):27–8.
Perán S, Gil JL, Ruiz F, Balbuena FR. Athletic competition and Down syndrome. *Down Syndrome: Research and Practice* 1996;**4**(1):43–4.
* Perán S, Gil JL, Ruiz F, Fernandez-Pastor V. Development of physical response after athletics training in adolescents with Down's syndrome. *Scandinavian Journal of Medicine & Science in Sports* 1997;**7**(5):283–8. [MEDLINE: 9338946]
Perán S, Gil JL, Ruiz F, Sánchez JJ. Improvements in physical performance and its clinical repercussions dispose people with Down syndrome to the entertainment in athletism [Evolución Del rendimiento físico y su repercusión sobre los aspectos clínicos tras el entrenamiento de atletismo en personas con síndrome de Down]. *Síndrome de Down. Artículos y Resumes Científicos* 1995;**25**:1–6.

Rimmer 2004 ***{published data only}***
Heller T, Hsieh K, Rimmer JH. Attitudinal and psychosocial outcomes of a fitness and health education program on adults with Down syndrome. *American Journal of Mental Retardation* 2004;**109**(2):175–85.
* Rimmer JH, Heller T, Wang E, Valerio I. Improvements in physical fitness in adults with Down syndrome. *American Journal of Mental Retardation* 2004;**109**(2):165–74. [MEDLINE: 15000673]
Valerio I, Rimmer J H, Heller T, Wang E. Improving physical fitness in adults with Down syndrome. *Medicine and Science in Sports and Exercise* 2003;**35 (Suppl)**(5):S374.

Shields 2008 ***{published data only}***
Shields N, Taylor NF, Dodd KJ. Effects of a community-based progressive resistance training program on muscle performance and physical function in adults with Down syndrome: a randomized controlled trial. *Archives of Physical Medicine & Rehabilitation* 2008;**89**(7):1215–20. [PUBMED: 18586124]

Skrobak 1980 ***{published data only}***
* Skrobak-Kaczynski J, Vavik T. Physical fitness and trainability of young male patients with Down syndrome. In: K. Berg& B. O. Ericksson editor(s). *Children and Exercise: IX. International Series on Sports Sciences*. Vol. **10**, Baltimore: Park Press, 1980:300–16.

Smith 2007 ***{published data only}***
Smith BA, Kubo M, Black DP, Holt KG, Ulrich BD. Effect of practice on a novel task - walking on a treadmill: preadolescents with and without Down syndrome. *Physical Therapy* 2007;**87**(6):766–77. [PUBMED: 17442836]

Tsimaras 2004 ***{published data only}***
Tsimaras V, Giagazoglou P, Fotiadou E, Christoulas K, Angelopoulou N. Jog-walk training cardiorespiratory fitness of adults with Down syndrome. *Perceptual & Motor Skills* 2003;**96**(3 [Pt 2]):1239–51.
* Tsimaras VK, Fotiadou EG. Effect of training on the muscle strength and dynamic balance ability of adults with down syndrome. *Journal of Strength & Conditioning Research* 2004;**18**(2):343–7. [MEDLINE: 15142004]

Ulrich 2001 ***{published data only}***
Rizzo T. Early intervention to facilitate walking in infants with Down syndrome (book). *Adapted Physical Activity Quarterly* 2002;**19**(3):397. [: 3000012613]
* 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. [MEDLINE: 11694668]

Weber 1986 ***{published data only}***
Weber RC, A P. Effects of strength development training programs for Down's Syndrome adolescents [Thesis]. ProQuest Information & Learning: US 1986.

Additional references

Achten 2003
Achten J, Jeukendrup AE. Maximal fat oxidation during exercise in trained men. *International Journal of Sports Medicine* 2003;**24**(8):603–8. [MEDLINE: 14598198]

Ahmaidi 1993
Ahmaidi S, Hardy JM, Varray A, Collomp K, Mercier J, Prefault C. Respiratory gas exchange indices used to detect the blood lactate accumulation threshold during an incremental exercise test in young athletes. *European Journal of Applied Physiology & Occupational Physiology* 1993;**66**(1): 31–36. [MEDLINE: 8425510]

Baptista 2005
Baptista F, Varela A, Sarbinha LB. Bone mineral mass in males and females with and without Down syndrome.

Osteoporosis International 2005;**16**:380–8. [DOI: 10.1007/s00198-004-1687-1]

Berg 1996
Berg JM, Shi Y. The galvanization of biology: a growing appreciation for the roles of zinc. *Science* 1996;**271**(5252):1081–5. [MEDLINE: 8599083]

Blake 2009
Blake H, Mo P, Malik S, Thomas S. How effective are physical activity interventions for alleviating depressive symptoms in older people? A systematic review. *Clinical Rehabilitation* 2009;**23**(10):873–87. [PUBMED: 19675114]

Bronks 1985
Bronks R, Parker AW. Anthropometric observation of adults with Down syndrome. *American Journal of Mental Deficiency* 1985;**90**(1):110–3. [MEDLINE: 3161328]

Cabelof 2009
Cabelof DC, Patel HV, Chen Q, van Remmen H, Matherly LH, Ge Y, et al.Mutational spectrum at GATA1 provides insights into mutagenesis and leukemogenesis in Down syndrome. *Blood* 2009;**114**(13):2752–63. [PUBMED: 19633202]

Cairney 2009
Cairney CJ, Sanguinetti G, Ranghini E, Chantry AD, Nostro MC, Bhattacharyya A, et al.A systems biology approach to Down syndrome: identification of Notch/Wnt dysregulation in a model of stem cells aging. *Biochimica et Biophysica Acta* 2009;**1792**(4):353–63. [PUBMED: 19419698]

Carmeli 2002
Carmeli E, Aylon M, Barchad S, Sheklow SL, Reznick AZ. Isokinetic leg strength of institutionalized older adults with mental retardation with and without Down's syndrome. *Journal of Strength & Conditioning Research* 2002;**16**(2):316–20. [MEDLINE: 11991788]

Carr 2003
Carr M, Jones J. Physiological effects of exercise on stroke survivors. *Topics in Stroke Rehabilitation* 2003;**9**(4):57–64.

Climstein 1993
Climstein M, Pitetti KH, Barret PJ, Campbell KD. The accuracy of predicting treadmill VO2max for adults with mental retardation, with and without Down's syndrome, using ACSM gender- and activity-specific regression equations. *Journal of Intellectual Disability Research* 1993;**37**(Pt 6):521–31. [MEDLINE: 8123998]

Conn 2009
Conn VS, Hafdahl AR, Brown LM. Meta-analysis of quality-of-life outcomes from physical activity interventions. *Nursing Research* 2009;**58**(3):175–83. [PUBMED: 19448521]

Coppus 2009
Coppus A, Evenhuis H, Verberne GJ, Visser F, van Gool P, Eikelenboom P, et al.Dementia and mortality in persons with Down's syndrome. *Journal of Intellectual Disability Research* 2006;**50**(Pt 10):768–77. [PUBMED: 16961706]

Coppus 2009b
Coppus AM, Evenhuis HM, Verberne GJ, Visser FE, Oostra BA, Eikelenboom P, et al.Survival in elderly persons with Down syndrome. *Journal of the American Geriatrics Society* 2008;**56**(12):2311–6. [PUBMED: 19093931]

DiLorenzo 1999
DiLorenzo TM, Bargman EP, Stucky-Ropp R, Brassington GS, Frensch PA, La Fountaine T. Long-term effects of aerobic exercise on psychological outcomes. *Preventive Medicine* 1999;**28**(1):75–85. [MEDLINE: 9973590]

Dodd 2005
Dodd KJ Shields N. A systematic review of the outcomes of cardiovascular exercise programs for people with Down syndrome. *Archives of Physical Medicine & Rehabilitation* 2005;**86**(10):2051–8.

Dyken 2003
Dyken ME, Lin-Dyken DC, Poulton S, Zimmerman MB, Sedars E. Prospective polysomnographic analysis of obstructive sleep apnea in down syndrome. *Archives of Pediatrics & Adolescent Medicine* 2003;**157**(7):655–60. [MEDLINE: 12860786]

Eberhard 1989
Eberhard Y, Eterradossi J, Rapacchi B. Physical aptitudes to exertion in children with Down's syndrome. *Journal of Mental Deficiency Research* 1989;**33**(Pt2):167–74. [MEDLINE: 2524596]

Egger 1997
Egger M, Davey-Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphic test. *British Medical Journal* 1997;**315**(7):629–34.

Fernhall 1996
Fernhall BO, Pitetti KH, Rimmer JH, McCubbin JA, Rintala P, Millar AL, et al.Cardiorespiratory capacity of individuals with mental retardation including Down syndrome. *Medicine & Science in Sports & Exercise* 1996;**28**(3):366–71. [MEDLINE: 8776225]

Fernhall 2001
Fernhall BO, McCubbin JA, Pitetti KH, Rintala P, Rimmer JH, Millar L, et al.Prediction of maximal heart rate in individuals with mental retardation. *Medicine & Science in Sports & Exercise* 2001;**33**(10):1655–60. [MEDLINE: 11581548]

Franklin 1986
Franklin BA. Pitfalls in estimating aerobic capacity from exercise time or workload. *Applied Cardiology* 1986;**14**:25–6.

Godoy 2005
Godoy JR, Barros J de F. Palmar force in Down syndrome people. Analysis of involved muscles [Força de preensão palmar em portadores da síndrome de Down e análise dos músculos envolvidos neste movimento]. *Acta Cirúrgica Brasileira* 2005;**20**(Suppl 1):159–66. [PUBMED: 17768804]

Guerra 2003
Guerra M, Liorenz N, Fernhall B. Chronotropic incompetence in persons with Down syndrome. *Archives*

of Physical Medicine & Rehabilitation 2003;**84**(11):1604–8. [MEDLINE: 14639558]

Handerson 2007

Henderson A, Lynch SA, Wilkinson S, Hunter M. Adults with Down's syndrome: the prevalence of complications and health care in the community. *British Journal of General Practice* 2007;**57**(534):50–5. [PUBMED: 17244425]

Hartman 1983

Hartman PE. Putative mutagens and carcinogens in foods. IV. Malonaldehyde (malondialdehyde). *Environ Mutagen* 1983;**5**(4):603–7. [MEDLINE: 6347681]

Haskell 2007

Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al.Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;**116**(9):1081–93. [PUBMED: 17671237]

Heller 2004

Heller T, Hsieh K, Rimmer JH. Attitudinal and psychosocial outcomes of a fitness and health education program on adults with Down syndrome. *American Journal of Mental Retardation* 2004;**109**(2):175–85. [MEDLINE: 15000672]

Hernandez 1996

Hernandez D, Fisher EMC. Down syndrome genetics: unravelling a multifactorial disorder. *Human Molecular Genetics* 1996;**5**:1411–6.

Higgins 2002

Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;**21**:1539–58.

Higgins 2008

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 [updated September 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org. Chichester, UK.

Irving 2008

Irving C, Basu A, RichmondS, Burn J, Wren C. Twenty-year trends in prevalence and survival of Down syndrome. *European Journal of Human Genetics* 2008;**16**(11):1336–40. [PUBMED: 18596694]

Khalili 2009

Khalili MA, Elkins MR. Aerobic exercise improves lung function in children with intellectual disability: a randomised trial. *The Australian Journal of Physiotherapy* 2009;**55**(3):171–5. [PUBMED: 19681738]

Kunz 2006

Kunz R, Vist G, Oxman AD. Randomisation to protect against selection bias in healthcare trials. *Cochrane Database of Systematic Reviews* 2006, Issue 1. [DOI: 10.1002/14651858.MR000012.pub2]

Lee 2008

Lee MJ, Kilbreath SL, Singh MF, Zeman B, Lord SR, Raymond J, Davis GM. Comparison of effect of aerobic cycle training and progressive resistance training on walking ability after stroke: a randomized sham exercise-controlled study. *Journal of the American Geriatrics Society* 2008;**56**(6):976–85. [PUBMED: 18422947]

Leijssen 2002

Leijssen DP, Saris WH, Wagenmakers AJ, Senden JM, Van Baak MA. Effects of exercise training at different intensities on fat metabolism of obese. *Obesity Research* 2002;**92**(3):1300–9.

Mead 2009

Mead GE, Morley W, CampbellP, Greig CA, McMurdo M, Lawlor DA. Exercise for depression. *Cochrane Database of Systematic Reviews* 2009, Issue 3. [DOI: 10.1002/14651858]

Melville 2005

Melville CA, Cooper SA, McGrother CW, Thorp CF, Collacott R. Obesity in adults with Down syndrome: a case-control study.. *Journal of Intellectual Disability Research* 2005;**49**(Pt 2):125–33. [PUBMED: 15634321]

Merrick 2002

Merrick J, Ezra E, Josef B, Hendel D, Steinberg DM, Wientroub S. Musculoskeletal problems in Down syndrome European paediatric orthopaedic society survey: the Israeli sample. *Journal of Pediatric Orthopaedics, Part B* 2002;**9**(3):185–92.

Millar 2004

Millar AL. Personal correspondence (email to Regis Andriolo concerning method of randomisation and missing data) 2004 (20 September).

Moreira 1999

Moreira WD, Fuchs FD, Ribeiro JP, Appel LJ. The effects of two aerobic training intensities on ambulatory blood pressure in hypertensive patients: results of a randomized trial. *Journal of clinical epidemiology* 1999;**52**(7):637–42. [MEDLINE: 10391657]

Myers 2002

Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among among men referred for exercising testing. *New England Journal of Medicine* 2002;**346**(11):793–801. [MEDLINE: 11893790]

Nadel 2003

Nadel L. Down's syndrome: a genetic disorder in biobehavioral perspective. *Genes Brain & Behavior* 2003;**2**(3):156–66.

Nespoli 1993

Nespoli L, Burgio GR, Ugazio AG, Maccario R. Immunological features of Down's syndrome: a review. *Journal of Intellectual Disability Research* 1993;**37**(Pt 6):543-51. [PUBMED: 8124000]

Nicham 2003

Nicham R, Weitzdorfer R, Hauser E, Freidl M, Schubert M, Wurst E, et al.Spectrum of cognitive, behavioural and emotional problems in children and young adults with Down syndrome. *Journal of Neural Transmission. Supplementum* 2003;**67**:173–91.

Norris 1990
Norris R, Carroll D, Cochrane R. The effects of aerobic and anaerobic training on fitness, blood pressure, and psychological stress and well-being. *Journal of Psychosomatic Research* 1990;**34**(4):367–75. [MEDLINE: 2376838]

Ogawa 2002
Ogawa O, Perry G, Smith MA. The "Down's" side of mitochondria. *Dev Cell* 2002;**2**(3):255–6. [MEDLINE: 11879629]

Pastore 2003
Pastore A, Tozzi G, Gaeta LM, Giannotti A, Bertini E, Federici G, et al.Glutathione metabolism and antioxidant enzymes in children with Down syndrome. *Journal of Pediatrics* 2003;**142**(5):583–5.

Pitetti 1992
Pitetti KH, Climstein M, Campbell KD, Barret PJ, Jackson JA. The cardiovascular capacities of adults with Down syndrome: a comparative study. *Medicine & Science in Sports & Exercise* 1992;**24**(1):13–9. [MEDLINE: 1532223]

Pitetti 1995
Pitetti KH, Boneh S. Cardiovascular fitness as related to leg strength in adults with mental retardation. *Medicine & Science in Sports & Exercise* 1995;**27**(3):423–8. [MEDLINE: 7752871]

Resta 2003
Resta O, Barbaro MP, Giliberti T, Caratozzolo G, Cagnazzo MG, Scarpelli F, et al.Sleep related breathing disorders in adults with Down syndrome. *Down's Syndrome, Research and Practice* 2003;**8**(3):115–9. [PUBMED: 14502839]

Roat 2007
Roat E, Prada N, Ferraresi R, Giovenzana C, Nasi M, Troiano L, et al.Mitochondrial alterations and tendency to apoptosis in peripheral blood cells from children with Down syndrome. *FEBS Letters* 2007;**581**(3):521–5. [PUBMED: 17250829]

Roberts 1996
Roberts TJ, Weber J-M, Hoppeler H, Weibel ER, Taylor CR. Design of the oxygen and substrate pathways. II. Defining the upper limits of carbohydrate and fat oxidation. *Journal of Experimental Biology* 1996;**199**:1651–8.

Saenz 1999
Saenz R. Primary Care of Infants and Young Children with Down Syndrome. *American Family Physician* 1999;**59**: 381–401.

Schjerve 2008
Schjerve IE, Tyldum GA, Tjønna AE, Stølen T, Loennechen JP, Hansen HE, et al.Both aerobic endurance and strength training programmes improve cardiovascular health in obese adults. *Clinical Science* 2008;**115**(9):283–93. [PUBMED: 18338980]

Schloo 1991
Schloo BL, Vawter GF, Reid LM. Down syndrome: Patterns of disturbed lung growth. *Human Pathology* 1991;**22**(9): 919–23. [MEDLINE: 1833304]

Seggar 1998
Segar ML, Katch VL, Roth RS, Garcia AW, Portner TI, Glickman SG, et al.The effect of aerobic exercise on self-esteem and depressive and anxiety symptoms among breast cancer survivors. *Oncology Nursing Forum* 1998;**25**(1): 107–13.

Spurway 1992
Spurway NC. Aerobic exercise, anaerobic exercise and the lactate threshold. *British Medical Bulletin* 1992;**48**(3): 569–91. [MEDLINE: 1450885]

Stewart 2003
Stewart KJ, Turner KL, Bacher AC, DeRegis Jr, Sung J, Tayback M, et al.Are fitness, activity, and fatness associated with health-related quality of life and mood in older persons?. *Journal of Cardiopulmonary Rehabilitation* 2003; **23**(2):115–21. [MEDLINE: 12668934]

Swain 1994
Swain DP, Abernathy KS, Smith CS, Lee SJ, Bunn SA. Target heart rates for the development of cardiorespiratory fitness. *Medicine & Science in Sports & Exercise* 1994;**26**(1): 112–6. [MEDLINE: 8133731]

Travis 1930
Travis LE, Dorsey JM. The relationship of "intelligence" and reflex conduction rate as found in hypophrenic children. *Journal of Experimental Psychology* 1930;**13**(4):370–2. [: 2005–14788–001]

Uhlig 1992
Uhlig S, Wendel A. The physiological consequences of glutathione variations. *Life Sciences* 1992;**51**(14):1083–94. [MEDLINE: 1518371]

Uong 2001
Uong EC, McDonough JM, Tayag-Kier CE, Zhao H, Haselgrove J, Mahboubi S, et al.Magnetic resonance imaging of the upper airways in children with Down syndrome. *American Journal of Respiratory and Critical Care Medicine* 2001;**163**(3 Pt 1):731–6. [MEDLINE: 11254532]

Urv 2008
Urv TK, Zigman WB, Silverman W. Maladaptive behaviors related to dementia status in adults with Down syndrome. *American Journal of Mental Retardation* 2008;**113**(2):73–86. [PUBMED: 18240877]

USDHHS 2002
United States Department of Health and Human Services. Physical activity fundamental to preventing disease. www.hhs.gov 2002.

Vilas Boas 2009
Vilas Boas LT, Albernaz EP, Costa RG. Prevalence of congenital heart defects in patients with Down syndrome. *Jornal de Pediatria* 2009;**85**(5):403–7. [PUBMED: 9662319]

Ware 1992
Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care* 1992;**30**(6):473–83.

Wasserman 1973

Wasserman K, Whipp BJ, Koyl SN, Beaver WL. Anaerobic threshold and respiratory gas exchange during exercise. *Journal of Applied Physiology* 1973;**35**(2):236–43. [MEDLINE: 4723033]

WHO 2009

WHO. Genes and human disease. http://www.who.int/genomics/public/geneticdiseases/en/index1.html 2009.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Carmelli 2002

Methods	Single-center, parallel RCT. Location: Israel
Participants	26 participants with Down syndrome. Age range: 57 to 65 years. Mean age: 63 years. Intelligence quotients (Stanford Binet Scale): 56 to 75. Cardiac disease: 15%
Interventions	Low endurance walking at 0% incline, 3 times/week, for 25 consecutive weeks, initially for 10 to 15 minutes and then gradually for as long as 45 minutes (at a speed below the threshold of breathlessness)
Outcomes	(1) Average power %BW for Knee extension (angular velocity at 60°/s), (2) Average power %BW for knee flexion (angular velocity at 60°/s), (3) walking performance (timed-up and go test, seconds)
Notes	Knee flexion and extension variables at angular velocities of 120°/s were not considered for analysis, since average power %BW was more one surrogate outcome, but composed by more than one variable

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Coin toss
Allocation concealment?	Unclear	not reported
Blinding? All outcomes	No	blinding of outcome assessors was not explicitly reported, and the characteristic of the intervention group (supervised physical exercise training) and control group (absence of supervised physical exercise training) would prevent participants and coaches to be blinded
Incomplete outcome data addressed? All outcomes	Unclear	no suspected withdrawals.
Free of selective reporting?	Unclear	none suspected

Millar 1993

Methods	Single-center, parallel RCT. Location: USA.
Participants	14 participants with Down syndrome. Age, 18.4 years ± 2.9 (SD) and 17.0 years ± 2.8 (SD); weight, 66.5 Kg ± 12.5 (SD) and 58.4 Kg ± 25.3 (SD); height, 153.7 cm ± 7.1 (SD) and 150.0 cm ± 15.8 (SD) age, 18.4 years ± 2.9 (SD) and 17.0 years ± 2.8 (SD) ; weight, 66.5 Kg ± 12.5 (SD) and 58.4 Kg ± 25.3 (SD); height, 153.7 cm ± 7.1 (SD) and 150.0 cm ± 15.8 (SD). Setting: county schools (living at home)
Interventions	Supervised 30 minutes of outside brisk/walking and jogging training with initial 10 minutes to warm-up, and 5 to 10 minutes to cool-down. Intensity: 65% - 75% of maximal HR. Session duration: 30 minutes. Period of training: 10 weeks
Outcomes	(1) Maximal heart rate, (2) Peak oxygen consumption (VO2 peak), (3) Respiratory exchange ratio (RER), (4) Pulmonary ventilation (VE), (5) Maximal treadmill grade (percentage of incline / gradient)
Notes	Maximal exercise test time was not reported. Biased method of monitoring of heart rate during the training bouts (at random, by palpation after subject slowing down the speed) . Informations not published: (1) the way in which exercise was performed: outside walking/jogging; (2) allocation concealment "using slips pulled by another person (first two slips with names to exercise, next one to control)"; (3) absence of blinding assessors of outcomes; and (4) anomaly in ECG as cause for one withdrawal (7% of randomised participants)

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"slips pulled by another person"
Allocation concealment?	Yes	"slips pulled by another person"
Blinding? All outcomes	No	patiens, therapists and outcome assessors were aware of the allocated group (Millar 2004)
Incomplete outcome data addressed? All outcomes	Yes	There was only 1 withdrawal after randomization and missing data could not be acquired because information concerning such matters was kept confidential on ethical grounds
Free of selective reporting?	Unclear	none suspected

Varela 2001

Methods	Single-center, parallel RCT. Location: Portugal.
Participants	16 males with Down syndrome. Age, 22.0 years ± 3.8 (SD) and 20.8 years ± 2.3 (SD) ; weight, 62.6 Kg ± 10.7 (SD) and 60.1 Kg ± 10.6 (SD); height, 153.6 cm ± 7.0 (SD) and 157.3 cm ± 4.1 (SD); IQ, 39.4 ± 12.2 (SD) and 38.4 ± 7.4 (SD). Setting: Local vocational and education training centers
Interventions	Supervised rowing training sessions on Gjessing 'Ergorow' ergometer, 3 times per week, for 16 weeks. Duration of exercise bouts: phase 1 (weeks 1-6), 15 minutes per session ; phase 2 (weeks 6-10), 5 minutes to total every 2 weeks til participants reached 25 mins per session; and phase 3 (weeks 10-16), maintenance at 25 minutes per session. Intensities of training: 75% of peak HR (heart rate) registered on TM GXT (treadmill graded exercise test) on phases 1 and 2 of study, and 79% of peak HR obtained on TM GXT on phase 3; The intensities mentioned corresponded with 83% of peak HR obtained from RE GXT (rowing ergometer graded exercise test) on phase 1 and phase 2, and 89% of peak HR in RE GXT on phase 3
Outcomes	(1) Maximal heart rate; (2) Peak oxygen consumption (VO2peak); (3) Respiratory exchange ratio (RER); (4) Pulmonary ventilation (VE); (5) Maximal test time (min); (6) Maximal treadmill grade (%); (7) Maximal rowing resistance (Kg); (8) Distance (meters) ; (9) Total turns of fan wheel; (10) Weight (Kg); (11) Body fat (%); (12) Lean mass (Kg) , (13) Fat mass (Kg) , and (14) Bone mineral content (Kg); (15) Red blood cells Mg (mg/L), (16) Red blood cells Se (microgram/L), (17) Red blood cells Cu (microgram/L) , (18) Red blood cells Zn (mg/L), (19) Plasma Mg (mg/L); (20) Plasma Se (microgram/ L), (21) Plasma Cu (mg/L) and (22) Plasma Zn (mg/L); (23) Red blood cells SOD (U/ mg Hb); (24) Red blood cells GSH (microgram/ g Hg) and (25) Red blood cells GSSG (microgram/ g Hg), (26) Plasma GSH (microgram/g prot.) and (27) Plasma GSSG (microgram/g prot.); (28) Plasma TBARS (mM)
Notes	Outcomes 12, 13 and 14 were extracted from Baptista 1996. Outcomes 15 to 28 were extracted from Monteiro 1997. The authors did not report any measure of adherence. Outcomes 1, 2, 3, 4 and 5 were measured on both TM GXT and RE GXT; Oucomes 7 and 9 were measured only on RE GXT; Outcomes 6 and 8 were measured only on TM GXT; Outcomes 10 to 28 were measured at rest.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	not reported
Allocation concealment?	Unclear	not reported
Blinding? All outcomes	No	blinding of outcome assessors was not explicitly reported, and the characteristic of the intervention group (supervised physical exercise training) and control group

Varela 2001 (*Continued*)

		(absence of supervised physical exercise training) would prevent participants and coaches to be blinded
Incomplete outcome data addressed? All outcomes	Unclear	no suspected withdrawals
Free of selective reporting?	Unclear	none suspected

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

Study	Reason for exclusion
Agiovlasitis 2009	Case-control
Aguiar 2008	Case-series
Angulo-Barroso 2008	Randomized controlled trial. Clinical condition out of interest (infants)
Black 2007	Case-control
Black 2009	Case-control
Bricout 2008	Case-control
Carmeli 2004	Non-randomised controlled trial
Chang 2009	Case-control
Dupont 1987	Non-randomized controlled trial. Clinical condition out of interest
Dyer 1994	Case-series. Participants 8-13 years old. Intervention: aerobic exercise combined together with weight training
Eberhard 1989	Case-control
Eberhard 1990	Case-series
Eberhard 1993	Case-series
Eberhard 1997	Case-series
Flore 2008	Case-control
Galli 2008	Case-control
Guerra 2009	Accuracy

(*Continued*)

Heffernan 2009	Case-control
Lafferty 2005	Case-series. Participants: Children
LaForme 2007	Non-randomized controlled trial. Intervention out of interest. Clinical condition out of interest (children)
LaForme 2009	Non-randomized controlled trial. Intervention out of interest. Clinical condition out of interest
Lewis 2005	Case-report. Participants: Children
Lloyd 2008	Case-control
Mendonça 2009	Case-control
Mendonça 2009a	Case-series
Ordoñez 2006	Case-series
Perán 1997	Case-series
Rimmer 2004	Randomised controlled trial. Intervention out of interest: aerobic exercise combined together with muscular strength and endurance training and education program. Current for another review
Shields 2008	Randomized controlled trial. Intervention out of interest (resistance training)
Skrobak 1980	Case-series. Intervention: Mixed activities.
Smith 2007	Case-control
Tsimaras 2004	Non-randomized controlled trial. Intervention: aerobic exercise combined together with both dynamic balance activities and plyometric exercises
Ulrich 2001	Randomised controlled trial. Clinical condition out of interest for this review: mean age, 307 days
Weber 1986	Intervention ou of interest (strength development training programs). Clinical condition out of interest (children)

DATA AND ANALYSES

Comparison 1. Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Peak VO2 (mL·Kg -1·min-1)	2	29	Mean Difference (IV, Random, 95% CI)	0.30 [-3.17, 3.77]
1.1 Walking/jogging training programmes	1	13	Mean Difference (IV, Random, 95% CI)	-0.68 [-7.86, 6.50]
1.2 Rowing training programmes	1	16	Mean Difference (IV, Random, 95% CI)	0.60 [-3.37, 4.57]
2 Peak heart rate (beats per minute)	2	29	Mean Difference (IV, Random, 95% CI)	2.84 [-5.05, 10.73]
2.1 Walking/jogging training programmes	1	13	Mean Difference (IV, Random, 95% CI)	-2.60 [-17.41, 12. 21]
2.2 Rowing training programmes	1	16	Mean Difference (IV, Random, 95% CI)	5.0 [-4.32, 14.32]
3 Respiratory exchange ratio (VCO2/VO2)	2	29	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.06, 0.04]
3.1 Walking/jogging training programmes	1	13	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.10, 0.08]
3.2 Rowing training programmes	1	16	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.07, 0.05]
4 Pulmonary ventilation (L·min-1)	2	29	Mean Difference (IV, Random, 95% CI)	5.86 [-4.34, 16.06]
4.1 Walking/jogging training programmes	1	13	Mean Difference (IV, Random, 95% CI)	1.0 [-14.59, 16.59]
4.2 Rowing training programmes	1	16	Mean Difference (IV, Random, 95% CI)	9.5 [-3.98, 22.98]
5 Maximal treadmill grade (%)	2	29	Mean Difference (IV, Random, 95% CI)	4.26 [2.06, 6.45]
5.1 Walking/jogging training programmes	1	13	Mean Difference (IV, Random, 95% CI)	5.0 [1.44, 8.56]
5.2 Rowing training programmes	1	16	Mean Difference (IV, Random, 95% CI)	3.80 [1.01, 6.59]
6 Maximal test time (minutes)	1	16	Mean Difference (IV, Random, 95% CI)	3.10 [0.96, 5.24]
6.1 Rowing training programmes	1	16	Mean Difference (IV, Random, 95% CI)	3.10 [0.96, 5.24]
7 Maximal distance (meters)	1	16	Mean Difference (IV, Random, 95% CI)	244.30 [98.53, 390. 07]
7.1 Walking/Jogging training programmes	1	16	Mean Difference (IV, Random, 95% CI)	244.30 [98.53, 390. 07]

Comparison 2. Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Peak VO2 (mL·Kg -1·min-1)	1	16	Mean Difference (IV, Fixed, 95% CI)	2.30 [-5.14, 9.74]
1.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	2.30 [-5.14, 9.74]
2 Peak heart rate (beats per minute)	1	16	Mean Difference (IV, Fixed, 95% CI)	3.0 [-18.08, 24.08]
2.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	3.0 [-18.08, 24.08]
3 Respiratory exchange ratio (VCO2/VO2)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.45, 0.39]
3.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.45, 0.39]
4 Pulmonary ventilation (L·min-1)	1	16	Mean Difference (IV, Fixed, 95% CI)	6.40 [-12.73, 25.53]
4.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	6.40 [-12.73, 25.53]
5 Maximal test time (minutes)	1	16	Mean Difference (IV, Fixed, 95% CI)	2.31 [1.06, 3.56]
5.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	2.31 [1.06, 3.56]
6 Distance (total turns of fan wheel divided by 100)	1	16	Mean Difference (IV, Fixed, 95% CI)	9.08 [1.49, 16.67]
6.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	9.08 [1.49, 16.67]
7 Resistance (Kg)	1	16	Mean Difference (IV, Fixed, 95% CI)	0.22 [0.08, 0.36]
7.1 Rowing traning programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	0.22 [0.08, 0.36]

Comparison 3. Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Weight (Kg)	1	16	Mean Difference (IV, Fixed, 95% CI)	-2.10 [-12.01, 7.81]
1.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-2.10 [-12.01, 7.81]
2 Body fat (%)	1	16	Mean Difference (IV, Fixed, 95% CI)	-1.40 [-5.72, 2.92]
2.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-1.40 [-5.72, 2.92]
3 Lean mass (Kg)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-4.87, 3.67]
3.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-4.87, 3.67]
4 Fat mass (Kg)	1	16	Mean Difference (IV, Fixed, 95% CI)	-1.5 [-8.46, 5.46]
4.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-1.5 [-8.46, 5.46]

5 Bone content mineral (Kg)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.45, 0.15]
5.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.45, 0.15]
6 Red blood cells magnesium (mg/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	1.0 [-3.41, 5.41]
6.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	1.0 [-3.41, 5.41]
7 Red blood cells selenium (mg/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	2.40 [-18.94, 23.74]
7.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	2.40 [-18.94, 23.74]
8 Red blood cells copper (microgram/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	-9.10 [-156.41, 138.21]
8.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-9.10 [-156.41, 138.21]
9 Red blood cells zinc (mg/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-2.40, 1.40]
9.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-2.40, 1.40]
10 Plasma magnesium (mg/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-1.71, 0.71]
10.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-1.71, 0.71]
11 Plasma selenium (microgram/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	-6.90 [-17.12, 3.32]
11.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-6.90 [-17.12, 3.32]
12 Plasma copper (mg/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.19, 0.13]
12.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.19, 0.13]
13 Plasma zinc (mg/L)	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.22, -0.02]
13.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.22, -0.02]
14 Red blood cells superoxide dismutase (U/mg Hb)	1	16	Mean Difference (IV, Fixed, 95% CI)	44.0 [-511.07, 599.07]
14.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	44.0 [-511.07, 599.07]
15 Red blood cells reduced glutatione (microgram/g Hb)	1	16	Mean Difference (IV, Fixed, 95% CI)	-261.0 [-586.66, 64.66]
15.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-261.0 [-586.66, 64.66]
16 Red blood cells oxidized glutathione (microgram/g Hb)	1	16	Mean Difference (IV, Fixed, 95% CI)	49.2 [38.65, 59.75]
16.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	49.2 [38.65, 59.75]
17 Plasma reduced glutathione (microgram/g prot/10)	1	16	Mean Difference (IV, Fixed, 95% CI)	169.90 [84.83, 254.97]
17.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	169.90 [84.83, 254.97]
18 Plasma oxidized glutathione (microgram/g prot)	1	16	Mean Difference (IV, Fixed, 95% CI)	-10.40 [-22.47, 1.67]
18.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-10.40 [-22.47, 1.67]
19 Plasma thiobarbituric acid reactive substances (mM)	1	16	Mean Difference (IV, Fixed, 95% CI)	-2.28 [-4.56, -0.00]

19.1 Rowing training programmes	1	16	Mean Difference (IV, Fixed, 95% CI)	-2.28 [-4.56, -0.00]
20 Average power for Knee extension (watts/Kg-angular velocity at 60/°s)	1	26	Mean Difference (IV, Fixed, 95% CI)	17.83 [16.00, 19.65]
20.1 Men	1	10	Mean Difference (IV, Fixed, 95% CI)	18.20 [16.32, 20.08]
20.2 Women	1	16	Mean Difference (IV, Fixed, 95% CI)	11.30 [3.46, 19.14]
21 Average power for Knee flexion (watts/Kg-angular velocity at 60/°s)	1	26	Mean Difference (IV, Fixed, 95% CI)	20.57 [16.56, 24.58]
21.1 Men	1	10	Mean Difference (IV, Fixed, 95% CI)	13.80 [5.74, 21.86]
21.2 Women	1	16	Mean Difference (IV, Fixed, 95% CI)	22.80 [18.18, 27.42]

Comparison 4. Aerobic exercise training programmes versus no intervention (data collection on medical isokinetic system)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Average power for Knee extension (watts/Kg-angular velocity at 60/°s)	1	26	Mean Difference (IV, Fixed, 95% CI)	17.72 [15.91, 19.53]
1.1 Men	1	10	Mean Difference (IV, Fixed, 95% CI)	18.20 [16.32, 20.08]
1.2 Women	1	16	Mean Difference (IV, Fixed, 95% CI)	11.30 [4.44, 18.16]
2 Average power for Knee flexion (watts/Kg-angular velocity at 60/°s)	1	26	Mean Difference (IV, Fixed, 95% CI)	20.57 [16.56, 24.58]
2.1 Men	1	10	Mean Difference (IV, Fixed, 95% CI)	13.80 [5.74, 21.86]
2.2 Women	1	16	Mean Difference (IV, Fixed, 95% CI)	22.80 [18.18, 27.42]

Comparison 5. Aerobic exercise training programmes versus no intervention (data collection on Timed-up and go test (s))

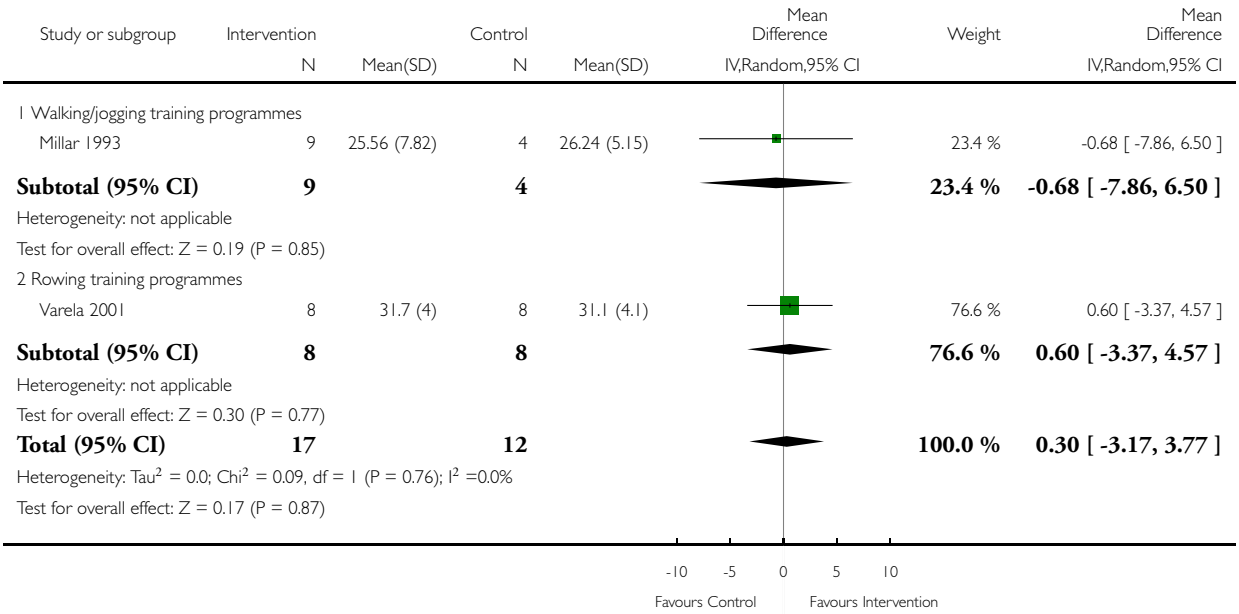
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Timed-up and go test (s)	1	26	Mean Difference (IV, Random, 95% CI)	3.20 [0.83, 5.57]

Analysis 1.1. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 1 Peak VO2 (mL·Kg -1·min-1).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 1 Peak VO2 (mL Kg -1 min-1)



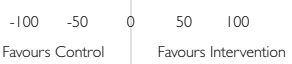
Analysis 1.2. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 2 Peak heart rate (beats per minute).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 2 Peak heart rate (beats per minute)

Study or subgroup	Favours Control N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Walking/jogging training programmes							
Millar 1993	9	167.2 (11.8)	4	169.8 (12.9)		28.4 %	-2.60 [-17.41, 12.21]
Subtotal (95% CI)	**9**		**4**			**28.4 %**	**-2.60 [-17.41, 12.21]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.34 (P = 0.73)							
2 Rowing training programmes							
Varela 2001	8	171 (10)	8	166 (9)		71.6 %	5.00 [-4.32, 14.32]
Subtotal (95% CI)	**8**		**8**			**71.6 %**	**5.00 [-4.32, 14.32]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.05 (P = 0.29)							
Total (95% CI)	**17**		**12**			**100.0 %**	**2.84 [-5.05, 10.73]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.72$, df = 1 (P = 0.39); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.71 (P = 0.48)							



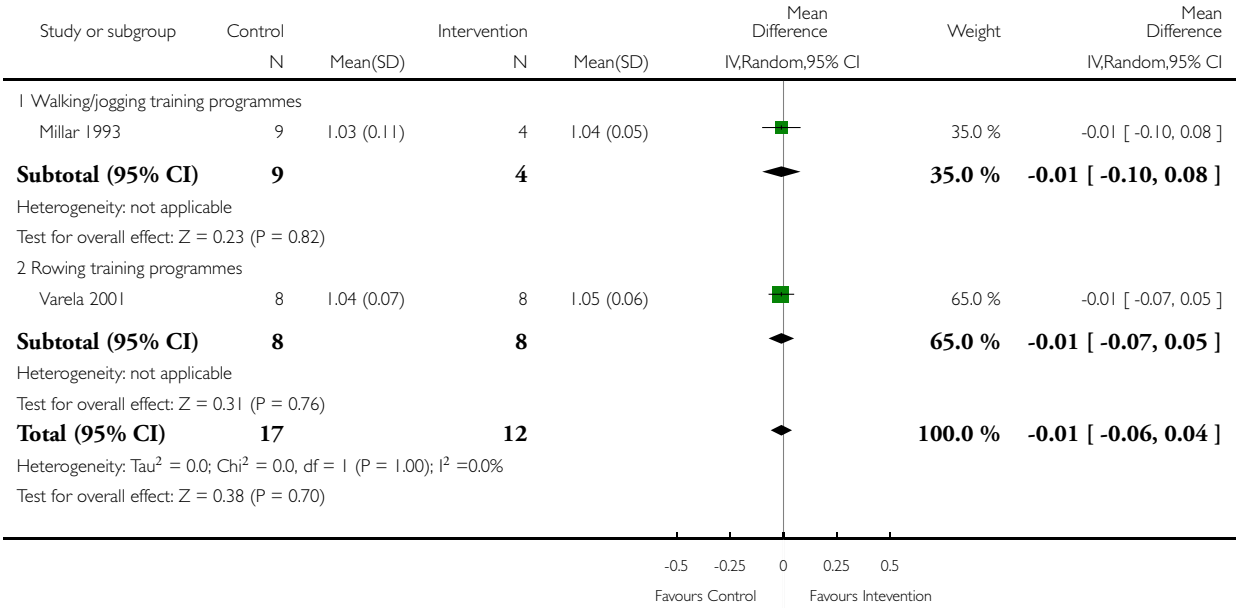
Analysis 1.3. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 3 Respiratory exchange ratio (VCO2/VO2).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 3 Respiratory exchange ratio (VCO2/VO2)

Study or subgroup	Control N	Mean(SD)	Intervention N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Walking/jogging training programmes							
Millar 1993	9	1.03 (0.11)	4	1.04 (0.05)		35.0 %	-0.01 [-0.10, 0.08]
Subtotal (95% CI)	**9**		**4**			**35.0 %**	**-0.01 [-0.10, 0.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.23 (P = 0.82)							
2 Rowing training programmes							
Varela 2001	8	1.04 (0.07)	8	1.05 (0.06)		65.0 %	-0.01 [-0.07, 0.05]
Subtotal (95% CI)	**8**		**8**			**65.0 %**	**-0.01 [-0.07, 0.05]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.31 (P = 0.76)							
Total (95% CI)	**17**		**12**			**100.0 %**	**-0.01 [-0.06, 0.04]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.0, df = 1 (P = 1.00); I^2 =0.0%							
Test for overall effect: Z = 0.38 (P = 0.70)							

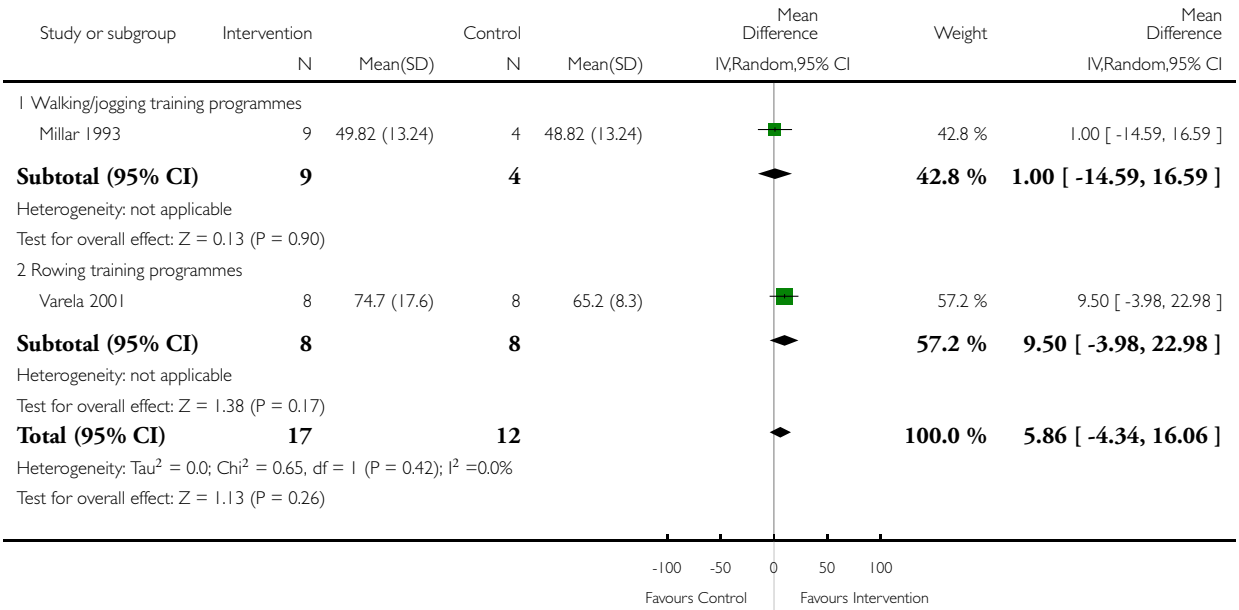


Analysis 1.4. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 4 Pulmonary ventilation (L·min-1).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 4 Pulmonary ventilation (L min-1)



Analysis 1.5. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 5 Maximal treadmill grade (%).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 5 Maximal treadmill grade (%)

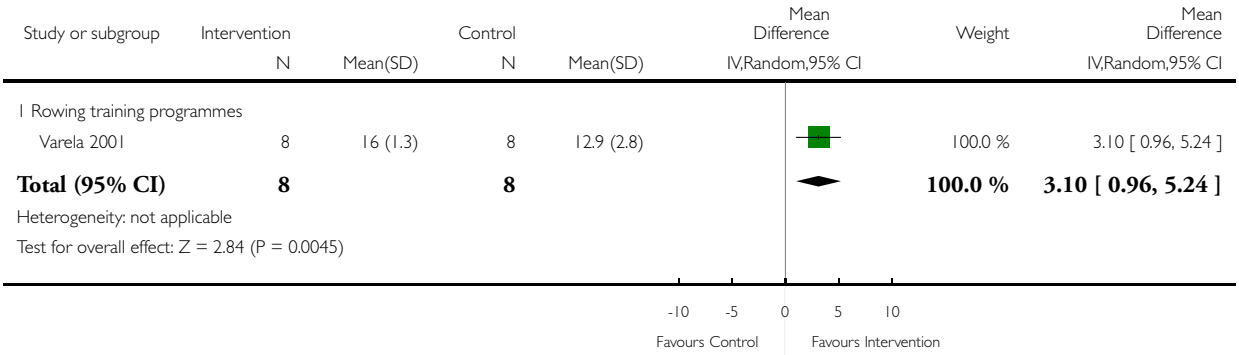
Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Walking/jogging training programmes							
Millar 1993	9	23.1 (4.1)	4	18.1 (2.4)		38.0 %	5.00 [1.44, 8.56]
Subtotal (95% CI)	**9**		**4**			**38.0 %**	**5.00 [1.44, 8.56]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.75 (P = 0.0060)							
2 Rowing training programmes							
Varela 2001	8	18.1 (1.8)	8	14.3 (3.6)		62.0 %	3.80 [1.01, 6.59]
Subtotal (95% CI)	**8**		**8**			**62.0 %**	**3.80 [1.01, 6.59]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.67 (P = 0.0076)							
Total (95% CI)	**17**		**12**			**100.0 %**	**4.26 [2.06, 6.45]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.27, df = 1 (P = 0.60); I^2 =0.0%							
Test for overall effect: Z = 3.80 (P = 0.00015)							

Analysis 1.6. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 6 Maximal test time (minutes).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 6 Maximal test time (minutes)

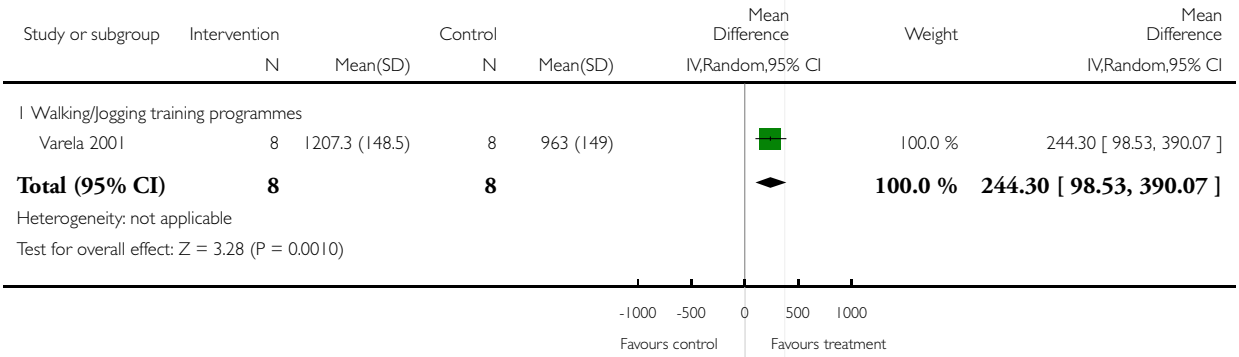


Analysis 1.7. Comparison 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test), Outcome 7 Maximal distance (meters).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 1 Aerobic exercise training programmes versus no intervention (data collection on treadmill test)

Outcome: 7 Maximal distance (meters)

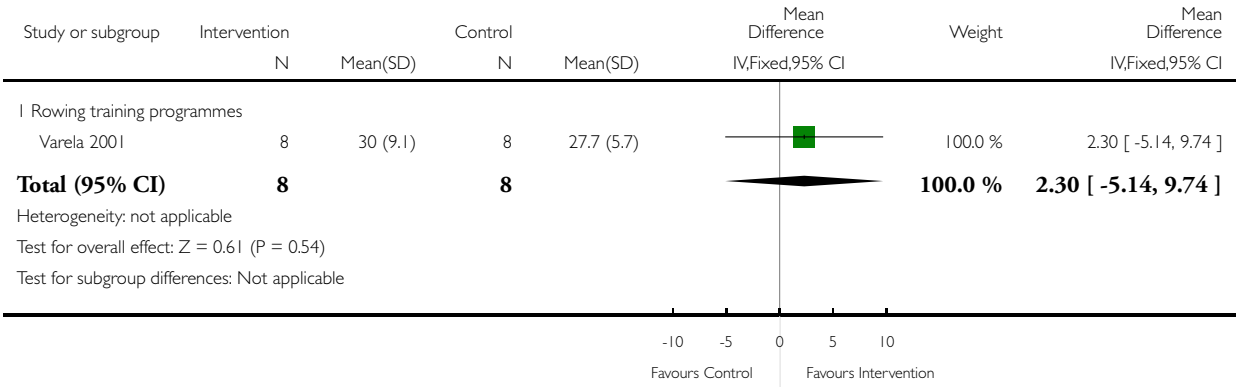


Analysis 2.1. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 1 Peak VO2 (mL·Kg -1·min-1).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

Outcome: 1 Peak VO2 (mL Kg -1 min-1)

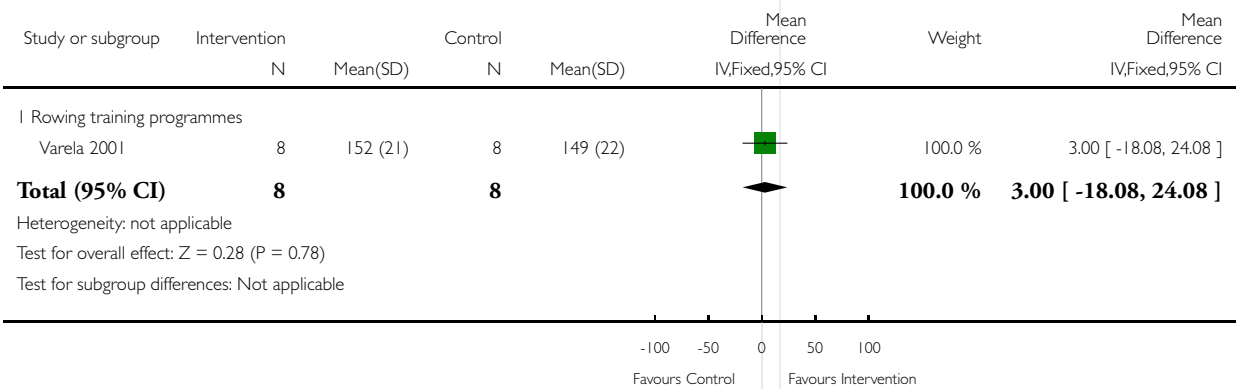


Analysis 2.2. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 2 Peak heart rate (beats per minute).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

Outcome: 2 Peak heart rate (beats per minute)



Analysis 2.3. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 3 Respiratory exchange ratio (VCO2/VO2).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

Outcome: 3 Respiratory exchange ratio (VCO2/VO2)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	1.01 (0.6)	8	1.04 (0.01)		100.0 %	-0.03 [-0.45, 0.39]
Total (95% CI)	**8**		**8**			**100.0 %**	**-0.03 [-0.45, 0.39]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.14 (P = 0.89)							
Test for subgroup differences: Not applicable							

Analysis 2.4. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 4 Pulmonary ventilation (L·min-1).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

Outcome: 4 Pulmonary ventilation (L min-1)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	67.3 (16.4)	8	60.9 (22.2)		100.0 %	6.40 [-12.73, 25.53]
Total (95% CI)	**8**		**8**			**100.0 %**	**6.40 [-12.73, 25.53]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.66 (P = 0.51)

Test for subgroup differences: Not applicable

Analysis 2.5. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 5 Maximal test time (minutes).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

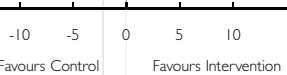
Outcome: 5 Maximal test time (minutes)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	9.62 (0.97)	8	7.31 (1.52)		100.0 %	2.31 [1.06, 3.56]
Total (95% CI)	**8**		**8**			**100.0 %**	**2.31 [1.06, 3.56]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.62 (P = 0.00029)

Test for subgroup differences: Not applicable



Analysis 2.6. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 6 Distance (total turns of fan wheel divided by 100).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

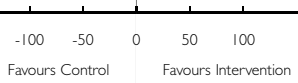
Outcome: 6 Distance (total turns of fan wheel divided by 100)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	33.7 (7.74)	8	24.62 (7.75)		100.0 %	9.08 [1.49, 16.67]
Total (95% CI)	**8**		**8**			**100.0 %**	**9.08 [1.49, 16.67]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.34 (P = 0.019)

Test for subgroup differences: Not applicable

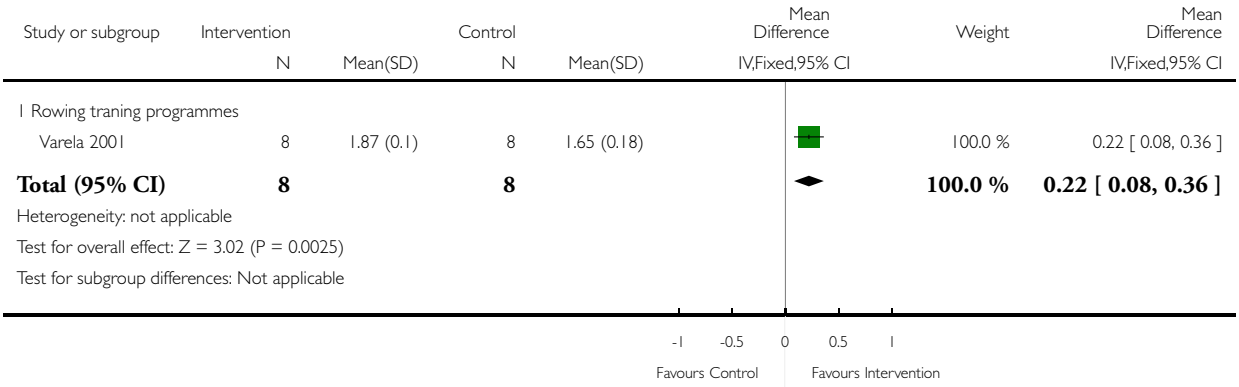


Analysis 2.7. Comparison 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test), Outcome 7 Resistance (Kg).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 2 Aerobic exercise training programmes versus no intervention (data collection on rowing ergometer test)

Outcome: 7 Resistance (Kg)

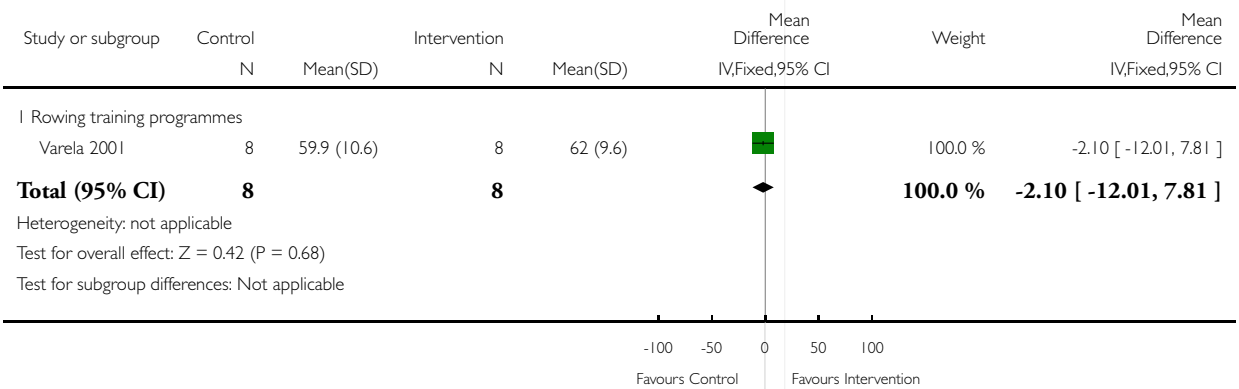


Analysis 3.1. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 1 Weight (Kg).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 1 Weight (Kg)



Analysis 3.2. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 2 Body fat (%).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 2 Body fat (%)

Study or subgroup	Control N	Mean(SD)	Intervention N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	21.4 (4.1)	8	22.8 (4.7)		100.0 %	-1.40 [-5.72, 2.92]
Total (95% CI)	**8**		**8**			**100.0 %**	**-1.40 [-5.72, 2.92]**

Heterogeneity: not applicable

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

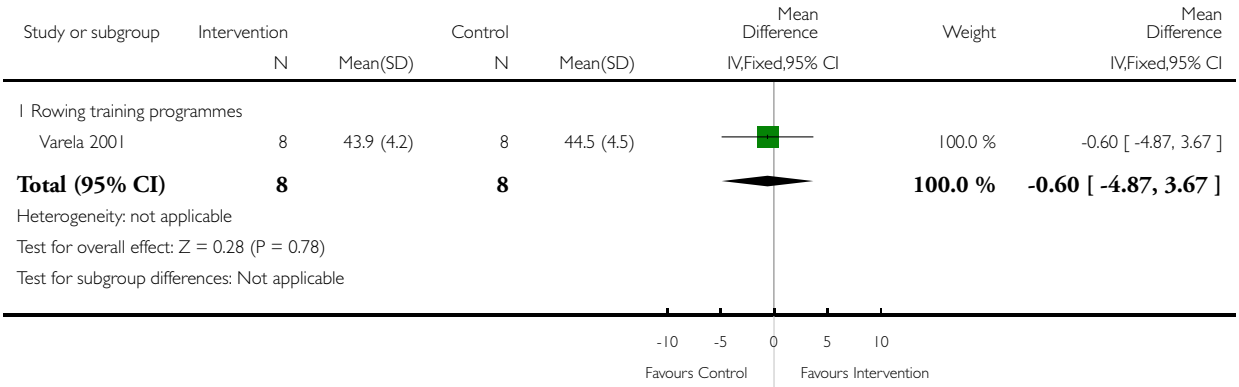
Test for subgroup differences: Not applicable

Analysis 3.3. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 3 Lean mass (Kg).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 3 Lean mass (Kg)

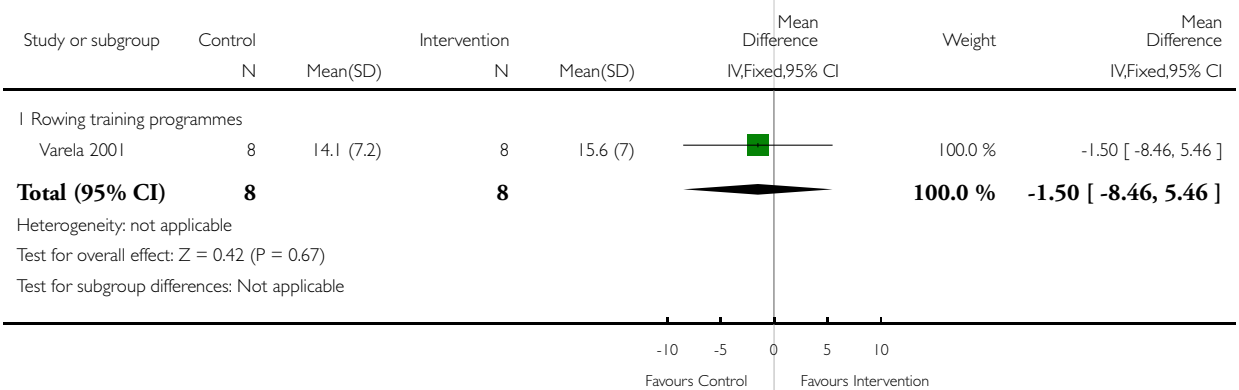


Analysis 3.4. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 4 Fat mass (Kg).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 4 Fat mass (Kg)



Analysis 3.5. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 5 Bone content mineral (Kg).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 5 Bone content mineral (Kg)

Study or subgroup	Control N	Mean(SD)	Intervention N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	1.9 (0.29)	8	2.05 (0.32)		100.0 %	-0.15 [-0.45, 0.15]
Total (95% CI)	**8**		**8**			**100.0 %**	**-0.15 [-0.45, 0.15]**

Heterogeneity: not applicable

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

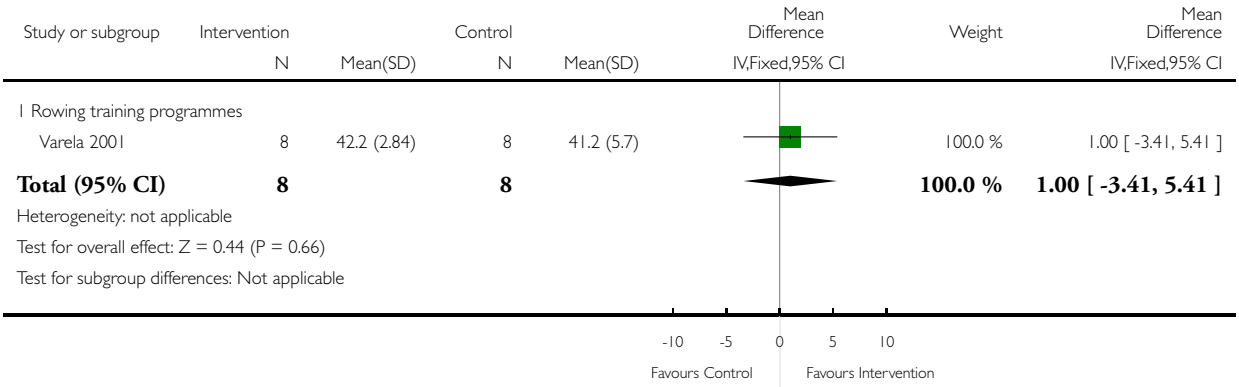
Test for subgroup differences: Not applicable

Analysis 3.6. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 6 Red blood cells magnesium (mg/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 6 Red blood cells magnesium (mg/L)

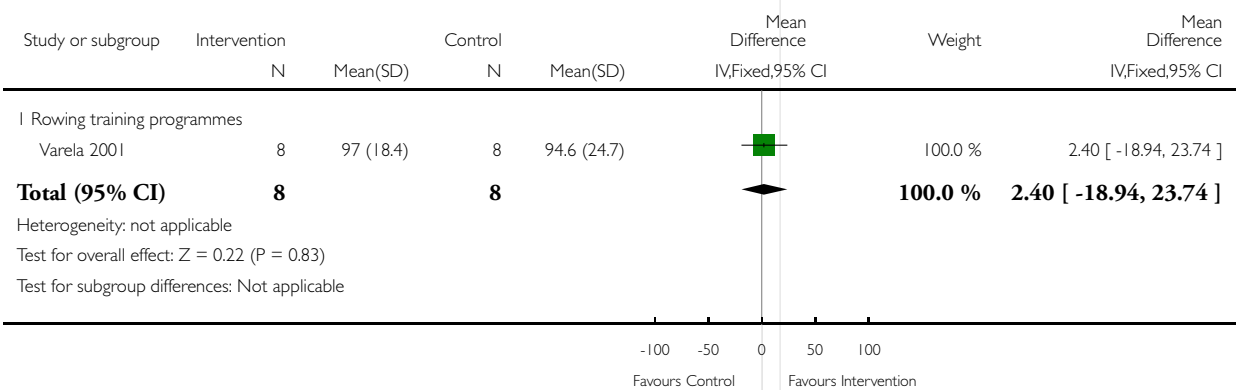


Analysis 3.7. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 7 Red blood cells selenium (mg/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 7 Red blood cells selenium (mg/L)



Analysis 3.8. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 8 Red blood cells copper (microgram/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 8 Red blood cells copper (microgram/L)

Study or subgroup	Intervention		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	751.9 (144.2)	8	761 (156.2)		100.0 %	-9.10 [-156.41, 138.21]
Total (95% CI)	**8**		**8**			**100.0 %**	**-9.10 [-156.41, 138.21]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.12 (P = 0.90)

Test for subgroup differences: Not applicable

Analysis 3.9. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 9 Red blood cells zinc (mg/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 9 Red blood cells zinc (mg/L)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	14.9 (1.02)	8	15.4 (2.55)		100.0 %	-0.50 [-2.40, 1.40]
Total (95% CI)	**8**		**8**			**100.0 %**	**-0.50 [-2.40, 1.40]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.51 (P = 0.61)

Test for subgroup differences: Not applicable

Analysis 3.10. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 10 Plasma magnesium (mg/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 10 Plasma magnesium (mg/L)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	19.9 (1.36)	8	20.4 (1.09)		100.0 %	-0.50 [-1.71, 0.71]
Total (95% CI)	**8**		**8**			**100.0 %**	**-0.50 [-1.71, 0.71]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.81 (P = 0.42)

Test for subgroup differences: Not applicable

Analysis 3.11. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 11 Plasma selenium (microgram/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 11 Plasma selenium (microgram/L)

Study or subgroup	Intervention		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	65 (6.78)	8	71.9 (13.1)		100.0 %	-6.90 [-17.12, 3.32]
Total (95% CI)	**8**		**8**			**100.0 %**	**-6.90 [-17.12, 3.32]**

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

Analysis 3.12. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 12 Plasma copper (mg/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

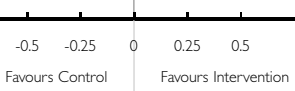
Outcome: 12 Plasma copper (mg/L)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	1.13 (0.1)	8	1.16 (0.21)		100.0 %	-0.03 [-0.19, 0.13]
Total (95% CI)	**8**		**8**			**100.0 %**	**-0.03 [-0.19, 0.13]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.36 (P = 0.72)

Test for subgroup differences: Not applicable



Analysis 3.13. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 13 Plasma zinc (mg/L).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

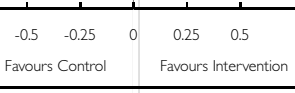
Outcome: 13 Plasma zinc (mg/L)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	0.98 (0.11)	8	1.1 (0.09)		100.0 %	-0.12 [-0.22, -0.02]
Total (95% CI)	**8**		**8**			**100.0 %**	**-0.12 [-0.22, -0.02]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.39 (P = 0.017)

Test for subgroup differences: Not applicable



Analysis 3.14. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 14 Red blood cells superoxide dismutase (U/mg Hb).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 14 Red blood cells superoxide dismutase (U/mg Hb)

Study or subgroup	Intervention		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	3192 (210)	8	3148 (773)		100.0 %	44.00 [-511.07, 599.07]
Total (95% CI)	**8**		**8**			**100.0 %**	**44.00 [-511.07, 599.07]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.16 (P = 0.88)

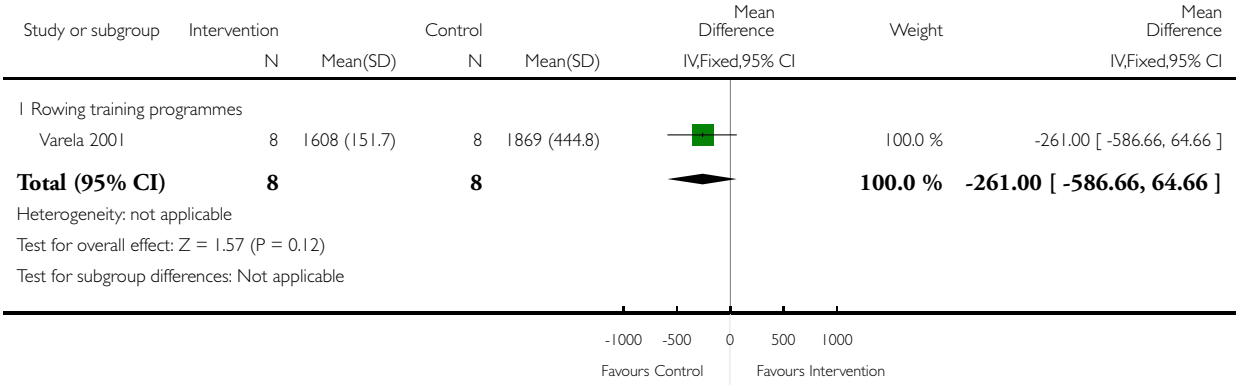
Test for subgroup differences: Not applicable

Analysis 3.15. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 15 Red blood cells reduced glutatione (microgram/g Hb).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 15 Red blood cells reduced glutatione (microgram/g Hb)

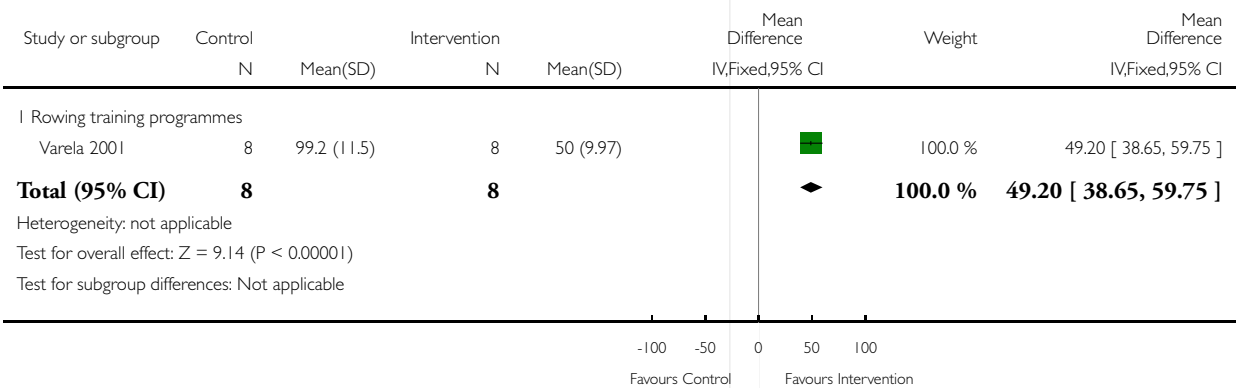


Analysis 3.16. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 16 Red blood cells oxidized glutathione (microgram/g Hb).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 16 Red blood cells oxidized glutathione (microgram/g Hb)



Analysis 3.17. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 17 Plasma reduced glutathione (microgram/g prot/10).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 17 Plasma reduced glutathione (microgram/g prot/10)

Study or subgroup	Intervention		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	836.8 (52.45)	8	666.9 (111)		100.0 %	169.90 [84.83, 254.97]
Total (95% CI)	**8**		**8**			**100.0 %**	**169.90 [84.83, 254.97]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.91 (P = 0.000091)

Test for subgroup differences: Not applicable

Analysis 3.18. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 18 Plasma oxidized glutathione (microgram/g prot).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 18 Plasma oxidized glutathione (microgram/g prot)

Study or subgroup	Control N	Mean(SD)	Intervention N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	61 (6.65)	8	71.4 (16.1)		100.0 %	-10.40 [-22.47, 1.67]
Total (95% CI)	**8**		**8**			**100.0 %**	**-10.40 [-22.47, 1.67]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.69 (P = 0.091)

Test for subgroup differences: Not applicable

Analysis 3.19. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 19 Plasma thiobarbituric acid reactive substances (mM).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

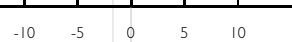
Outcome: 19 Plasma thiobarbituric acid reactive substances (mM)

Study or subgroup	Control N	Mean(SD)	Intervention N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Rowing training programmes							
Varela 2001	8	5.21 (1.63)	8	7.49 (2.85)		100.0 %	-2.28 [-4.56, 0.00]
Total (95% CI)	**8**		**8**			**100.0 %**	**-2.28 [-4.56, 0.00]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.96 (P = 0.050)

Test for subgroup differences: Not applicable



Analysis 3.20. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 20 Average power for Knee extension (watts/Kg-angular velocity at 60/°s).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 20 Average power for Knee extension (watts/Kg-angular velocity at 60/ s)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Men							
Carmelli 2002	6	58.4 (2)	4	40.2 (1)		94.6 %	18.20 [16.32, 20.08]
Subtotal (95% CI)	**6**		**4**			**94.6 %**	**18.20 [16.32, 20.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 19.01 (P < 0.00001)							
2 Women							
Carmelli 2002	6	45.4 (9)	10	34.1 (5)		5.4 %	11.30 [3.46, 19.14]
Subtotal (95% CI)	**6**		**10**			**5.4 %**	**11.30 [3.46, 19.14]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.82 (P = 0.0047)							
Total (95% CI)	**12**		**14**			**100.0 %**	**17.83 [16.00, 19.65]**
Heterogeneity: Chi^2 = 2.81, df = 1 (P = 0.09); I^2 =64%							
Test for overall effect: Z = 19.14 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 2.81, df = 1 (P = 0.09), I^2 =64%							

Analysis 3.21. Comparison 3 Aerobic exercise training programmes versus no intervention (data collection at rest), Outcome 21 Average power for Knee flexion (watts/Kg-angular velocity at 60/°s).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 3 Aerobic exercise training programmes versus no intervention (data collection at rest)

Outcome: 21 Average power for Knee flexion (watts/Kg-angular velocity at 60/ s)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Men							
Carmelli 2002	6	39.9 (8)	4	26.1 (5)		24.8 %	13.80 [5.74, 21.86]
Subtotal (95% CI)	**6**		**4**			**24.8 %**	**13.80 [5.74, 21.86]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.36 (P = 0.00079)							
2 Women							
Carmelli 2002	10	33.8 (7)	6	11 (2)		75.2 %	22.80 [18.18, 27.42]
Subtotal (95% CI)	**10**		**6**			**75.2 %**	**22.80 [18.18, 27.42]**
Heterogeneity: not applicable							
Test for overall effect: Z = 9.66 (P < 0.00001)							
Total (95% CI)	**16**		**10**			**100.0 %**	**20.57 [16.56, 24.58]**
Heterogeneity: Chi^2 = 3.60, df = 1 (P = 0.06); I^2 =72%							
Test for overall effect: Z = 10.05 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 3.60, df = 1 (P = 0.06), I^2 =72%							

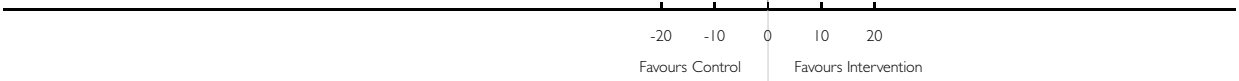
Analysis 4.1. Comparison 4 Aerobic exercise training programmes versus no intervention (data collection on medical isokinetic system), Outcome 1 Average power for Knee extension (watts/Kg-angular velocity at 60/°s).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 4 Aerobic exercise training programmes versus no intervention (data collection on medical isokinetic system)

Outcome: 1 Average power for Knee extension (watts/Kg-angular velocity at 60/ s)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Men							
Carmelli 2002	6	58.4 (2)	4	40.2 (1)		93.0 %	18.20 [16.32, 20.08]
Subtotal (95% CI)	**6**		**4**			**93.0 %**	**18.20 [16.32, 20.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 19.01 (P < 0.00001)							
2 Women							
Carmelli 2002	10	45.4 (9)	6	34.1 (5)		7.0 %	11.30 [4.44, 18.16]
Subtotal (95% CI)	**10**		**6**			**7.0 %**	**11.30 [4.44, 18.16]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.23 (P = 0.0013)							
Total (95% CI)	**16**		**10**			**100.0 %**	**17.72 [15.91, 19.53]**
Heterogeneity: Chi^2 = 3.61, df = 1 (P = 0.06); I^2 =72%							
Test for overall effect: Z = 19.19 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 3.61, df = 1 (P = 0.06), I^2 =72%							



Analysis 4.2. Comparison 4 Aerobic exercise training programmes versus no intervention (data collection on medical isokinetic system), Outcome 2 Average power for Knee flexion (watts/Kg-angular velocity at 60/°s).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 4 Aerobic exercise training programmes versus no intervention (data collection on medical isokinetic system)

Outcome: 2 Average power for Knee flexion (watts/Kg-angular velocity at 60/ s)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Men							
Carmelli 2002	6	39.9 (8)	4	26.1 (5)		24.8 %	13.80 [5.74, 21.86]
Subtotal (95% CI)	**6**		**4**			**24.8 %**	**13.80 [5.74, 21.86]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.36 (P = 0.00079)							
2 Women							
Carmelli 2002	10	33.8 (7)	6	11 (2)		75.2 %	22.80 [18.18, 27.42]
Subtotal (95% CI)	**10**		**6**			**75.2 %**	**22.80 [18.18, 27.42]**
Heterogeneity: not applicable							
Test for overall effect: Z = 9.66 (P < 0.00001)							
Total (95% CI)	**16**		**10**			**100.0 %**	**20.57 [16.56, 24.58]**
Heterogeneity: Chi^2 = 3.60, df = 1 (P = 0.06); I^2 =72%							
Test for overall effect: Z = 10.05 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 3.60, df = 1 (P = 0.06), I^2 =72%							

Analysis 5.1. Comparison 5 Aerobic exercise training programmes versus no intervention (data collection on Timed-up and go test (s)), Outcome 1 Timed-up and go test (s).

Review: Aerobic exercise training programmes for improving physical and psychosocial health in adults with Down syndrome

Comparison: 5 Aerobic exercise training programmes versus no intervention (data collection on Timed-up and go test (s))

Outcome: 1 Timed-up and go test (s)

Study or subgroup	Control N	Mean(SD)	Intervention N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Carmelli 2002	10	29.1 (3)	16	25.9 (3)		100.0 %	3.20 [0.83, 5.57]
Total (95% CI)	**10**		**16**			**100.0 %**	**3.20 [0.83, 5.57]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.65 (P = 0.0081)

Test for subgroup differences: Not applicable

APPENDICES

Appendix 1. General search strategy for clinical condition and intervention of interest used across all databases

#1 down syndrome
#2 syndrome, down
#3 mongolism
#4 trisomy 21
#5 down's syndrome
#6 downs syndrome
#7 syndrome, down's
#8 trisomy 21, meiotic nondisjunction
#9 trisomy 21, mitotic nondisjunction
#10 down syndrome, partial trisomy 21
#11 partial trisomy 21 down syndrome
#12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13 aerobic exercise
#14 aerobic exercises
#15 athletic
#16 bicycling
#17 calisthenic
#18 cyclic
#19 dance
#20 dancing

#21 physical train
#22 exercise activities
#23 exercise activity
#24 exercise behaviour
#25 exercise education
#26 exercise educations
#27 exercise intervention
#28 exercise interventions
#29 exercise lifestyle
#30 exercise program
#31 exercise recreation
#32 exercise recreations
#33 exercise study
#34 exercise therapy
#35 exercise training
#36 exercise, aerobic
#37 exercise, isometric
#38 exercise, physical
#39 exercise, warm-up
#40 exercises
#41 exercises, aerobic
#42 exercises, isometric
#43 exercises, physical
#44 xercises, warm-up
#45 exertion
#46 exertions
#47 football
#48 gymnastic
#49 isometric exercise
#50 isometric exercises
#51 mountaineer
#52 physical activities
#53 physical activity
#54 physical behavior
#55 physical behaviour
#56 physical education
#57 physical exercise
#58 physical exercises
#59 physical habit
#60 physical habits
#61 physical intervention
#62 physical interventions
#63 physical program
#64 physical programme
#65 physical programmes
#66 physical programs
#67 physical recreation
#68 physical studies
#69 physical study
#70 physical training
#71 ramble
#72 rambling
#73 rowing

#74 running
#75 skate
#76 skating
#77 soccer
#78 swim
#79 swimming
#80 training program
#81 training programme
#82 training programmes
#83 training programs
#84 walk
#85 walking
#86 warm up exercise
#87 warm-up exercise
#88 warm-up exercises
#89 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88
#89 #12 AND #88

Appendix 2. Search filter for RCTs used in Medline (PUBMED)

#1 randomized controlled trial [pt]
#2 controlled clinical trial [pt]
#3 randomized controlled trials [mh]
#4 random allocation [mh]
#5 double-blind method [mh]
#6 single-blind method [mh]
#7 clinical trial [pt]
#8 clinical trials [mh]
#9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
#10 clinical trial [tw]
#11 singl* [tw]
#12 doubl* [tw]
#13 trebl* [tw]
#14 tripl* [tw])
#15 #10 OR #11 OR #12 OR #13 OR #14
#16 mask* [tw]
#17 blind* [tw]
#18 #16 OR #17
#19 #15 AND #18
#20 placebos [mh]
#21 placebo* [tw]
#22 random* [tw]
#23 research design [mh:noexp]
#24 comparative study [mh]
#25 evaluation studies [mh]
#26 follow-up studies [mh]
#27 prospective studies [mh]

#28 control* [tw]
#29 prospectiv* [tw]
#30 volunteer* [tw])
#31 #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30
#32(animals [mh] NOT human [mh])
#33 #9 OR #19 OR #31 NOT #32

Appendix 3. Search filter for RCTs used in Lilacs (Bireme)

#1 Pt RANDOMIZED CONTROLLED TRIAL
#2 Pt CONTROLLED CLINICAL TRIAL
#3 Mh RANDOMIZED CONTROLLED TRIALS
#4 Mh RANDOM ALLOCATION
#5 Mh DOUBLE-BLIND METHOD
#6 Mh SINGLE-BLIND METHOD
#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6
#8 Ct ANIMAL AND NOT (Ct HUMAN and Ct ANIMAL)
#9 #7 AND NOT #8
#10 Pt CLINICAL TRIAL
#11 Ex E05.318.760.535$ <explode Mh CLINICAL TRIALS>
#12 Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR
Tw experim$ OR Tw investiga$)
#13 Tw singl$ OR Tw simple$ OR Tw doubl$ OR Tw doble$ OR
Tw duplo$ OR Tw trebl$ OR Tw trip$
#14 Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR
Tw mascar$
#15 #18 #13 AND #14
#16 Mh PLACEBOS
#17 Tw placebo$
#18 Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$
OR Tw azar OR Tw aleator$
#19 Mh RESEARCH DESIGN
#20 #10 OR #11 OR #12 OR #15 OR #16 OR #17 OR #18
OR #19
#21 Ct ANIMAL AND NOT (Ct HUMAN and Ct ANIMAL)
#22 #20 AND NOT #21
#23 #22 AND NOT #9
#24 Ct COMPARATIVE STUDY
#25 Ex E05.337$ <explode Mh EVALUATION STUDIES)>
#26 Mh FOLLOW-UP STUDIES
#27 Mh PROSPECTIVE STUDIES
#28 Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$
#29 #24 OR #25 OR #26 OR #27 OR #28
#30 Ct ANIMAL AND NOT (Ct HUMAN and Ct ANIMAL)
#31 #29 AND NOT #30
#32 #31 AND NOT (#9 OR #23)
#33 #9 OR #23 OR #32

Appendix 4. Search filter for RCTs for EMBASE

#1 random$
#2 factorial$
#3 crossover$
#4 cross over$
#5 placebo$
#6 doubl$ adj blind$
#7 singl$ adj blind$
#8 assign$
#9 allocat$
#10 volunteer$
#11 crossover-procedure
#12 double-blind procedure
#13 randomized controlled trial
#14 single-blind procedure

Appendix 5. Search Strategy - The Cochrane Library

#1 MeSH descriptor Down Syndrome explode all trees
#2 MeSH descriptor Exercise explode all trees
#3 MeSH descriptor Physical Education and Training explode all trees
#4 MeSH descriptor Swimming explode all trees
#5 MeSH descriptor Walking explode all trees
#6 MeSH descriptor Running explode all trees
#7 MeSH descriptor Motor Activity explode all trees
#8 MeSH descriptor Physical Fitness explode all trees
#9 MeSH descriptor Physical Therapy (Specialty) explode all trees
#10 MeSH descriptor Physical Endurance explode all trees
#11 MeSH descriptor Physical Therapy Modalities explode all trees
#12 (physical exercise$)
#13 (rowing)
#14 (EXERCISE TRAIN$)
#15 (TRAINING PROGRAM$)
#16 (physical education$)
#17 (training)
#18 (AEROBIC TRAINING)
#19 (#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18)
#20 (#1 AND #19)

F E E D B A C K

Comments regarding excluded study, 28 February 2009

Summary

The study Carmelli 2002a has been excluded from this review on the grounds that it is not randomised. However, on page 107, under the heading "Walking Training Protocol", it states: "Participants in the study were randomly assigned to either the WG or the CG by means of a coin toss." This study has also been confirmed as being randomised by two independent raters on the PEDro database of randomised trials in physiotherapy: www.pedro.fhs.usyd.edu.au

Reply

We have now reassessed and included the Carmelli 2002 trial and at the same time, thoroughly updated the review. We would like to thank Mark Elkins and the staff of PEDro database for their feedback, which has made us look again at this issue.

Contributors

This feedback was prepared by Jane Dennis, feedback editor for CDPLPG, in consultation with the submitter, the authors, the co-ordinating editor and the managing editor.

WHAT'S NEW

Last assessed as up-to-date: 18 February 2010.

Date	Event	Description
8 December 2010	Amended	Author contact details updated

HISTORY

Protocol first published: Issue 1, 2005

Review first published: Issue 3, 2005

Date	Event	Description
28 April 2010	Amended	References updated
14 April 2010	New citation required but conclusions have not changed	Review reinstated after temporary withdrawal
14 April 2010	New search has been performed	Full update undertaken in light of feedback received
14 April 2010	Feedback has been incorporated	Updated in response to feedback
13 May 2009	New search has been performed	Temporary withdrawal

(*Continued*)

8 July 2008	Amended	Converted to new review format.
1 March 2007	Amended	Searches for this version of the review were run in March 2007. No studies identified met inclusion criteria; however, relevant material has been added to the Discussion section
21 March 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Luiz Roberto Ramos (LRR) was responsible for conception of this review. Design and overall coordination of this protocol was done by Regis Andriolo (RA). RA was responsible for the search strategy, in collaboration with trial search coordinators Eileen Brunt and Jo Abbott of the Cochrane Developmental, Psychosocial and Learning Problems Group. RA ran searches and, in collaboration with Regina El Dib, screened search results, obtained papers, screened retrieved papers against inclusion criteria, appraised quality of papers and extracted data. RA wrote to authors of papers for additional information and to locate potentially relevant unpublished or ongoing studies.

RA was responsible for data management for the review, although data was entered independently by the two reviewers. RA analysed and interpreted data and wrote up the results, whilst seeking clinical, methodological, policy and consumer perspectives.

ANA and EMKS updated the review and inserted considerations on "Discussion".

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Capes - Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brazil.

Coordination of Improvement of Higher Education

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Assessment of risk of bias of included studies

The items to evaluate the risk of systematic error were modified according to suggested by the updated Cochrane Handbook (Higgins 2008).

Types of outcomes

Besides validated methods to evaluate the outcomes, the authors of this review will also accept studies with methods tested for their internal validity (eg., concordance inter- and intra-observer or comparison with an acceptable reference standard).

Outcomes were properly divided to "primary outcomes" and "secondary outcomes".

Sensitivity analysis

Impact of study quality on treatment effect will be analysed using sensitivity analysis. Intention-to-treat analysis versus available data analysis will also be investigated in future versions of this systematic review, because until now there was insufficient data to enable any sensitivity analysis.

NOTES

This review was temporarily withdrawn following the authors' attention being brought to a misclassification of an excluded study. This updated version now includes that study, and has been fully updated with new searches.

INDEX TERMS

Medical Subject Headings (MeSH)

*Exercise [physiology; psychology]; Down Syndrome [*physiopathology; *psychology]; Physical Fitness [physiology; psychology]; Program Evaluation; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Adult; Aged; Humans; Middle Aged; Young Adult