Strength training and aerobic exercise training for muscle disease (Review)

Voet NBM, van der Kooi EL, Riphagen II, Lindeman E, van Engelen BGM, Geurts ACH
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Strength training and aerobic exercise training for muscle disease

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ABSTRACT

Background

Strength training or aerobic exercise programmes might optimise muscle and cardiorespiratory function and prevent additional disuse atrophy and deconditioning in people with a muscle disease. This is an update of a review first published in 2004.

Objectives

To examine the safety and efficacy of strength training and aerobic exercise training in people with a muscle disease.

Search methods

We searched the Cochrane Neuromuscular Disease Group Specialized Register (July 2012), CENTRAL (2012 Issue 3 of 4), MEDLINE (January 1946 to July 2012), EMBASE (January 1974 to July 2012), EMBASE Classic (1947 to 1973) and CINAHL (January 1982 to July 2012).

Selection criteria

Randomised or quasi-randomised controlled trials comparing strength training or aerobic exercise programmes, or both, to no training, and lasting at least six weeks, in people with a well-described diagnosis of a muscle disease.

We did not use the reporting of specific outcomes as a study selection criterion.

Data collection and analysis

Two authors independently assessed trial quality and extracted the data obtained from the full text-articles and from the original investigators. We collected adverse event data from included studies.
Main results

We included five trials (170 participants). The first trial compared the effect of strength training versus no training in 36 people with myotonic dystrophy. The second trial compared aerobic exercise training versus no training in 14 people with polymyositis and dermatomyositis. The third trial compared strength training versus no training in a factorial trial that also compared albuterol with placebo, in 65 people with facioscapulohumeral muscular dystrophy (FSHD). The fourth trial compared combined strength training and aerobic exercise versus no training in 18 people with mitochondrial myopathy. The fifth trial compared combined strength training and aerobic exercise versus no training in 35 people with myotonic dystrophy type 1.

In both myotonic dystrophy trials and the dermatomyositis and polymyositis trial there were no significant differences between training and non-training groups for primary and secondary outcome measures. The risk of bias of the strength training trial in myotonic dystrophy and the aerobic exercise trial in polymyositis and dermatomyositis was judged as uncertain, and for the combined strength training and aerobic exercise trial, the risk of bias was judged as adequate. In the FSHD trial, for which the risk of bias was judged as adequate, a +1.17 kg difference (95% confidence interval (CI) 0.18 to 2.16) in dynamic strength of elbow flexors in favour of the training group reached statistical significance. In the mitochondrial myopathy trial, there were no significant differences in dynamic strength measures between training and non-training groups. Exercise duration and distance cycled in a submaximal endurance test increased significantly in the training group compared to the control group. The differences in mean time and mean distance cycled till exhaustion between groups were 23.70 min (95% CI 2.63 to 44.77) and 9.70 km (95% CI 1.51 to 17.89), respectively. The risk of bias was judged as uncertain. In all trials, no adverse events were reported.

Authors’ conclusions

Moderate-intensity strength training in myotonic dystrophy and FSHD and aerobic exercise training in dermatomyositis and polymyositis and myotonic dystrophy type I appear to do no harm, but there is insufficient evidence to conclude that they offer benefit. In mitochondrial myopathy, aerobic exercise combined with strength training appears to be safe and may be effective in increasing submaximal endurance capacity. Limitations in the design of studies in other muscle diseases prevent more general conclusions in these disorders.

Plain Language Summary

Strength training or comprehensive aerobic exercise training for muscle disease

Strength training, which is performed to improve muscle strength and muscle endurance, or aerobic exercise programmes, which are designed to improve cardiorespiratory endurance, might optimise physical fitness and prevent additional muscle wasting in people with muscle disease. However, people with muscle disease and some clinicians are still afraid of overuse and have a cautious approach to training. This updated review (most recent date of search 2 July 2012) included two eligible trials of strength training in people with facioscapulohumeral muscular dystrophy (FSHD) and myotonic dystrophy (101 participants), two trials of strength training combined with aerobic exercise in people with mitochondrial myopathy (18 participants) and myotonic dystrophy type I (35 participants) and one trial of aerobic exercise in people with polymyositis and dermatomyositis (14 participants). These trials showed that moderate-intensity strength training in people with myotonic dystrophy or with FSHD, and aerobic exercise training in people with dermatomyositis or polymyositis appear not to harm muscles. Strength training combined with aerobic exercise appears to be safe in myotonic dystrophy type I and may be effective in increasing endurance in people with mitochondrial myopathy. Evidence suggests that strength training is not harmful in people in FSHD, myotonic dystrophy, mitochondrial disorders and dermatomyositis and polymyositis, but further research is needed to determine potential benefit.
### Summary of Findings for the Main Comparison

**Strength training compared to usual care for facioscapulohumeral muscular dystrophy**

**Patient or population:** facioscapulohumeral muscular dystrophy  
**Settings:** at home  
**Intervention:** strength training  
**Comparison:** usual care

<table>
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<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
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<td><strong>Assumed risk</strong></td>
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<td>Strength training</td>
<td>The mean difference in dynamic muscle strength of elbow flexors in the control groups was <strong>1.39 Nm</strong></td>
<td>The mean difference in dynamic muscle strength of elbow flexors in the intervention groups was <strong>1.17 higher</strong> (0.18 to 2.16 higher)</td>
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*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).*

**GRADE Working Group grades of evidence**

- **High quality:** Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low quality:** We are very uncertain about the estimate.

1 The lower confidence limit crosses the minimal important difference.
BACKGROUND

The term ‘muscle disease’ comprises a large group of conditions. Skeletal muscles are primarily affected but in some disorders other organ systems may also be involved. Most conditions are progressive, causing the muscles to gradually weaken over time. When a person is diagnosed as having a muscle disease, questions arise about the prognosis, possible interventions and genetics. However, people with muscle disease are usually also concerned about everyday issues such as participation in sports, work and hobbies. We cannot give evidence-based advice about these issues, because we do not know how physical exercise affects the diseased muscular system or the cardiorespiratory system. To answer these questions, controlled trials of aerobic exercise and strength training in people with a muscle disease are needed.

Weakness and impaired cardiorespiratory function are common in people with muscle disease; pain and fatigue may also be common symptoms, all of which contribute to a decreased quality of life. In healthy persons the best intervention to improve strength and cardiorespiratory function is physical training. Strength training or aerobic exercise programmes in people with muscle disease might maximise muscle and cardiorespiratory function and prevent additional disuse atrophy (Vignos 1983). However, reports of progression of weakness after exercise in people with myopathies have encouraged a cautious approach to training (Brouwer 1992; Fowler 1984; Johnson 1971). Therefore, many people with a muscle disease were advised to avoid physical exertion (Fowler 1982). Thus the benefit from strength training or aerobic exercise training in muscle diseases is still not clear (Kilmer 1998).

The relative rarity of many muscle diseases has led researchers to group participants with different neuromuscular disorders together in one study, including myopathies, neuropathies and motor neuron disease (Aitkens 1993; Dawes 2006; Kilmer 1994; Kilmer 2005; McCartney 1988; Milner-Brown 1988a; Milner-Brown 1988b; Wright 1996). As the pathophysiology of these disorders differs, their reaction to an intervention might also be different. Therefore, conclusions about the effect of training derived from these mixed populations cannot readily be extrapolated to people with specific muscular disorders (Lindeman 1995).

In this review we systematically analysed randomised controlled trials (RCTs) of these interventions for people with specified muscle diseases. This review was first published in 2004, with the most recent update of the searches in 2012.

OBJECTIVES

To examine the safety and efficacy of strength training and aerobic exercise training in people with a muscle disease.

METHODS

Criteria for considering studies for this review

Types of studies

We included all RCTs or quasi-RCTs that made any of the following comparisons:

- strength training versus no training;
- aerobic exercise training versus no training;
- combined strength training and aerobic exercise versus no training.

Quasi-RCTs are trials that allocate participants to experimental or control groups based on a method that is not truly random, for example, hospital record number or date of birth.

Types of participants

We selected all trials that included participants with a well-described diagnosis of a muscle disease, such as inflammatory myopathies, metabolic myopathies, muscular dystrophies, muscle diseases with myotonia and other well-defined myopathies. We decided not to include studies looking at strength training or aerobic exercise training for people in whom muscle weakness was not the primary feature, but might have been secondary to chronic renal insufficiency, chronic heart failure, renal or heart transplantation, or corticosteroid use. We did not review the effects of respiratory muscle training. We did not include studies regarding aerobic exercise training for McArdle disease because there is a separate Cochrane review available for this metabolic myopathy (Quinlivan 2011). We excluded studies in which participants had a variety of muscle diseases if we could not obtain results for each condition separately. We assessed the diagnostic criteria of each study; diagnosis has to be confirmed by muscle biopsy or genetic testing.

Types of interventions

To date, there is no evidence or recommendation for a minimum duration of training in muscle disease. However, in the first six weeks, the change in muscle strength or aerobic capacity is generally caused by neural adaptation. Therefore, we included all forms of strength training and aerobic exercise training lasting at least six weeks. We excluded all studies using a within-subjects design with the non-exercised limb as a control. If exercises are performed to increase muscle strength on one side of the body, voluntary strength can increase on the contralateral side. This concept is called cross-education, and has been described with different forms of exercises. A meta-analysis of 16 randomised studies concluded that, on average, the magnitude of cross-education is eight per cent of the initial strength of the untrained limb (Munn 2004). Neural adaptations to training and learning effects due to testing are postulated as explanations (Lee 2007; Munn 2005; Sale 1988; Shima 2002). Moreover, the results may well be confounded by
the presence of asymmetric weakness of both limbs, as the absolute gain in muscle strength resulting from strength training is related to pre-exercise muscle weakness (Kilmer 2002). For this reason, a non-exercised limb is not an appropriate control, even if training is randomly assigned. For this reason, we have excluded studies using such a within-subjects design.

Definitions

- Training, or physical fitness training: a planned, structured regimen of regular physical exercise deliberately performed to improve one or more of the following components of physical fitness: cardiorespiratory fitness, body composition, muscle strength and endurance, and flexibility (Garber 2011).
- Strength training: a systematic program of exercises designed to increase an individual’s ability to exert or resist force, for example, weights, weight machines or elastic cords (Garber 2011).
- Aerobic exercise training, or cardiorespiratory fitness training: training that is designed to improve the capacity and efficiency of aerobic energy-producing systems and is effective for improving cardiorespiratory endurance. It consists of an activity or combination of activities that uses large muscle groups, that can be maintained continuously, and is rhythmical and aerobic in nature, for example walking, running, cycling, aerobic dance exercise or swimming (Garber 2011).

Types of outcome measures

Primary outcomes

The primary outcome measure for strength training was:
- change in muscle strength, expressed in measures of static (that is, isometric) or dynamic strength between baseline and six weeks.

The primary outcome measure for aerobic exercise training was:
- change in aerobic capacity, expressed in measures of work capacity between baseline and six weeks.

Secondary outcomes

The secondary outcome measure specific to strength training was:
- change in muscle endurance muscle endurance or muscle fatigue between baseline and six weeks.

The secondary outcome measure specific to aerobic exercise training was:
- change in aerobic capacity, expressed in measures of oxygen consumption, parameters of cardiac function or parameters of respiratory function between baseline and six weeks.

Secondary outcome measures applicable to both strength training and aerobic exercise training showing a change from baseline and six weeks were:
- timed-scored functional assessments of muscle performance, such as a six-minute walk test (Florence 2008);
- quality of life measures, such as the Short Form 36 (SF-36) Health Survey (Ware 2000);
- parameters of muscle membrane permeability (serum creatine kinase level, myoglobin level) to assess safety;
- pain assessed by an analogue pain scale (Kahl 2005);
- experienced fatigue assessed by questionnaires, eg. Checklist Individual Strength (CIS-fatigue) (Vercoulen 1999);
- adverse effects requiring withdrawal of the participant from the study: acute rhabdomyolysis, increasing muscle pain, injury, etc;

We compared data on outcome measures at baseline with those obtained after at least six weeks of training. When there were assessments at more than one time (during the intervention, after cessation of the intervention), our preference was for data on outcome measures obtained at the end of the intervention.

Search methods for identification of studies

We searched the following databases: the Cochrane Neuromuscular Disease Group Specialized Register (July 2012), the Cochrane Central Register of Controlled Trials (CENTRAL, in The Cochrane Library 2012, Issue 7 of 12), MEDLINE (January 1946 to July 2012), EMBASE (January 1974 to July 2012), EMBASE Classic (1947 to 1973) and CINAHL (January 1982 to July 2012). We reviewed the bibliographies of the trials identified and other reviews of the subject, and contacted some of the authors in the field to identify additional published and unpublished data.

Data collection and analysis

Selection of studies

Two review authors (Voet, van der Kooi) checked the references identified by the search strategy. We obtained the full text of all potentially relevant studies for independent assessment by both authors. We decided which trials fitted the inclusion criteria.

Data extraction and management

Two review authors (Voet, van der Kooi) independently extracted the data from the included trials onto a specially designed data extraction form, and graded the risk of bias and certain other aspects of the design of the included trials.

Assessment of risk of bias in included studies

We assessed the risk of bias and other aspects according to the Cochrane approach using the updated guidance in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011).
We assessed the included studies for randomisation sequence generation, allocation concealment, blinding (participants and outcome assessors), incomplete outcome data, selective outcome reporting and other sources of bias. When there was uncertainty, we contacted authors for clarification. We resolved disagreements about fulfilment of inclusion or quality criteria by discussion between the two authors. We made a judgement on each of the 'Risk of bias' criteria, of "High risk of bias", "Low risk of bias" or "Unclear risk of bias". Whenever characteristics of study design or drop-out rates were likely to cause a higher risk of bias, we planned to make a note of this and investigate the possibility of differences in treatment effects varying with the degree of this problem.

**Data synthesis**

We intended to combine trial results for appropriate pairings of treatments by calculating a mean of the difference between their effects using the Cochrane statistical package Review Manager 5 (RevMan) (RevMan 2012). Because pooling of the results of trials in different muscle diseases is usually not appropriate, we expressed, when possible, the results per muscle disease as mean differences (MD) with 95% confidence intervals (CI) for continuous outcomes, and risk ratios (RR) with 95% CI for dichotomous outcome measures. The intended testing for heterogeneity, and consequent actions, turned out to be unnecessary.

**Subgroup analysis and investigation of heterogeneity**

We decided, in advance, not to perform subgroup analyses based on sex or age because we anticipated that the differences in muscle disease severity would have a much bigger influence on outcome than sex or age. Moreover, the American College of Sports Medicine stated in their Position Stand (Garber 2011) that relative improvements resulting from aerobic and strength training are similar for young and old, male and female. We presented data for individual muscle diseases separately. As the pathophysiology of each muscle disease differs, we considered that their reaction to training might be different. If in future data are available for meta-analysis, we will consider investigating the effect of different durations of exercise or training intervention.

**RESULTS**

**Description of studies**

In this review, the search retrieved approximately 7400 records. After assessing the titles and abstracts, we identified 61 studies for potential inclusion: 26 completed trials that studied strength training as an intervention, 20 trials studying aerobic exercise training, and 15 trials studying combined strength training and aerobic exercise, sometimes incorporated in more comprehensive rehabilitation programmes. Most strength training trials included people with the following muscle diseases: slowly progressive dystrophies (mostly myotonic dystrophy, limb-girdle dystrophies, facioscapulohumeral muscular dystrophy (FSHD)) and in the older studies, non-specified progressive muscular dystrophies and inflammatory myopathies. Studies on the effects of aerobic exercise training included mainly people with slowly progressive dystrophies and metabolic myopathies (mostly unspecified mitochondrial myopathies).

Studies have generally been limited by small sample sizes. We excluded 48 studies because there was no randomised controlled comparison between training and non-training participants and six studies because of a within-subjects design (see Characteristics of excluded studies).

Only seven studies were RCTs making a comparison between training and non-training participants (Cejudo 2005; Dawes 2006; Kierkegaard 2011; Lindeman 1995; van der Kooi 2004; Wiesinger 1998a; Wiesinger 1998b). Regrettably, the extension of the initially randomised, controlled six-week aerobic exercise study in people with dermatomyositis and polymyositis by Wiesinger et al (Wiesinger 1998b) lost its randomised controlled design due to a decision of the ethics committee. The randomised controlled strength training combined with aerobic exercise trial which compared eight weeks of walking and strengthening exercises versus no training in 20 participants with different muscle diseases (Dawes 2006) has been excluded as both study groups consisted of participants with various muscle diseases and the outcome measures were not presented for each muscle disease separately. As the pathophysiology of each muscle disease differs, their reaction to training might be different. It is not known if the effect of strength training and aerobic exercise training is the same for every muscle disease. Therefore, data should be presented and analysed for each disease individually, and the power should be sufficient for each individual disorder. For this reason, no conclusions can be drawn with regard to the effect of exercise training for each specific muscle disease in the trial. Finally, no specific details about the exercise programme were provided and the risk of bias of the trial was high.

In conclusion, we included two strength training trials (Lindeman 1995; van der Kooi 2004), one aerobic exercise trial (Wiesinger 1998a) and two strength training combined with aerobic exercise trials (Cejudo 2005; Kierkegaard 2011) (see Characteristics of included studies). The first strength training trial compared the effect of 24 weeks of training versus no training in 36 adults with myotonic dystrophy and 30 adults with hereditary motor and sensory neuropathy types I or II (Lindeman 1995). As this review is concerned with muscle disease, we will not discuss the results of the hereditary motor and sensory neuropathy participant group. The aerobic exercise trial compared six weeks of cycle and step aerobics exercise with no training in nine adults with dermatomyositis and five adults with polymyositis (Wiesinger 1998a). The sec-
ond strength training trial compared 52 weeks of strength training versus no training in a factorial trial that also compared albuterol with placebo after the first 26 weeks of training in 65 adult participants with FSHD (van der Kooi 2004). Only the results for the comparison strength training versus no training will be discussed in this review. The first combined aerobic exercise and strength training trial compared 12 weeks of cycle exercises and dynamic and isokinetic strength training versus no training in 18 people with mitochondrial myopathy (Cejudo 2005) (see Characteristics of included studies). The second combined aerobic exercise and strength training trial compared 14 weeks of balance exercises, aerobic activities, flexibility exercises, strength exercises and a brisk walk versus no training in 35 people with myotonic dystrophy type 1 (Kierkegaard 2011).

Risk of bias in included studies

Strength training trial in myotonic dystrophy

In the first myotonic dystrophy trial (Lindeman 1995), participants with myotonic dystrophy were individually matched for muscle strength and performance in a stair-climbing test. Within each matched pair, participants were randomly assigned to the training or control group. There was no published information on the method of randomisation or on allocation concealment but the first author (Lindeman) informed us that two independent persons drew one sealed name per matched pair and allocated it to the training or non-training group by tossing a coin. We graded the intention to blind the clinical evaluators as adequate, although approximately 20% of the myotonic dystrophy participants revealed information to the clinical evaluators that resulted in unblinding during the course of the trial. The authors considered the baseline comparability of the groups as suboptimal because the training group had longer time scores for stair climbing (a measure of functional ability) and had higher knee torques (a measure of muscle strength). They argued that the first three items could have resulted in an underestimation of the training effect, whereas the last item could have resulted in an overestimation of the training effect. They concluded that the differences in experimental group composition did not seem to explain the absence of differences in outcomes between treatment groups. We considered the way the authors presented and discussed the baseline differences as adequate. Three of the initially 36 randomised participants withdrew before disclosure of treatment allocation. The 33 participants starting the trial made 15 matched pairs. During the trial one person dropped out because of knee problems. Because of the matched pair design only complete pairs were analysed, thus eventually 28 of the initial 36 randomised participants were analysed. Follow-up was therefore incomplete and analysis was not by intention-to-treat. However, the flow path of participants was well documented.

Dermatomyositis and polymyositis trial

In the dermatomyositis and polymyositis trial (Wiesinger 1998a), nine people with dermatomyositis and five with polymyositis were randomly assigned to the training or control group using distinct randomisation lists. The training group received six weeks of bicycle exercises and step aerobics. Participants in the control group did not undergo any training and continued their previous way of life. There was no published information on allocation concealment and our attempts to obtain further information on this were not successful. During the strength measurements, the clinical evaluator was blinded to the treatment allocation. The success of blinding of assessors was not formally checked as blinding of participants is not possible in an exercise study. There was no published information on blinding during the other measurements. Baseline characteristics were presented for both groups. The authors considered the two groups to be well balanced with respect to most baseline characteristics. There was complete follow-up of all participants.

Facioscapulohumeral muscular dystrophy (FSHD)

In the FSHD trial (van der Kooi 2004), 65 participants were stratified into two groups based on muscle strength. Participants in both strata were randomly assigned to one of the four treatment groups according to a computer-generated randomisation list. The treatments consisted of training plus albuterol, training plus placebo, non-training plus albuterol, or non-training plus placebo. Training or non-training was the first intervention, starting just after the baseline visit until after the final visit at 52 weeks. Information on the assignment to training or non-training was disclosed to the participants by the physical therapist (supervising the training programme) after their baseline visit. The clinical evaluator was blinded for the assignment to both interventions. The participants, physical therapist and the neurologist evaluating side effects were blinded to the treatment allocation. The blinding of the clinical evaluator was considered adequate, although one of the main secondary outcome measures, the one-repetition maximum (1RM) measurement for assessing dynamic strength, was performed by the physical therapist who supervised the training, and who was therefore not blinded to the allocation to training or non-training. Allocation to the training or non-training group was unmasked in three cases, due to unintentional remarks. The success of blinding was not formally checked. Baseline characteristics were presented for all treatment groups. One participant stopped training but still attended all trial visits, resulting in complete follow-up of all participants. Data analysis was by the intention-to-treat principle. As no statistically significant interactions between the two interventions (that is, training versus non-training) could be detected, the effect sizes, being the differences in mean change from baseline, were presented for each intervention.
Combined aerobic exercise and strength training trial in mitochondrial myopathy

In the mitochondrial myopathy trial (Cejudo 2005), 20 participants were randomly assigned to the training or control group. There was no published information on the method of randomisation, allocation concealment, or blinding of the evaluators. The author (Cejudo) informed us that participants were randomly assigned according to a computer generated randomisation list. The evaluators were not blinded to the intervention allocation, but knew to which group each participant was assigned. One participant in each group failed to finish the study for personal reasons. Baseline characteristics were presented for both groups, except for the participants lost to follow-up. Follow-up was therefore incomplete and analysis was not done by intention-to-treat. No flow path of participants was documented. The authors considered both groups as comparable with respect to age and gender, as well as to each measured variable at baseline.

Combined aerobic exercise and strength training trial in myotonic dystrophy type 1

In the second myotonic dystrophy trial (Kierkegaard 2011), the median value of the results of the six-minute walk test was used to divide the 35 participants into two strata from which they were divided into the training or the control group. The lots consisted of folded pieces of paper with the name of the participant and were drawn by a person not involved in any part of the study. Since participants were recruited before randomisation, concealed allocation procedures were applied. An intention-to-treat analysis was applied. Three participants had missing data for perceived exertion at baseline and one person in the control group did not attend the measurement after the intervention but still completed the questionnaires. There was no significant difference in sex or age of participants between groups in the study; however, the mean muscular impairment scale (MIRS) grade was higher in the exercise group, indicating that participants in the exercise group were more severely impaired than participants in the control group. The training group received a comprehensive group exercise training programme, they were also asked to perform an active 30 min walk every week. The participants in the control group were advised to live their normal lives and to maintain their degree of physical activity during the study period. The degree of activity of both groups was not objectively checked.

We ranked each criterion using the Cochrane 'Risk of bias' tool. The review authors’ judgements about each risk of bias item for included studies are presented in Figure 1.
**Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.**

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<th>Allocation concealment (selection bias)</th>
<th>Blinding (performance bias and detection bias)</th>
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<th>Selective reporting (reporting bias)</th>
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<td>Lindeman 1995</td>
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<td>van der Kooi 2004</td>
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<td>Wiesinger 1998a</td>
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</table>
Quality of diagnostic criteria

This assessment took into account if and how diagnoses were verified. In the first myotonic dystrophy trial (Lindeman 1995), participants were recruited via neurologists, physiatrists and the Dutch association for neuromuscular diseases (Vereniging Spierziekten Nederland) on clinical grounds and without genetic verification. We therefore considered the quality of the diagnostic criteria as inadequate. In the second myotonic dystrophy (type I) trial (Kierkegaard 2011), the diagnosis was genetically confirmed in all participants and the diagnostic criteria are therefore adequate.

In the dermatomyositis and polymyositis trial (Wiesinger 1998a), all the participants had an established diagnosis of primary inflammatory muscle disease as defined by the established criteria of Bohan and Peter, with a disease duration of at least six months (Bohan 1975a; Bohan 1975b). In all participants, muscle biopsies, electromyograms and laboratory studies had been performed to establish the diagnosis. We therefore considered the quality of the diagnostic criteria to be adequate.

In the FSHD trial (van der Kooi 2004), participants or a first-degree relative had the associated deletion at chromosome 4 (Deidda 1996). The quality of the diagnosis was therefore adequate. In the mitochondrial myopathy trial (Cejudo 2005) participants were recruited from a larger group of patients followed at the university hospital of Sevilla, Spain. Diagnosis was based on clinical and muscle biopsy data. Biopsy findings were determined by biochemical and histological techniques without genetic verification. One participant in each group had only a probable diagnosis of mitochondrial myopathy. The quality of the diagnostic criteria is therefore uncertain.

Quality of training programme

The training programmes of the first myotonic dystrophy (Lindeman 1995), FSHD (van der Kooi 2004), mitochondrial myopathy (Cejudo 2005) and dermatomyositis and polymyositis (Wiesinger 1998a) trials fulfilled most of the minimum requirements as defined by the American College of Sports Medicine (ACSM) Position Stand (Garber 2011). In the second myotonic dystrophy type I trial (Kierkegaard 2011), the intervention consisted of a comprehensive group exercise training programme supported by music. The author could not give the exact training load of each strength training exercise as a percentage of repetition maximum (RM) as it was not tested that way. However, all major muscle groups were trained: arm, back, leg and abdominal muscles (Kierkegaard 2011). The training scheme for the other strength training trials was inadequate only with respect to the number of muscle groups trained, as the ACSM recommends eight to 10 exercises of all the major muscle groups. Only four muscle groups were trained in the first myotonic dystrophy trial (Lindeman 1995), two in the FSHD trial (van der Kooi 2004) and three in the mitochondrial myopathy trial (Cejudo 2005). All studies except the combined aerobic exercise and strength training in myotonic dystrophy type I trial (Kierkegaard 2011), focused on a limited number of muscle groups for reasons of effect evaluation, safety and time restraints per training session.

In the dermatomyositis and polymyositis trial (Wiesinger 1998a), the training frequency was only twice a week in the first two weeks, but increased to three times a week in the remaining four weeks. In the mitochondrial myopathy trial (Cejudo 2005), there was no published information regarding supervision. In the other trials (Kierkegaard 2011; Lindeman 1995; van der Kooi 2004), a physiotherapist supervised training. A description of the training programmes is given in the Characteristics of included studies.

Effects of interventions

See: Summary of findings for the main comparison Strength training compared to usual care for facioscapulohumeral muscular dystrophy; Summary of findings 2 Aerobic exercise and strength training compared to usual care for mitochondrial myopathy.

We intended to combine trial results for appropriate pairings of treatments by calculating a mean of the difference between their effects using the Cochrane statistical package RevMan. Because we could not obtain the original data for the mitochondrial myopathy (Cejudo 2005), dermatomyositis and polymyositis (Wiesinger 1998a) and myotonic dystrophy trials, we describe the results of these trials as published in the article. We were unable to produce MDs and 95% CIs for the myotonic dystrophy trial (Lindeman 1995) because of the matched pair design. We report the findings of the study as given in the paper.

Primary outcome measure for strength training: muscle strength, expressed in measures of static (ie. isometric) or dynamic strength

Muscle strength was the primary outcome measure for the first myotonic dystrophy (Lindeman 1995) and FSHD trials (van der Kooi 2004). In the first myotonic dystrophy trial (Lindeman 1995), differences in muscle strength were measured isokinetically on a dynamometer as maximum concentric knee torques at three velocities, and isometrically as maximum voluntary contraction. Knee torques of the myotonic dystrophy group did not show any statistically significant difference between the training and control groups, as found with a paired t-test. After 24 weeks, mean change in isokinetic knee torque extension was 1.4 Nm (SD 8.2) for the control group and 5.3 Nm (SD 12.9) for the training group, P = 0.34. Mean change in isokinetic knee torque flexion was 3.7 Nm (SD 8.6) for the control group and 7.4 (SD 11.4) for the
training group, \( P = 0.34 \) and mean change in maximum isometric voluntary contraction was 6.6 Nm (SD 11.0) for the control group and 8.7 Nm (SD 14.71) for the training group, \( P = 0.67 \).

The primary outcome measure in the FSHD trial (van der Kooi 2004) was a change in maximum voluntary isometric strength of the elbow flexors and ankle dorsiflexors, measured on a Quantitative Muscle Assessment fixed myometry testing system. After 12 weeks the isometric strength of the elbow flexors did not differ significantly between the training and non-training group, for the right side the difference in the means was 0.54 kgF (95% CI 0.38 to 1.46) (Analysis 2.1), with the better score being for the training group. Dynamic strength was evaluated using the one-repetition maximum (1RM), the weight a person can lift once, but not twice, at a steady controlled pace through the full range of joint motion. The 1RM of the elbow flexors showed a significantly larger increase in the training group compared to the non-training group (for the right side the difference in the means was 1.17 kg (95% CI 0.18 to 2.16) (Analysis 2.2). Both strength measures of the ankle dorsiflexors decreased significantly and markedly in all treatment groups. This decrease was not influenced by training (on the right side the difference in the means in maximum voluntary contraction (MVIC) was 0.43 kgF (95% CI 1.62 to 2.48) (Analysis 2.3) more for the training group, in 1RM the difference was -0.44 kg (95% CI -1.77 to 0.89) (Analysis 2.4) less for the training group). Differences between groups for the left-sided trained muscles did not materially differ from those for the right side.

Muscle strength was a secondary outcome in the mitochondrial myopathy trial (Cejudo 2005). In this trial, weight-lifting capacity was measured as the heaviest weight that could be lifted throughout the complete range of movement (1RM test). After the study period, all participants showed increases in all 1RM tests. After 12 weeks, weight-lifting capacity did not differ significantly between the training and non-training group. The differences in mean 1RM between groups were -5.00 kg (95% CI -14.71 to 4.71) less for the training group for the butterfly exercise (Analysis 3.1), 6.40 kg (95% CI -2.89 to 15.69) in favour of the training group for the butterfly exercise (Analysis 3.2) and 7.30 kg (95% CI -2.91 to 17.51) in favour of the training group for the biceps curls exercise (Analysis 3.3).

**Primary outcome measure for aerobic exercise training: aerobic capacity, expressed in measures of work capacity**

This outcome was published in the mitochondrial myopathy trial (Cejudo 2005) and was a primary outcome in the combined aerobic exercise and strength training trial in myotonic dystrophy (Kierkegaard 2011). In the inflammatory muscle disease trial (Wiesinger 1998a), no primary outcome measure was defined and aerobic capacity was not measured. In the mitochondrial myopathy trial (Cejudo 2005), work capacity was measured in a cycle test and in the shuttle walking test. Endurance time was measured in a submaximal cycling test at a constant workload of 70% of the maximum power output achieved during the baseline increment-

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**Secondary outcome measures for aerobic exercise or strength training, or both**

**Aerobic capacity, expressed in measures of oxygen uptake (ie. VO\textsubscript{2 max})**

This outcome was available for the mitochondrial myopathy (Cejudo 2005) and inflammatory muscle disease trial (Wiesinger 1998a).

In the inflammatory muscle disease trial (Wiesinger 1998a), work capacity was measured during an incremental cycle test on a cycle ergometer. Maximal oxygen uptake (VO\textsubscript{2 max}) was defined as the highest \( O_2 \) consumption obtained during the symptom-limited exercise test. After six weeks, the difference in mean VO\textsubscript{2 max} (ml/min/kg) was 14.6% higher for the training group (95% CI -0.96 to 30.16) (Analysis 2.1).

In the mitochondrial myopathy trial (Cejudo 2005), VO\textsubscript{2 max} was noninvasively determined in a maximal incremental cycle exercise test. After 12 weeks, the difference in mean VO\textsubscript{2 max} was 400 ml/min (95% CI 61.97 to 861.97) in favour of the training group (Analysis 3.9).

**Muscle strength, expressed in measures of endurance or fatigue**

This outcome was published for the first myotonic dystrophy (Lindeman 1995) and FSHD (van der Kooi 2004) studies. In the myotonic dystrophy trial (Lindeman 1995), endurance was measured as maximum duration of contraction at 80% of MVC on an isokinetic dynamometer. After 24 weeks, the difference in MVC for the control group was -7.4 s (SD 12.0) and for the training
group 5.7 s (SD 17.0), P = 0.09. This difference was mainly due to a decrease in endurance in the non-training group.

In the FSHD trial (van der Kooi 2004), muscle endurance was expressed as a Force-Time Integral (FTI30) of a sustained 30 s maximal isometric contraction measured on a Quantitative Muscle Assessment fixed myometry testing system. After 52 weeks, the FTI30 of the elbow flexors did not differ significantly between the training and non-training group. The FTI30 of the ankle dorsiflexors decreased significantly and markedly in all treatment groups. This decrease was not influenced by training (for the right side the difference in the means was -1 kgF (95% CI -42 to 41). Changes in FTI30 for the left-sided trained muscle groups did not differ significantly from the right-sided results.

(Time-scored) functional assessments of muscle performance

This outcome was available for all trials (Kierkegaard 2011; Lindeman 1995; van der Kooi 2004; Wiesinger 1998a) except the mitochondrial myopathy trial (Cejudo 2005). In the first myotonic dystrophy trial (Lindeman 1995), functional assessments comprised the following time-scored activities: ascending and descending stairs, rising from a chair, rising from supine, walking 50 m as fast as possible, and walking 6 m at natural speed. In the inflammatory muscle disease trial (Wiesinger 1998a), the modified Functional Assessment Screening Questionnaire was used for evaluating disability (Millard 1989) (Analysis 1.3).

In the FSHD trial (van der Kooi 2004) the functional tests consisted of the assessment of a functional upper extremity grade and functional lower extremity grade (Personius 1994), and the following timed-scored tasks: standing from lying supine, standing from sitting, walking 30 feet (9.14 m), and climbing three standard stairs (Personius 1994). In the combined aerobic exercise and strength training trial in myotonic dystrophy type 1 (Kierkegaard 2011), the timed-stands test, and the timed up-and-go test were used for evaluation of effects of the exercises (Analysis 4.2; Analysis 4.3).

In all trials (Kierkegaard 2011; Lindeman 1995; van der Kooi 2004; Wiesinger 1998a), no differences between groups in functional assessments were reported.

Quality of life

This outcome was assessed in the FSHD trial (van der Kooi 2004) using the Sickness Impact Profile (SIP) and the Symptom-Checklist (SCL-90-R). The mean total of the SIP and its subscales did not demonstrate relevant or significant changes for either the training or non-training groups. In addition, for both groups the mean SCL total did not change between the baseline and final visit.

In the mitochondrial myopathy trial (Cejudo 2005), the Nottingham Health Profile (NHP) questionnaire was used. Scores ranged from 0 (no problem) to 100 (maximum problem). The MD in overall mean score between both groups was -9.80 (95% CI -25.70 to 6.14) (Analysis 3.7).

In the aerobic exercise and strength training trial in myotonic dystrophy type 1 (Kierkegaard 2011), quality of life was measured by the SF-36 Health Survey. The scores on all subscales of the SF-36 did not demonstrate relevant or significant changes for either the training or non-training group.

Parameters of muscle membrane permeability (serum creatine kinase level, serum myoglobin level, serum aldolase level)

This outcome was available for the first myotonic dystrophy trial (Lindeman 1995), mitochondrial myopathy trial (Cejudo 2005) and inflammatory muscle disease trial (Wiesinger 1998a). In the myotonic dystrophy trial (Lindeman 1995), serum myoglobin levels were assessed just before and one hour after the measurement session at the baseline visit and at the final visit. Changes in serum myoglobin activity one hour after a standardised test should reflect changes in muscle fibre permeability due to muscle damage. The mean rise in serum myoglobin levels did not differ significantly between the training and the non-training group (-21.00 ng/l, 95% CI -48.35 to 6.35) (Analysis 3.8). In the inflammatory muscle disease trial (Wiesinger 1998a), serum levels of creatine kinase and aldolase were measured weekly on Monday after a weekend recovery phase without exercise. There was no statistically significant change in serum creatine kinase level and serum aldolase level during the observation period either in the control group (mean -13.9%, 95% CI -41.74 to 13.54) or in the training group (mean -6%, 95% CI -22.66 to 10.66) (Analysis 1.2).

In the mitochondrial myopathy trial (Cejudo 2005), the authors state that the participants’ serum creatine kinase levels remained unaltered after the intervention period. However, data for the serum creatine kinase level were not published. In the FSHD trial (van der Kooi 2004), one participant stopped training because of recurring, training-related muscle soreness and fatigue. A diagnostic work-up revealed a mitochondrial myopathy as well as FSHD. In the mitochondrial myopathy trial (Cejudo 2005), cancellations of exercise sessions by participants happened because of muscle soreness associated with the exercise activity. However, every participant was able to tolerate the exercise training regimen without complications. In the first myotonic dystrophy trial (Lindeman 1995), a few participants complained of muscle soreness and transient strength reduction after eight weeks. However, no signs of muscle damage were found at the final visit after 24 weeks. In the second myotonic dystrophy trial (Kierkegaard 2011), one person had periods of atrial arrhythmia; however, this was not in connection with the training and the participant was allowed to complete the study by a cardiologist. No other adverse effects were reported.

In all trials no other signs of overuse, such as a decline in strength measures (Cejudo 2005; Lindeman 1995; van der Kooi 2004) or training-related increase in pain or fatigue (van der Kooi 2004)
were reported.

Pain
This outcome was available in both the FSHD (van der Kooi 2004) and mitochondrial myopathy trials (Cejudo 2005). In the FSHD trial (van der Kooi 2004), 11 out of 34 participants in the training group reported pain in the neck and shoulder region to the physical therapist during home visits. Five people mentioned a period with elbow complaints. However, the number of people with neck-shoulder and elbow complaints did not differ between treatment groups at baseline nor at the final visit. Moreover, the number of participants with neck-shoulder and elbow complaints slightly decreased in both groups. RR at the final visit was 1.02 (95% CI 0.66 to 1.58) for neck-shoulder and 1.82 (95% CI 0.17 to 19.13) for elbow complaints in favour of the non-training group. Although not formally quantified, the authors mentioned that participants experienced no notable muscle soreness after training. At the final visit, scores on the VAS for pain and the mean daily rated pain scores did not demonstrate significant changes for either group.

In the mitochondrial myopathy trial (Cejudo 2005), participants’ arm and leg myalgia was recorded by a simple questionnaire and scored as mild, moderate or severe. Two people in the exercise group and three people in the control group reported severe myalgia in arms and legs. Seven people in the exercise group and five people in the control group reported moderate myalgia in arms and legs. After the 12-week training programme no participants in the exercise group and five participants in the control group still reported symptoms of myalgia.

Experienced fatigue
In the FSHD trial (van der Kooi 2004), experienced fatigue was measured by the subscale “fatigue severity” of the Checklist Individual Strength (CIS-fatigue). At the final visit, the mean score on the CIS-fatigue did not change significantly between the baseline and final visit for either group. The mean daily rated fatigue score of the participants in the training group slightly decreased, whereas the score in the non-training group showed a small increase.

In the mitochondrial myopathy trial (Cejudo 2005), participants’ usual fatigability was recorded in a simple questionnaire and scored as mild, moderate or severe. Three participants in the exercise group and five participants in the control group reported severe fatigue in arms and legs. At the end of the study period, no participants in the exercise group and five participants in the control group reported moderate fatigue. Six participants in the exercise group and two participants in the control group reported severe fatigue in arms and legs. After the intervention period, five participants in the exercise group and two participants in the control group still reported moderate fatigue.

Adverse events
There were no serious adverse effects related to strength or aerobic training.
### ADDITIONAL SUMMARY OF FINDINGS

Aerobic exercise and strength training compared to usual care for mitochondrial myopathy

**Patient or population:** mitochondrial myopathy  
**Settings:** unclear  
**Intervention:** aerobic exercise and strength training  
**Comparison:** usual care

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed risk</td>
<td>Corresponding risk</td>
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<tr>
<td></td>
<td>Usual care</td>
<td>Aerobic exercise and strength training</td>
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<tr>
<td>Difference in work capacity - mean time until exhaustion in cycle test electronically braked ergo cycle Follow-up: mean 12 weeks</td>
<td>The mean difference in work capacity - mean time until exhaustion in cycle test in the control groups was -2.7 min</td>
<td>The mean difference in work capacity - mean time until exhaustion in cycle test in the intervention groups was 23.7 higher (2.63 to 44.77 higher)</td>
<td>18 (1 study)</td>
<td>⬠⬠⬠⃝</td>
<td>moderate¹</td>
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<tr>
<td>Difference in work capacity - mean distance until exhaustion in cycle test electronically braked ergo cycle Follow-up: mean 12 weeks</td>
<td>The mean difference in work capacity- mean distance until exhaustion in cycle test in the control groups was -0.9 km</td>
<td>The mean difference in work capacity- mean distance until exhaustion in cycle test in the intervention groups was 9.7 higher (1.51 to 17.89 higher)</td>
<td>18 (1 study)</td>
<td>⬠⬠⬠⃝</td>
<td>moderate¹</td>
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</table>

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).  
**CI:** confidence interval
GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

In this trial, clinical evaluators were not blinded, which may have led to an overestimation of the training effect on muscle strength and aerobic capacity. Analysis in this trial was not by intention-to-treat.
DISCUSSION

Only six out of the 60 identified studies on the effect of training in people with muscle disease used a randomised controlled design (Cejudo 2005; Dawes 2006; Lindeman 1995; van der Kooi 2004; Wiesinger 1998a; Kierkegaard 2011). The randomised controlled strength training combined with aerobic exercise trial which compared eight weeks of walking and strengthening exercises versus no training in 20 participants with different muscle diseases (Dawes 2006) has been excluded because the outcome measures were not presented separately for each different muscle disease. Moreover, no specific details about the exercise programme were provided and the risk of bias of the trial was judged as ‘high’.

The strength training trial in FSHD participants (van der Kooi 2004) had minor methodological shortcomings. One of the main secondary outcome measures, the 1RM strength measurement, was performed by a physical therapist not blinded to the allocation to training or non-training. The overall risk of bias was, therefore, judged as ‘low’.

The dermatomyositis and polymyositis trial (Wiesinger 1998a) had several uncertainties regarding the generation of the randomisation list, allocation concealment and blinding of the assessor. No primary or secondary outcome measures were defined. The overall risk of bias was, therefore, judged as ‘unclear’.

In the myotonic dystrophy strength training trial (Lindeman 1995) diagnoses were not adequately verified. Furthermore, analysis was not by intention-to-treat partly due to the matched-pair design. Because of these major methodological shortcomings, we judged the overall risk of bias as ‘unclear’.

In the mitochondrial myopathy trial (Cejudo 2005), clinical evaluators were not blinded, which may have led to an overestimation of the training effect on muscle strength and aerobic capacity. Analysis in this trial was not by intention-to-treat. The overall risk of bias was therefore judged as ‘unclear’.

Most differences in mean muscle strength outcomes (isometric, dynamic and endurance) between groups in all trials showed small, non-significant beneficial effects in favour of the training groups. In the first myotonic dystrophy trial (Lindeman 1995), only changes in the endurance measure (13.10 s longer maximum duration of an isometric contraction (95% CI 2.20 to 24.00)) and in the FSHD trial (van der Kooi 2004) only the dynamic strength measure for the elbow flexors (concentric contraction with 1.20 kg heavier weight (95% CI 0.18 to 2.16)) reached statistical significance. However, no adjustments were made for multiple comparisons.

The absent or limited positive effects of strength training on muscle strength could reflect the inability of the diseased muscular system to respond with normal neural and trophic adaptations to the applied training stimuli. However, part of this lack of response could be due to the specificity of the training (Lindeman 1995).

All adaptations to training are specific to the stimuli applied. Specific strength training essentially involves exercising the muscles in the same manner as the expected use (Kraemer 2002). This means that a training programme with dynamic exercises increases dynamic strength more than isometric strength, and vice versa. This phenomenon of specificity of training has implications for the sensitivity of the outcome measures; for example, the positive effect of a dynamic strength training programme may be captured by using a dynamic evaluation technique, but might be missed using an isometric strength measure. The size of the carry-over effect from, for example, dynamic strength to isometric strength cannot be predicted and it may be that there is a diminished ability of the diseased muscular system to transfer effects of a specific training programme from one strength modality to another (van der Kooi 2004).

In the FSHD trial (van der Kooi 2004), training did not influence strength of the ankle dorsiflexors, in contrast to the elbow flexors. The authors thought that a difference in grade of muscle weakness at baseline between elbow and ankle dorsiflexors might provide the explanation for the difference in their response to training. In this study elbow flexors were eligible for testing and training when strength according to the MRC scale grade was three or more, whereas ankle dorsiflexors were eligible when the muscles moved the ankle joint in a position between dorsiflexion and plantarflexion, which potentially includes MRC grades less than three (Medical Research Council 1981). Therefore, pre-exercise weakness might have been more severe in ankle dorsiflexors compared to elbow flexors. In people with a muscle disease, it is assumed that absolute gain in muscle strength resulting from strength training is probably related to pre-exercise muscle strength, and that severely weakened muscles (< 10% of normal strength) may not be able to improve. However, this widely reported assumption is based on one published observation only (Milner-Brown 1988a).

In the mitochondrial myopathy trial (Cejudo 2005), the MD in aerobic capacity as measured in a submaximal cycle test differed significantly between the training and non-training group after the study period. Participants in the training group cycled, on average 23.70 min (95% CI 2.63 to 44.77) and 9.70 km longer (95% CI 1.51 to 17.89) than participants in the control group. The distance walked in the shuttle walking test did not differ between groups. This could be explained by the specificity of training, because training consisted of cycling rather than walking exercises.

The timed-scored functional assessments did not demonstrate any relevant or significant changes between treatment groups in the two myotonic dystrophy trials (Lindeman 1995; Kierkegaard 2011), the dermatomyositis and polymyositis trial (Wiesinger 1998a) or the FSHD trial (van der Kooi 2004). This may be due to the small number of muscle groups trained, the absent or limited effects on muscle strength, and the specificity of the training stimuli applied.
In all trials no signs of overuse were reported. This is of major clinical importance because these findings do not support the notion of increased risk of muscle strain in slowly progressive muscular dystrophies. However, adverse events were only mentioned in general and not compared between groups. Only in the dermatomyositis and polymyositis trial (Wiesinger 1998a), were serum levels of enzymes mentioned for both groups. Moreover, several participants in all trials experienced muscle soreness. An enhanced liability for overwork weakness in more severely affected FSHD patients cannot be excluded, because patients unable to walk independently were not included in the FSHD trial (van der Kooi 2004). Furthermore, all training studies, including the studies included in this review, imposed a controlled strain for a relatively short period. Hence, exertion of longer duration may still have an undetermined effect on disease progression.

Based on the evidence of the five selected RCTs in this review concerning myotonic dystrophy (Lindeman 1995) and myotonic dystrophy type I (Kierkegaard 2011), dermatomyositis and polymyositis (Wiesinger 1998a), FSHD (van der Kooi 2004) and mitochondrial myopathy (Cejudo 2005), people with these specific disorders can be advised that ‘normal’ participation in sports and work appears not to harm their muscles. Yet there is still insufficient evidence for general prescription of strength training and aerobic exercise programmes in myotonic dystrophy, polymyositis and dermatomyositis and FSHD. Nevertheless, there is some evidence for training effects in mitochondrial myopathy. Unfortunately, no clearly defined exercise protocols can be drawn from the current research evidence.

Evidence from non-randomised studies and other designs, such as pre-post studies or case-control studies showed that aerobic exercise training appears to be safe and effective in adults with various muscle diseases and that strength training appears to be safe and effective in adults with slowly progressive muscle diseases (Cup 2007; Ansved 2008) but limitations in the design of these studies prevent valid conclusions. The number of recent studies lacking a randomised controlled design is striking. At least for the relatively frequent muscle diseases, one should aim for randomised controlled training studies. Preferably, homogeneous groups of people with the same muscle disease should be included. When people with different neuromuscular disorders but with similar distribution and severity of muscle weakness participate in the same study, the data should also be presented for each major type of muscle disease separately to detect possible disease-specific trends. Because we cannot pool the results of the trials in different muscle diseases in this review, it is not possible to define the optimal exercise duration for people with a specific muscle disease.

Specific diagnostic criteria should be given for all muscle diseases included. Information on the severity of the muscle disease in participants should also be presented so as to allow readers to assess the generalisability of the results to other people with the similar type and severity of muscle disease. In trials with a small sample size, participants should be stratified for disease severity. Another related characteristic that may influence outcome is the level of activity (sedentary versus active) at baseline, because in the healthy population untrained persons respond with higher percentages and rates of gain in strength, compared to trained individuals (Garber 2011). Activity level and change in activity level for each participant should be monitored objectively during the trial period, for example with an accelerometer.

Participants in an active training group may experience additional non-specific benefits (that is, Hawthorne effects), for instance from regular interaction with a skilled therapist, in contrast to those in a non-treatment or usual care group. As it is well known that such Hawthorne effects may affect outcome (Parsons 1974), future studies should preferably have an appropriate control intervention rather than ‘no training’ in order to assess the specific benefits of aerobic exercise and strength training. For example, the control group might receive weekly counselling sessions with general information about exercise.

In strength training and aerobic exercise intervention studies, the training programme should be described in detail, just as the prescription of drugs would be. Authors should provide information about the type(s) of exercises, the intensity (including progression rate), frequency, duration per exercise session, the duration of the entire programme, as well as the trained muscle groups, and the supervision of training.

The recommendations from the ACSM Position Stand on ‘The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults’ (Garber 2011) can be used as requirements for an effective, safe and individualised exercise prescription, taking into account the pre-training level of fitness. The ACSM recommendations were almost all adhered to by most of the included and excluded studies in this review. The only criterion that was rarely met was that eight to 10 major muscle groups should be exercised in strength training programmes. This is probably partly due to limitations in time available to evaluate the effects of training by multiple assessments covering the different outcome measures. In addition, expenses for (adjusted) training equipment can be high. Thirdly, investigators were perhaps too cautious in order not to strain participants too much. Moreover, strength training for fewer than eight muscle groups could be adequate in people with a muscle disease, who are generally untrained.

More studies that evaluate the level of basic muscle function and aerobic capacity are needed on the effects of aerobic exercise and strength training programmes in people with specific muscle diseases. There are well-validated outcome measures that are able to assess positive and, at least equally important, negative effects on the diseased muscular system. The expertise to deliver training programmes in healthy individuals is already present in sports medicine and experts in exercise physiology should be consulted.
If strength training and aerobic exercise training programmes prove to be effective for people with a muscle disease, we can then aim to develop and evaluate programmes adjusted to each different muscle disease. In people with muscular disorders, combinations of muscle weakness, fatigue, pain and difficulty exercising can all lead to reduced physical activity and a sedentary lifestyle (McDonald 2002). Physical inactivity negatively impacts quality of life and health outcomes (McDonald 2002).

In healthy young adults, in the elderly, and in cardiac patients, increasing physical activity and participation by comprehensive exercise programmes incorporating aerobic activities, strength training and flexibility exercises has been shown to reduce the risk of several chronic diseases (for example, coronary heart disease, obesity, diabetes and osteoporosis) (Garber 2011). Therefore, indicators of chronic disease risk such as blood pressure, resting heart rate, body mass, glucose tolerance and bone density could be useful as additional outcome measures (Kilmer 2002), although little is known about the risks of comorbidity in people with a muscle disease. Cost-benefit analyses are only relevant if the benefit of training is much higher than studies have shown so far.

In summary, the authors’ recommendations for future studies are as follows.

- Participants with different muscle disorders can participate in one study, but data should be presented for each major type of muscle disease separately.

- Randomised controlled comparisons should be made with participants having the same muscle disease. The effect of training in people with a muscle disease should be compared to a non-exercising control group of people with the same muscle disease and not to healthy individuals, or to contralateral non-exercised limbs.

- An appropriate placebo intervention is recommended in order to measure exercise-specific benefits.

- Stratified randomisation is strongly advised with regard to disease severity, particularly in studies with a small sample size. It should also be considered for pre-training level of activity (sedentary versus active), particularly in aerobic intervention studies.

- The following aspects of the training intervention should be specified: type(s) of exercise training, intensity and progression rate, frequency, duration per exercise session and of the entire programme, trained muscle groups, and supervision of training. Duration of the training intervention should be at least six weeks.

- Outcomes should at least include measures of muscle function (for example, strength, endurance measured by the maximum duration of contraction) and aerobic capacity (for example, work capacity measured by an incremental cycle test), and functional assessments such as a six-minute walk test. Researchers should be aware of the specificity of training effects in their choice of outcome measures. The following evaluations are strongly advised: measures of quality of life, pain and experienced fatigue.

  - Outcomes assessors should be blinded to interventions, to avoid measurement bias.

  - Activity level of participants in the control group should be monitored objectively in order to assess the specific benefits of aerobic exercise and strength training exercise.

AUTHORS’ CONCLUSIONS

Implications for practice

Based on the evidence from five RCTs in this review, moderate-intensity strength training in myotonic dystrophy (Lindeman 1995) and FSHD (van der Kooi 2004), aerobic exercise therapy in dermatomyositis and polymyositis (Wiesinger 1998a) and a combination of strength and aerobic exercise training in myotonic dystrophy type I (Kierkegaard 2011) show no harm, but there is insufficient evidence to conclude that they offer benefit. A combination of aerobic exercise and strength training in mitochondrial myopathy shows no harm and could be beneficial for aerobic capacity (Cejudo 2005). The small number of included studies and limitations in study design of the other studies prevent general conclusions in other muscle diseases.

Implications for research

There is a need for more research to establish whether strength training and aerobic exercise training is beneficial in all forms of muscle disease, and to define the optimal exercise programmes for people with a muscle disease.

ACKNOWLEDGEMENTS

The Netherlands Organisation for Scientific Research (NWO), The Netherlands Organisation for Health Research and Development (ZonMw) and the Princess Beatrix Fund (the Dutch Public Fund for Neuromuscular Disorders) for supporting three of the authors (Voet, van der Kooi, Lindeman) in related neuromuscular research projects.

Editorial support from the Cochrane Neuromuscular Disease Group for this update was supported by the MRC Centre for Neuromuscular Diseases and the Muscular Dystrophy Campaign.
Strength training and aerobic exercise training for muscle disease (Review)

References to studies included in this review

Cejudo 2005 [published data only]

Kierkeaard 2011 [published data only]

Lindeman 1995 [published and unpublished data]


References to studies excluded from this review

Abramson 1952 [published data only]

Aitkens 1993 [published data only]

Aldehag 2005 [published data only]

Alexanderson 1999 [published data only]

Alexanderson 2000 [published data only]

Alexanderson 2007 [published data only]

Arnardottir 2003 [published data only]

Chung 2007 [published data only]

Dastmalchi 2007 [published data only]
Strength training and aerobic exercise training for muscle disease (Review)

Dawes 2006  {published data only}

De Lateur 1979  {published data only}

Escalante 1993  {published data only}

Florence 1984a  {published data only}

Florence 1984b  {published data only}

Fowler 1965  {published data only}

Heikkila 2001  {published data only}

Hicks 1989  {published data only}

Hoberman 1955  {published data only}

Jeppesen 2006  {published data only}

Jeppesen 2009a  {published data only}

Johnson 2007  {published data only}

Johnson 2009  {published data only}

Kelm 2001  {published data only}

Kilm 2004  {published data only}

Kilm 2005  {published data only}

Lenman 1959  {published data only}

Mate-Munoz 2007  {published data only}

McCarty 1988  {published data only}

Mielke 1990  {published data only}

Milner-Brown 1988a  {published data only}

Milner-Brown 1988b  {published data only}
Milner-Brown HS, Miller RG. Muscle strengthening through electric stimulation combined with low-resistance

**Milner-Brown 1990** *(published data only)*


**Murphy 2008** *(published data only)*


**Na 1996** *(published data only)*


**Nader 2010** *(published data only)*


**Olsen 2005** *(published data only)*


**Omori 2010** *(published data only)*


**Orngreen 2005** *(published data only)*


**Scott 1981** *(published data only)*


**Siciliano 2000** *(published data only)*


**Spector 1997** *(published data only)*


**Sunnerhagen 2004** *(published data only)*


**Sveen 2007** *(published data only)*


**Sveen 2008** *(published data only)*


**Taivassalo 1998** *(published data only)*


**Taivassalo 1999** *(published data only)*


**Taivassalo 2001** *(published data only)*


**Taivassalo 2006** *(published data only)*


**Tollbäck 1999** *(published data only)*


**Trenell 2006** *(published data only)*


**Varju 2003** *(published data only)*


**Vignos 1966** *(published data only)*

Wiesinger 1998b  [published data only]

Wright 1996  [published data only]

Yildirim 2007  [published data only]

References to studies awaiting assessment

Alexanderson 2009  [published data only]

References to ongoing studies

Jansen 2010  [published data only]

Voet 2010  [published data only]

Additional references

Ansved 2008

Bohan 1975a

Bohan 1975b

Brouwer 1992

Cup 2007

Deidda 1996

Florence 2008

Fowler 1982

Fowler 1984

Garber 2011

Higgins 2011

Johnson 1971

Kahl 2005

Kilmer 1998
Kilmer 2002

Kraemer 2002

Lee 2007

McDonald 2002

Medical Research Council 1981

Millard 1989

Munn 2004

Munn 2005

Parsons 1974

Personius 1994

Quinlivan 2011

RevMan 2012

Sale 1988

Shima 2002

Vercoulen 1999

Vignos 1983

Ware 2000

* Indicates the major publication for the study
### Characteristics of included studies  
ordered by study ID

#### Cejudo 2005

<table>
<thead>
<tr>
<th>Methods</th>
<th>Parallel group RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>20 adults with mitochondrial myopathy, diagnosed on the basis of clinical, familial and muscle biopsy data</td>
</tr>
</tbody>
</table>
| Interventions | Strength training and aerobic exercise training versus no training  
 **Type of training and exercise**  
 Endurance bicycle training, dynamic isotonic with weights  
 **Intensity**  
 Aerobic training: individualised work rate, 30 min leg exercise on an ergo cycle, 70% of the peak work rate; strength training: one set dynamic and isotonic of 10 to 15 repetitions at 50% 1RM load, to 2 or 3 sets. Adjustments on workload changed every 2 weeks  
 **Frequency**  
 3 times/week  
 **Duration**  
 Session: approximately 60 min. Programme: 24 weeks  
 **Muscle groups**  
 Shoulder, upper back, arm, pectoralis major, biceps brachii and brachialis muscles  
 **Supervision**  
 Supervised training programme by specialised nurses and a physiatrist specialist in a rehabilitation unit on an outpatient basis |
| Outcomes | Primary: exercise capacity - expressed in measures of oxygen uptake (ie. VO\textsubscript{2} max), endurance time and distance walked in the shuttle walking test. Secondary outcomes were: peripheral muscle strength (1RM test), quality of life, symptoms of myalgia, cramps and fatigability and functional exercise capacity |
| Notes | - |

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias) | Low risk | Quote: “Patients were randomly assigned to a training group or control group”  
 Comment: no published information on the sequence generation. The author (Cejudo) informed us that patients were randomly assigned according to a computer generated randomisation list |
| Allocation concealment (selection bias) | Unclear risk | Quote: “Patients were randomly assigned to a training group or control group”  
 Comment: no published information on the allocation concealment. The author (Cejudo) informed us that patients were ran- |
### Cejudo 2005 (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>High risk</td>
<td>Comment: no published information on the blinding of the outcome assessors and personnel. The author (Cejudo) told us that the evaluators knew to which group each patient was assigned.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>High risk</td>
<td>Quote: &quot;...one patient in each group failed to finish the study for personal reasons&quot;. Comment: baseline outcome data assessed, but not available for these patients. So 1/10 missing from intervention group and 1/10 missing from control group.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>High risk</td>
<td>No primary and secondary outcome(s) defined in the article</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No risk of bias from other sources detected</td>
</tr>
</tbody>
</table>

### Kierkegaard 2011

<table>
<thead>
<tr>
<th>Methods</th>
<th>Evaluator blind, parallel group RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>35 adults with myotonic dystrophy type 1, genetically confirmed</td>
</tr>
<tr>
<td>Interventions</td>
<td>Strength training and aerobic exercise training versus no training</td>
</tr>
<tr>
<td></td>
<td><strong>Type of training and exercise</strong></td>
</tr>
<tr>
<td></td>
<td>Strength training, aerobic exercise, balance exercises</td>
</tr>
<tr>
<td></td>
<td><strong>Intensity</strong></td>
</tr>
<tr>
<td></td>
<td>Strength exercises for arm, leg, back and abdominal muscles 16-20 repetitions, for 6-7 min, balance exercises for 3-4 min, aerobic activities for 11-12 min at 60-80% of maximum heart rate. Once a week a 30-min brisk walk</td>
</tr>
<tr>
<td></td>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td></td>
<td>2 times/week and once a week a brisk walk</td>
</tr>
<tr>
<td></td>
<td><strong>Duration</strong></td>
</tr>
<tr>
<td></td>
<td>Session: 60 min and a 30-min walk. Programme: 14 weeks</td>
</tr>
<tr>
<td></td>
<td><strong>Muscle groups</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Supervision</strong></td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary: distance walked in the 6-min walk test</td>
</tr>
<tr>
<td></td>
<td>Secondary: timed-stands test, timed up-and-go test</td>
</tr>
<tr>
<td>Notes</td>
<td>Participants were stratified before randomisation by their results in the 6-min walk test</td>
</tr>
</tbody>
</table>

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
### Kierkegaard 2011

<table>
<thead>
<tr>
<th>Bias</th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low</td>
<td>Quote: “The lots were drawn by a person who was not involved in any other part of the study”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low</td>
<td>Quote: “Participants were recruited before randomisation”</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias)</td>
<td>Low</td>
<td>Quote: “Data was collected before and after the intervention by two independent experienced physiotherapists, blinded to group allocation and each assessing the same participants on both occasions”</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low</td>
<td>Quote: “one person in the control group did not attend the data collection after the intervention”</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low</td>
<td>No evidence found for selective reporting</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low</td>
<td>No risk of bias from other sources detected</td>
</tr>
</tbody>
</table>

### Lindeman 1995

<table>
<thead>
<tr>
<th>Methods</th>
<th>Evaluator blind, matched-control RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>36 adults with myotonic dystrophy (2 congenital form, 34 classical adult type), diagnosis not verified</td>
</tr>
<tr>
<td>Interventions</td>
<td>Strength training versus no training</td>
</tr>
<tr>
<td><strong>Type of training and exercise</strong></td>
<td>Dynamic strength training with weights</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Individualised progressive overload, 3 sets from 25 repetitions at 60% of 1RM, via 15 repetitions at 70%, to 10 repetitions at 80%</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>3 times/week</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Session: within 30 min. Programme: 24 weeks</td>
</tr>
<tr>
<td><strong>Muscle groups</strong></td>
<td>Knee extensors and flexors, hip extensors and abductors</td>
</tr>
<tr>
<td><strong>Supervision</strong></td>
<td>Supervised home training programme</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Primary: muscle strength by isokinetically measured knee torques and isometrically as MVIC. Main secondary outcomes were: endurance by maximum duration of contraction at 80% of MVIC, functional performance by timed motor performance tests and by questionnaires. Serum myoglobin levels to detect changes in muscle fibre membrane permeability</td>
</tr>
</tbody>
</table>
**Notes**
Participants were matched based on muscle strength (knee extension torque/body weight) and on performance in a stair-climbing test. Only complete pairs were analysed.

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Comment: there was no published information on the sequence generation but the author (Lindeman) informed us that 2 independent persons drew a sealed lot per matched pair and allocated it by tossing a coin to the training or non-training group.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Comment: there was no published information on the method of allocation concealment but the author (Lindeman) informed us that 2 independent persons allocated the training, after tossing the coin, to the training or non-training group.</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>Low risk</td>
<td>Quote: “observers of the outcome measurements were blinded for treatment allocation” Comment: approximately 20% of the myotonic dystrophy participants revealed information to the clinical evaluators that resulted in unblinding during the course of the trial</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>High risk</td>
<td>3 of the initially 36 randomised participants withdrew before disclosure of treatment allocation. The 33 participants starting the trial made 15 matched pairs. During the trial 1 person dropped out. Because of the matched pair design only complete pairs were analysed, therefore eventually 28 of the initial 36 randomised participants were analysed. Follow-up was therefore incomplete and analysis was not by intention-to-treat. However, the flow path of participants was well documented</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence found for selective reporting</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No risk of bias from other sources detected</td>
</tr>
</tbody>
</table>
van der Kooi 2004

<table>
<thead>
<tr>
<th>Methods</th>
<th>Evaluator blind, parallel group, RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>65 adults with FSHD, genetically confirmed</td>
</tr>
</tbody>
</table>
| Interventions | Strength training versus no training (and as add-on in a double blind randomised controlled design albuterol or placebo)  
**Type of training and exercise**  
Dynamic and isometric strength training with weights  
**Intensity**  
Individualised progressive overload, 2 sets dynamic from 10 repetitions at 10RM, via 8 repetitions at 8RM, to 5 repetitions at 5RM, and 30s isometric with same weight  
**Frequency**  
3 times/week  
**Duration**  
Session: Within 30 min. Programme: 52 weeks  
**Muscle groups**  
Elbow flexors, ankle dorsiflexors  
**Supervision**  
Supervised home training programme |
| Outcomes | Primary: difference in muscle strength of elbow flexors and ankle dorsiflexors after 52 weeks using the MVIC. Main secondary outcomes were muscle endurance (MVIC Force-Time Integral) and dynamic muscle strength (1RM). Other measures included functional tests and timed motor performance tasks |
| Notes | Outcomes are presented for the 4 treatment groups (ie. the 4 combinations of training versus non-training, and albuterol versus placebo). Effect sizes are presented by intervention as well |

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: “...participants were randomly assigned to one of the four treatment groups according to a computer generated randomisation list”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Quote: “information on the assignment to training or non-training was disclosed to the participants by the physical therapist”</td>
</tr>
</tbody>
</table>
| Blinding (performance bias and detection bias) All outcomes | Low risk | Quote: “The RM measurements were performed by the physical therapist, who was not blinded for the allocation to training or non-training, as this specific measurement carried too great a risk of unblinding the clinical evaluator”  
Comment: adequate although one of the main secondary outcome measures, the 1RM mea-
van der Kooi 2004  (Continued)

| Incomplete outcome data (attrition bias) | Low risk | Quote: "One patient stopped training because of recurring, training-related muscle soreness and fatigue. Four participants stopped using their study medication because of side effects. Data for the participants who discontinued an intervention were analysed in the assigned treatment group."
| Selective reporting (reporting bias) | Low risk | No evidence found for selective reporting
| Other bias | Low risk | No risk of bias from other sources detected

Wiesinger 1998a

| Methods | Parallel group RCT |
| Participants | 9 adults with dermatomyositis and 5 adults with polymyositis  
Diagnosis of primary inflammatory muscle disease was defined by the criteria of Bohan and Peter |
| Interventions | Aerobic exercise training versus no training  
**Type of training and exercise**  
Endurance bicycle training, endurance step aerobics  
**Intensity**  
Bicycle training: 30 min, slowly increased on an individual basis. Resistance was increased until a heart rate of 60% of maximum. Step aerobics: 30 min  
**Frequency**  
During the first 2 weeks, twice weekly, during the remaining 4 weeks, 3 times weekly  
**Duration**  
Session: 60 min. Programme: 6 weeks  
**Muscle groups**  
Not applicable  
**Supervision**  
Supervised by a physiotherapist |
| Outcomes | No primary outcome or secondary outcomes defined. Study outcomes: activities of daily living score, peak isometric torque of knee extensors and hip flexors, peak oxygen consumption and creatine kinase and aldolase levels |
Outcomes are not presented separately for the dermatomyositis and polymyositis patients

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Quote: “Distinct randomisation lists were used”. Comment: there was no information about the generation of the list. It is not clear what is meant by “distinct randomisation lists”.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Comment: there was no published information on the method of allocation concealment</td>
</tr>
<tr>
<td>Blinding (performance bias and detection bias) All outcomes</td>
<td>Unclear risk</td>
<td>Quote: “Muscle strength assessments were carried out by the same person who was unaware of the group to which the individual patients belonged”. Comment: there was no published information about blinding of the assessor of the other measurements</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>Comment: complete follow-up of all participants</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>High risk</td>
<td>Comment: no primary or secondary outcomes are defined</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No risk of bias from other sources detected. Outcomes are not presented for dermatomyositis and polymyositis separately</td>
</tr>
</tbody>
</table>

MVIC: maximum voluntary isometric strength
RCT: randomised controlled trial
RM: repetition maximum
VO₂ max: maximal oxygen uptake

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abramson 1952</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Aitkens 1993</td>
<td>Not a RCT. Exercised versus non-exercised control limb (randomly assigned) and patients versus healthy volunteers</td>
</tr>
<tr>
<td>Aldehag 2005</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Year</td>
<td>Details</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Alexanderson 1999</td>
<td>Pilot study. Not a RCT</td>
</tr>
<tr>
<td>Alexanderson 2007</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Arnardottir 2003</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Chung 2007</td>
<td>No non-exercising control group</td>
</tr>
<tr>
<td>Dastmalchi 2007</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Dawes 2006</td>
<td>Excluded because of serious insufficiencies in the study design</td>
</tr>
<tr>
<td>De Lateur 1979</td>
<td>Not a RCT. Exercised versus non-exercised control limb (randomly assigned)</td>
</tr>
<tr>
<td>Escalante 1993</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Florence 1984a</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Florence 1984b</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Fowler 1965</td>
<td>Not a RCT. Exercise combined with medication</td>
</tr>
<tr>
<td>Heikkila 2001</td>
<td>Not a RCT. Training programme duration of 3 weeks</td>
</tr>
<tr>
<td>Hicks 1989</td>
<td>Not a RCT. Training programme duration of 1 month</td>
</tr>
<tr>
<td>Hoberman 1955</td>
<td>Not a RCT. 3 drugs added to a comprehensive regimen of therapies, including breathing and resistive exercises</td>
</tr>
<tr>
<td>Jeppesen 2006</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Jeppesen 2009a</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Johnson 2007</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Johnson 2009</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Kelm 2001</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Kilmer 1994</td>
<td>Not a RCT. Exercised versus non-exercised control limb (randomly assigned) and patients versus healthy volunteers</td>
</tr>
<tr>
<td>Kilmer 2005</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Lenman 1959</td>
<td>Not a RCT. Training programme duration for participants with muscle disorders ranged from approximately 1 to 21 months</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td>Mate-Munoz 2007</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>McCartney 1988</td>
<td>Not a RCT. Exercised versus non-exercised control limb (randomly assigned)</td>
</tr>
<tr>
<td>Mielke 1990</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Milner-Brown 1988a</td>
<td>Not a RCT. Training programme duration for participants with muscle disorders ranged from approximately 2 to 48 months</td>
</tr>
<tr>
<td>Milner-Brown 1988b</td>
<td>Not a RCT. Intervention is not training versus non-training, but training added to electric stimulation or electric stimulation only in 1 limb versus a non-stimulated, non-exercised control limb</td>
</tr>
<tr>
<td>Milner-Brown 1990</td>
<td>Not a RCT. Intervention is not training versus no training, but amitriptyline added to strength training</td>
</tr>
<tr>
<td>Murphy 2008</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Na 1996</td>
<td>Not a RCT. Intervention is not training versus non-training, but training and daily quinine sulfate</td>
</tr>
<tr>
<td>Nader 2010</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Olsen 2005</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Omori 2010</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Orngreen 2005</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Scott 1981</td>
<td>A RCT that makes a comparison between 2 different training regimes. No comparison of training versus non-training participants</td>
</tr>
<tr>
<td>Siciliano 2000</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Spector 1997</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Sunnerhagen 2004</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Sveen 2007</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Sveen 2008</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Taivassalo 1998</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Taivassalo 1999</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Taivassalo 2001</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Taivassalo 2006</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Tollbäck 1999</td>
<td>Not a RCT. Exercised versus non-exercised control limb (randomly assigned)</td>
</tr>
</tbody>
</table>
(Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trenell 2006</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Varju 2003</td>
<td>Not a RCT. Training programme duration of 3 weeks</td>
</tr>
<tr>
<td>Vignos 1966</td>
<td>Not a RCT.</td>
</tr>
<tr>
<td>Wiesinger 1998b</td>
<td>A non-randomised extension of a RCT (Wiesinger 1998a)</td>
</tr>
<tr>
<td>Wright 1996</td>
<td>Not a RCT</td>
</tr>
<tr>
<td>Yildirim 2007</td>
<td>Not a RCT</td>
</tr>
</tbody>
</table>

RCT: randomised controlled trial

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

**Alexanderson 2009**

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Patients with recent onset dermatomyositis and polymyositis</td>
</tr>
<tr>
<td>Interventions</td>
<td>A resistive home exercise program versus no training</td>
</tr>
<tr>
<td>Outcomes</td>
<td>-</td>
</tr>
<tr>
<td>Notes</td>
<td>The study will be submitted early 2012</td>
</tr>
</tbody>
</table>

RCT: randomised controlled trial

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

**Jansen 2010**

<p>| Trial name or title | Physical training in boys with Duchenne Muscular Dystrophy: the protocol of the No Use is Disuse study. This study consists of two separate studies. Study 1 &quot;Dynamic leg and arm training for ambulant and recently wheelchair-dependent boys with DMD. Study 2 &quot;Functional training with arm support for boys with DMD who have been confined to a wheelchair for several years&quot; |
| Methods             | Study 1: an explorative RCT with multiple baseline measurements. Study 2: a within-group repeated measurements design |</p>
<table>
<thead>
<tr>
<th>Jansen 2010</th>
<th>(Continued)</th>
</tr>
</thead>
</table>
| **Participants** | Study 1: 30 boys with a DNA-established diagnosis of DMD  
Study 2: 10 boys with a DNA-established diagnosis of DMD already confined to a wheelchair for several years |
| **Interventions** | Study 1: 6-months physical training during which boys train their legs and arms with active or assisted cycling training equipment  
Study 2: 6-months physical training program consisting of 1) computer-assisted training and 2) functional training with an arm support |
| **Outcomes** | Study 1: the primary study outcomes are muscle endurance and functional abilities, assessed with a 6-min bicycle test and the Motor Function Measure  
Study 2: the primary study outcome is functional abilities of the upper extremity, assessed with the Action Research Arm Test |
| **Starting date** | - |
| **Contact information** | m.jansen@reval.umcn.nl |
| **Notes** | The study will finish at the end of 2010 and results are expected in 2012 |

<table>
<thead>
<tr>
<th>Voet 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial name or title</strong></td>
</tr>
<tr>
<td><strong>Methods</strong></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
</tr>
</tbody>
</table>
| **Interventions** | Participants will be randomised to one of 3 groups:  
- a control group (usual care alone, consisting of no therapy at all or occasional (conventional) physical therapy)  
- CBT plus usual care  
- AET, compromising cycle exercises for 4 months plus usual care  
After an intervention period of 16 weeks and a follow-up of 3 months, the third (control) group will be randomised to either AET or CBT (approximately 7 months after inclusion) |
| **Outcomes** | Primary outcome measure: experienced fatigue as measured with the CIS. Outcomes will be assessed at baseline, immediately post intervention and at 3 and 6 months follow-up |
| **Starting date** | January 2009 |
| **Contact information** | N.Voet@reval.umcn.nl |
| **Notes** | The study will finish at the end of 2012 and results are expected in 2013 |

AET: aerobic exercise therapy
### Data and Analyses

**Comparison 1. Aerobic exercise training versus control in polymyositis and dermatomyositis**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Aerobic capacity</td>
<td>1</td>
<td>14</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>14.6 [-0.96, 30.16]</td>
</tr>
<tr>
<td>2 Creatine kinase and aldolase serum level</td>
<td>1</td>
<td>14</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>7.9 [-24.20, 40.00]</td>
</tr>
<tr>
<td>3 Functional assessment - functional assessment screening questionnaire.</td>
<td>1</td>
<td>14</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>17.6 [-5.58, 40.78]</td>
</tr>
</tbody>
</table>

**Comparison 2. Strength training versus control in facioscapulohumeral muscular dystrophy**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Muscle strength elbow flexors - maximum voluntary isometric contraction</td>
<td>1</td>
<td>65</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.54 [-0.38, 1.46]</td>
</tr>
<tr>
<td>2 Muscle strength elbow flexors - dynamic strength</td>
<td>1</td>
<td>65</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>1.17 [0.18, 2.16]</td>
</tr>
<tr>
<td>3 Muscle strength ankle dorsiflexors - maximum isometric voluntary contraction</td>
<td>1</td>
<td>65</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>0.43 [-1.62, 2.48]</td>
</tr>
<tr>
<td>4 Muscle strength ankle dorsiflexors - dynamic strength</td>
<td>1</td>
<td>65</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-0.44 [-1.77, 0.89]</td>
</tr>
</tbody>
</table>

**Comparison 3. Aerobic exercise and strength training versus control in mitochondrial myopathy**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Muscle strength shoulder press - maximum dynamic isotonic voluntary contraction</td>
<td>1</td>
<td>18</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-3.00 [-14.71, 4.71]</td>
</tr>
<tr>
<td>2 Muscle strength butterfly - maximum dynamic isotonic voluntary contraction</td>
<td>1</td>
<td>18</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>6.4 [-2.89, 15.69]</td>
</tr>
<tr>
<td>3 Muscle strength biceps curls - maximum isotonic dynamic voluntary contraction</td>
<td>1</td>
<td>18</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>7.3 [-2.91, 17.51]</td>
</tr>
</tbody>
</table>
Comparison 4. Aerobic exercise and strength training versus control in myotonic dystrophy type 1

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Distance walked in 6-minute walk test</td>
<td>1</td>
<td>35</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>11.0 [-66.92, 88.92]</td>
</tr>
<tr>
<td>2 Timed-stands test</td>
<td>1</td>
<td>35</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-1.0 [-6.76, 4.76]</td>
</tr>
<tr>
<td>3 Timed-up-and-go tests</td>
<td>1</td>
<td>35</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-0.5 [-1.86, 0.86]</td>
</tr>
</tbody>
</table>

Analysis 1.1. Comparison 1 Aerobic exercise training versus control in polymyositis and dermatomyositis, Outcome 1 Aerobic capacity.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 1 Aerobic exercise training versus control in polymyositis and dermatomyositis

Outcome: 1 Aerobic capacity

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiesinger 1998a</td>
<td>12 (12.44)</td>
<td>7 -2.6 (16.93)</td>
<td>IV/Fixed, 95% CI</td>
<td>100.0 %</td>
<td>14.60 [-0.96, 30.16]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>7</td>
<td>7</td>
<td>14.60 [-0.96, 30.16]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 1.84 (P = 0.066)

Test for subgroup differences: Not applicable
Analysis 1.2. Comparison of Aerobic exercise training versus control in polymyositis and dermatomyositis, Outcome 2: Creatine kinase and aldolase serum level.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 1. Aerobic exercise training versus control in polymyositis and dermatomyositis

Outcome: 2. Creatine kinase and aldolase serum level

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean(SD) [%]</td>
<td>N</td>
<td>Mean(SD) [%]</td>
<td>Mean(SD) [%]</td>
<td>N</td>
</tr>
<tr>
<td>Wiesinger 1998a</td>
<td>7</td>
<td>-6 (22.49)</td>
<td>7</td>
<td>-1.39 (37.04)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>7</td>
<td>7</td>
<td>100.0%</td>
<td>7.90 [-24.20, 40.00 ]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.48 (P = 0.63)

Test for subgroup differences: Not applicable

---


Review: Strength training and aerobic exercise training for muscle disease

Comparison: 1. Aerobic exercise training versus control in polymyositis and dermatomyositis

Outcome: 3. Functional assessment - functional assessment screening questionnaire

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>Mean(SD)</td>
<td>N</td>
</tr>
<tr>
<td>Wiesinger 1998a</td>
<td>7</td>
<td>20.5 (10.87)</td>
<td>7</td>
<td>2.9 (29.34)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>7</td>
<td>7</td>
<td>100.0%</td>
<td>17.60 [-5.58, 40.78 ]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 1.49 (P = 0.14)

Test for subgroup differences: Not applicable
### Analysis 2.1. Comparison 2 Strength training versus control in facioscapulohumeral muscular dystrophy, Outcome 1 Muscle strength elbow flexors - maximum voluntary isometric contraction.

**Review:** Strength training and aerobic exercise training for muscle disease

**Comparison:** 2 Strength training versus control in facioscapulohumeral muscular dystrophy

**Outcome:** 1 Muscle strength elbow flexors - maximum voluntary isometric contraction

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>van der Kooi 2004</td>
<td>34 -0.06 (1.93)</td>
<td>31 -0.6 (1.87)</td>
<td>1.15 (P = 0.25)</td>
<td>0.54 [-0.38, 1.46]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>34 31</td>
<td>100.0 %</td>
<td>0.54 [-0.38, 1.46]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** not applicable

**Test for overall effect:** Z = 1.15 (P = 0.25)

**Test for subgroup differences:** Not applicable

### Analysis 2.2. Comparison 2 Strength training versus control in facioscapulohumeral muscular dystrophy, Outcome 2 Muscle strength elbow flexors - dynamic strength.

**Review:** Strength training and aerobic exercise training for muscle disease

**Comparison:** 2 Strength training versus control in facioscapulohumeral muscular dystrophy

**Outcome:** 2 Muscle strength elbow flexors - dynamic strength

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>van der Kooi 2004</td>
<td>34 2.56 (2.09)</td>
<td>31 1.39 (1.97)</td>
<td>2.32 (P = 0.02)</td>
<td>1.17 [0.18, 2.16]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>34 31</td>
<td>100.0 %</td>
<td>1.17 [0.18, 2.16]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** not applicable

**Test for overall effect:** Z = 2.32 (P = 0.020)

**Test for subgroup differences:** Not applicable
**Analysis 2.3. Comparison 2 Strength training versus control in facioscapulohumeral muscular dystrophy, Outcome 3 Muscle strength ankle dorsiflexors - maximum isometric voluntary contraction.**

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 2 Strength training versus control in facioscapulohumeral muscular dystrophy

Outcome: 3 Muscle strength ankle dorsiflexors - maximum isometric voluntary contraction

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Control</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>van der Kooi 2004</td>
<td>34</td>
<td>-1.13 (4.28)</td>
<td>31</td>
<td>-1.56 (4.16)</td>
<td>100.0%</td>
<td>0.43 [ -1.62, 2.48 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>34</td>
<td>31</td>
<td>100.0%</td>
<td>0.43 [ -1.62, 2.48 ]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.41 (P = 0.68)

Test for subgroup differences: Not applicable

---

**Analysis 2.4. Comparison 2 Strength training versus control in facioscapulohumeral muscular dystrophy, Outcome 4 Muscle strength ankle dorsiflexors - dynamic strength.**

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 2 Strength training versus control in facioscapulohumeral muscular dystrophy

Outcome: 4 Muscle strength ankle dorsiflexors - dynamic strength

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Control</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>van der Kooi 2004</td>
<td>34</td>
<td>-1.5 (2.68)</td>
<td>31</td>
<td>-1.06 (2.78)</td>
<td>100.0%</td>
<td>-0.44 [ -1.77, 0.89 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>34</td>
<td>31</td>
<td>100.0%</td>
<td>-0.44 [ -1.77, 0.89 ]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.65 (P = 0.52)

Test for subgroup differences: Not applicable
Analysis 3.1. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 1 Muscle strength shoulder press - maximum dynamic isotonic voluntary contraction.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

Outcome: 1 Muscle strength shoulder press - maximum dynamic isotonic voluntary contraction

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Mean(SD)</th>
<th>Control</th>
<th>Mean(SD)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9</td>
<td>5.7 (11)</td>
<td>9</td>
<td>10.7 (10)</td>
<td>-5.00 [-14.71, 4.71]</td>
<td>100.0 %</td>
<td>-5.00 [-14.71, 4.71]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9</td>
<td></td>
<td>9</td>
<td></td>
<td>100.0 %</td>
<td>-5.00 [-14.71, 4.71]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable
Test for overall effect: Z = 1.01 (P = 0.31)
Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 2 Muscle strength butterfly - maximum dynamic isotonic voluntary contraction.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

Outcome: 2 Muscle strength butterfly - maximum dynamic isotonic voluntary contraction

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Mean(SD)</th>
<th>Control</th>
<th>Mean(SD)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9</td>
<td>7 (9)</td>
<td>9</td>
<td>0.6 (11)</td>
<td>6.40 [-2.89, 15.69]</td>
<td>100.0 %</td>
<td>6.40 [-2.89, 15.69]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9</td>
<td></td>
<td>9</td>
<td></td>
<td>100.0 %</td>
<td>6.40 [-2.89, 15.69]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable
Test for overall effect: Z = 1.35 (P = 0.18)
Test for subgroup differences: Not applicable
**Analysis 3.3. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 3 Muscle strength biceps curls - maximum isotonic dynamic voluntary contraction.**

**Review:** Strength training and aerobic exercise training for muscle disease

**Comparison:** 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

**Outcome:** 3 Muscle strength biceps curls - maximum isotonic dynamic voluntary contraction

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9 8 (10)</td>
<td>9 0.7 (12)</td>
<td>100.0 %</td>
<td>7.30 [-2.91, 17.51]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9 9</td>
<td>100.0 %</td>
<td>7.30 [-2.91, 17.51]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

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

Test for subgroup differences: Not applicable

---

**Analysis 3.4. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 4 Work capacity - mean time until exhaustion in cycle test.**

**Review:** Strength training and aerobic exercise training for muscle disease

**Comparison:** 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

**Outcome:** 4 Work capacity - mean time until exhaustion in cycle test

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
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<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9 21 (28)</td>
<td>9 -2.7 (16)</td>
<td>100.0 %</td>
<td>23.70 [2.63, 44.77]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9 9</td>
<td>100.0 %</td>
<td>23.70 [2.63, 44.77]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 2.20 (P = 0.027)

Test for subgroup differences: Not applicable
Analysis 3.5. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 5 Work capacity - mean distance until exhaustion in cycle test.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

Outcome: 5 Work capacity - mean distance until exhaustion in cycle test

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>---</td>
<td>-----</td>
<td>---</td>
<td>-----</td>
<td>-----------------</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9</td>
<td>8.8 (11)</td>
<td>9</td>
<td>-0.9 (6)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9</td>
<td>9</td>
<td>100.0 %</td>
<td>9.70 [1.51, 17.89]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 2.32 (P = 0.020)

Test for subgroup differences: Not applicable

-100 -50 0 50 100
Favours control Favours training

Analysis 3.6. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 6 Work capacity - mean distance walked until exhaustion in shuttle walking test.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

Outcome: 6 Work capacity - mean distance walked until exhaustion in shuttle walking test

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
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</thead>
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<tr>
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<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>---</td>
<td>-----</td>
<td>---</td>
<td>-----</td>
<td>-----------------</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9</td>
<td>95 (222)</td>
<td>9</td>
<td>17 (259)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9</td>
<td>9</td>
<td>100.0 %</td>
<td>78.00 [-144.86, 300.86]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Not applicable

-200 -100 0 100 200
Favours control Favours training

Strength training and aerobic exercise training for muscle disease (Review)
Copyright © 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
### Analysis 3.7. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 7 Quality of life.

**Review:** Strength training and aerobic exercise training for muscle disease

**Comparison:** 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

**Outcome:** 7 Quality of life

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV/Fixed, 95% CI</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9</td>
<td>-8.3 (16.8)</td>
<td>9</td>
<td>1.5 (17.7)</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>9</td>
<td>9</td>
<td>100.0 %</td>
<td>-9.80 [-25.74, 6.14]</td>
<td></td>
</tr>
</tbody>
</table>

- Heterogeneity: not applicable
- Test for overall effect: Z = 1.20 (P = 0.23)
- Test for subgroup differences: Not applicable

### Analysis 3.8. Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 8 Myoglobin.

**Review:** Strength training and aerobic exercise training for muscle disease

**Comparison:** 3 Aerobic exercise and strength training versus control in mitochondrial myopathy

**Outcome:** 8 Myoglobin

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV/Fixed, 95% CI</td>
</tr>
<tr>
<td>Lindeman 1995</td>
<td>15</td>
<td>20 (34)</td>
<td>15</td>
<td>41 (42)</td>
<td>100.0 %</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>15</td>
<td>15</td>
<td>100.0 %</td>
<td>-21.00 [-48.35, 6.35]</td>
<td></td>
</tr>
</tbody>
</table>

- Heterogeneity: not applicable
- Test for overall effect: Z = 1.51 (P = 0.13)
- Test for subgroup differences: Not applicable
### Analysis 3.9.  Comparison 3 Aerobic exercise and strength training versus control in mitochondrial myopathy, Outcome 9 VO2 max in maximal incremental cycle exercise test.

**Review:** Strength training and aerobic exercise training for muscle disease  
**Comparison:** 3 Aerobic exercise and strength training versus control in mitochondrial myopathy  
**Outcome:** 9 VO2 max in maximal incremental cycle exercise test

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Cejudo 2005</td>
<td>9 400 (500)</td>
<td>9 0 (500)</td>
<td>100.0 %</td>
<td>400.00</td>
<td>[-61.97, 861.97]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>9</td>
<td>9</td>
<td>100.0 %</td>
<td>400.00</td>
<td>[-61.97, 861.97]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable  
Test for overall effect: Z = 1.70 (P = 0.090)  
Test for subgroup differences: Not applicable

### Analysis 4.1.  Comparison 4 Aerobic exercise and strength training versus control in myotonic dystrophy type 1, Outcome 1 Distance walked in 6-minute walk test.

**Review:** Strength training and aerobic exercise training for muscle disease  
**Comparison:** 4 Aerobic exercise and strength training versus control in myotonic dystrophy type 1  
**Outcome:** 1 Distance walked in 6-minute walk test

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Kierkegaard 2011</td>
<td>18 9 (116)</td>
<td>17 -2 (119)</td>
<td>100.0 %</td>
<td>11.00</td>
<td>[-66.92, 88.92]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>18</td>
<td>17</td>
<td>100.0 %</td>
<td>11.00</td>
<td>[-66.92, 88.92]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable  
Test for overall effect: Z = 0.28 (P = 0.78)  
Test for subgroup differences: Not applicable
### Analysis 4.2. Comparison 4 Aerobic exercise and strength training versus control in myotonic dystrophy type 1, Outcome 2 Timed-stands test.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 4 Aerobic exercise and strength training versus control in myotonic dystrophy type 1

Outcome: 2 Timed-stands test

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kierkegaard 2011</td>
<td>18</td>
<td>17</td>
<td>-0.6 (7.2)</td>
<td></td>
<td>-1.00 [-6.76, 4.76]</td>
</tr>
<tr>
<td><strong>Total</strong> (95% CI)</td>
<td>18</td>
<td>17</td>
<td></td>
<td>100.0%</td>
<td>-1.00 [-6.76, 4.76]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.34 (P = 0.73)

Test for subgroup differences: Not applicable

---

### Analysis 4.3. Comparison 4 Aerobic exercise and strength training versus control in myotonic dystrophy type 1, Outcome 3 Timed-up-and-go tests.

Review: Strength training and aerobic exercise training for muscle disease

Comparison: 4 Aerobic exercise and strength training versus control in myotonic dystrophy type 1

Outcome: 3 Timed-up-and-go tests

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Training</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kierkegaard 2011</td>
<td>18</td>
<td>17</td>
<td>-0.5 (2.2)</td>
<td></td>
<td>-0.50 [-1.86, 0.86]</td>
</tr>
<tr>
<td><strong>Total</strong> (95% CI)</td>
<td>18</td>
<td>17</td>
<td></td>
<td>100.0%</td>
<td>-0.50 [-1.86, 0.86]</td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 0.72 (P = 0.47)

Test for subgroup differences: Not applicable
APPENDICES

Appendix 1. Cochrane Central Register of Controlled Trials (CENTRAL) (through Wiley Interscience, The Cochrane Library 2012, Issue 7 of 12) search strategy

#1 "muscle dis*" or "muscle weakness" or "muscular dis*" or "neuromuscular dis*" or myopath* or dystroph* or myotoni* or myositis or polio* or "muscle fibre*" or "muscle strength" or fibromyalgia
#2 "exercise therapy" or "exercise training" or "exercise program*" or "strength training" or "aerobic training" or "aerobic exercise" or "training program" or "resistive exercise" or "endurance training" or "muscle exercise"
#3 (#1 AND #2) (total database: 1299 hits)

Appendix 2. Cochrane Neuromuscular Disease Group Specialized Register search strategy

("muscle dis*" or "muscle weakness" or "muscular dis*" or "neuromuscular dis*" or myopath* or dystroph* or myotoni* or myositis or polio* or "muscle fibre*" or "muscle strength" or fibromyalgia) and ("exercise therapy" or "exercise training" or "exercise program*" or "strength training" or "aerobic training" or "aerobic exercise" or "training program" or "resistive exercise" or "endurance training" or "muscle exercise")

Appendix 3. MEDLINE (through OvidSP 1946 to 2012 July week 2) search strategy

1 (muscle disease* or muscle disorder* or muscular disease* or muscular disorder* or neuromuscular disease* or neuromuscular disorder* or myopath* or dystroph* or myotoni* or myositis).mp. or exp muscle disease/
2 (exercise therapy or exercise program* or exercise training or strength training or aerobic training or aerobic exercise* or training program* or resistive exercise* or resistive training or endurance exercise* or endurance training or muscle exercise*).mp. or exp exercise/ or exp muscle exercise/ or exp excessive training/ or exp kinesiotherapy/
3 (trial* or random*).mp. or exp clinical trial/ or major clinical study/ or exp controlled study/
4 1 and 2 and 3 (total database: 820 hits)

Appendix 4. EMBASE (through OvidSP 2012 week 30) and EMBASE Classic (through OvidSp) search strategy

1 (muscle disease* or muscle disorder* or muscular disease* or muscular disorder* or neuromuscular disease* or neuromuscular disorder* or myopath* or dystroph* or myotoni* or myositis).mp. or exp muscle disease/
2 (exercise therapy or exercise program* or exercise training or strength training or aerobic training or aerobic exercise* or training program* or resistive exercise* or resistive training or endurance exercise* or endurance training or muscle exercise*).mp. or exp exercise/ or exp muscle exercise/ or exp excessive training/ or exp kinesiotherapy/
3 (trial* or random*).mp. or exp clinical trial/ or major clinical study/ or exp controlled study/
4 1 and 2 and 3 (total database lim to Embase: 5475 hits)

Appendix 5. Cumulative Index to Nursing and Allied Health Literature (CINAHL) (through EBSCOhost 1982 to July 2012) search strategy

S1 TX (muscle disease* or muscle disorder* or muscular disease* or muscular disorder* or neuromuscular disease* or neuromuscular disorder* or myopath* or dystroph* or myotoni* or myositis) or MH "Muscular Diseases+
S2 TX (exercise therap* or exercise program* or exercise training or strength training or aerobic training or aerobic exercise* or training program* or resistive exercise* or resistive training or endurance exercise* or endurance training or muscle exercise*) or MH "Therapeutic exercise+
S3 TX Trial* OR Tx random* OR PT Systematic review OR PT Clinical trial OR MH "Clinical trials+
S4 S1 and S2 and S3 (total database: 489 hits)
Search mode - Boolean/Phrase (July 31 2012)
WHAT'S NEW

Last assessed as up-to-date: 2 July 2012.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
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<tbody>
<tr>
<td>26 August 2012</td>
<td>New citation required and conclusions have changed</td>
<td>Review updated to include a study of people with dermatomyositis and polymyositis and a study with people with myotonic dystrophy type I. The results and conclusions of the review amended accordingly</td>
</tr>
<tr>
<td>2 July 2012</td>
<td>New search has been performed</td>
<td>Searches updated to July 2012. One new trial identified from searches. In this update we have included studies with an exercise programme duration of at least six, instead of 10, weeks. Therefore, one trial which was previously excluded in the former update is now also included</td>
</tr>
</tbody>
</table>

HISTORY

Protocol first published: Issue 4, 2002
Review first published: Issue 1, 2005

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>15 June 2011</td>
<td>Amended</td>
<td>Additional acknowledgement added.</td>
</tr>
<tr>
<td>20 July 2009</td>
<td>New citation required and conclusions have changed</td>
<td>Search updated to July 2009. Review updated to include a new study of people with mitochondrial myopathy (Cejudo 2005). The results and conclusions of the review have been amended accordingly</td>
</tr>
<tr>
<td>2 July 2008</td>
<td>Amended</td>
<td>Converted to new review format.</td>
</tr>
<tr>
<td>23 September 2004</td>
<td>New citation required and conclusions have changed</td>
<td>Substantive amendment.</td>
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</tbody>
</table>
CONTRIBUTIONS OF AUTHORS

I Riphagen searched all databases. NBM Voet and EL van der Kooi identified and assessed potentially relevant studies, and extracted the data from included studies. NBM Voet prepared the final draft. ACH Geurts, EL van der Kooi and E Lindeman edited each draft and approved the final text of the review.

Eline Lindeman died in September 2012, but contributed to this update. There were moderately substantive changes to the review subsequent to her involvement.

DECLARATIONS OF INTEREST

E van der Kooi carried out a RCT on the effect of strength training and albuterol in FSHD (van der Kooi 2004).

E Lindeman: author deceased; declarations of interest in previously published version of the review: "Another [author] (Lindeman) has co-ordinated a RCT on the effects of strength training in myotonic dystrophy (Lindeman 1995).

ACH Geurts: “Other than being the principle investigator in the Facts-2-FSHD trial (not yet published) on the effects of cognitive behavioural therapy and physical exercises on chronic fatigue in patients with FSHD, I have no competing interests.”

II Riphagen: none known.

NBM Voet: none known.

Dr. van Engelen is research director of the European Neuromuscular Centre and receives institutional support from the Radboud University Nijmegen Medical Centre and the ENMC, grant support from the Global FSH, Netherlands Organization for Scientific Research, Prinses Beatrix Fonds, and the Dutch FSHD Foundation.

SOURCES OF SUPPORT

Internal sources

• New Source of support, Not specified.

External sources

• No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As stated in a previous update, we excluded all studies using a within-subjects design with the non-exercised limb as a control (Aitkens 1993; De Lateur 1979; Kilmer 1994; McCartney 1988; Tollbäck 1999).

At this update (2012) additional changes were:

• inclusion of exercise programmes with a minimum duration of six, rather than 10 weeks as previously specified. Because of this change of protocol, we included one trial which was excluded in the previous update (Wiesinger 1998a) and one new trial (Kierkegaard 2011);

• we added a statement that we would exclude studies in which outcomes were not presented separately for each muscle disease. One randomised controlled strength training combined with aerobic exercise trial has been excluded for this reason. No specific details about the exercise programme were provided and the methodological quality of the trial was considered poor (Dawes 2006);

• we updated the definitions in Types of interventions;

• we have updated and changed the diagnostic criteria to "confirmed by muscle biopsy or genetic testing";
• we have updated the exercise guidelines (Garber 2011);
• we searched the Cochrane Rehabilitation and Related Therapies Field Register in October 2002, August 2008 and July 2009. As, in the past, it yielded no results and is no longer available, it has been removed from the Methods section.

INDEX TERMS

Medical Subject Headings (MeSH)
*Exercise; Dermatomyositis [rehabilitation]; Mitochondrial Myopathies [rehabilitation]; Muscular Diseases [*rehabilitation]; Muscular Dystrophy, Facioscapulohumeral [rehabilitation]; Myotonic Dystrophy [rehabilitation]; Physical Fitness; Polymyositis [rehabilitation]; Randomized Controlled Trials as Topic; Resistance Training [*methods]

MeSH check words
Humans