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Exercise training for adults with chronic kidney disease (Review)

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Exercise training for adults with chronic kidney disease.

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Exercise training for adults with chronic kidney disease (Review)

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[Intervention Review]

Exercise training for adults with chronic kidney disease

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ABSTRACT

Background

Chronic kidney disease (CKD) is a worldwide public health problem. In the National Kidney Foundation Disease Outcomes Quality Initiative guidelines it is stressed that lifestyle issues such as physical activity should be seen as cornerstones of the therapy. The physical fitness in adults with CKD is so reduced that it impinges on ability and capacity to perform activities in everyday life and occupational tasks. An increasing number of studies have been published regarding health effects of various regular exercise programmes in adults with CKD and in renal transplant patients.

Objectives

We aimed to: 1) assess the effects of regular exercise in adults with CKD and kidney transplant patients; and 2) determine how the exercise programme should be designed (e.g. type, duration, intensity, frequency of exercise) to be able to affect physical fitness and functioning, level of physical activity, cardiovascular dimensions, nutrition, lipids, glucose metabolism, systemic inflammation, muscle morphology and morphometrics, dropout rates, compliance, adverse events and mortality.

Search methods

We searched the Cochrane Renal Group's specialised register, CENTRAL, MEDLINE, EMBASE, CINAHL, Web of Science, Biosis, Pedro, Amed, AgeLine, PsycINFO and KoreaMed. We also handsearched reference lists of review articles and included studies, conference proceeding's abstracts. There were no language restrictions.

Date of last search: May 2010.

Selection criteria

We included any randomised controlled trial (RCT) enrolling adults with CKD or kidney transplant recipients undergoing any type of physical exercise intervention undertaken for eight weeks or more. Studies using less than eight weeks exercise, those only recommending an increase in physical activity, and studies in which co-interventions are not applied or given to both groups were excluded.

Data collection and analysis

Data extraction and assessment of study and data quality were performed independently by the two authors. Continuous outcome data are presented as standardised mean difference (SMD) or mean difference (MD) with 95% confidence intervals (CI).

Main results

Forty-five studies, randomising 1863 participants were included in this review. Thirty two studies presented data that could be meta-analysed. Types of exercise training included cardiovascular training, mixed cardiovascular and resistance training, resistance-only training and yoga. Some studies used supervised exercise interventions and others used unsupervised interventions. Exercise intensity was classed as 'high' or 'low', duration of individual exercise sessions ranged from 20 minutes/session to 110 minutes/session, and study duration was from two to 18 months. Seventeen per cent of studies were classed as having an overall low risk of bias, 33% as moderate, and 49% as having a high risk of bias.

The results shows that regular exercise significantly improved: 1) physical fitness (aerobic capacity, 24 studies, 847 participants: SMD -0.56, 95% CI -0.70 to -0.42; walking capacity, 7 studies, 191 participants: SMD -0.36, 95% CI -0.65 to -0.06); 2) cardiovascular dimensions (resting diastolic blood pressure, 11 studies, 419 participants: MD 2.32 mm Hg, 95% CI 0.59 to 4.05; resting systolic blood pressure, 9 studies, 347 participants: MD 6.08 mm Hg, 95% CI 2.15 to 10.12; heart rate, 11 studies, 229 participants: MD 6 bpm, 95% CI 10 to 2); 3) some nutritional parameters (albumin, 3 studies, 111 participants: MD -2.28 g/L, 95% CI -4.25 to -0.32; pre-albumin, 3 studies, 111 participants: MD -44.02 mg/L, 95% CI -71.52 to -16.53; energy intake, 4 studies, 97 participants: SMD -0.47, 95% CI -0.88 to -0.05); and 4) health-related quality of life. Results also showed how exercise should be designed in order to optimise the effect. Other outcomes had insufficient evidence.

Authors' conclusions

There is evidence for significant beneficial effects of regular exercise on physical fitness, walking capacity, cardiovascular dimensions (e.g. blood pressure and heart rate), health-related quality of life and some nutritional parameters in adults with CKD. Other outcomes had insufficient evidence due to the lack of data from RCTs. The design of the exercise intervention causes difference in effect size and should be considered when prescribing exercise with the aim of affecting a certain outcome. Future RCTs should focus more on the effects of resistance training interventions or mixed cardiovascular- and resistance training as these exercise types have not been studied as much as cardiovascular exercise.

PLAIN LANGUAGE SUMMARY

Exercise training for adults with chronic kidney disease

Exercise regimens are based on the frequency, intensity and duration of exercise training as well as the type of activity and the individual's initial level of physical fitness. All these factors have to be taken into account when aiming to achieve the goal with the regular exercise training and or rehabilitation.

Forty-five studies, randomising 1863 participants were included in this review. Thirty two studies presented data that could be included in the meta-analyses. This review showed that regular exercise training significantly improved physical fitness, physical functioning (e.g. walking capacity), and health-related quality of life in adults with chronic kidney disease (CKD). Beneficial effects were also seen on other outcome measures, such as blood pressure, but where the level of evidence is somewhat lower due to too few research studies and or small study populations. Beneficial effects were present in both adults with CKD but not yet in need of dialysis treatment, patients with dialysis (haemodialysis and peritoneal dialysis) and kidney transplant recipients.

This systematic review and meta-analysis presents evidence-based data to clinicians and patients on which type of exercise regimen (type of exercises, intensity, frequency and duration of exercise) that should be used to optimise the effect size. The results should be implemented by clinicians who should encourage and inform adults with CKD that there is scientific evidence for beneficial effects of regular exercise training, and who should use an adequate exercise intervention in order to achieve the patient's and the clinician's goal with the regular exercise.

BACKGROUND

Chronic kidney disease (CKD) is a worldwide public health problem. Adverse outcomes of CKD include loss of kidney function and cardiovascular disease. The disease is defined as either: 1) kidney damage that is present for three months or more and with or without decreased glomerular filtration rate (GFR); or 2) GFR less than 60 mL/min/1.73 m² that is present for three months or more with or without kidney damage (KDOQI 2002). There are primary and secondary causes of CKD. Examples of primary CKD are glomerulonephritis, interstitial nephritis and polycystic kidney disease. Secondary causes can be diabetes mellitus, nephrosclerosis, and systemic diseases such as systemic lupus erythematosus, rheumatic diseases and systemic vasculitis. There are five stages of CKD (KDOQI 2002).

- Stage 1: GFR > 90 mL/min/1.73 m² (kidney damage with normal or increased kidney function)
- Stage 2: GFR 60-89 mL/min/1.73 m² (kidney damage with mild reduction in kidney function)
- Stage 3: GFR 30-59 mL/min/1.73 m² (moderate kidney function)
- Stage 4: GFR 15-29 mL/min/1.73 m² (severely reduced kidney function)
- Stage 5: GFR < 15 mL/min/1.73 m² (kidney failure)
- Stage 5D: on haemodialysis (HD) or peritoneal dialysis (PD)

The complications to CKD may be problems in themselves, but they may also increase the risk for other adverse events, for instance increase the risk for cardiovascular disease (KDOQI 2002). In the National Kidney Foundation Disease Outcomes Quality Initiative guidelines it is stressed that lifestyle issues such as physical activity habits should be seen as cornerstones of the therapy, especially when aiming at managing cardiovascular risk factors (KDOQI 2002).

The physical fitness and physical functioning (the ability and capacity to perform activities of daily living) is severely reduced in adults with CKD (Bohannon 1994; Clyne 1993; Heiwe 2001; Heiwe 2003; Heiwe 2005; Johansen 2003; Kempeneers 1990b; Kettner 1987; Kouidi 1997b; Kouidi 1998a; Kutner 1992), declining from 70% of the expected norm at early stages of CKD, to 50% of the expected norm when starting dialysis therapy (Brodin 2001; Clyne 1991b; Heiwe 2001; Kettner 1987; Painter 1986b). Kidney transplant patients have a physical fitness of approximately 70% to 80% of the expected norm (Painter 1986b). Thus, the physical fitness in adults with CKD is so reduced that it impinges on their ability and capacity to perform activities in everyday life and occupational tasks (Heiwe 2003; Wilmore 1999).

The main causes for the decline in physical exercise capacity in this group of patients are renal anaemia and skeletal muscle disorder (Clyne 1987; Diesel 1990; Kouidi 1998a; McMahon 1999; Thompson 1996). These factors cause fatigue and inactivity that, in turn, further reduces the physical exercise capacity. Today renal anaemia is successfully corrected by treatment with recombinant human erythropoietin (EPO), which improves, but does not normalise, maximal physical exercise capacity (Barany 1993; CESC 1990; Clyne 1992; Laupacis 1991; Lim 1989; Painter 2002b). There is however no significant changes in muscle metabolism after correction of renal anaemia, which implies that oxygen delivery is not the only limiting factor for aerobic metabolism in adults with CKD (Thompson 1996). The muscle weakness is predominant in the proximal muscle groups and in particular in the lower extremities (Brautbar 1983;

Kettner 1987). When analysing muscle biopsies histopathological abnormalities are seen already in the pre-dialysis stages (Heiwe 2005). The causes of muscular weakness have, however, not been fully elucidated. Muscle atrophy, a neuropathic process, and myopathy are potential causes of the muscular weakness. It is suggested that myopathy is due to abnormal energy metabolism (Thompson 1996), secondary hyperparathyroidism (Ritz 1980), malnutrition (Guarnieri 1983), prolonged physical inactivity (Jones 1990), and to uraemia itself (Sakkas 2003b).

Insulin resistance as well as reduced insulin sensitivity is also present in adults with CKD (Eidemak 1995). There is a positive correlation between maximal exercise capacity and insulin sensitivity of the tissues (Eidemak 1995). Insulin resistance and metabolic acidosis, both common in CKD, causes an increased muscle proteolysis. Studies performed on uraemic rats have shown that regular exercise training reduces muscle protein catabolism, and that the reduction is combined with improved insulin sensitivity (Davis 1983; Davis 1987).

During the last 30 years there have been a significantly increasing number of published studies concerning effects of regular exercise training in adults with CKD. There is however a lack of evidence-based guidelines for exercise training in adults with CKD. Therefore there is a need for a review in this area to clarify: 1) the effects of regular physical exercise training in adults with CKD and kidney transplant patients; and 2) how the exercise training programme should be designed (e.g. type of exercises, duration, intensity, frequency) to be able to affect clinically important outcomes in this group of patients.

OBJECTIVES

To assess the effects of regular physical exercise training in adults with CKD and kidney transplant recipients on the following clinically important health outcomes: physical fitness and functioning; cardiovascular dimensions; nutrition; level of physical activity; depression; health-related quality of life; blood lipids; muscle morphology and morphometric systemic inflammation; glucose metabolism; dropout rates; adverse events; and mortality.

METHODS

Criteria for considering studies for this review

Types of studies

Design

All randomised controlled trials (RCTs) and quasi-RCTs, assessing the effects of regular physical exercise training in adults with CKD were included. Crossover studies were considered if the starting period of intervention was randomly allocated.

Duration

Studies of eight weeks regular exercise or longer were included since the aim was to evaluate the effects of regular ongoing physical exercise training. An exercise training period of less than eight weeks would be too short to show alteration in nutritional status, inflammation, cardiac function, physical activity, fitness and functioning, and psychological well-being.

Exclusion criteria

Studies where the intervention involved only the recommendation of increased physical activity were not included as it was not possible to quantify the exercise stimulus. Studies where there was a co-intervention in the experimental group was not applied to the control group. Studies with an exercise intervention less than two months were excluded as this period has been found too short for achieving changes in many of the outcome measures that this review focuses on (ACSM 2006) and also as this review is focused on effects of long-term regular exercise training interventions.

Types of participants

All adults (male or female) with any stage CKD or who have received a kidney transplant were included.

Studies investigating the effects of regular physical exercise training in adults with acute kidney injury (AKI) and studies in children were excluded.

Types of interventions

Exercise regimens needed to be planned, structured and repetitive. They needed to include specific recommendations for the type, intensity, frequency and duration of exercise training with a specific objective (i.e. increase fitness or health, Bouchard 1994). Studies were classified as short-term (three months or less, but not less than two months regular exercise), medium-term (four to six months regular exercise), long term (six to 12 months or longer regular exercise) based on the presented exercise intervention period.

As the intention of the review was to measure the effect of regular exercise training, only studies where the only difference in interventions between groups was regular exercise training were included. The review includes studies involving the following types of interventions.

1. Regular physical exercise training versus non-exercise control.
2. Regular physical exercise training plus a co-intervention versus just that co-intervention, i.e. physical exercise training plus erythropoietin treatment versus erythropoietin treatment.

Types of outcome measures

This review focused on clinically important outcomes, measured using physiological and psychological variables associated with CKD and its complications.

Outcome data at the end of the intervention were used.

Primary outcomes

1. Physical fitness: aerobic capacity; muscular strength and endurance
2. Physical functioning and activity: walking capacity; stair climbing capacity; activities of daily living (ADL) capacity
3. Cardiovascular dimensions: resting blood pressure (diastolic and systolic); maximum heart rate; resting heart rate
4. Nutritional measures: albumin; pre-albumin; Subjective Global Assessment (SGA); energy intake; protein intake; transferrin; body mass indices (muscle mass, fat mass, anthropometric measures - waist circumference, mid-arm circumference, calf circumference; mid-thigh circumference)

5. Systemic inflammation: serum interleukin 6; lymphocytes; protein catabolic rate
6. Physical activity
7. Depression
8. Health-related quality of life (using well established reliable and validated instruments such as SF-36, EuroquoI).

Secondary outcomes

1. Blood lipids: triglycerides; total cholesterol; high-density lipoprotein (HDL) cholesterol; low-density lipoprotein (LDL) cholesterol; very low-density lipoprotein (VLDL) cholesterol; intermediate-density lipoproteins (IDL); apolipoprotein (APO) A1; APO B
2. Muscle morphology and morphometrics: type I, IIa and IIb muscle fibre area; proportion type I, IIa and IIb muscle fibres; thigh muscle cross sectional area, thigh muscle attenuation
3. Cardiovascular dimensions: heart rate variability (HRV) index; mean RR; mean standard deviation of all the normal RR intervals (SDNN); arrhythmias (Lown class > I); left ventricular internal dimension at end-diastole, left ventricular internal dimension at end-systole; intraventricular septal thickness at end-diastole; left ventricular posterior wall thickness at end-diastole; left ventricular mass; left ventricular mass index
4. Glucose metabolism: fasting plasma glucose; fasting plasma insulin; glucose disappearance
5. Dropout rates
6. Compliance
7. Adverse events (exercise induced injuries)
8. Mortality

Search methods for identification of studies

The search for studies was performed by one of the author using the Cochrane Renal Group search strategy. The searches were performed with the assistance of the Cochrane Renal Group Trials Search Coordinator; librarian Susanne Gustafsson, Karolinska Institutet University Library; and librarian Marie Källberg, Karolinska University Hospital Library.

Electronic searches

The following databases were searched (see Appendix 1).

1. The Cochrane Renal Group's specialised register and the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (from start to May 2010)
2. MEDLINE (from 1966 to May 2010)
3. EMBASE (from 1980 to May 2010)
4. CINAHL (from 1982 to May 2010)
5. Science citation index (from 1945 to May 2010)
6. Social science citation index (from 1956 to May 2010)
7. BIOSIS (from 1969 to May 2010)
8. PEDRO (from 1929 to May 2010)
9. Amed (from 1985 to May 2010)
10. AgeLine (from 1978 to May 2010)
11. PsycINFO (from 1806 to May 2010)
12. KoreaMed (from start (year unknown) to May 2010)

We placed no language restrictions on either the search or the included studies.

Searching other resources

The reference lists of review articles and included studies were handsearched for other potentially eligible studies. Conference proceeding's abstracts from nephrology scientific meetings were obtained from CENTRAL and the Renal Group's specialised register. These contain the handsearched results of conference proceedings from general and speciality meetings. This is an ongoing activity across the Cochrane Collaboration and is both retrospective and prospective. Please refer to The Cochrane Renal Group's Module in The Cochrane Library for the most up-to-date list of conference proceedings ([Renal Group 2011](#)). Conference proceeding's abstracts were also handsearched (American Society of Nephrology to May 2010, European Dialysis Transplant Association to May 2010, EDTNA-ERCA to May 2010, International Society of Nephrology to May 2010, World Congress of Nephrology 2001 to May 2010). Authors of included studies who were contacted due to need of clarification of methods or results were also asked if they knew of any other relevant studies.

Data collection and analysis

Selection of studies

Two authors independently reviewed the titles, abstract sections and keywords of every record retrieved from the electronic search. If the information given in the title, abstract and or keywords suggested that the study might fit the inclusion criteria of the systematic review, the full article was retrieved for further assessment. From the full articles, the decision to eliminate a study was based on agreement by both authors. Studies that did not fulfil the selection criteria of the systematic review were eliminated. Once a study was excluded, a record of the article, including the reason for exclusion, was retained. Cohen's kappa statistic was to be used to measure inter-rater assessment of the studies. This was, however, not necessary as the authors were unanimous in their initial choices of abstracts for further investigation.

Data extraction and management

Data from each study were independently extracted by both authors. Variations in data extraction were to be resolved by consensus, referring back to the original data. Data were extracted using a standard data extraction form, which included the following:

1. General information: published/unpublished, title, authors, source, contact address, country, setting, language, year of publication, duplicate publication, source of funding.
2. Study characteristics: design, randomisation (and method if stated), allocation concealment, blinding of outcome assessors.
3. Participants: if randomised, inclusion criteria, exclusion criteria, total number in intervention/control groups, sex, age, baseline characteristics, diagnostic criteria, similarity of groups at baseline. We also extracted data concerning the number of participants who refused or were excluded from entering the study as well as number of withdrawals/losses to end of intervention follow-up. Further, we sought information on the reasons for discontinuation of all participants allocated to the intervention.
4. Intervention and comparator, duration of study.

5. All outcomes.
6. Results: for continuous variables, we extracted the number of participants, and the baseline and post-intervention means with SD (or standard error of the mean (SEM) or 95% confidence interval (95% CI)) for the intervention and control groups. We transformed SEM or 95% CI into SD, if appropriate. For dichotomous variables, we extracted proportions.

Assessment of risk of bias in included studies

Both authors independently assessed each study for the risk of bias. If there was a disagreement in the assessment of a study, a third party was to adjudicate. Since there was no difference in the authors' assessment, a third party was never used and the level of inter-rater agreement was therefore not calculated.

Bias was then assessed based on criteria specified below and with the component of allocation concealment added to the checklist ([Jadad 1996](#); [Moher 1998](#); [Schulz 1995](#)).

1. Minimisation of selection bias
 - Was the recruitment procedure completely described and adequate?
 - Was the randomisation procedure adequate?
 - Was the allocation concealment adequate?
2. Minimisation of detection bias:
 - Were the outcome assessors blind to the intervention?
 - Blinding of the individuals who administered the intervention
 - Were the participants in the study blinded?
3. Minimisation of attrition bias:
 - Were withdrawals and dropouts completely described?
 - Was compliance to the intervention described and adequate?
 - Was the analysis by intention-to treat?

Each study was classified into one of the following three categories ([Higgins 2005](#))

- Low risk of bias: all quality criteria met (A).
- Moderate risk of bias: one or more of the quality criteria only partially met (B).
- High risk of bias: one or more quality criteria not met (C).

In this review assessments of bias were used to explain differences in results between studies and in sensitivity analyses.

In the present review and meta-analysis, investigators have been sought for additional information when necessary. When we could not obtain additional information and data, this was reported as 'missing data' and 'not reported'.

Measures of treatment effect

All outcomes were analysed using both a fixed and a random-effects model. If the fixed and random-effects meta-analyses gave similar results, the results from the fixed-effect model were presented. If the results from the fixed and the random-effects meta-analyses differed, the results from the random-effects model were presented. The choice between using a fixed or a random-effects model was also affected by the presence of heterogeneity.

Dealing with missing data

Where possible, investigators of studies were contacted to obtain information or data required that could not be found in the published reports. Additional information was sought, when necessary, for all studies that appeared to meet the inclusion criteria. Studies with data only available in graph form were included in the review but excluded from the meta-analysis rather than estimate the mean and SD from the graph. When post-intervention measures of dispersion (SD, SEM or 95% CI) were not available (e.g. when post-intervention information was expressed as percentage change from baseline values) the result was excluded from the meta-analysis and noted as missing data. When an article contained missing data the primary investigator was contacted for clarification of results. If the investigators' present contact information was not found or the investigators were not able to provide the missing data, the result was excluded from the meta-analysis and noted as missing data. Fourteen authors were contacted for clarification and/or to request raw data. See [Characteristics of included studies](#).

Assessment of heterogeneity

Heterogeneity between studies was analysed using the Cochran Q test of N-1 degrees of freedom (P of 0.10 used for statistical significance). The I^2 parameter was used to quantify any inconsistency ($I^2 = [(Q - df)/Q] \times 100\%$, where Q is the χ^2 statistic and df is its degrees of freedom, ([Higgins 2002](#); [Higgins 2003](#)). When there was no heterogeneity ($I^2 \leq 50\%$, $P > 0.10$) the results from the fixed-effect meta-analyses were presented. If there was evidence of heterogeneity between included studies, a visual inspection of the CIs was used as a help to get an idea of the amount of statistical heterogeneity and to decide whether it would be reasonable to combine the results of these studies.

Assessment of reporting biases

If a sufficient number of studies were identified for the intervention, a funnel plot was used to assess publication bias ([Higgins 2005](#)).

Data synthesis

Data were summarised statistically, when it was sufficiently uniform and of sufficient quality. For dichotomous outcomes results were expressed as a risk ratios (RR) with 95% CI. Where continuous scales of measurement were used to assess the effects of the exercise training intervention, mean difference (MD) was used between the post-intervention values of the intervention and control groups to analyse the size of the intervention effects, or standardised mean difference (SMD) if different scales had been used.

Subgroup analysis and investigation of heterogeneity

Where heterogeneity was found, the following was undertaken.

1. Data entry was checked.
2. Heterogeneity was explored by conducting subgroup analyses.

3. If the heterogeneity could not be explained and there was a small but significant heterogeneity ($I^2 < 50\%$, $P < 0.10$), the random-effects model was used as this model is the most conservative option.
4. If the studies had collect continuous outcome data using different scales or different units, the effect measure was changed to SMD as extreme heterogeneity may be apparent when using the MD but not when the more appropriate SMD was used.
5. No meta-analysis was conducted if a considerable variation ($I^2 > 50\%$) in results still remained, and if there was inconsistency in the direction of effect.

The different subgroups were type of physical exercise training, duration, frequency and intensity of physical exercise training. We also performed length of intervention subgroup analyses for outcome measures, when there were sufficient data (three months or less, four to six months, six to 12 months or longer). Other subgroup analyses planned (but with insufficient data to pursue) were: sex (male or female); exercise frequency (less than three times/week, more than three times/week); and post-intervention follow-up timing (less than six months, six to 12 months, more than 12 months). We did not run subgroup analysis for age, gender and type of patients (CKD stages 1-5, HD, continuous ambulatory PD (CAPD), kidney transplant), respectively.

Sensitivity analysis

We explored the influence of potential biases, as specified above, on effect size by repeating the analysis. In this review the sensitivity analysis was conducted on studies classified as A or B (low or moderate bias) versus A, B and C (low, moderate or high bias), and which had data in a form that could be included in this analysis.

RESULTS

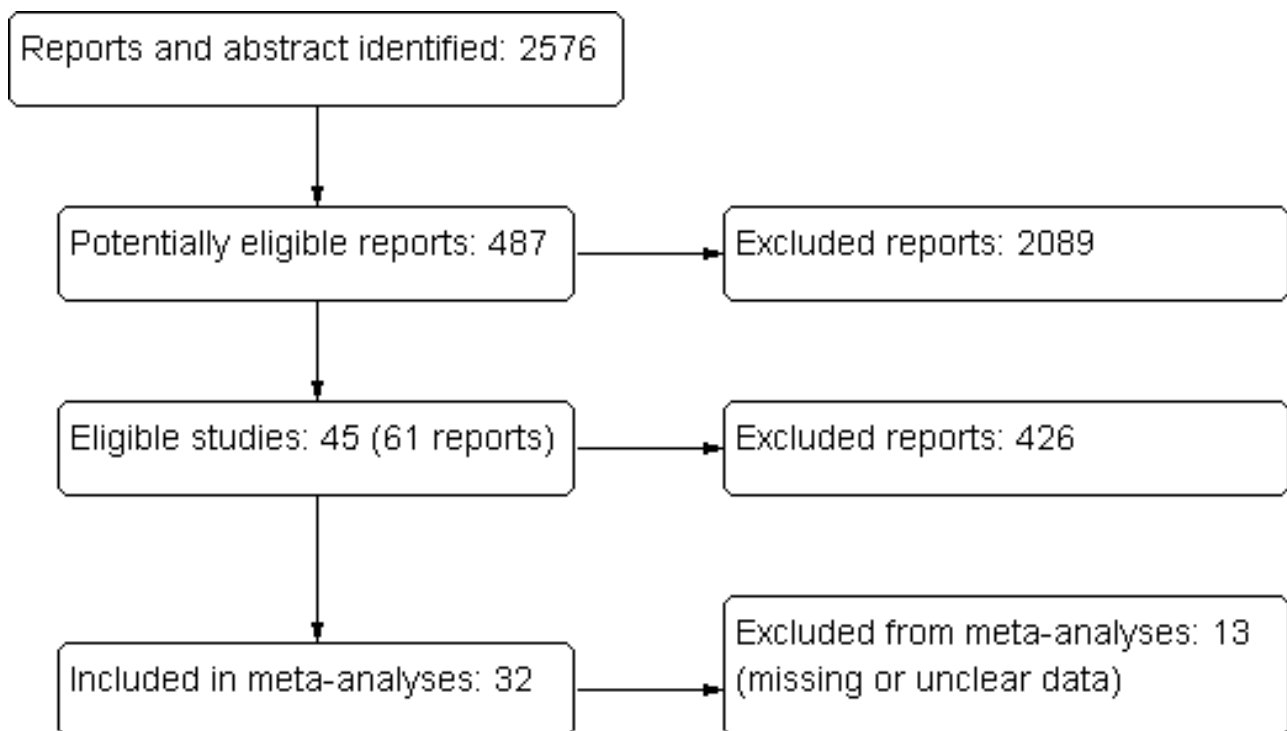
Description of studies

Results of the search

From the initial search of the databases all abstracts were screened to identify potentially relevant studies. During the initial screening reports were excluded on basis of the information presented in the abstracts, because they were not relevant to the question under study (i.e. it was clear that the study did not have an exercise intervention, that it was not a RCT). In many cases it was not possible to decide whether to include or exclude a study based on the information in the abstract or because there was no abstract presented in the database. In those cases, full papers were retrieved and screened. A total of 2576 reports were screened and 487 potential reports of studies were identified. We excluded 365 reports as they were not relevant to the question under study. From the reports selected for closer examination, 45 studies (61 reports) finally qualified for inclusion in the review.

See [Figure 1](#) for flow diagram showing study selection.

Figure 1. Flow diagram showing study identification and selection



Included studies

Forty-five studies, randomising 1863 participants, were identified and retained for this review. Details of the characteristics of the included studies are given in the Table: 'Characteristics of included studies' and in Appendix 2. The following gives a brief overview.

- Twenty-three studies were single centre studies, seven were multi-centre studies, and 15 did not provide this information.
- All used a parallel group RCT design.
- Inclusion criteria were moderate kidney failure, dialysis treatment or kidney transplantation. The most common was HD treatment.
- Exclusion criteria were mainly severe cardiovascular disease and orthopaedic, psychiatric or neurological disorder that would preclude outcome assessment and/or exercise training.
- Number of participants randomised in each study varied from 11 (Frey 1999; Parsons 2004) to 167 (Painter 2002a).
- Studies were from Australia (Koh 2010a; Koh 2010b; PEAK Study 2005; Toussaint 2008), Canada (DePaul 2002; Parsons 2004), Denmark (Eidemak 1997; Molsted 2004), Germany (Dimeo 2007), Greece (Deligiannis 1999; Deligiannis-HI 1999; Deligiannis-LI 1999; Konstantinidou-D 2002; Konstantinidou-ND 2002; Konstantinidou-US 2002; Kouidi 1997a; Kouidi 2002a; Kouidi 2002b; Kouidi 2003a; Kouidi 2004a; Ouzouni 2009), Japan (Akiba 1995; Matsumoto 2007), Korea (Jong 2004; Lee 2001), Netherlands (van Vilsteren 2005), Spain (Segura-Orti 2009), Turkey (Yurtkuran 2007), UK (Koufaki 2002a; Koufaki 2003), USA (Carmack 1995; Carney 1987; Castaneda 2001; Chen 2010; Chatoth 2005; Fitts 1995; Fitts 1999; Frey 1999; Goldberg 1983; Harter 1985; Leehey 2009; Painter 2002a; Painter 2002b; Painter 2003), and finally a USA and Greece collaboration (Kouidi 2009).

Participants

- The number of participants/study ranged from 11 (Frey 1999) to 167 (Painter 2002a).
- Mean age of participants varied from 36 ± 3 years (Harter 1985) to 71 ± 13 years (Chen 2010).
- There were a higher proportion of male participants in the studies, which reflects the higher male prevalence of CKD.
- The level of kidney insufficiency as assessed by CKD stage was moderate or severe (Castaneda 2001; Eidemak 1997; Leehey 2009), but in most studies the participants had CKD Stage 5 and were treated with regular dialysis. Three studies studied the effect of regular exercise training in adults with a kidney transplant (Dimeo 2007; Kouidi 2002a; Painter 2003).

Results from the present review are generalizable to patients with CKD (all stages) and kidney transplant recipients who do not have unstable hypertension, congestive heart failure (NYHA ≥ II), cardiac arrhythmias (III according to Lown), recent myocardial infarction or unstable angina, and who have a physical or mental impairment that precluded undergoing submaximal/maximal exercise tolerance tests and participating in an exercise programme.

Interventions

Types of exercise

The studies in this systematic review included all types of regular exercise training interventions. The most common exercise training intervention was cardiovascular exercise training (Akiba 1995; Carmack 1995; Deligiannis 1999; Deligiannis-LI 1999; Eidemak 1997; Frey 1999; Goldberg 1983; Jong 2004; Koh 2010a; Koh 2010b; Konstantinidou-US 2002; Koufaki 2002a; Kouidi 1997a; Leehey 2009; Painter 2002a; Painter 2002b; Painter 2003;

Parsons 2004; Toussaint 2008; Tsuyuki 2003; i.e. aerobic exercise training), followed by mixed cardiovascular and resistance training (Deligiannis 1999; Deligiannis-HI 1999; Deligiannis-LI 1999; DePaul 2002; Fitts 1995; Konstantinidou-D 2002; Konstantinidou-ND 2002; Kopple 2007a; Kouidi 2009; Ouzouni 2009; van Vilsteren 2005), resistance training (Castaneda 2001; Chen 2010; Johansen 2006; Kopple 2007a; PEAK Study 2005; Segura-Orti 2009), and yoga (Yurtkuran 2007).

Some studies used supervised exercise interventions (Akiba 1995; Castaneda 2001; Chen 2010; Deligiannis 1999; Deligiannis-HI 1999; DePaul 2002; Eidemak 1997; Frey 1999; Goldberg 1983; Johansen 2006; Koh 2010a; Konstantinidou-D 2002; Konstantinidou-ND 2002; Koufaki 2002a; Kouidi 1997a; Kouidi 2009; Leehey 2009; Ouzouni 2009; Painter 2002b; Painter 2003; Parsons 2004; PEAK Study 2005; Segura-Orti 2009; Tsuyuki 2003; van Vilsteren 2005; Yurtkuran 2007) and others used unsupervised exercise training interventions (Carmack 1995; Deligiannis-LI 1999; Eidemak 1997; Fitts 1995; Jong 2004; Koh 2010b; Konstantinidou-US 2002; Leehey 2009; Painter 2002a; Painter 2003; Toussaint 2008).

Intensity of exercise intervention

Only a few studies did not report the intensity of the exercise training intervention studies and one study used a mixed low and high intensity exercise intervention (Leehey 2009). Most studies used a high intensity exercise intervention (Akiba 1995; Castaneda 2001; Chen 2010; Deligiannis 1999; Deligiannis-HI 1999; DePaul 2002; Eidemak 1997; Fitts 1995; Frey 1999; Goldberg 1983; Johansen 2006; Jong 2004; Koh 2010a; Koh 2010b; Konstantinidou-D 2002; Konstantinidou-ND 2002; Koufaki 2002a; Kouidi 1997a; Kouidi 2009; Ouzouni 2009; Painter 2002a; Painter 2003; PEAK Study 2005; Segura-Orti 2009; van Vilsteren 2005), and a few studies used a low intensity exercise training intervention (Deligiannis-LI 1999; Konstantinidou-US 2002; Parsons 2004; Tsuyuki 2003; van Vilsteren 2005). Percentage of the maximal oxygen uptake, peak oxygen uptake, maximum heart rate or the Borg RPE-scale were scales used to define the percentage effort required in the interventions.

Frequency

The highest frequency of exercise training was seven times/week (Eidemak 1997) and the lowest frequency was twice/week (Molsted 2004). Most studies did however use three or five times/week as frequency of exercise training intervention. Some studies did not report frequency of the exercise training intervention.

Duration/exercise session (minutes)

The duration of individual exercise sessions varied from 20 minutes/session (Akiba 1995; Matsumoto 2007) to 110 minutes/session (Deligiannis 1999), and was not reported in some studies. Less than 30 minutes duration/exercise session was reported in five studies (Akiba 1995; Carmack 1995; Koufaki 2002a; Matsumoto 2007; van Vilsteren 2005); 30 to 60 min/sessions in 21 studies (Carney 1987; Castaneda 2001; Deligiannis-LI 1999; DePaul 2002; Eidemak 1997; Fitts 1995; Fitts 1999; Frey 1999; Koh 2010a; Koh

2010b; Konstantinidou-US 2002; Koufaki 2003; Lee 2001; Leehey 2009; Ouzouni 2009; Toussaint 2008; Painter 2002b; Painter 2003; Parsons 2004; PEAK Study 2005; Tsuyuki 2003; Yurtkuran 2007), and ≥ 60 min/sessions in eight studies (Deligiannis 1999; Deligiannis-HI 1999; Goldberg 1983; Harter 1985; Konstantinidou-D 2002; Konstantinidou-ND 2002; Kouidi 1997a; Kouidi 2009; Molsted 2004). The remaining studies did not report duration of exercise/session.

Duration of exercise intervention (months)

Exercise interventions ranged from two months (Frey 1999) to 18 months duration (Chatoth 2005; Eidemak 1997). Duration of the intervention was three months in 17 studies, four to six months in 14 studies, and seven to 12 months in 14 studies.

Exercise supervision

Supervised exercise was carried out in 26 studies. Fifteen studies used exercise interventions supervised by a physiotherapist or an exercise physiologist (Akiba 1995; Kouidi 1997a; Deligiannis 1999; Deligiannis-HI 1999; DePaul 2002; Goldberg 1983; Konstantinidou-D 2002; Konstantinidou-ND 2002; Koufaki 2002a; Kouidi 2009; Ouzouni 2009; Painter 2002b; Parsons 2004; Segura-Orti 2009; Tsuyuki 2003; van Vilsteren 2005).

Outcomes

The reporting of outcome measures was variable. Different methods had often been used when measuring the same outcome, e.g. aerobic capacity (measured as VO₂ peak, VO₂ max, maximal exercise duration, maximal METs) and muscular strength (peak torque, one repetition maximum, five repetition maximum). The most common outcome measure when assessing the effect of regular physical exercise training on physical functioning was aerobic capacity.

Excluded studies

Excluded studies and the reasons for excluding them are given in [Characteristics of excluded studies](#).

Risk of bias in included studies

The risk of bias assessments of the included studies are summarised in [Figure 2](#) and [Figure 3](#). When assessing total risk of bias of the included studies eight were classified as A (DePaul 2002; Johansen 2006; Koh 2010a; Molsted 2004; Painter 2002a; PEAK Study 2005; Segura-Orti 2009; Yurtkuran 2007), 15 as B (Carmack 1995; Carney 1987; Castaneda 2001; Konstantinidou-D 2002; Koufaki 2002a; Kouidi 1997a; Kouidi 2009; Leehey 2009; Matsumoto 2007; Ouzouni 2009; Painter 2002b; Painter 2003; Parsons 2004; Toussaint 2008; van Vilsteren 2005); and 22 as C (Akiba 1995; Chen 2010; Chatoth 2005; Deligiannis 1999; Deligiannis-HI 1999; Dimeo 2007; Eidemak 1997; Fitts 1995; Fitts 1999; Frey 1999; Goldberg 1983; Harter 1985; Jong 2004; Kopple 2007a; Koufaki 2003; Kouidi 2002a; Kouidi 2002b; Kouidi 2003a; Kouidi 2004a; Kouidi 2005; Lee 2001; Tsuyuki 2003).

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

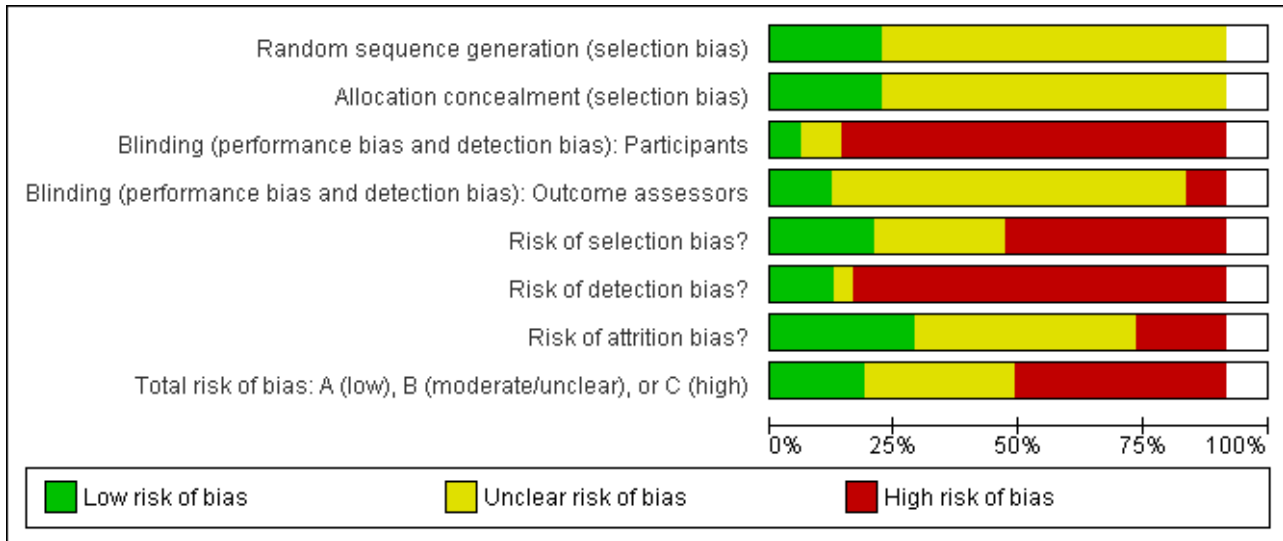


Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias): Participants	Blinding (performance bias and detection bias): Outcome assessors	Risk of selection bias?	Risk of detection bias?	Risk of attrition bias?	Total risk of bias: A (low), B (moderate/unclear), or C (high)
Akiba 1995	?	?	-	?	-	-	?	-
Carmack 1995	?	?	-	?	?	-	+	?
Carney 1987	?	?	-	?	?	-	?	?
Castaneda 2001	?	?	+	+	?	+	+	+
Chatoth 2005	?	?	-	?	-	-	-	-
Chen 2010	?	?	+	-	?	?	+	?
Deligiannis 1999	?	?	-	?	-	-	?	-
Deligiannis-HI 1999	?	?	-	?	-	-	?	-
Deligiannis-LI 1999								
DePaul 2002	+	+	-	+	+	+	+	+
Dimeo 2007	?	?	?	?	-	-	-	-
Eidemak 1997	?	?	-	?	-	-	?	-
Fitts 1995	?	?	-	?	-	-	+	-
Fitts 1999	?	?	?	?	-	-	?	-
Frey 1999	?	?	-	?	-	-	+	-
Goldberg 1983	?	?	-	?	-	-	?	-
Harter 1985	?	?	-	?	-	-	-	-
Johansen 2006	+	+	-	-	+	-	+	+

Figure 3. (Continued)

Johansen 2006	+	+	-	-	+	-	+	+
Jong 2004	?	?	-	?	-	-	?	-
Koh 2010a	+	+	-	-	+	-	+	+
Koh 2010b								
Konstantinidou-D 2002	?	?	-	?	?	-	?	?
Konstantinidou-ND 2002								
Konstantinidou-US 2002								
Kopple 2007a	?	?	-	?	-	-	?	-
Koufaki 2002a	+	+	-	?	+	-	?	?
Koufaki 2003	?	?	-	?	-	-	-	-
Kouidi 1997a	?	?	-	?	?	-	?	?
Kouidi 2002a	?	?	-	?	-	-	?	-
Kouidi 2002b	?	?	-	?	-	-	-	-
Kouidi 2003a	?	?	-	?	-	-	-	-
Kouidi 2004a	?	?	?	?	-	-	-	-
Kouidi 2005	?	?	-	?	-	-	-	-
Kouidi 2009	?	?	-	?	?	-	+	?
Lee 2001	?	?	?	?	-	-	-	-
Leehey 2009	+	?	-	-	?	-	?	?
Matsumoto 2007	?	?	-	?	?	-	?	?
Molsted 2004	+	+	-	+	+	+	?	+
Ouzouni 2009	?	?	-	?	-	-	+	?
Painter 2002a	+	+	-	?	+	-	+	+
Painter 2002b	?	?	-	?	?	-	?	?
Painter 2003	+	+	-	?	+	-	?	?
Parsons 2004	?	?	-	?	?	-	?	?
PEAK Study 2005	+	+	-	+	+	+	?	+
Segura-Orti 2009	+	+	+	?	+	?	+	+
Toussaint 2008	?	+	-	?	?	-	?	?
Tsuyuki 2003	?	?	-	?	-	-	?	-
van Vilsteren 2005	?	?	-	+	?	+	+	?

Figure 3. (Continued)

van Vilsteren 2005	?	?	-	+	?	+	+	?
Yurtkuran 2007	+	+	-	+	+	+	+	+

Allocation

Eligible/considered for inclusion

Seventeen of the studies included in the review described number of patients eligible/considered for inclusion (Carmack 1995; Carney 1987; Castaneda 2001; Chen 2010; DePaul 2002; Frey 1999; Johansen 2006; Koh 2010a; Konstantinidou-D 2002; Kouidi 2009; Leehey 2009; Molsted 2004; Painter 2002a; Segura-Orti 2009; PEAK Study 2005; van Vilsteren 2005; Yurtkuran 2007). The proportion between 'eligible/considered for inclusion' and 'enrolled/randomised' were: < 10% (Castaneda 2001); 11% to 20% (Chen 2010); 21% to 30% (Johansen 2006; Yurtkuran 2007); 31% to 40% (DePaul 2002; Molsted 2004); 41% to 50% (Konstantinidou-D 2002; Segura-Orti 2009); 51% to 60% (none); 61% to 70% (Koh 2010a; Leehey 2009; Painter 2002a; PEAK Study 2005); 71% to 80% (van Vilsteren 2005); 81% to 90% (none); and 91% to 100% (Carmack 1995; Carney 1987; Frey 1999).

Method of recruitment

Twenty one studies described where the recruitment had occurred (Carmack 1995; Carney 1987; Castaneda 2001; Chen 2010; DePaul 2002; Johansen 2006; Koh 2010a; Konstantinidou-D 2002; Kouidi 1997a; Kouidi 2009; Leehey 2009; Matsumoto 2007; Molsted 2004; Painter 2002a; Painter 2002b; Painter 2003; Parsons 2004; Segura-Orti 2009; PEAK Study 2005; Toussaint 2008; Yurtkuran 2007), but very few of the included studies described how the recruitment had been performed.

Method of randomisation

All of the included studies were described as randomised, but only 10 studies reported the method of randomisation (DePaul 2002; Johansen 2006; Koh 2010a; Kouidi 2009; Leehey 2009; Koufaki 2002a; Painter 2002a; Painter 2003; Segura-Orti 2009; Yurtkuran 2007). Randomisation was done using the following methods.

- Randomisation table and randomising in blocks (DePaul 2002; Johansen 2006; Leehey 2009; Segura-Orti 2009).
- Flip of a coin (Koufaki 2002a).
- Restricted randomisation method (Painter 2002a; Painter 2003).
- Computer-generated randomisation (Koh 2010a; PEAK Study 2005; Yurtkuran 2007).

All but one study (Chatoth 2005) reported number of patients enrolled/randomised.

Allocation concealment

Only 11/45 studies had used adequate allocation concealment (Chen 2010; DePaul 2002; Johansen 2006; Koh 2010a; Koufaki 2002a; Molsted 2004; Painter 2002a; Painter 2003; Segura-Orti 2009; PEAK Study 2005; Yurtkuran 2007); 34 studies had unclear allocation concealment, and none of the included studies had inadequate allocation concealment.

When assessing total risk of selection bias in the included studies, 10 were classified as A (DePaul 2002; Johansen 2006; Koh 2010a; Koufaki 2002a; Molsted 2004; Painter 2002a; Painter 2003; PEAK Study 2005; Segura-Orti 2009; Yurtkuran 2007), 13 as B (Carmack 1995; Carney 1987; Castaneda 2001; Chen 2010; Konstantinidou-D 2002; Kouidi 1997a; Kouidi 2009; Leehey 2009; Matsumoto 2007; Painter 2002b; Parsons 2004; Toussaint 2008; van Vilsteren 2005); and the remaining 22 as C.

Blinding

When assessing total risk of detection bias, five were classified as A (Castaneda 2001; DePaul 2002; Molsted 2004; PEAK Study 2005; van Vilsteren 2005; Yurtkuran 2007), two as B (Chen 2010; Segura-Orti 2009), and the remaining were classified as C.

Masked outcome assessment

Six out of 45 studies had used masked outcome assessments (Castaneda 2001; DePaul 2002; Molsted 2004; PEAK Study 2005; van Vilsteren 2005; Yurtkuran 2007).

Blinding of participants

Three studies had blinded participants (Castaneda 2001; Chen 2010; Segura-Orti 2009), in one study it was unclear (Yurtkuran 2007), and the rest of the studies the participants could not or were not blinded.

Blinding of administrators

None of the studies used blinded administrators.

Incomplete outcome data

Most studies accounted for all the randomised participants. Twenty-four of the 45 studies had followed over 80% of the initially included patients (Carney 1987; Castaneda 2001; Chen 2010; Deligiannis 1999; Deligiannis-HI 1999; Eidemak 1997; Fitts 1995; Jong 2004; Frey 1999; Johansen 2006; Jong 2004; Kouidi 1997a; Kouidi 2002a; Kouidi 2009; Konstantinidou-D 2002; Leehey 2009; Ouzouni 2009; Painter 2003; Segura-Orti 2009; PEAK Study 2005; Toussaint 2008; Tsuyuki 2003; van Vilsteren 2005; Yurtkuran 2007), 12 studies followed between 40% to 80% of the initially included patients (Akiba 1995; Carmack 1995; DePaul 2002; Fitts 1999; Goldberg 1983; Koh 2010a; Kopple 2007a; Koufaki 2002a; Matsumoto 2007; Molsted 2004; Painter 2002a; Painter 2002b; Parsons 2004), and nine studies did not report per cent followed (Dimeo 2007; Chatoth 2005; Harter 1985; Koufaki 2003; Kouidi 2002b; Kouidi 2003a; Kouidi 2004a; Kouidi 2005; Lee 2001).

Fifteen of 45 studies reported compliance to the intervention (Carmack 1995; Castaneda 2001; Chen 2010; DePaul 2002; Fitts 1995; Frey 1999; Koh 2010a; Kouidi 2009; Molsted 2004; Painter 2002a; PEAK Study 2005; Segura-Orti 2009; Toussaint 2008; van Vilsteren 2005; Yurtkuran 2007).

When assessing total risk of attrition bias 16 studies were classified as A (Carmack 1995; Castaneda 2001; Chen 2010; DePaul 2002; Fitts 1995; Frey 1999; Johansen 2006; Koh 2010a; Kouidi 2009; Molsted 2004; Ouzouni 2009; Painter 2002a; PEAK Study 2005; Segura-Orti 2009; van Vilsteren 2005; Yurtkuran 2007), 19 as B, and 10 as C.

Studies excluded from the meta-analyses

After extracted methodological information and research data needed for the meta-analysis, 12 reports had to be completely excluded from the meta-analysis (Carney 1987; Chatoth 2005; Fitts 1999; Harter 1985; Koufaki 2003; Kouidi 2002a, Kouidi 2002b; Kouidi 2003a; Kouidi 2004a; Kouidi 2005; Matsumoto 2007; Molsted 2004). Reasons for not being included in the meta analysis were missing or unclear data concerning: 1) number of patients analysed, for each outcome measure, in the control and the exercise group, respectively; 2) mean and SD of the outcome measure/s for the exercise group and or the control group, respectively.

Thirty-two studies were finally included in the meta-analysis (Akiba 1995; Carmack 1995; Castaneda 2001; Chen 2010, Deligiannis 1999; Deligiannis-HI 1999; Deligiannis-LI 1999; DePaul 2002; Eidemak 1997; Fitts 1995; Frey 1999; Goldberg 1983; Johansen 2006; Jong 2004; Koh 2010a; Koh 2010b; Konstantinidou-D 2002; Kopple 2007a; Koufaki 2002a; Kouidi 1997a; Kouidi 2009; Lee 2001; Leehey 2009; Ouzouni 2009; Painter 2002a; Painter 2002b; Painter 2003; Parsons 2004; PEAK Study 2005; Segura-Orti 2009; Toussaint 2008; Tsuyuki 2003; van Vilsteren 2005; Yurtkuran 2007).

Eight studies had missing data for some of their reported outcomes (Dimeo 2007; Eidemak 1997; Goldberg 1983; Jong 2004; Kopple 2007a; Matsumoto 2007; Parsons 2004; Toussaint 2008) and were therefore excluded from those particular meta-analyses.

Effects of interventions

Primary outcome measures

Physical fitness

Aerobic capacity

Physical exercise training (regardless of type of exercise, intensity, length of intervention, or with or without supervision) significantly increased aerobic capacity when compared to control (Analysis 1.1 (24 studies, 847 participants): SMD -0.56, 95% CI -0.70 to -0.42, $P < 0.00001$; $I^2 = 12\%$, $P = 0.19$), subgrouped by time of assessment.

Exercise Intensity

Both high and low intensity exercise training had a positive effect on aerobic capacity. High intensity exercise training improved aerobic capacity (Analysis 2.1 (17 studies, 647 participants): SMD -0.61, 95% CI -0.77 to -0.45, $P < 0.00001$; $I^2 = 28\%$, $P = 0.14$) more than low intensity exercise training interventions (Analysis 3.1 (5 studies, 182 participants): SMD -0.39, 95% CI -0.69 to -0.09, $P = 0.01$; $I^2 = 0\%$, $P = 0.42$). Based on subgroup analysis, the increase in aerobic capacity in high intensity exercise training studies (-0.59) was more pronounced than the increase for all the studies combined (-0.56).

Length of time of the exercise

Aerobic capacity increased significantly following three months (Analysis 1.1.1 (7 studies, 241 participants): SMD -0.39, 95% CI -0.65 to -0.13, $P = 0.003$; $I^2 = 0\%$, $P = 0.53$), four to six months (Analysis 1.1.2 (11 studies, 268 participants): SMD -0.81, 95% CI -1.08 to -0.54, $P < 0.00001$; $I^2 = 14\%$, $P = 0.31$), and seven to 12 months

of regular physical exercise training (Analysis 1.1.3 (6 studies, 338 participants): SMD -0.52, 95% CI -0.74 to -0.30, $P < 0.00001$; $I^2 = 28\%$, $P = 0.23$). The results show that three to 7-12 months regular exercise training has positive effect on aerobic capacity. Based on subgroup analysis, the increase in aerobic capacity in four to six months studies (-0.81) was more pronounced than the increase for all the studies combined (-0.56).

Type of exercise

Cardiovascular exercise training (Analysis 4.1 (16 studies, 503 participants): SMD -0.53, 95% CI -0.71 to -0.35, $P < 0.00001$; $I^2 = 25\%$, $P = 0.17$) and mixed cardiovascular and resistance training significantly improved aerobic capacity (Analysis 5.1 (9 studies, 353 participants): SMD -0.77, 95% CI -1.06 to -0.48, $P < 0.00001$; $I^2 = 33\%$, $P = 0.16$). Resistance training alone had no significant effect on aerobic capacity (Analysis 6.1). Based on subgroup analysis, the increase in aerobic capacity in mixed cardiovascular and resistance training studies (-0.77) was more pronounced than the increase for all the studies combined (-0.56).

Exercise supervision

Supervised exercise interventions showed a statistically significant increase in aerobic capacity (Analysis 7.1 (15 studies, 538 participants): SMD -0.68, 95% CI -0.91 to -0.45, $P < 0.00001$; $I^2 = 34\%$, $P = 0.09$). Unsupervised exercise also showed a positive effect on aerobic capacity (Analysis 8.1 (8 studies, 333 participants): SMD -0.48, 95% CI -0.70 to -0.26, $P < 0.0001$; $I^2 = 0\%$, $P = 0.46$). Based on subgroup analysis, the increase in aerobic capacity in supervised exercise intervention studies (-0.68) was more pronounced than the increase for all the studies combined (-0.56).

Muscular strength

Ten of 11 studies reporting muscular strength used different measurement methods. In two studies the outcome measure showed increased muscular strength when the outcome had a lower value than at baseline (Koufaki 2002a; van Vilsteren 2005), while in the remaining nine studies an increased value indicated increased muscular strength. Data from these nine studies showed increased muscular strength with regular physical exercise training (regardless of type of exercise, intensity, length of intervention, with or without supervision, (Analysis 1.2 (9 studies, 358 participants): SMD -0.52, 95% CI -0.73 to -0.31, $P < 0.00001$; $I^2 = 0\%$, $P = 0.94$). This was also seen in the two studies using methods where a reduced value was equal to improved muscular strength (Analysis 1.3 (2 studies, 148 participants): SMD 0.58, 95% CI 0.25 to 0.92, $P = 0.0007$; $I^2 = 22\%$, $P = 0.28$).

Exercise intensity

High intensity exercise training showed an increase in muscular strength (Analysis 2.2 (8 studies, 322 participants): SMD -0.50, 95% CI -0.72 to -0.27, $P = 0.0001$; $I^2 = 0\%$, $P = 0.92$); (Analysis 2.3 (3 studies, 148 participants): SMD 0.58, 95% CI 0.25 to 0.92, $P = 0.0007$; $I^2 = 22\%$, $P = 0.28$).

Low intensity exercise training had a positive effect on muscular strength (Analysis 3.2 (1 study, 96 participants): SMD 0.77, 95% CI 0.35 to 1.19, $P = 0.0003$).

Length of time of the exercise intervention

Three months of regular exercise training significantly increased muscular strength (Analysis 1.2.1 (5 studies, 177 participants): SMD

-0.60, 95% CI -1.90 to -0.29, $P = 0.0001$; $I^2 = 0\%$, $P = 0.78$) and (Analysis 1.3.1 (2 studies, 123 participants): SMD 0.69, 95% CI 0.32 to 1.05, $P = 0.0002$; $I^2 = 0\%$, $P = 0.41$).

Four to six months of regular exercise training significantly increased muscular strength in those studies reporting an increased value for increased muscular strength (Analysis 1.2.2 (3 studies, 86 participants): SMD -0.37, 95% CI -0.97 to -0.08, $P = 0.02$; $I^2 = 0\%$, $P = 0.83$), but not in the study reporting a decreased value for increased muscular strength (Analysis 1.3.2 (1 study, 25 participants): SMD 0.04, 95% CI -0.80 to 0.88, $P = 0.92$).

Seven to 12 months of regular exercise showed no statistically significant difference in muscular strength between exercise and control group (Analysis 1.2 (1 study, 95 participants): SMD -0.37, 95% CI -0.78 to 0.04, $P = 0.08$).

Type of exercise

Cardiovascular exercise training (Analysis 4.2 (4 studies, 165 participants): SMD -0.23, 95% CI -0.57 to 0.12, $P = 0.19$; $I^2 = 10\%$, $P = 0.34$) and mixed cardiovascular and resistance training (Analysis 5.2, DePaul 2002 (29 participants): SMD -0.54, 95% CI -1.28 to 0.20; van Vilsteren 2005 (96 participants): SMD 0.77, 95% CI 0.35 to 1.19) did not improve muscular strength.

Regular resistance training significantly increased muscular strength (Analysis 6.2 (4 studies, 153 participants): SMD -0.60, 95% CI -0.92 to -0.27, $P = 0.0003$; $I^2 = 0\%$, $P = 0.64$).

Yoga significantly increased muscular strength (Analysis 9.1 (1 study 37 participants): SMD -0.70, 95% CI -1.37 to -0.03)

Exercise intensity

Both supervised exercise training (Analysis 7.2 (7 studies, 248 participants): SMD -0.57, 95% CI -0.83 to -0.32, $P < 0.0001$; $I^2 = 0\%$, $P = 0.90$); (Analysis 7.3 (3 studies, 148 participants): SMD 0.58, 95% CI 0.25 to 0.92, $P = 0.0007$; $I^2 = 22\%$, $P = 0.28$) and unsupervised exercise training (Analysis 8.2 (2 studies, 123 participants): SMD -0.39, 95% CI -0.75 to -0.03; $P = 0.03$, $I^2 = 0\%$, $P = 0.86$) showed a significant increase in muscular strength compared to no exercise or control.

Muscular endurance ('Sit-to-Stand-to-Sit-60' method)

Neither three months of high intensity ($\geq 60\%$), supervised, cardiovascular exercise training (Analysis 1.4.1 (1 study, 27 participants): MD -2.80 sec, 95% CI -7.89 to 2.29, $P = 0.28$) nor six months supervised, high intensity, resistance training (Analysis 1.4.2 (1 study, 25 participants): MD -5.70 sec, 95% CI -7.93 to 2.28, $P = 0.16$) improved muscular endurance.

Physical functioning

Walking capacity

Seven studies reported walking capacity, all used different methods of measurement. Walking capacity was significantly increased following regular exercise training (Analysis 1.5 (7 studies, 191 participants): SMD -0.48, 95% CI -0.79 to -0.17; $P = 0.003$; $I^2 = 2\%$, $P = 0.41$).

Type of exercise

Only studies using a high intensity ($\geq 60\%$) exercise training intervention reported walking capacity, and it was therefore not possible to compare high versus low intensity exercise training.

Length of time of the exercise intervention

Three months exercise showed a significant increase in walking capacity (Analysis 1.5.1 (4 studies 122 participants): SMD -0.50, 95% CI -0.86 to 0.13, $P = 0.007$; $I^2 = 0\%$, $P = 0.86$) however there was no significant increase with four to six months of regular exercise (Analysis 1.5.2 (3 studies, 69 participants): SMD -0.09, 95% CI -0.60 to 0.41, $P = 0.72$; $I^2 = 46\%$, $P = 0.15$).

Type of exercise

Neither cardiovascular exercise (Analysis 4.4 (3 studies, 71 participants): SMD -0.38, 95% CI -0.86 to 0.10, $P = 0.12$; $I^2 = 0\%$, $P = 0.83$) nor mixed cardiovascular and resistance training (Analysis 5.3 (2 studies, 46 participants): SMD -0.43, 95% CI -1.02 to 0.16, $P = 0.15$; $I^2 = 0\%$, $P = 0.81$) improved walking capacity. Three months resistance exercise training used by PEAK Study 2005 improved walking capacity significantly (Analysis 6.5.1 (1 study, 49 participants): SMD -0.68, 95% CI -1.25 to -0.10, $P = 0.02$), however the four to six months resistance training used by Segura-Orti 2009 did not improve walking capacity (Analysis 6.5.2 (1 study, 25 participants): SMD 0.56, 95% CI -0.29 to 1.42, $P = 0.20$).

Exercise supervision

There was a significant improvement in walking capacity with supervised exercise training (Analysis 7.5 (5 studies, 160 participants): SMD -0.26, 95% CI -0.68 to -0.04, $P = 0.03$; ($P = 0.20$); $I^2 = 33\%$, $P = 0.20$). The heterogeneity was as a result of Segura-Orti 2009. When it was removed from the analysis the result remains significant, however the I^2 was zero (SMD -0.51, 95% CI -0.85 to -0.17, $P = 0.04$; $I^2 = 0\%$, $P = 0.85$).

There was no significant difference in walking capacity when unsupervised exercise training was compared to control (Analysis 8.3 (2 studies, 47 participants): SMD -0.37, 95% CI -0.94 to 0.21, $P = 0.22$; $I^2 = 0\%$, $P = 0.69$).

Stair climbing capacity

One study (Koufaki 2002a), using three months of supervised, high intensity, cardiovascular exercise training showed no change in stair climbing capacity (Analysis 1.6 (1 study, 27 participants): MD -1.50 sec, 95% CI -5.67 to 2.67, $P = 0.48$).

Activities of daily living (ADL) capacity

There was no significant effect of four to six months supervised or unsupervised, high or low intensity, resistance or cardiovascular exercise training on ADL (Analysis 1.7 (3 studies, 87 participants): SMD 0.05, 95% CI -0.39 to 0.48, $P = 0.83$; $I^2 = 0\%$, $P = 0.44$).

Cardiovascular dimensions

Resting diastolic blood pressure

Physical exercise training (regardless of type, intensity, length of intervention, or supervision) decreased resting diastolic blood pressure when compared to control (Analysis 1.8 (11 studies, 419 participants): MD 2.32 mm Hg, 95% CI 0.59 to 4.05, $P = 0.009$; $I^2 = 46\%$, $P = 0.05$).

Exercise intensity

High intensity exercise training showed a significant decrease in resting diastolic blood pressure (Analysis 2.8 (6 studies, 254 participants): MD 3.98 mm Hg, 95% CI 1.90 to 6.05, $P = 0.0002$; $I^2 =$

0%, $P = 0.71$). There was no significant change in resting diastolic blood pressure with low intensity exercise training ([Analysis 3.4](#) (3 studies, 147 participants): MD -1.77 mm Hg, 95% CI -5.26 to 1.73, $P = 0.32$; $I^2 = 0\%$, $P = 0.55$).

Length of time of the exercise intervention

Exercise training intervention for three months did not decrease resting diastolic blood pressure ([Analysis 1.8.1](#) (3 studies, 144 participants): MD -0.88 mm Hg, 95% CI -4.58 to 2.81, $P = 0.64$; $I^2 = 13\%$, $P = 0.32$).

Four to six months exercise training intervention did not decrease resting diastolic blood pressure ([Analysis 1.8.2](#) (4 studies, 78 participants): MD 1.39 mm Hg, 95% CI -1.78 to 4.56, $P = 0.39$; $I^2 = 61\%$, $P = 0.05$). The heterogeneity was as a result of [Leehey 2009](#) which was the only study that showed a significant decrease in resting diastolic blood pressure. When it was removed from the analysis the result was still not significant and the I^2 decreased to 45% (MD 0.39 mm Hg, 95% CI -2.78 to 3.70, $P = 0.82$; $I^2 = 45\%$, $P = 0.16$).

Seven to 12 months of exercise showed a significant decrease in resting diastolic blood pressure ([Analysis 1.8.3](#) (4 studies, 197 participants): MD 4.37 mm Hg, 95% CI 1.87 to 6.87, $P = 0.0006$; $I^2 = 0\%$, $P = 0.46$).

Type of exercise

Cardiovascular exercise training did not decrease resting diastolic blood pressure ([Analysis 4.7](#) (6 studies, 202 participants): MD -0.11 mm Hg, 95% CI -2.88 to 2.66, $P = 0.96$; $I^2 = 45\%$, $P = 0.11$).

Mixed cardiovascular and resistance training significantly decreased resting diastolic blood pressure ([Analysis 5.5](#) (5 studies, 229 participants): MD 3.77 mm Hg, 95% CI 1.61 to 5.94, $P = 0.0006$; $I^2 = 17\%$, $P = 0.14$).

This outcome was not reported in studies using resistance training.

Exercise supervision

Supervised exercise training significantly decreased resting diastolic blood pressure ([Analysis 7.8](#) (7 studies, 282 participants): MD 2.93 mm Hg, 95% CI 0.20 to 5.66, $P = 0.04$; $I^2 = 35\%$, $P = 0.16$).

Unsupervised exercise training intervention showed no effect on resting diastolic blood pressure ([Analysis 8.5](#) (4 studies, 148 participants): MD 0.27 mm Hg, 95% CI -2.72 to 3.26, $P = 0.86$; $I^2 = 55\%$, $P = 0.08$).

Resting systolic blood pressure

Exercise resulted in a significant decrease in resting systolic blood pressure ([Analysis 1.9](#) (9 studies, 347 participants): MD 6.08 mm Hg, 95% CI 2.15 to 10.12, $P = 0.002$; $I^2 = 12\%$, $P = 0.33$). Two studies were excluded from this analysis because of their inconsistency in the direction of the effect, resulting in significant heterogeneity. [Kouidi 2009](#) showed a significant increase in resting systolic blood pressure while [Tsuyuki 2003](#) showed no effect on resting systolic blood pressure. When they were included, physical exercise did not decrease resting systolic blood pressure (11 studies, 419 participants): MD 3.01 mm Hg, 95% CI -3.25 to 9.26; $I^2 = 71\%$, $P = 0.0002$).

Exercise intensity

High intensity exercise training significantly decreased resting systolic blood pressure ([Analysis 2.9](#) (5 studies, 211 participants): MD 4.60 mm Hg, 95% CI 0.37 to 8.83, $P = 0.03$, $I^2 = 0\%$, $P = 0.84$). [Kouidi 2009](#) was excluded from the analysis because of its inconsistency in the direction of effect, resulting in significant heterogeneity. When it was included, high intensity exercise did not decrease resting systolic blood pressure (6 studies, 254 participants): MD 0.34 mm Hg, 95% CI -3.42 to 4.10, $P = 0.86$; $I^2 = 75\%$, $P = 0.001$).

Low intensity exercise training showed no significant decrease in resting systolic blood pressure ([Analysis 3.5](#) (3 studies, 147 participants): MD 0.86 mm Hg, 95% CI -6.10 to 7.82, $P = 0.81$; $I^2 = 36\%$, $P = 0.21$).

Length of time of the exercise intervention

Length of time of the exercise did not affect resting systolic blood pressure, not after three months ([Analysis 1.9.1](#) (3 studies, 144 participants): MD 6.38 mm Hg, 95% CI -1.08 to 13.84), four to six months ([Analysis 1.9.2](#) (3 studies, 49 participants): MD 10.62 mm Hg, 95% CI -1.38 to 22.62), or seven to 12 months ([Analysis 1.9.3](#) (3 studies, 154 participants): MD 3.16 mm Hg, 95% CI -1.94 to 8.27).

Type of exercise

Six studies used cardiovascular exercise training, however data were not pooled due to significant heterogeneity. Only [Leehey 2009](#) showed any significant decrease on resting systolic blood pressure ([Analysis 4.8](#)).

None of the included studies using a resistance training intervention reported resting systolic blood pressure.

Mixed cardiovascular and resistance training showed a significant decrease in resting systolic blood pressure ([Analysis 5.6](#) (5 studies, 186 participants): MD 5.80 mm Hg, 95% CI 1.19 to 10.41, $P = 0.02$, $I^2 = 0\%$, $P = 0.92$). [Kouidi 2009](#) showed a significant increase in resting systolic blood pressure, resulting in significant heterogeneity and was excluded from the analysis.

Exercise supervision

Supervised exercise significantly decreased resting systolic blood pressure ([Analysis 7.9](#) (5 studies, 211 participants): MD 5.88 mm Hg, 95% CI 1.42 to 10.34, $P = 0.01$, $I^2 = 0\%$, $P = 0.97$). Two studies were excluded from this analysis because of their inconsistency in the direction of the effect, resulting in significant heterogeneity. [Kouidi 2009](#) showed a significant increase in resting systolic blood pressure while [Tsuyuki 2003](#) showed no effect on resting systolic blood pressure. When they were included, supervised exercise did not decrease resting systolic blood pressure (MD 0.64 mm Hg, 95% CI -7.27 to 8.54, $P = 0.87$; $I^2 = 74\%$, $P = 0.0008$).

Four studies used unsupervised exercise training, however data were not pooled due to significant heterogeneity. Only [Leehey 2009](#) showed any significant decrease on resting systolic blood pressure ([Analysis 8.6](#)).

Heart rate maximum (bpm)

Compared to control, any physical exercise training (regardless of type, intensity, length of intervention or supervision) significantly

increased maximum heart rate ([Analysis 1.10](#) (11 studies, 229 participants): MD 6 bpm, 95% CI 10 to 2, $P = 0.002$; $I^2 = 0\%$, $P = 0.94$).

Exercise intensity

High intensity exercise training increased maximum heart rate ([Analysis 2.10](#) (7 studies, 169 participants): MD 6 bpm, 95% CI 11 to 2, $P = 0.006$; $I^2 = 0\%$, $P = 0.81$).

Low intensity exercise training showed no effect on maximum heart rate ([Analysis 3.6](#) (3 studies, 73 participants): 4 bpm MD, 95% CI 10 to -2, $P = 0.16$; $I^2 = 0\%$, $P = 0.77$).

Length of time of the exercise intervention

Three months of regular exercise training increased maximum heart rate in [Akiba 1995](#) (13 participants: MD 19 bpm, 95% CI 36 to 2) while [Koufaki 2002a](#) showed no increase in maximum heart rate (33 participants: MD 2 bpm, 95% CI 18 to -14). Combined these studies showed no significant increase in bpm, however there was significant heterogeneity ([Analysis 1.10.1](#) (2 studies, 46 participants): MD 10 bpm, 95% CI 22 to -2, $P = 0.09$; $I^2 = 52\%$, $P = 0.15$).

Four to six months of regular exercise training increased maximum heart rate ([Analysis 1.10.2](#) (8 studies, 150 participants): MD 6 bpm, 95% CI 11 to 1, $P = 0.01$, $I^2 = 0\%$, $P = 0.98$).

Seven to 12 months of regular exercise (33 participants randomised) and showed no significant change in maximum heart rate ([Analysis 1.10.3](#) (1 study, 33 participants): MD 5 bpm, 95% CI 12 to -3).

Type of exercise

Regular cardiovascular exercise significantly increased maximum heart rate ([Analysis 4.9](#) (7 studies, 154 participants): MD 6 bpm, 95% CI 11 to 1, $P = 0.01$; $I^2 = 0\%$, $P = 0.63$).

Mixed cardiovascular and resistance training significantly increased maximum heart rate ([Analysis 5.7](#) (4 studies, 99 participants): MD 5 bpm MD, 95% CI 10 to 1, $P = 0.03$; $I^2 = 0\%$, $P = 0.98$).

None of the included studies using a resistance training intervention reported maximum heart rate.

Exercise supervision

Supervised exercise increased maximum heart rate ([Analysis 7.10](#) (8 studies, 194 participants): MD 7 bpm, 95% CI 11 to 2, $P = 0.003$; $I^2 = 0\%$, $P = 0.88$).

Unsupervised exercise showed no significant change in maximum heart rate ([Analysis 8.7](#) (3 studies, 55 participants): MD 4 bpm, 95% CI 10 to -2, $P = 0.18$; $I^2 = 0\%$, $P = 0.59$).

Resting heart rate (bpm)

Physical exercise training (regardless of type, intensity, length of intervention, or supervision) significantly reduced resting heart rate ([Analysis 1.11](#) (7 studies, 179 participants): MD 4 bpm, 95% CI 2 to 7, $P = 0.002$, $I^2 = 0\%$, $P = 0.48$).

Exercise intensity

High intensity exercise training significantly reduced resting heart rate ([Analysis 2.11](#) (4 studies, 129 participants): MD 4 bpm, 95% CI 1 to 7; $P = 0.002$; $I^2 = 0\%$, $P = 0.48$).

Low intensity exercise training showed no significant change in resting heart rate ([Analysis 3.7](#) (2 studies, 51 participants): MD 3 bpm, 95% CI 3 to 9, $P = 0.33$; $I^2 = 0\%$; $P = 0.87$).

Length of time of the exercise intervention

None of the studies using three months of exercise training reported resting heart rate.

Four to six months of regular exercise training did not significantly change resting heart rate ([Analysis 1.11.2](#) (4 studies, 78 participants): MD 3 bpm, 95% CI -2 to 8, $P = 0.25$; $I^2 = 0\%$, $P = 0.70$).

Seven to 12 months of regular exercise training did not significantly change resting heart rate ([Analysis 1.11.3](#) (3 studies, 101 participants): MD 3 bpm, 95% CI -2 to 8, $P = 0.23$; $I^2 = 48\%$, $P = 0.15$).

Type of exercise

Cardiovascular exercise training did not affect resting heart rate ([Analysis 4.10](#) (4 studies, 87 participants): MD 1 bpm, 95% CI -4 to 6, $P = 0.77$; $I^2 = 0\%$, $P = 0.53$).

Mixed cardiovascular and resistance training significantly reduced resting heart rate ([Analysis 5.8](#) (3 studies, 104 participants): MD 5 bpm, 95% CI 2 to 8, $P = 0.0005$; $I^2 = 0\%$, $P = 0.53$).

None of the studies using resistance exercise training reported resting heart rate.

Exercise supervision

Supervised exercise training reduced resting heart rate ([Analysis 7.11](#) (5 studies, 158 participants): MD 4 bpm, 95% CI 2 to 7, $P = 0.001$; $I^2 = 0\%$, $P = 0.42$).

Unsupervised exercise did not alter resting heart rate ([Analysis 8.8](#) (2 studies, 33 participants): MD 2 bpm, 95% CI -6 to 10, $P = 0.62$; $I^2 = 18\%$, $P = 0.27$).

Nutrition

Albumin (g/L)

Three months of physical exercise training (regardless of type, intensity, length of intervention, or supervision) significantly decreased albumin ([Analysis 1.12](#) (3 studies, 111 participants): MD -2.28 g/L, 95% CI -4.25 to -0.32, $P = 0.02$; $I^2 = 46\%$, $P = 0.16$). [Koufaki 2002a](#) was excluded from this analysis because of their inconsistency in the direction of the effect, resulting in significant heterogeneity. When it was included physical exercise did not decrease albumin levels (4 studies, 144 participants): MD -0.89 g/L, 95% CI -4.08 to 2.31, $P = 0.59$; $I^2 = 81\%$, $P = 0.001$).

Exercise intensity

This outcome was not reported in any of the studies using either high or low intensity exercise training.

Length of exercise the intervention

This outcome was not reported in any of the studies using either four to six months or seven to 12 months exercise training.

Type of exercise

Due to heterogeneity, data from the cardiovascular exercise studies could not be pooled for albumin. Cardiovascular exercise training

increased albumin in [Jong 2004](#) ([Analysis 4.11](#) (36 participants): MD -5.20 g/L, 95% CI -8.90 to -1.50), whereas the cardiovascular exercise training used in [Koufaki 2002a](#) decreased levels of albumin ([Analysis 4.11](#) (33 participants): MD 5.30 g/L, 95% CI 1.47 to 9.13).

None of the studies using a mixed cardiovascular and resistance training intervention reported albumin levels.

Resistance training significantly decreased albumin levels ([Analysis 6.6](#) (2 studies, 75 participants): MD -1.46 g/L, 95% CI -2.89 to -0.84, $P = 0.04$; $I^2 = 0\%$, $P = 0.61$).

Exercise supervision

Supervised exercise training significantly decreased albumin ([Analysis 7.12](#) (2 studies, 75 participants): MD -1.46 g/L, 95% CI -2.89 to -0.04, $P = 0.04$; $I^2 = 0\%$, $P = 0.61$). [Koufaki 2002a](#) was excluded from this analysis because of their inconsistency in the direction of the effect, resulting in significant heterogeneity. When it was included exercise supervision did not decrease albumin levels (3 studies, 108 participants): MD 0.32 g/L, 95% CI -3.13 to 3.77, $P = 0.86$; $I^2 = 81\%$, $P = 0.005$).

Unsupervised exercise training increased albumin levels ([Analysis 8.9](#) (1 study, 36 participants): MD -5.20 g/L, 95% CI -8.90 to -1.50).

Pre-albumin (mg/L)

Three months of regular, high intensity exercise training significantly decreased pre-albumin levels ([Analysis 1.13](#) (3 studies, 111 participants): MD -44.02 mg/L, 95% CI -71.52 to -16.53; $P = 0.002$; $I^2 = 0\%$, $P = 0.92$).

Exercise intensity

This outcome was not reported in any of the studies using low intensity exercise interventions.

Length of the exercise intervention

This outcome was not reported in any of the studies using either four to six months or seven to 12 months exercise training.

Type of exercise

Cardiovascular exercise did not decrease pre-albumin levels ([Analysis 4.12](#) (1 study, 11 participants): MD -33.30 mg/L, 95% CI -130.63 to 64.03).

None of the studies using a mixed cardiovascular and resistance training reported pre-albumin levels.

Resistance training significantly increased pre-albumin levels ([Analysis 6.7](#) (2 studies, 75 participants): MD -45.24 mg/L, 95% CI -73.90 to -16.57; $P = 0.002$; $I^2 = 0\%$, $P = 0.79$).

Exercise supervision

This outcome was not reported in any of the studies using unsupervised exercise training.

Subjective Global Assessment (SGA)

Three months of supervised, high intensity ($\geq 60\%$), cardiovascular exercise training did not change the SGA score ([Analysis 1.14](#) (1 study, 33 participants): MD -0.10, 95% CI -0.75 to 0.55).

Energy intake

Regular exercise training (regardless of type, intensity, length of intervention, or supervision) showed a significant increase in energy intake following exercise training ([Analysis 1.15](#) (4 studies, 97 participants): SMD -0.47, 95% CI -0.88 to -0.05; $P = 0.03$; $I^2 = 12\%$, $P = 0.33$).

Exercise intensity

High intensity exercise training significantly increased energy intake following exercise training ([Analysis 2.15](#) (3 studies, 86 participants): SMD -0.57, 95% CI -1.01 to -0.13, $P = 0.01$; $I^2 = 0\%$, $P = 0.49$).

This outcome was not reported in any of the studies using low intensity exercise training.

Type of exercise

Due to heterogeneity, data from the cardiovascular exercise studies were not pooled. Neither [Frey 1999](#) nor [Leehey 2009](#) reported any significant increase in energy intake following cardiovascular exercise ([Analysis 4.14](#)).

This outcome was not reported in any of the studies using mixed cardiovascular and resistance exercise training.

Resistance training did not significantly increase energy intake ([Analysis 6.8](#) (2 studies, 75 participants): MD -3.70 kcal/kg/d, 95% CI -7.46 to 0.06, $P = 0.05$; $I^2 = 5\%$, $P = 0.31$).

Exercise supervision

This outcome was not reported in any of the studies using unsupervised exercise training.

Protein intake

Three months of supervised, high intensity exercise training did not significantly increase protein intake ([Analysis 1.16](#) (2 studies, 60 participants): SMD -0.50, 95% CI -1.01 to 0.02, $P = 0.06$; $I^2 = 0\%$, $P = 0.75$).

Type of exercise

Cardiovascular exercise training did not increase protein intake ([Analysis 4.15](#) (1 study, 11 participants): MD -21.00 g/day, 95% CI -57.82 to 15.82).

None of the studies using a mixed cardiovascular and resistance training reported protein intake.

Resistance exercise training did not increase protein intake ([Analysis 6.9](#) (1 study, 49 participants): MD -0.15 g/kg body weight/day, 95% CI -0.33 to 0.03).

Transferrin (g/L)

Due to heterogeneity ($I^2 = 90\%$, $P = 0.001$) data have not been pooled but are presented separately.

Two months of supervised, high intensity cardiovascular exercise training did not significantly increase serum transferrin ([Analysis 1.17](#) (1 study, 11 participants): MD 0.05 g/L, 95% CI -0.35 to 0.45).

Three months of supervised, high intensity resistance training significantly increased in serum transferrin ([Analysis 1.17](#) (1 study, 26 participants): MD -0.81 g/L, 95% CI -1.15 to -0.47).

Body mass indices (muscle mass, fat mass, anthropometric measures)

Twelve studies reported body mass indices (muscle mass, fat mass, anthropometric measures) as an outcome measure, however none reported muscle mass.

Exercise training in general did not significantly reduce fat mass ([Analysis 1.18](#) (5 studies, 237 participants): SMD 0.08, 95% CI -0.19 to 0.34, $P = 0.57$; $I^2 = 61%$, $P = 0.04$). Heterogeneity was due to [Leehey 2009](#) who used four to six months of unsupervised, mixed intensity walking program and showed a significant decrease in fat mass ([Analysis 1.18.2](#) (1 study, 11 participants): SMD 2.10, CI 0.45 to 3.74).

Anthropometric measures were only reported in [PEAK Study 2005](#). Three months of supervised, high intensity resistance training did not reduce waist circumference ([Analysis 1.19](#): MD 3.30 cm, 95% CI -6.32 to 12.92; $P = 0.50$), mid-arm circumference ([Analysis 1.20](#): MD -0.70 cm, 95% CI -2.66 to 1.26), mid-calf circumference ([Analysis 1.21](#): MD 0.50 cm, 95% CI -1.44 to 2.44; $P = 0.61$), or mid-thigh circumference ([Analysis 1.22](#): MD 0.60 cm, 95% CI -2.16 to 3.36).

Systemic inflammation

Serum interleukin 6

There was no difference in serum interleukin 6 levels between the exercise and control group when using three months supervised high intensity resistance training ([Analysis 1.23](#) (1 study, 26 participants): MD 3.10 pg/mL, 95% CI -3.41 to 9.61).

Lymphocytes

There was no difference in lymphocytes between the exercise and control group when using three months supervised, high intensity resistance training ([Analysis 1.24](#) (1 study, 49 participants): MD 0.08 x 10⁹ L, 95% CI -0.26 to 0.42).

Protein catabolic rate

There was no difference in protein catabolic rate between the exercise and control group when using three months supervised, high intensity resistance training ([Analysis 1.25](#) (1 study, 49 participants): MD -0.01 g/kg BW/d, 95% CI -0.17 to 0.15).

Physical activity

Regular exercise training (regardless of type, intensity, length of intervention, or supervision) showed a significant increase in the level of physical activity ([Analysis 1.26](#) (4 studies, 121 participants): SMD -0.43, 95% CI -0.80 to -0.05, $P = 0.02$; $I^2 = 0%$, $P = 0.85$). There was no significant difference in physical activity between the exercise and control group after three months of exercise ([Analysis 1.26](#) (1 study, 33 participants): SMD -0.33, 95% CI -1.02 to 0.36). The effect occurred in the studies with four to six months of exercise training ([Analysis 1.26.2](#) (3 studies, 88 participants): SMD -0.46, 95% CI -0.09 to -0.83, $P = 0.04$; $I^2 = 0%$, $P = 0.71$).

Cardiovascular exercise training did not increase physical activity ([Analysis 4.18](#) (3 studies, 77 participants): SMD -0.30, 95% CI -0.77 to 0.17, $P = 0.21$; $I^2 = 0%$, $P = 0.98$).

None of the studies using a mixed cardiovascular and resistance training reported physical activity.

Resistance exercise training did not increase physical activity ([Analysis 6.19](#) (1 study, 44 participants): MD -0.30, 95% CI -1.22 to 0.62).

Depression

Due to significant heterogeneity ($I^2 = 79%$, $P = 0.002$) data were not pooled ([Analysis 1.27](#)) but have been presented separately.

[van Vilsteren 2005](#) found three months of supervised low intensity mixed cardiovascular and resistance training and found a decreased level of depression ([Analysis 1.27.1](#) (96 participants): SMD 0.47, 95% CI 0.06 to 0.88), while [Carmack 1995](#) found no difference ([Analysis 1.27.1](#) (21 participants): SMD -0.26, 95% CI -1.12 to 0.60).

There was no change in depression after four to six months of exercise ([Analysis 1.27.2](#) (1 study, 31 participants): SMD 0.31, 95% CI -0.05 to 1.47).

Ten months of supervised, high intensity, mixed cardiovascular and resistance training ([Ouzouni 2009](#)) decreased the level of depression ([Analysis 1.27.3](#) (1 study, 33 participants): SMD 1.99, 95% CI 1.13 to 2.85).

Health-related quality of life

Eighteen studies reported the effect of regular exercise training on health-related quality of life in adults with CKD. Different instruments had been used. Most studies had used a generic instrument and not a disease-specific instrument. In some cases only a total score had been used. Data from each study has been tabulated and is presented in [Appendix 2 - Health-related quality of life assessment](#). In summary, 14/18 studies showed improved total scores and/or sub-scores following regular exercise training and 4/18 studies showed no effect of exercise training on health-related quality of life in adults with CKD.

Secondary outcome measures

Blood lipids

Triglycerides

Regular exercise (regardless of type, intensity, length of intervention, or supervision) showed no significant change in triglycerides ([Analysis 1.28](#) (4 studies, 100 participants): MD 0.05 mmol/L, 95% CI -0.23 to 0.33, $P = 0.72$; $I^2 = 0%$, $P = 0.87$). Analyses based on length of intervention ([Analysis 1.28](#)), intensity of exercise ([Analysis 2.28](#)), type of exercise ([Analysis 4.20](#); [Analysis 9.3](#)), and with ([Analysis 7.28](#)) or without ([Analysis 8.14](#)) supervision, showed no effect of exercise on triglycerides.

Total cholesterol

Regular exercise (regardless of type, intensity, length of intervention, or supervision) showed no significant change in cholesterol ([Analysis 1.29](#) (6 studies, 292 participants): MD 0.17 mmol/L, 95% CI -0.12 to 0.46, $P = 0.25$; $I^2 = 20%$, $P = 0.28$). All six studies used supervised exercise training interventions. Analyses based on length of intervention ([Analysis 1.29](#)), intensity of exercise ([Analysis 2.29](#); [Analysis 3.9](#)) or type of exercise ([Analysis 4.21](#); [Analysis 5.11](#); [Analysis 9.4](#)) showed no effect on total cholesterol.

HDL cholesterol

Regular exercise (regardless of type, intensity, length of intervention, or supervision) showed a statistically significant decrease in HDL cholesterol ([Analysis 1.30](#) (4 studies, 166 participants): MD -0.14 mmol/L MD, 95% CI -0.23 to -0.04, $P = 0.005$; $I^2 = 0%$, $P = 0.67$).

LDL and VLDL cholesterol

Three studies measured LDL cholesterol (Eidemark 1997; Goldberg 1983; Leehey 2009) and two studies measured VLDL cholesterol (Eidemark 1997; Goldberg 1983). Unfortunately data were missing from Goldberg 1983 and Eidemark 1997 and they could therefore not be meta-analysed.

Four to six months of a supervised, mixed intensity walking program showed no significant effect on LDL cholesterol (Analysis 1.31 (1 study, 11 participants): MD 0.39 mmol/L, 95% CI -0.21 to 0.99).

Intermediate-density lipoprotein (IDL), apolipoprotein (APO) A1 and APO-B

These outcomes were not reported in any of the included studies.

Muscle morphology and morphometrics

Type I, IIa and IIb muscle fibre area

Three months of regular, supervised, high intensity, resistance training showed no statistically significant difference in type I muscle fibre area between the exercise and control group (Analysis 1.32 (1 study, 26 participants): MD -861.00 μm^2 , 95% CI -1791.12 to 69.12).

Type IIa and type IIb muscle fibre areas had not been analysed separately.

Proportion type I, IIa and IIb muscle fibres (%)

These outcomes were not reported in any of the included studies.

Mid-thigh muscle area (cm^2)

Overall, regular exercise (regardless of type, intensity, length of intervention, or supervision) showed a significant increase in mid-thigh muscle area (Analysis 1.33 (4 studies, 162 participants): MD 7.51 cm^2 , 95% CI 11.37 to 3.65, $P < 0.0001$; $I^2 = 5\%$, $P = 0.37$). After three months there was no significant increase in mid-thigh muscle area using a supervised, high intensity, resistance training program (Analysis 1.33.1 (3 studies, 111 participants): MD 3.22 cm^2 , 95% CI 9.67 to -3.24, $P = 0.33$; $I^2 = 0\%$, $P = 0.77$). However after four to six months of cardiovascular exercise training there was a significant increase in mid-thigh muscle area (Analysis 4.24 (1 study, 24 participants): MD 13.10 cm^2 , 95% CI -21.13 to 5.07).

Thigh muscle attenuation

After three months of supervised, high intensity resistance training significantly increased thigh muscle attenuation was significantly increased (Analysis 1.34 (1 study, 49 participants): MD 1.50 Hounsfield units, 95% CI 0.21 to 2.79).

Cardiovascular dimensions

HRV index, SDNN, arrhythmias

HRV index was significantly improved after six months of supervised, high intensity mixed cardiovascular and resistance training (Analysis 1.35 (1 study, 60 participants): MD -6.00, 95% CI -10.08 to -1.92).

Six and 10 months of mixed cardiovascular and resistance training significantly improved mean cardiac R-R interval (Analysis 1.36 (2 studies, 119 participants): MD -0.06 sec, 95% CI -0.09 to -0.02, $P = 0.001$; $I^2 = 0\%$, $P = 0.58$) and SDNN (Analysis 1.37 (2 studies, 119

participants): MD -0.02, 95% CI -0.03 to -0.01, $P < 0.00001$; $I^2 = 0\%$, $P = 1.00$).

Six months of supervised, high intensity mixed cardiovascular and resistance training did not significantly decrease arrhythmias (Analysis 1.38 (1 study, 60 participants): RR 0.62, 95% CI 0.30 to 1.27).

Left ventricular internal dimension at end-diastole, Left ventricular internal dimension at end-systole, Intraventricular septal thickness at end-diastole, Left ventricular posterior wall thickness at end-diastole, Left ventricular mass, Left ventricular mass index

Six months of supervised, cardiovascular exercise training did not change left ventricular internal dimension at end-diastole (Analysis 1.39 (2 studies, 38 participants): MD -1.44 mm, 95% CI -4.94 to 2.06), left ventricular internal dimension at end-systole (Analysis 1.40 (2 studies, 38 participants): MD 0.06 mm, 95% CI -3.16 to 3.27), intraventricular septal thickness at end-diastole (Analysis 1.41 (2 studies, 38 participants): MD 0.04 mm, 95% CI -1.28 to 1.36), left ventricular posterior wall thickness at end-diastole (Analysis 1.42 (2 studies, 38 participants): MD 0.20 mm, 95% CI -0.93 to 1.33), or left ventricular mass (Analysis 1.43 (2 studies, 38 participants): MD -5.66 g, 95% CI -50.23 to 38.91).

Left ventricular mass index was not significantly changed after six or 10 months of exercise (Analysis 1.44 (3 studies, 97 participants): MD -1.77 g/m^2 , 95% CI -7.26 to 3.73, $P = 0.53$; $I^2 = 0\%$, $P = 0.77$).

Glucose metabolism

Fasting plasma glucose (mmol/L), fasting plasma insulin (mmol/L), glucose disappearance (%/min)

Twelve months of supervised, high intensity cardiovascular exercise did not significantly change fasting plasma glucose (Analysis 1.45 (1 study, 13 participants): MD 0.39 mmol/L, 95% CI -0.30 to 1.08), fasting plasma insulin (Analysis 1.46 (1 study, 13 participants): MD 8.00 mmol/L, 95% CI -7.58 to 23.58), or glucose disappearance (Analysis 1.47 (1 study, 13 participants): MD -1.00 %/min, 95% CI -2.62 to 0.62).

Dropout rates (%)

The dropout rates are presented in the Characteristics of included studies. Some studies did not report dropout rates and in some cases dropout rates were unclear. Thirty four of 45 studies reported dropout rates. Twenty-seven had a dropout rate between zero and 30% (Carney 1987; Castaneda 2001; Chen 2010, Deligiannis 1999; Deligiannis-HI 1999; Deligiannis-LI 1999; DePaul 2002; Eidemark 1997; Fitts 1995; Frey 1999; Johansen 2006, Koh 2010a, Jong 2004; Konstantinidou-D 2002; Konstantinidou-ND 2002; Konstantinidou-US 2002; Kouidi 1997a; Kouidi 2009, Leehey 2009, Matsumoto 2007, Ouzouni 2009, Painter 2002b; Painter 2003; Parsons 2004; PEAK Study 2005; Segura-Orti 2009, Toussaint 2008, Tsuyuki 2003; van Vilsteren 2005, Yurtkuran 2007), six studies had a dropout rate of between 30% and 50% (Akiba 1995; Fitts 1999; Kopple 2007a, Koufaki 2002a; Molsted 2004; Painter 2002a), one study had a dropout rate of between 50% and 70% (Carmack 1995), and no study had a dropout rate greater than 70%.

Compliance

Compliance was reported in 14 studies. Eleven studies had high compliance (> 70%) (Carmack 1995; Castaneda 2001; Chen 2010, Fitts 1995; Koh 2010a, Kouidi 2009, Molsted 2004; PEAK Study

2005; Segura-Orti 2009; Toussaint 2008; Yurtkuran 2007); one study had moderate compliance (> 50% to 70%) (Painter 2002a); and no study had low compliance (< 50%). van Vilsteren 2005 reported high compliance to the aerobic exercise and moderate compliance to the resistance training. DePaul 2002 did not report compliance, but the authors reported that the results of a per-protocol analysis including only patients who completed 75% of training sessions were no different from results of the intention-to-treat (ITT) analysis.

Adverse events (exercise-induced injuries)

Only one study had included exercise-induced injuries as an outcome (PEAK Study 2005). They defined adverse events as 'any injury or exacerbation of underlying disease potentially attributed to the progressive resistance training (PRT) regimen'. They compared common dialysis-related complaints (such as headaches, hypotension, cramping, and fistula cannulation difficulties), fistula infections, angina, incidence of falls, acute illness, and number of health care professional visits, and found no difference between the exercise and control group. They did however identify one adverse event in one of the participants who after six weeks of exercise training suffered partial tearing of musculus supraspinatus.

Molsted 2004 did not have adverse events as an outcome measure, but reported that there were no drop-outs caused by adverse events.

Mortality

This outcome was not reported by any of the included studies.

Heterogeneity

Of the outcomes tested, there was substantial heterogeneity in the results of studies for the outcomes of heart rate maximum (three months); walking capacity (four to six months); resting diastolic blood pressure (four to six months); resting systolic blood pressure (cardiovascular exercise, four to six months); albumin; transferrin and depression.

Two studies reported maximum heart rate (Analysis 1.10.1) (Akiba 1995; Koufaki 2002a) and the results showed heterogeneity although these were not statistically significant. Akiba 1995 showed no beneficial effect on maximum heart rate, whereas Koufaki 2002a did show beneficial effects. The results from Akiba 1995 are based on 13 randomised participants, while Koufaki 2002a randomised 23 participants.

Five studies reported walking capacity (Analysis 1.5) (Koh 2010a; Koh 2010b; Koufaki 2002a; PEAK Study 2005; Segura-Orti 2009), and there was heterogeneity although not significant. The observed heterogeneity was caused by data from Segura-Orti 2009, whose results caused inconsistency in the direction of effect. Segura-Orti 2009 enrolled only eight participant to the exercise group and showed no beneficial effects on walking capacity following six months of supervised, high intensity, intra-dialytic resistance training (frequency: three times/week; 15 reps and 1 set/exercise).

Resting diastolic blood pressure was reported in ten studies (Analysis 1.8) (Deligiannis-HI 1999; Deligiannis-LI 1999; DePaul 2002; Goldberg 1983; Leehey 2009; Ouzouni 2009; Painter 2003; Toussaint 2008; Tsuyuki 2003; van Vilsteren 2005). There was no heterogeneity for either the three months or more than seven to 12

months data, however four to six months data showed significant heterogeneity. This was caused by Leehey 2009 who, contrary to all other four to six months data, showed significant improvement in walking capacity following six weeks of a supervised, mixed intensity walking program followed by 18 weeks unsupervised, mixed intensity walking program with the goal to increase step count by 10% each week. This finding is in concordance with the positive effects found for more than seven to 12 months exercise training (Analysis 1.8).

Resting systolic blood pressure was reported in nine studies and showed heterogeneity (Analysis 1.9) (Deligiannis-HI 1999; Deligiannis-LI 1999; DePaul 2002; Goldberg 1983; Leehey 2009; Ouzouni 2009; Painter 2003; Toussaint 2008; van Vilsteren 2005). Kouidi 2009 and Tsuyuki 2003 data showed inconsistency in direction of effect. Tsuyuki 2003 reported five months of low intensity cardiovascular exercise training two to three times/week increased resting systolic blood pressure. Kouidi 2009 reported 10 months of intra-dialytic mixed cardiovascular and resistance training also increased resting systolic blood pressure. We were unable to determine the reason for this inconsistency in direction of effect.

Four studies had reported serum albumin as measure for nutrition (Koufaki 2002a; Castaneda 2001; Jong 2004; PEAK Study 2005). Data showed an inconsistency in the direction of effect when Koufaki 2002a was included in the meta-analysis. In the study by Koufaki 2002a albumin levels decreased following three months of supervised, high intensity cardiovascular exercise whereas albumin levels increased in the three other studies. When we investigated possible explanations for this inconsistency, looking at high (Castaneda 2001; Koufaki 2002a; PEAK Study 2005) versus low intensity (Jong 2004); cardiovascular (Jong 2004; Koufaki 2002a) versus resistance training (Castaneda 2001; PEAK Study 2005); supervised (Castaneda 2001; Koufaki 2002a; PEAK Study 2005) versus unsupervised training (Jong 2004); and pre-dialysis (Castaneda 2001; PEAK Study 2005) versus dialysis patients (Jong 2004; Koufaki 2002a), however the reasons remained unclear.

Transferrin had been used as an outcome measure in only two studies (Frey 1999; Castaneda 2001) and pooled data showed substantial heterogeneity. Castaneda 2001 showed statistically significant benefits on transferrin, whereas Frey 1999 found no change in transferrin levels following regular exercise training. Both studies used supervised, high intensity exercise, however Frey 1999 used regular cardiovascular exercise whereas Castaneda 2001 used regular resistance training. It is also possible that the difference in the duration of the exercise training (two months in Frey 1999 versus three months in Castaneda 2001) may explain the inconsistency in results.

Depression was reported in four studies (Analysis 1.27) (Carmack 1995; Kouidi 1997a; Ouzouni 2009; van Vilsteren 2005). Due to significant heterogeneity data could not be pooled across the different time periods. Ten weeks of cardiovascular exercise training of unknown intensity (Carmack 1995), 12 weeks of low intensity mixed cardiovascular and resistance training (van Vilsteren 2005) and six months of supervised high intensity cardiovascular training (Kouidi 1997a) had no significant effect on the level of depression. However 10 months of supervised, high intensity, mixed cardiovascular and resistance training (Ouzouni 2009) did show a significant improvement in the level of depression.

Sensitivity analyses

Sensitivity analyses were run on the primary outcomes of this systematic review and meta-analysis. Data from at least 50 randomised participants had to be available when running the sensitivity analyses.

The sensitivity analysis was conducted based on study quality assessment (please see [Characteristics of included studies](#)). Nine studies were classified as having the highest risk of bias, CCC (Chatoth 2005; Dimeo 2007; Harter 1985; Koufaki 2003; Kouidi 2002b; Kouidi 2003a; Kouidi 2004a; Kouidi 2005; Lee 2001) and had been excluded from the initial meta-analysis due to missing

and or unclear data. When we also excluded those classified as ACC (Fitts 1995; Frey 1999) or BCC (Akiba 1995; Deligiannis 1999; Deligiannis-HI 1999; Deligiannis-LI 1999; Eidemak 1997; Fitts 1999; Goldberg 1983; Jong 2004, Kopple 2007a, Tsuyuki 2003), sensitivity analyses showed that findings reported above were unchanged in this analysis.

Assessment of publication bias

An assessment of publication bias was conducted for the main outcomes that contained enough study data and where a fixed-effect model had been used. Funnel plots were visually assessed as reasonably symmetrical, indicating little publication or small study bias (see [Figure 4](#); [Figure 5](#); [Figure 6](#)).

Figure 4. Funnel plot of comparison: 1 Any exercise versus control (no exercise/placebo exercise), outcome: 1.1 Aerobic capacity.

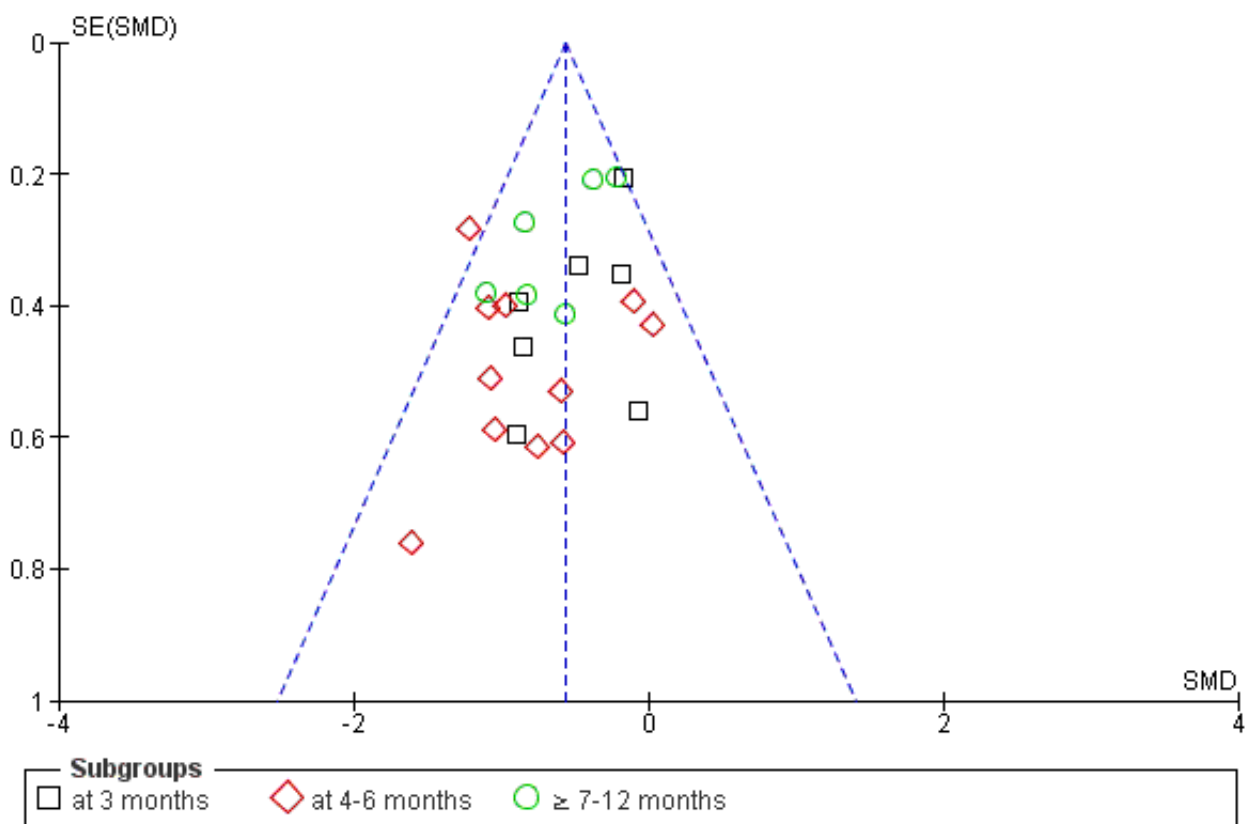


Figure 5. Funnel plot of comparison: 1 Any exercise versus control (no exercise/placebo exercise), outcome: 1.2 Muscular strength (high value = improved).

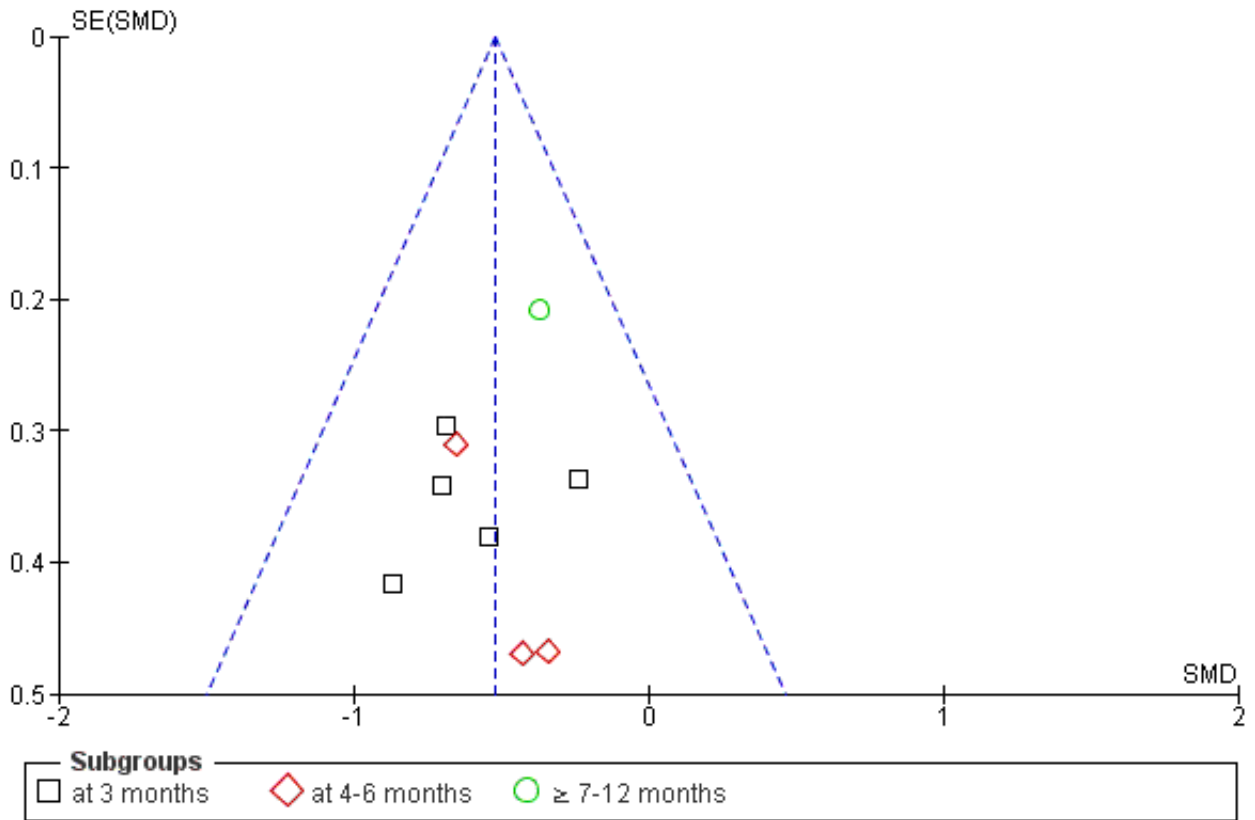
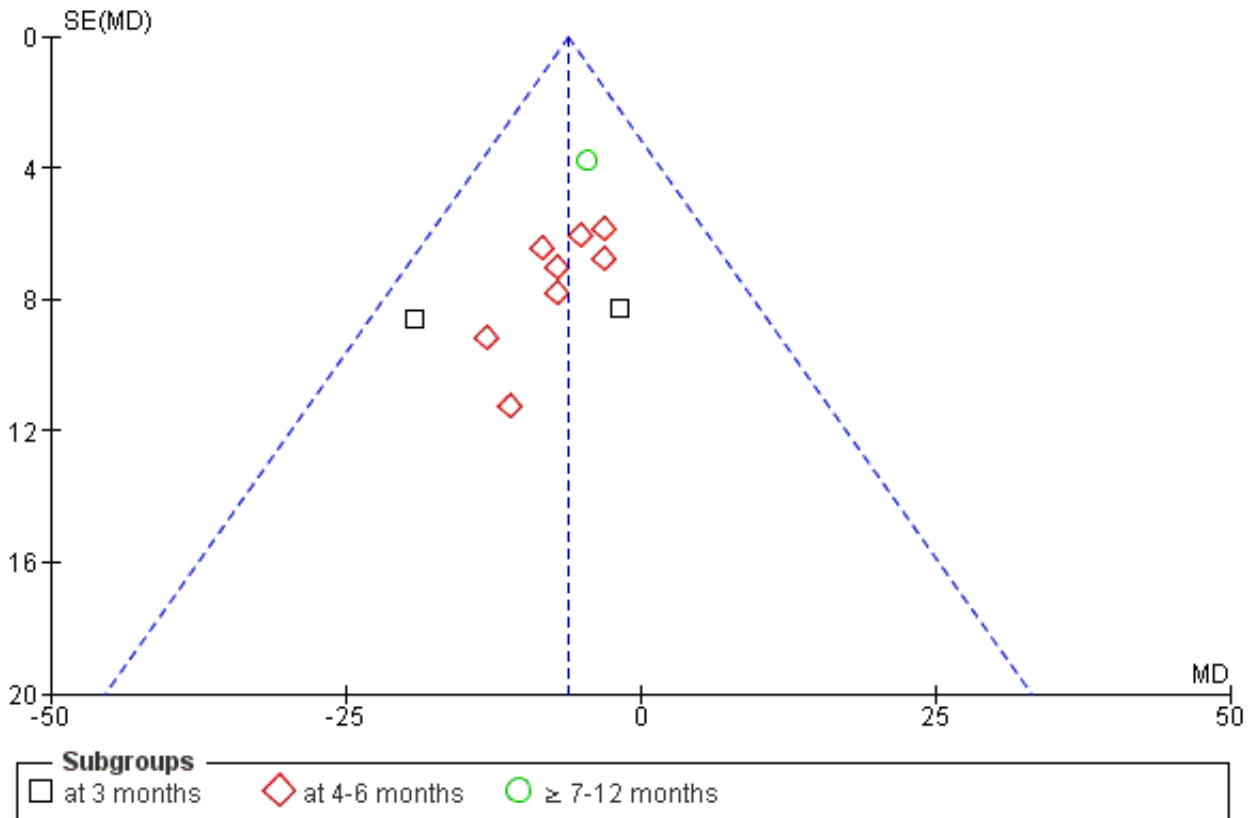


Figure 6. Funnel plot of comparison: 1 Any exercise versus control (no exercise/placebo exercise), outcome: 1.10 Heart rate: maximum [bpm].



Follow-up

Three studies provided follow-up data on the randomised groups (Carmack 1995; Carney 1987; DePaul 2002).

- Carmack 1995 provided follow-up aerobic capacity data four weeks after the end of the 10 week exercise training. During the 10 week observation period, aerobic capacity increased significantly in the exercise group whereas the control group's aerobic capacity had not changed. Four weeks after the end of the exercise training there was no significant difference in aerobic capacity between control and exercise group, showing that the exercisers' did not maintain their increased aerobic capacity at one month follow-up.
- Carney 1987 provided follow-up depression data on the randomised groups 18 months after the end of the six month exercise training. The exercise and comparison groups' follow-up data could not be compared since three participants in the control group started exercising during the follow-up period. Follow-up data for the exercise group showed continued low levels of depressed mood and significantly more performance of pleasant activities. All but one exerciser was continuing to exercise at 18 months, but less often than during the structured exercise program.
- DePaul 2002 provided follow-up data on aerobic capacity, muscular strength, walking capacity, and health-related quality of life data on the randomised groups, five months after the end of the three month exercise training. There were no significant

differences between the exercise and control groups, showing that the significant effects of the three month exercise training did not remain five months after the end of treatment. At the five month follow-up, 41% of the control group and only 35% of the exercise training group were still doing home exercises.

Results from included studies completely or partly excluded from the meta-analyses

Ten of the review's included studies were completely excluded from the meta-analyses (Carney 1987; Chatoth 2005; Fitts 1999; Goldberg 1983; Harter 1985; Koufaki 2003; Kouidi 2002b; Kouidi 2003a; Kouidi 2004a; Kouidi 2005; Molsted 2004). Their individual data and reasons for exclusion are presented below and in Characteristics of included studies.

- Carney 1987 was excluded due to missing outcome data (mean and SD for all outcomes). The study showed that six to 18 months regular high intensity cardiovascular exercise training significantly increased aerobic capacity and decreased depressed mood, and after 18 months of regular exercise training the participants performed significantly more pleasant activities than prior to the study. No changes were observed in the control group.
- Dimeo 2007 was excluded because the number of patients in the exercise and control group were not reported.

- [Chatoth 2005](#) was excluded because all result data were missing. The study used 18 months of regular high intensity resistance training and its results have not been found.
 - [Fitts 1999](#) SD data were missing for walking capacity and resting heart rate. The study used 12 months of regular low intensity cardiovascular exercise training and showed that exercise training increased walking capacity and health-related quality of life, but did not affect resting heart rate enough to make it a statistically significant difference. No changes were observed in the control group.
 - [Goldberg 1983](#) and [Harter 1985](#) report findings concerning the same outcomes from the same study. They had studied effects of 12 months of regular high intensity cardiovascular exercise training on the following outcomes: aerobic capacity, resting blood pressure, lipids, glucose metabolism and psychosocial functioning. Similarity between exercise and control group at baseline was unclear concerning outcome measures. Due to missing data (mean and or SD for the different outcome measures, groups, and the number of participants analysed for each outcome measure) and to inconsistency between results presented in the text and those presented in tables or figures, it was decided that the results from [Harter 1985](#) and [Goldberg 1983](#) would be presented separately and not be included in the meta analysis. Their data showed that 12 months of high intensity cardiovascular exercise training significantly increased aerobic capacity, reduced depression, decreased dosages of antihypertensive medications, decreased plasma triglycerides, increased HDL cholesterol levels, and improved insulin sensitivity (increase in glucose disappearance rates in spite of decrease in fasting insulin levels). No changes were observed in the control group.
 - [Kopple 2007a](#) did not present the mean and SD for physical capacity at baseline and end of intervention for the cardiovascular exercise group, resistance training group, mixed cardiovascular and resistance training group and the control group. As there is no information regarding intensity or supervision, the data have not been included in these subgroup analysis.
 - [Koufaki 2003](#) was excluded due to missing data for the control group and concerning number of participants in each group. The study used three months of regular high intensity cardiovascular exercise training + EPO versus control + EPO, and showed that the exercise training intervention increased aerobic capacity, peripheral muscle oxygen utilisation and activity of daily living-related functional capacity. No changes were observed in the control group. The researchers underscore the importance of exercise training if the benefits of anaemia treatment are to be maximised.
 - [Kouidi 2002b](#), [Kouidi 2003a](#) and [Kouidi 2005](#) were all excluded due to missing data in the control group, and [Kouidi 2004a](#) was excluded as the mean and SD data for all outcomes and groups were missing. All four were abstracts that had been presented at the ERA-EDTA Congress. The data from the completed studies were not to be found and the researcher did not have the missing data. [Kouidi 2002b](#) showed that 12 months regular cardiovascular exercise training (of unknown intensity) significantly increased the aerobic capacity, improved the heart rate variability and reduced the level of depression. Data for the control group were reported to have remained 'almost unchanged'. [Kouidi 2003a](#) used the same exercise intervention and showed increased aerobic capacity and improved cardiac vagal activity. [Kouidi 2004a](#) used six months of cardiovascular exercise training (of unknown intensity) and showed that the exercise intervention increased aerobic capacity by 19% and muscular strength by 20%. There was, however, no significant difference in any parameter of cardiac function between the intervention and control group. No changes in either outcome were observed in the control group. [Kouidi 2005](#) used 10 months cardiovascular exercise training (of unknown intensity and frequency) and showed significant increase in aerobic capacity, health-related quality of life and a reduced level of depression. The most severely depressed patients had the greatest beneficial outcomes from the exercise intervention. No changes were observed in the control group.
 - [Matsumoto 2007](#) the mean and SD for serum albumin and health-related quality of life at end of intervention is missing. Data were only presented in a figure.
 - [Molsted 2004](#) data were presented as median (range) and it was therefore not possible to include the data. The study used five months of high intensity, mixed cardiovascular and resistance training twice a week ([Characteristics of included studies](#)) and showed that aerobic capacity, muscular strength and physical functioning increased significantly in the exercise group, with no significant change in the control group. Health-related quality of life was assessed by SF-36 and post-intervention data from the exercise group showed improvement in three sub-scales (physical function, bodily pain, physical component scale), but no difference between the control and exercise group concerning all other sub-scales. The study also showed that the exercise intervention that had been used did not affect resting blood pressure or lipids. No changes were observed in the control group.
- Some studies were included in the meta-analysis but had missing data concerning some of their outcomes (i.e. no data for the control group or missing SD for an outcome measure). This information is presented in [Characteristics of included studies](#) and each study's results concerning these outcomes are presented below.
- [Eidemak 1997](#) mean and/or SD data were missing for some outcome measures. The study showed that 18 months of regular high intensity, cardiovascular exercise training did not significantly change either resting blood pressure or lipids. No changes were observed in the control group.
 - [Goldberg 1983](#) mean, SD data and/or numbers analysed were missing for some outcome measures. The study showed that 12 months of progressive high intensity cardiovascular exercise training reduced fasting plasma triglyceride levels by 33%, VLDL lipoprotein triglyceride levels by 38% and VLDL lipoprotein cholesterol by 55%. HDL cholesterol levels increased by 16% and there was no change in either total cholesterol levels or in mean body mass. Exercise training also significantly improved scores on the Beck Depression Inventory. No changes were observed in the control group.
 - [Jong 2004](#) mean and SD data were missing for some outcome measures. The study showed that three months of regular cardiovascular exercise training (of unknown intensity) had no effect on triglycerides, cholesterol, HDL cholesterol, or LDL cholesterol levels. No changes were observed in the control group.
 - [Parsons 2004](#) mean and SD were missing for resting systolic and diastolic blood pressure. The study used two months of low

intensity cardiovascular exercise training during haemodialysis and showed that this exercise intervention did not affect resting blood pressure or health-related quality of life. The researchers did however observe that pulse pressure tended to increase in the control group but decrease in the exercise group, which might indicate that exercise training has beneficial effects on the cardiovascular system in adults with CKD. Seeing no effect of the exercise intervention on health-related quality of life is argued by the researchers to be most likely caused by the short duration of the exercise intervention (two months) and the high-functioning level that the study's study population had at baseline. No changes were observed in the control group.

DISCUSSION

Results from this study show that all regular exercise training (regardless of type of exercise, intensity, length of intervention, or supervision) improves aerobic capacity, but it also showed that when aiming to increase aerobic capacity as effectively as possible in adults with CKD the following exercise regimen is recommended: four to six months supervised, regular (three sessions/week) high intensity mixed cardiovascular and resistance training lasting 30 to 90 minutes. To maintain this peak effect the patient has to continue with the regular exercise training intervention. This finding is in concordance with the recommended quantity and quality of exercise training for developing cardiorespiratory fitness in healthy adults (ACSM 1998). Modes of activities that were shown to improve aerobic capacity in adults with CKD were activities that use large muscle groups and that can be maintained continuously, such as cycling, walking, and jogging.

Muscular strength progressively reduces in adults with CKD. Adults with CKD were shown to improve their muscular strength by using any regular high intensity exercise training. Positive effects could be observed after only three months of regular exercise training. Whether the beneficial effect can be achieved by using a low intensity exercise intervention remains unclear as only one of included studies had used a low intensity exercise intervention. All types of exercise training showed positive effects of exercise training on muscular strength. Resistance training had a significant beneficial effect on muscular strength. There was however too few included studies using cardiovascular exercise or mixed cardiovascular and resistance training, to be able to draw conclusions concerning the type of exercise required for an optimal enhancement of muscular strength. Only two studies used unsupervised exercise (Koh 2010a; Painter 2002a). Painter 2002a used a resistance training program whereas Koh 2010a used a cardiovascular exercise training program. Pooled data showed significant beneficial effects on muscular strength. Severely reduced muscle endurance is a common problem among adults with CKD. Only two of the included studies had used muscular endurance as an outcome measure (Koufaki 2002a; Segura-Orti 2009). More research focusing on the if and how exercise training can affect the muscular endurance are needed before conclusions can be drawn in this area.

Changing one's lifestyle is an important factor for the prevention, treatment and control of hypertension. Previous research have shown that exercise training is a cornerstone therapy and that the most blood pressure lowering effect of exercise training is observed when using regular (three sessions/week) low intensity (40% to 60%) dynamic cardiovascular exercise training (> 30 minutes/

session) (ACSM 2004). Meta-analyses have shown no effects of exercise frequency, type, intensity and duration of training on the positive blood pressure response in adults with hypertension and without CKD (Kelley 1997; Kelley 1999; Kelley 2001; Whelton 2002). In concordance with previous research, the present study shows that regular exercise training had a significant effect on resting blood pressure in adults with CKD. To achieve this effect the analysis showed that it is not possible to use any exercise (regardless of type of exercise, intensity, length of intervention, supervision or not). Subgroup analysis based on intensity, length of intervention and type of exercise training did however show that when using four to six months of high intensity, mixed cardiovascular and resistance training programme there was a significant decrease in resting systolic and diastolic blood pressure in adults with CKD. This decrease was approximately 4 to 7 mm Hg following regular exercise training. This is of importance as even a small reduction (2 mm Hg) in an average population's systolic blood pressure can reduce coronary heart disease, stroke and all-cause mortality (ACSM 2004; Stamler 1989; Whelton 2002). To be able to detect smaller decreases in blood pressure, large enough sample sizes have to be used.

Even modest reductions in body mass indices can improve an individual's health (Goldstein 1992). In combination with reduced energy intake, regular exercise training is used as a strategy to affect body mass indices in adults with overweight or obesity. The optimal exercise regimen for these individuals has been shown to be a progressive increase of physical exercise training from 150 to 200 to 300 minutes of exercise training/week. Adopting more than 280 minutes of exercise training/week (e.g. >2000 kcal/week) has been shown to be important for maintaining weight loss in the long-term (Evans 2007; Jakicic 1999; Jakicic 2001). However little is known about the difference in effects between different exercise regimens. Regular exercise training was not shown to significantly affect body mass indices in adults with CKD, except for one study with only 11 participants, and this result remained unchanged when we investigated type, intensity, intervention period and supervision of exercise. The result is however based on a relatively small sample size and further research is needed before drawing scientific conclusions concerning the effect that regular exercise training programmes can have on body mass indices. Also, it is well known that exercise training alone does not reduce weight and has to be combined with a reduced energy intake. In the present study body mass indices were used as an outcome measure, but the reader should be aware of that none of the included studies have used an intervention that was primarily designed for weight loss (e.g. there was no combined energy intake and exercise intervention).

Today, the main cause for CKD is diabetes mellitus. Mild to moderate intensity endurance and resistance exercise training (40% to 70% VO₂ max ESKD) has been shown to have favourable effects on glucose control and insulin sensitivity in adults with type 2 diabetes (Albright 2000). These favourable effects are however a reflection of the last individual exercise bout rather than exercise training per se, and to sustain the favourable effects it is therefore important that the exercise training is regular (5 sessions/week)(Albright 2000). In the present study there was not enough data to draw scientific conclusions about the effect of regular exercise training on glucose metabolism in adults with CKD. The single RCT that had investigated this did not see any significant effect of 12 months regular, supervised, high intensity cardiovascular exercise training on glucose metabolism (Goldberg

1983). The study sample was however only on 13 randomised participants and the exercise regimen used differed from that recommended for adults with type 2 diabetes in order to affect glucose metabolism (Goldberg 1983). They used high intensity exercise training, whereas the exercise regimen that has been shown to be effective in adults with type 2 diabetes consists of low to moderate intensity exercise training at least three times/week and with a minimum cumulative energy expenditure of 1000 kcal/week (Albright 2000; Blair 1992; Gordon 1995). Also, the type of exercise training used by Goldberg 1983 was strictly cardiovascular, whereas today's exercise guidelines for adult with type 2 diabetes recommend that resistance training should be included as part of the exercise program (Albright 2000). Several studies (Fennicchia 2004; Fluckey 1994), have found that resistance training results in improved glucose tolerance and insulin sensitivity in normal and glucose-intolerant adults. It has also been shown that a mixed cardiovascular and resistance training programme have significant beneficial effects on glucose metabolism in adults with type 2 diabetes (Maiorana 2002; Tokmatidis 2004). It is possible that a mixed cardiovascular and resistance training program would have affected the glucose metabolism in Goldberg 1983. Further research is necessary to investigate whether regular exercise training has the capacity to affect glucose metabolism in adults with CKD, and if so to investigate the exercise regimen required for the optimal enhancement.

Depression can be present when having CKD. Results from the present study indicate that 3 to 10 months supervised high or low intensity, mixed cardiovascular and resistance training interventions should be used when aiming to decrease level of depression. More research data are needed in order to draw conclusions concerning the effect of regular exercise training on level of depression in adults with CKD, and also to be able to compare the effects depending on the type, intensity, duration, and supervision of the exercise intervention.

Results from the present study show that there is insufficient research data from RCTs concerning several outcome measures that might be affected by regular exercise training. Future research should focus on designing RCTs evaluating the effects of various exercise regimens on the following outcome measures in adults with CKD: muscular endurance, muscle morphology and morphometrics, physical functioning (e.g. stair climbing), cardiovascular dimensions (e.g. arrhythmias), nutrition, systemic inflammation, level of physical activity in daily living, depression, lipids, glucose metabolism, drop-out rates, compliance, adverse events and mortality. Future RCTs should also focus more on the effects of resistance training interventions and or mixed cardiovascular and resistance training as these exercise types has not been studied as much as cardiovascular exercise training. It would also be of interesting to study the effect of a regular exercise regimen versus a pharmacological treatment or as a complement to a pharmacological treatment, i.e. statin versus regular exercise regimen design to affect lipids, or the effect of a combination between statin and a regular exercise regimen designed to positively affect lipids.

This review has some potential limitations. First, in some studies the outcome measures were not blindly assessed and ITT analysis was not used in all studies. This could have inflated the apparent results (Hollis 1999; Jadad 1996). During the process of writing this review it also became evident that researchers and editors

within this field need to improve the report of methodological and result information (i.e. method of randomisation, drop-out rate, compliance to the intervention and control) that is important for the reader when assessing the quality of the study. The reader should be aware that in this review a study that may have been classified as having lower quality than it actually had as data and/or information was missing from the reports. During the review process a large number of exercise studies were excluded as participants had not been randomised. Future exercise studies in adults with CKD should therefore strive for randomisation of participants, which would increase knowledge of effects of various exercise regimens. Another problem was outcome measurement. For example muscular fitness (strength and endurance) was measured in several different ways (i.e. one repetition maximum or peak torque). This complicates comparisons between studies and also the meta-analysis of studies results. Being able to achieve a consensus concerning which methods to be used when measuring muscular fitness and health-related quality of life in adults with CKD would make it easier to compare results from different studies with one another and increase the quality of meta-analysis and future research within this field.

Duration of exercise varied from three months (17 studies), four to six months (14 studies), and seven to 12 months (14 studies). Studies with longer duration of exercise intervention (12 to 24 months) are needed to be able to evaluate long-term benefits (e.g. morbidity and mortality) of regular exercise training in adults with CKD. When evaluating the effects of regular exercise training the reader and researcher also have to bear in mind that there is also important intrinsic limitation to regular exercise training, including the reluctance of individuals to regularly adhere to a prescribed exercise training intervention. Some individuals have a low compliance to exercise training, whereas others have a high compliance. Most exercisers do however have a relatively good compliance in the beginning but gradually decreases the compliance to regular exercise training in a long-term perspective. Clinical experience also shows that a high compliance to exercise training is usually achieved as long as the participant's exercise is supervised, but when the individual should continue to exercise on its own the compliance decreases. This was also seen in the studies in this review, where a follow-up period was used. Future studies should focus on long-term benefits of regular exercise training; on developing beneficial exercise and behavioural modification interventions with high compliance (also following the treatment); and include long-term follow-up of the treatment.

AUTHORS' CONCLUSIONS

Implications for practice

Clinicians should inform adults with CKD that there is scientific evidence showing that by exercising regularly for > 30 minutes/session and three times/week they would improve their physical fitness, walking capacity, cardiovascular dimensions (e.g. blood pressure and heart rate), some nutritional parameters and health-related quality of life. Beneficial effects are present in both adults with CKD stages 1 to 5, patients with dialysis (haemodialysis and peritoneal dialysis) and kidney transplant recipients. Clinicians should encourage adults with CKD to participate in regular exercise regimens. Exercise regimens should be based on the frequency, intensity and duration of exercise training as well as the type of activity and the individual's initial level of physical fitness. All these

factors have to be taken into account when aiming to achieve the goal with the regular exercise training and or rehabilitation.

Implications for research

Outcomes that need more research are muscular endurance, muscle morphology and morphometrics, physical functioning (e.g. stair climbing), cardiovascular dimensions (e.g. arrhythmias), nutrition (e.g. muscle mass), systemic inflammation, level of physical activity in daily living, depression, lipids, glucose metabolism, drop-out rates, compliance, adverse events and mortality. Future RCTs should focus more on the effects of resistance training interventions and/or mixed cardiovascular and resistance training as these exercise types has not been studied as much as cardiovascular exercise training.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Akiba 1995

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Japan Setting: Multicentre study Hb (mean \pm SD g/dL): Treatment group (6.6 ± 0.9); Control group (6.4 ± 0.7) Duration on HD (mean \pm SD months): Treatment group (73.8 ± 47.2); control group (68.3 ± 41.5) Frequency of HD (times/week): 3 Duration of HD session (hours): 4 Number: 20 randomised Age (mean \pm SD years): Treatment group (38.4 ± 9.5); control group (40.6 ± 10.8) Ethnicity: NS Sex (M/F): Treatment group (2/8); control group (7/3) <p>Exclusion criteria: NS</p>
Interventions	<p>After improvement of anaemia by rHuEPO, patients were randomised into 2 groups.</p> <p>Treatment group</p> <ul style="list-style-type: none"> 12 weeks of supervised exercise training using a bicycle ergometer. Unclear whether the exercise training was performed prior to the HD or during the HD. <ul style="list-style-type: none"> For the first 3 weeks the exercise training consisted of 5 min warm-up, 10 min exercise and 5 min cooling down. Starting workload was 80% of maximal performance at the exercise tolerance test. When the RPE was less than 12, the duration of exercise was increased to 30 min (5 min warm-up, 20 min exercise, 5 min cooling down). This duration of exercise was then fixed during the observation period, and the workload was increased by 10 watts every third week as long as the RPE was less than 12. The starting workload was 80% of maximal performance. <p>Control group</p> <ul style="list-style-type: none"> No exercise training <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of exercise intervention: 12 weeks End of intervention data has been used.
Outcomes	<ul style="list-style-type: none"> Relevant to our study <ul style="list-style-type: none"> Watt max VO2 max Heart rate max Not relevant to our study <ul style="list-style-type: none"> maximum lactate level; Hb

Akiba 1995 (Continued)

- Notes
- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment (10), control (10)
 - Analysed: Treatment (7), control (6)
 - Per cent followed: Treatment (70), control (60)
 - Compliance: NS
 - Similarity between groups at baseline: Yes
 - Number of patients in the exercise and the control group, respectively, differ between the text and the figures. We have chosen to use the number of patients reported in the text
 - Missing information: Unclear whether the exercise training was performed prior to the HD or during the HD, and the study has therefore not been used in the comparisons between exercise training before, during and after HD, respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Carmack 1995

- Methods
- Recruitment: Three local outpatient HD clinics
 - Study design: Parallel group RCT
 - ITT analysis: No
- Participants
- Inclusion criteria
- Country: USA
 - Setting: Multicentre study
 - Patients undergoing HD treatment
 - Hb (g/L): NS
 - Duration on HD (months): NS

Carmack 1995 (Continued)

- Frequency of HD (times/week): NS
- Duration of HD session (hours): NS
- Number: 48 randomised
- Age: NS
- Ethnicity: African American (86%); White (NS); Latino (NS); Asian (NS)
- Sex (M/F): 73% male

Exclusion criteria

- physical or mental impairment that precluded undergoing submaximal exercise tolerance tests and participating in an exercise programme; severe cardiac problems; leg vascular access; leg prosthesis

Interventions

Treatment group

- Individualized exercise treatment program containing ergometer bicycling three times/week for 20-30 min during HD treatment.
- The exercise training was unsupervised.
- Each subject kept a record of exercise sessions during HD and any additional exercise (type of exercise, duration of exercise, rate of perceived exertion, and number of breaks taken during exercise).
 - Letters sent home to the family members served as an attempt to elicit family members' support and reinforcement for subjects' participation in the exercise program.
- Intensity of exercise training: NS
- Duration: 10 weeks

Control group

- Subjects in the waiting-list control condition received the information that they could engage in an individualized exercise program after 10 weeks, when equipment became available.
- To control for attention given to the exercise group, experimenters spent 3-5 min, 3 days/week, engaging in positive social conversation with control-group subjects.
 - Experimenters did not provide advice or discuss treatment protocol with these subjects. All discussions centred on neutral topics, such as recent events, local news and sports.

Follow-up assessment

- One month following treatment
- End of intervention: 10 weeks
- End of intervention data has been used.

Outcomes

- Relevant to our study
 - VO2 peak
 - Depression
- Not relevant to our study
 - Stress appraisal measures; anxiety; frequency of physical complaints and symptoms

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 48
 - Enrolled/randomised: Treatment (23); control (25)
 - Analysed: Treatment (10); control (11)
 - Per cent followed: Treatment (43); control (44)
- Compliance: 84.2%
- Similarity between groups at baseline
 - Outcome measures: Yes
 - Demographic data: Unclear
- Since data concerning exercise intensity is missing, the study has not been included in the meta-analysis investigating the difference in effect between high- and low intensity exercise.

Carmack 1995 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Carney 1987

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: UK Setting: Single centre Minimum of 6 months of HD; stable medication; diet and dialysis schedule; age between 18 and 70 years; willingness and motivation to participate Hb: NS Duration on HD (mean \pm SD months): Treatment group (30 \pm 8.1); control group (40 \pm 13.2) Frequency of HD (times/week): NS Duration of HD session (hr): NS Number: 21 randomised Age (mean \pm SD years): Treatment group (36.1 \pm 3.2); control group (40.7 \pm 5.3) Ethnicity: NS Sex (M/F): Treatment group (5%); control group (3/4) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Coexisting disease such as: unstable coronary artery disease; cardiac arrhythmias; clinically significant valvular heart disease; congestive heart failure; severe retinal disease; insulin-dependent DM; hypothyroidism; poorly controlled hypertension

Carney 1987 (Continued)

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Training sessions were held 3 times/week for 45-60 min on a 17 lap/mile banked indoor track in a temperature-controlled facility. <ul style="list-style-type: none"> ◦ The initial training sessions were at 50-60% of VO₂ max and usually included repetitive callisthenics, 5 min sessions on a stationary bicycle ergometer and fast walking interspersed with 5 min rest periods. Within 6-8 weeks most patients progressed to bicycling continuously for 8-10 min at 60-65% of their VO₂ max. The intensity and duration of training sessions were gradually increased based upon each patient's ability to complete the prescribed session without excessive fatigue or an abnormal cardiovascular (heart rate, blood pressure) response. ◦ All patients were provided with bicycle ergometers for home use at 16 weeks and by 20 weeks most were walking 1 lap and jogging 1-2 laps for 5-7 min, and riding the bicycle ergometer at 70-80% of VO₂ max for 10-15 min. At 6 months of exercise, most patients could jog 3 laps and walk 1 lap continuously for 7-10 min. ◦ The duration and intensity of the training sessions at this time were 45 min 3 times/week at 70-80% of VO₂ max. <p>Control group</p> <ul style="list-style-type: none"> • Group used in order to control for attention, expectation of positive psychological benefits, supportive group effects, and other non-specific treatment effects present in the exercise group. • The patients were informed that the purpose of the support group was to provide a setting where they could share their concerns, frustrations and problems relating to ESKD and HD treatment. The group leader had extensive experience in conducting group and individual psychotherapy for patients with HD. the group met for 60-90 min once or twice each week, for 24 weeks to match the duration of exercise. <p>Follow-up assessment</p> <ul style="list-style-type: none"> • End of intervention: 6 months • 18 months after treatment • End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> • Psychopathology • Frequency of enjoyment of pleasant activities performed during the previous month • Frequency and associated displeasure of unpleasant activities for the previous month • Severity of depression • VO₂ max <p>Not relevant to our study: none</p>
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: 21 ◦ Enrolled/randomised: Treatment (11); control (10) ◦ Analysed: Treatment (10); control (7) ◦ Per cent followed: Treatment (91), control (70) • Compliance: NS • Missing data: Mean and SD concerning VO₂ max and depression. • Not been able to find primary investigators for clarifying results.
Risk of bias	
Bias	Authors' judgement Support for judgement
Random sequence generation (selection bias)	Unclear risk NS

Carney 1987 (Continued)

Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Castaneda 2001

Methods	<ul style="list-style-type: none"> Recruitment: Nephrology clinic at New England Medical centre, Saint Elizabeth's and Newton Wellesley Hospitals, and the Lahey Hitchcock Clinic, all in Boston (MA) Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: Single centre SCr between 133-442 $\mu\text{mol/L}$ and physician approval to follow a low-protein diet Number: 26 randomised Age (mean \pm SD years): Treatment group (65 \pm 9); control group (64 \pm 13) Ethnicity (White/African American/Latino/Asian): Treatment group (11/3/0/0); control group (9/2/1/0) Sex (M/F): Treatment group (8/6); control group (9/3) HCT (%): Treatment group (31.6); control group (32.1) GFR (median; mL/min/ 1.73 m²): Treatment group (24.76); control group (27.53) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Myocardial infarction (within the past 6 months); any unstable chronic condition; dementia; alcoholism; dialysis or previous kidney transplantation; current resistance training; recent involuntary weight change (\pm 2 kg); albumin level < 30 g/L; proteinuria > 10 g/d; abnormal stress test results at screening
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Low-protein diet plus resistance training <ul style="list-style-type: none"> Patients were counselled to reduce their habitual protein intake by eating food sources with less protein or by reducing portion sizes of higher-protein foods. Behaviour modification strategies, including tips, recipes, food models, and self-monitoring tools for protein counts, were provided. Resistance training was performed 3 times/week under the supervision of an exercise physiologist. Patients who performed resistance training had monthly 1RM testing on each machine. Workload

Castaneda 2001 (Continued)

during training was adjusted to reflect 80% of the most recent 1RM. In addition, patients' workloads were progressively increased as appropriate according to the trainer's objective perception of patients' difficulty with workloads at each session. Patients performed three sets of eight repetitions on each machine/session, which lasted about 45 min.

- o Duration: 12 weeks.

Control group

- Low-protein diet plus sham exercises
 - o Patients were counselled to reduce their habitual protein intake by eating food sources with less protein or by reducing portion sizes of higher-protein foods. Behaviour modification strategies, including tips, recipes, food models, and self-monitoring tools for protein counts, were provided.
 - o Patients also performed 5-8 sham exercises (gentle movements while standing, sitting, and bending) for the upper and lower body. These were designed not to have a physiological impact but to provide trainer contact time similar to that of the treatment group
- Duration: 12 weeks

Follow-up assessment

- End of intervention: 12 weeks
- End of intervention data has been used.

Outcomes	Relevant to our study <ul style="list-style-type: none"> • Insulin-like growth factor 1 level • Serum prealbumin • Energy intake • Protein intake • Lower body strength • Muscle fibre area • Mid-thigh muscle area Not relevant to our study <ul style="list-style-type: none"> • leucine synthesis; leucine oxidation; urinary creatinine concentration; serum urea nitrogen level; SCr
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> o Eligible/considered for inclusion: 300 o Enrolled/randomised: Treatment group (14); control group (12) o Analysed: Treatment group (14); control group (12) o Per cent followed: Treatment group (100); control group (100) • Compliance/adherence <ul style="list-style-type: none"> o Resistance training (91 ± 9%); sham exercise sessions (90 ± 10%) o Low-protein diet: Treatment group (108 ± 8% of the target protein level); control group (112 ± 12%); determined by urinary urea nitrogen level • Similarity between groups at baseline: Yes • Missing data: type IIa, IIb and IIX muscle fibre area has not been analysed separately.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)

Castaneda 2001 (Continued)

Blinding (performance bias and detection bias) Participants	Low risk	Blinded
Blinding (performance bias and detection bias) Outcome assessors	Low risk	The study dietician and exercise trainer were not blinded to group assignment. However, baseline muscle strength was assessed before randomisation. Outcome assessors blinded to group assignment performed all other study measurements.
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	Low risk	Low risk of detection bias (A)
Risk of attrition bias?	Low risk	Low risk of selection bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias: all quality criteria met (A)

Chatoth 2005

Methods	<ul style="list-style-type: none"> Recruitment: NS Study Design: Parallel group RCT ITT analysis: NS
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: NS Moderate kidney failure Number: NS Age: NS Ethnicity: NS Sex (M/F): NS HCT (%): NS GFR (median; mL/min/1.73 m²): NS <p>Exclusion criteria: NS</p>
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Standard care + resistance exercise training No details presented <p>Treatment group 2</p> <ul style="list-style-type: none"> Low protein diet No details presented <p>Treatment group 3</p> <ul style="list-style-type: none"> Low protein diet + resistance exercise training No details presented <p>Control group</p> <ul style="list-style-type: none"> Standard care

Chatoth 2005 (Continued)

- No details presented

Follow-up assessment

- End of intervention: 18 months

Outcomes	Relevant to our study <ul style="list-style-type: none"> • Body composition • Muscular strength • Physical functioning • Muscle mass • Immune function Not relevant to our study <ul style="list-style-type: none"> • Progression of CKD; nitrogen balance
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: NS ◦ Analysed: NS ◦ Per cent followed: NS • Compliance: NS • Similarity between groups at baseline: NS • Missing data: The completed study report could not be found. Tried contacting primary investigator for clarification of method and results, but without result.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High: one or more quality criteria not met (C).

Chen 2010

Methods	<ul style="list-style-type: none"> Recruitment: Outpatient dialysis facilities Study design: Parallel group RCT ITT analysis: Yes
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA. Setting: Multicentre HD thrice weekly for at least 3 months with $\geq 80\%$ compliance; age ≥ 30 years; serum albumin < 4.2 g/dL HCT (%): NS Duration of HD (mean \pm SD years): Treatment group (2.6 ± 2.6); control group (4.8 ± 5.2) Frequency of HD (times/week): 3 Duration of HD (hours): NS Number: 50 randomised Age (mean \pm SD years): Treatment group (71 ± 13); control group (67 ± 13) Ethnicity (White/African American/Latino/Asian): Treatment group (8/7/1/6); control group (7/5/1/9) Sex (M/F): Treatment group (12/10); control group (11/11) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Unstable cardiovascular disease or any uncontrolled chronic condition; cardiac surgery; retina laser therapy; myocardial infarction; joint replacement or lower extremity fracture within the last 6 months; severe cognitive impairment; lower extremity amputation; current strength training
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Supervised exercise <ul style="list-style-type: none"> Patients followed a 6-month supervised exercise training program. The training sessions were performed twice a week during the second hour of HD. Exercise began with 5 minute warm-up and ended with a minute cool-down. Resistance exercise was performed by using ankle weights that progressively incremented from 0.5 to 20 lbs. Muscle groups exercised: quadriceps, hamstrings, hip adductors, tibialis anterior, gastrocnemius, soleus, abdominal and lower back muscles. Intensity 50% of one-repetition maximum. Two sets of eight repetitions for each exercise. 1-2 minutes rest between sets. <p>Control group</p> <ul style="list-style-type: none"> Attention control group who did stretching exercises and were to continue their usual activities. <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 6 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> Muscular strength Physical performance Whole-body lean mass Whole-body fat mass Leisure-time physical activity Health-related quality of life <p>Not relevant to our study: None</p>
Notes	<ul style="list-style-type: none"> Completeness of follow-up <ul style="list-style-type: none"> Eligible/considered for inclusion: 250

Chen 2010 (Continued)

- Enrolled/randomised: 59/50
- Analysed: Treatment group (22); control group (22)
- Per cent followed: Treatment group (88); control group (88)
- Compliance: Treatment group (89 ± 14%); control group (90 ± 17%)
- Similarity between groups at baseline: Yes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	Low risk	Attention-control participants
Blinding (performance bias and detection bias) Outcome assessors	High risk	Not blinded
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	Unclear risk	Moderate risk of detection bias (B)
Risk of attrition bias?	Low risk	Low risk of attribution bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate: one or more quality criteria only partially met (B).

Deligiannis 1999

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> • Country: Greece • Setting: NS • Undergoing HD • Duration of HD (mean ± SD years): Treatment group (6.3 ± 3.0); control group (6.2 ± 3.6) • Frequency of HD (times/week): Treatment group (3); control group (3) • Duration of HD (hours): Treatment group (4); control group (4) • HCT (mean ± SD%): Treatment group (31 ± 4); control group (31 ± 5) • Number: 60 randomised • Age (mean ± SD years): Treatment group (48 ± 12); control group (48 ± 11) • Ethnicity NS • Sex (M/F): Treatment group (17/13); control group (15/15)

Deligiannis 1999 (Continued)

Exclusion criteria

- Documented myocardial infarction during the previous 6 months; symptoms of angina or heart failure (NYHA class \geq II); severe hypertension, DM, or any other disease that might interfere with autonomic regulation; sinus rhythm during a resting ECG; medication that might interfere with autonomic regulation (i.e. beta-blockers)

Interventions

Treatment group

- Supervised exercise rehabilitation program
 - Patients performed a 6-month exercise rehabilitation program 3-4 times/week on non-dialysis days. All training sessions were continuously supervised by a physician, an exercise physiologist, and a physical education instructor. Each session consisted of a 10-min warm-up (bicycling and/or walking), a 50-min aerobic exercise program (callisthenics, steps, swimming, or ball games), a 20-min stretching and low-weight resistance program, and a 10-min cool down period (bicycling and/or walking). The intensity was prescribed on individual basis so that the heart rate remained within 60-70% of the maximum heart rate achieved during the initial VO₂ max test. Exercise regimens were adjusted periodically to encourage a gradual increase in exercise performance.

Control group

- Patients were asked to remain their sedentary lifestyle.

Follow-up assessment

- End of the intervention period: 6 months
- End of intervention data has been used

Outcomes

Relevant to our study

- Exercise time (min)
- VO₂ max
- Arrhythmias: Low class > II (no)
- HRV index
- Mean RR (sec)
- SDNN (sec)

Not relevant to our study

- Sum of heart beats; 24h mean heart rate

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (30); control group (30)
 - Analysed: Treatment group (30); control group (30)
 - Per cent followed: Treatment group (100); control group (100)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)

Deligiannis 1999 (Continued)

Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Deligiannis-HI 1999

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> Country: Greece Setting NS Patients requiring HD HCT (mean \pm SD%): Supervised exercise (31.1 ± 4.2); home exercise (31.7 ± 4.3); control (30.8 ± 2.8) Duration on HD (mean \pm SD months): Supervised exercise (78 ± 62); home exercise (62 ± 37); control group (79 ± 86) Frequency of HD (times/week): 3 Duration of HD (hours): 4 Number: 38 randomised Age (mean \pm SD years): Supervised exercise (46.4 ± 13.9); home exercise (51.4 ± 12.5); control group (50.2 ± 7.9) Ethnicity: NS Sex (M/F): Supervised exercise (11/5); Home exercise (8/2); control (4/8) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Unstable hypertension; congestive heart failure (NYHA \geq II); cardiac arrhythmias (III according to Lown); recent myocardial infarction or unstable angina; DM; active liver disease; serious anaemia; peripheral vascular disease
Interventions	<p>Supervised exercise group</p> <ul style="list-style-type: none"> Patients followed a 6-month supervised exercise training program. <ul style="list-style-type: none"> The training sessions were performed three times/week, 90 min each time, on the non-dialysis days. Patients were divided into subgroups, each consisting of three or four persons according to age, gender, and dialysis days. Each training session consisted of a 10-min warm-up (ergometer cycling or treadmill), a 50-min intermittent aerobic exercise program (including callisthenics, steps and flexibility exercises) and a 10-min cool down period. After 2 months of training, a 10-min stretching and low-weight resistance training program was added to the program. The intensity

Deligiannis-HI 1999 (Continued)

was prescribed on an individual basis, so that during the first 2 months the heart rate remained within 60-70% of the max heart rate achieved during the initial maximal exercise test. After the first 3 months the younger patients were playing basketball and football once a week, whereas the older patients were swimming.

Home exercise group

- Patients followed a moderate exercise training program at home.
 - They were supplied with ergometer cycles and given instructions regarding the performance of simple exercises. The researchers kept close contact with these patients, to answer any questions they had and to become aware of their course. The patients had to cycle at least five times a week, 30 min each time, at a heart rate of 50-60% of the maximal heart rate each had performed during the baseline treadmill test. After that, the patients performed simple flexibility and muscular extension exercises. Progress checks were carried out at each patient's home every month to check physical adaptation and to modify the exercise program, if necessary.

Control group

- Patients were asked to continue their usual lifestyle.

Follow-up assessment

- End of the intervention period: 6 months
- End of intervention data has been used

Outcomes

Relevant to our study

- Heart rate
- Blood pressure
- Left ventricular internal dimension (diastole and systole)
- IVS
- PW
- Left ventricular mass index
- Exercise time (min)
- METS
- VO2 max

Not relevant to our study

- Ventilatory max; lactic acid

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Supervised exercise (16); home exercise (10); control (12)
 - Analysed: NS
 - Per cent followed: NS
- Compliance: NS
- Similarity between groups at baseline: Yes

This is the same study as [Deligiannis-LI 1999](#), but the study has been given different names (HI, LI) to separate data from the high intensity exercise group and the low intensity exercise group, respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS

Deligiannis-HI 1999 (Continued)

Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of selection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Deligiannis-LI 1999

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Deligiannis-HI 1999 , but the study has been given different names (HI, LI) to separate data from the supervised, high intensity exercise group and the unsupervised, low intensity exercise group, respectively.

DePaul 2002

Methods	<ul style="list-style-type: none"> Recruitment: Progressive Care HD Unit at the St Joseph's Hospital and Bayshore Dialysis Centre in Hamilton (ON) Canada Study design: Parallel group RCT ITT analysis: Yes
Participants	Inclusion criteria <ul style="list-style-type: none"> Country: Canada Setting: Single centre HD therapy > 3 months; administered EPO for the treatment of anaemia, Hb > 9 g/dL (90 g/L); able to maintain sitting and standing balance without assistance, and ambulatory without assistance Hb (mean ± SD g/dL): Treatment group (11.6 ± 1.2); control group (11.1 ± 1.4) Duration of HD (mean ± SD months): Treatment group (4.2 ± 4.8); control group (4.6 ± 4.5) Frequency of HD (times/week): NS Duration of HD session (hours): NS

DePaul 2002 (Continued)

- Number: 38 randomised
- Age (mean \pm SD years): Treatment group (55 \pm 16); control group (54 \pm 14)
- Ethnicity: NS
- Sex (M/F): Treatment group (10/10); control group (13/4)

Exclusion criteria

- Ischaemic heart disease; recent myocardial infarction of less than 6 months; uncontrolled hypertension; pericardial or pleural friction rub; aortic stenosis; active musculoskeletal lower-extremity problem; history of vertebral fracture caused by osteoporosis; patients who participated in team sports or formal organized exercise programs

Interventions

Treatment group

- Aerobic exercise training on a Monark Rehab Trainer that was positioned and stabilised in front of the participant while sitting in the dialysis chair during HD. After a 2 minute warm up, the resistance was adjusted so that individuals were working at a level of perceived exertion of "somewhat strong" (BORG RPE-scale). Either before or after the dialysis session, based on convenience, participants performed strength training for hamstrings and quadriceps. The workload was initially 50% 5-RM and was then gradually increased during 12 weeks. The participants performed 10 reps, 3 sets (3 times/week, 12 weeks).

Control group

- 30 minutes of non-progressive, non-resisted, low intensity, range-of-motion exercises of the lower extremities and free upper extremity, performed sitting during HD (3 times/week, 12 weeks).

Follow-up assessment

- After an intervention period: 12 weeks
- After 6 months, during which no intervention was provided.
- End of intervention data has been used.

Outcomes

Relevant to our study

- Watt max
- Muscular strength
- Six-minute walk (m)
- Health-related quality of life

Not relevant to our study: None

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 108
 - Enrolled/randomised: Treatment group (20); control group (18)
 - Analysed at 12 weeks: Treatment group (15); control group (14)
 - Per cent followed at 12 weeks: Treatment group (75); control group (78)
 - Analysed at 5 months: Treatment group (10); control group (10)
 - Per cent followed at 5 months: Treatment group (67); control group (71)
- Compliance: NS, but the authors write that results of a per-protocol analysis including only patients who completed 75% of training sessions were not different from results of the ITT-analysis.
- Similarity between groups at baseline: Yes, except for number of individuals reporting having arthritis at baseline

Risk of bias
Bias
Authors' judgement
Support for judgement

DePaul 2002 (Continued)

Random sequence generation (selection bias)	Low risk	Randomisation table and randomising in blocks of four
Allocation concealment (selection bias)	Low risk	Used concealed assignments
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Low risk	Blinded
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	Low risk	Low risk of detection bias (A)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Dimeo 2007

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: NS
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Germany Setting: NS Kidney transplant recipients Hb (g/dL): NS. Number: 24 randomised Age (range): 35-68 years Ethnicity: NS Sex (M/F): 15/9 <p>Exclusion criteria: NS</p>
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 8 weeks high intensity cardiovascular exercise training Supervised or not: NS Duration of exercise/session: NS Frequency of exercise: 3 times/week <p>Control group</p> <ul style="list-style-type: none"> No exercise intervention <p>Follow-up assessment</p>

Dimeo 2007 (Continued)

- After an intervention period: 2 months

Outcomes	Relevant to our study <ul style="list-style-type: none"> • VO2 max • Health-related quality of life Not relevant to our study: None
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: 24 ◦ Analysed: NS ◦ Per cent followed: NS • Compliance: NS • Similarity between groups at baseline: Yes • Missing data: number of patients in the treatment group and the control group was not stated and data has therefore only been included in the review and not in the meta-analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias) Participants	Unclear risk	NS
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Eidemak 1997

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: Yes
Participants	Inclusion criteria:

Eidemak 1997 (Continued)

- Country: Denmark
- Setting: Single centre
- Moderate progressive CKD
- Hb (g/dL): NS
- GFR (mL/min/1.73 m²; range): Treatment group (26; 10-38); control group (29; 9-43)
- Number: 30 randomised
- Age (years; range): Treatment group (45; 22-70); control group (44; 28-65)
- Ethnicity: NS
- Sex (M/F): Treatment group (8/8); control group (5/10)

Exclusion criteria

- DM

Interventions

Treatment group

- Individual exercise training designed to match each patient's physical capacity.
 - The training program consisted mainly of bicycle ergometer exercise in the patient's home, and running, swimming and walking. Exercise duration and intensity was gradually increased, the latter up to 60-75% of maximal exercise capacity. The intensity of exercise was related to the patient's VO₂ max by monitoring heart rate during the exercise session and adjusting running/walking/swimming speed, or resistance on the bicycle ergometer, to elicit the heart rate equivalent to the desired per cent of VO₂ max. The relationship between heart rate and O₂ uptake was determined by measuring VO₂ and heart rate during submaximal and maximal stages of the bicycle exercise tests performed each month. The goal was to raise the energy consumption by 2.000 kcal/week corresponding to approximately 30 min of bicycling or an equal amount of other activities daily.
 - Exercise capacity was measured every month in the treatment group in order to secure the participant's continuous interest for training.

Control group

- Patients were asked to maintain their usual, mostly sedentary lifestyle.

Follow-up assessment

- Median intervention time in the treatment group was 18 months (range 8-28) and in the control group 20 months (range 10-30).
- End of intervention data has been used.

Outcomes

Relevant to our study

- VO₂ max
- Blood pressure
- Heart rate
- Total cholesterol
- Triglyceride
- VLDL cholesterol
- LDL cholesterol
- HDL cholesterol.

Not relevant to our study

- GFR

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (15); control group (15)
 - Analysed: Treatment group (15); control group (15)

Eidemak 1997 (Continued)

- Per cent followed: Treatment group (100); control group (100)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: blood pressure, heart rate SD, VO2 max SD, mean and SD VLDL cholesterol, LDL cholesterol and HDL cholesterol in the control group. Contacted primary investigators for clarification of results. They have provided the reviewer with missing VO2 max data, but do not have the rest of the missing data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Fitts 1995

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> • Country: USA • Setting: Single centre • Patients with CKD expected to require dialysis within about 6 months. • HCT (mean %): Treatment group (31.6); control group (32.4) • Number: 20 randomised. • Age (mean years; range): all patients (44; 22-67); treatment group (46); control group (44) • Ethnicity: NS • Sex (M/F): Treatment group (6/4); control group (5/5) <p>Exclusion criteria</p>

Fitts 1995 (Continued)

- Serious medical conditions in addition to CKD (including diabetes, cancer or cardiac, orthopaedic, neurological conditions)

Interventions
Treatment group

- Exercise coaching in biweekly meetings to clarify goals, develop individual programs, practice measurement and experience of target heart rate (75% maximum), demonstrate exercises, review exercise diaries and discuss motivational literature. Individual programs emphasized aerobic exercise (usually walking), but also included stretching and strengthening components as needed. The goal was to exercise for 30 min, 5 days/week.

Control group

- Patients were told to continue their usual activities.

Co-interventions

- EPO was given to all who needed to correct anaemia.

Follow-up assessment

- End of the intervention period: 3 months
- End of intervention data has been used

Outcomes
Relevant to our study

- Walking distance
- Heart rate
- Perceived exertion

Not relevant to our study: None
Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (10); control group (10)
 - Analysed: Treatment group (10); control group (10)
 - Per cent followed: Treatment group (100); control group (100)
- Data for treatment (9) and control (8) participants who did not change their perceived exertion more than one point between baseline and post intervention has been used in the meta analysis.
- Compliance: Goal was to exercise for 30 min, 5 days/week; the mean reported was 23 min, 4 days/week
- Similarity between groups at baseline: Unclear

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS, however balanced for age and sex
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS

Fitts 1995 (Continued)

Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Fitts 1999

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> Country: USA Setting: NS Patients in either the pre-dialysis phase ("expected to commence dialysis within 6-12 months after enrolment") or on HD (on dialysis for 1-5 years at the time of enrolment) Hb (g/dL): NS GFR (mL/min/1.73 m²): NS Time to dialysis start (mean ± SD months): PR treatment group (12.1 ± 3.0); PC control group (12.1 ± 3.3) Duration of HD (mean ± SD months): DR treatment group (28.2 ± 3.5); DC control group (29.6 ± 3.6) Frequency of HD (times/week): NS Duration of HD session (hours): NS Number: Pre-dialysis phase (26); dialysis phase (24) Age (mean ± SD years): PR treatment group (44.4 ± 11.4); DR treatment group (44.7 ± 9.4); PC control group (50.1 ± 12.1); DC control (48.7 ± 14.6) Ethnicity: NS Sex (M/F): PR treatment group (6/3); DR treatment group (6/3); PC control group (3/6); DC control group (5/4) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Serious coexisting disease (e.g. diabetes); patients without current or recent employment (within the preceding year)
Interventions	<p>Treatment groups (DR and PR)</p> <ul style="list-style-type: none"> DR: Dialysis patients receiving rehabilitation counselling and exercise coaching PR: Pre-dialysis patients receiving rehabilitation counselling and exercise coaching Individual rehabilitation counselling and exercise coaching was given for up to 1 hour/week for months 1-3, then up to 1 hour/month for months 4-6 (a total of 16 hours). Months 6-12 were a no-treatment follow-up period. Coaching and counselling sessions were scheduled according to patient's preferences, usually early in a dialysis session, but often by telephone or in a small conference room. Most patients chose to exercise at home, but a few joined community activities or exercised with the coach at a physical therapy gym near the dialysis centre. The goal was to help patients find strategies and motivation to improve physical functioning. The exercise program consisted of individual instruction and coaching based on the 'Simplecise' routine: 14 low intensity strengthening and stretching exercises. Each patient kept an exercise diary. The exercise coach discussed the diary with each patient weekly (months 1-3) or monthly (4-6) to give encouragement and adjust exercise intensity as appropriate. The goal

Exercise training for adults with chronic kidney disease (Review)

Fitts 1999 (Continued)

was to exercise for 30 min, 5 days/week for the 26-week program. The patients were also encouraged to walking, jogging or cycling.

Control groups (DC and PC)

- DC: Dialysis patients were asked to maintain their usual lifestyle.
- PC: DC: Pre-dialysis patients were asked to maintain their usual lifestyle.

Follow-up assessment

- End of intervention: 6 months
- End of the observation period: 12 months
- End of intervention data has been used.

Co-interventions

- All patients with anaemia had equal access to EPO to eliminate the potential confounding variable of anaemia.

Outcomes	Relevant to our study <ul style="list-style-type: none"> • Walking distance • Health-related quality of life • Resting heart rate Not relevant to our study: None
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: Pre-dialysis patients (26); dialysis patients (24) ◦ Analysed questionnaires: DR (9); DC (9); PR (9); PC (9) ◦ Analysed exercise tests: DR (8); DC (8); PR (9); PC (8) ◦ Per cent followed exercise tests: Pre-dialysis patients (65); dialysis patients (67) ◦ Per cent followed questionnaires: Pre-dialysis patients (69); dialysis patients (75) • Compliance: NS • Similarity between groups at baseline: Unclear • Missing data: SD for walking distance and resting heart rate, respectively. Contacted primary investigators for clarification of the results, but the data were missing.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	2x2x4 factorial design, with two between-group variables. Sequence generation method: NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	Unclear risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)

Fitts 1999 (Continued)

Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Frey 1999

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: Single centre Undergoing HD treatment; 25-65 years HB (g/dL): NS Number: 11 randomised Age (mean \pm SD years): treatment group (40 \pm 11); control group (53 \pm 13) Ethnicity: NS Sex (M/F): Treatment group (3/2); control group (3/3) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Blood pressure > 160 mm Hg systolic and > 95 mm Hg diastolic at the beginning of the second hour of dialysis; average inter-dialytic weight gain > 3.5 kg between dialysis treatments; DM; unstable angina
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> During the second hour of dialysis treatment the patients exercised each dialysis day (3 times per week). <ul style="list-style-type: none"> The patients cycled on stationary bicycle ergometers. The exercise consisted of a 5-minute warm-up and 5-minute cool-down. After the warm-up session all cycling sessions were followed by gradually increasing the workload until 60 or 80% of maximal heart rate (or approximately 11-16 on the RPE scale) was achieved. During the first 4 weeks exercise time was increased each day by 3 minutes and at the end of week 4 45 minutes of exercise had been achieved. During the following 4 weeks the patients exercised for 45 minutes with an intensity of 60-80% of maximal heart rate (or 11-16 on the RPE scale). <p>Control group</p> <ul style="list-style-type: none"> Patients remained sedentary throughout the 12-week study. <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 8 weeks End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> Kilocalorie and protein intake Serum prealbumin Serum transferrin

Frey 1999 (Continued)

Not relevant to our study

- Pre-dialysis and post-dialysis albumin; Kt/V

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 11
 - Enrolled/randomised: Treatment group (5); control group (6)
 - Analysed: Treatment group (5); control group (6)
 - Per cent followed: Treatment group (100); control group (100)
- Compliance: Treatment group 83% compliance to the exercise sessions during the last 4 weeks of exercise.
- Similarity between groups at baseline: Yes
- Missing data: None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Goldberg 1983

Methods

- Recruitment: NS
- Study design: Parallel group RCT
- ITT analysis: No

Participants

Inclusion criteria

- Country: USA
- Setting: Single centre
- Undergoing HD treatment
- HB (g/dL): 8.0 ± 2.0
- Duration on HD (mean \pm SD months): Treatment group (22.2 ± 17.1); control group (40.1 ± 29.7)

Goldberg 1983 (Continued)

- Frequency of HD (times/week): 3
- Duration of HD session (hours): 4-6
- Number: 25 randomised.
- Age (mean \pm SD years): Treatment group (38 \pm 15); control group (37 \pm 12)
- Ethnicity (White/African American/Latino/Asian): Treatment group 9/5/0/0; control group (9/6/0/0)
- Sex (M/F): Treatment group (8/6); control group (7/4)

Exclusion criteria

- Patients with unstable angina pectoris; cardiac arrhythmias; haemodynamically significant valvular heart disease; congestive heart failure; poorly controlled hypertension; severe retinal disease; insulin-dependent DM; hypothyroidism

Interventions

Treatment group

- Exercise training 3 times/week.
 - Each session began with 10-min of stretching and low intensity walking as a warm-up. Workouts usually lasted 45 min and concluded with a 5-10 min period of low intensity exercise. The initial exercise sessions were at an intensity of 50-60% of VO₂ max and usually included four 5-min sessions on a bicycle ergometer or walking. Within 4-6 weeks, most patients progressed to bicycling 8-10 min at an intensity of 65% of VO₂ max. By 12 weeks, most patients exercised at an intensity of 70-75% of VO₂ max, alternating 23 laps of walking with 1 lap of jogging for 5-7 min. At 20 weeks, exercise sessions were increased to walk 1 lap, jog 1-2 laps for 5-7 min, and 10-15 min on the bicycle ergometer at an intensity of 70-80% of VO₂ max. This exercise was repeated after a 5-min rest for 45-60 min. By 9 months, exercise sessions were 45-60 min at an intensity of 70-80% of VO₂ max., and most patients could jog 3 laps and walk 1 lap continuously for 7-10 min.

Control group

- Patients remained sedentary throughout the study period.

Follow-up assessment

- End of the intervention period: 12 months
- End of intervention data has been used.

Outcomes

Relevant to our study

- Graded exercise treadmill duration
- VO₂ max
- Heart rate
- Blood pressure
- Psychological function
- Plasma triglyceride levels
- Plasma HGL cholesterol levels
- Fasting plasma glucose
- Fasting plasma insulin
- Glucose disappearance

Not relevant to our study

- red cell mass; HCT

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (14); control group (11)
 - Analysed (exercise testing): Treatment group (14); control group (11)
 - Per cent followed (exercise testing): Treatment group (100); control group (100)
 - Analysed (lipid metabolism): Unclear

Goldberg 1983 (Continued)

- Per cent followed (lipid metabolism): Unclear
- Analysed (glucose metabolism): Treatment group (8); control group (5)
- Per cent followed (glucose metabolism): Treatment group (57); control group (45)
- Analysed (psychological assessments): Treatment group (9); control group (9)
- Per cent followed (psychological assessments): Treatment group (64); control group (82)
- Compliance: NS
- Missing data
 - Mean and SD for post intervention for outcomes measures: depression, VLDL Triglyceride, LDL cholesterol, mean body mass
 - Data from the control group was sometimes missing.
 - Numbers analysed concerning lipids: Unclear
 - Tried contacting primary investigators for clarification of results, but not been able to locate them.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Harter 1985

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> • Country: USA • Setting: Single centre • Undergoing HD • Hb (g/dL): NS • Duration on HD (mean ± SD months): Treatment group (23 ± 5); control group (40 ± 9)

Harter 1985 (Continued)

- Frequency of HD (times/week): 3
- Duration of HD session (hours): 4-6
- Number: 27 randomised
- Age (mean \pm SD years): Treatment group (40 ± 4); control group (36 ± 3)
- Ethnicity (White/African American/Latino): Treatment group (9/4/0); control group (6/6/0)
- Sex (M/F): Treatment group (8/5); control group (7/5)

Exclusion criteria

- Unstable angina pectoris; cardiac arrhythmias; haemodynamically significant valvular heart disease; clinically significant or symptomatic cerebrovascular; peripheral vascular, or coronary atherosclerosis; congestive heart failure; poorly controlled hypertension; electrolyte imbalance; severe retinal disease; insulin-dependent DM, hypothyroidism.

Interventions

Treatment group

- Exercise sessions which began with 10 min callisthenics.
 - Initial exercise was at the intensity of 50% VO₂ max on a bicycle ergometer for 3-5 min, followed by a 5-min rest or until pulse and blood pressure returned to baseline before repeating the workout. Training was exclusively on a bicycle ergometer the first 6 weeks of the program. The intensity and duration of exercise was gradually increased as the patients adapted to the exercise training regimen.
 - At 12 weeks most patients were exercising at an intensity of 60-65% of VO₂ max and walking and jogging was started. At 20 weeks all patients were walk-jogging 1 mile/session, and by 28 weeks most patients were exercising continuously for 10 min, alternating jogging with walking for 2 miles/session and bicycling at an intensity of 70% of VO₂ max. Exercise intensity and duration was increased until the 36th week of exercising, when most of the patients were walk-jogging and bicycling at 70-80% of their VO₂ max for a total workout of 45 min/session.

Control group

- Patients remained sedentary throughout the study period.

Follow-up assessment

- End of the intervention period: at least 12 months
- End of intervention data has been used.

Outcomes

Relevant to our study

- VO₂ max
- Blood pressure
- Lipoprotein parameters
- Plasma glucose
- Plasma insulin
- Insulin receptor binding
- Psychosocial functioning

Not relevant to our study

- Haematological function

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 31
 - Enrolled/randomised: 27; 1 patient in the exercise group moved and one exerciser's data were excluded from the analysis due to significant weight loss during the programme. Two of the sedentary controls participated in the exercise group after serving as controls for 6 and 9 months.
 - Analysed (aerobic capacity): Treatment group (13); control group (12)
 - Per cent followed: Treatment group (100); control group (100)

Harter 1985 (Continued)

- Analysed (lipoprotein metabolism): Treatment group (13); control group (11)
- Analysed (carbohydrate metabolism): Treatment group (8); control group: (NS)
- Compliance: NS
- Similarity between groups at baseline: Yes concerning demographic data, unclear concerning outcome measures
- Missing data: The article does not present mean and SD for the different outcomes and groups, respectively. Mean and SD for VO₂ peak is presented only for the exercise group, showing an increase from 22 ± 2 to 25 ± 2 mL/kg/min. All other outcomes are presented as % increase / decrease. There are also figures in which data is presented on an individual or a group basis. For carbohydrate metabolism the number of patients in the control group is not presented. We have tried to use the figures to calculate mean ± SD for the outcomes, but have decided that instead of including approximate outcome data (based on our calculations from the figures) into the meta-analysis, which would increase the risk of errors, the results from the study were not be used in the meta analysis. Instead results were described separately under the heading 'Results'.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Johansen 2006

Methods	<ul style="list-style-type: none"> • Recruitment: Outpatient dialysis facilities affiliated with the University of California • Study design: Parallel group RCT • ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> • Country: USA • Setting: Multicentre • Kt/V ≥ 1.2; good compliance with dialysis treatment (i.e. not missing more than two dialysis treatment session in the month before enrolment)

Johansen 2006 (Continued)

- Hb (mean \pm SD mmol/L): Treatment group (119 \pm 9); control group (115 \pm 16)
- Duration of HD (years): NS
- Frequency of HD (times/week): 3
- Duration of HD (hours): NS
- Number: 79 randomised
- Age (mean \pm SD years): Treatment group (54 \pm 14); control group (57 \pm 14)
- Ethnicity (White/African American/Latino/Asian): 4/46/10/19
- Sex (M/F): Treatment group (12/8); control group (14/6)

Exclusion criteria

- Dialysis < 3 months; catabolic state; unable to give informed consent; active IV drug users; thigh dialysis graft; contraindications to resistance training such as myocardial infarction within 6 months; active angina; uncompensated congestive heart failure; orthopaedic or musculoskeletal limitations

Interventions

Treatment group

- Placebo + supervised exercise
- 3 months supervised high intensity (60% max) intra-dialytic resistance training of the lower extremities. 2-3 sets of 10 reps/exercise.

Control group

- Placebo + no exercise

Follow-up assessment

- End of the intervention period: 3 months
- End of intervention data has been used.

Patients were randomised into 4 groups

- placebo + no exercise; nandrolone decanoate + no exercise; placebo + exercise; nandrolone decanoate + exercise
- We have used data from placebo + no exercise (control group); placebo + exercise (treatment group).

Outcomes

Relevant to our study

- Mean body mass
- Lean body mass
- Fat mass
- Muscle size
- Quadriceps muscle area
- Muscular strength
- Physical performance
- Physical activity
- Health-related quality of life

Not relevant to our study: None

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 278
 - Enrolled/randomised: 79; treatment group (20); control group (20)
 - Analysed: Treatment group (19); control group (17)
 - Per cent followed: Treatment group (95); control group (85)
- Compliance: NS
- Similarity between groups at baseline: Yes

Johansen 2006 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Yes; 1:1:1:1 manner by the research pharmacist using variable block sized.
Allocation concealment (selection bias)	Low risk	Adequate
Blinding (performance bias and detection bias) Participants	High risk	No blinding
Blinding (performance bias and detection bias) Outcome assessors	High risk	No blinding
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Jong 2004

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> Country: Korea Setting: NS Hb (g/L): NS Duration on CAPD (months): NS Number: 36 randomised Age (mean years): Treatment group (48.8); control group (49.8) Ethnicity: NS Sex (M/F): Treatment group (12/7); control group (11/6) Exclusion criteria: NS
Interventions	Treatment group <ul style="list-style-type: none"> Walking exercise program which consisted of an exercise education protocol, an exercise regimen and a counselling protocol based on a framework of self-efficacy promotion. The patients were educated according to the exercise education protocol and performed walking exercise for 2-4 times a week upon taking verbal persuasion biweekly through telephone or face to face interview for 12 weeks. Intensity and duration of walking exercise: NS

Jong 2004 (Continued)

Control group

- No exercise intervention.

Follow-up assessment

- End of the intervention: 12 weeks
- End of intervention data has been used.

Outcomes

Relevant to our study

- VO2 max
- Serum albumin
- Cholesterol
- Triglyceride
- HDL cholesterol
- LDL cholesterol
- Health-related quality of life

Not relevant to our study

- HCT; serum urea; SCr

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (19); control group (17)
 - Analysed: Treatment group (19), control group (17)
 - Per cent followed: Treatment group (100); control group (100)
- Compliance: NS
- Similarity between groups at baseline: NS
- Missing data
 - Data concerning VO2 peak and albumin has been included in the meta-analysis.
 - Data concerning cholesterol, triglyceride, HDL cholesterol and LDL cholesterol is NS in the abstract. Contacted the Department of Internal Medicine, College of Medicine, Yonsei University, Seoul, Korea for clarification of methods and results, but without result. As there was no information about the intensity of the exercise, it has not been possible to use data from this study in the comparisons between the effects of high versus low intensity exercise.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)

Jong 2004 (Continued)

Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C)

Koh 2010a

Methods	<ul style="list-style-type: none"> Recruitment: 3 Tasmanian renal units Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Australia Setting: Multicentre Aged 18 years on stable, adequate dialysis therapy with urea reduction ratio 70% for 3 months Hb (mmol/L): NS Duration of HD (years): NS Frequency of HD (times/week): NS Duration of HD (hours): NS Number: 70 randomised Age (mean \pm SD years): Intra-dialytic exercise group (52 ± 11); home-based exercise group (52 ± 14); control group (51 ± 14) Ethnicity: NS Sex (M/F): Intra-dialytic exercise group (10/5); home-based exercise group (11/4); control group (8/8) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Unstable angina; lower-limb amputation; or those who met or exceeded the exercise recommendation of 120 minutes of moderate intensity physical activity/week
Interventions	<p>Supervised intra-dialytic exercise group</p> <ul style="list-style-type: none"> 6 months supervised, intra-dialytic cardiovascular training. Frequency: Three times weekly and progressively increased from 15 to 45 minutes/session. During the first 2 hours of HD sessions. Intensity: 12-13 on the Borg RPE-scale <p>Unsupervised home-based exercise group</p> <ul style="list-style-type: none"> 6 months unsupervised walking exercise. Frequency: 3 times/week and progressively increased from 15 to 45 minutes at 6 months. Intensity: 12-13 on the Borg RPE-scale <p>Control group</p> <ul style="list-style-type: none"> No intervention <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 6 months End of intervention data has been used.

Koh 2010a (Continued)

Outcomes	Relevant to our study <ul style="list-style-type: none"> • Walking capacity • Physical functioning • Muscular strength • Level of physical activity • Health-related quality of life Not relevant to our study: None
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Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: 113 ◦ Enrolled/randomised: 74/70; intra-dialytic exercise group (27); home-based exercise group (21); control group (22) ◦ Analysed: Intra-dialytic exercise group (15); home-based exercise group (15); control group (16) ◦ Per cent followed: Intra-dialytic exercise group (71); home-based exercise group (71); control group (73) • Compliance: Intra-dialytic exercise group (75 ± 19%); home-based exercise group (71 ± 13%) • Similarity between groups at baseline: Yes
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned by an individual not associated with the study using unrestricted computer-generated random numbers.
Allocation concealment (selection bias)	Low risk	Adequate (A)
Blinding (performance bias and detection bias) Participants	High risk	No blinding
Blinding (performance bias and detection bias) Outcome assessors	High risk	No blinding
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Koh 2010b

Methods

Participants

Koh 2010b (Continued)

Interventions

Outcomes

Notes This is the same study as [Koh 2010a](#) but the study has been given different names (2010a, 2010b) to separate data from the intra-dialytic exercise group and the home-based exercise group, respectively.

Konstantinidou-D 2002

Methods

- Recruitment: the Renal Unit of AHEPA Hospital
- Study design: Parallel 4-group RCT
- ITT analysis: No

Participants

Inclusion criteria

- Country: Greece
- Setting: single centre
- HD treatment
- Hb (g/dL): NS
- Duration on HD (mean \pm SD months): Treatment group 1 (78 \pm 62); treatment group 2 (72 \pm 66); treatment group 3 (62 \pm 37); control group (79 \pm 86)
- Frequency of HD (times/week): 3
- Duration of HD session (hours): 4
- Number: 48 randomised.
- Age (mean \pm SD years): Treatment group 1 (46.4 \pm 13.9); treatment group 2 (48.3 \pm 12.1); treatment group 3 (51.4 \pm 12.5); control group (50.2 \pm 7.9)
- Ethnicity: NS
- Sex (M/F): Treatment group 1 (11/5); treatment group 2 (8/2); treatment group 3 (8/2); control group (4/8)

Exclusion criteria

- Unstable hypertension; congestive heart failure (grade >II according to NYHA); cardiac arrhythmias (\geq III according to Lown); recent myocardial infarction or unstable angina; persistent hyperkalaemia before dialysis; DM; active liver disease; bone disease that puts the patient at risk of fracture; arthritic or orthopaedic problems limiting exercise; peripheral vascular disease; undisciplined patients

Interventions

Treatment group 1

- Participated in a 6-month outpatient supervised exercise training program on the non-dialysis days. 3 weekly sessions (60 min/session) of aerobic and strengthening training.
- Intensity aerobic exercise: 60-70%
- Intensity resistance training: low (NS exact intensity); reps (NS); sets (NS)

Treatment group 2

- 6-month supervised exercise training program during their HD sessions. 3 weekly sessions(60 min/ session) of aerobic and strengthening training.
- Intensity aerobic exercise: 70%
- Intensity resistance training (NS exact intensity); reps (NS) sets (NS)

Treatment group 3

- Moderate unsupervised exercise training program for 6 months at home. 5 weekly sessions (30 min/ session) of aerobic training followed by simple flexibility and muscular extension exercises.
- Intensity aerobic exercise: 50-60%

Konstantinidou-D 2002 (Continued)

Control group

- Continued their usual lifestyle

Co-interventions

- Patients were given EPO in order to keep the Hb/HCT level stable throughout the study period

Follow-up: at the end of the intervention period of 6 months. End of intervention data has been used.

Outcomes

Relevant to our study

- Heart rate
- Blood pressure
- VO2 peak
- Exercise time

Not relevant to our study

- Ventilation; respiratory exchange ration

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 120
 - Enrolled/randomised: Treatment group 1 (21); treatment group 2 (12); treatment group 3 (12); control group (13)
 - Analysed: Treatment group 1 (16); treatment group 2 (10); treatment group 3 (10); control group (12)
 - Per cent followed: Treatment group 1 (76); treatment group 2 (83); treatment group 3 (83); control group (100)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: None

This is the same study as [Konstantinidou-ND 2002](#) and [Konstantinidou-US 2002](#), but the study has been given different names (D, ND, us) to separate data from the during dialysis exercise group, the exercise group that exercised on non-dialysis days and the unsupervised, respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)

Konstantinidou-D 2002 (Continued)

Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Konstantinidou-ND 2002

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Konstantinidou-D 2002 and Konstantinidou-US 2002 , but the study has been given different names (D, ND, us) to separate data from the during dialysis exercise group, the exercise group that exercised on non-dialysis days and the unsupervised, respectively.

Konstantinidou-US 2002

Methods	
Participants	
Interventions	
Outcomes	
Notes	This is the same study as Konstantinidou-ND 2002 and Konstantinidou-US 2002 , but the study has been given different names (D, ND, US) to separate data from the during dialysis exercise group, the exercise group that exercised on non-dialysis days and the unsupervised, respectively.

Kopple 2007a

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: NS Undergoing HD treatment Hb (mean \pm SD mmol/L): Cardiovascular exercise (113 \pm 13); resistance training (129 \pm 3); mixed cardiovascular and resistance training (134 \pm 4); control group (130 \pm 4) Duration on HD (mean \pm SD months): Cardiovascular exercise (46 \pm 14); resistance training (52 \pm 12); mixed cardiovascular and resistance training (38 \pm 6); control group (51 \pm 21) Frequency of HD (times/week): NS

Kopple 2007a (Continued)

- Duration of HD session (hours): NS
- Number: 80 randomised
- Age (mean \pm SD years): Cardiovascular exercise (46 ± 4); resistance training (46 ± 3); mixed cardiovascular and resistance training (43 ± 4); control group (41 ± 3)
- Ethnicity (African American/Latino): Cardiovascular exercise (6/2/2); resistance training (5/9/1); mixed cardiovascular and resistance training (5/7/0); control group (4/5/5)
- Sex (M/F): cardiovascular exercise (6/4); resistance training (9/6); mixed cardiovascular and resistance training (7/5); control group (9/5)

Exclusion criteria: NS

Interventions

Cardiovascular exercise group

- 5 months cardiovascular exercise
- Intensity: NS
- Frequency: NS
- Description of exercise interventions: NS
- Supervision: NS

Resistance training group

- 5 months resistance training
- Intensity: NS
- Frequency: NS
- Description of exercise interventions: NS
- Supervision: NS

Mixed cardiovascular and resistance training group

- 5 months mixed cardiovascular and resistance training
- Intensity: NS
- Frequency: NS
- description of exercise interventions: NS
- Supervision: NS

Control group

- Patients remained sedentary throughout the study period.

Follow-up assessment

- End of the intervention period: 5 months
- End of intervention data has been used.

Outcomes

Relevant to our study

- Mean body mass
- Fat mass
- Body Mass Index
- Mid-thigh muscle area

Not relevant to our study

- mRNA levels for various growth factors

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: 80
 - Analysed: 51

Kopple 2007a (Continued)

- Per cent followed: 64
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data
 - The article does not present mean and SD for physical capacity at baseline and end of intervention for the cardiovascular exercise group; resistance training group; mixed cardiovascular and resistance training group and control group, respectively.
 - As there is no information regarding intensity or supervision, the studies data has not been included in these subgroup analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias) Participants	High risk	No blinding
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attribution bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Koufaki 2002a

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> • Country: UK • Setting: Single centre • Undergoing CAPD or HD treatment • Hb (g/dL): Treatment group (12.1±1.4); control group (12.1±1.3) • Duration on HD (mean ± SD months): Treatment group (36.7 ± 45.5); control group (47.4 ± 50.7) • Frequency of HD (times/week): NS • Duration of HD session (hours): NS • Number: 48 randomised

Koufaki 2002a (Continued)

- Age (mean \pm SD years): Treatment group (57.3 \pm 14.3); control group (50.5 \pm 19)
- Ethnicity: NS
- Sex (M/F): NS

Exclusion criteria

- Evidence of recent myocardial infarction (within 6 weeks); uncontrolled dysrhythmias; uncontrolled hypertension; unstable angina; severe uncontrolled diabetes; symptomatic left ventricular dysfunction or neurological disorder with functional deficit; demonstrating an inter-dialytic weight \geq 2.5 kg, pre-dialysis potassium \geq 5.5 mmol/L and urea clearance (Kt/V \leq 1 mL/min/L)

Interventions

Treatment group

- 3 months of aerobic exercise on a cycle ergometer.
 - Patients with CAPD exercised 3 times/week under the supervision of an exercise physiologist. Patients with HD exercised during the first 2 h of dialysis also under the supervision of an exercise physiologist in a recumbent position. Patients who paused their exercise training for more than 2 weeks had to start from the exercise workload that they stopped at or the work load that they could sustain. Patients who had to pause their exercise training for more than 4 weeks had to start from the beginning. All patients had to complete 12 weeks of exercise training. Exercise intensity was 90% of VO₂ peak. Each exercise session was divided into a warm-up, conditioning and cool down session. The exercise started gently with all patients having to perform 3 separate bouts on a bike, each of 6-8 min duration. After the first 2 weeks, exercise duration of cycling was gradually increased by adding 1 min extra to each conditioning bout also depending on the patients' response to the exercise training. The aim was that all patients were to be able to perform 2 separate bouts of continuous cycling of 20 min each on the cycle ergometer, or one of 30-35 min duration. The patients in this group were asked not to get involved in any other physical activities except the ones performed within the study.

Control group

- Patients were instructed to maintain their usual level of physical activity.

Co-interventions

- All patients, except one, were receiving EPO to maintain a constant Hb.

Follow-up assessment

- End of the observation period: 12 weeks
- End of intervention data has been used.

Outcomes

Relevant to our study

- Nutritional status
- Level of physical activity
- VO₂ peak
- Heart rate functional capacity

Not relevant to our study

- Comorbidity score

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (26); control group (22)
 - Analysed: Treatment group (18); control group (15)
 - Per cent followed: Treatment group (69); control group (68)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: none

Koufaki 2002a (Continued)

- Since the participants is a mix of patients with CAPD and patients with HD treatment it has not been possible to include data from the study in the comparison between effects of exercise training during HD versus on a non-dialysis day or versus before HD.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	By flip of a coin after eligible participants entered the study
Allocation concealment (selection bias)	Low risk	Adequate (A)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Koufaki 2003

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> • Country: UK • Setting: NS • Hb (g/L): NS • Duration on dialysis (months): NS • Frequency of HD (times/week): NS • Duration of HD session (hours): NS • Number: 12 randomised. • Age (mean \pm SD years): total (47.8 \pm 20.3); treatment group (NS); control group (NS) • Ethnicity: NS • Sex (M/F): NS Exclusion criteria: NS
Interventions	Patients' anaemia was first partially corrected with EPO (mean interval 5 months) before randomisation

Koufaki 2003 (Continued)

Treatment group

- EPO-therapy + exercise training
 - Cycle ergometer exercise training 3 sessions/week (progressing to accumulate 40 min/session) and at an exercise intensity equivalent to ventilatory threshold.

Control group

- EPO-therapy + no exercise
 - Patients were instructed to maintain their usual level of physical activity.

Follow-up assessment

- End of the observation period: 12 weeks
- End of intervention data has been used.

Outcomes

 Relevant to our study: VO₂ peak, walk performance.

Not relevant to our study: Hb, oxygen uptake at the ventilatory threshold, oxygen uptake kinetics.

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: total (12); treatment group (NS); control group (NS)
 - Analysed: NS
 - Per cent followed: NS
- Compliance: NS
- Similarity between groups at baseline: NS
- Missing data
 - Number of patients in each group, mean and SD values for VO₂ peak and WALK test.
 - Contacted the Centre for Biophysical and Clinical Research into Human Movement, Manchester Metropolitan University, Cheshire, United Kingdom for clarification of methods and results, but without result.
 - The study has been included but not used in the meta-analysis due to missing data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)

Koufaki 2003 (Continued)

Total risk of bias: A (low), B (moderate/unclear), or C (high) High risk High, one or more quality criteria not met (C).

Kouidi 1997a

Methods	<ul style="list-style-type: none"> Recruitment: Renal Unit, AHEPA Hospital Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Greece Setting: Single centre HCT (mean \pm SD %): Treatment group (30.6 \pm 4.2); control group (32.7 \pm 3.5) Duration on HD (mean \pm SD years): Treatment group (5.9 \pm 4.9); control group (6.2 \pm 5.4) Frequency of HD (times/week): 3 Duration of HD session (hours): 4 Number: 36 randomised Age (mean \pm SD years): Treatment group (49.6 \pm 12.1); control group (52.8 \pm 10.2) Ethnicity: NS Sex (M/F): Treatment group (11/9); control group (4/7) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Symptomatic cardiovascular disease; DM; musculoskeletal limitation or other medical problems contraindicating participation in an exercise training program
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 6-month exercise renal rehabilitation program <ul style="list-style-type: none"> The intensity and duration of the exercise sessions was gradually increased as the patients adapted to the supervised training regimen. After 6-8 weeks of exercise training all patients were exercised in subgroups at 50-60% of their VO₂ max or 60-70% of their heart rate max for 90 min, 3-4 times/week on the non-dialysis days. Each exercise session consisted of stationary cycling, walking or jogging, callisthenics, aerobics, as well as swimming and/or game sports such as basketball and football in the last 8-12 weeks. <p>Control group</p> <ul style="list-style-type: none"> No exercise intervention <p>Co-interventions</p> <ul style="list-style-type: none"> Patients remained on a stable medication regimen, diet and dialysis schedule during the study. Antihypertensive and erythropoietin therapy was only changed as needed. <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 6 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> VO₂ max Heart rate Blood pressure

Kouidi 1997a (Continued)

- Health-related quality of life
- Severity of depression

Not relevant to our study

- Traits of personality

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (24); control group (12)
 - Analysed: Treatment group (20); control group (11)
 - Per cent followed: Treatment group (83); control group (92)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: None
- The exercise group has exercised at an intensity between 50, 60 and 70%. We have chosen to classify the exercise training intervention as high intensive ($\geq 60\%$).
- As the EPO therapy was changed as needed the study has been included in the comparison between exercise training + EPO versus control + EPO

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Kouidi 2002a
Methods

- Recruitment: NS
- Study design: Parallel group RCT
- ITT analysis: No

Participants

Inclusion criteria

Kouidi 2002a (Continued)

- Country: Greece
- Setting: NS
- Kidney transplant recipients
- Hb (g/dL): NS
- Number: 18 randomised
- Age (mean \pm SD years): Treatment group (50.2 \pm 10.4); control age (matched)
- Ethnicity: NS
- Sex (M/F): NS

Exclusion criteria: NS

Interventions	Treatment group <ul style="list-style-type: none"> • Cardiovascular exercise training with stationary bicycles • Intensity: NS • Frequency: 3 times/week • Duration: 8 months Control group <ul style="list-style-type: none"> • No exercise Follow-up assessment <ul style="list-style-type: none"> • End of the intervention period: 8 months • End of intervention data has been used.
Outcomes	<ul style="list-style-type: none"> • Heart rate variability parameters: SDNN, RMSSD, pNN50, LF, HF, LF/HF
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: Treatment group (9); control group (9) ◦ Analysed: Treatment group (9); control group (9) ◦ Per cent followed: Treatment group (100), control group (100) • Compliance: NS • Similarity between groups at baseline: NS • Missing data <ul style="list-style-type: none"> ◦ No data for the control group. Contacted primary investigator for clarification of method and results. The results are missing. ◦ Primary investigator confirmed that this is a RCT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias)	Unclear risk	NS

Kouidi 2002a (Continued)

Outcome assessors

Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Kouidi 2002b

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Greece Setting: NS Hb (g/L): NS HCT (%): NS Duration of HD (years): NS Frequency of HD (times/week): 3 Duration of HD (hours): NS Number: 44 randomised Age (mean \pm SD years): Treatment group (46.3\pm11.2); control group (NS; two groups were matched for age) Ethnicity: NS Sex (M/F): NS, two groups were matched for sex <p>Exclusion criteria: NS</p>
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Exercise training with stationary bicycles during HD sessions Intensity: NS Frequency: 3 times/week Duration: 1 year <p>Control group</p> <ul style="list-style-type: none"> No exercise <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 12 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> VO₂ peak SDNN RMSSD

Kouidi 2002b (Continued)

- Depression scores

Not relevant to our study

- pNN50, LF/HF ratio

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (24); control group (20)
 - Analysed: Treatment group (NS); control group (NS)
 - Per cent followed: Treatment group (NS); control group (NS)
- Compliance: NS
- Similarity between groups at baseline: NS
- Missing data
 - No data for the control group. Contacted primary investigator for clarification of method and results. The results are missing.
 - Primary investigator confirmed that this is a RCT

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Kouidi 2003a
Methods

- Recruitment: NS
- Study design: Parallel group RCT
- ITT analysis: No

Participants

- Inclusion criteria
- Country: Greece

Kouidi 2003a (Continued)

- Setting: NS
- Hb (g/L): NS
- HCT (%): NS
- Duration on HD (years): NS
- Frequency of HD (times/week): 3
- Duration of HD session (hours): NS
- Number: 30 randomised
- Age (mean \pm SD years): Treatment group (50.6 \pm 10.8); control group (51.3 \pm 9.9)
- Ethnicity: NS
- Sex (M/F): NS

Exclusion criteria

- Other systemic disease; clinical symptoms of heart disease

Interventions

Treatment group

- Supervised training program
 - Stationary bicycles during the HD sessions (3 times/week) for one year.
 - Intensity and duration: NS

Control group

- Remained untrained.

Follow-up assessment

- End of intervention: 12 months
- End of intervention data has been used.

Outcomes

Relevant to our study

- VO₂ peak
- SDNN

Not relevant to our study

- LVEF; LF/HF; LP; TWA

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (15); control group (15)
 - Analysed: NS
 - Per cent followed: NS
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data
 - Data concerning mean \pm SD for VO₂ peak and heart rate variability for the control group is missing in the abstract. Contacted primary investigator for clarification of method and results. The researcher does not have the missing data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS

Kouidi 2003a (Continued)

Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Kouidi 2004a

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Greece Setting: NS Hb (g/L): NS HCT (%): NS Duration on HD (years): NS Frequency of HD (times/week): NS Duration of HD session (hours): NS Number: 21 randomised Age (range years): Total (60-72); mean \pm SD for each group (NS) Ethnicity: NS Sex (M/F): NS <p>Exclusion criteria</p> <ul style="list-style-type: none"> Not fully reported. It's reported that screening was performed to "...exclude severe cardiovascular abnormalities, DM, active hepatitis etc."
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Supervised exercise sessions <ul style="list-style-type: none"> Stationary bicycle during HD treatment (3 times/week) Duration: NS Intensity: NS <p>Control group</p>

Kouidi 2004a (Continued)

- Maintained pre-randomisation physical activity levels.

Follow-up assessment

- End of intervention: 6 months
- End of intervention data has been used.

Outcomes	Relevant to our study <ul style="list-style-type: none"> • VO2 peak • peak torque Not relevant to our study <ul style="list-style-type: none"> • Ejection fraction; cardiac output index; transmittal flow; isovolemic relaxation time
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: Treatment group (11); control group (10) ◦ Analysed: NS ◦ Per cent followed: Treatment group (NS); control group (NS) • Compliance: NS • Similarity between groups at baseline: NS • Missing data <ul style="list-style-type: none"> ◦ Data concerning mean \pm SD for VO2 peak for all outcome measures is missing. Contacted primary investigator for clarification of methods and results, but the data is missing.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	Unclear risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Kouidi 2005

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> • Country: Greece • Setting: NS • HCT (%): NS • Duration on HD (years): NS • Frequency of HD (times/week): 3 • Duration of HD session (hours): NS • 33 patients were randomised • Age: 48.8 ± 13.9 years • Age (mean ± SD years): NS • Ethnicity: NS • Sex (M/F): 27/6 <p>Exclusion criteria: NS</p>
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Supervised exercise aerobic exercise <ul style="list-style-type: none"> ◦ Stationary bicycle during HD treatment 3/week for 10 months ◦ Intensity: NS ◦ Duration: NS <p>Control group</p> <ul style="list-style-type: none"> • No exercise training <p>Co-interventions</p> <ul style="list-style-type: none"> • The dose of EPO was changed as needed, according to the level of Hb, aiming to keep it constant during the study. <p>Follow-up assessment</p> <ul style="list-style-type: none"> • End of intervention: 10 months • End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> • VO2 peak • Depression scores • Quality of life <p>Not relevant to our study</p> <ul style="list-style-type: none"> • Personality
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: Treatment group (19); control group (14) ◦ Analysed: NS ◦ Per cent followed: Treatment group (NS); control group (NS) • Compliance: NS • Similarity between groups at baseline: Yes

Kouidi 2005 (Continued)

- Missing data
 - Data concerning mean \pm SD for VO₂ peak, depression scores and quality of life scores is missing for the control group.
 - Contacted E. Kouidi at Lab of Sports Medicine, Aristotle University of Thessaloniki, Greece for clarification of methods and results, but the data is missing

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Kouidi 2009

Methods	<ul style="list-style-type: none"> • Recruitment: Renal units of the American Hellenic Educational Progressive Association University Hospital and the General Clinic of Thessaloniki in Greece • Study design: Parallel group RCT • ITT analysis: No
Participants	Inclusion criteria <ul style="list-style-type: none"> • Country: Greece, USA • Setting: Multicentre • HD thrice weekly for at least 6 months; in sinus rhythm and able to reach sufficient workload during ergometry (definition for 'sufficient workload' NS) • Hb (mean \pm SD mmol/L): Treatment group (11.0 \pm 0.7); control group (11.0 \pm 0.5) • Duration of HD (mean \pm SD years): Treatment group (6.3 \pm 3.7); control group (6.2 \pm 3.9) • Frequency of HD (times/week): 3 • Duration of HD (hours): 4 • Number: 63 randomised • Age (mean \pm SD years): Treatment group (55 \pm 9); control group (53 \pm 6) • Ethnicity: NS • Sex (M/F): Treatment group (18/12); control group (16/13)

Kouidi 2009 (Continued)

	<p>Exclusion criteria</p> <ul style="list-style-type: none"> • Bundle branch block; unstable hypertension; DM; severe congestive heart failure; recent myocardial infarction; unstable angina
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Supervised exercise <ul style="list-style-type: none"> ◦ 10 months intra-dialytic mixed cardiovascular and resistance training program. Three times weekly under supervision and for 90 minutes each time during the first 2 hours of HD sessions. Intensity 60-70% of maximum heart rate. 10 minutes warm-up, 40 minutes intra-dialytic cycling, then 30 minutes strengthening and flexibility exercises for the abdomen and lower limbs (3 sets of 15 reps for each exercise, and finally 10 minutes cool-down. <p>Control group</p> <ul style="list-style-type: none"> • No intervention <p>Follow-up assessment</p> <ul style="list-style-type: none"> • End of the intervention period: 10 months • End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> • Peak oxygen consumption • Left ventricular mass index • SD of the normal RR intervals (SDNN) • Mean RR interval <p>Not relevant to our study</p> <ul style="list-style-type: none"> • Left ventricular ejection fraction; mean 24-h heart rate; LF/HF ratio; signal-averaged electrocardiogram
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: 167 ◦ Enrolled/randomised: 74/63; treatment group (32); control group (31) ◦ Analysed: Treatment group (30); control group (29) ◦ Per cent followed: Treatment group (94); control group (94) • Compliance: Treatment group (88.3%) • Similarity between groups at baseline: Yes <p>From the same study 60 patients volunteered to participate in an included substudy where baroreflex sensitivity was primary outcome measure. They measured this after 7 months but the original study continued for 10 months as presented in the article by Kouidi 2009. Data concerning blood pressure and heart rate has been extracted from Petraki's article.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation by lot
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias)	High risk	Not blinded

Kouidi 2009 (Continued)

Participants

Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Lee 2001

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> • Country: Korea • Setting: NS • Undergoing HD • Hb (mmol/L): NS • Duration of HD (years): NS • Frequency of HD (times/week): NS • Duration of HD (hours): NS • Number: 46 randomised • Age: NS • Ethnicity: NS • Sex (M/F): NS <p>Exclusion criteria: NS</p>
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Supervised exercise <ul style="list-style-type: none"> ◦ 3 months cardiovascular exercise training 2 or 4 times a week for a total exercise time of 10-40 min per session. ◦ Intensity NS ◦ Supervision: NS <p>Control group</p> <ul style="list-style-type: none"> • No intervention <p>Follow-up assessment</p> <ul style="list-style-type: none"> • End of the intervention period: 3 months
Outcomes	Relevant to our study

Lee 2001 (Continued)

- Serum lipid profiles
- Physical work capacity
- Physical fitness

Not relevant to our study: none

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (25); control group (21)
 - Analysed: NS
 - Per cent followed: NS
- Compliance: NS
- Similarity between groups at baseline: NS

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias) Participants	Unclear risk	NS
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	High risk	High risk of attrition bias (C)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

Leehey 2009
Methods

- Recruitment: NS
- Study design: Parallel group RCT
- ITT analysis: No

Participants
Inclusion criteria

- Country: USA
- Setting: Single centre
- CKD stages 2-4; body mass index (≥ 30), proteinuria; treatment with ACEi or ARB, aspirin and statin (if low density lipoprotein >100)
- Hb (mean \pm SD g/dL): Treatment group (12.7 ± 2.1); control group (11.8 ± 1.9)

Leehey 2009 (Continued)

- GFR (mL/min/ 1.73 m²): NS
- Number: 13 randomised
- Age (median, range): 66 years (55-81)
- Ethnicity: NS
- Sex (M/F): All male

Exclusion criteria

- hyperparathyroidism/osteoporosis; symptomatic neuropathy/retinopathy; positive stress test due to coronary arterial disease; symptomatic cardiovascular disease; congestive heart failure (NYHD class >II); chronic obstructive pulmonary disease; cerebrovascular disease/cognitive impairment; inability to walk on treadmill, illness or disability that would preclude exercise testing and training; participation in a formal exercise program within the previous 12 weeks

Interventions

Treatment group

- Supervised and unsupervised mixed intensity program
 - Supervised (6 weeks), mixed intensity walking program followed by 18 weeks unsupervised, mixed intensity walking program and the goal to increase step count by 10% each week. Three-five min warm-up, range of motion exercises, interval walking, cool-down and post-exercise range-of-motion exercises. Total exercise time began at 30 min and gradually increased by 5 min every two weeks.

Control group

- Maintain usual, mostly sedentary lifestyle

Follow-up assessment

- Median intervention time in the treatment group was 18 weeks (range 8-28) and in the control, group 20 months (range 10-30).
- End of intervention data has been used.

Outcomes

Relevant to our study

- VO₂ max
- Blood pressure
- Heart rate
- Total cholesterol
- Triglyceride
- LDL cholesterol
- HDL cholesterol
- Calorie intake
- Body weight
- Fat weight
- Lean weight

Not relevant to our study

- Kidney function parameters

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 20
 - Enrolled/randomised: Treatment group (7); control group (6)
 - Analysed: Treatment group (7); control group (4)
 - Per cent followed: Treatment group (100); control group (57)
- Compliance: NS
- Similarity between groups at baseline: Yes

Leehey 2009 (Continued)

- Missing data: None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	2x2 block randomisation scheme
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	High risk	No blinded outcome assessors
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Matsumoto 2007

Methods	<ul style="list-style-type: none"> • Recruitment: Sawada Dialysis centre • Study design: Parallel group RCT • ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> • Country: Japan • Setting: Single centre • HD for more than three years and taking standard medications • Hb (mean \pm SD mmol/L): Treatment group (11 ± 1); control group (11 ± 1) • Duration on HD (mean \pm SD years): Treatment group (12 ± 7); control group (13 ± 8) • Frequency of HD (times/week): 3. • Duration of HD session (hours): 4. • Number: 55 randomised. • Age (mean \pm SD years): Treatment group (61 ± 10); control group (57 ± 8) • Ethnicity: NS • Sex (M/F): Treatment group (5/12); control group (15/17) <p>Exclusion criteria</p> <ul style="list-style-type: none"> • Chronic lung disease; current ischaemic heart disease; uncontrolled arrhythmias or hypertension; haemodynamic instability; inability to pedal a stationary cycle; Hb < 85 mmol/L; albumin levels > 40 mg/dL

Matsumoto 2007 (Continued)

Interventions	Treatment group <ul style="list-style-type: none"> • Supervised cardiovascular exercise training <ul style="list-style-type: none"> ◦ 3 times/week (prior to every dialysis session) with the intensity of 60-70% of peak heart rate. ◦ Duration/session: 20 minutes Control group <ul style="list-style-type: none"> • No intervention Follow-up assessment <ul style="list-style-type: none"> • End of intervention: 12 months
Outcomes	Relevant to our study <ul style="list-style-type: none"> • Albumin • Health-related quality of life Not relevant to our study <ul style="list-style-type: none"> • Creatinine generation rate
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: Treatment group (22); control group (33) ◦ Analysed: Treatment group (17); control group (32) ◦ Per cent followed: Treatment group (77); control group (97) • Compliance: NS • Similarity between groups at baseline: Yes, with the exception of BP and RE on the SF-36 scale where the control group had higher BP scores and RE scores at baseline. • Missing data <ul style="list-style-type: none"> ◦ Mean and SD for serum albumin and health-related quality of life at end of interventions missing. Data is only presented in a figure. ◦ As no exact data is available the study has been included in the review but not in the meta-analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS
Blinding (performance bias and detection bias) Participants	High risk	No
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)

Matsumoto 2007 (Continued)

Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Molsted 2004

Methods	<ul style="list-style-type: none"> Recruitment: Dialysis Centre at University Hospital of Copenhagen, Rigshospitalet, Denmark Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Denmark Setting: Single centre > 18 years; treated by HD for more than 3 months Hb (median, range; mmol/L): Treatment group (118; 103-127), control group (122; 97-129) Duration on HD (years): Treatment group (2); control group (1.5). Frequency of HD (times/week): NS Duration of HD session (hours): NS Number: 33 randomised Age (median, range; years): Treatment group (59; 25-58); control group (48; 23-58) Ethnicity: NS Sex (M/F): Treatment group (14/8); control group (8/3) <p>Exclusion criteria</p> <ul style="list-style-type: none"> DM, symptomatic heart disease; orthopaedic limitations; severe peripheral polyneuropathy; dementia; participation in other studies with the risk of affecting the results; inability to speak either Danish or English excluded patients from the entire study whereas those patients able to speak English were only excluded from the questionnaire
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Exercise training 1 hour, twice a week for a period of 5 months. <ul style="list-style-type: none"> The programme consisted of 10 min warm-up, 20-30 min strength and aerobic exercises like step and circuit training, high and low impact aerobics and 15-20 min spin at variable intensity. Intensity: 14-17 using Borg's RPE. The spin included at least 9 times of spin in 20 s on an intensity as 17 on the Borg scale. The session was concluded by 5-10 min stretching and cooling down. In the first two months the intensity was adjusted every other week and thereafter every second week. <p>Control group</p> <ul style="list-style-type: none"> No exercise intervention <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 5 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> Health-related quality of life Physical functioning

Molsted 2004 (Continued)

- VO2 max
- Blood pressure
- Lipids

Not relevant to our study: None

Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: 100 ◦ Enrolled/randomised: Treatment group (22); control group (11) ◦ Analysed: Treatment group (11); control group (9) ◦ Per cent followed: Treatment group (50); control group (82) • Compliance: 74% • Similarity between groups at baseline: Yes • Missing data <ul style="list-style-type: none"> ◦ It was not been possible to use data from the study in the meta analysis, as all data in the study are presented as median (range) and not mean \pm SD. Contacted primary investigator to clarify whether the data has been skewed or if they can provide information about mean \pm SD of all outcome measures, but without result. Data from the study were presented separately under the heading 'Results from studies included in the systematic review but excluded from the meta-analysis'.
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The patients were randomly assigned to either an exercise- or a control group (ratio 2:1), however method not stated
Allocation concealment (selection bias)	Low risk	Envelope method
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Low risk	All tests were carried out by blinded testers.
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	Low risk	Low risk of detection bias (A)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Ouzouni 2009

Methods	<ul style="list-style-type: none"> • Recruitment: NS • Study design: Parallel group RCT • ITT analysis: No
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Participants	Inclusion criteria
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Ouzouni 2009 (Continued)

- Country: Greece
- Setting: NS
- >18 years; treated by HD 3 days/week, 4 hours/session for at least 4 months
- Hb (mmol/L): NS
- Duration on HD (years): Treatment group (2); control group (1.5)
- Frequency of HD (times/week): NS
- Duration of HD session (mean \pm SD hours): Treatment group (7.7 \pm 7.0); control group (8.6 \pm 6.0)
- Number: 35 randomised
- Age (mean \pm SD years): Treatment group (47 \pm 16); control group (51 \pm 12)
- Ethnicity: NS
- Sex (M/F): Treatment group (14/5); control group (13/1)

Exclusion criteria

- Unstable hypertension; heart failure (NYHA class >II); cardiac arrhythmias (>III according to Lown); recent myocardial infarction or unstable angina; DM; active liver disease or orthopaedic problems limiting exercise

Interventions

Treatment group

- Supervised, high intensity, mixed cardiovascular and resistance training
 - 3 times/week for 10 months. 60-90 minutes duration each session.
 - Cycling: 5 min warm-up, 20 min at desired workload and 5 min cool-down.
 - Resistance training design included the abdominal and lower limbs. Therabands were used.
 - No information concerning number of repetitions, sets.

Control group

- No exercise intervention

Follow-up assessment

- End of the intervention period: 10 months
- End of intervention data has been used.

Outcomes

Relevant to our study

- Health-related quality of life
- VO₂ peak
- Exercise time
- METs
- Heart rate maximum
- Blood pressure
- Depression

Not relevant to our study

- double product; maximum pulmonary ventilation

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: 35
 - Analysed: Treatment group (19); control group (14)
 - Per cent followed: Treatment group (95); control group (95)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: None

Ouzouni 2009 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk of selection bias (C)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Painter 2002a

Methods	<ul style="list-style-type: none"> Recruitment: University Hospital Study design: Parallel group RCT ITT analysis: Yes
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: Single centre Kidney transplantation within 2 months Hb (mean \pm SD g/dL): Treatment group (113 \pm 17); control group (116 \pm 16) Number: 167 randomised (54% of the eligible patients) Age (mean \pm SD years): Treatment group (39.7 \pm 12.6); control group (43.7 \pm 10.7) Ethnicity (White/African American/Latino/Asian/other): Treatment group (27/6/12/0/4); control group (20/6/10/4/3) Sex (M/F): Treatment group (30/24); control group (30/13) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Transplant rejection or psychiatric or neurologic disorder that would preclude exercise testing or training; unavailable for regular follow-up; any absolute contraindications to exercise testing as established by the American Heart Association or the American College of Sports Medicine; or any medical complications that would prevent regular participation
Interventions	Treatment group

Painter 2002a (Continued)

- Independent home-based exercise, including cardiovascular exercise (primary walking or cycling) with a frequency of at least 4 times/week, a duration that worked up to at least 30 min/session, and an intensity that was initially 60-65% of maximum heart rate and gradually (~ every 2 weeks) increased to 75-80% of maximum heart rate.
- Every other week adherence was measured through exercise logs and telephone follow-up.

Control group

- Usual care

Follow up assessment

- During the study: 6 months
- End of the intervention period: 12 months
- End of intervention (12 months) data has been used.

Outcomes	Relevant to our study <ul style="list-style-type: none"> • VO2 peak • % age-predicted VO2 peak • Peak torque • Peak torque/body wt. • Fat mass • Health-related quality of life. Not relevant to our study <ul style="list-style-type: none"> • Peak respiratory exchange ratio; bone mineral density
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: 257 ◦ Enrolled/randomised: Treatment group (83); control group (84) ◦ Analysed: Treatment group (54); control group (43) ◦ Per cent followed: Treatment group (64); control group (51) • Compliance: 58% at 6 months and 67% at 12 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate. Randomisation was performed using a restricted randomisation procedure, which was managed using prepared sealed envelopes containing a card indicating the allocated treatment group. After the baseline testing, the next envelope was opened.
Allocation concealment (selection bias)	Low risk	Sealed envelopes containing a card indicating the allocated treatment (A)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Low risk	Low risk of selection bias (A)

Painter 2002a (Continued)

Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Painter 2002b

Methods	<ul style="list-style-type: none"> Recruitment: five dialysis clinics (5) Study design: Parallel 4-group RCT ITT analysis: Yes, but only for VO2 peak
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: Single centre ≥ 18 years; CKD, been treated with HD for at least 3 months; mean HCT 30% ± 3% for 4 weeks prior to study enrolment Hb (mean ± SD g/dL): Treatment group 1 (10.4 ± 0.6); treatment group 2 (10.5 ± 1.5); control group 1 (10.6 ± 0.8); control group 2 (10.5 ± 0.7) Duration on HD (mean ± SD months): Treatment group 1 (23.1 ± 24.6); Treatment group 2 (60.4 ± 80.0); control group 1 (61.8 ± 72.9); control group 2 (67.8 ± 54.4) Frequency of HD (times/week): NS Duration of HD session (hours): NS <ul style="list-style-type: none"> Authors have reported dialysis regimen (mean ± SD min/week): Treatment group 1 (421 ± 80); Treatment group 2 (582 ± 73); control group 1 (534 ± 104); control group 2 (531 ± 100) Number: 65 randomised Age (mean ± SD years): Treatment group 1 (47.6 ± 11.9); treatment group 2 (43.5 ± 10.5); control group 1 (43.3 ± 9.8); control group 2 (50.1 ± 13.8) Ethnicity: NS Sex (M/F): Treatment group 1 (5/5); treatment group 2 (5/7); control group 1 (6/8); control group 2 (5/7) <p>Exclusion criteria</p> <ul style="list-style-type: none"> musculoskeletal problems that would prevent exercise testing or training; current evidence of ischaemic heart disease
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Usual HCT (30-33%) plus exercise training <p>Treatment group 2</p> <ul style="list-style-type: none"> Normalised HCT (40-42%) plus exercise training <p>Control group 1</p> <ul style="list-style-type: none"> Usual HCT (30-33%) with no exercise training <p>Control group 2</p> <ul style="list-style-type: none"> Normalised HCT (40-42%) with no exercise training <p>Co-interventions</p>

Painter 2002b (Continued)

- HCT management: EPO was administered by a dialysis nurse intravenously 3 times/week according to the randomisation groups.

Exercise training

- Performed during the HD treatment by using a stationary cycle. Patients started with 10-15 minutes of no-resistance exercise and progressed by increasing the duration by 2-3 minutes per session until they achieved a goal of 30 minutes continuous cycling.
- Intensity: RPE 12-14 and 70% of peak heart rate
- Intervals of 2-3 minutes of more intense exertion (RPE of 15-17) were interspersed throughout the session once 20 minutes of continuous cycling was tolerated.
- All exercise training was supervised.

Follow-up assessment

- End of intervention period: 5 months
- End of intervention data has been used.

Outcomes	Relevant to our study <ul style="list-style-type: none"> • VO₂ peak • Physical functioning • Health-related quality of life • Heart rate maximum Not relevant to our study <ul style="list-style-type: none"> • HCT; Hb; EPO dose; respiratory exchange ratio; blood pressure maximum
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: 65 ◦ Analysed: 48; the ITT-analysis includes all 55 patients who had at least 1 post-baseline measurement ◦ Per cent followed: 74 • Compliance: NS • Similarity between groups at baseline: Yes • Missing data <ul style="list-style-type: none"> ◦ Data concerning health related quality of life. Contacted primary investigator for clarification, but the data is missing. ◦ SF-36 total scores and scores from the SF-36 PF scale. Contacted primary author for clarification of results, but she does not have the data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was stratified by age (< 50 versus ≥ 50) and sex. No further description of the randomisation method is reported.
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias)	Unclear risk	NS

Painter 2002b (Continued)

Outcome assessors

Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of selection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Painter 2003

Methods	<ul style="list-style-type: none"> Recruitment: University Hospital Study design: Parallel group RCT ITT analysis: Yes
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: USA Setting: single centre study. Within 1 month of kidney transplantation Hb concentration (g/dL): NS Number: 96 randomised Age (mean \pm SD years): Treatment group (39.7 \pm 12.6); control group (43.7 \pm 10.6) Ethnicity: NS Sex (M/F): Treatment group 29/22; control group 31/14 <p>Exclusion criteria</p> <ul style="list-style-type: none"> transplant rejection; psychiatric or neurological disorder that would preclude participation; orthopaedic limitations that would preclude exercise training; lack of availability for regular follow-up; any absolute contraindications to exercise testing, established by the American Heart Association or the American College of Sports Medicine; or any medical complications that would prevent regular participation
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Independent home-based exercise, including cardiovascular exercise (primary walking or cycling) with a frequency of at least 4 times/week, a duration that worked up to at least 30 min/session, and an intensity that was initially 60-65% of maximum heart rate and gradually (~every 2 weeks) increased to 75-80% of maximum heart rate. Every other week adherence was measured through exercise logs and telephone follow-up. <p>Control group</p> <ul style="list-style-type: none"> Usual care <p>Follow up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 12 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> Blood pressure

Painter 2003 (Continued)

- Cholesterol
- Maximum METs

Not relevant to our study

- Total cardiovascular disease risk

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (51); control group (45)
 - Analysed: Treatment group (51); control group (45)
 - Per cent followed: Treatment group (100); control group (100)
- Compliance: NS
- Similarity between groups at baseline: Yes
- Missing data: None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Adequate. Randomisation was performed using a restricted randomisation procedure, which was managed using prepared sealed envelopes containing a card indicating the allocated treatment group. After the baseline testing, the next envelope was opened.
Allocation concealment (selection bias)	Low risk	Prepared sealed envelopes containing a card indicating the allocated treatment group (A)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Parsons 2004
Methods

- Recruitment: Kingston General Hospital Burr Wing satellite dialysis unit
- Study design: Parallel group RCT
- ITT analysis: No

Participants

- Inclusion criteria
- Country: Canada

Parsons 2004 (Continued)

- Setting: Single centre
- Self-care HD patients
- Hb (mean \pm SD g/dL): Treatment group (119 \pm 9); control group (110 \pm 17)
- Duration on HD (mean \pm SD months): Treatment group (25 \pm 25); control group (49 \pm 26)
- Frequency of HD (times/week): 3
- Duration of HD session (hours): approximately 4
- Number: 18 randomised
- Age (mean \pm SD years): Treatment group (60 \pm 17); control group (49 \pm 25)
- Ethnicity: NS
- Sex (M/F): Treatment group (3/3); control group (4/3)

Exclusion criteria

- Cardiovascular, neurological or orthopaedic impairment which would preclude the ability to exercise during the 8-week protocol

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Three 15-minutes bouts of ergometer cycling at an intensity of 40-50% of their maximum workload. This was done during each of the first 3 hours of dialysis. If improvements in work capacity were observed at week 4 of the study, the exercise intensity (40-50% of maximum workload) was increased accordingly for the remainder of the exercise program. <p>Control group</p> <ul style="list-style-type: none"> • Continued with their normal dialysis regimen and were asked to complete an activity log on a weekly basis <p>Co-interventions</p> <ul style="list-style-type: none"> • EPO therapy was only changed as needed <p>Follow-up assessment</p> <ul style="list-style-type: none"> • End of intervention period: 12 weeks • End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> • Maximal work capacity • Resting blood pressure • Health-related quality of life <p>Not relevant to our study</p> <ul style="list-style-type: none"> • Blood urea clearance; dialysate urea clearance
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: NS ◦ Enrolled/randomised: 18 ◦ Analysed: Treatment group (6); control group (7) ◦ Per cent followed: 72% • Compliance: NS. • Similarity between groups at baseline: Yes • Missing data <ul style="list-style-type: none"> ◦ Resting systolic and diastolic blood pressure post exercise training intervention for both the exercise group and the control group. • As the EPO therapy was changed as needed the study has been included in the comparison between 'exercise training + EPO' versus control + EPO'

Parsons 2004 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS; Patients were matched according to age, maximal work capacity and protein catabolic rate
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

PEAK Study 2005

Methods	<ul style="list-style-type: none"> Recruitment: All patients attending the dialysis unit on a regular basis were evaluated for eligibility between October 2002 and July 2005 Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Australia Setting: Single centre ≥ 18 years; HD for > 3 months; willingness to be randomised and to undergo study protocol Hb concentration (g/L): NS Duration on HD (median, range years): Treatment group (3.3, 0.3-16.7); control group (1.6, 0.6-10.3) Frequency of HD (times/week): NS Duration of HD session (min): NS Number: 49 randomised Age (mean ± SD years): Treatment group (60.0 ± 15.3); control group (65.0 ± 12.9) Ethnicity: NS Sex (M/F): Treatment group (17/7); control group (17/8) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Acute or chronic medical condition precluding exercise training or collection of outcome measures; not able to walk ≥ 50 metres with or without an assistive device; Kt/V < 1.2 and unstable during dial-

PEAK Study 2005 (Continued)

ysis; cognitive dysfunction or language difficulties making it hard for patient to understand research procedures and to provide written informed consent

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Supervised progressive resistance training during HD treatment. Intensity: high (15-17 on the Borg RPE-scale) Sets: 2. Reps: 8/set Frequency: 3 times/week Duration: NS <p>Control group</p> <ul style="list-style-type: none"> Provided usual care but no instructions to exercise or access to equipment <p>Follow up assessment</p> <ul style="list-style-type: none"> End of the intervention period: 3 months End of intervention data has been used.
Outcomes	<p>Related to our study</p> <ul style="list-style-type: none"> CRP Muscular strength Cross sectional muscle fibre area Health-related quality of life Physical performance <p>Not related to our study</p> <ul style="list-style-type: none"> BMI
Notes	<ul style="list-style-type: none"> Completeness of follow-up <ul style="list-style-type: none"> Eligible/considered for inclusion: 77 Enrolled/randomised: Treatment group (24); control group (25) Analysed: Treatment group (20); control group (24) <ul style="list-style-type: none"> Baseline data carried forward and included in analysis giving treatment group (24); control group (25) Per cent followed: Treatment group (83); control group (96) Compliance: 85.1% Similarity between groups at baseline: Yes, but with a trend for a higher proportion of diabetics in the control group and longer time on HD in the treatment group Missing data <ul style="list-style-type: none"> Contacted primary investigator for clarification of method and results. Cheema B. (which is primary investigator has provided data of the completed study (the PEAK study) which are to be published soon. The preliminary findings of the PEAK study are presented in the abstract. The study is now completed, and Cheema et al have recently submitted two manuscripts for peer-review. The author has provided the reviewer with data from the finished study. Depression scale data and Physical functioning (subjective rating from 0 to 100) has not been used in the meta-analysis as the data for mean and SD at end of intervention is missing (only expressed as %-change).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomly-permuted blocks stratified by gender in blocks of four to Exercise training + usual care, or usual care control

PEAK Study 2005 (Continued)

Allocation concealment (selection bias)	Low risk	Adequate (A)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Low risk	Yes for body composition, nutritional status, biochemical measures
Risk of selection bias?	Low risk	Low risk of bias for selection bias (A)
Risk of detection bias?	Low risk	Low risk for detection bias (A)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Segura-Orti 2009

Methods	<ul style="list-style-type: none"> Recruitment: 2 Spanish HD units Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Spain Setting: Multicentre Stable condition under their medication and undertaking HD sessions for at least 3 months Hb (mean \pm SD g/dL): Treatment group (120 \pm 20); control group (123 \pm 80) Duration on HD (mean \pm SD months): Treatment group (37.3 \pm 34.9); control group (53.7 \pm 42.0) Frequency of HD (times/week): 3 Duration of HD session (hours): approximately 4 Number: 27 randomised Age (mean \pm SD years): Treatment group (54 \pm 18); control group (60 \pm 21) Ethnicity: NS Sex (M/F): Treatment group (11/6); control group (7/1) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Recent myocardial infarction (6 weeks); uncontrolled hypertension; malignant arrhythmias; unstable angina and any disorder that could be exacerbated by physical activity
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 6 months supervised, high intensity, intra-dialytic resistance training. Frequency: 3 times/week; 15 reps and 1 set <p>Control group:</p> <ul style="list-style-type: none"> Placebo exercise <p>Follow-up assessment</p>

Segura-Orti 2009 (Continued)

- end of intervention period: 6 months
- End of intervention data has been used.

Outcomes	Relevant to our study <ul style="list-style-type: none"> • Aerobic capacity • Muscular strength • Physical functioning • Health-related quality of life Not relevant to our study: None
Notes	<ul style="list-style-type: none"> • Completeness of follow-up <ul style="list-style-type: none"> ◦ Eligible/considered for inclusion: 59 ◦ Enrolled/randomised: Treatment group (19); control group (8) ◦ Analysed: Treatment group (17); control group (8) ◦ Per cent followed: Treatment group (89); control group (100) • Compliance: Treatment group (80%), control group (88%) • Similarity between groups at baseline: Yes • Missing data: None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Table of random numbers, stratified by age and gender
Allocation concealment (selection bias)	Low risk	Adequate (A)
Blinding (performance bias and detection bias) Participants	Low risk	Control group: placebo exercise
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	Unclear risk	Moderate risk of detection bias (C)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

Toussaint 2008

Methods	<ul style="list-style-type: none"> • Recruitment: a satellite HD unit • Study design: Parallel group RCT • ITT analysis: No
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Toussaint 2008 (Continued)

Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Australia Setting: Single centre HD treatment > 3 months; able to give informed consent; able or willing to commit to regular exercise for 3 months Hb (mmol/L): NS Duration on HD (mean \pm SD months): Treatment group (35 \pm 31); control group (72 \pm 56) Frequency of HD (times/week): 3 Duration of HD session (hours): 4-5 Number: 20 randomised Age (median, range years): Treatment group (67, 60-83); control group (70, 28-77) Ethnicity: NS Sex (M/F): Treatment group (5/4); control group (4/6) <p>Exclusion criteria</p> <ul style="list-style-type: none"> Active or symptomatic cardiovascular or respiratory disease; musculoskeletal abnormalities that limited exercise ability
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Unsupervised, cardiovascular, intra-dialytic exercise for 30 minutes at each HD session Intensity NS Duration: 3 months <p>Control group</p> <ul style="list-style-type: none"> No exercise intervention <p>Follow-up assessment</p> <ul style="list-style-type: none"> End of intervention: 3 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> Blood pressure Albumin <p>Not relevant to our study</p> <ul style="list-style-type: none"> Augmentation index; brain-natriuretic peptide; pulse pressure; pulse wave velocity
Notes	<ul style="list-style-type: none"> Completeness of follow-up <ul style="list-style-type: none"> Eligible/considered for inclusion: NS Enrolled/randomised: 20 Analysed: Treatment group (9), control group (10) Per cent followed: Treatment group (100), control group (100) Compliance: Treatment group (88%) Similarity between groups at baseline: Yes Since data concerning exercise intensity is missing, the study has not been included in the meta-analysis investigating the difference in effect between high and low intensity exercise.
Risk of bias	
Bias	Authors' judgement Support for judgement

Toussaint 2008 (Continued)

Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding (performance bias and detection bias) Participants	High risk	Not blinding
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	Unclear risk	Moderate risk of selection bias (B)
Risk of detection bias?	High risk	High risk of detection bias (C)
Risk of attrition bias?	Unclear risk	Moderate risk of attrition bias (B)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B).

Tsuyuki 2003

Methods	<ul style="list-style-type: none"> Recruitment: NS Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Japan Setting: NS Regular HD treatment Hb (mean \pm SD g/L): Treatment group (77 ± 0); control group (75 ± 10) Duration on HD (mean \pm SD years): Treatment group (2.1 ± 2.5); control group (2.7 ± 2.6) Frequency of HD (times/week): NS Duration of HD session (min): NS Number: 29 randomised Age (mean \pm SD years): Treatment group (40.1 ± 11.9); control group (39.7 ± 10.7); ≥ 65 years (41%) Ethnicity: NS Sex (M/F): Treatment group (9/8); control group (5/7) <p>Exclusion criteria</p> <ul style="list-style-type: none"> hypertension ($>170/110$ mm Hg); anaemia ($< 18\%$ of HCT); weight gain (< 3.0 kg); heart disease; liver dysfunction; DM; chronic obstructive pulmonary disease
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> On non-dialysis days, the patients underwent a combination training of cycling, walking and jogging for 30 minutes under supervision. The intensity was: 50-60% of the peak heart rate. Frequency of exercise training: 2-3 times/week

Tsuyuki 2003 (Continued)

Control group

- No exercise training

Follow up assessment

- End of the intervention period: 5 months
- End of intervention data has been used.

Outcomes

Related to our study

- VO2 peak
- Heart rate
- Blood pressure

Not related to our study

- Minute ventilation; carbon dioxide output; respiratory ratio; tidal volume; anaerobic threshold

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: NS
 - Enrolled/randomised: Treatment group (17); control group (12)
 - Analysed: Treatment group (17); control group (12)
 - Per cent followed: Treatment group (100); control group (100)
- Compliance: NS
- Similarity between groups at baseline: NS
- Missing data: Contacted K Tsuyuki at Laboratory of Exercise Physiology, Odawara Cardiovascular Hospital, Odawara for clarification of methods, but without result.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	NS
Risk of selection bias?	High risk	High risk for selection bias
Risk of detection bias?	High risk	High risk for detection bias
Risk of attrition bias?	Unclear risk	Moderate risk for attrition bias
Total risk of bias: A (low), B (moderate/unclear), or C (high)	High risk	High, one or more quality criteria not met (C).

van Vilsteren 2005

Methods	<ul style="list-style-type: none"> Recruitment: Dialysis Centre Study design: Parallel group RCT ITT analysis: No
Participants	<p>Inclusion criteria</p> <ul style="list-style-type: none"> Country: Netherlands Setting: Single centre Patients with HD and a sedentary physical activity status according to ACSM criteria Hb (mean \pm SD mmol/L; analysed groups only): Treatment group (7.52 ± 0.85); control group (7.44 ± 0.83) Duration of HD (mean \pm SD years): Treatment group (3.22 ± 4.08); control group (3.90 ± 4.41) Frequency of HD (times/week): NS Duration of HD (hours): NS Number: 103 randomised Age (mean \pm SD years; analysed groups only): Treatment group (52 ± 15); control group (58 ± 16) Ethnicity: NS Sex (M/F; randomised patients only): Treatment group (38/22); control group (30/13) <p>Exclusion criteria:</p> <ul style="list-style-type: none"> Severe cardiovascular disease; use of beta-blockers; unstable angina pectoris; orthopaedic complaints
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Pre-dialysis strength training programme and a cycling (during dialysis) program. <ul style="list-style-type: none"> The strength training program consisted of: a 5-10 min warm-up, 20 min of callisthenics, steps, flexibility and low weight resistance exercises, and a 5-10 min cool down period. The cycling was performed 2-3 times/week for ~20-30 min within the first 2 hours of dialysis. Intensity: 60% of maximal capacity. Motivational interviewing techniques were also used for exercise counselling. The study has been classified as low intensity due to the combination of low-weight exercise training and cycling at 60% of maximal capacity. During the intervention the counsellors met with the patients four times. Duration of intervention: 12 weeks. <p>Control group</p> <ul style="list-style-type: none"> No exercise or exercise counselling <p>Follow up assessment</p> <ul style="list-style-type: none"> End of the observation period: 3 months End of intervention data has been used.
Outcomes	<p>Relevant to our study</p> <ul style="list-style-type: none"> Muscle strength Physical functioning VO2 peak Health-related quality of life Blood pressure Heart rate Cholesterol Depression <p>Not relevant to our study</p>

van Vilsteren 2005 (Continued)

- Kt/V; HCT levels; Hb levels; behavioural change; mean body weight

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 128
 - Enrolled/randomised: Treatment group (60); control group (43)
 - Analysed: Treatment group (53); control group (43)
 - Per cent followed: Treatment group (88); control group (100)
- Compliance: Mean frequency cycling (2.73 ± 0.69), mean frequency resistance training (1.86 ± 0.86)
- Similarity between groups at baseline: Yes
- Missing data: None
- The exercise intervention in this study has used a mix of resistance training with a low intensity and cardiovascular exercise training with an intensity of ~60%. Due to this mix of intensity, the studies exercise training programme has been classified as low intensity mixed cardiovascular- and resistance exercise training in this meta-analysis.
- As the exercise intervention contains both exercise that has been performed pre-dialysis and exercise training that has been performed during dialysis, this study has not been included in the comparison between effects of exercise training performed on non-dialysis days, before dialysis or during dialysis, respectively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NS. Extra patients were randomised into the exercise group to compensate for the effects of drop-out.
Allocation concealment (selection bias)	Unclear risk	NS (B)
Blinding (performance bias and detection bias) Participants	High risk	Not blinded
Blinding (performance bias and detection bias) Outcome assessors	Low risk	Blinded
Risk of selection bias?	Unclear risk	Moderate risk for selection bias (B)
Risk of detection bias?	Low risk	Low risk for detection bias (A)
Risk of attrition bias?	Low risk	Low risk for attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Unclear risk	Moderate, one or more of the quality criteria only partially met (B)

Yurtkuran 2007

Methods

- Recruitment: University dialysis unit
- Study design: Parallel group RCT
- ITT analysis: No

Participants

Inclusion criteria

Yurtkuran 2007 (Continued)

- Country: Turkey
- Setting: Single centre
- HD for at least 6 months (4h/d; 3 times/week); use of analgesic or non-steroid anti-inflammatory drugs and musculoskeletal pain score ≥ 2 on the 0-10 visual analogue scale
- Hb (g/dL): NS
- Duration on HD (median; mean \pm SD months): 10.5; 21.9 \pm 14.2 (all 40 patients)
- Frequency of HD (times/week): 3
- Duration of HD session (hours): 4
- Number: 40 randomised
- Age (mean \pm SD years): Treatment group (38 \pm 14); control group (41 \pm 10)
- Ethnicity: NS
- Sex (M/F): Treatment group (9/11), control group (7/13)

Exclusion criteria

- Unstable hypertension; arrhythmia or cardiac angina after 10 min of fast pedaling; ischaemic cardiac pain; unstable angina; congestive heart failure grade II; significant cardiac valve disease; conduction abnormalities on the electrocardiogram; cerebrovascular disease; electrolyte imbalance; persistent hyperkalaemia before dialysis; DM; active liver disease; arthritic or orthopaedic problems limiting exercise; peripheral vascular disease; 'undisciplined patients'

Interventions
Treatment group

- Supervised, modified yoga exercise (12 weeks)
 - 30 minutes/session, twice/week, intensity progressively increased
 - Intensity: NS
 - Exercises in standing, sitting and lying positions.
 - Yoga exercise postures: ardhha chakrasana; trikonasana; pranayama; nitambasana; uddiyana; paschimothanasana; salabhasana.
 - Relaxation technique
 - Home-based active range of motion exercises once a day for 10 minutes.

Control group

- Home-based active range of motion exercises once a day for 10 minutes.
- No other change in life-style.

Follow-up assessment

- End of exercise intervention: 12 weeks
- End of intervention data has been used.

Outcomes
Relevant to our study

- Grip strength
- Cholesterol
- HDL cholesterol
- Triglyceride

Not relevant to our study

- Pain; fatigue; sleep disturbance; urea; creatinine; calcium; alkaline phosphatase; phosphorus; erythrocyte; HCT

Notes

- Completeness of follow-up
 - Eligible/considered for inclusion: 157
 - Enrolled/randomised: Treatment group (20), control group (20)
 - Analysed: Treatment group (19), control group (18)

Yurtkuran 2007 (Continued)

- Per cent followed: Treatment group (95), control group (90)
- Compliance: 3 patients missed 3 sessions and adhered poorly to the exercise instructions and were therefore excluded.
- Similarity between groups at baseline: Yes
- Missing information: None

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated table of random numbers
Allocation concealment (selection bias)	Low risk	Adequate (A)
Blinding (performance bias and detection bias) Participants	High risk	No
Blinding (performance bias and detection bias) Outcome assessors	Low risk	Yes
Risk of selection bias?	Low risk	Low risk of selection bias (A)
Risk of detection bias?	Low risk	Low risk of detection bias (A)
Risk of attrition bias?	Low risk	Low risk of attrition bias (A)
Total risk of bias: A (low), B (moderate/unclear), or C (high)	Low risk	Low risk of bias (A)

ACEi - Angiotensin converting enzyme inhibitor; ARB - angiotensin receptor blocker; CAPD - continuous ambulatory peritoneal dialysis; CKD - chronic kidney disease; DM - diabetes mellitus; ESKD - end-stage kidney disease; EPO - erythropoietin; GFR - glomerular filtration rate; Hb - haemoglobin; HCT - haematocrit; HD - haemodialysis; ITT - intention-to-treat; NS - not stated; rHuEPO - recombinant human erythropoietin; RPE - rating of perceived exertion; Scr - serum creatinine

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Adams 2006	Not a RCT
Adorati 2000	Not a RCT
Ahn 2000	No control group
Ahn 2001	No control group
Amaral 1999	Not a RCT
Anderson 2001	Not a RCT

Study	Reason for exclusion
Anderson 2004	Wrong study design. Have used a A-B-A design
Anonymous 1998	No exercise intervention
Anonymous 2001	This article is a summary of Castaneda 2001
Antonoff 1988	This article consists of comments on a previously published article on exercise and patients with haemodialysis treatment.
Argani 2001	No control group
Baiardi 2002	No exercise intervention
Bandel 1983	Review
Banerjee 2004	Studied acute response to physical exercise
Bavikati 2008	Studies life style change and not the effects of a specific exercise intervention
Beddhu 2009	No exercise intervention
Bernardi 2005	No exercise intervention
Beto 1998	Review
Biehl 1997	No control group
Biolo 2005	Review
Blagg 1994	No exercise intervention
Bolanos 1993	Review
Boone 1987	Review
Borregaard 2003	Not a RCT
Boyce 1997	Not a RCT
Brawner 1999	Case report
Bronas 2009	Review
Brunier 1993	No exercise intervention
Bullock 1984	No exercise intervention
Burke 1985	No exercise intervention
Cade 1995	Case report
Cade 1997	Case report
Cade 2004	Not a RCT

Study	Reason for exclusion
Capitanini 2008	Not a RCT
Cappy 1999	No control group
Carey 1997	Review
Carlson 1999	No exercise intervention
Carney 1983	Not a RCT
Cashion 2000	Not a RCT
Castaneda 1998	Review
Castellino 1987	Studied acute response to physical exercise
Chan 2007	Review
Cheema 2005a	Review
Cheema 2005b	Review
Cheema 2006	Not a RCT
Chen 2005	Not a RCT
Cheng 2003	Not a RCT
Clark 1996	Studied acute response to maximal physical exercise
Clyne 1991a	Not a RCT
Clyne 1996	Review
Clyne 2004a	Review
Clyne 2004b	Review
Colangelo 1997	Review
Cook 2008	Not a RCT
Copley 1999	No exercise intervention
Copley 2001	No exercise intervention
Cowan 2000	Not a RCT
Cowan 2001	No control group
Cowen 1995	No ESRD control group
Curtin 2002	No exercise intervention
Dasselaar 2004	Not a RCT

Study	Reason for exclusion
Daul 1990	No control group
Daul 2004	Review
Death 1999	No control group
Deligiannis 2002	No exercise intervention
Deligiannis 2004a	Review
Deligiannis 2004b	Review
Derici 2005	No control group
Desmet 2003	No exercise intervention
Donwerth 1994	Review
Endo 1995	No CKD control group
Endo 1996	No control group
Evans 2004	Review
Farese 2008	No exercise intervention
Fatouros 2008	Studied acute effects of single bout exercise
Ferreira 2003	Animal study
Finkelstein 2002	No exercise intervention
Fitts 1996	No exercise intervention
Fitts 1997	Review
Forrest 2004	Not a RCT
Francavilla 2002	Review
Franssen 2002	No exercise intervention.
Fritschka 2000	No exercise intervention
Fritschka 2001	No control group
Fritschka 2003	No control group
Fuhrmann 2004	Review
Fuiano 2004	No exercise intervention
Fulignati 2002	Not a RCT
Furuland 1998	No exercise intervention

Study	Reason for exclusion
Gavin 1982	Not a RCT
Germain 1985	No exercise intervention
Goldberg 1979a	No control group
Goldberg 1979b	No control group
Goldberg 1980a	No control group
Goldberg 1980b	No control group
Goldberg 1984	Review
Golper 1984	Not a RCT
Gonzales 1993	Randomised to exercise or to lovastatin
Gonzales 1996	Randomised to exercise or to lovastatin
Goodman 2004	No exercise intervention
Gordon 2005	Not a RCT
Gordon 2009	Not a RCT
Grant 2004	Not a RCT
Green 1979	Not a RCT
Greinert 1986	Review
Guarnieri 2005	Review
Gültekin 2003	Not a RCT
Habedank 2009	No exercise intervention
Haber 1988	No control group
Hagberg 1983	Not a RCT
Haouzi 1994	Not a RCT
Hase 1983	No exercise intervention
Hauser 1995	No control group
Headley 2002	Not a RCT
Headley 2008	Study of acute response to exercise
Hebbar 2000	No control group
Heiwe 2001a	Not a RCT

Study	Reason for exclusion
Heiwe 2005	Not a RCT
Hensel 1973	Study of acute response to physical exercise
Henson 2010	Not a RCT
Hiramatsu 2003	Not a RCT
Hollis 2005	No control group
Horber 1985	Not a RCT
Hori 1992	Review
Huber 1985	Study of acute response to physical exercise
Hughes 1986	Wrong population (healthy subjects)
Hung 2002	No exercise intervention.
Hung 2003	Not a RCT
Iborra 2000	No exercise intervention
Itoh 1992	No exercise intervention
Jang 2009	Not a RCT
Jassal 1998	Not a RCT
Jassal 2002	No exercise intervention
Jette 1977	Not a RCT
Jindal 2004	Review
Johansen 1999	Review
Johansen 2000	No exercise intervention
Johansen 2003a	No exercise intervention
Johansen 2003b	No exercise intervention
Johansen 2005a	Review
Johansen 2005b	No exercise intervention
Johansen 2007	Review
Johansen 2008	Review
Johansen 2010	Review
Johnstone 2002	Not a RCT

Study	Reason for exclusion
Juskowa 2006	Only 4-5 weeks exercise intervention
Kalevrosoglou 1999	No control group
Kalogerakou 2006	Not a RCT
Karamouzi 2002	Not a RCT
Karamouzis 2009	Not a RCT
Karmiel 1996	No control group
Karmiel 1999	No exercise intervention
Kempeneers 1988	No control group
Kempeneers 1990a	Not a RCT
Kerby 2007	Not a RCT
Kern 2009	Wrong outcome measures
Kesi 2010	Study of acute response to single bout of exercise
Kettner 1982	Review
Kettner 1984a	Study of acute response to physical exercise
Kettner 1984b	Study of acute response to physical exercise
Kielstein 1995	No control group
Kim 1991	Not a RCT
Kirkpatrick 1990	Review
Kiss 2005	Review
Kjaer 1995	Study of acute response to physical exercise
Kjaer 1999	Review
Klang 1997	No exercise intervention
Knap 2005	Review
Kocak 2003	No control group
Kolewaski 2005	Not a RCT
Kong 1999a	Not a RCT
Kong 1999b	Not a RCT
Kontos 2007	Not a RCT

Study	Reason for exclusion
Kopple 2003	No control group
Kopple 2005	Review
Kopple 2007b	Wrong outcome measures
Kosmadakis 2007	Editorial
Kosmadakis 2010	Review
Koufaki 2002b	They have an exercise intervention, but only a healthy control group and no CKD control group.
Kouidi 1998b	No control group
Kouidi 1999	Not a RCT
Kouidi 2000	Has two exercise intervention groups but no control group
Kouidi 2001	Review
Kouidi 2002c	Not a RCT
Kouidi 2002d	Editorial review
Kouidi 2003b	Not a RCT
Kouidi 2004b	RCT with no control group
Kouidi 2004c	Review
Kramer 2006	Review
Krause 1990	No control group
Krause 1993a	No control group
Krause 1993b	Review
Krause 1993c	Not a RCT
Krause 1994	No exercise intervention
Krause 2003a	No exercise intervention
Krause 2003b	No control group
Krause 2004a	No exercise intervention
Krause 2004b	Not a RCT
Krause 2004c	No control group
Kuge 2005	Wrong population (healthy control group)

Study	Reason for exclusion
Kutner 1982	No exercise intervention
Kutner 1992	No exercise intervention
Kutner 1994	No exercise intervention
Kutner 1997	Review
Kutner 2000	No exercise intervention
Kutner 2007	Review
Kutsuna 2010	No exercise intervention
Latos 1987	Study of acute response to physical exercise training
Laville 1995	Review
Leaf 2003a	Wrong type of outcome: the effect of a formal exercise program on the size of native veins.
Leaf 2003b	No control group
Leaf 2004	Not a RCT
Lee 2005	Not a RCT
Leikis 2004	No exercise intervention
Lennon 1986	No control group
Lens 1989	No control group
Leung 1999	Not a RCT
Leung 2000	Not a RCT
Leung 2003	Review
Leung 2004	Study of acute response to physical exercise
Levendoglu 2004	Not a RCT
Ling 2003	No control group
Lisy 1981	Not a RCT
Lo 1998	Not a RCT
Lopez 1990	No exercise intervention
LORD Study 2009	No exercise intervention
Low 2004	No exercise intervention

Study	Reason for exclusion
Lundin 1987	Study of acute response to physical exercise
Lundin 1991	No exercise intervention
MacDonald 2004	Not a RCT
MacDonald 2005	Not a RCT
Macdonald 2009	Review
MacDougal 1998	No exercise intervention
MacLaughlin 2010	Not a RCT
Majchrzak 2008	No exercise intervention
Malagoni 2008	Not a RCT
Mancuso 2002	Not a RCT
Manfredini 2009	Not a RCT
Mao 2002	Not a RCT
Marlowe 2001	Review
Martin 2003	No exercise intervention
Matsuoka 1991	No exercise intervention
Mercer 2002	Not a RCT
Mercer 2003	No control group
Mercer 2004	Review
Miller 1987	No control group
Miller 2002	Not a RCT
Mishkin 1998	No control group
Miskulin 1999	Not a RCT
Miyamura 2000	Review
Moinuddin 2008	Review
Momen 2005	Study of acute response to physical exercise
Moore 1990	Not a RCT
Moore 1993	Not a RCT
Moore 1998	No control group

Study	Reason for exclusion
Morales 2002	No exercise intervention
Moran 1984	No CKD control group
Moros 1993	No exercise intervention
Moros 1995	No control group
Moug 2004	RCT, duration of exercise training intervention was only 6 weeks
Mustata 2004	No control group
Mustata 2005	No control group
Mustata 2007	Not a RCT
Naish 2001	No exercise intervention
Navaneethan 2009	Review
Noakes 1993	Not a RCT
Noviana 2004	Not a RCT
Nowicki 2006	Not a RCT
Nyberg 1995	No exercise intervention
Oberley 1994	No exercise intervention
Oberley 1996	Review
Oberley 2000	Review
Oder 2003	Not a RCT
Oh-Park 2002	No control group
O´Hare 2003	Not an RCT
O´Moore 1999	No exercise intervention
Painter 1983	Review
Painter 1985	Not a RCT
Painter 1986a	No exercise intervention
Painter 1986b	Not a RCT
Painter 1986c	Study of acute response to physical exercise
Painter 1986d	Review
Painter 1987	Wrong type of outcome: have studied compliance to physical exercise training

Study	Reason for exclusion
Painter 1988a	Wrong type of outcome: this report describes average exercise participation rates
Painter 1988b	Review
Painter 1994a	Review
Painter 1994b	Review
Painter 1994c	Case study
Painter 1994d	No exercise intervention
Painter 1995	Review
Painter 1997	Not a RCT
Painter 1998	No exercise intervention
Painter 1999a	Review
Painter 1999b	Review
Painter 1999c	Review
Painter 1999d	Review
Painter 1999e	Not a RCT
Painter 1999f	Not a RCT
Painter 2000a	Not a RCT
Painter 2000b	Not a RCT
Painter 2005	Review
Painter 2006	Not a RCT
Painter 2008	Review
Painter 2009	Book
Pardell 2005	No CKD patients
Park 2008	Study of acute response to single bout exercise
Parrish 1981	Study of acute response to physical exercise
Payne 1972	Study of acute response to physical exercise
Pechter 2003a	Not a RCT
Pechter 2003b	Not a RCT

Study	Reason for exclusion
Pedersen 1986	Study of acute response to physical exercise
Pennell 2004	No control group
Pewen 1990	No control group
Phanish 2003	Not a RCT
Pianta 1999a	Review
Pianta 1999b	No control group
Plentz 2003	No control group
Poortmans 1997	Study of acute response to physical exercise
Poortmans 1998	Review
Price 1996	No control group
Pugh-Clarke 2002	Not a RCT
Pupim 2004	Study of acute response to physical exercise
Qing 1999	No control group
Rehacek 1979	No control group
Richard 2005	No exercise intervention
Richardson 1999a	RCT, exercise intervention period is < 8 weeks
Richardson 1999b	Not a RCT
Ridley 1999	Not a RCT
Rieu 1996	Not a RCT
Rodicio 2001	No exercise intervention
Ronco 1995	Wrong type of outcome measures
Rosales 1998	No control group
Ross 1989	No control group
Rus 2003	No control group
Rössler 1979	No control group
Sabry 2009	No exercise intervention
Sacksteder 2001	Not a RCT
Sadler 1998	No exercise intervention

Study	Reason for exclusion
Sagiv 1988	No exercise intervention
Saitoh 2007	Not a RCT
Sakkas 2003a	No control group
Sakkas 2008	Not a RCT
Sam 1992	RCT, physical exercise training versus physical exercise training plus EPO-treatment, no control group for exercise training
Sam 1993	Not a RCT
Schatell 1999	No exercise intervention
Schrag 1999	No exercise intervention
Segura-Orti 2008	Not a RCT
Segura-Orti 2010	Review
Shalom 1984	No control group
Sharif 2008	No exercise intervention
Shield 2002	No exercise intervention
Sietsema 2004	No exercise intervention
Smith 1981	Not a RCT
Smith 2006	Not a RCT
Smye 1998	A theoretical model
Snyder 1989	No control group
Soffritti 2006	Not a RCT
Solomon 1999	No exercise intervention
Sorensen 1986	Study of acute response to physical exercise
Squires 1985	No control group
Stanley 1989	No exercise intervention
Starky 2005	No exercise intervention
Stefanovic 2005	Review
Stenvinkel 2000	No exercise intervention
Stephens 1991	Not a RCT

Study	Reason for exclusion
Sternweiler 1970	No exercise intervention
Stewart 1981	Review
Stewart 1999	Not a RCT
Stivers 1996	No control group
Storer 1999	No control group
Storer 2005	Not a RCT
Straub 2008	Not a RCT
Suh 2002	No control group
Surgit 2001	No control group
Svarstad 2002	Study of acute response to physical exercise
Svoboda 2004	Not a RCT
Södergård 1991	Not a RCT
Tang 1999	No control group
Tawney 2000	No exercise intervention
Tawney 2003	Review
Tentori 2008	Not a RCT
Tobita 2009	Tests a support programme and not an exercise intervention
Triolo 1989	Not a RCT
Triolo 1991	RCT, physical exercise training in combination with a specific diet (group A) versus a different type of diet and no exercise training (group B).
Tsai 1995	Not a RCT
Tsay 2005	No exercise intervention
Tykarski 2003	No exercise intervention
Tzamaloukas 2003	Not a RCT
Vaithilingam 2004	RCT, wrong outcome measure
van den Ham 2001	Not a RCT
van den Ham 2005	No exercise intervention
van den Ham 2006	Not a RCT

Study	Reason for exclusion
van den Ham 2007	No CKD control group
van Zuilen 2005	No exercise intervention
Violan 2001	No control group
Violan 2002	No control group
Vlcek 1990	Study of acute response to physical exercise training
Wagner 2001	Study of acute response to physical exercise training
Weinberg 1988	Case report
Weissgarten 1998	Animal study
Wellard 2003	No exercise intervention
Wenger 1998	Review
Wiberg 2003	No control group
Williams 1991	Study of factors affecting compliance to physical exercise training, and not effects of physical exercise training.
Winchester 2003	Editorial comment
Wolfe 1985	Not a RCT
Worel 1985	Not a RCT
Yamaka 1984	No control group
Yoshida 2003	Animal study
Young 1993	No exercise intervention
Zabetakis 1982	Not a RCT
Zaluska 2002a	No control group
Zaluska 2002b	No control group
Zamojska 2005	No exercise intervention
Zeier 2001	No exercise training intervention
Zinna 2003	Review

DATA AND ANALYSES

Comparison 1. Any exercise versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	24	847	Std. Mean Difference (IV, Fixed, 95% CI)	-0.56 [-0.70, -0.42]
1.1 at 3 months	7	241	Std. Mean Difference (IV, Fixed, 95% CI)	-0.39 [-0.65, -0.13]
1.2 at 4-6 months	11	268	Std. Mean Difference (IV, Fixed, 95% CI)	-0.81 [-1.08, -0.54]
1.3 ≥ 7-12 months	6	338	Std. Mean Difference (IV, Fixed, 95% CI)	-0.52 [-0.74, -0.30]
2 Muscular strength (high value = improved)	9	358	Std. Mean Difference (IV, Fixed, 95% CI)	-0.52 [-0.73, -0.31]
2.1 at 3 months	5	177	Std. Mean Difference (IV, Fixed, 95% CI)	-0.60 [-0.90, -0.29]
2.2 at 4-6 months	3	86	Std. Mean Difference (IV, Fixed, 95% CI)	-0.53 [-0.97, -0.08]
2.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.78, 0.04]
3 Muscular strength (low value = improved)	3	148	Std. Mean Difference (IV, Fixed, 95% CI)	0.58 [0.25, 0.92]
3.1 3 months	2	123	Std. Mean Difference (IV, Fixed, 95% CI)	0.69 [0.32, 1.05]
3.2 at 4-6 months	1	25	Std. Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.80, 0.88]
3.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60	2	52	Mean Difference (IV, Fixed, 95% CI)	-3.64 [-7.93, 0.65]
4.1 at 3 months	1	27	Mean Difference (IV, Fixed, 95% CI)	-2.80 [-7.89, 2.29]
4.2 at 4-6 months	1	25	Mean Difference (IV, Fixed, 95% CI)	-5.70 [-13.68, 2.28]
4.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Walking capacity	7	191	Std. Mean Difference (IV, Fixed, 95% CI)	-0.36 [-0.65, -0.06]
5.1 at 3 months	4	122	Std. Mean Difference (IV, Fixed, 95% CI)	-0.50 [-0.86, -0.13]
5.2 at 4-6 months	3	69	Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.60, 0.41]
5.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Stair climbing capacity: stair climb test (22 steps)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 ADL capacity	3		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 at 3 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 at 4-6 months	3	87	Std. Mean Difference (IV, Random, 95% CI)	0.05 [-0.39, 0.48]
7.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Diastolic blood pressure: resting	11	419	Mean Difference (IV, Fixed, 95% CI)	2.32 [0.59, 4.05]
8.1 at 3 months	3	144	Mean Difference (IV, Fixed, 95% CI)	-0.88 [-4.58, 2.81]
8.2 at 4-6 months	4	78	Mean Difference (IV, Fixed, 95% CI)	1.39 [-1.78, 4.56]
8.3 ≥ 7-12 months	4	197	Mean Difference (IV, Fixed, 95% CI)	4.37 [1.87, 6.87]
9 Systolic blood pressure: resting	9	347	Mean Difference (IV, Fixed, 95% CI)	5.88 [2.28, 9.48]
9.1 at 3 months	3	144	Mean Difference (IV, Fixed, 95% CI)	6.38 [-1.08, 13.84]
9.2 at 4-6 months	3	49	Mean Difference (IV, Fixed, 95% CI)	10.46 [3.53, 17.40]
9.3 ≥ 7-12 months	3	154	Mean Difference (IV, Fixed, 95% CI)	3.16 [-1.94, 8.27]
10 Heart rate: maximum	11	229	Mean Difference (IV, Fixed, 95% CI)	-6.19 [-10.06, -2.32]
10.1 at 3 months	2	46	Mean Difference (IV, Fixed, 95% CI)	-10.11 [-21.79, 1.57]
10.2 at 4-6 months	8	150	Mean Difference (IV, Fixed, 95% CI)	-6.23 [-11.15, -1.32]
10.3 ≥ 7-12 months	1	33	Mean Difference (IV, Fixed, 95% CI)	-4.5 [-11.93, 2.93]
11 Heart rate: resting	7	179	Mean Difference (IV, Fixed, 95% CI)	3.96 [1.45, 6.48]
11.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	4	78	Mean Difference (IV, Fixed, 95% CI)	2.90 [-2.02, 7.82]
11.3 ≥ 7-12 months	3	101	Mean Difference (IV, Fixed, 95% CI)	4.34 [1.41, 7.27]
12 Albumin	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.1 at 3 months	3	111	Mean Difference (IV, Fixed, 95% CI)	-1.95 [-3.28, -0.62]
12.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13 Pre-albumin	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.1 at 3 months	3	86	Mean Difference (IV, Fixed, 95% CI)	-44.29 [-71.78, -16.79]
13.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 SGA	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
14.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Energy intake	4	97	Std. Mean Difference (IV, Fixed, 95% CI)	-0.47 [-0.88, -0.05]
15.1 at 3 months	3	86	Std. Mean Difference (IV, Fixed, 95% CI)	-0.57 [-1.01, -0.13]
15.2 at 4-6 months	1	11	Std. Mean Difference (IV, Fixed, 95% CI)	0.37 [-0.87, 1.62]
15.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Protein intake	2		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
16.1 at 3 months	2	60	Std. Mean Difference (IV, Fixed, 95% CI)	-0.50 [-1.01, 0.02]
16.2 at 4-6 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Transferrin	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
17.1 at 3 months	2		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
18 Fat mass	5	237	Std. Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.19, 0.34]
18.1 at 3 months	1	36	Std. Mean Difference (IV, Fixed, 95% CI)	-0.26 [-0.92, 0.40]
18.2 at 4-6 months	3	106	Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [-0.30, 0.53]
18.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.24, 0.57]
19 Waist circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
19.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Mid-arm circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
20.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Mid-calf circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
21.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Mid-thigh circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
22.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Interleukin 6	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
23.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Lymphocytes (x 10⁹ L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
24.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Protein catabolic rate	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
25.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

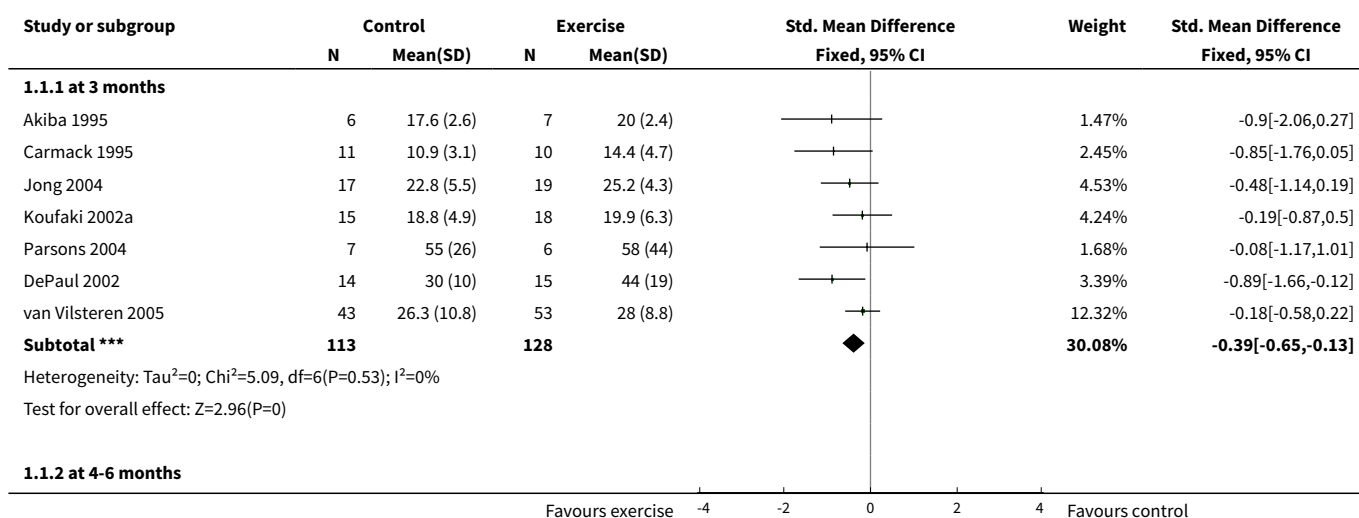
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
26 Physical activity	4	121	Std. Mean Difference (IV, Fixed, 95% CI)	-0.43 [-0.80, -0.05]
26.1 at 3 months	1	33	Std. Mean Difference (IV, Fixed, 95% CI)	-0.33 [-1.02, 0.36]
26.2 at 4-6 months	3	88	Std. Mean Difference (IV, Fixed, 95% CI)	-0.46 [-0.90, -0.02]
26.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
27 Depression	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
27.1 at 3 months	2	117	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.47, 0.89]
27.2 at 4-6 months	1	31	Std. Mean Difference (IV, Random, 95% CI)	0.71 [-0.05, 1.47]
27.3 ≥ 7-12 months	1	33	Std. Mean Difference (IV, Random, 95% CI)	1.99 [1.13, 2.85]
28 Triglycerides	4	100	Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.23, 0.33]
28.1 at 3 months	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.32, 0.32]
28.2 at 4-6 months	1	11	Mean Difference (IV, Fixed, 95% CI)	0.51 [-0.83, 1.84]
28.3 ≥ 7-12 months	2	52	Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.48, 0.81]
29 Total cholesterol	6	292	Mean Difference (IV, Random, 95% CI)	0.17 [-0.12, 0.46]
29.1 at 3 months	2	133	Mean Difference (IV, Random, 95% CI)	0.29 [-0.26, 0.83]
29.2 at 4-6 months	1	11	Mean Difference (IV, Random, 95% CI)	0.47 [-0.46, 1.39]
29.3 ≥ 7-12 months	3	148	Mean Difference (IV, Random, 95% CI)	-0.14 [-0.62, 0.33]
30 HDL cholesterol	4	166	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.23, -0.04]
30.1 at 3 months	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.33, 0.19]
30.2 at 4-6 months	1	11	Mean Difference (IV, Fixed, 95% CI)	-0.21 [-0.38, -0.04]
30.3 ≥ 7-12 months	2	118	Mean Difference (IV, Fixed, 95% CI)	-0.11 [-0.24, 0.02]
31 LDL cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
31.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32 Type I muscle fibre area	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

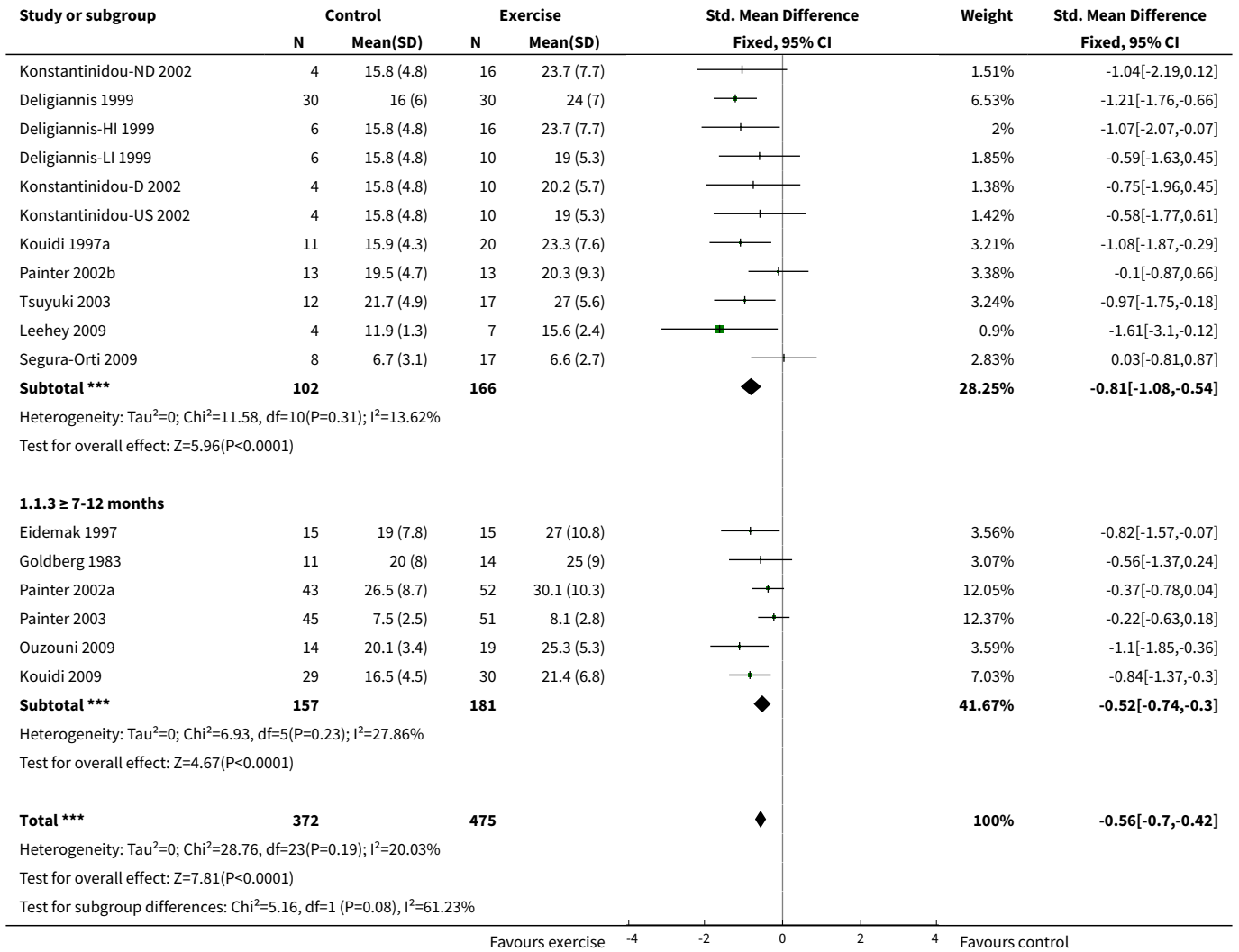
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
32.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
33 Mid-thigh muscle area	4	162	Mean Difference (IV, Fixed, 95% CI)	-7.51 [-11.37, -3.65]
33.1 at 3 months	3	111	Mean Difference (IV, Fixed, 95% CI)	-3.22 [-9.67, 3.24]
33.2 at 4-6 months	1	51	Mean Difference (IV, Fixed, 95% CI)	-9.90 [-14.72, -5.08]
33.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34 Thigh muscle attenuation (Hounsfield units)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
34.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35 HRV index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
35.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
36 Mean cardiac R-R interval	2	119	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.09, -0.02]
36.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
36.2 at 4-6 months	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.10, -0.00]
36.3 ≥ 7-12 months	1	59	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.12, -0.02]
37 SDNN	2	119	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.03, -0.01]
37.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
37.2 at 4-6 months	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.04, -0.00]
37.3 ≥ 7-12 months	1	59	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.03, -0.01]
38 Arrhythmias: Low class > II (no)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
38.1 at 3 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
38.2 at 4-6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
38.3 ≥ 7-12 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
39 Left ventricular internal dimension at end-diastole	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
39.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
39.2 at 4-6 months	2	38	Mean Difference (IV, Fixed, 95% CI)	-1.44 [-4.94, 2.06]
39.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
40 Left ventricular internal dimension at end-systole	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
40.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
40.2 at 4-6 months	2	38	Mean Difference (IV, Fixed, 95% CI)	0.06 [-3.16, 3.27]
40.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
41 Intraventricular septal thickness at end-diastole	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
41.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
41.2 at 4-6 months	2	38	Mean Difference (IV, Fixed, 95% CI)	0.04 [-1.28, 1.36]
41.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
42 Left ventricular posterior wall thickness at end-diastole	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
42.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
42.2 at 4-6 months	2	38	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.93, 1.33]
42.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
43 Left ventricular mass	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
43.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
43.2 at 4-6 months	2	38	Mean Difference (IV, Fixed, 95% CI)	-5.66 [-50.23, 38.91]
43.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
44 Left ventricular mass index	3	97	Mean Difference (IV, Fixed, 95% CI)	-1.77 [-7.26, 3.73]

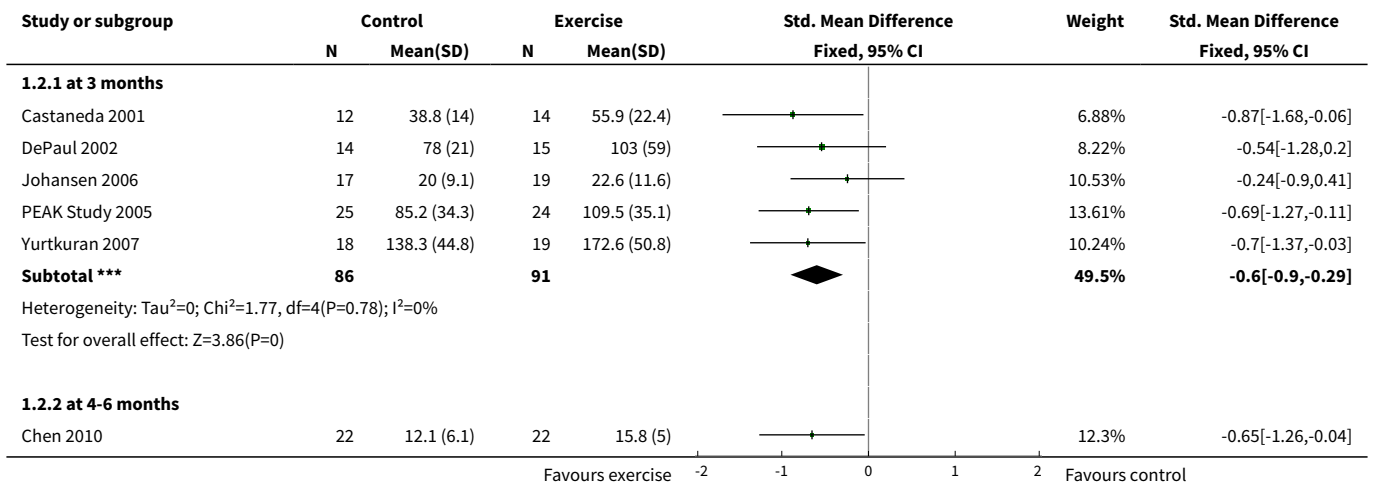
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
44.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
44.2 at 4-6 months	2	38	Mean Difference (IV, Fixed, 95% CI)	-10.44 [-34.79, 13.90]
44.3 ≥ 7-12 months	1	59	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-6.94, 4.34]
45 Fasting plasma glucose	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
45.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
45.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
45.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46 Fasting plasma insulin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
46.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
47 Glucose disappearance	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
47.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
47.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
47.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

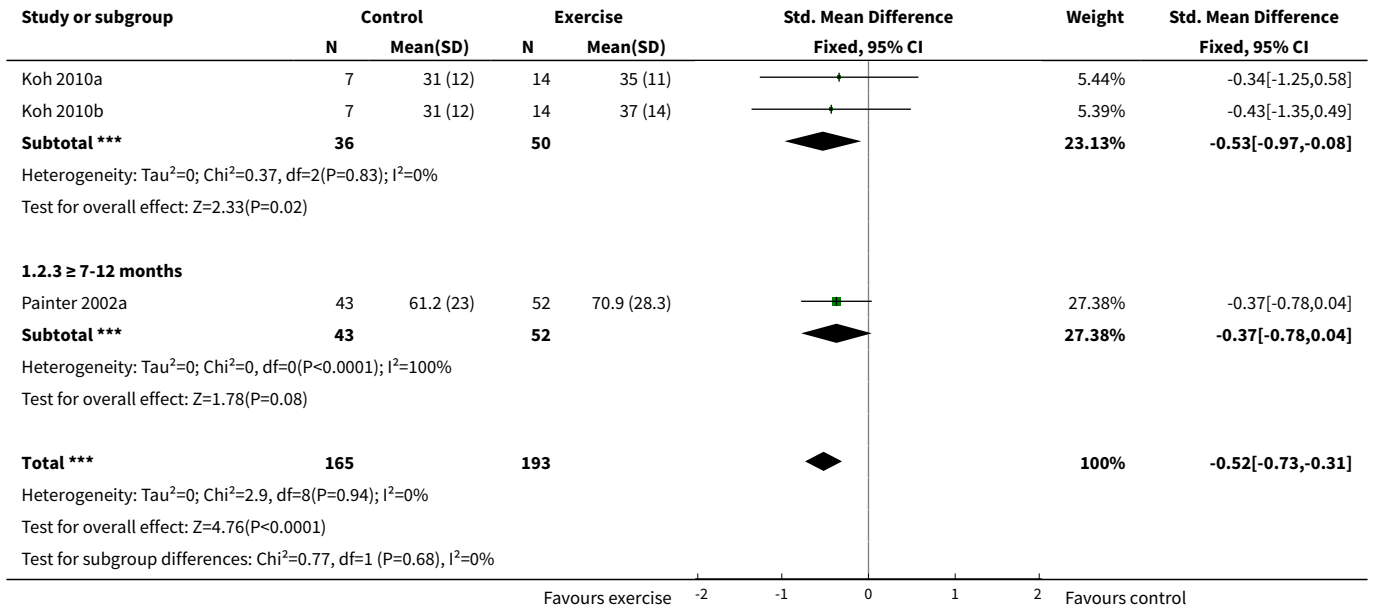
Analysis 1.1. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.



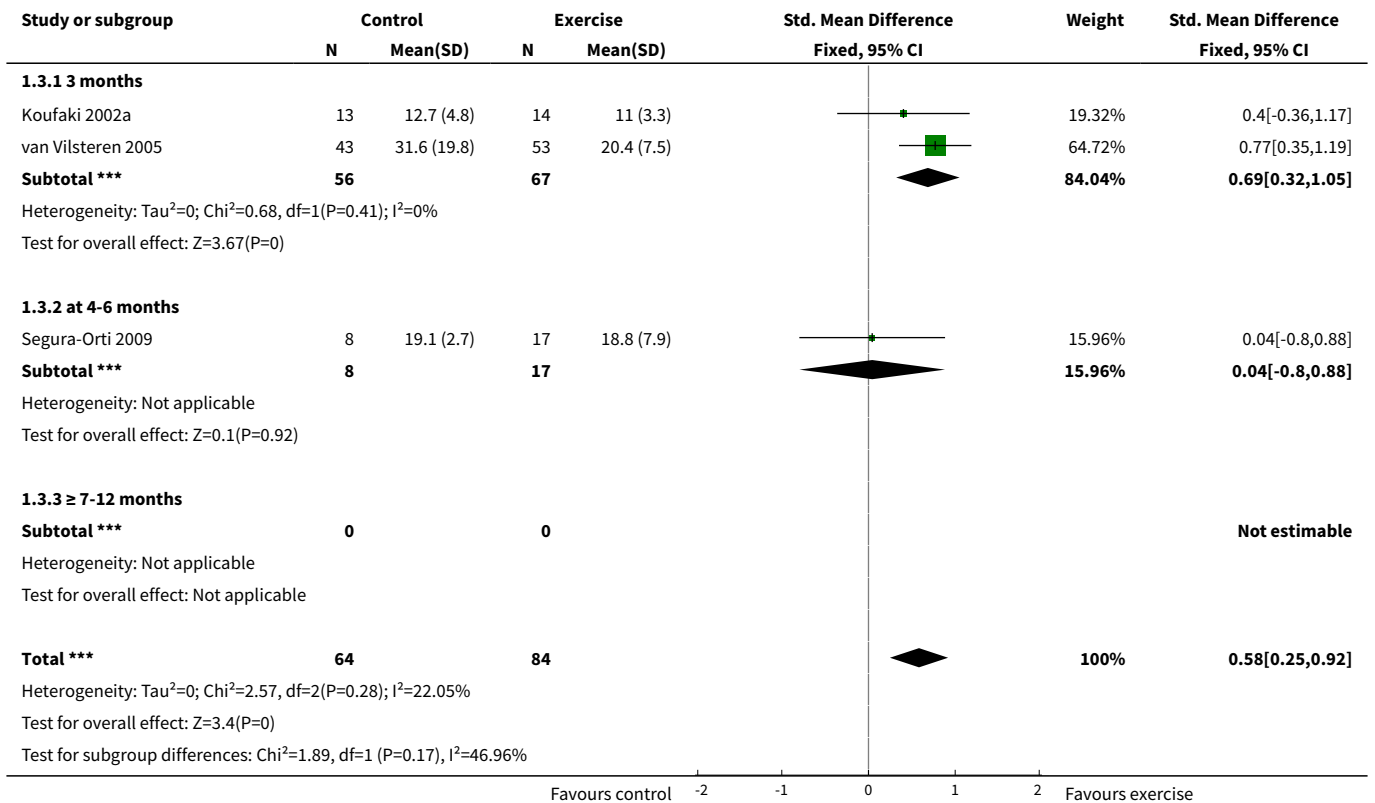


Analysis 1.2. Comparison 1 Any exercise versus control (no exercise/ placebo exercise), Outcome 2 Muscular strength (high value = improved).

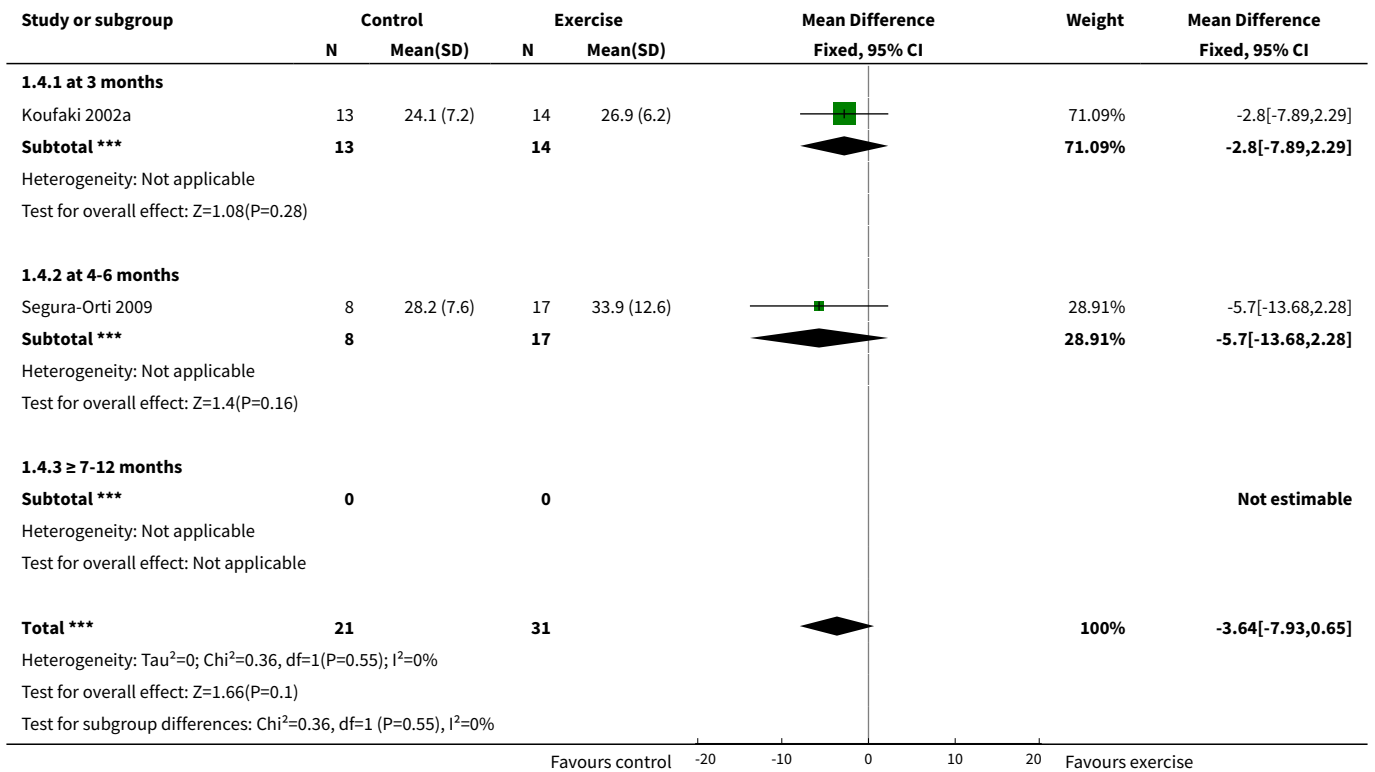




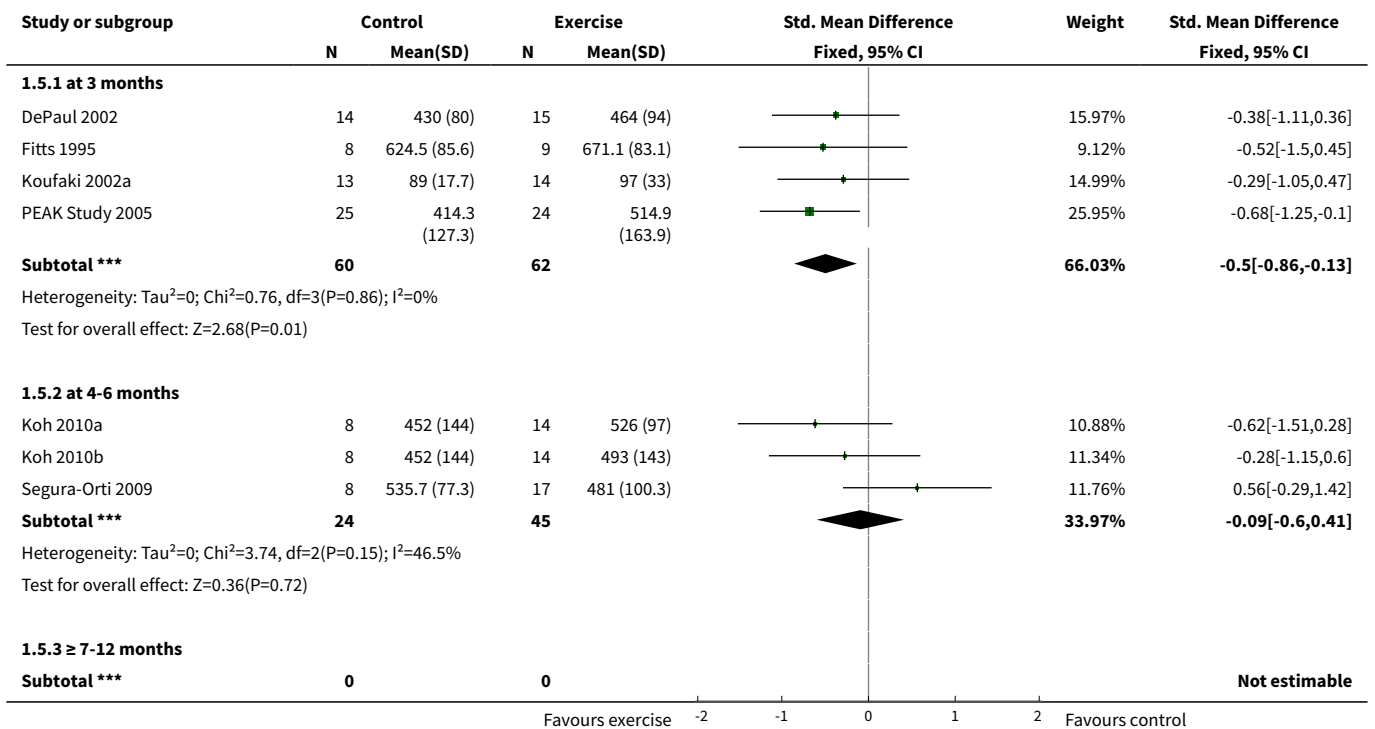
Analysis 1.3. Comparison 1 Any exercise versus control (no exercise/ placebo exercise), Outcome 3 Muscular strength (low value = improved).

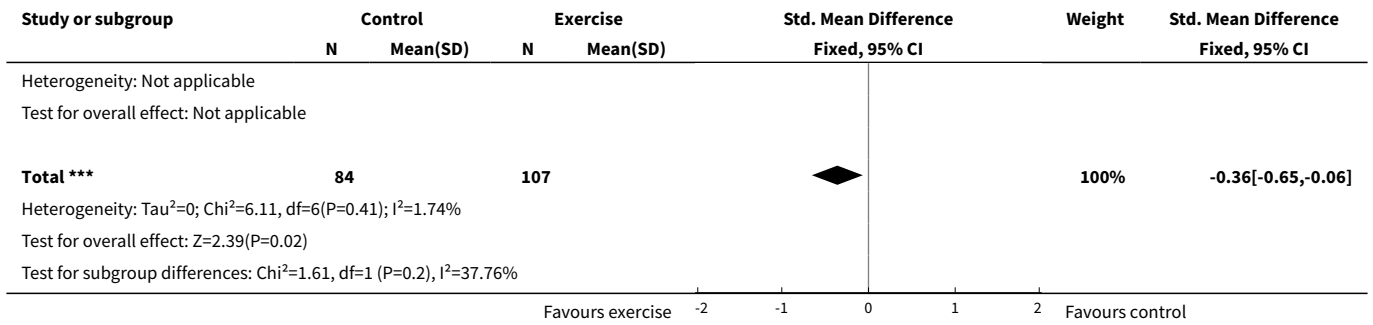


Analysis 1.4. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60.



Analysis 1.5. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 5 Walking capacity.

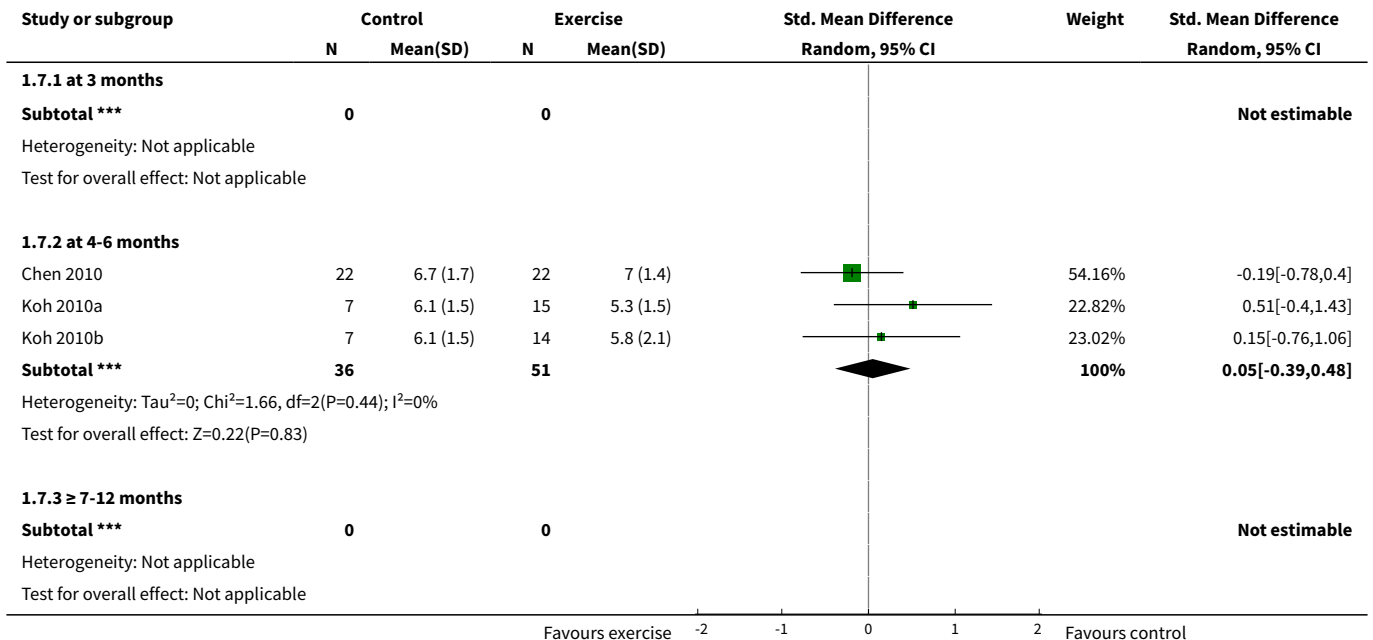




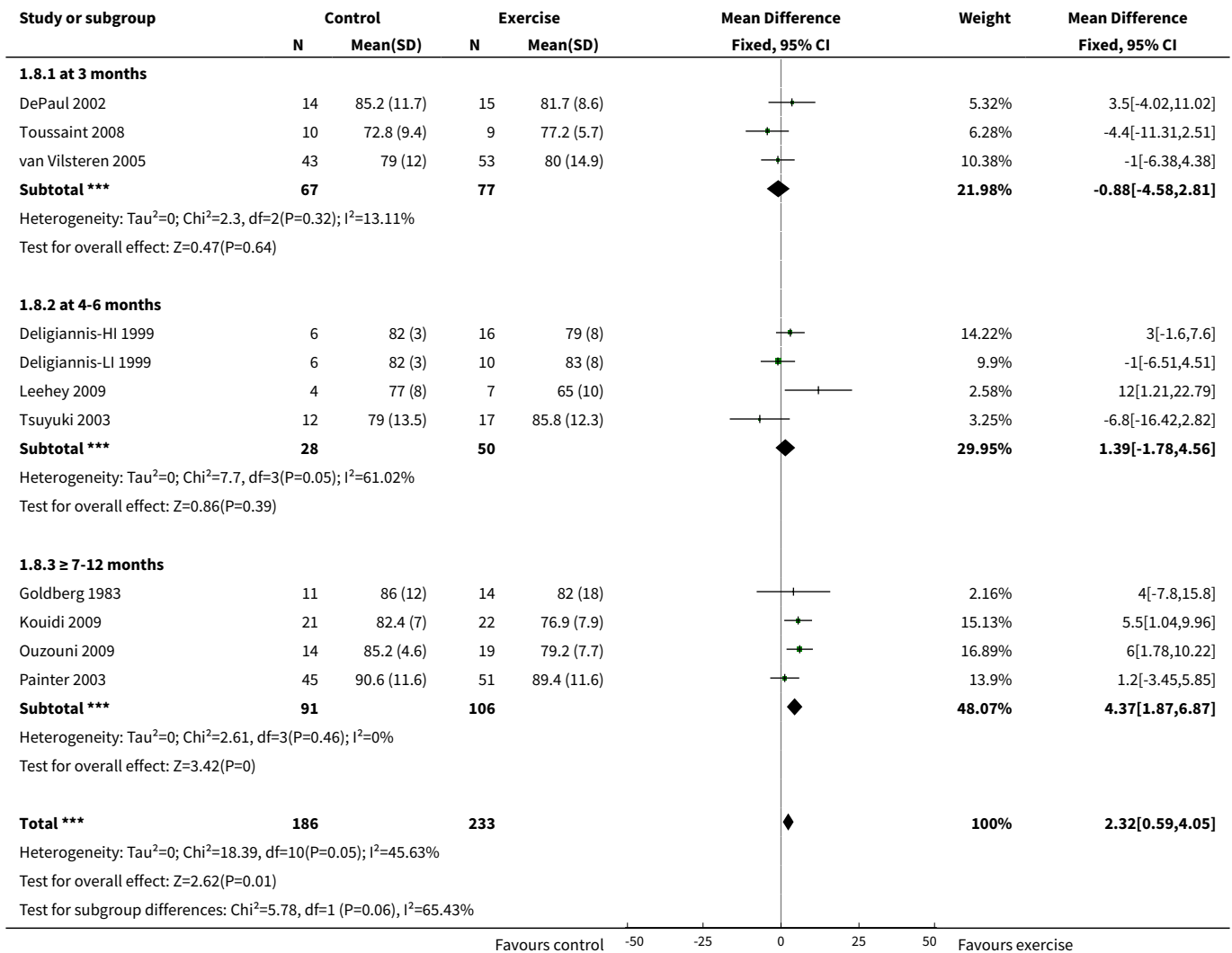
Analysis 1.6. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 6 Stair climbing capacity: stair climb test (22 steps).



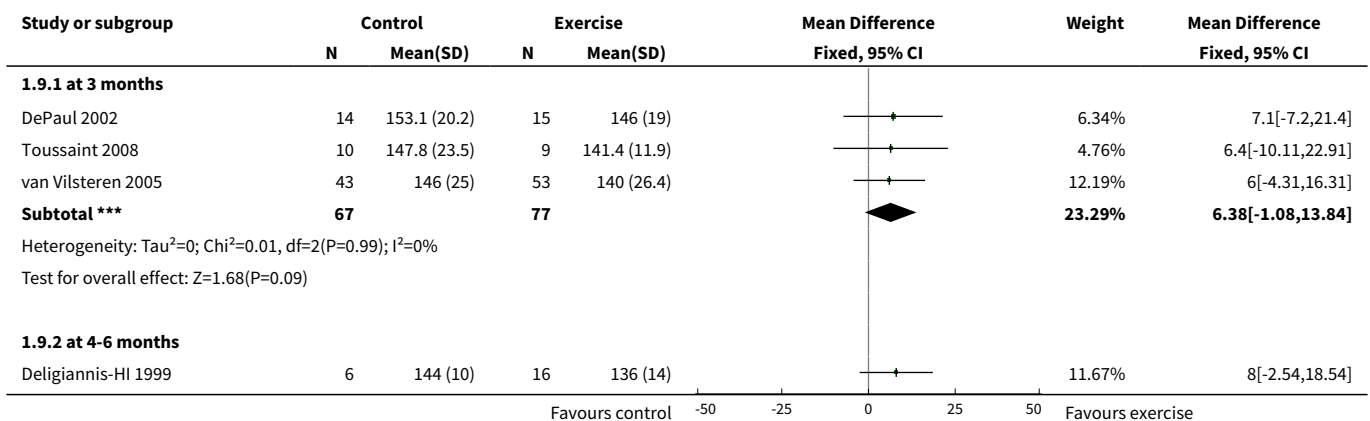
Analysis 1.7. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 7 ADL capacity.

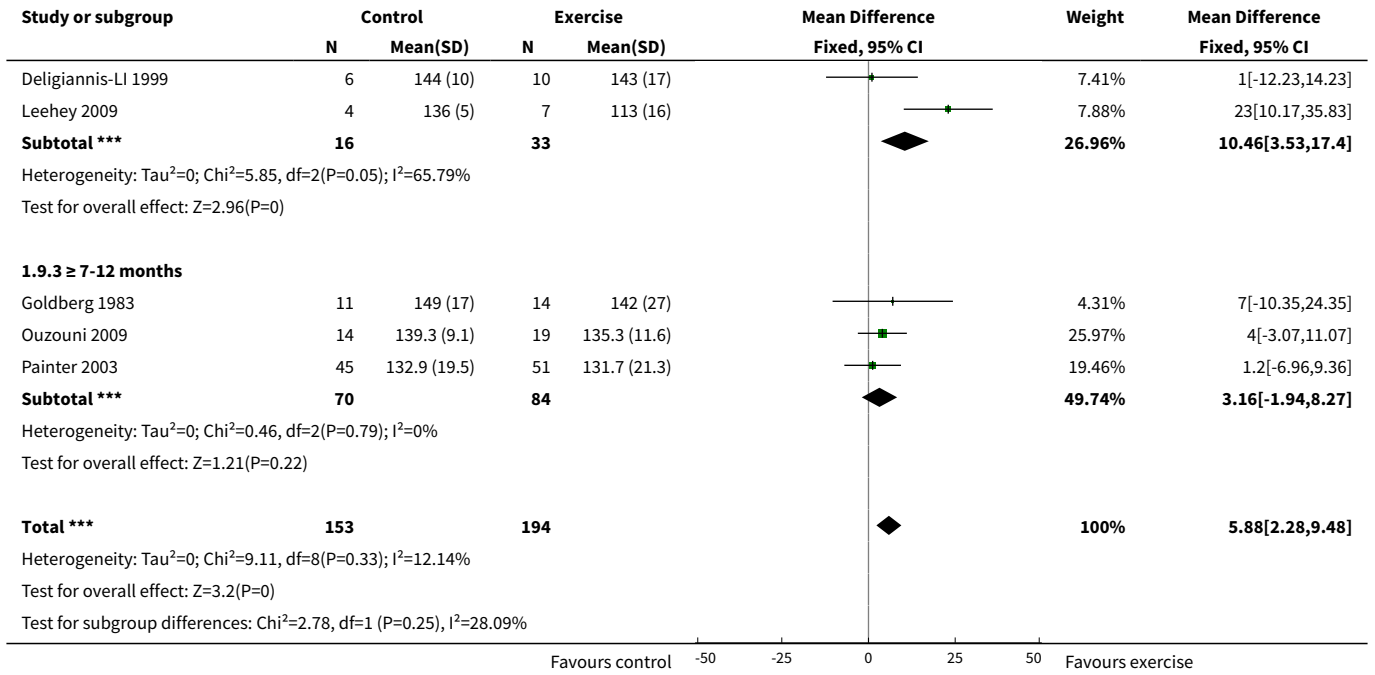


Analysis 1.8. Comparison 1 Any exercise versus control (no exercise/ placebo exercise), Outcome 8 Diastolic blood pressure: resting.

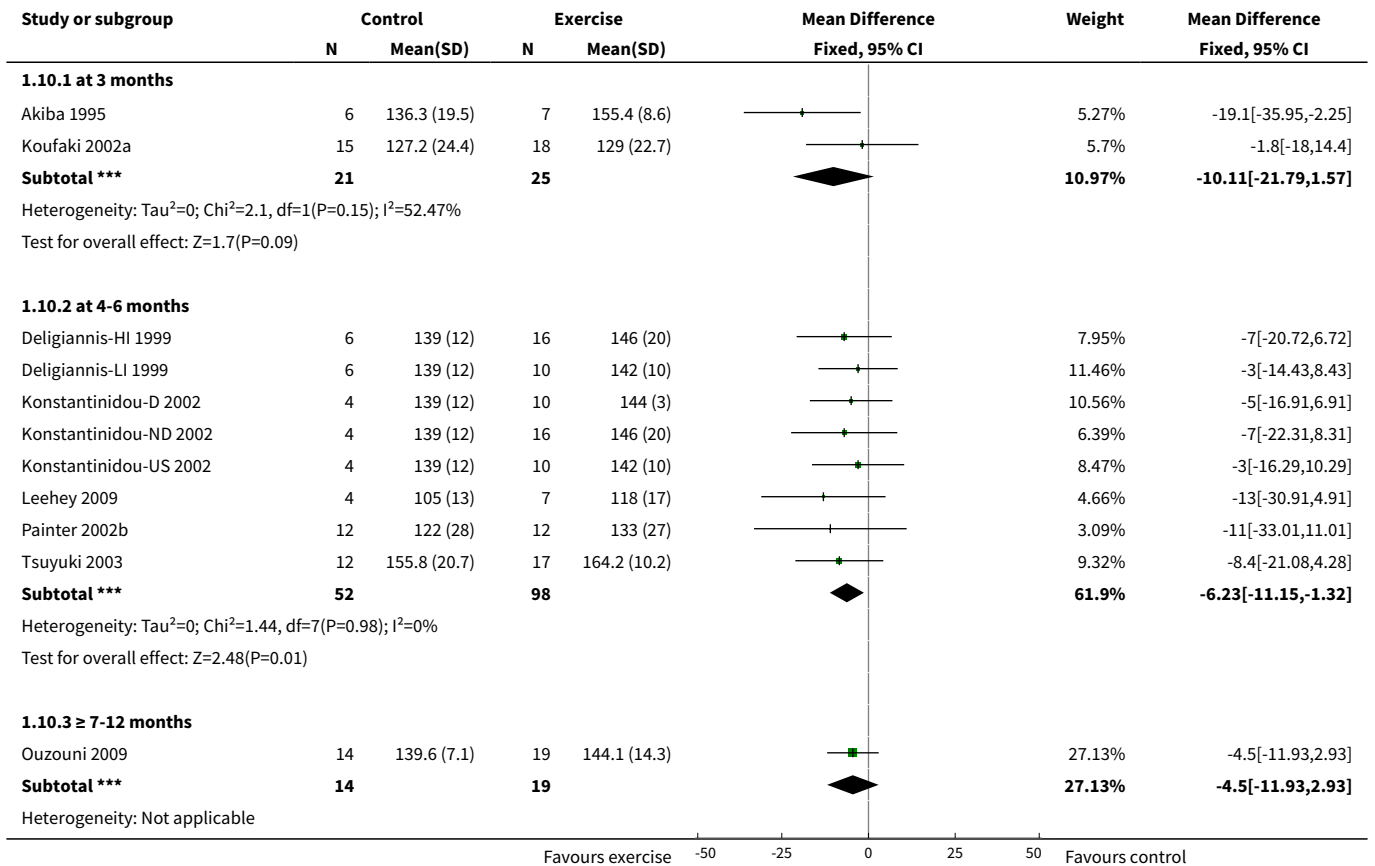


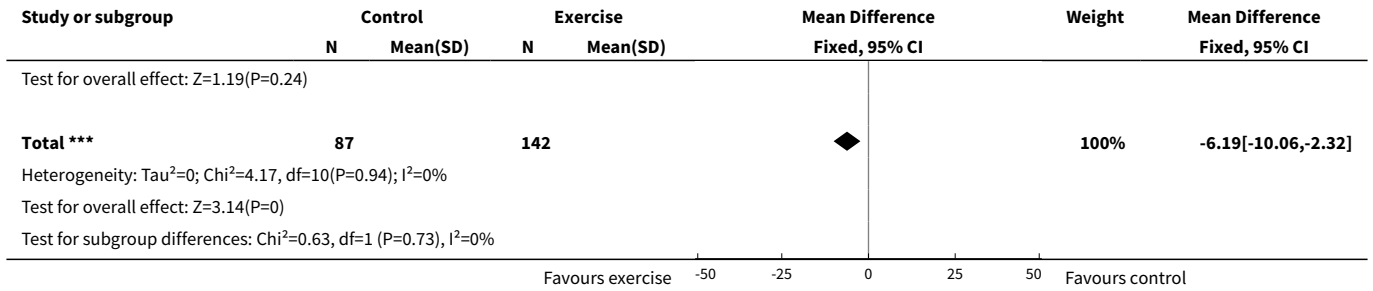
Analysis 1.9. Comparison 1 Any exercise versus control (no exercise/ placebo exercise), Outcome 9 Systolic blood pressure: resting.



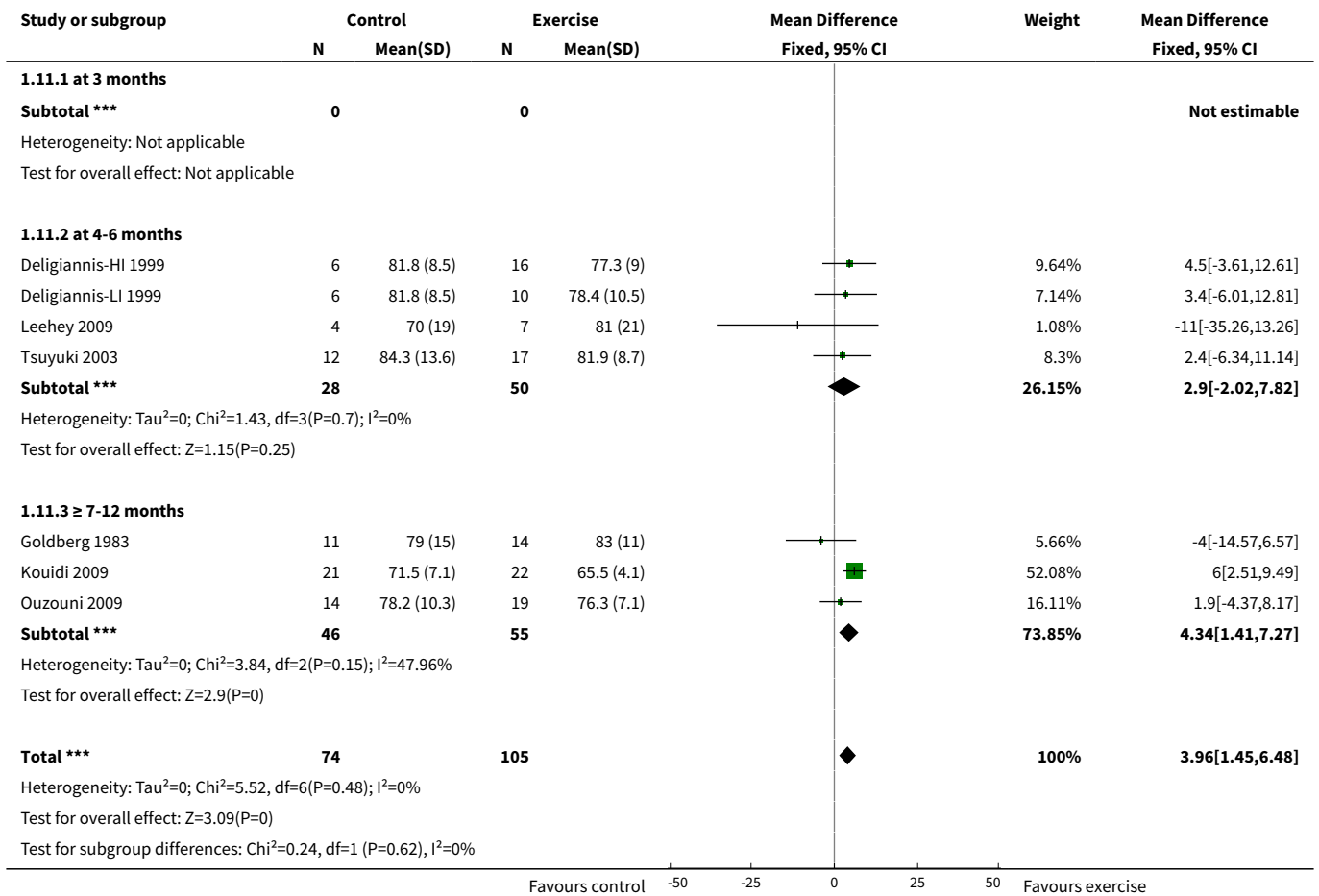


Analysis 1.10. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 10 Heart rate: maximum.

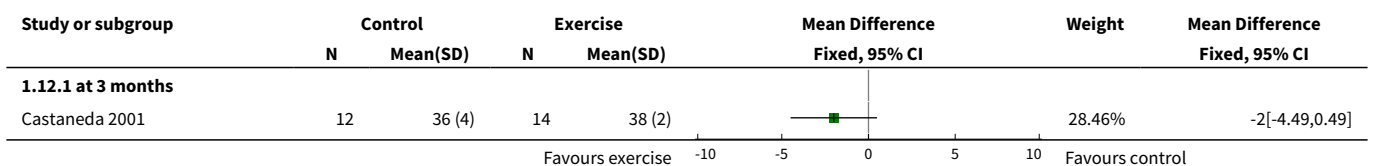


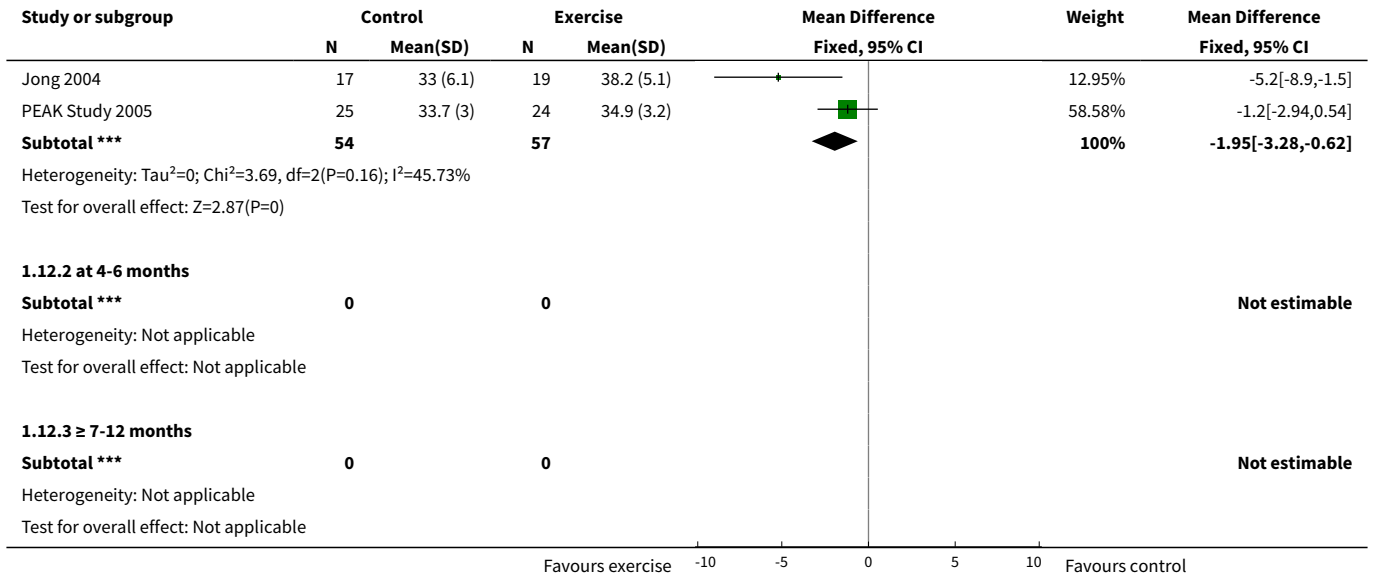


Analysis 1.11. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 11 Heart rate: resting.

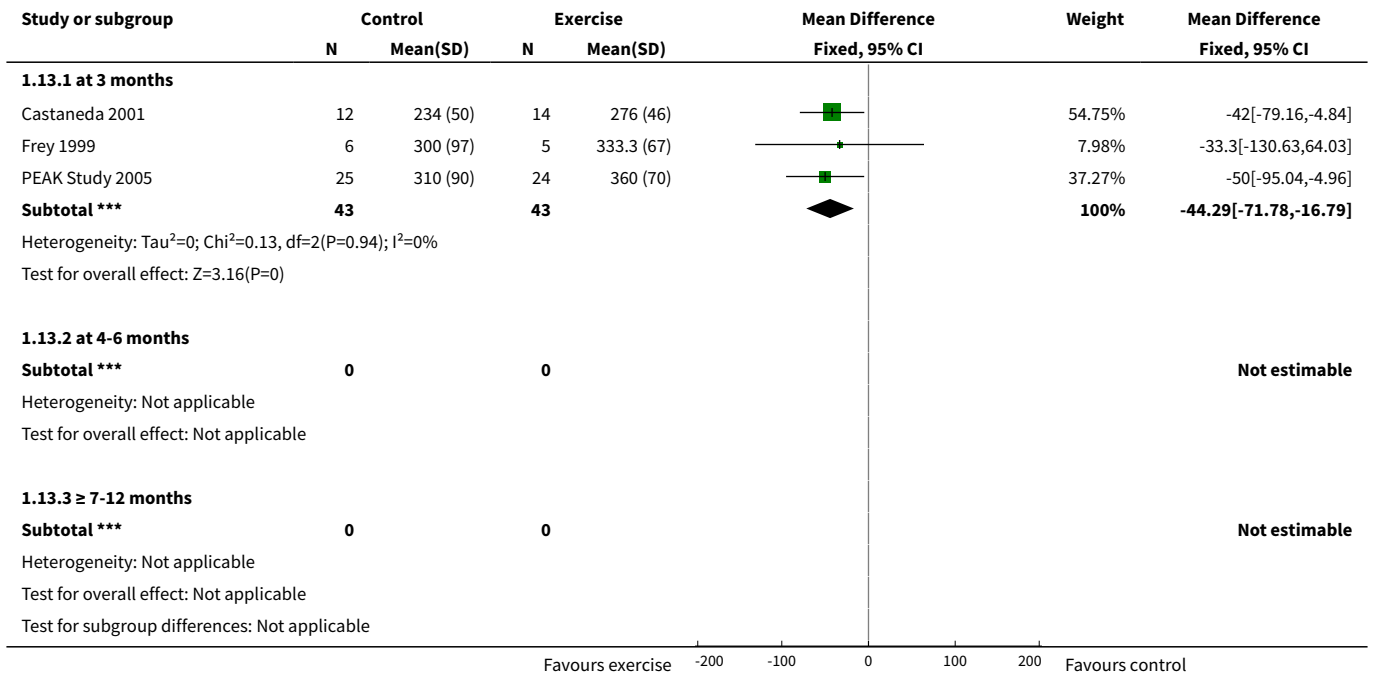


Analysis 1.12. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 12 Albumin.

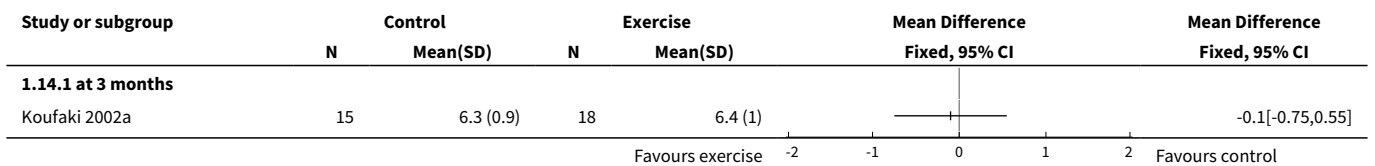


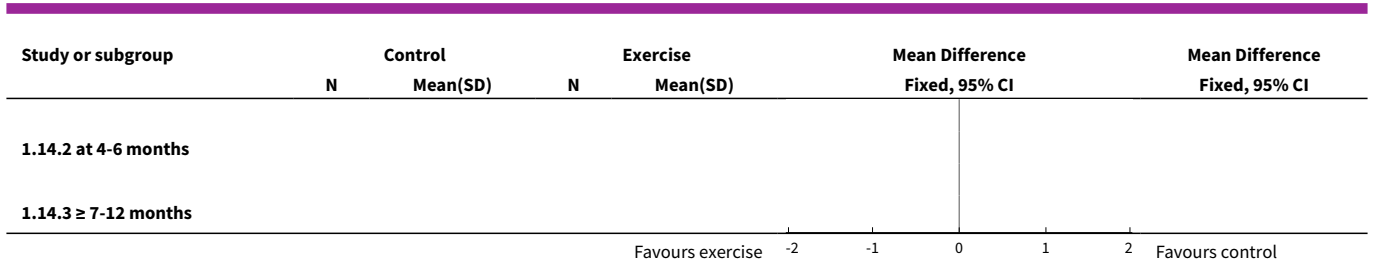


Analysis 1.13. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 13 Pre-albumin.

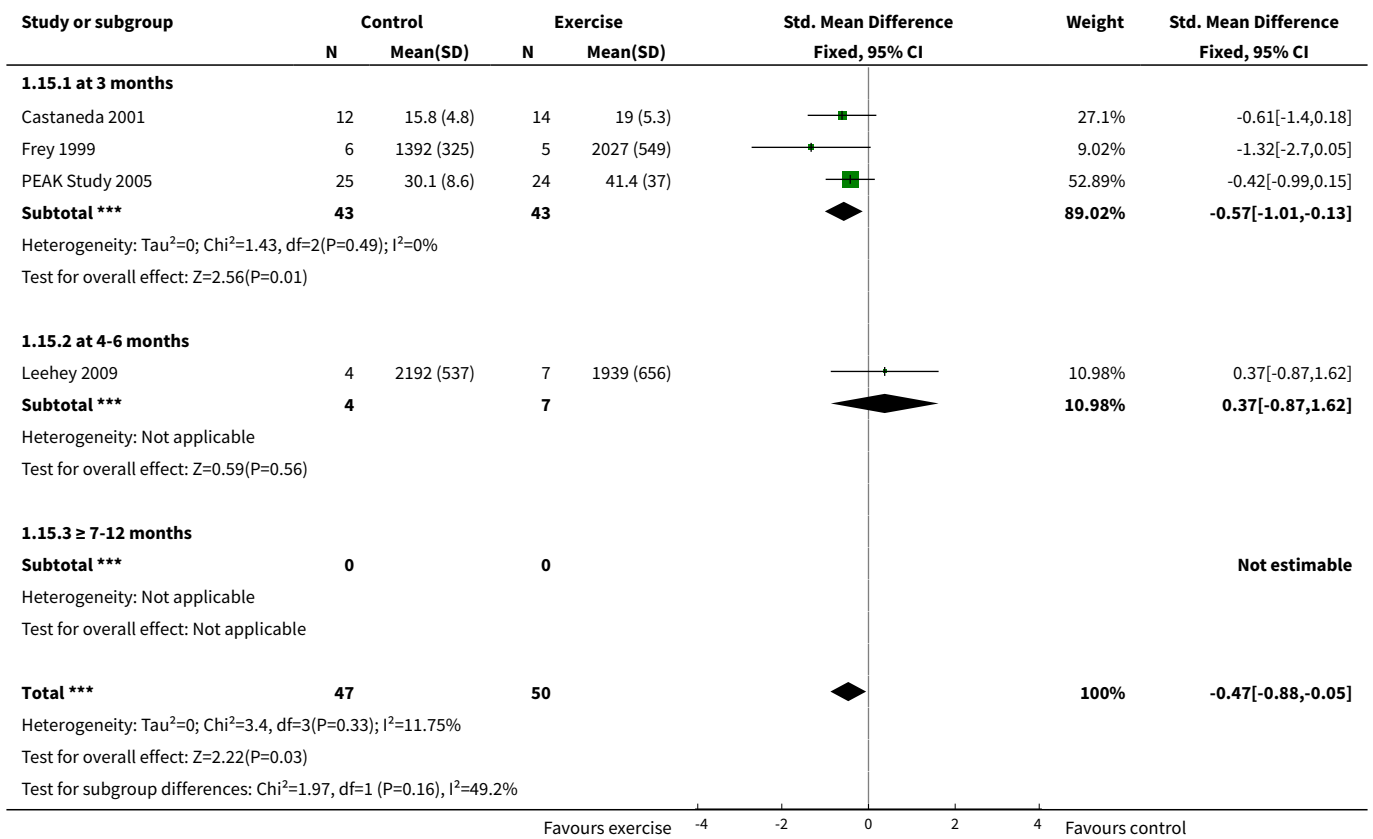


Analysis 1.14. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 14 SGA.

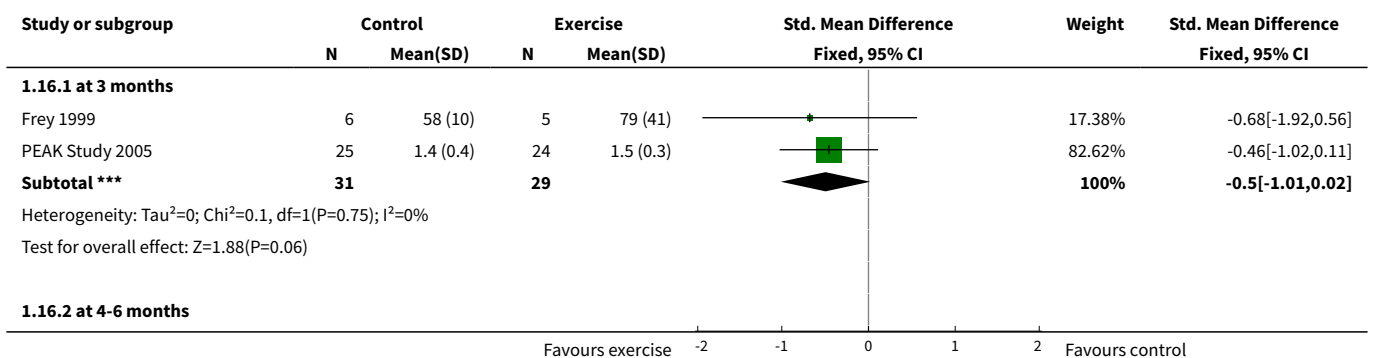


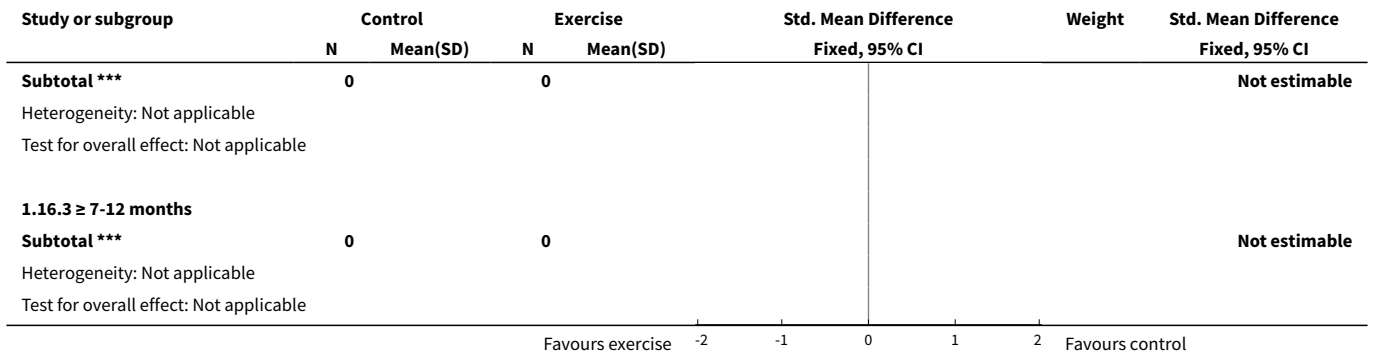


Analysis 1.15. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 15 Energy intake.

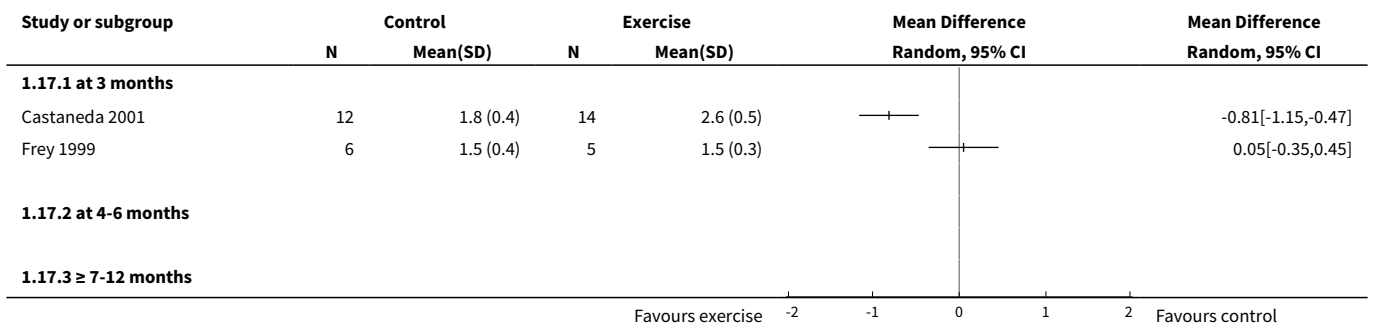


Analysis 1.16. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 16 Protein intake.

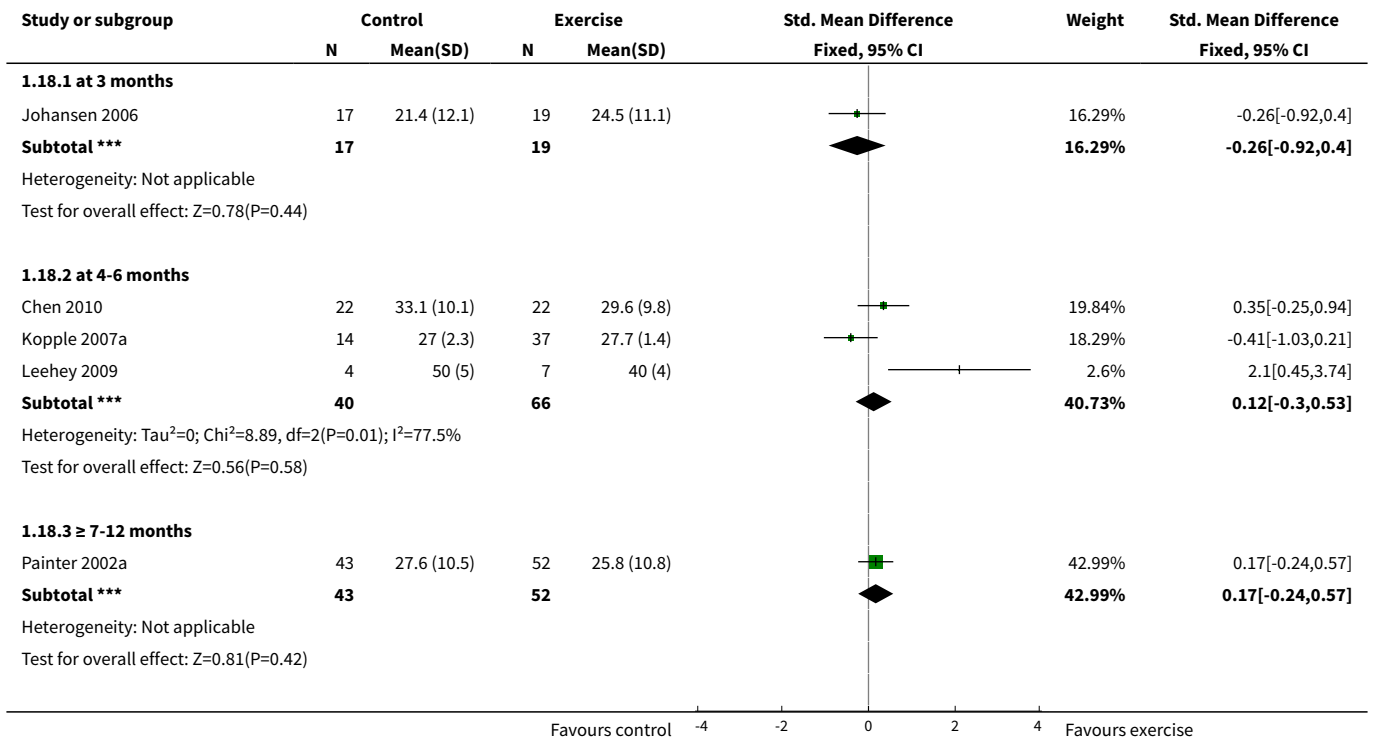


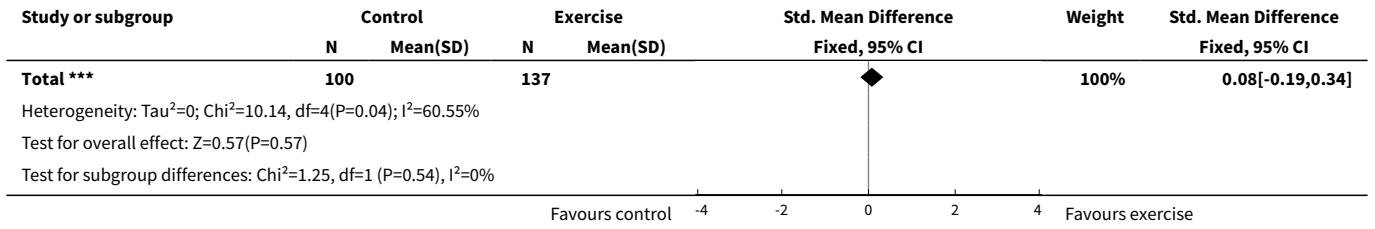


Analysis 1.17. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 17 Transferrin.

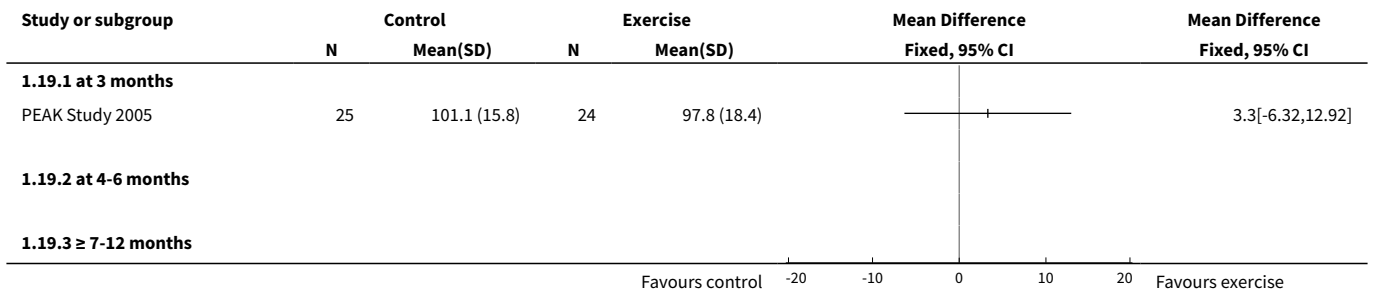


Analysis 1.18. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 18 Fat mass.

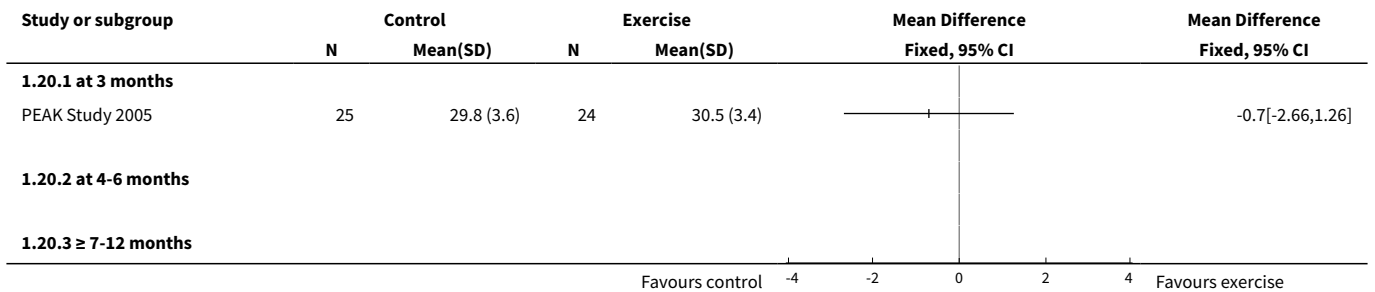




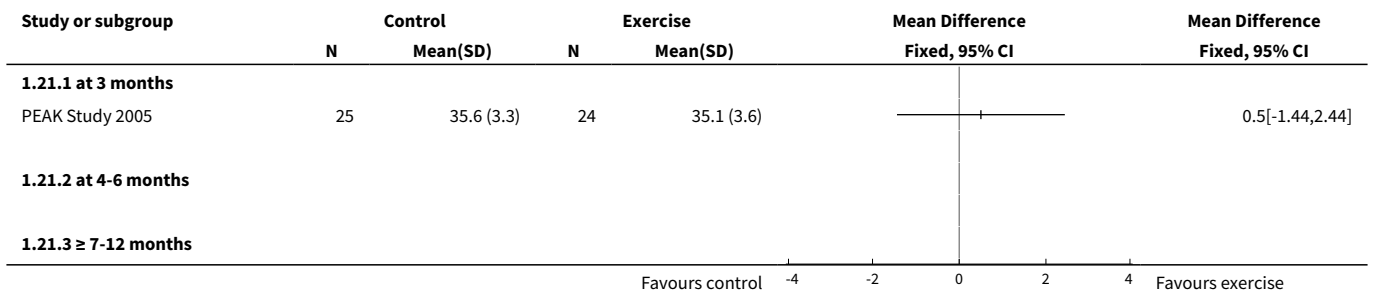
Analysis 1.19. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 19 Waist circumference.



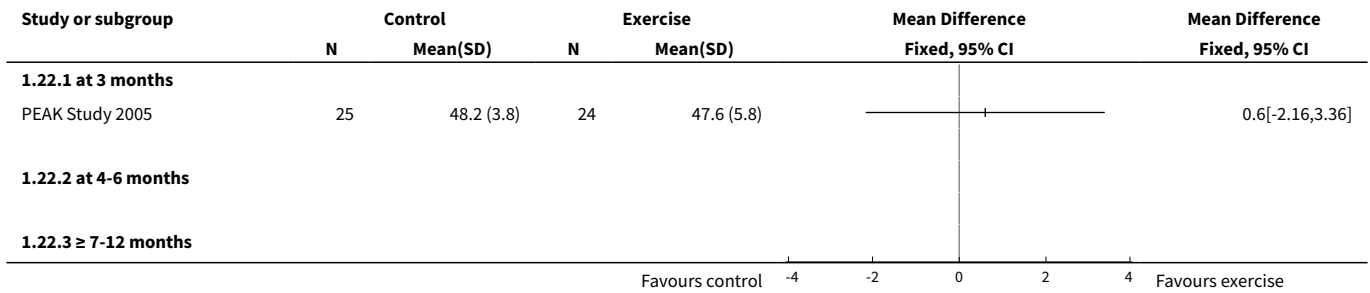
Analysis 1.20. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 20 Mid-arm circumference.



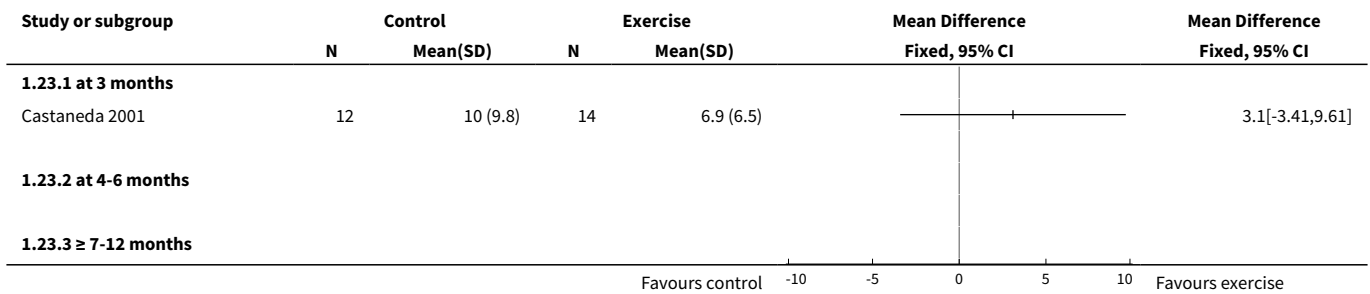
Analysis 1.21. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 21 Mid-calf circumference.



Analysis 1.22. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 22 Mid-thigh circumference.



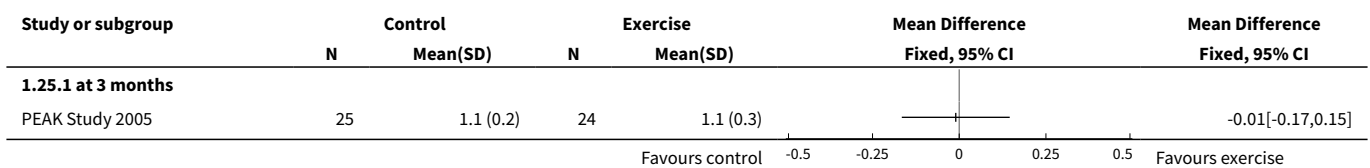
Analysis 1.23. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 23 Interleukin 6.



Analysis 1.24. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 24 Lymphocytes (x 10⁹ L).



Analysis 1.25. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 25 Protein catabolic rate.



Study or subgroup	Control		Exercise		Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.25.2 at 4-6 months						
1.25.3 ≥ 7-12 months						

Favours control -0.5 -0.25 0 0.25 0.5 Favours exercise

Analysis 1.26. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 26 Physical activity.

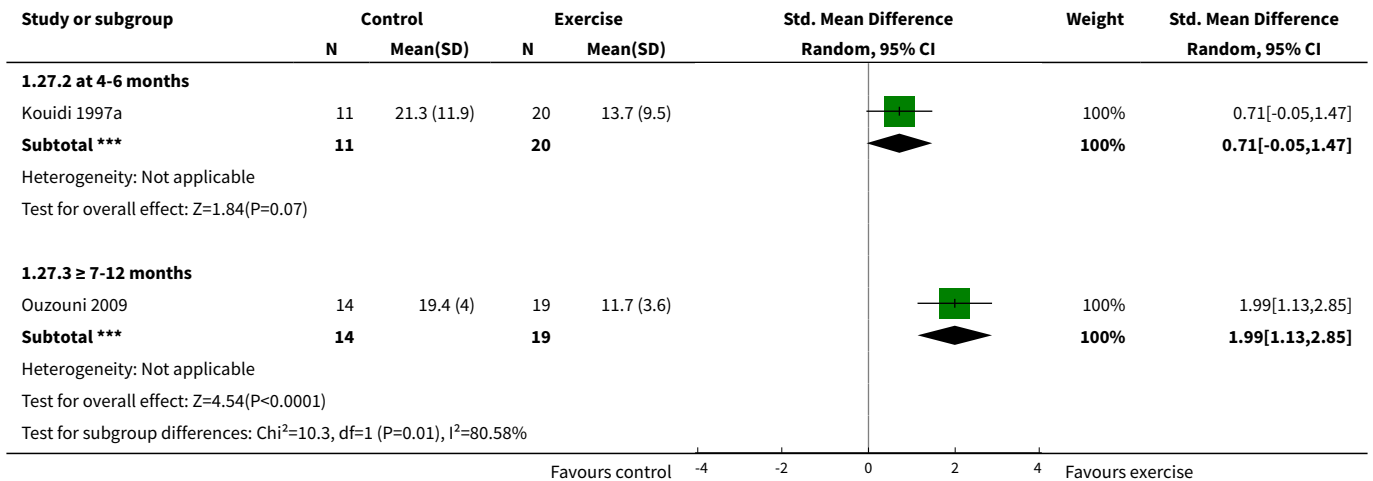
Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
1.26.1 at 3 months							
Koufaki 2002a	15	34.3 (1.7)	18	35.4 (4.1)		28.86%	-0.33[-1.02,0.36]
Subtotal ***	15		18			28.86%	-0.33[-1.02,0.36]
Heterogeneity: Not applicable Test for overall effect: Z=0.94(P=0.35)							
1.26.2 at 4-6 months							
Chen 2010	22	22.7 (30.5)	22	57.5 (69.3)		37.31%	-0.64[-1.25,-0.03]
Koh 2010a	7	943 (1701)	15	1920 (3273)		16.86%	-0.32[-1.23,0.58]
Koh 2010b	7	943 (1701)	15	1712 (3868)		16.98%	-0.22[-1.12,0.68]
Subtotal ***	36		52			71.14%	-0.46[-0.9,-0.02]
Heterogeneity: Tau ² =0; Chi ² =0.69, df=2(P=0.71); I ² =0% Test for overall effect: Z=2.07(P=0.04)							
1.26.3 ≥ 7-12 months							
Subtotal ***	0		0				Not estimable
Heterogeneity: Not applicable Test for overall effect: Not applicable							
Total ***	51		70			100%	-0.43[-0.8,-0.05]
Heterogeneity: Tau ² =0; Chi ² =0.79, df=3(P=0.85); I ² =0% Test for overall effect: Z=2.25(P=0.02) Test for subgroup differences: Chi ² =0.1, df=1 (P=0.75), I ² =0%							

Favours exercise -2 -1 0 1 2 Favours control

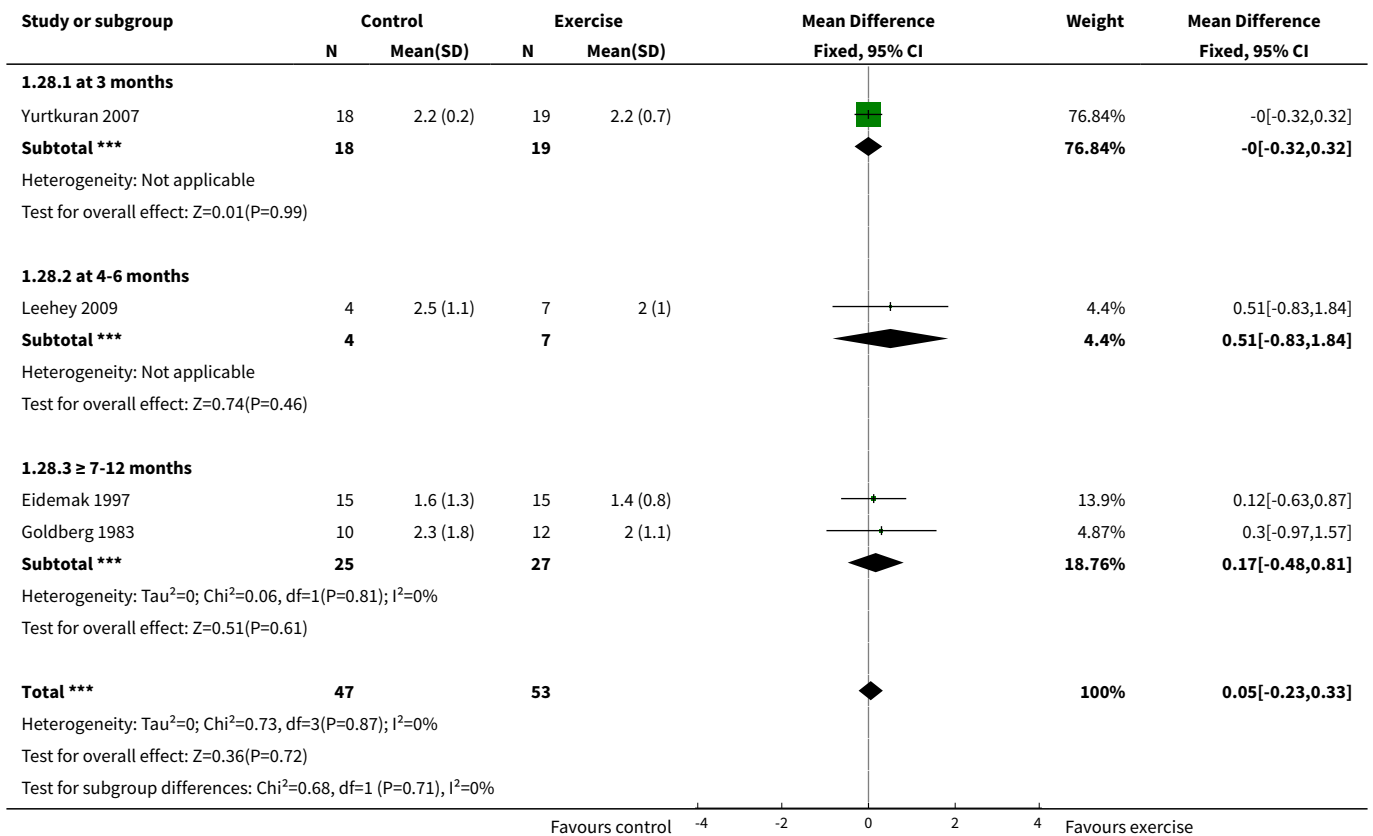
Analysis 1.27. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 27 Depression.

Study or subgroup	Control		Exercise		Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
1.27.1 at 3 months							
Carmack 1995	11	5 (5)	10	6.8 (8.2)		35.79%	-0.26[-1.12,0.6]
van Vilsteren 2005	43	41.4 (9.6)	53	37.2 (8.3)		64.21%	0.47[0.06,0.88]
Subtotal ***	54		63			100%	0.21[-0.47,0.89]
Heterogeneity: Tau ² =0.15; Chi ² =2.23, df=1(P=0.14); I ² =55.13% Test for overall effect: Z=0.6(P=0.55)							

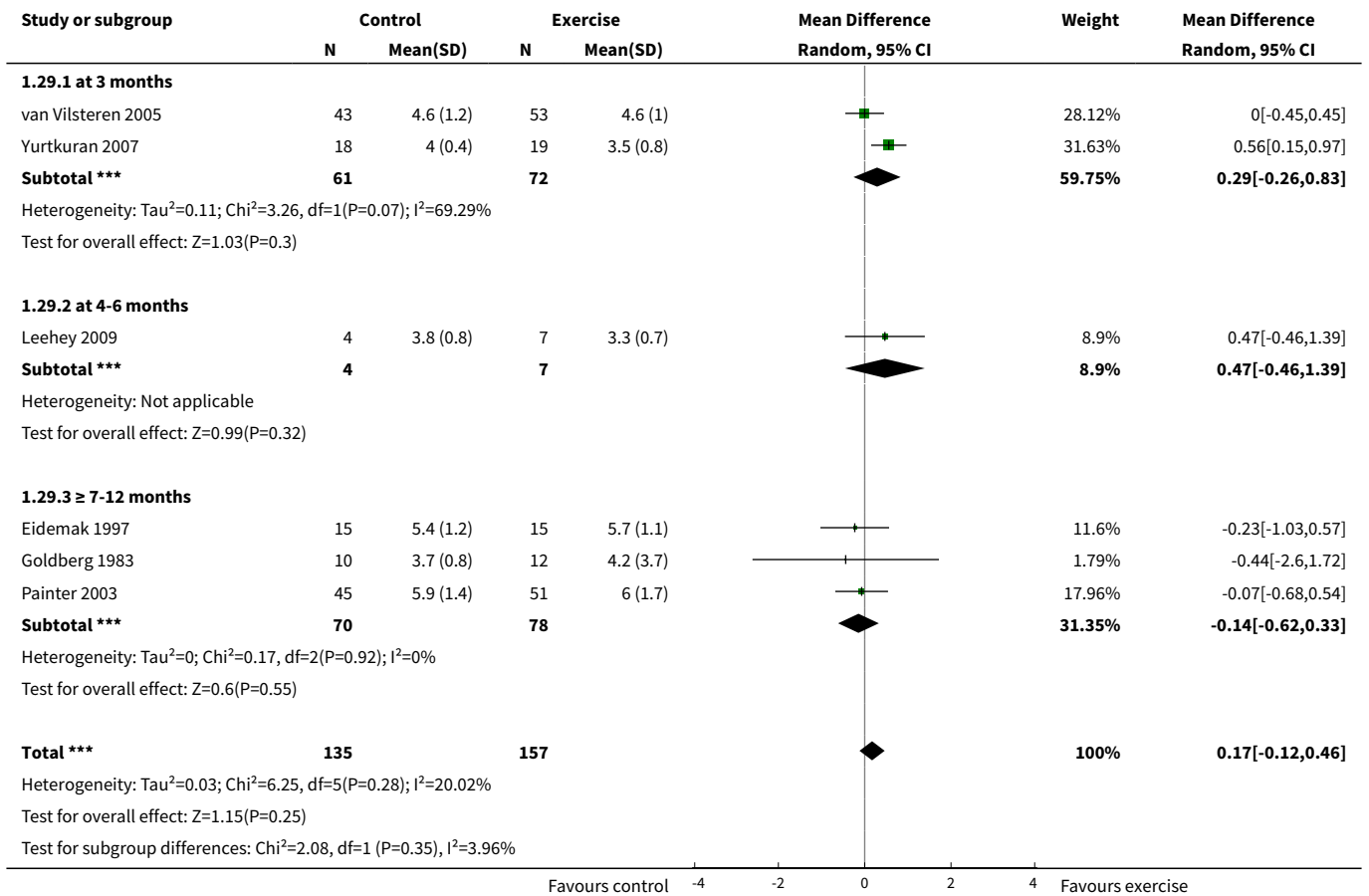
Favours control -4 -2 0 2 4 Favours exercise



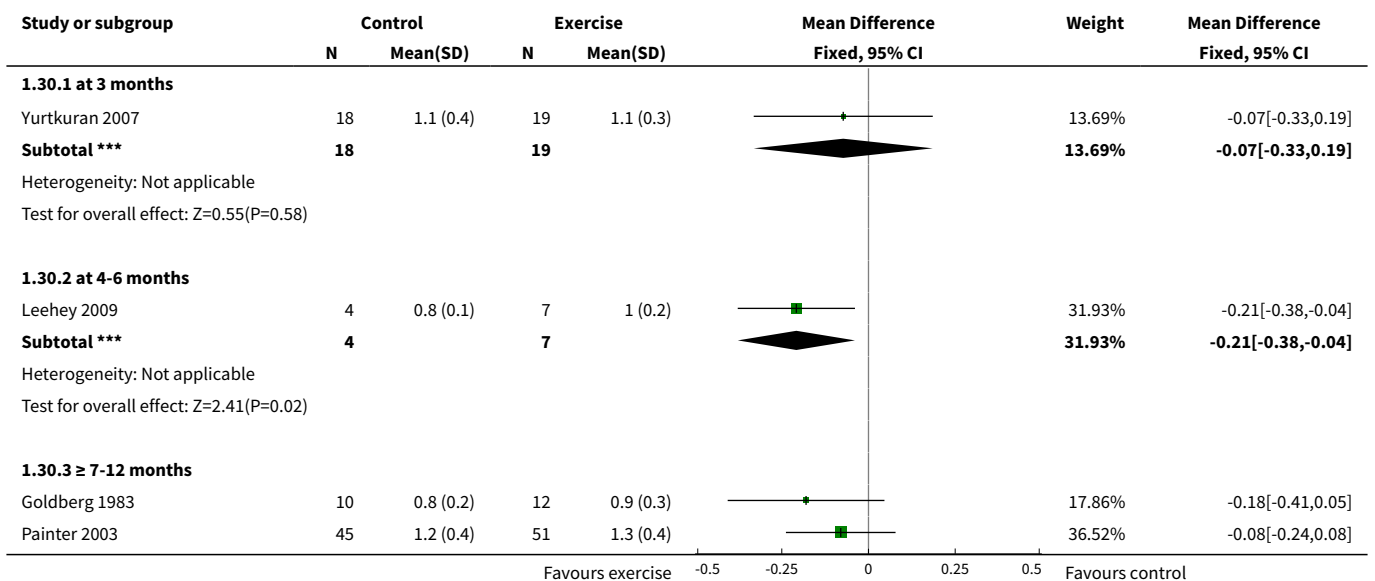
Analysis 1.28. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 28 Triglycerides.

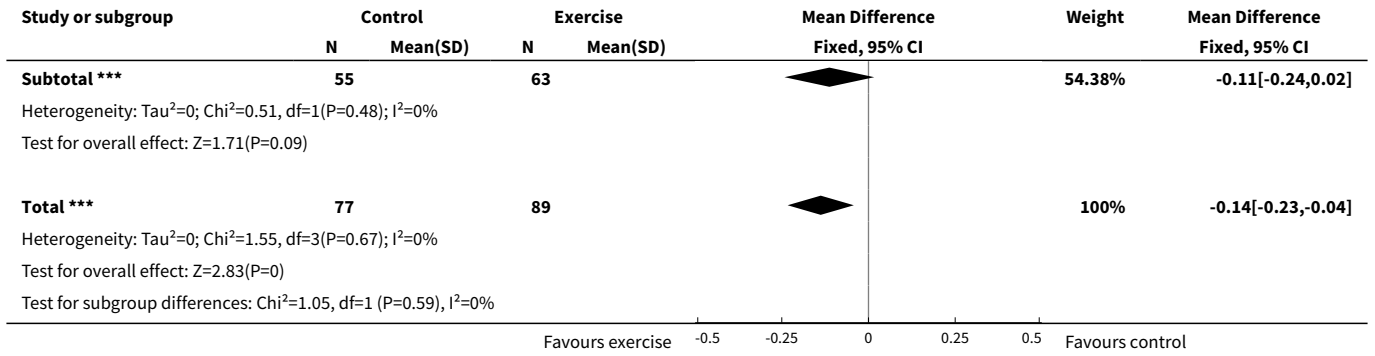


Analysis 1.29. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 29 Total cholesterol.



Analysis 1.30. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 30 HDL cholesterol.

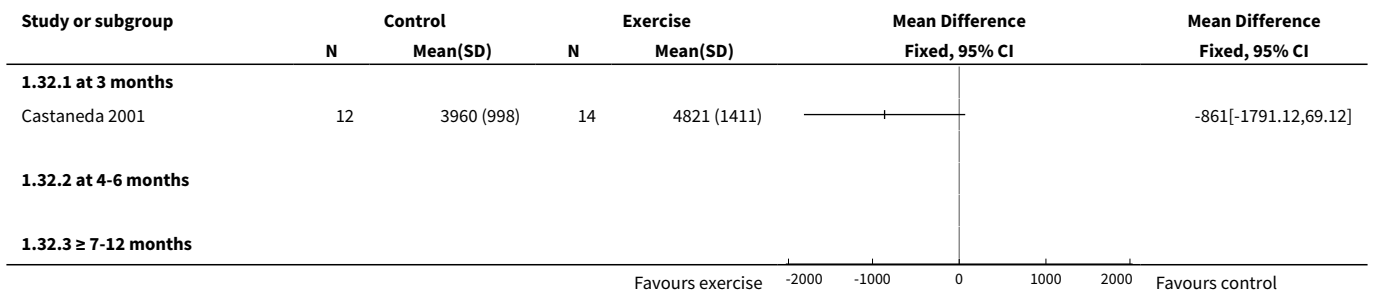




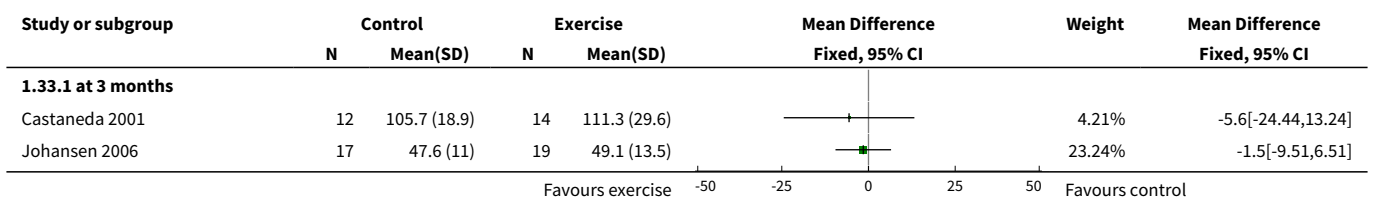
Analysis 1.31. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 31 LDL cholesterol.

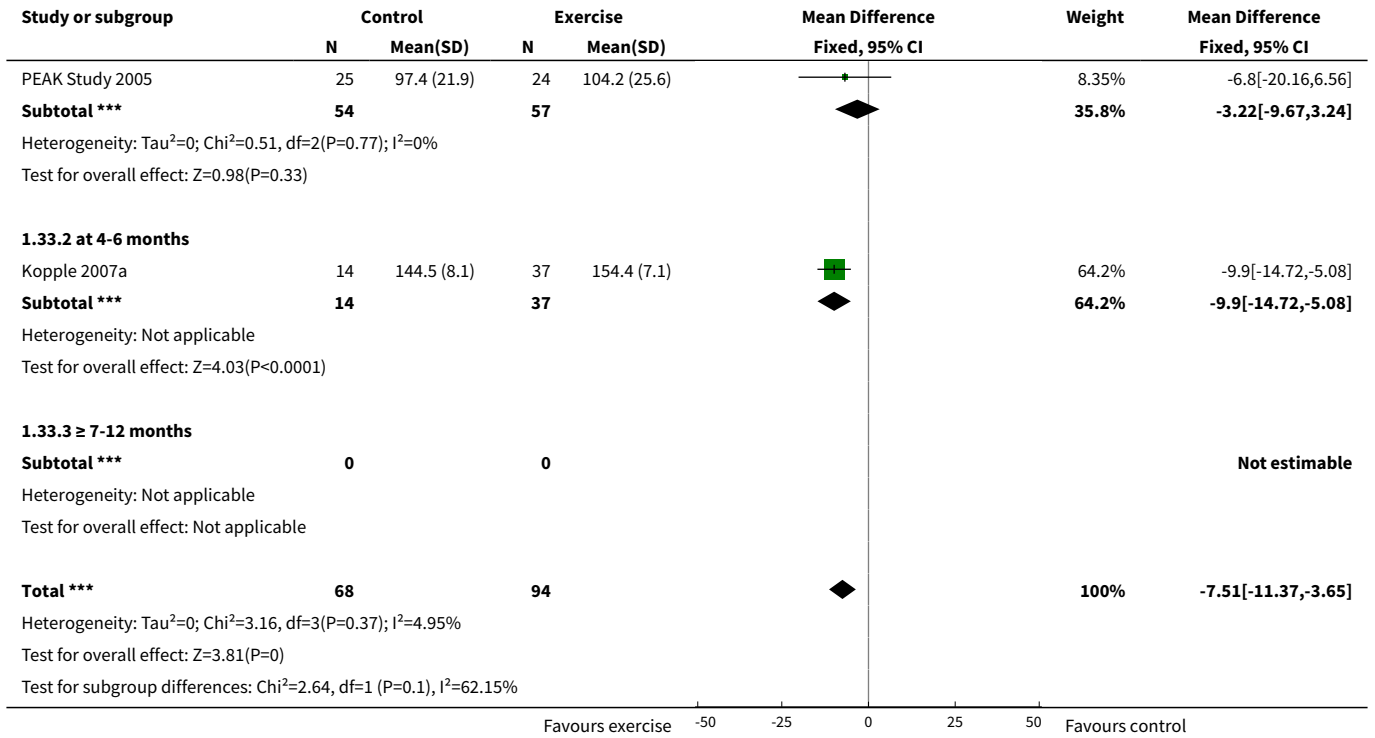


Analysis 1.32. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 32 Type I muscle fibre area.

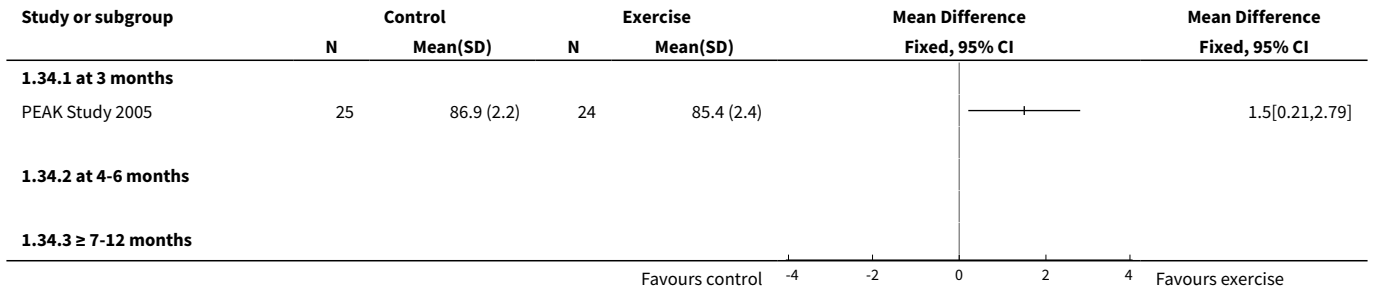


Analysis 1.33. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 33 Mid-thigh muscle area.

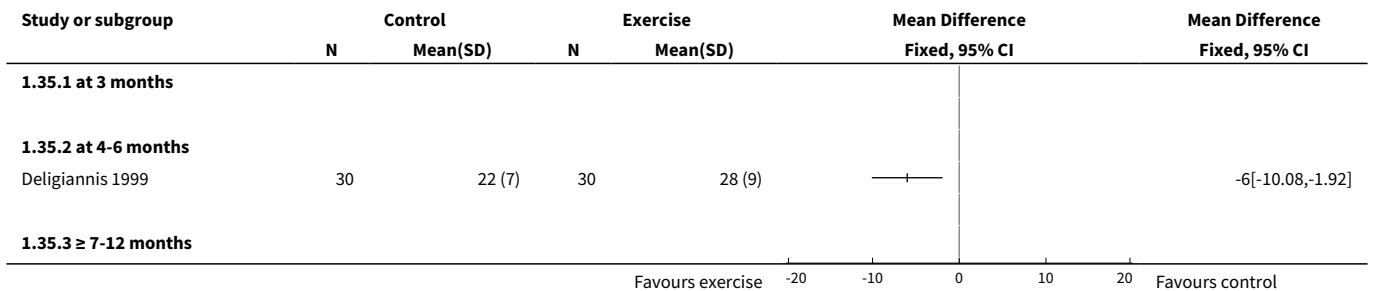




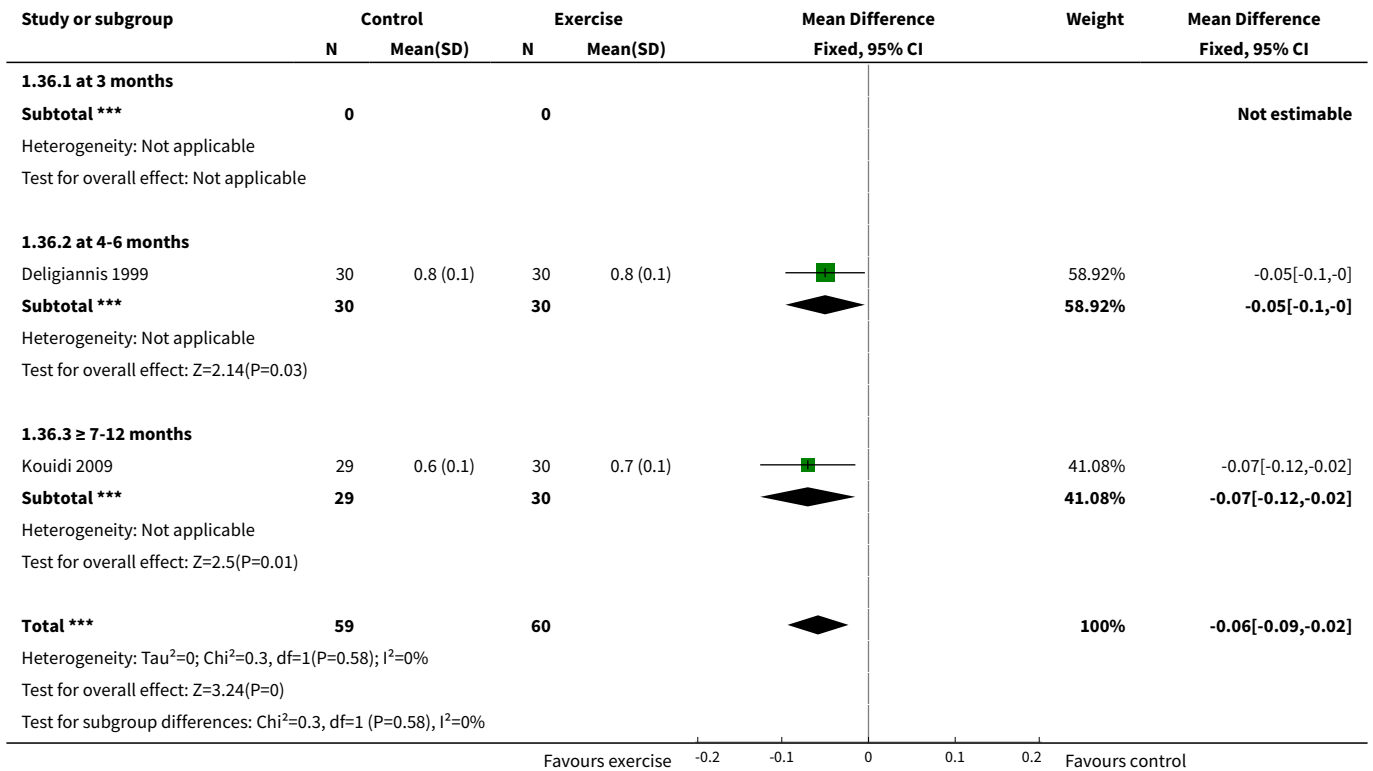
Analysis 1.34. Comparison 1 Any exercise versus control (no exercise/ placebo exercise), Outcome 34 Thigh muscle attenuation (Hounsfield units).



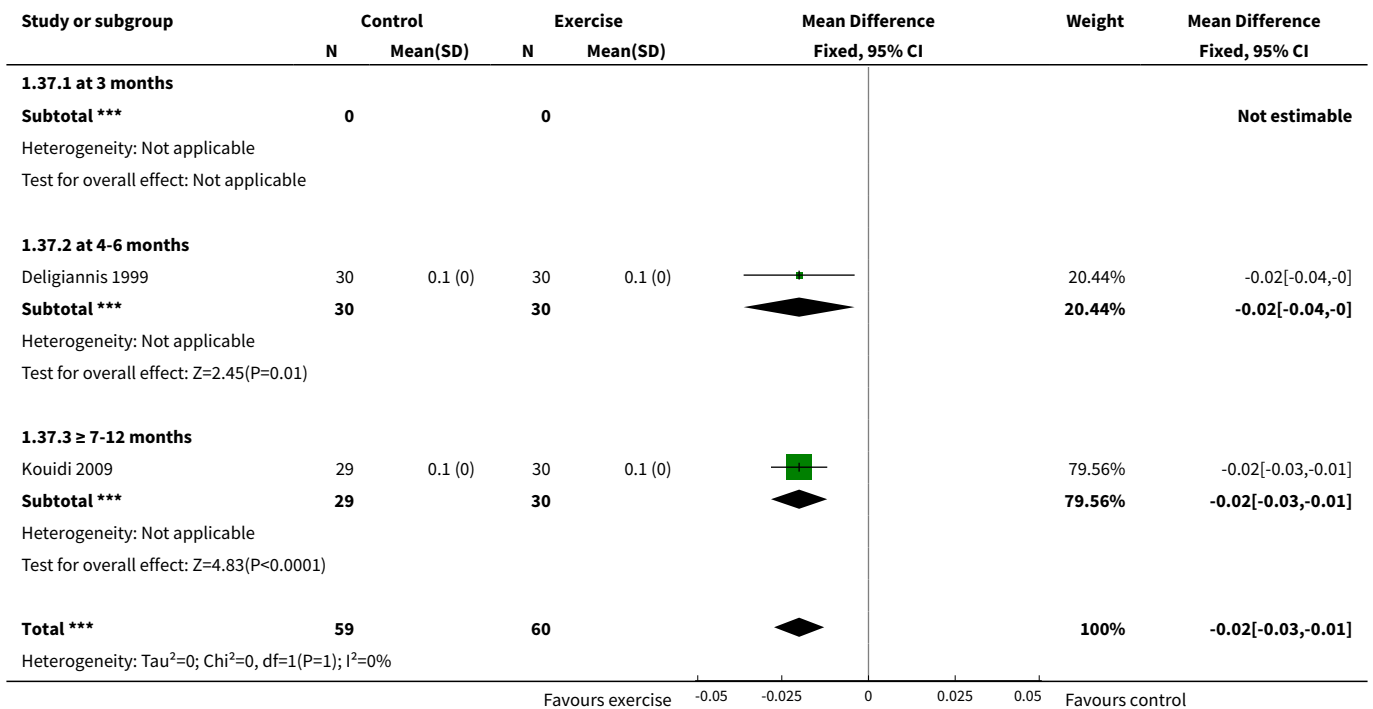
Analysis 1.35. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 35 HRV index.

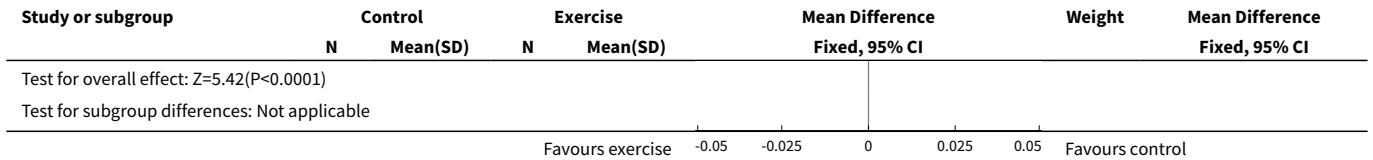


Analysis 1.36. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 36 Mean cardiac R-R interval.

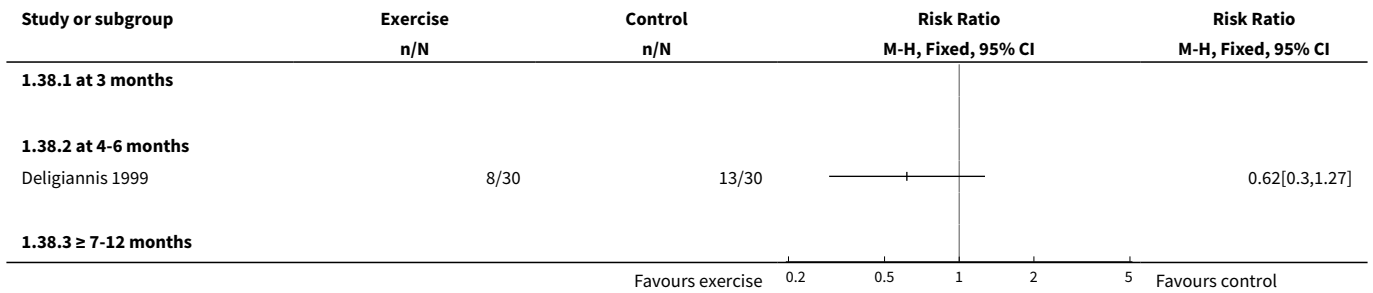


Analysis 1.37. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 37 SDNN.

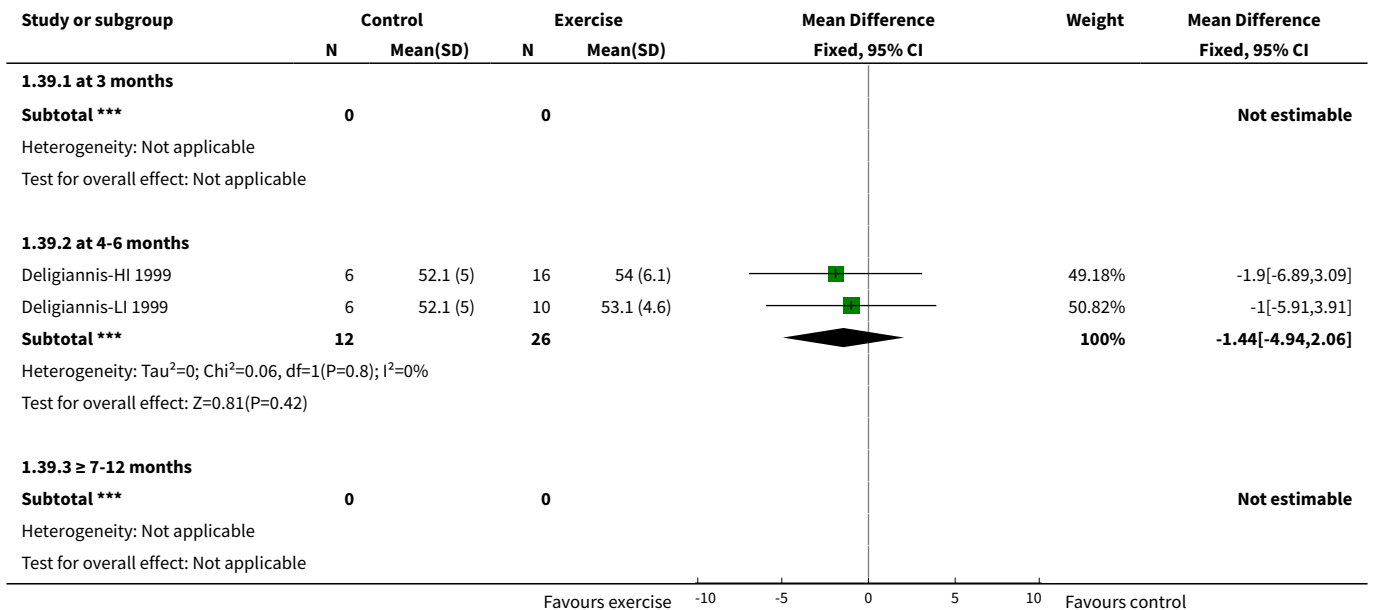




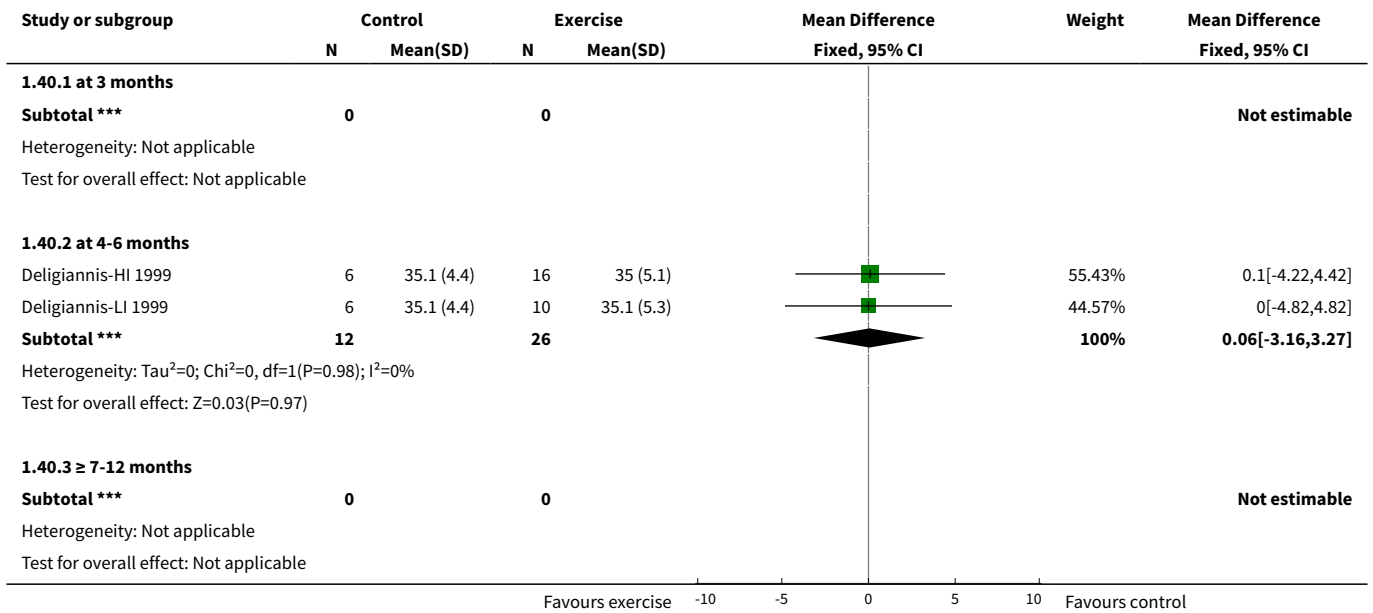
**Analysis 1.38. Comparison 1 Any exercise versus control (no exercise/
placebo exercise), Outcome 38 Arrhythmias: Lown class > II (no).**



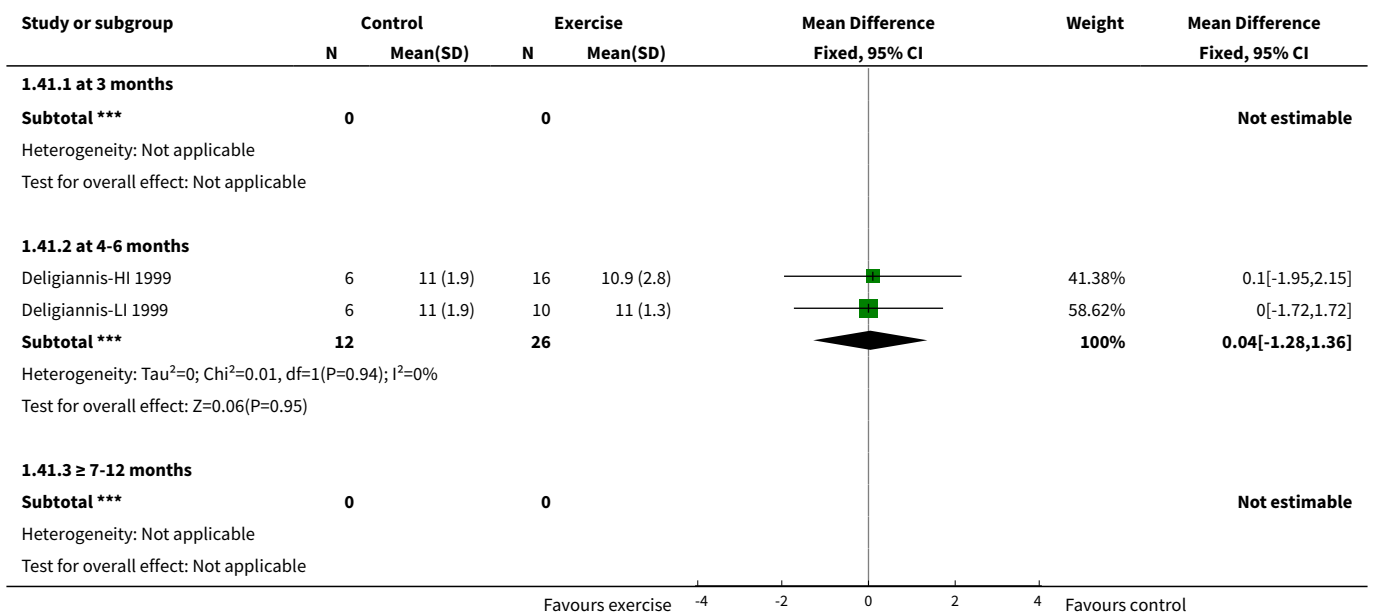
**Analysis 1.39. Comparison 1 Any exercise versus control (no exercise/
placebo exercise), Outcome 39 Left ventricular internal dimension at end-diastole.**



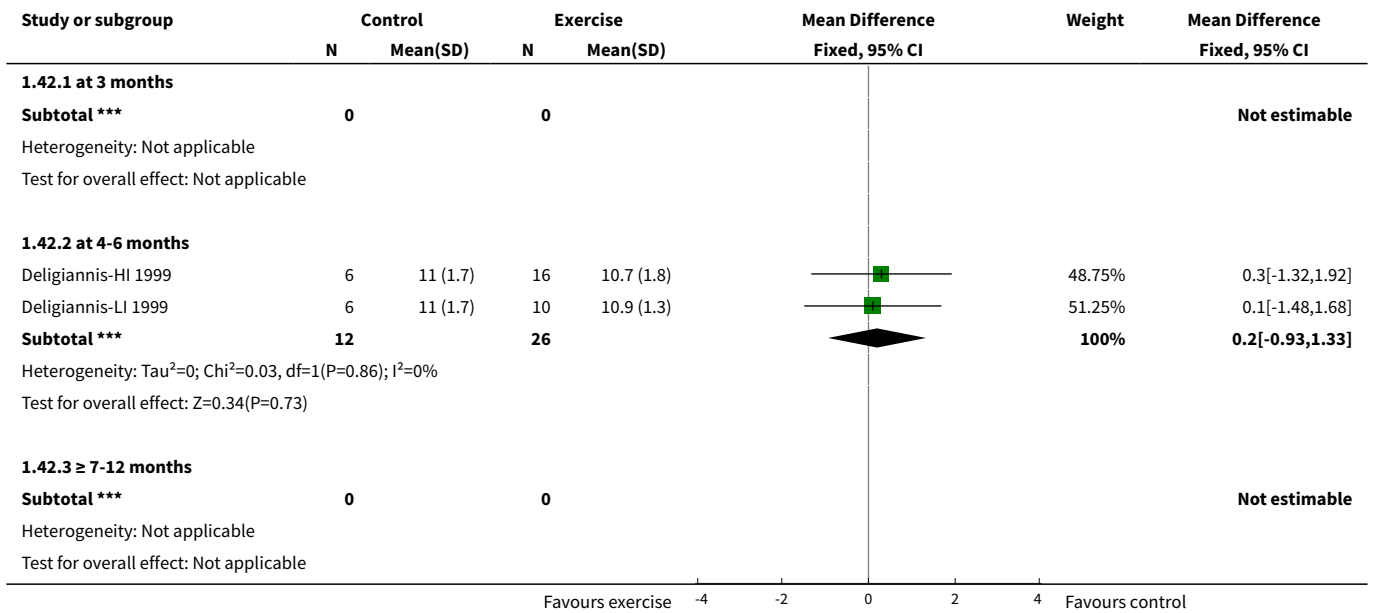
Analysis 1.40. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 40 Left ventricular internal dimension at end-systole.



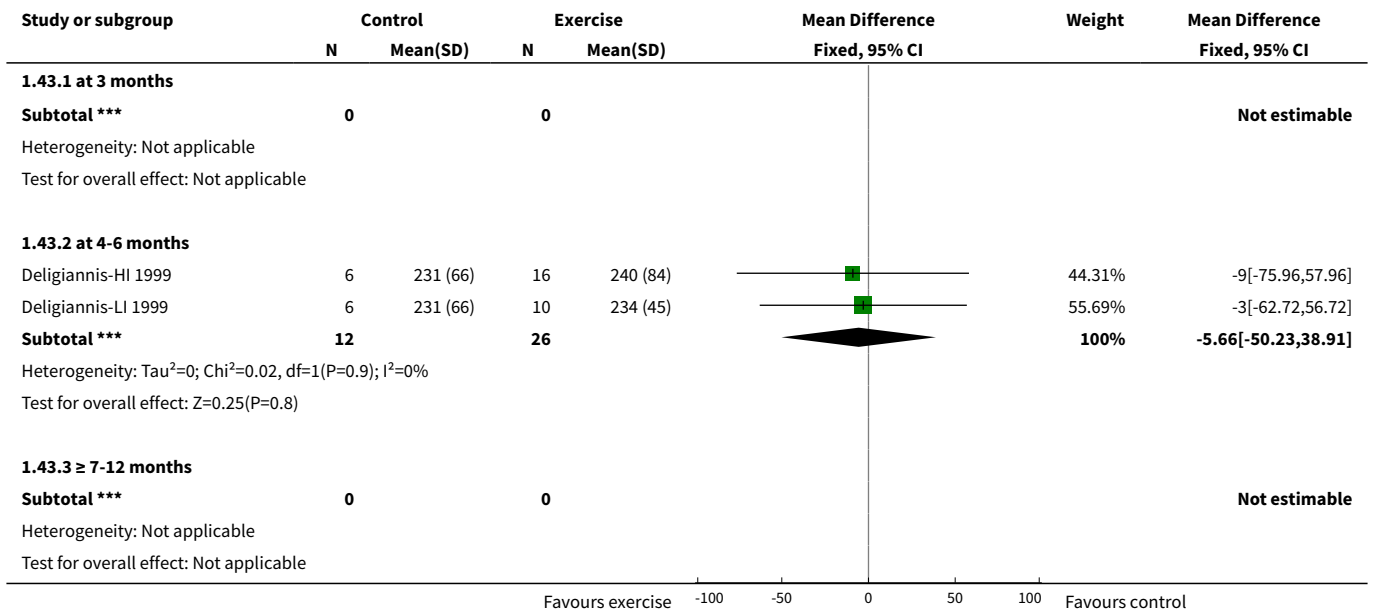
Analysis 1.41. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 41 Intraventricular septal thickness at end-diastole.



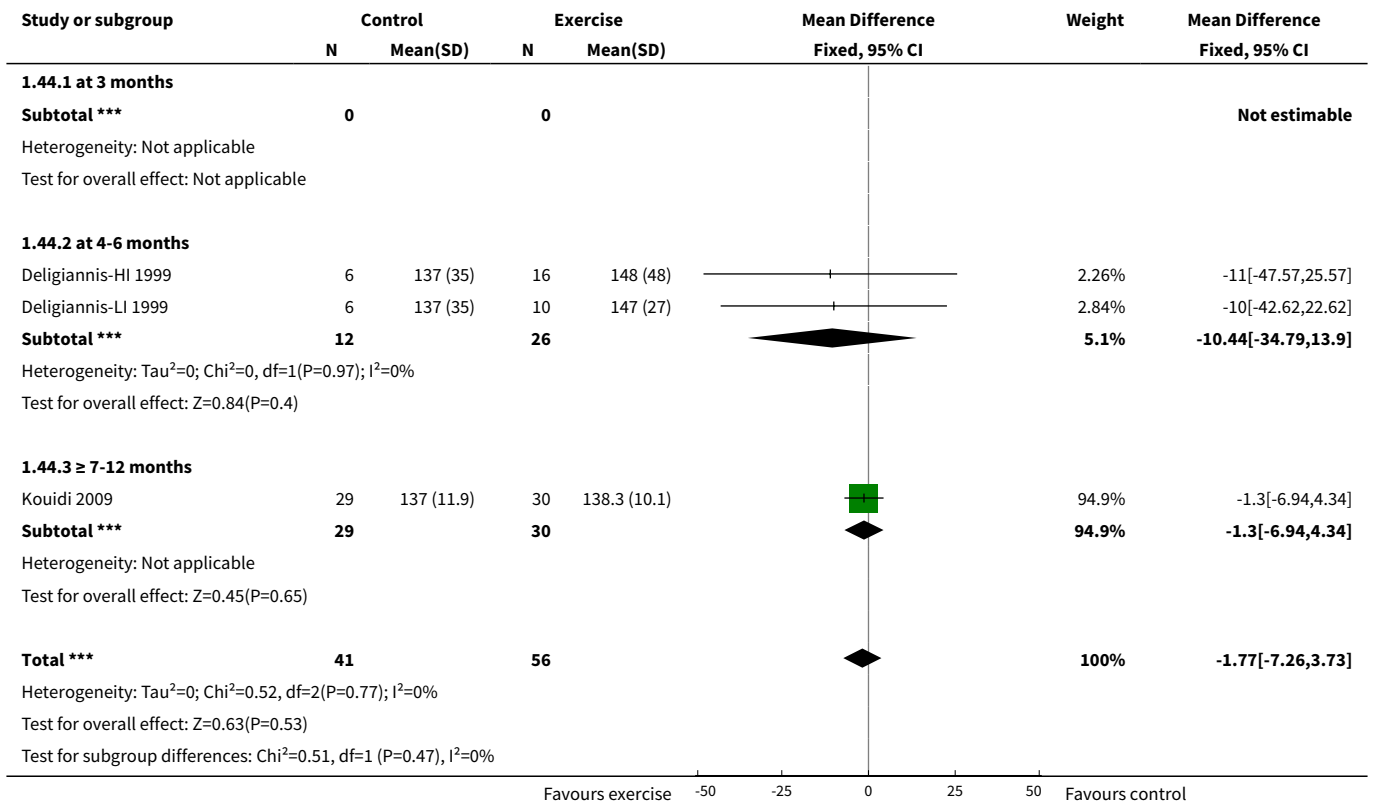
Analysis 1.42. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 42 Left ventricular posterior wall thickness at end-diastole.



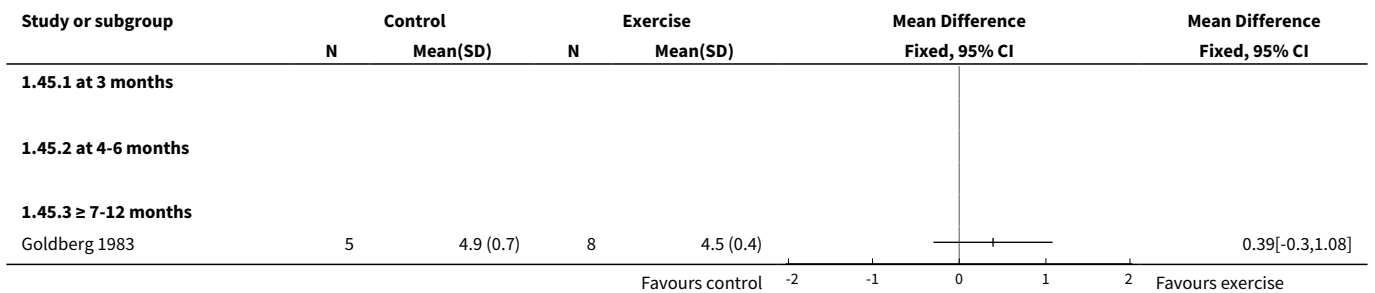
Analysis 1.43. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 43 Left ventricular mass.



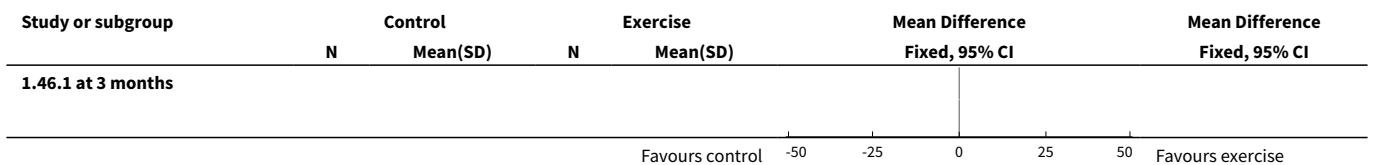
Analysis 1.44. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 44 Left ventricular mass index.



Analysis 1.45. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 45 Fasting plasma glucose.

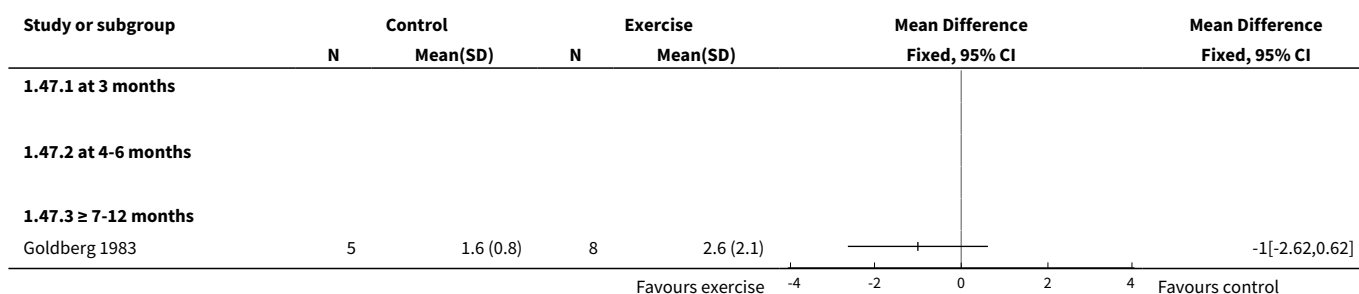


Analysis 1.46. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 46 Fasting plasma insulin.





Analysis 1.47. Comparison 1 Any exercise versus control (no exercise/placebo exercise), Outcome 47 Glucose disappearance.



Comparison 2. High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	17	647	Std. Mean Difference (IV, Fixed, 95% CI)	-0.61 [-0.77, -0.45]
1.1 at 3 months	4	102	Std. Mean Difference (IV, Fixed, 95% CI)	-0.54 [-0.94, -0.13]
1.2 at 4-6 months	7	207	Std. Mean Difference (IV, Fixed, 95% CI)	-0.82 [-1.12, -0.53]
1.3 ≥ 7-12 months	6	338	Std. Mean Difference (IV, Fixed, 95% CI)	-0.52 [-0.74, -0.30]
2 Muscular strength (high value = improved)	8	322	Std. Mean Difference (IV, Fixed, 95% CI)	-0.50 [-0.72, -0.27]
2.1 at 3 months	4	140	Std. Mean Difference (IV, Fixed, 95% CI)	-0.57 [-0.91, -0.23]
2.2 at 4-6 months	3	87	Std. Mean Difference (IV, Fixed, 95% CI)	-0.53 [-0.97, -0.08]
2.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.78, 0.04]
3 Muscular strength (low value = improved)	3	148	Std. Mean Difference (IV, Fixed, 95% CI)	0.58 [0.25, 0.92]
3.1 3 months	2	123	Std. Mean Difference (IV, Fixed, 95% CI)	0.69 [0.32, 1.05]
3.2 at 4-6 months	1	25	Std. Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.80, 0.88]
3.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60	2	52	Mean Difference (IV, Fixed, 95% CI)	-3.64 [-7.93, 0.65]
4.1 at 3 months	1	27	Mean Difference (IV, Fixed, 95% CI)	-2.80 [-7.89, 2.29]
4.2 at 4-6 months	1	25	Mean Difference (IV, Fixed, 95% CI)	-5.70 [-13.68, 2.28]
4.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Walking capacity	7	191	Std. Mean Difference (IV, Random, 95% CI)	-0.36 [-0.65, -0.06]
5.1 at 3 months	4	122	Std. Mean Difference (IV, Random, 95% CI)	-0.50 [-0.86, -0.13]
5.2 at 4-6 months	3	69	Std. Mean Difference (IV, Random, 95% CI)	-0.10 [-0.79, 0.59]
5.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 Stair climbing capacity: stair climb test (22 steps)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 ADL capacity	3		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 at 3 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 at 4-6 months	3	88	Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.39, 0.48]
7.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Diastolic blood pressure: resting	6	254	Mean Difference (IV, Fixed, 95% CI)	3.98 [1.90, 6.05]
8.1 at 3 months	1	29	Mean Difference (IV, Fixed, 95% CI)	3.5 [-4.02, 11.02]
8.2 at 4-6 months	1	28	Mean Difference (IV, Fixed, 95% CI)	3.0 [-1.27, 7.27]
8.3 ≥ 7-12 months	4	197	Mean Difference (IV, Fixed, 95% CI)	4.37 [1.87, 6.87]
9 Systolic blood pressure: resting	5	211	Mean Difference (IV, Fixed, 95% CI)	4.60 [0.37, 8.83]
9.1 at 3 months	1	29	Mean Difference (IV, Fixed, 95% CI)	7.10 [-7.20, 21.40]
9.2 at 4-6 months	1	28	Mean Difference (IV, Fixed, 95% CI)	8.0 [-0.89, 16.89]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.3 ≥ 7-12 months	3	154	Mean Difference (IV, Fixed, 95% CI)	3.16 [-1.94, 8.27]
10 Heart rate: maximum	7	169	Mean Difference (IV, Fixed, 95% CI)	-6.30 [-10.76, -1.84]
10.1 at 3 months	2	46	Mean Difference (IV, Fixed, 95% CI)	-10.11 [-21.79, 1.57]
10.2 at 4-6 months	4	90	Mean Difference (IV, Fixed, 95% CI)	-6.49 [-12.83, -0.15]
10.3 ≥ 7-12 months	1	33	Mean Difference (IV, Fixed, 95% CI)	-4.5 [-11.93, 2.93]
11 Heart rate: resting	4	129	Mean Difference (IV, Random, 95% CI)	3.90 [0.60, 7.20]
11.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	1	28	Mean Difference (IV, Random, 95% CI)	4.5 [-2.03, 11.03]
11.3 ≥ 7-12 months	3	101	Mean Difference (IV, Random, 95% CI)	3.02 [-1.89, 7.94]
12 Albumin	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 at 3 months	2	75	Mean Difference (IV, Random, 95% CI)	-1.46 [-2.89, -0.04]
12.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Pre-albumin	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.1 at 3 months	3	86	Mean Difference (IV, Fixed, 95% CI)	-44.02 [-71.52, -16.53]
13.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 SGA	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
14.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15 Energy intake	3		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
15.1 at 3 months	3	86	Std. Mean Difference (IV, Random, 95% CI)	-0.57 [-1.01, -0.13]
15.2 at 4-6 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16 Protein intake	3		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
16.1 at 3 months	3	86	Std. Mean Difference (IV, Fixed, 95% CI)	-0.34 [-0.77, 0.09]
16.2 at 4-6 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Transferrin	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
17.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
18 Fat mass	3	175	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.17, 0.42]
18.1 at 3 months	1	36	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.92, 0.40]
18.2 at 4-6 months	1	44	Std. Mean Difference (IV, Random, 95% CI)	0.35 [-0.25, 0.94]
18.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.24, 0.57]
19 Waist circumference	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
19.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
19.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
20 Mid-arm circumference	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
20.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
20.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
21 Mid-calf circumference	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
21.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
21.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
21.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
22 Mid-thigh circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
22.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Interleukin 6	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
23.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
23.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
23.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
24 Lymphocytes (x 10⁹ L)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
24.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
24.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
24.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
25 Protein catabolic rate	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
25.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Physical activity	4	121	Std. Mean Difference (IV, Random, 95% CI)	-0.43 [-0.80, -0.05]
26.1 at 3 months	1	33	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.02, 0.36]
26.2 at 4-6 months	3	88	Std. Mean Difference (IV, Random, 95% CI)	-0.46 [-0.90, -0.02]
26.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
27 Depression	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
27.1 at 3 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

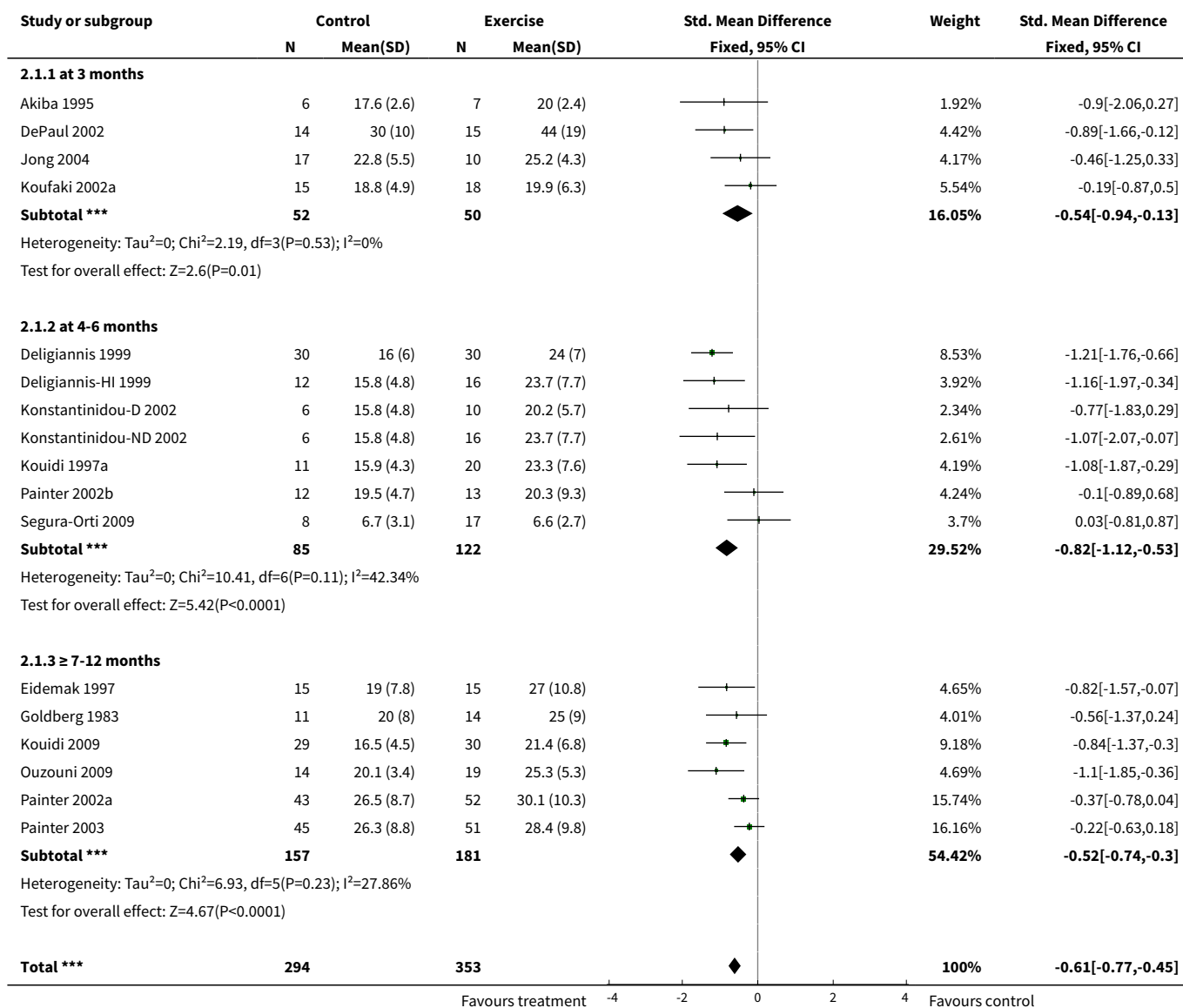
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
27.2 at 4-6 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
27.3 ≥ 7-12 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
28 Triglycerides	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
28.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
28.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
28.3 ≥ 7-12 months	2	52	Mean Difference (IV, Random, 95% CI)	0.22 [-0.43, 0.86]
29 Total cholesterol	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
29.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
29.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
29.3 ≥ 7-12 months	3	148	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.62, 0.33]
30 HDL cholesterol	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
30.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
30.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
30.3 ≥ 7-12 months	2	118	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.24, 0.02]
31 Type I muscle fibre area	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
31.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
31.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
31.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
32 Mid-thigh muscle area	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
32.1 at 3 months	3	111	Mean Difference (IV, Random, 95% CI)	-3.22 [-9.67, 3.24]
32.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
32.3 ≥ 7-12 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
33 Thigh muscle attenuation (Hounsfield units)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
33.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
33.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

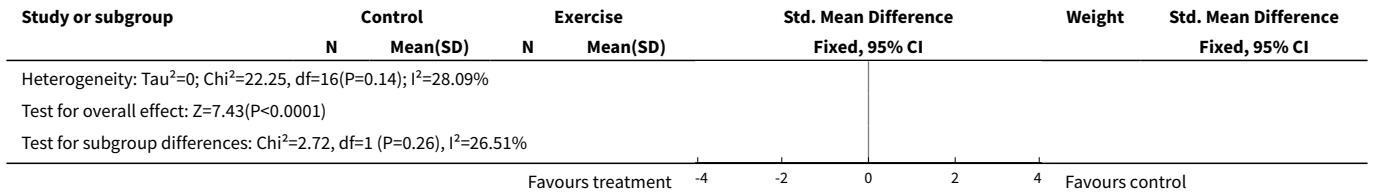
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
33.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
34 HRV index	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
34.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
34.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
34.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
35 Mean cardiac R-R interval	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
35.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
35.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
35.3 ≥ 7-12 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
36 SDNN	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
36.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
36.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
36.3 ≥ 7-12 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
37 Arrhythmias: Low class > II (no)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
37.1 at 3 months	0		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
37.2 at 4-6 months	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
37.3 ≥ 7-12 months	0		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
38 Left ventricular internal dimension at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
38.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
38.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
38.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
39 Left ventricular internal dimension at end-systole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
39.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
39.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
39.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
40 Intraventricular septal thickness at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
40.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
40.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
40.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
41 Left ventricular posterior wall thickness at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
41.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
41.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
41.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
42 Left ventricular mass	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
42.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
42.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
42.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
43 Left ventricular mass index	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
43.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
43.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
43.3 ≥ 7-12 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
44 Fasting plasma glucose	2	57	Mean Difference (IV, Random, 95% CI)	0.73 [-1.35, 2.81]
44.1 at 3 months	2	44	Mean Difference (IV, Random, 95% CI)	2.93 [-3.84, 9.70]
44.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
44.3 ≥ 7-12 months	1	13	Mean Difference (IV, Random, 95% CI)	0.39 [-0.30, 1.08]
45 Fasting plasma insulin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
45.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
45.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

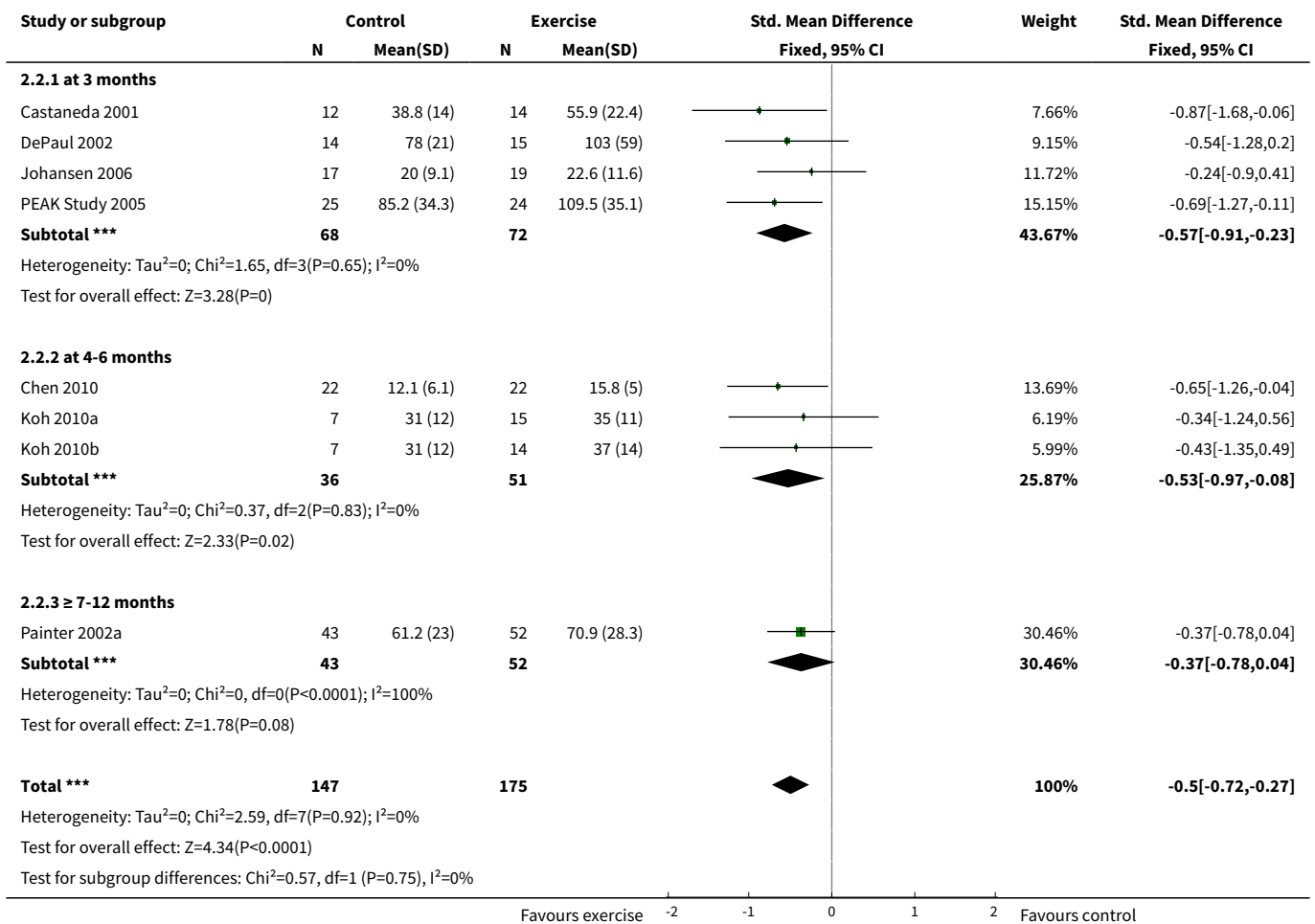
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
45.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46 Glucose disappearance	1	38	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-1.96, -0.04]
46.1 at 3 months	1	25	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-2.20, 0.20]
46.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46.3 ≥ 7-12 months	1	13	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-2.62, 0.62]

Analysis 2.1. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.

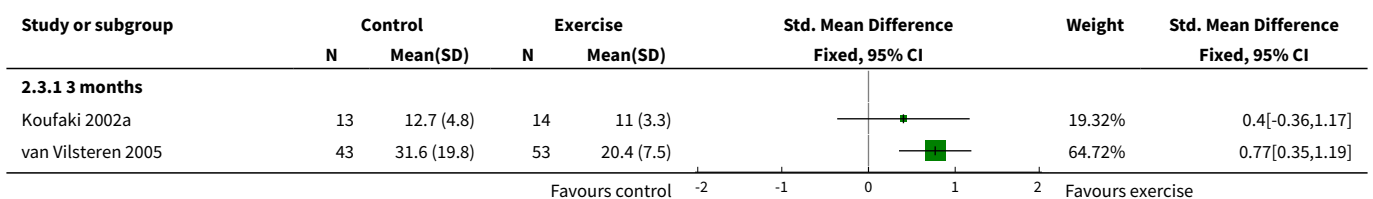


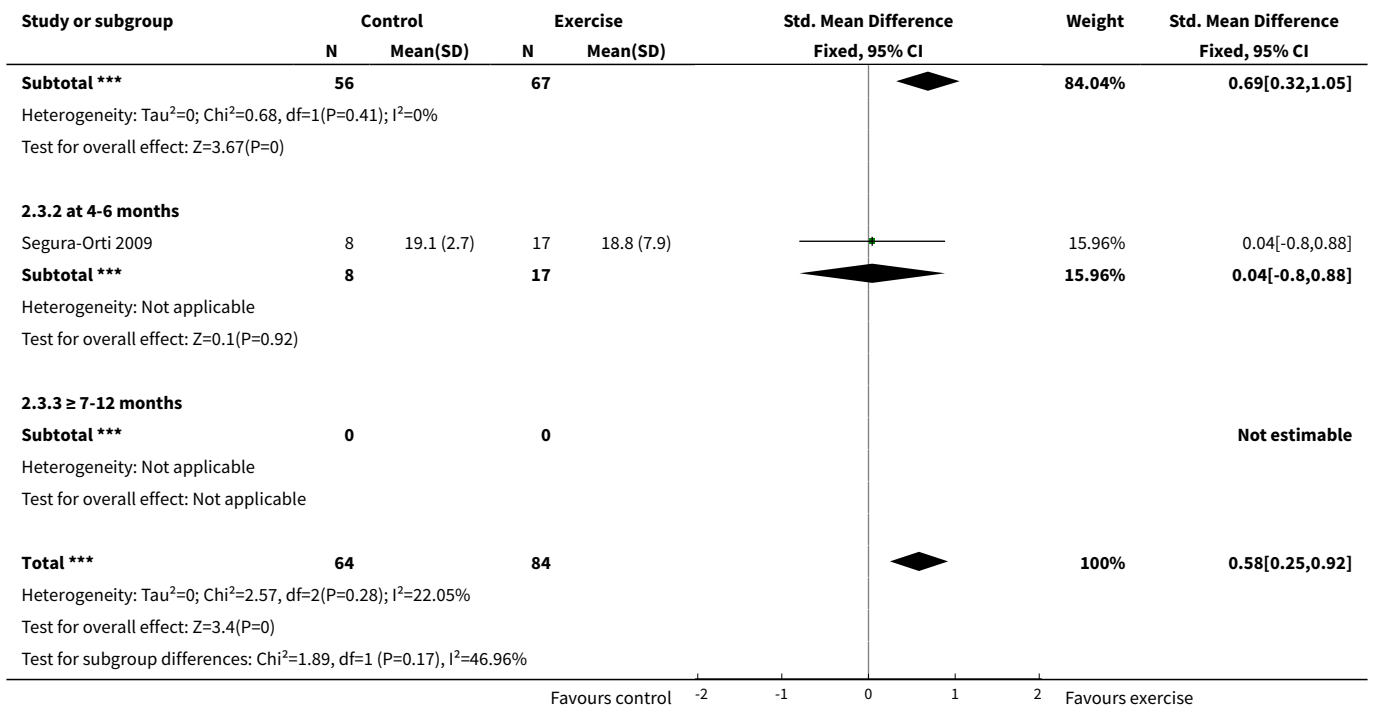


Analysis 2.2. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 2 Muscular strength (high value = improved).

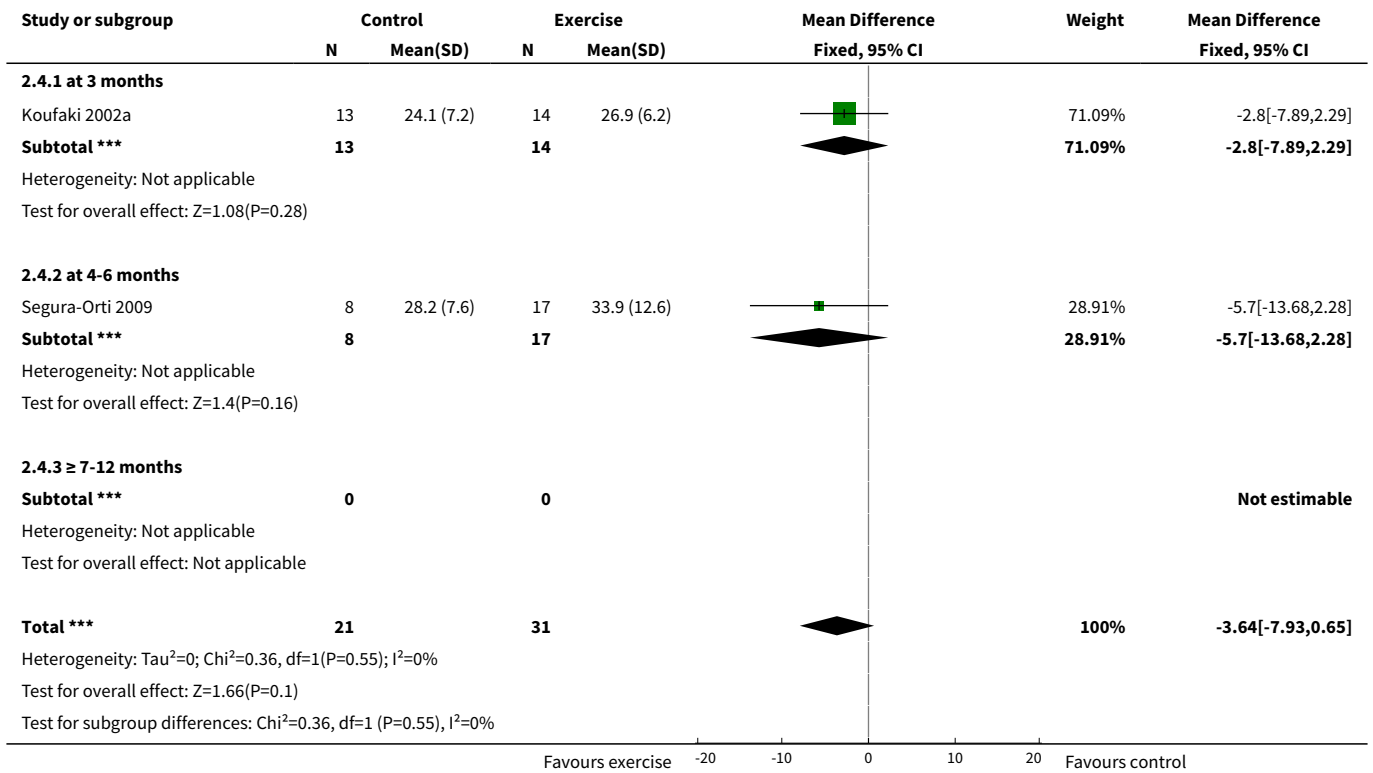


Analysis 2.3. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 3 Muscular strength (low value = improved).

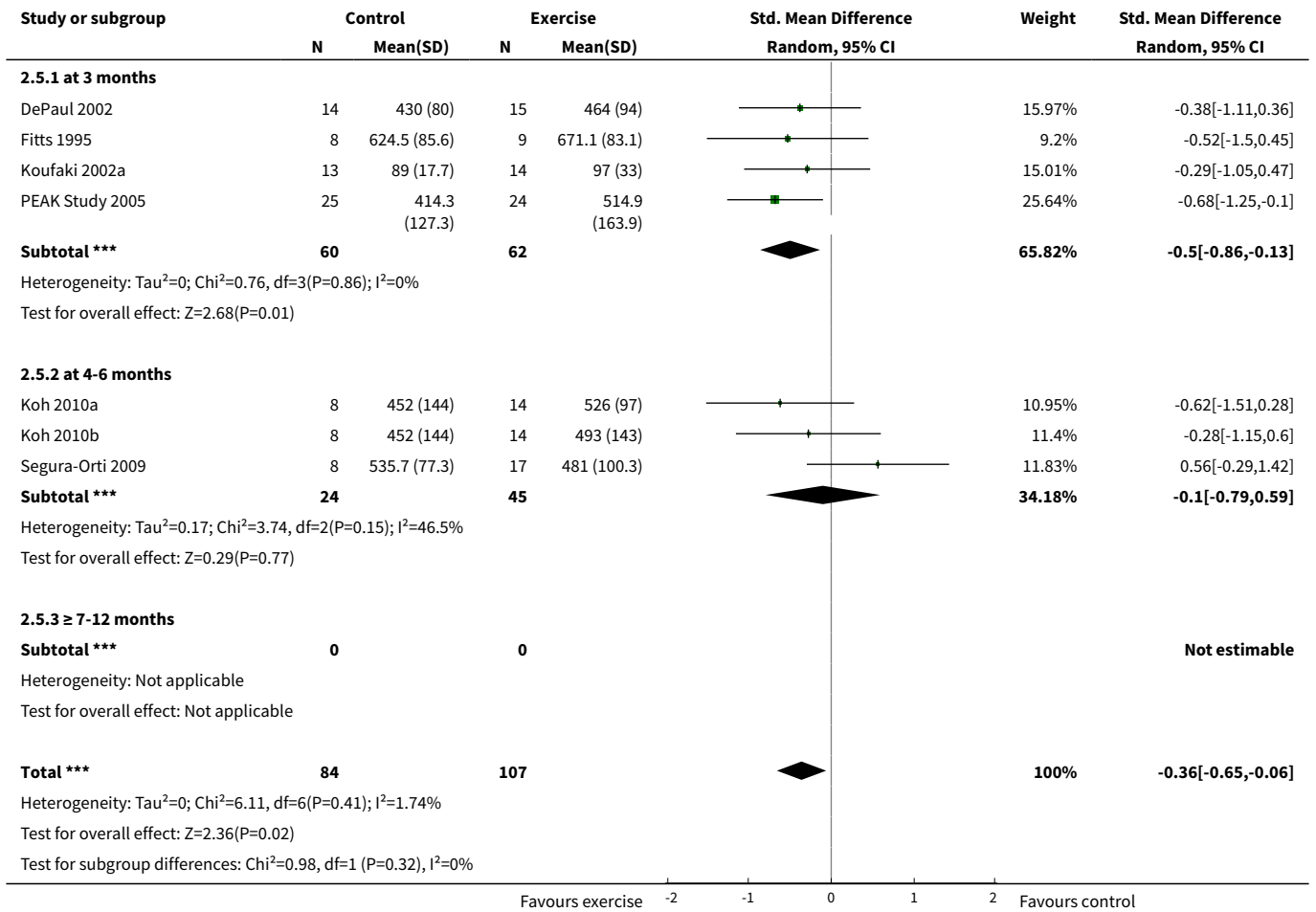




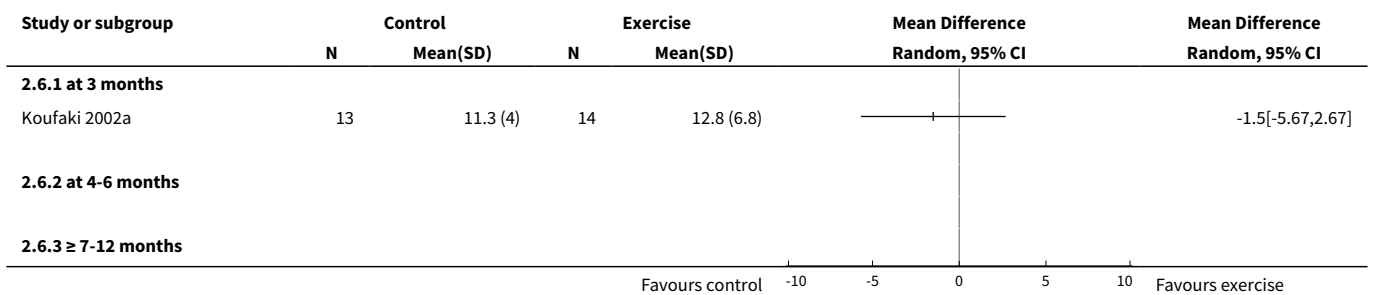
Analysis 2.4. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/ placebo exercise), Outcome 4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60.



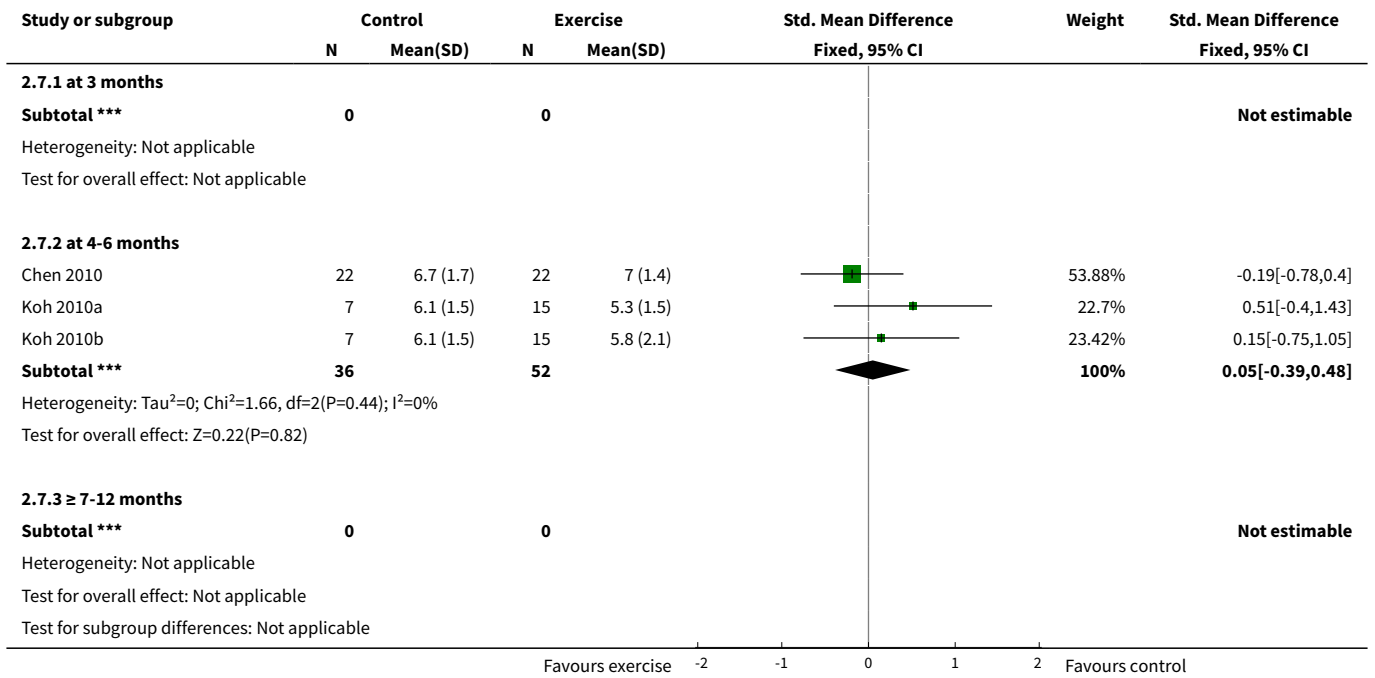
Analysis 2.5. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 5 Walking capacity.



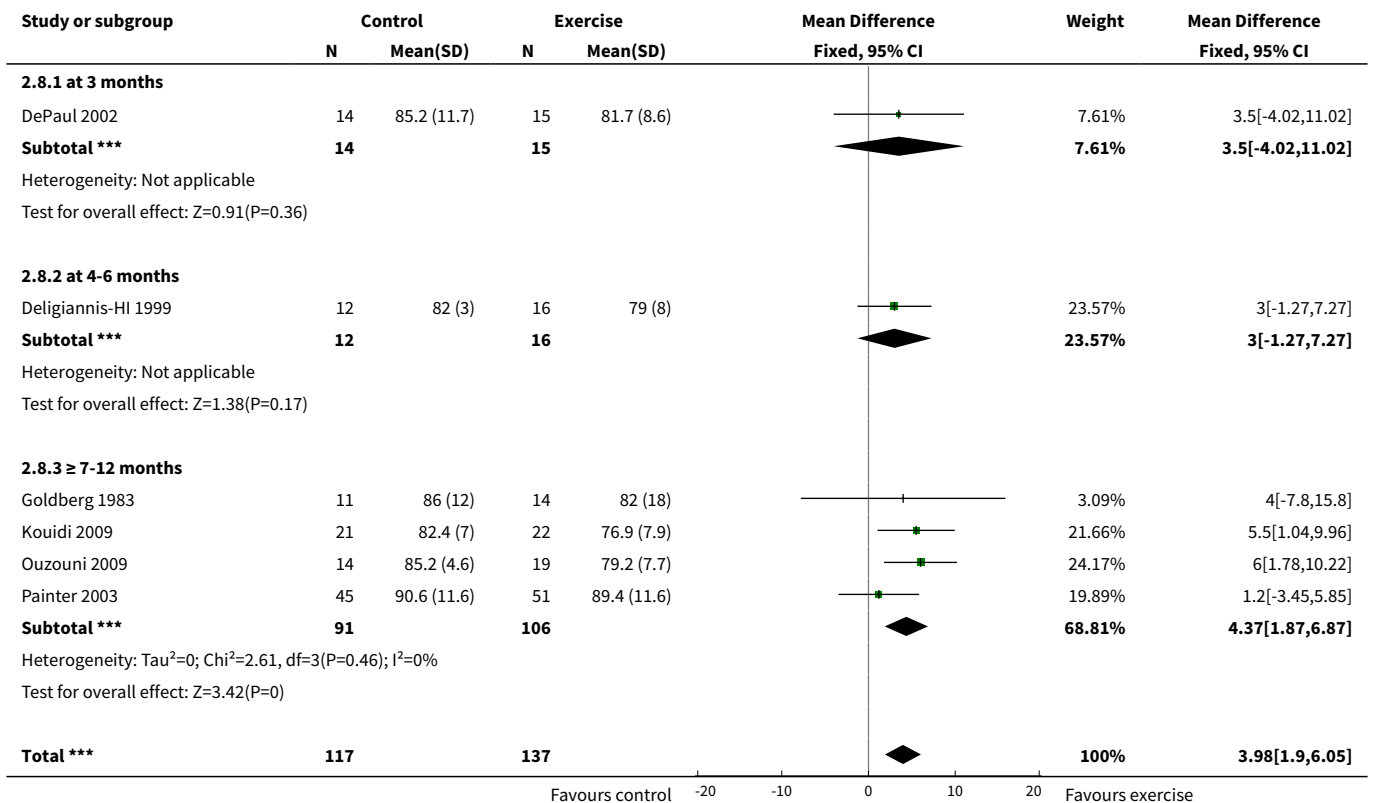
Analysis 2.6. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 6 Stair climbing capacity: stair climb test (22 steps).



Analysis 2.7. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 7 ADL capacity.



Analysis 2.8. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 8 Diastolic blood pressure: resting.



Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			

Heterogeneity: Tau²=0; Chi²=2.92, df=5(P=0.71); I²=0%
 Test for overall effect: Z=3.76(P=0)
 Test for subgroup differences: Chi²=0.31, df=1 (P=0.86), I²=0%

Favours control -20 -10 0 10 20 Favours exercise

Analysis 2.9. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 9 Systolic blood pressure: resting.

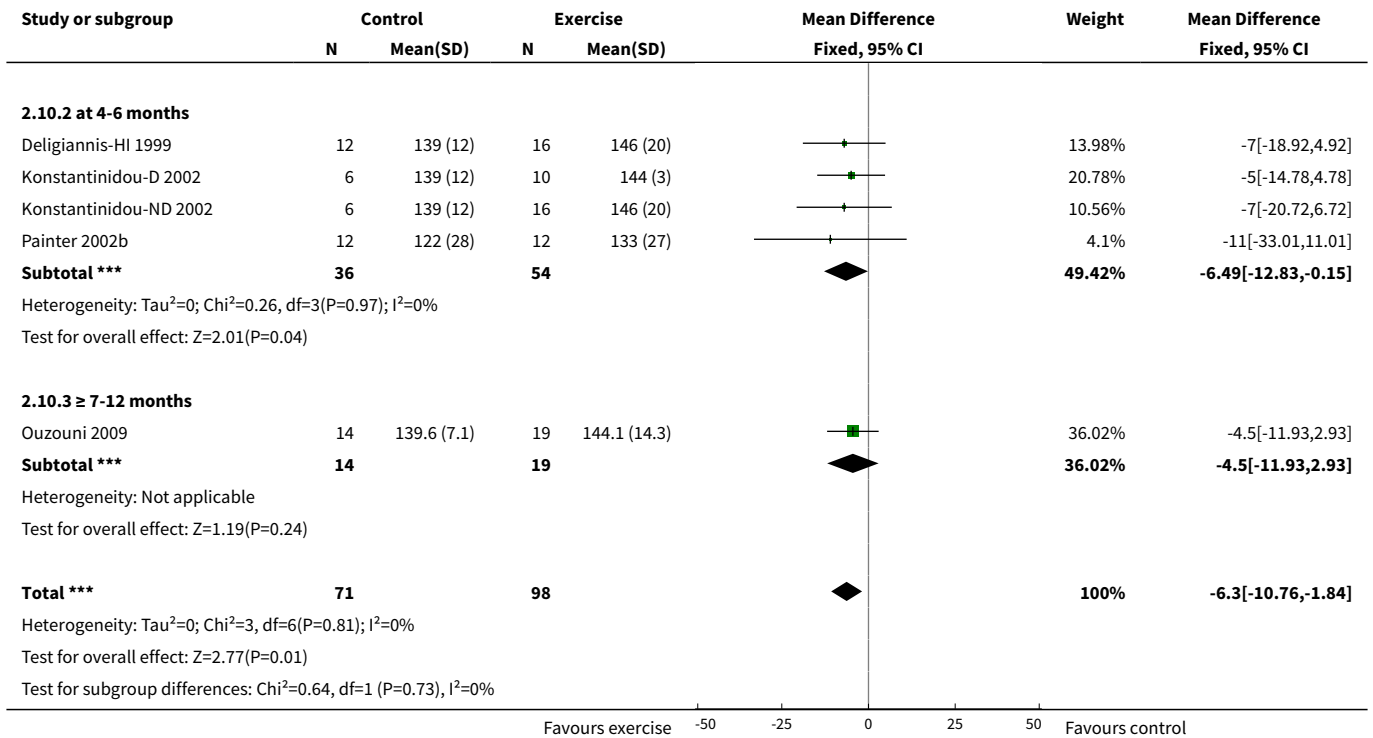
Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
2.9.1 at 3 months							
DePaul 2002	14	153.1 (20.2)	15	146 (19)		8.75%	7.1[-7.2,21.4]
Subtotal ***	14		15			8.75%	7.1[-7.2,21.4]
Heterogeneity: Not applicable Test for overall effect: Z=0.97(P=0.33)							
2.9.2 at 4-6 months							
Deligiannis-HI 1999	12	144 (10)	16	136 (14)		22.63%	8[-0.89,16.89]
Subtotal ***	12		16			22.63%	8[-0.89,16.89]
Heterogeneity: Not applicable Test for overall effect: Z=1.76(P=0.08)							
2.9.3 ≥ 7-12 months							
Goldberg 1983	11	149 (17)	14	142 (27)		5.94%	7[-10.35,24.35]
Ouzouni 2009	14	139.3 (9.1)	19	135.3 (11.6)		35.83%	4[-3.07,11.07]
Painter 2003	45	132.9 (19.5)	51	131.7 (21.3)		26.85%	1.2[-6.96,9.36]
Subtotal ***	70		84			68.62%	3.16[-1.94,8.27]
Heterogeneity: Tau ² =0; Chi ² =0.46, df=2(P=0.79); I ² =0% Test for overall effect: Z=1.21(P=0.22)							
Total ***	96		115			100%	4.6[0.37,8.83]
Heterogeneity: Tau ² =0; Chi ² =1.45, df=4(P=0.84); I ² =0% Test for overall effect: Z=2.13(P=0.03) Test for subgroup differences: Chi ² =0.98, df=1 (P=0.61), I ² =0%							

Favours control -50 -25 0 25 50 Favours exercise

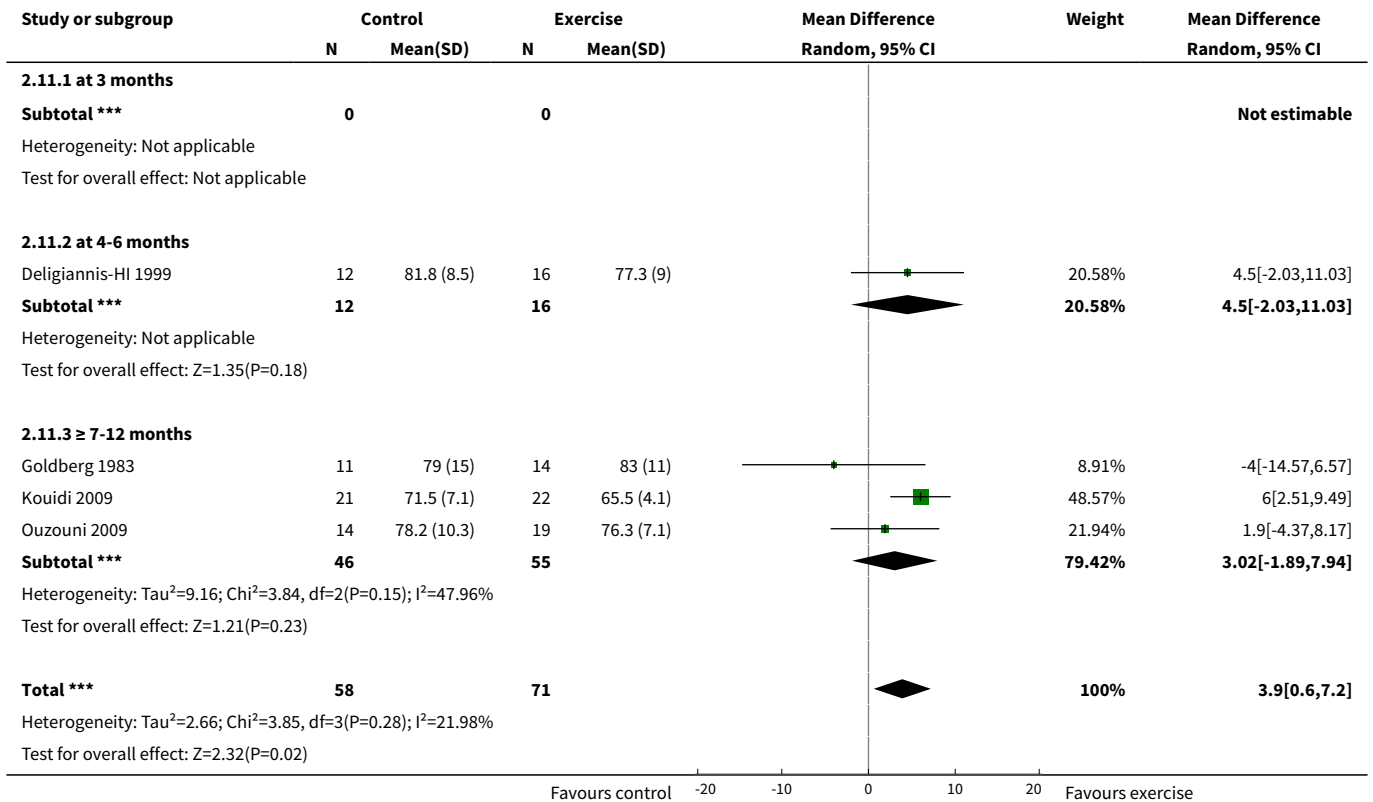
Analysis 2.10. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 10 Heart rate: maximum.

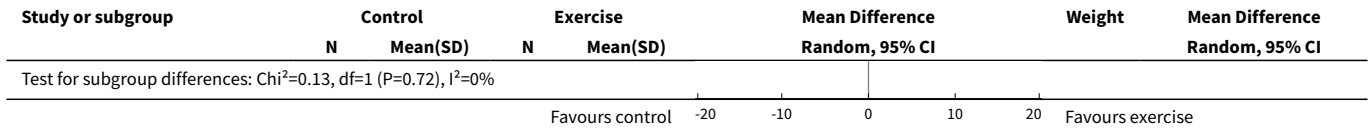
Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
2.10.1 at 3 months							
Akiba 1995	6	136.3 (19.5)	7	155.4 (8.6)		7%	-19.1[-35.95,-2.25]
Koufaki 2002a	15	127.2 (24.4)	18	129 (22.7)		7.57%	-1.8[-18,14.4]
Subtotal ***	21		25			14.57%	-10.11[-21.79,1.57]
Heterogeneity: Tau ² =0; Chi ² =2.1, df=1(P=0.15); I ² =52.47% Test for overall effect: Z=1.7(P=0.09)							

Favours exercise -50 -25 0 25 50 Favours control

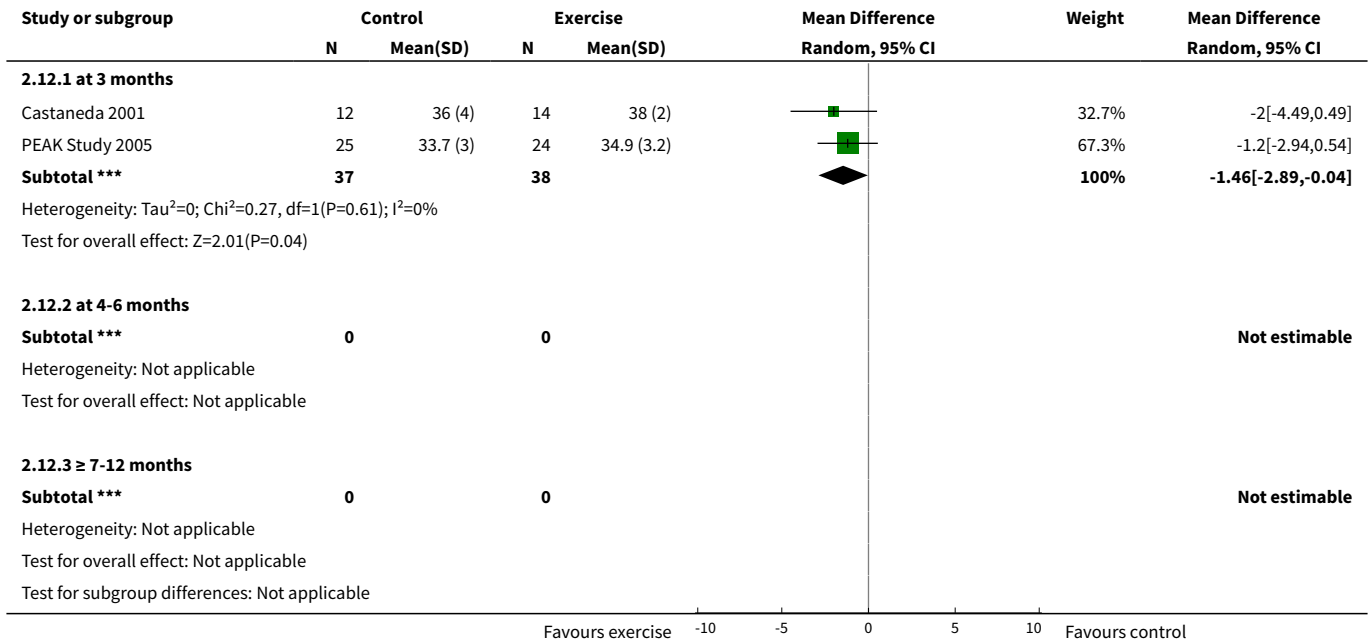


Analysis 2.11. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 11 Heart rate: resting.

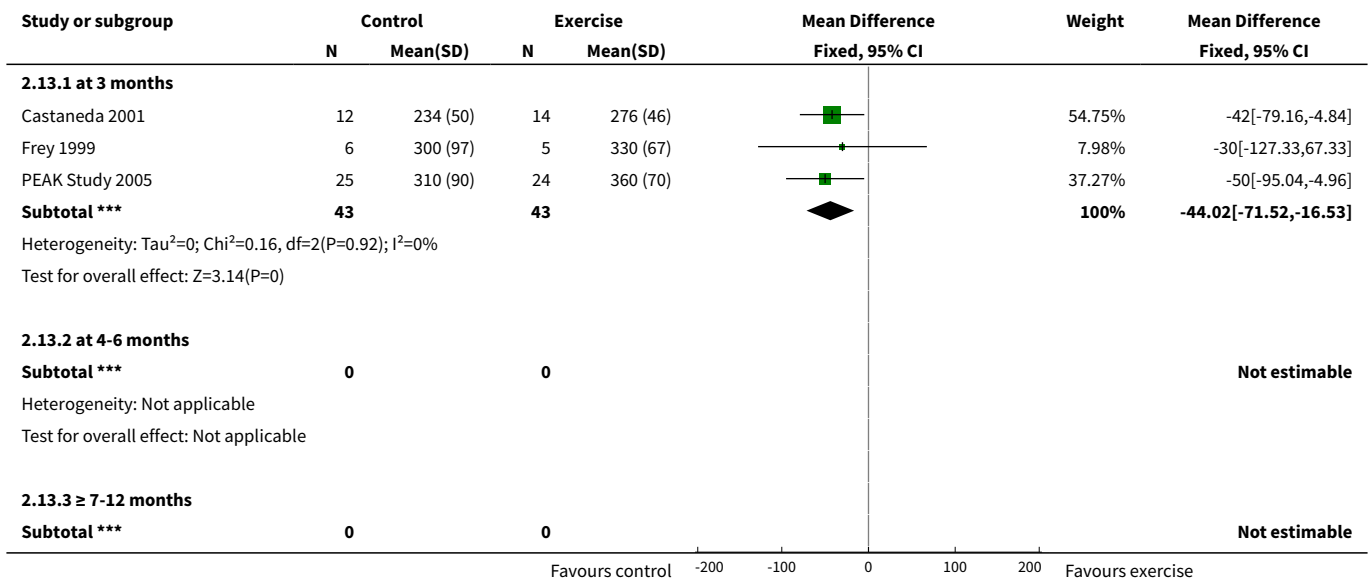


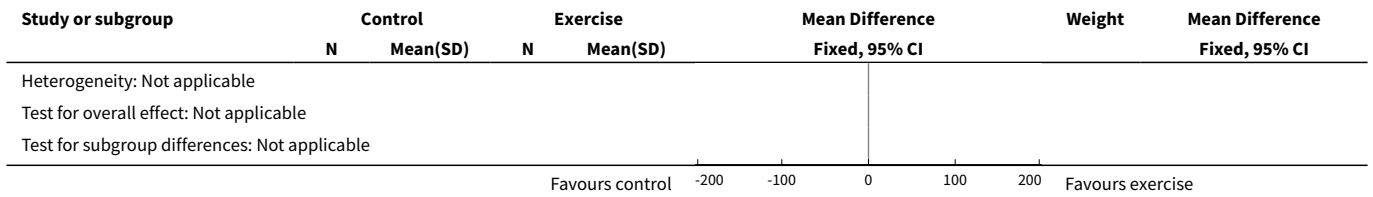


Analysis 2.12. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 12 Albumin.

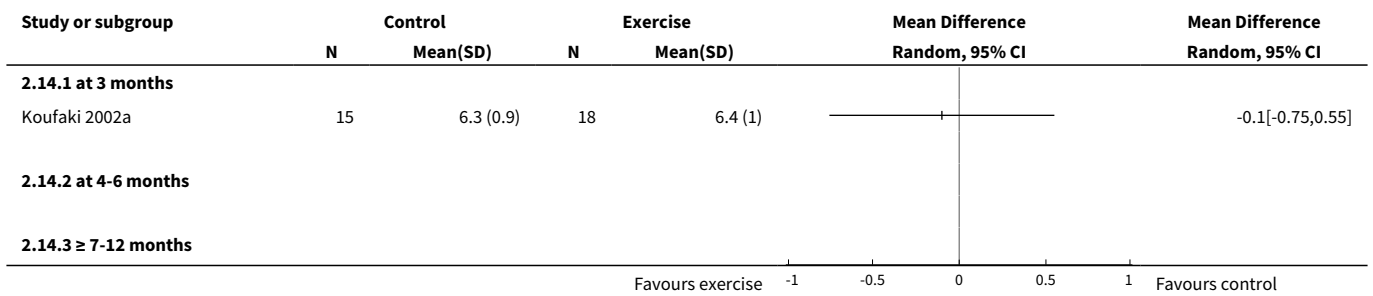


Analysis 2.13. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 13 Pre-albumin.

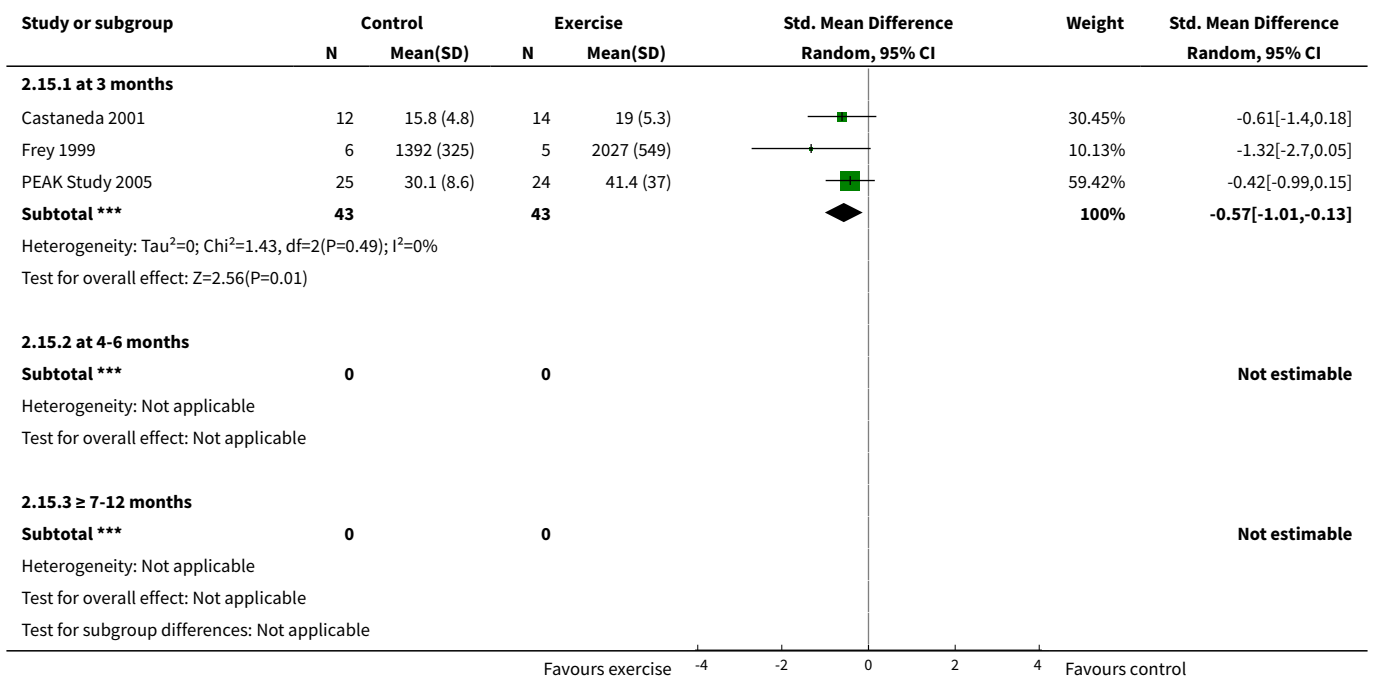




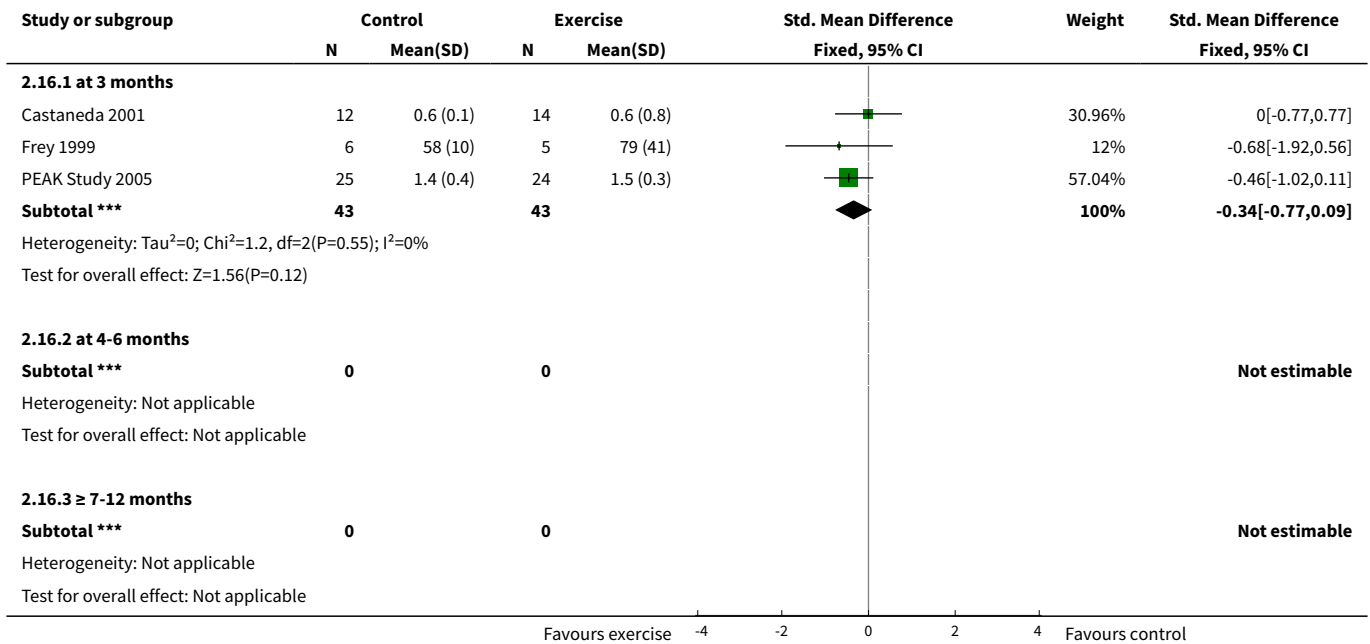
Analysis 2.14. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 14 SGA.



Analysis 2.15. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 15 Energy intake.



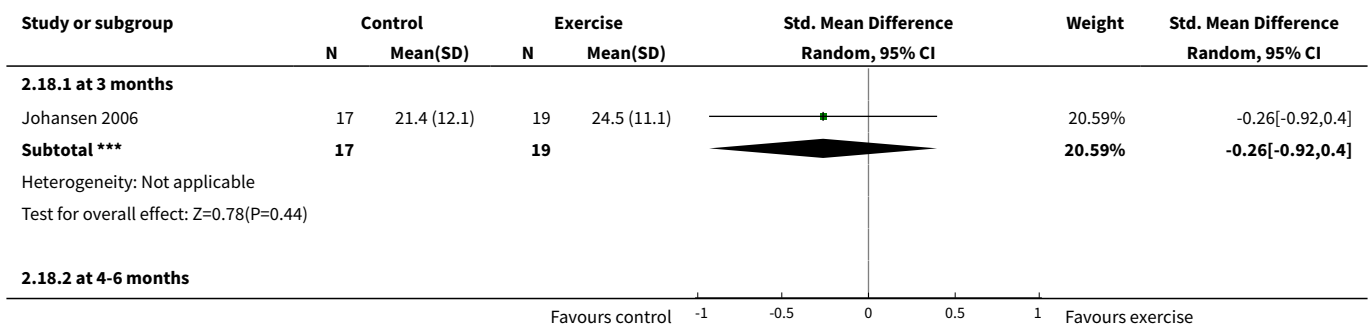
Analysis 2.16. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 16 Protein intake.

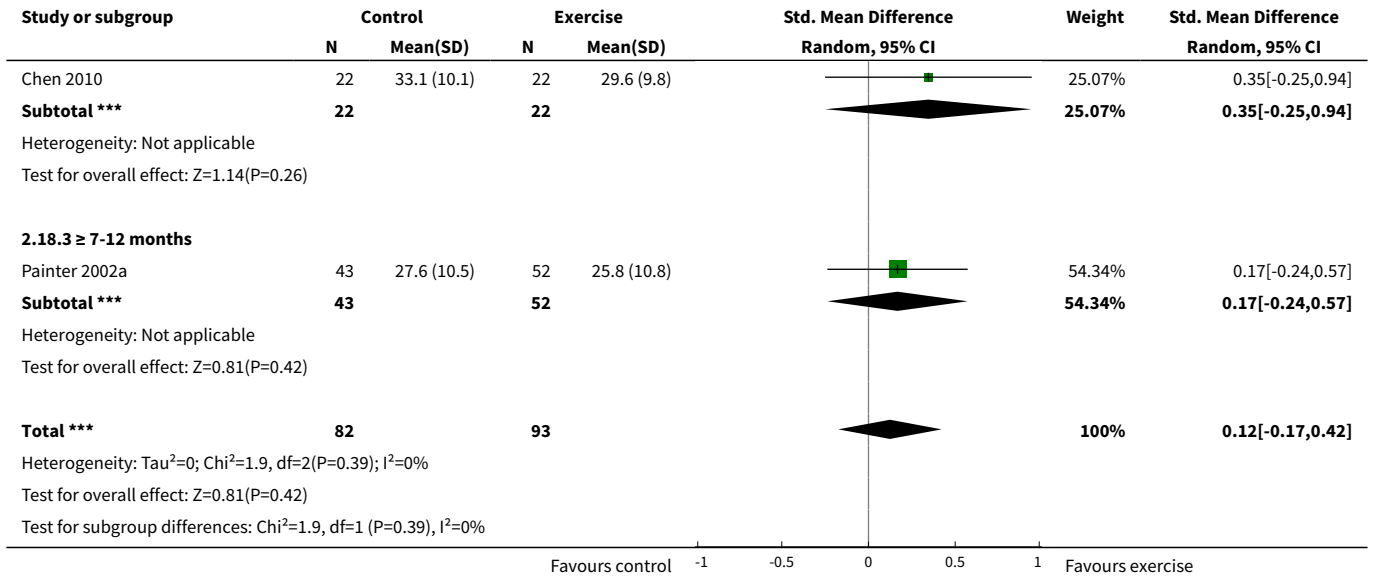


Analysis 2.17. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 17 Transferrin.



Analysis 2.18. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 18 Fat mass.





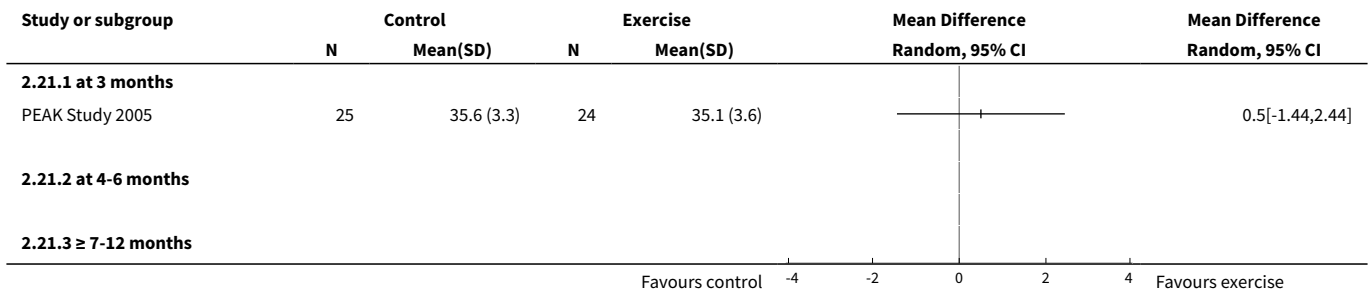
Analysis 2.19. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 19 Waist circumference.



Analysis 2.20. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 20 Mid-arm circumference.



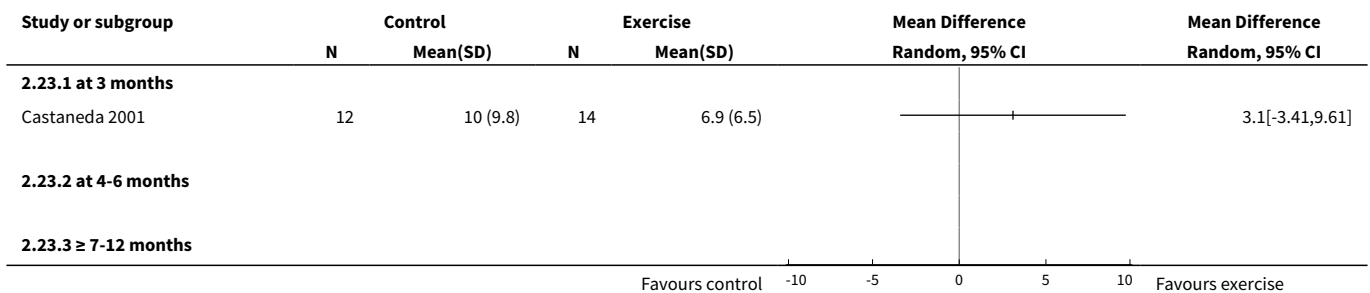
Analysis 2.21. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 21 Mid-calf circumference.



Analysis 2.22. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 22 Mid-thigh circumference.



Analysis 2.23. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 23 Interleukin 6.



Analysis 2.24. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 24 Lymphocytes ($\times 10^9$ L).



Study or subgroup	Control		Exercise		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
2.24.2 at 4-6 months						
2.24.3 ≥ 7-12 months						

Favours control -0.5 -0.25 0 0.25 0.5 Favours exercise

Analysis 2.25. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 25 Protein catabolic rate.

Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
2.25.1 at 3 months						
PEAK Study 2005	25	1.1 (0.2)	24	1.1 (0.3)		-0.01[-0.17,0.15]
2.25.2 at 4-6 months						
2.25.3 ≥ 7-12 months						

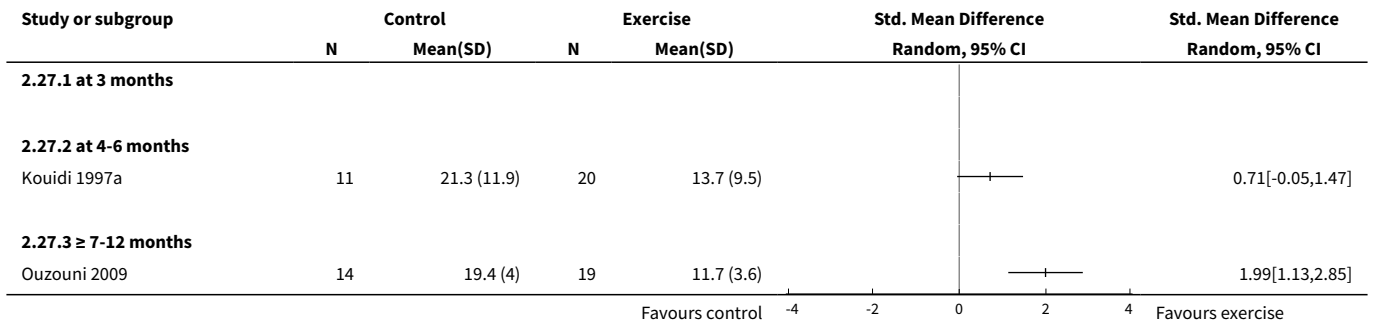
Favours control -0.2 -0.1 0 0.1 0.2 Favours exercise

Analysis 2.26. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 26 Physical activity.

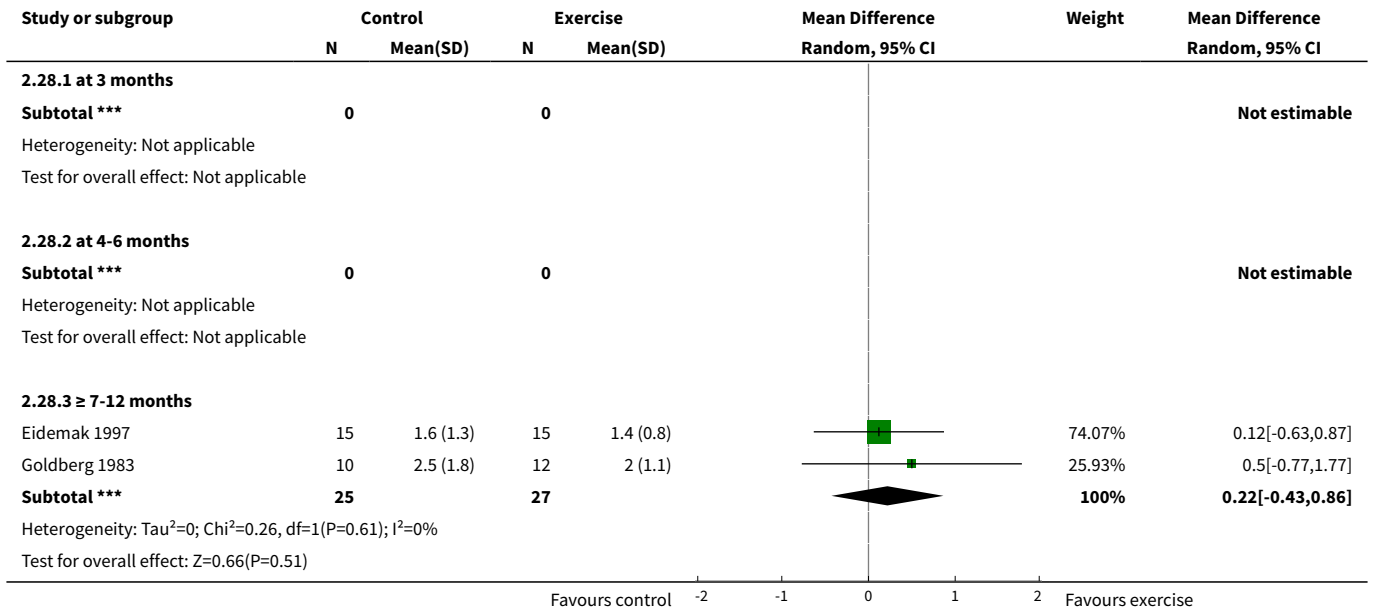
Study or subgroup	Control		Exercise		Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
2.26.1 at 3 months							
Koufaki 2002a	15	34.3 (1.7)	18	35.4 (4.1)		28.86%	-0.33[-1.02,0.36]
Subtotal ***	15		18			28.86%	-0.33[-1.02,0.36]
Heterogeneity: Not applicable Test for overall effect: Z=0.94(P=0.35)							
2.26.2 at 4-6 months							
Chen 2010	22	22.7 (30.5)	22	57.5 (69.3)		37.31%	-0.64[-1.25,-0.03]
Koh 2010a	7	943 (1701)	15	1920 (3273)		16.86%	-0.32[-1.23,0.58]
Koh 2010b	7	943 (1701)	15	1712 (3868)		16.98%	-0.22[-1.12,0.68]
Subtotal ***	36		52			71.14%	-0.46[-0.9,-0.02]
Heterogeneity: Tau ² =0; Chi ² =0.69, df=2(P=0.71); I ² =0% Test for overall effect: Z=2.07(P=0.04)							
2.26.3 ≥ 7-12 months							
Subtotal ***	0		0				Not estimable
Heterogeneity: Not applicable Test for overall effect: Not applicable							
Total ***	51		70			100%	-0.43[-0.8,-0.05]
Heterogeneity: Tau ² =0; Chi ² =0.79, df=3(P=0.85); I ² =0% Test for overall effect: Z=2.25(P=0.02) Test for subgroup differences: Chi ² =0.1, df=1 (P=0.75), I ² =0%							

Favours exercise -2 -1 0 1 2 Favours control

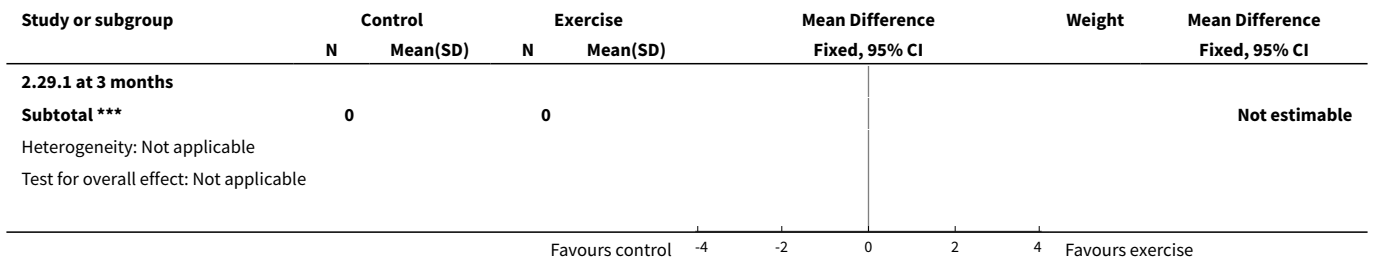
Analysis 2.27. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 27 Depression.

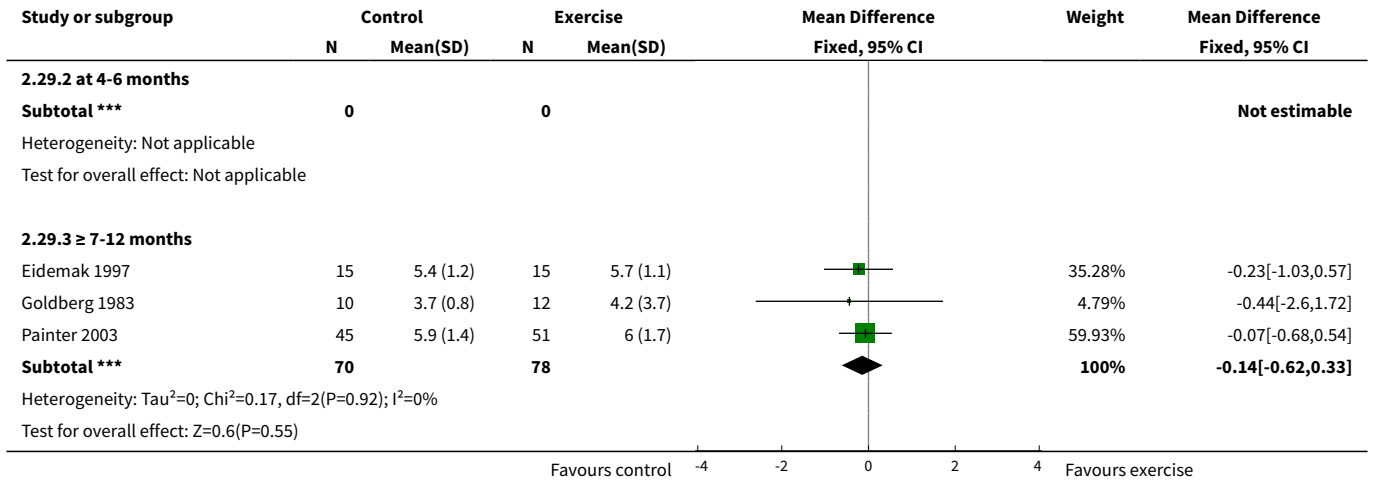


Analysis 2.28. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 28 Triglycerides.

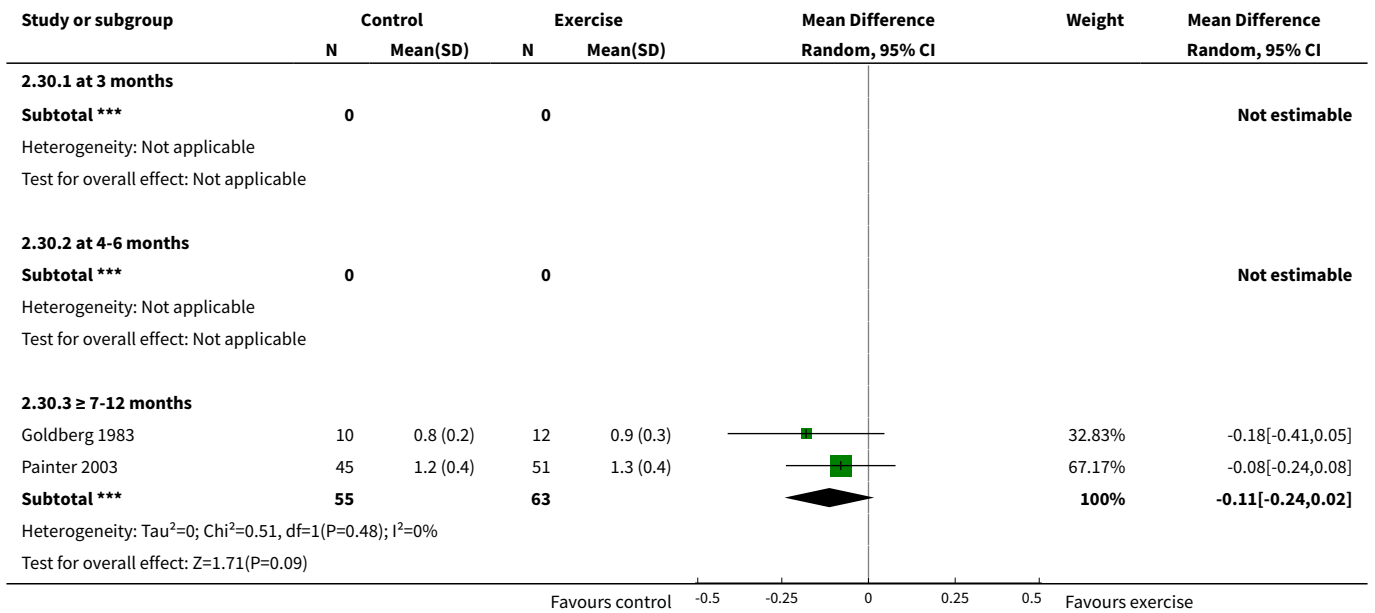


Analysis 2.29. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 29 Total cholesterol.

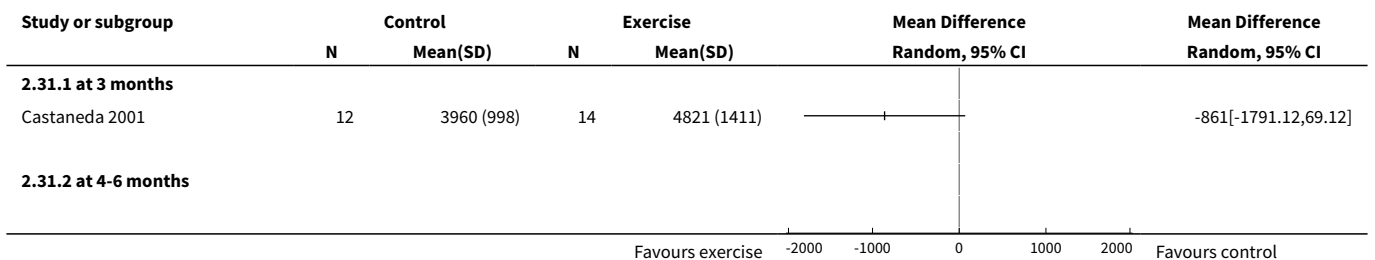


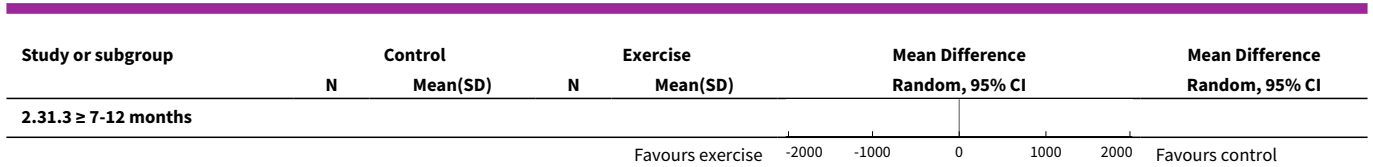


Analysis 2.30. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 30 HDL cholesterol.

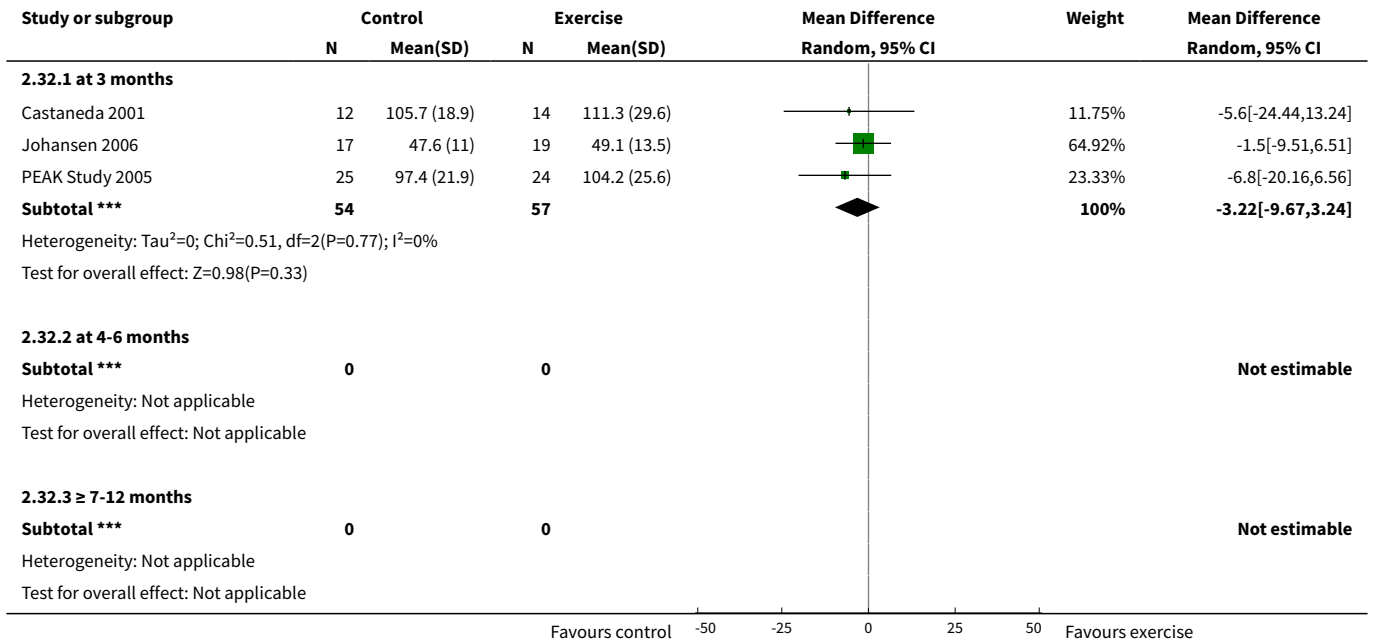


Analysis 2.31. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 31 Type I muscle fibre area.

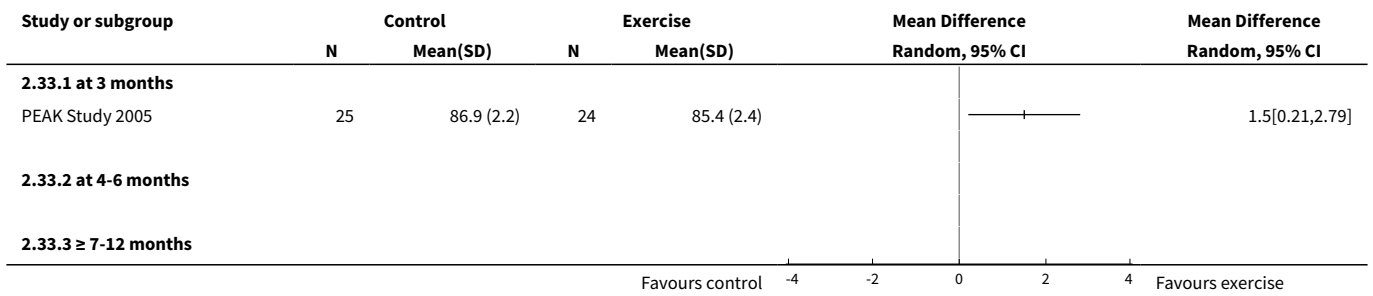




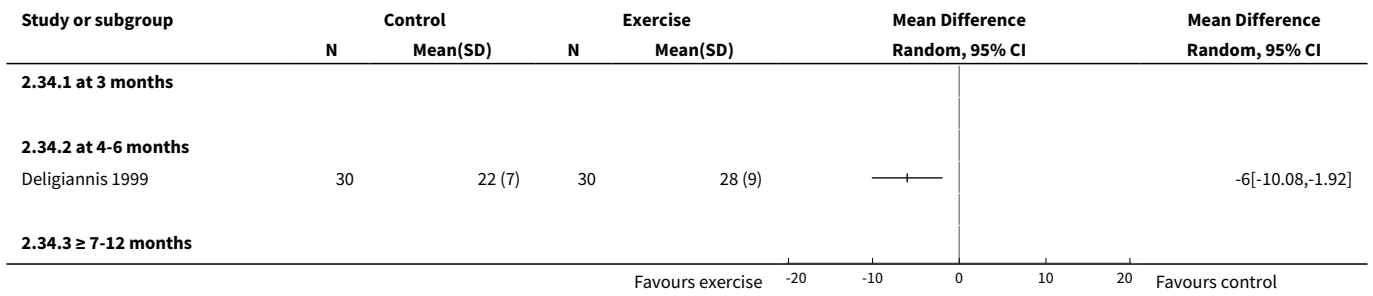
Analysis 2.32. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 32 Mid-thigh muscle area.



Analysis 2.33. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/placebo exercise), Outcome 33 Thigh muscle attenuation (Hounsfield units).



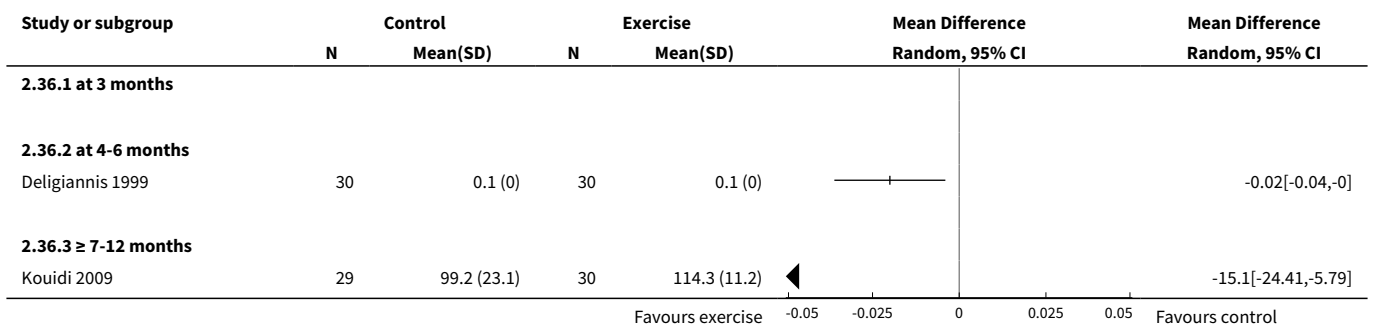
Analysis 2.34. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 34 HRV index.



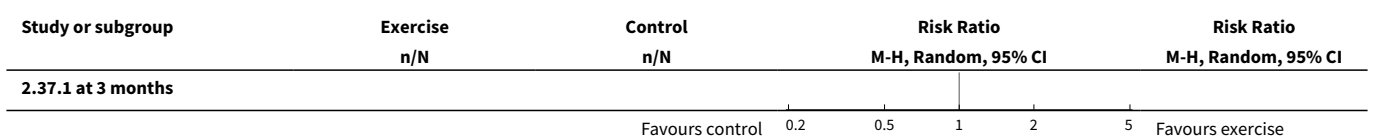
Analysis 2.35. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 35 Mean cardiac R-R interval.

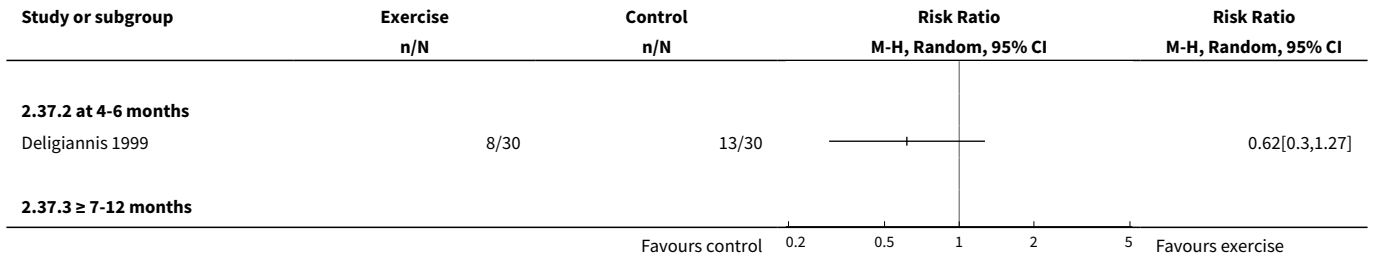


Analysis 2.36. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 36 SDNN.

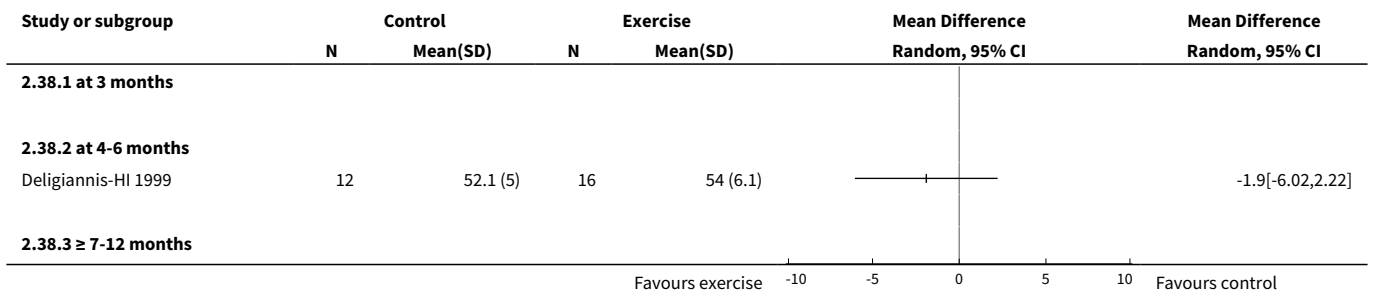


Analysis 2.37. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 37 Arrhythmias: Lown class > II (no).

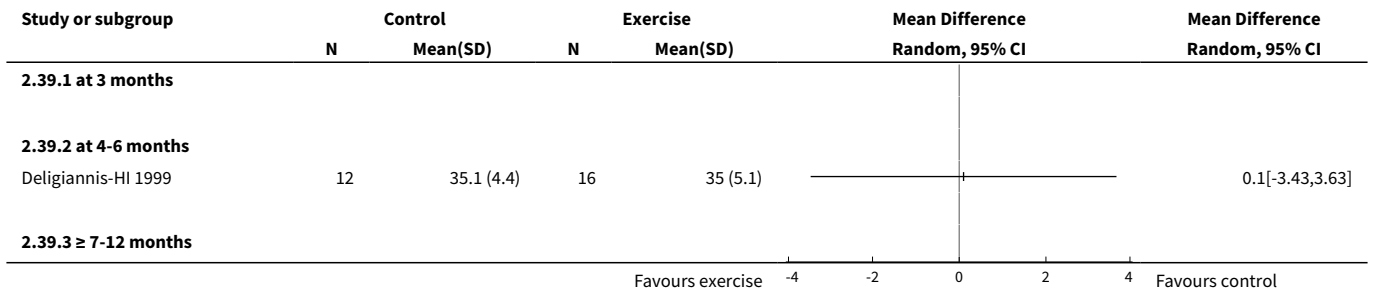




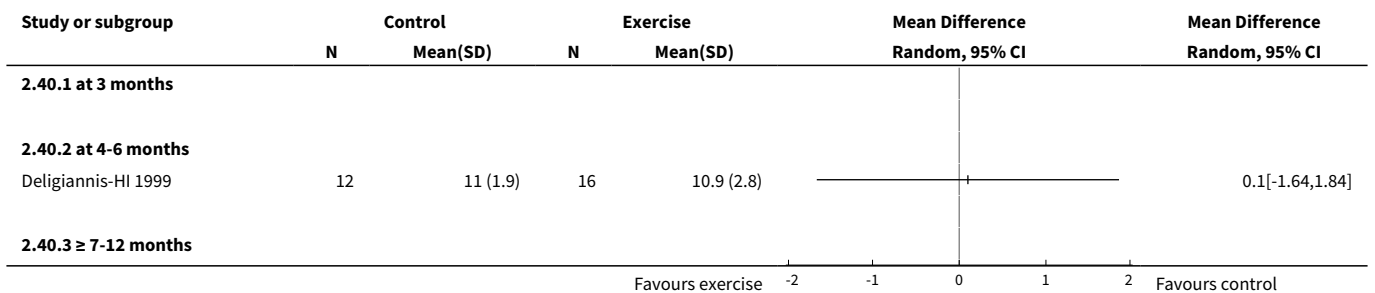
Analysis 2.38. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/ placebo exercise), Outcome 38 Left ventricular internal dimension at end-diastole.



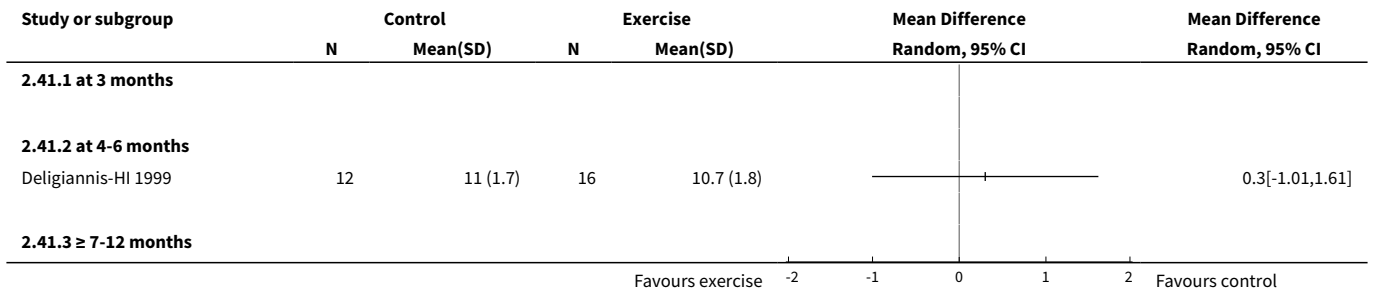
Analysis 2.39. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/ placebo exercise), Outcome 39 Left ventricular internal dimension at end-systole.



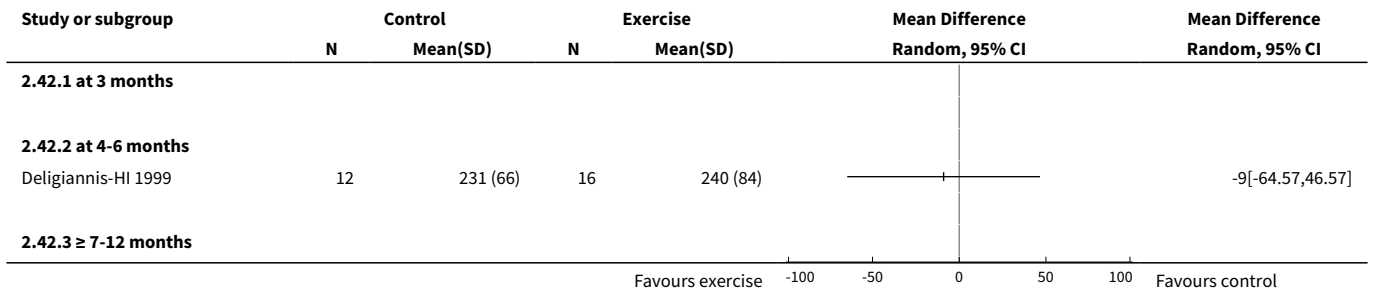
Analysis 2.40. Comparison 2 High intensity (≥ 60%) exercise versus control (no exercise/ placebo exercise), Outcome 40 Intraventricular septal thickness at end-diastole.



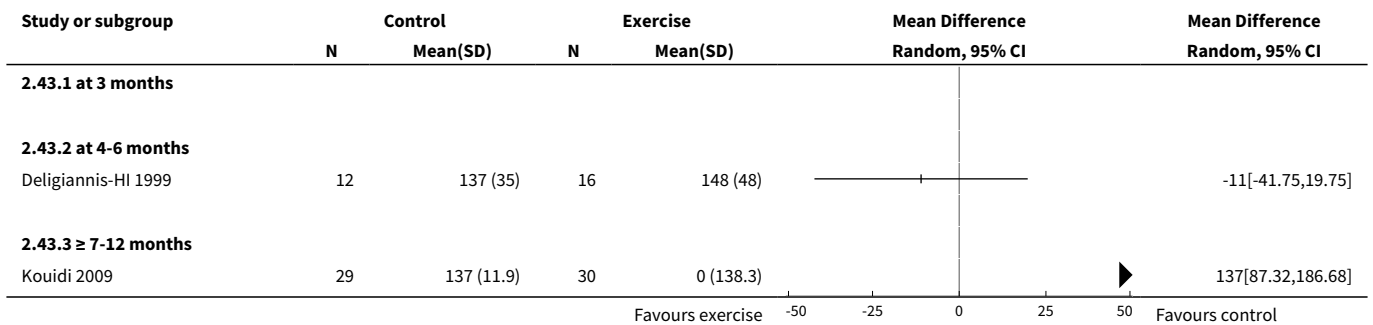
Analysis 2.41. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/ placebo exercise), Outcome 41 Left ventricular posterior wall thickness at end-diastole.



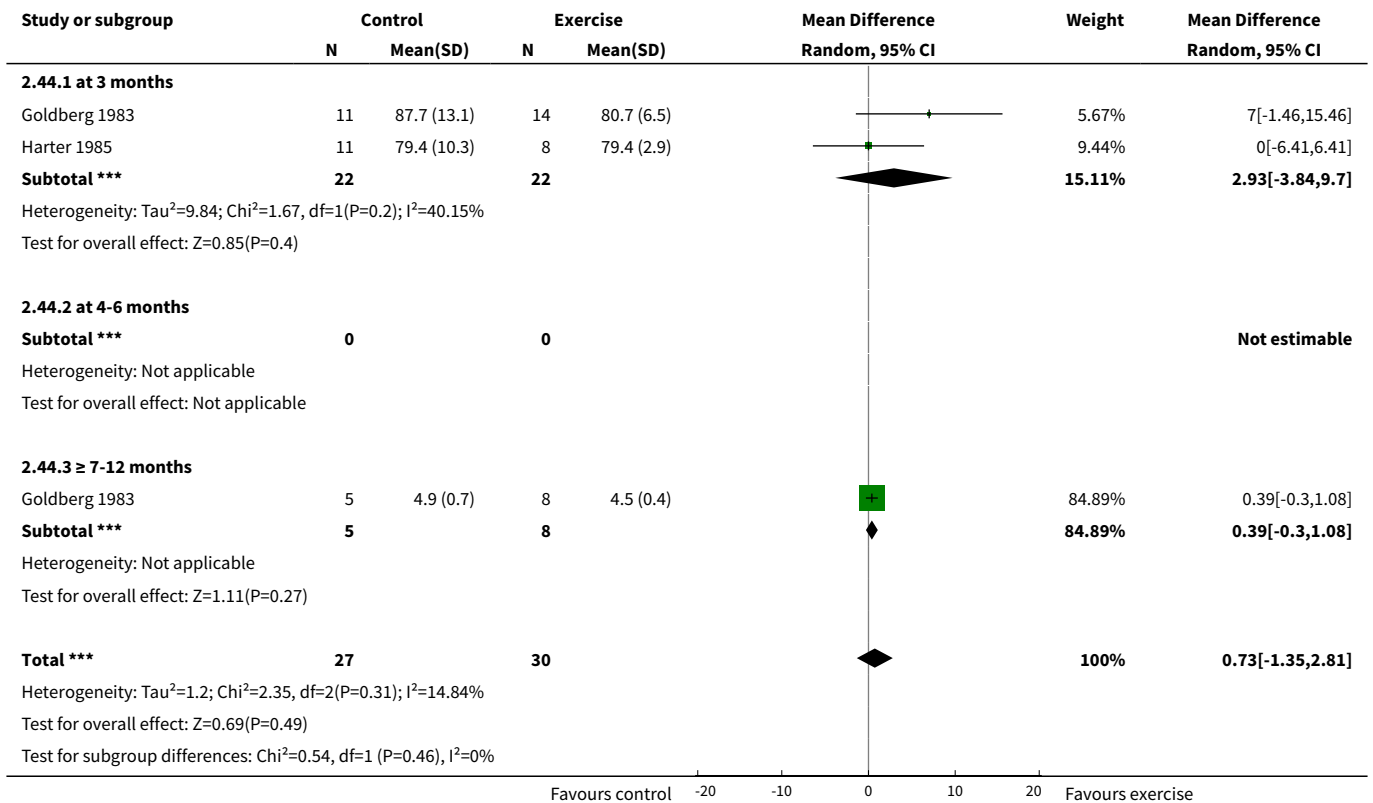
Analysis 2.42. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 42 Left ventricular mass.



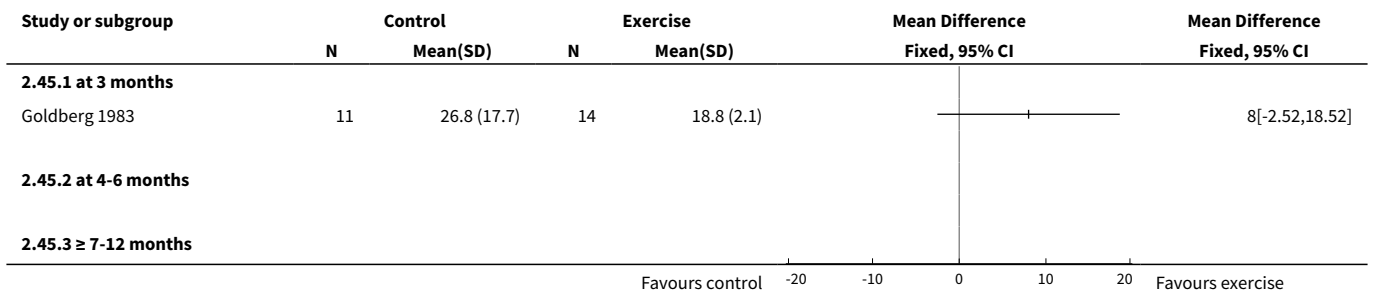
Analysis 2.43. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 43 Left ventricular mass index.



Analysis 2.44. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 44 Fasting plasma glucose.

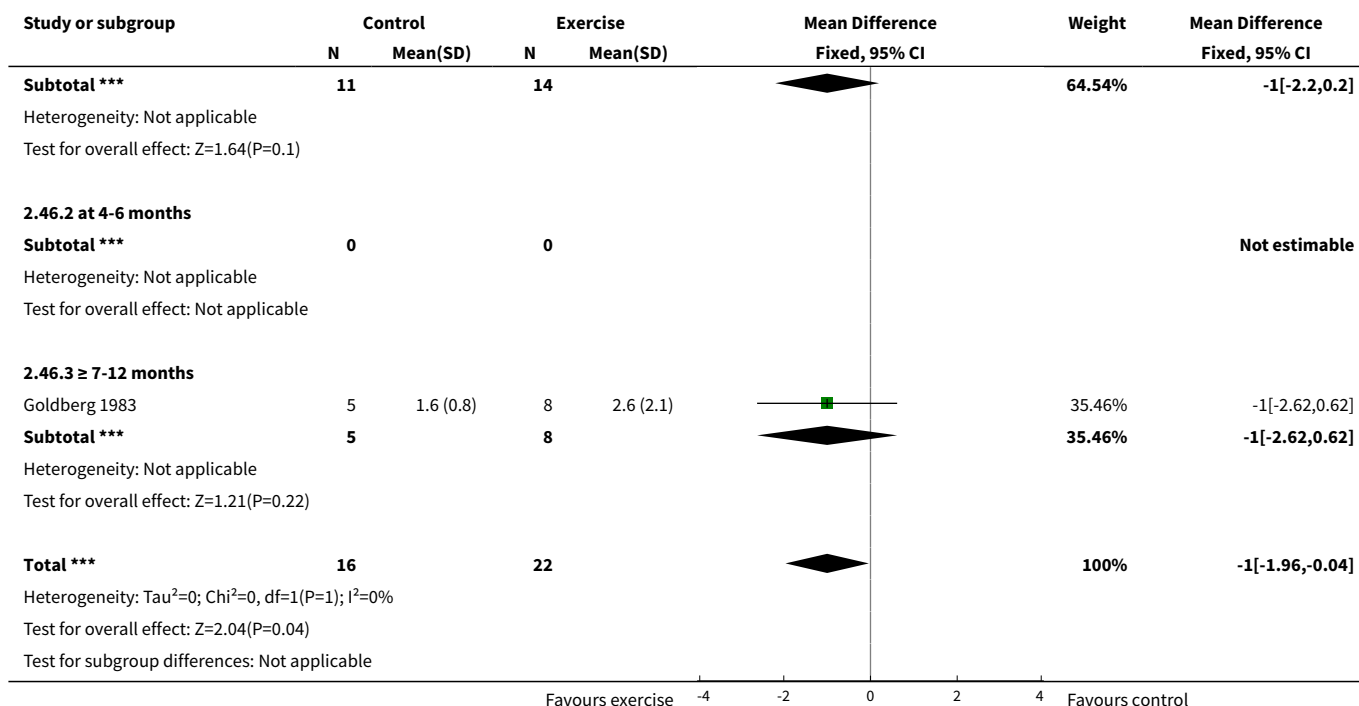


Analysis 2.45. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 45 Fasting plasma insulin.



Analysis 2.46. Comparison 2 High intensity ($\geq 60\%$) exercise versus control (no exercise/placebo exercise), Outcome 46 Glucose disappearance.





Comparison 3. Low intensity (< 60%) exercise versus control (no exercise/placebo exercise)

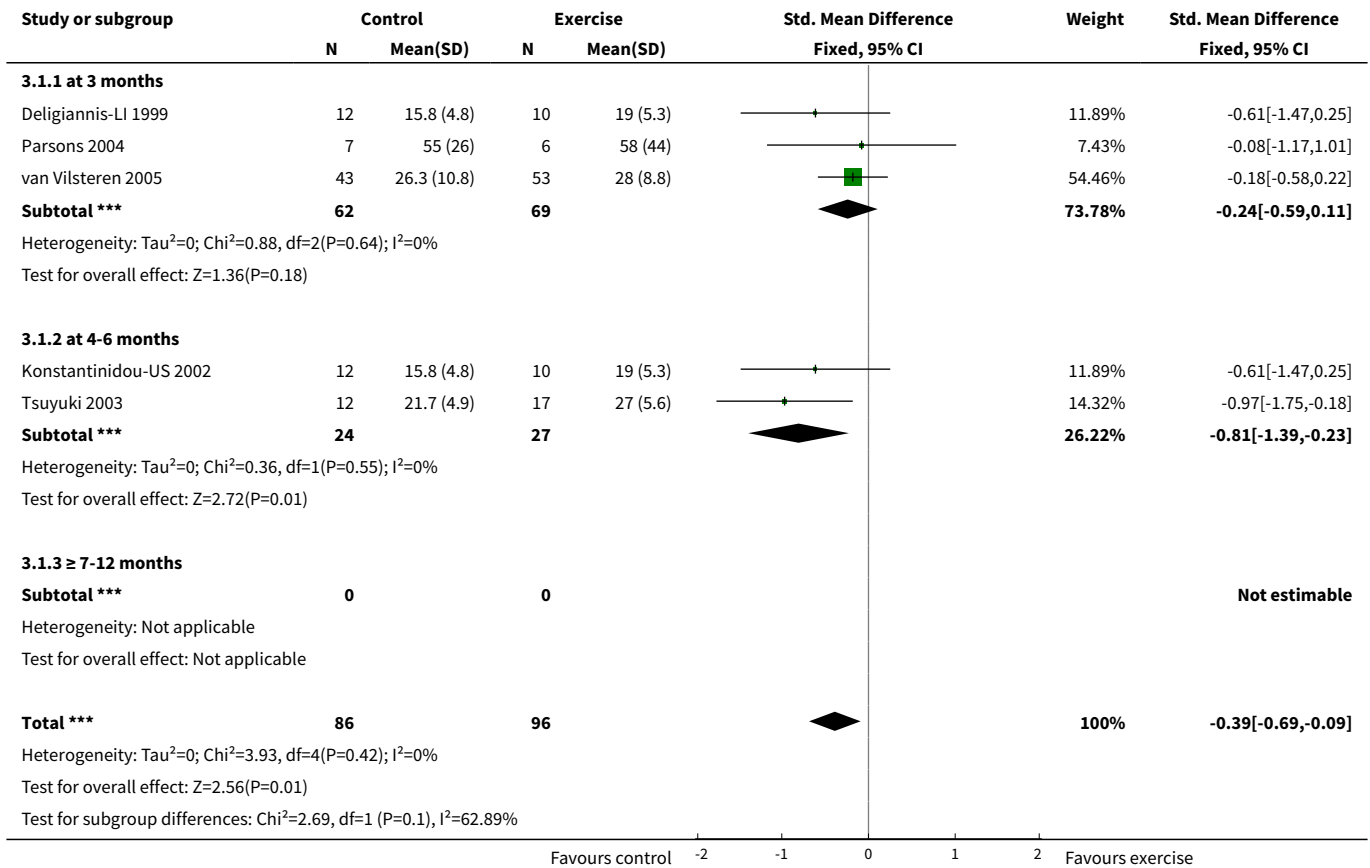
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	5	182	Std. Mean Difference (IV, Fixed, 95% CI)	-0.39 [-0.69, -0.09]
1.1 at 3 months	3	131	Std. Mean Difference (IV, Fixed, 95% CI)	-0.24 [-0.59, 0.11]
1.2 at 4-6 months	2	51	Std. Mean Difference (IV, Fixed, 95% CI)	-0.81 [-1.39, -0.23]
1.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Muscular strength (low value = improved)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 at 4-6 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 ADL capacity	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 ≥ 7-12 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Diastolic blood pressure: resting	3	147	Mean Difference (IV, Fixed, 95% CI)	-1.77 [-5.26, 1.73]
4.1 at 3 months	1	96	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-6.38, 4.38]
4.2 at 4-6 months	2	51	Mean Difference (IV, Fixed, 95% CI)	-2.33 [-6.93, 2.27]
4.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Systolic blood pressure: resting	3	147	Mean Difference (IV, Fixed, 95% CI)	0.86 [-6.10, 7.82]
5.1 at 3 months	1	96	Mean Difference (IV, Fixed, 95% CI)	6.0 [-4.31, 16.31]
5.2 at 4-6 months	2	51	Mean Difference (IV, Fixed, 95% CI)	-3.43 [-12.86, 5.99]
5.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Heart rate: maximum	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 at 4-6 months	3	73	Mean Difference (IV, Fixed, 95% CI)	-4.11 [-9.89, 1.68]
6.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Heart rate: resting	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 at 4-6 months	2	51	Mean Difference (IV, Fixed, 95% CI)	2.94 [-1.00, 8.87]
7.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Depression	1		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
8.1 at 3 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 at 4-6 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
9 Total cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

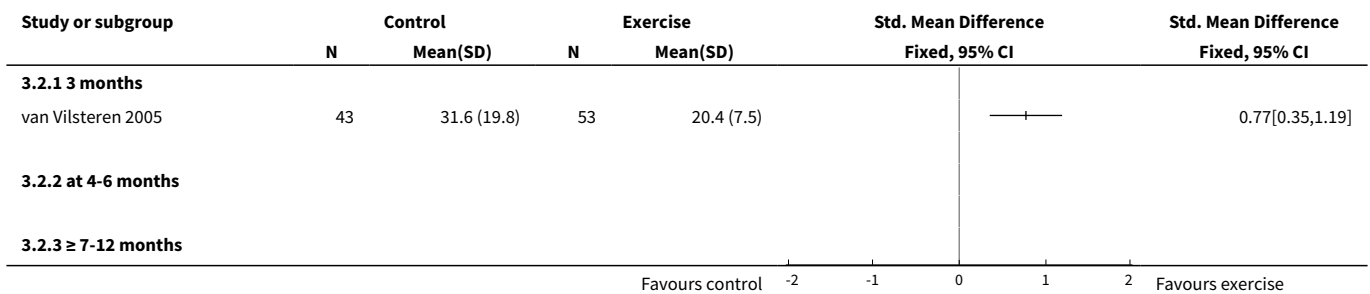
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10 Left ventricular internal dimension at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
10.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11 Left ventricular internal dimension at end-systole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
11.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12 Intraventricular septal thickness at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
12.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Left ventricular posterior wall thickness at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
13.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Left ventricular mass	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
14.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15 Left ventricular mass index	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
15.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

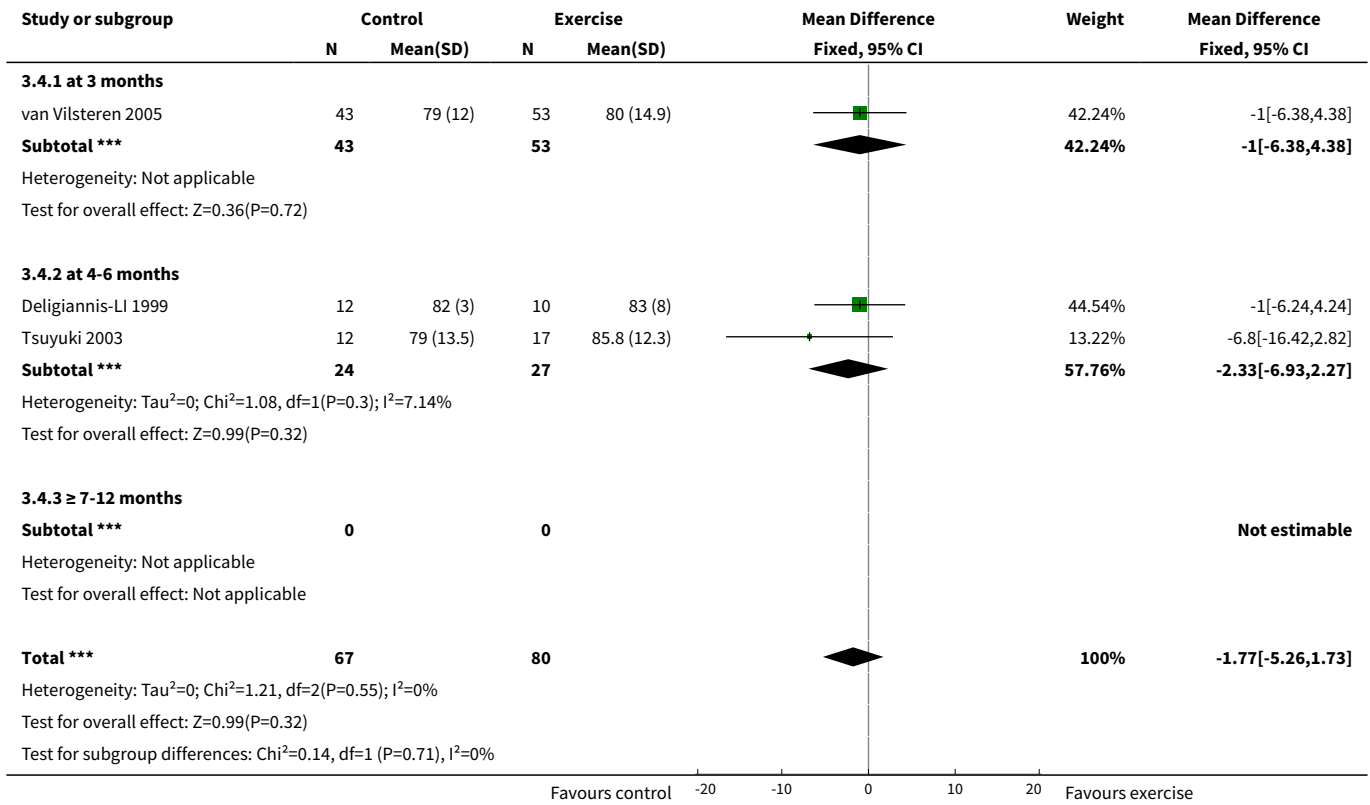
Analysis 3.1. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.



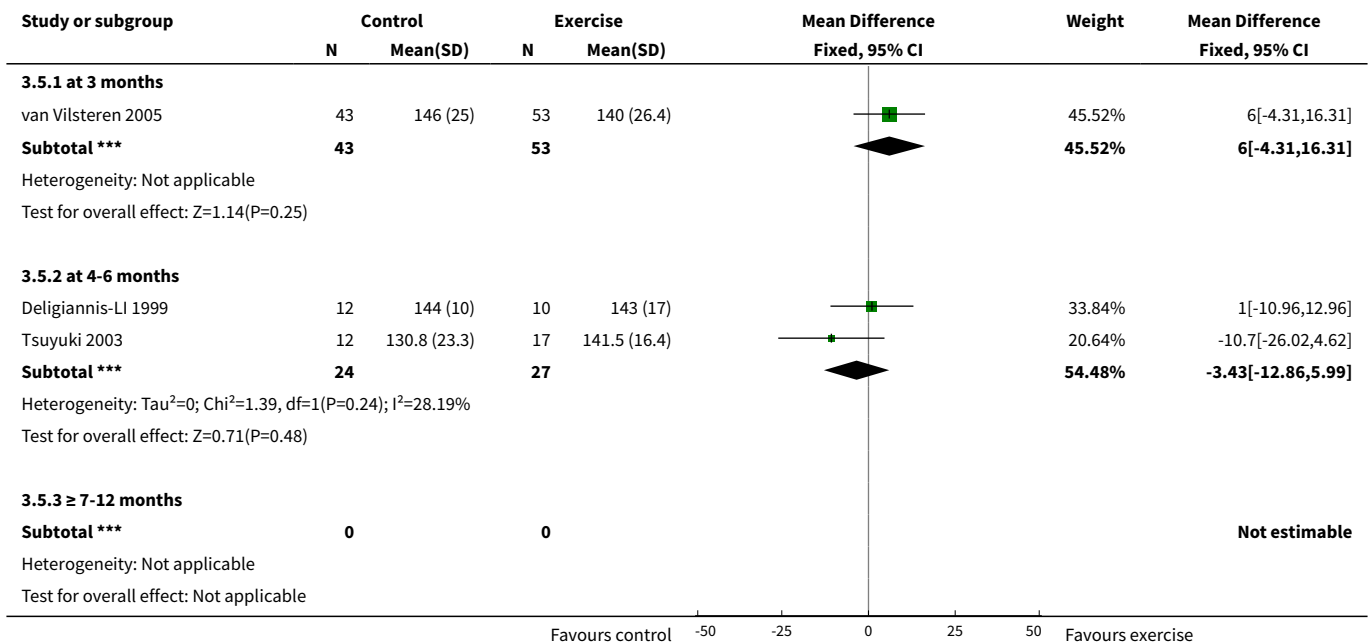
Analysis 3.2. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 2 Muscular strength (low value = improved).

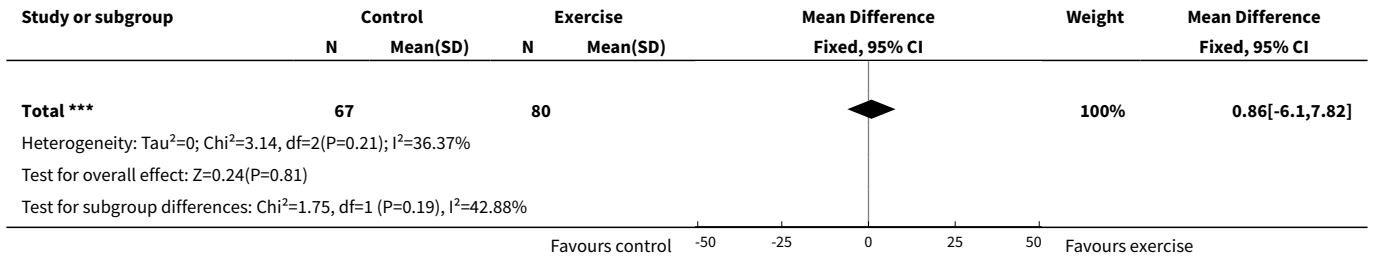


Analysis 3.4. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 4 Diastolic blood pressure: resting.

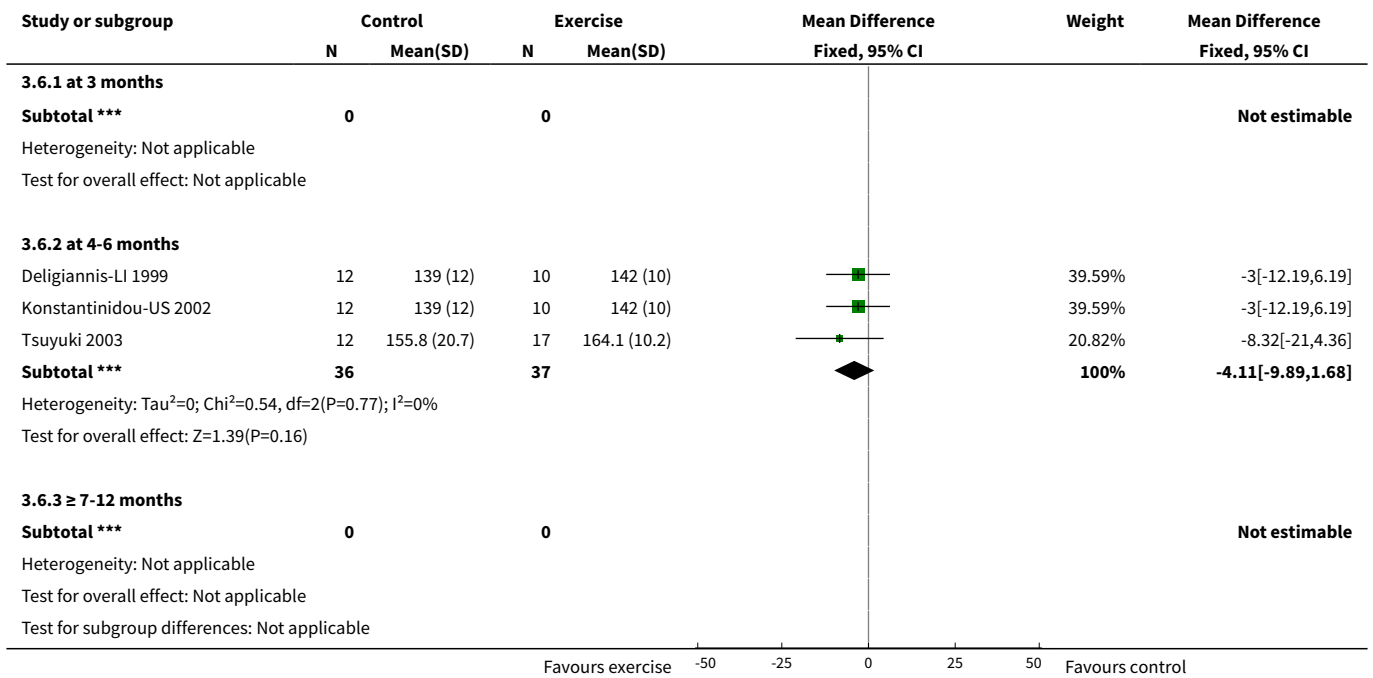


Analysis 3.5. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 5 Systolic blood pressure: resting.

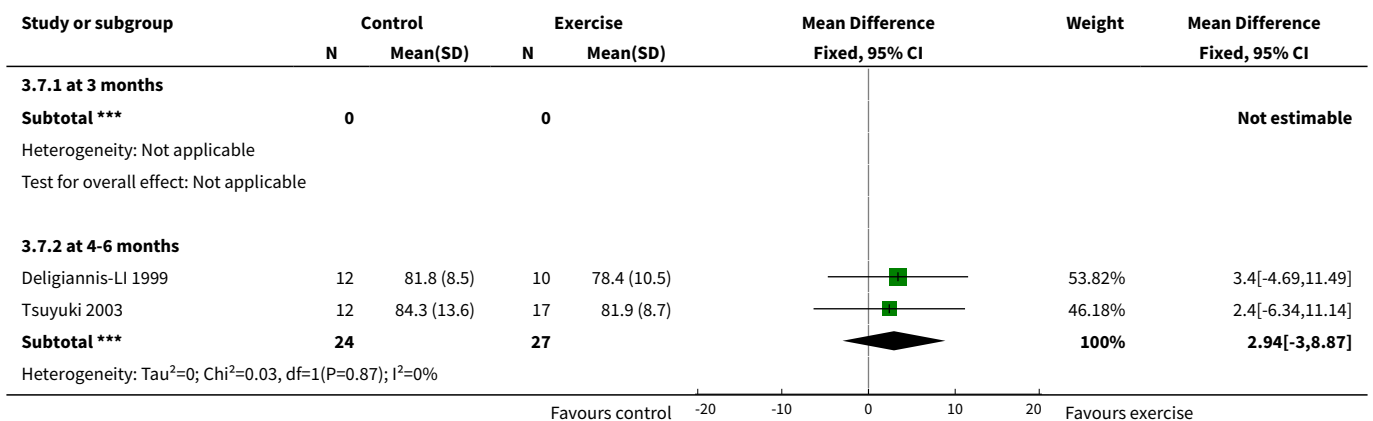


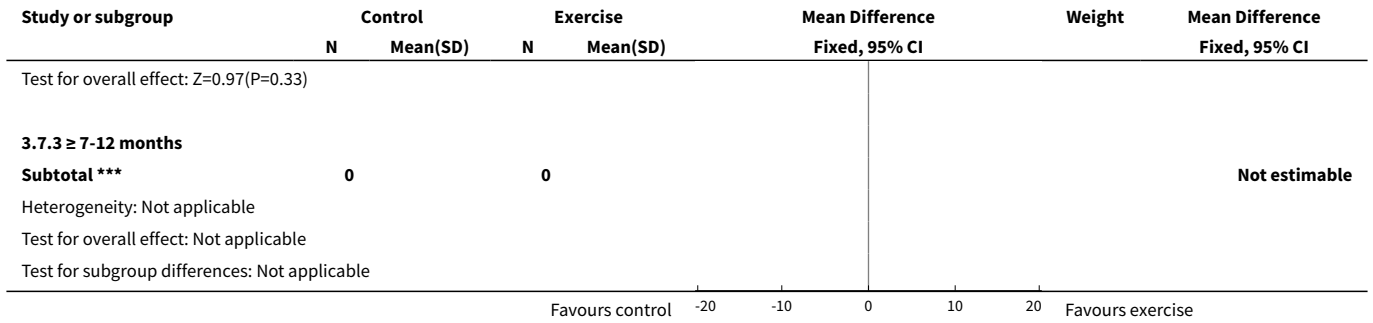


Analysis 3.6. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 6 Heart rate: maximum.

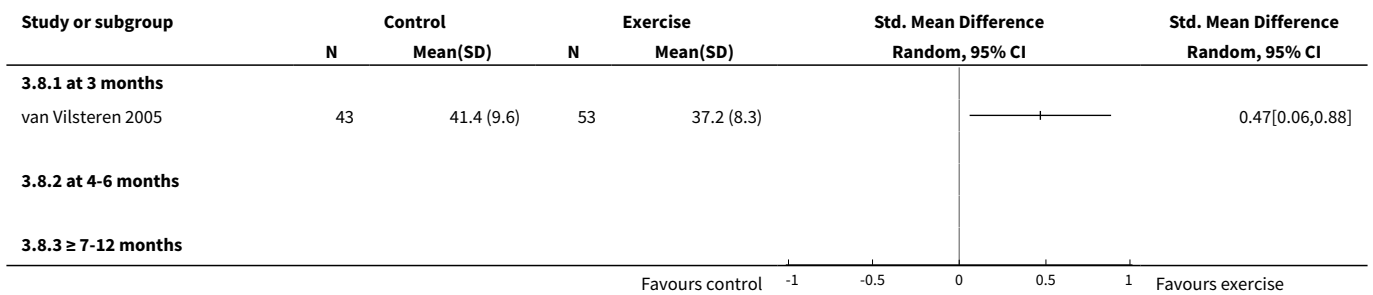


Analysis 3.7. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 7 Heart rate: resting.

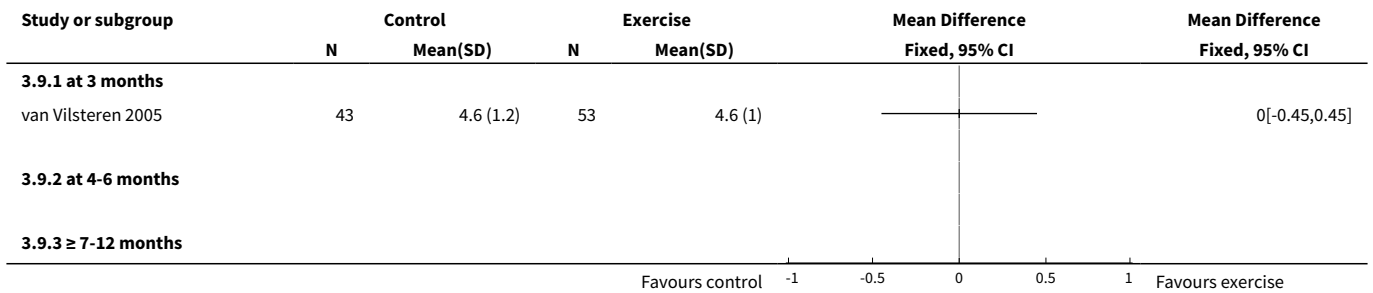




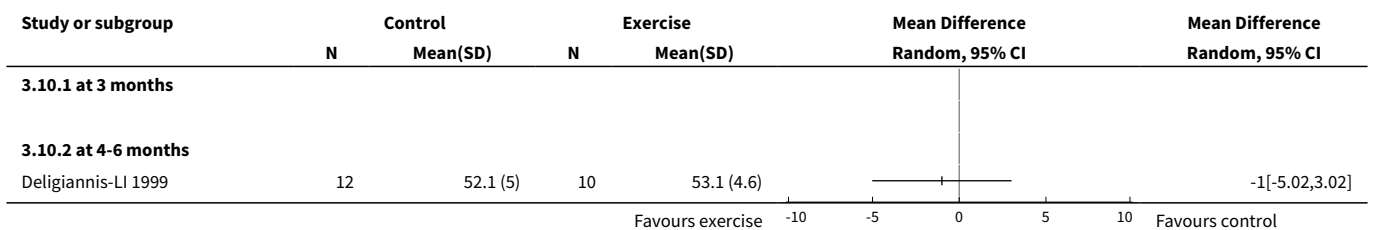
Analysis 3.8. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 8 Depression.

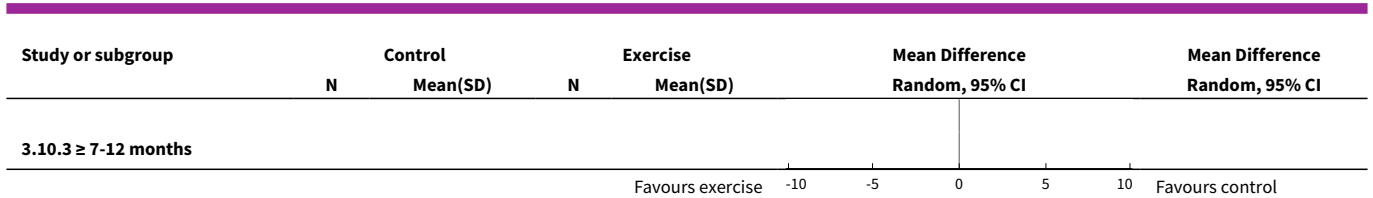


Analysis 3.9. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 9 Total cholesterol.

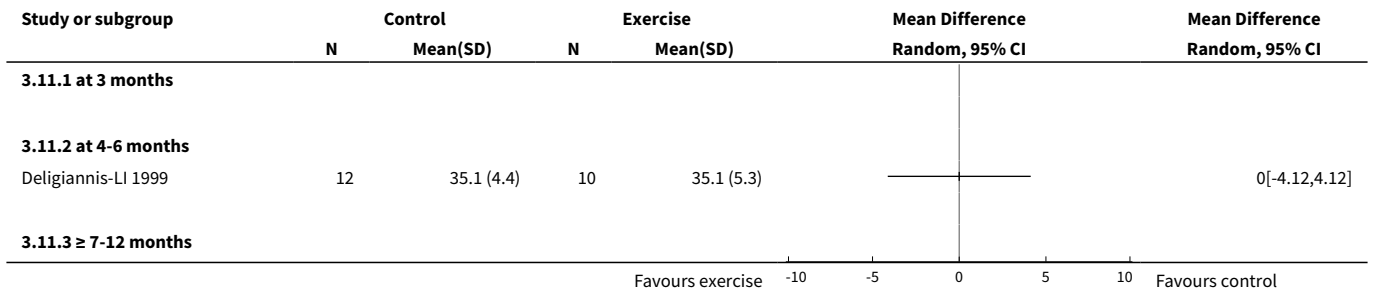


Analysis 3.10. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 10 Left ventricular internal dimension at end-diastole.

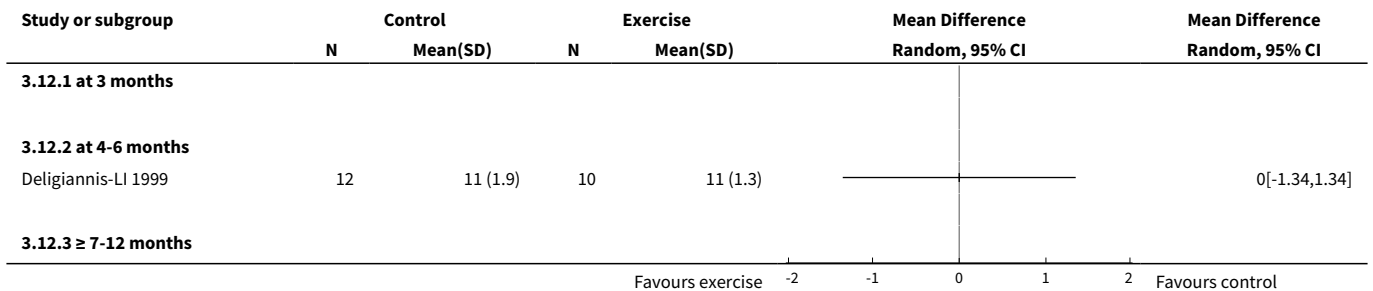




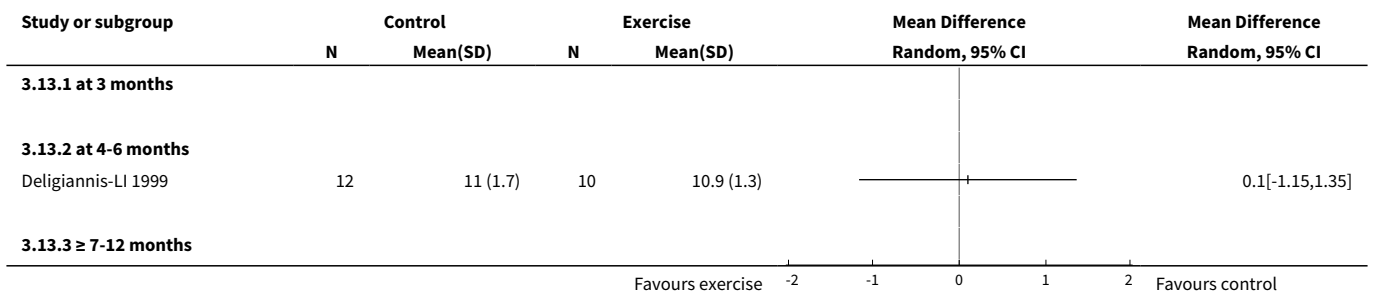
Analysis 3.11. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/ placebo exercise), Outcome 11 Left ventricular internal dimension at end-systole.



Analysis 3.12. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/ placebo exercise), Outcome 12 Intraventricular septal thickness at end-diastole.



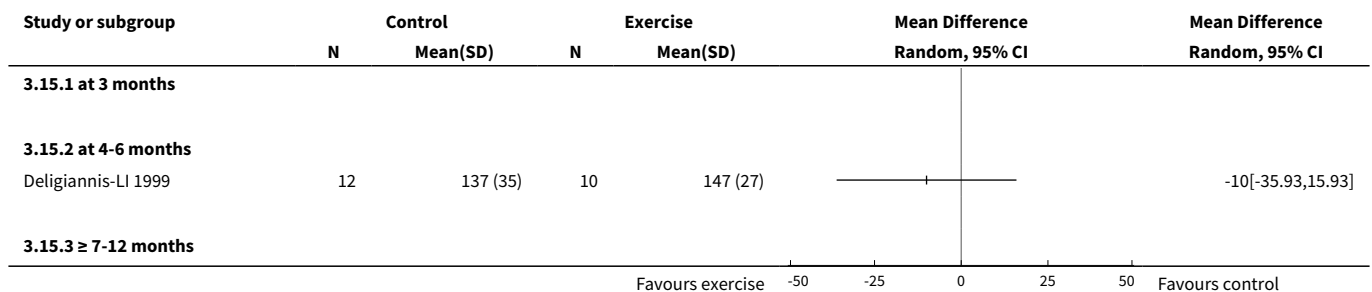
Analysis 3.13. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/ placebo exercise), Outcome 13 Left ventricular posterior wall thickness at end-diastole.



Analysis 3.14. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 14 Left ventricular mass.



Analysis 3.15. Comparison 3 Low intensity (< 60%) exercise versus control (no exercise/placebo exercise), Outcome 15 Left ventricular mass index.



Comparison 4. Cardiovascular exercise versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	16	514	Std. Mean Difference (IV, Fixed, 95% CI)	-0.53 [-0.71, -0.35]
1.1 at 3 months	5	116	Std. Mean Difference (IV, Fixed, 95% CI)	-0.45 [-0.82, -0.08]
1.2 at 4-6 months	7	152	Std. Mean Difference (IV, Fixed, 95% CI)	-0.87 [-1.22, -0.52]
1.3 ≥ 7-12 months	4	246	Std. Mean Difference (IV, Fixed, 95% CI)	-0.38 [-0.64, -0.13]
2 Muscular strength	4	165	Std. Mean Difference (IV, Random, 95% CI)	-0.23 [-0.57, 0.12]
2.1 at 3 months	1	27	Std. Mean Difference (IV, Random, 95% CI)	0.40 [-0.36, 1.17]
2.2 at 4-6 months	2	43	Std. Mean Difference (IV, Random, 95% CI)	-0.38 [-1.03, 0.26]
2.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Random, 95% CI)	-0.37 [-0.78, 0.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Walking capacity	3	71	Std. Mean Difference (IV, Fixed, 95% CI)	-0.38 [-0.86, 0.10]
4.1 at 3 months	1	27	Std. Mean Difference (IV, Fixed, 95% CI)	-0.29 [-1.05, 0.47]
4.2 at 4-6 months	2	44	Std. Mean Difference (IV, Fixed, 95% CI)	-0.44 [-1.07, 0.18]
4.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Stair climbing capacity: stair climb test (22 steps)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
6 ADL capacity	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 at 4-6 months	2	44	Mean Difference (IV, Fixed, 95% CI)	0.58 [-0.43, 1.60]
6.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Diastolic blood pressure: resting	6	202	Mean Difference (IV, Fixed, 95% CI)	-0.11 [-2.88, 2.66]
7.1 at 3 months	1	19	Mean Difference (IV, Fixed, 95% CI)	-4.40 [-11.31, 2.51]
7.2 at 4-6 months	3	62	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-4.35, 4.11]
7.3 ≥ 7-12 months	2	121	Mean Difference (IV, Fixed, 95% CI)	1.58 [-2.75, 5.90]
8 Systolic blood pressure: resting	6		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
8.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 at 4-6 months	3		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 ≥ 7-12 months	2		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9 Heart rate: maximum	7	154	Mean Difference (IV, Fixed, 95% CI)	-6.15 [-11.01, -1.30]
9.1 at 3 months	2	46	Mean Difference (IV, Fixed, 95% CI)	-10.11 [-21.79, 1.57]
9.2 at 4-6 months	5	108	Mean Difference (IV, Fixed, 95% CI)	-5.33 [-10.66, 0.00]
9.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Heart rate: resting	4	87	Mean Difference (IV, Fixed, 95% CI)	0.74 [-4.32, 5.80]
10.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 at 4-6 months	3	62	Mean Difference (IV, Fixed, 95% CI)	2.15 [-3.62, 7.92]
10.3 ≥ 7-12 months	1	25	Mean Difference (IV, Fixed, 95% CI)	-4.0 [-14.57, 6.57]
11 Albumin	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 at 3 months	2		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Pre-albumin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
12.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 SGA	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
13.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Energy intake	2		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
14.1 at 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Protein intake	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
15.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

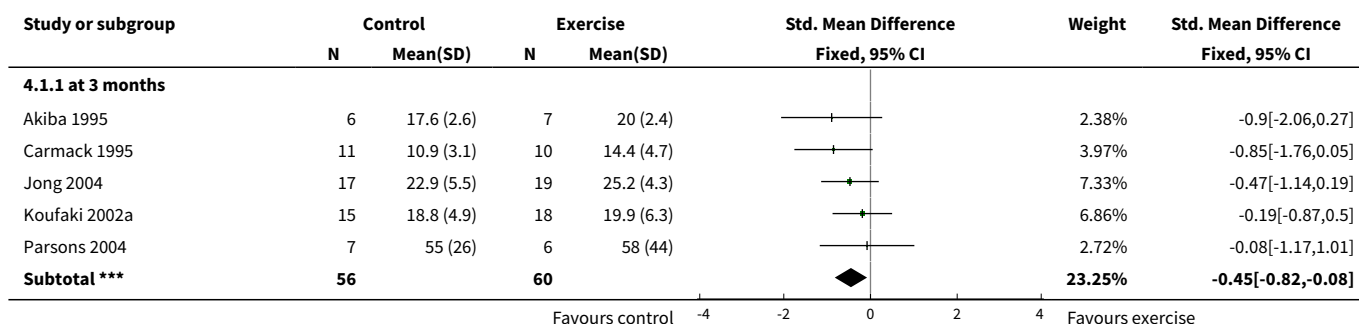
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Transferrin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
16.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Fat mass	3	130	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.29, 0.42]
17.1 at 3 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 at 4-6 months	2	35	Std. Mean Difference (IV, Fixed, 95% CI)	-0.31 [-1.08, 0.46]
17.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.24, 0.57]
18 Physical activity	3	77	Std. Mean Difference (IV, Random, 95% CI)	-0.30 [-0.77, 0.17]
18.1 at 3 months	1	33	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-1.02, 0.36]
18.2 at 4-6 months	2	44	Std. Mean Difference (IV, Random, 95% CI)	-0.27 [-0.91, 0.37]
18.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
19 Depression	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
19.1 at 3 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
19.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
20 Triglycerides	3	63	Mean Difference (IV, Random, 95% CI)	0.27 [-0.31, 0.85]
20.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	1	11	Mean Difference (IV, Random, 95% CI)	0.51 [-0.83, 1.84]
20.3 ≥ 7-12 months	2	52	Mean Difference (IV, Random, 95% CI)	0.22 [-0.43, 0.86]
21 Total cholesterol	4	159	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.40, 0.34]
21.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

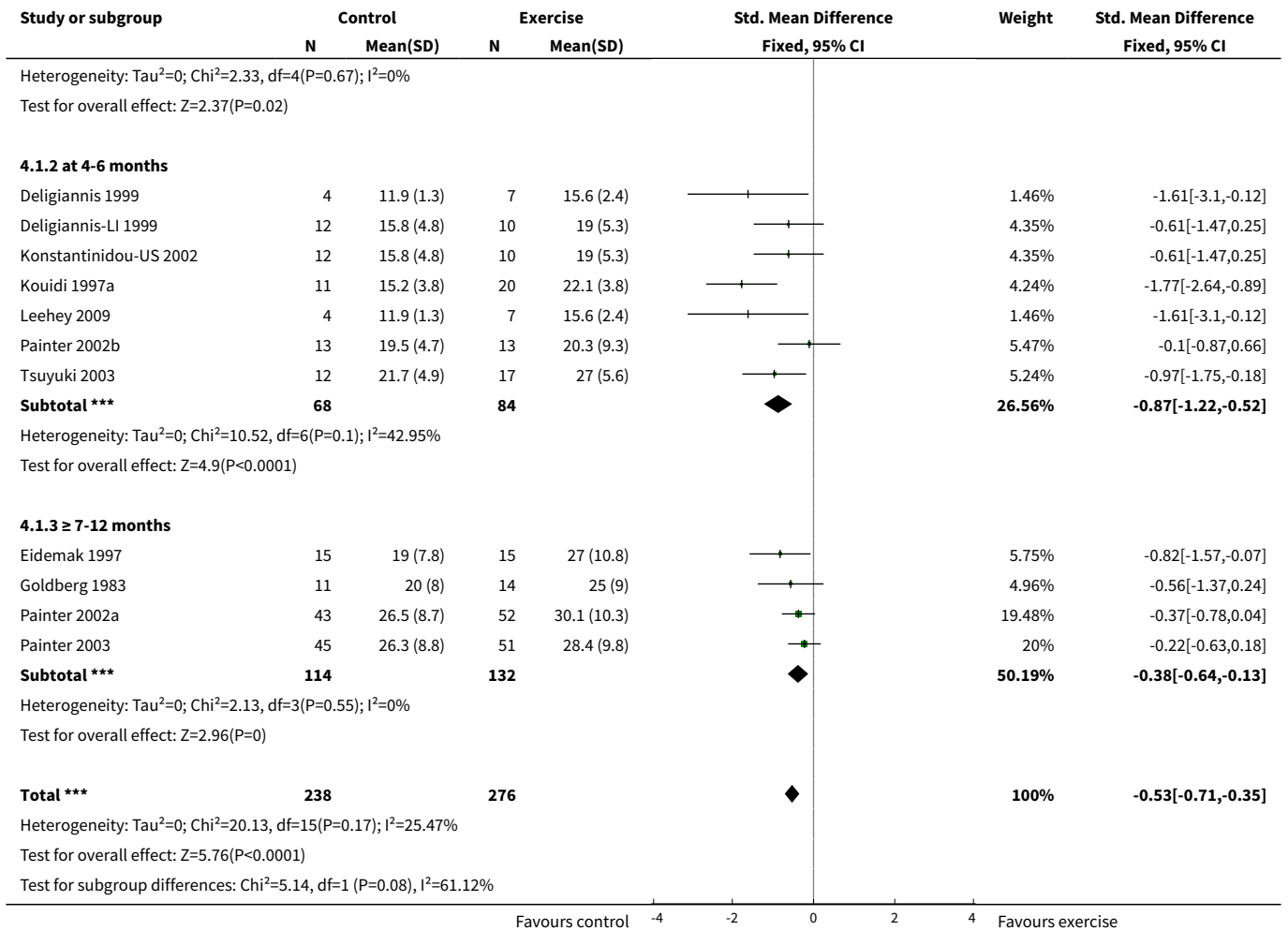
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.2 at 4-6 months	1	11	Mean Difference (IV, Random, 95% CI)	0.47 [-0.46, 1.39]
21.3 ≥ 7-12 months	3	148	Mean Difference (IV, Random, 95% CI)	-0.12 [-0.52, 0.28]
22 HDL cholesterol	3	129	Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.25, -0.05]
22.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	1	11	Mean Difference (IV, Fixed, 95% CI)	-0.21 [-0.38, -0.04]
22.3 ≥ 7-12 months	2	118	Mean Difference (IV, Fixed, 95% CI)	-0.11 [-0.24, 0.02]
23 LDL cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
23.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Mid-thigh muscle area	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
24.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 HRV index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
25.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Mean cardiac R-R interval	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
26.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
27 SDNN	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
27.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
27.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
27.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
28 Arrhythmias: Low class > II (no)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
28.1 at 3 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
28.2 at 4-6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
28.3 ≥ 7-12 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
29 Left ventricular internal dimension at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
29.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
29.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
29.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
30 Left ventricular internal dimension at end-systole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
30.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
30.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
30.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31 Intraventricular septal thickness at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
31.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32 Left ventricular posterior wall thickness at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
32.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
33 Left ventricular mass	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
33.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
33.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

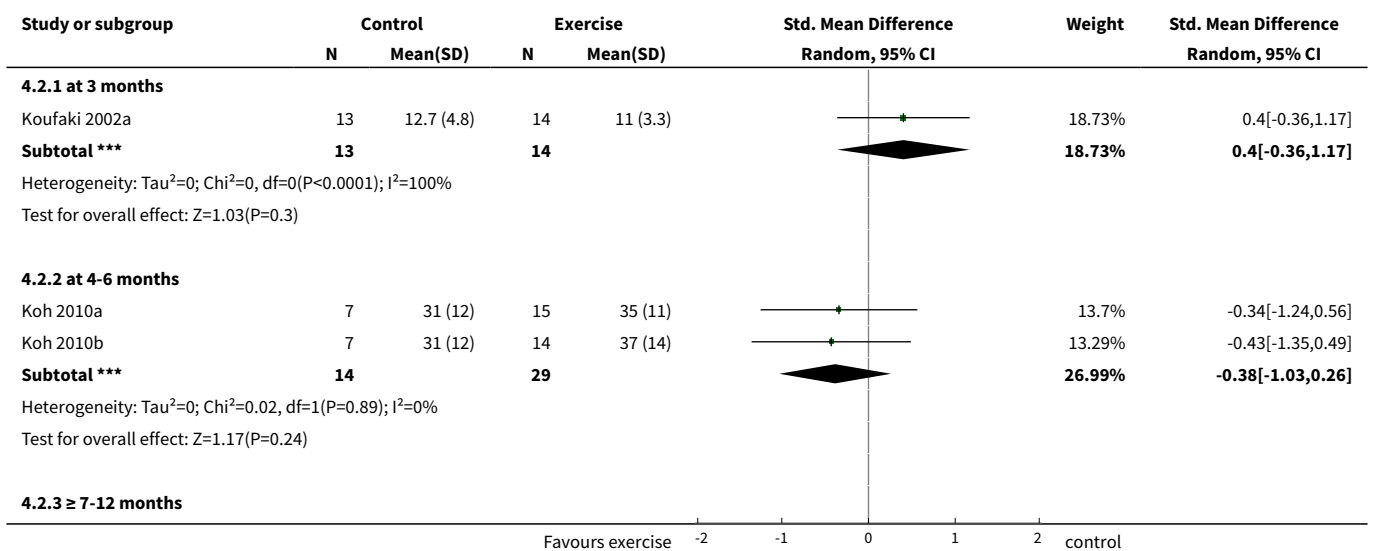
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
33.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34 Left ventricular mass index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
34.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35 Fasting plasma glucose	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
35.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
36 Fasting plasma insulin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
36.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
36.2 at 5 to 6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
36.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
37 Glucose disappearance	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
37.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
37.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
37.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

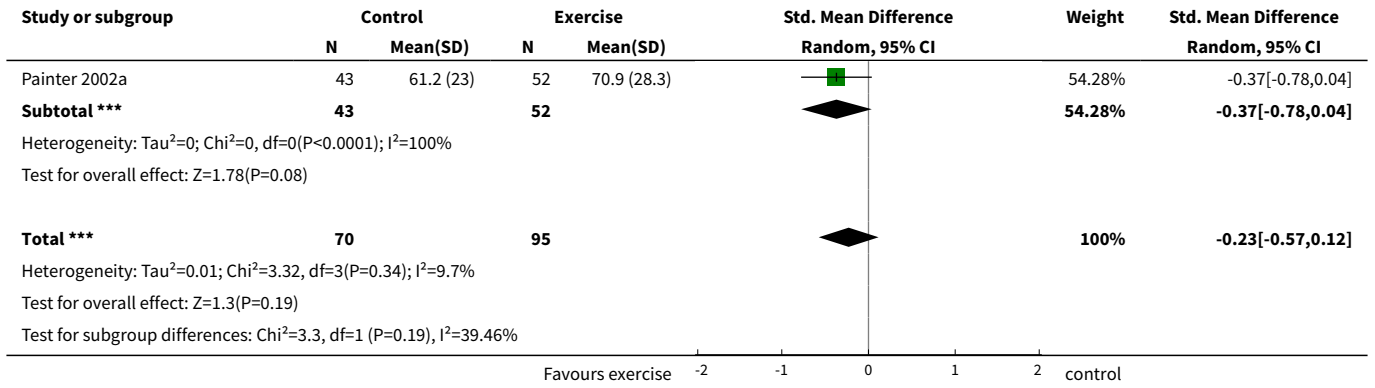
Analysis 4.1. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.



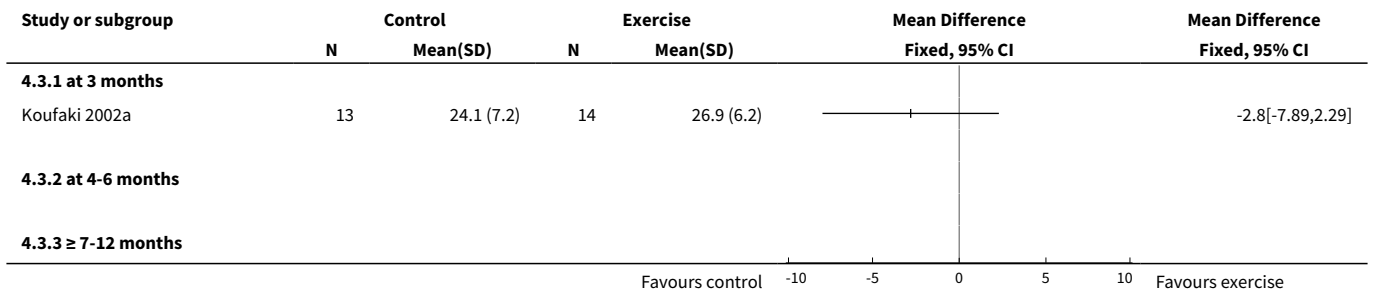


Analysis 4.2. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 2 Muscular strength.

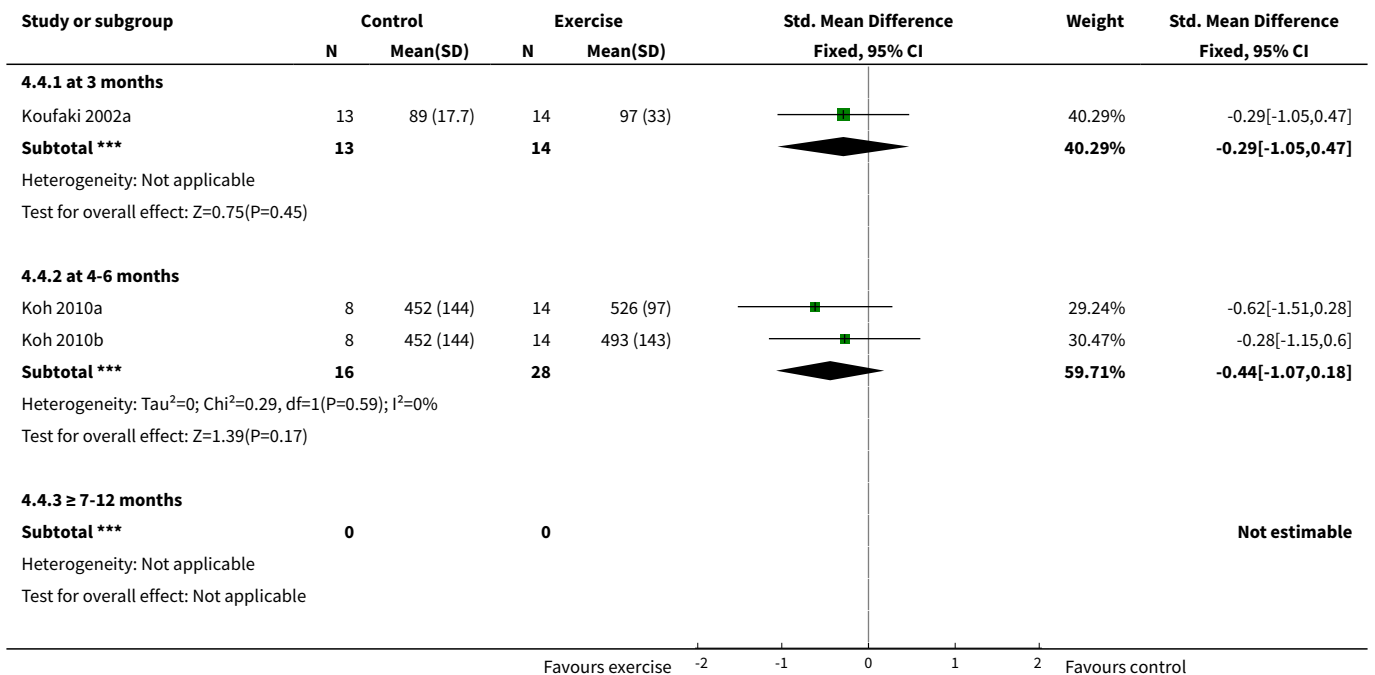


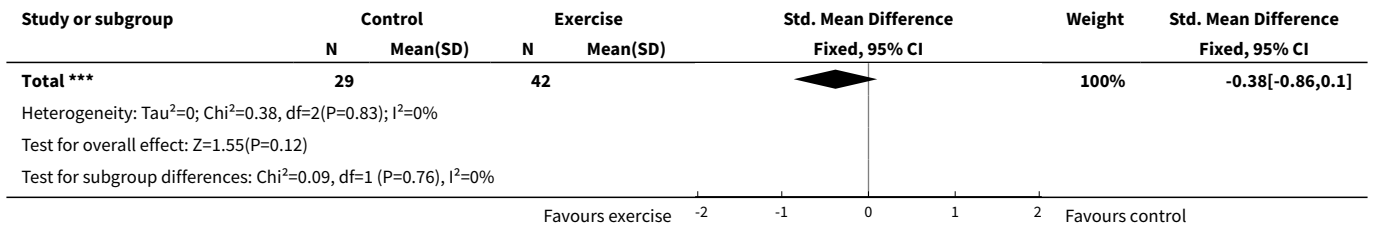


Analysis 4.3. Comparison 4 Cardiovascular exercise versus control (no exercise/ placebo exercise), Outcome 3 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60.

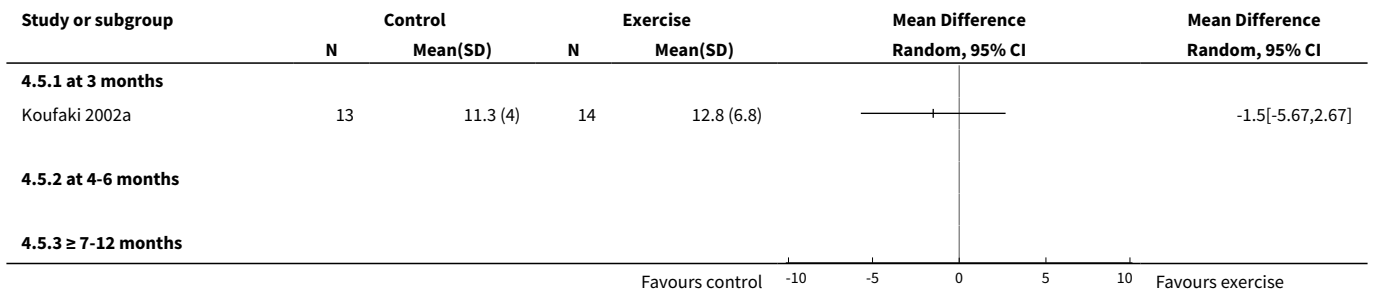


Analysis 4.4. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 4 Walking capacity.

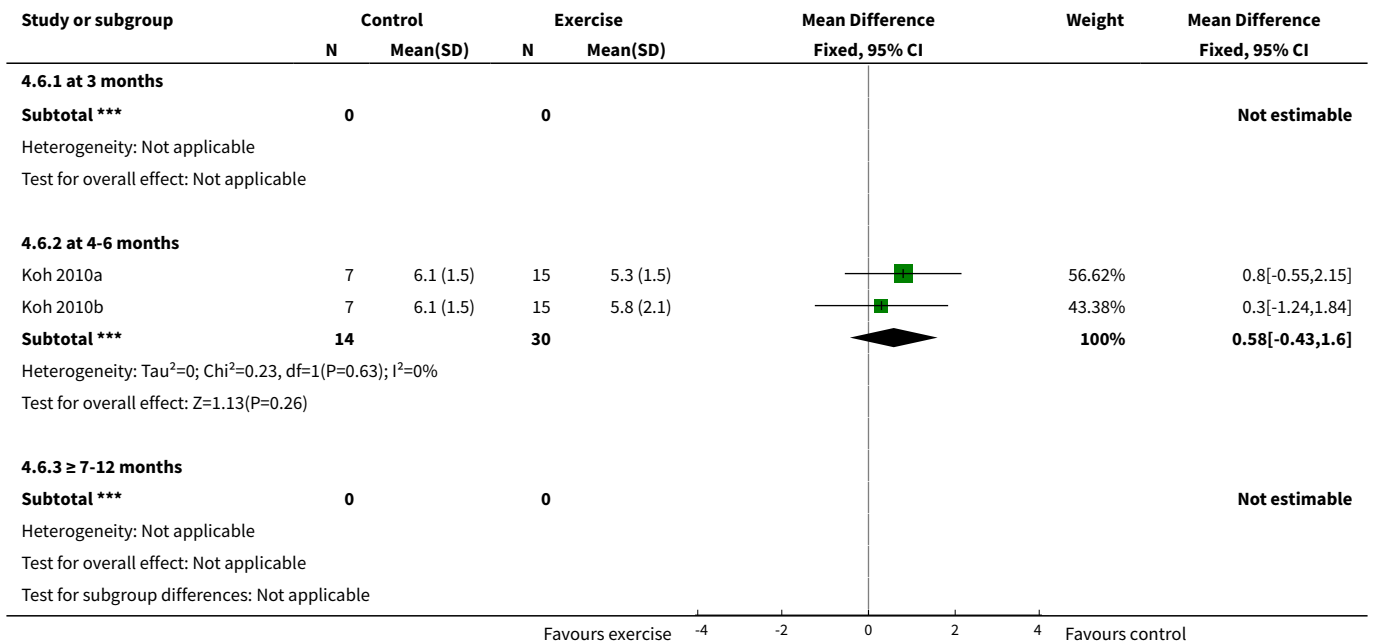




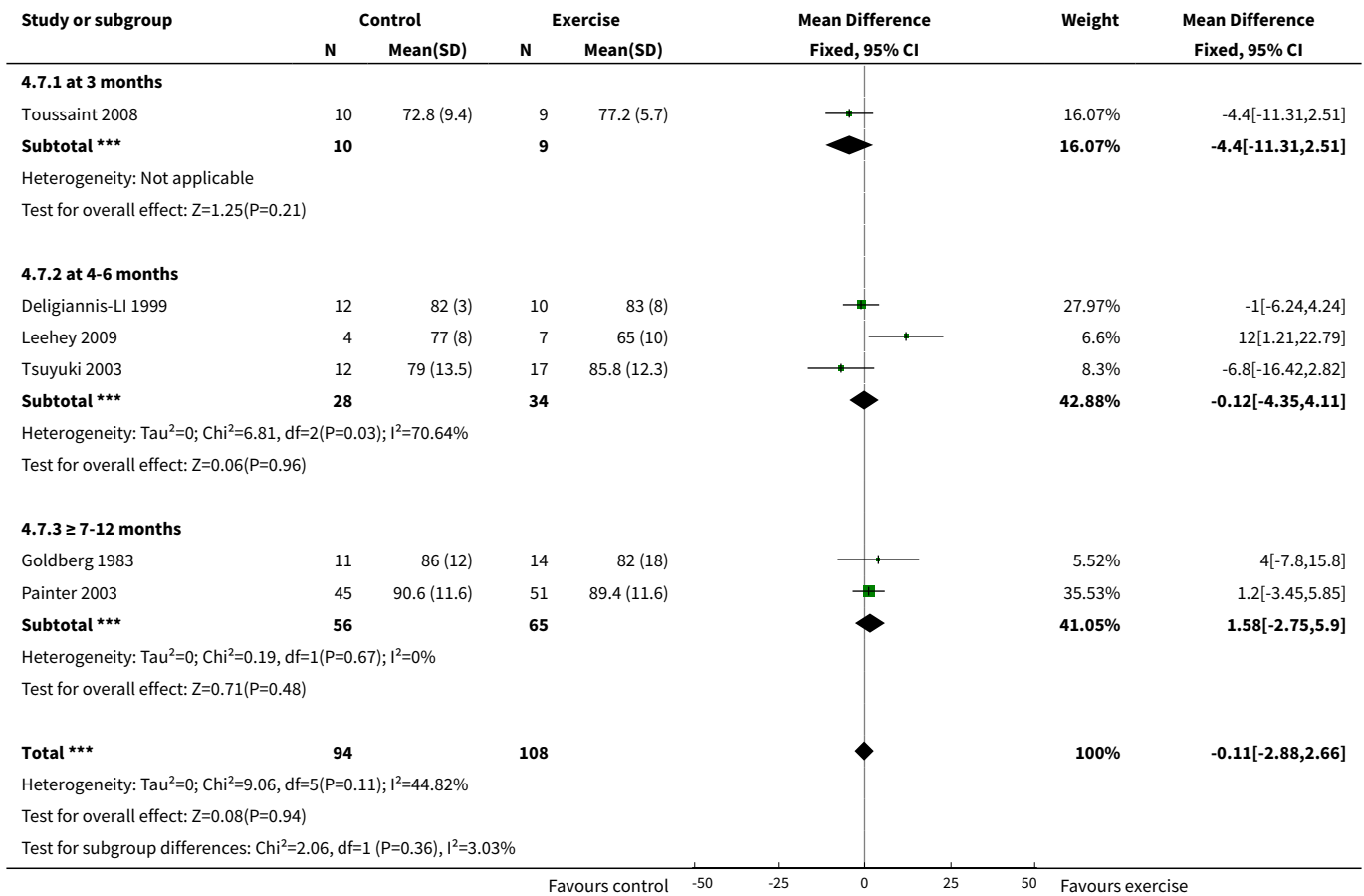
Analysis 4.5. Comparison 4 Cardiovascular exercise versus control (no exercise/ placebo exercise), Outcome 5 Stair climbing capacity: stair climb test (22 steps).



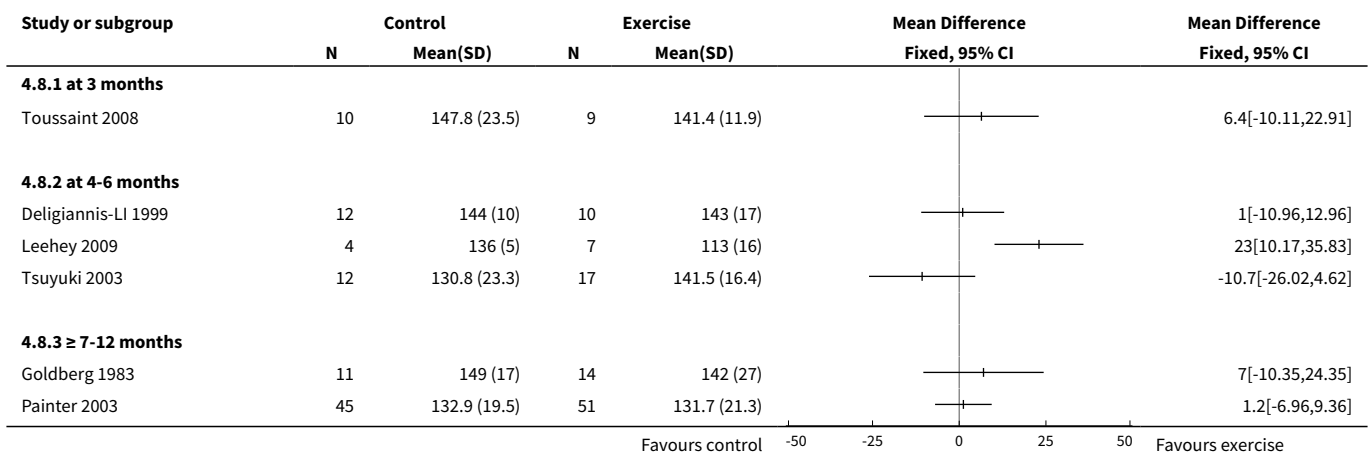
Analysis 4.6. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 6 ADL capacity.



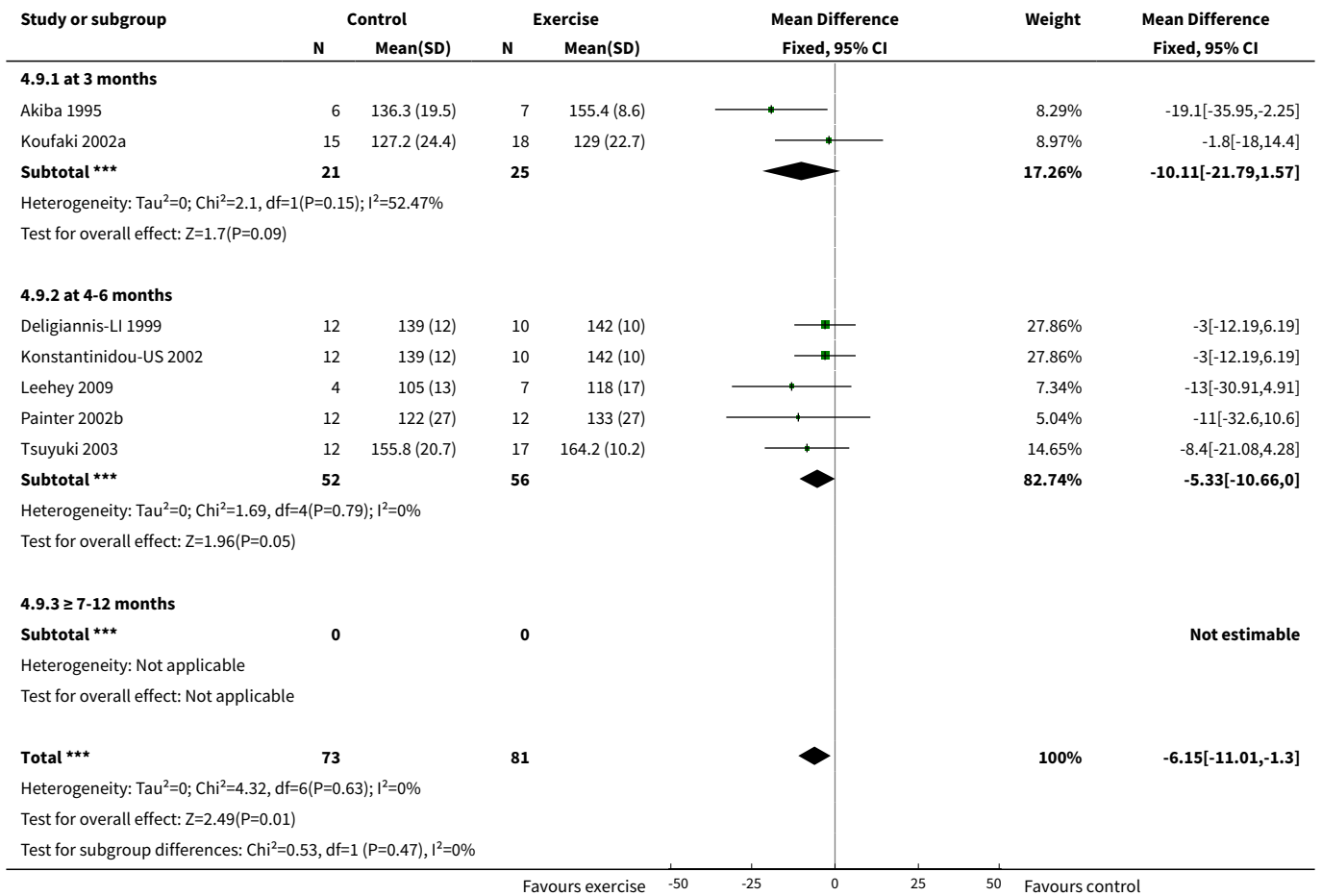
Analysis 4.7. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 7 Diastolic blood pressure: resting.



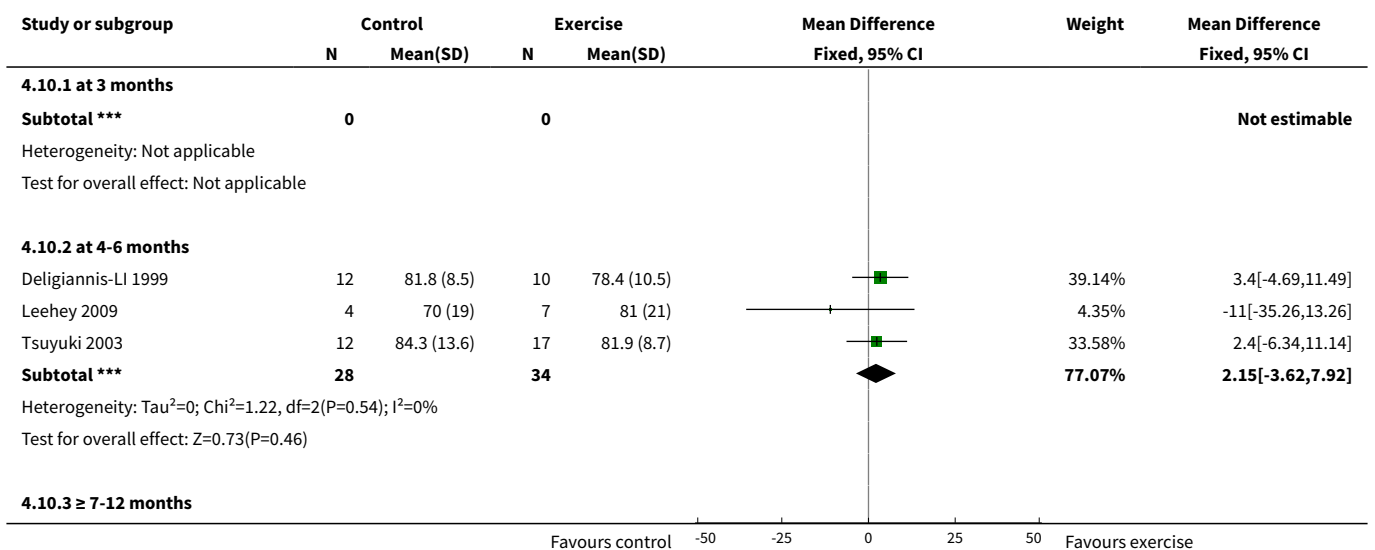
Analysis 4.8. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 8 Systolic blood pressure: resting.

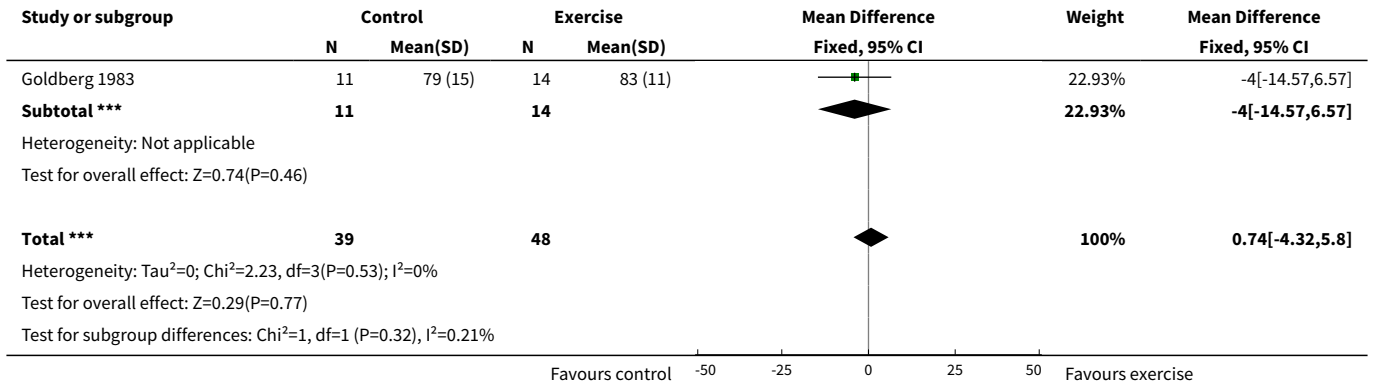


Analysis 4.9. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 9 Heart rate: maximum.

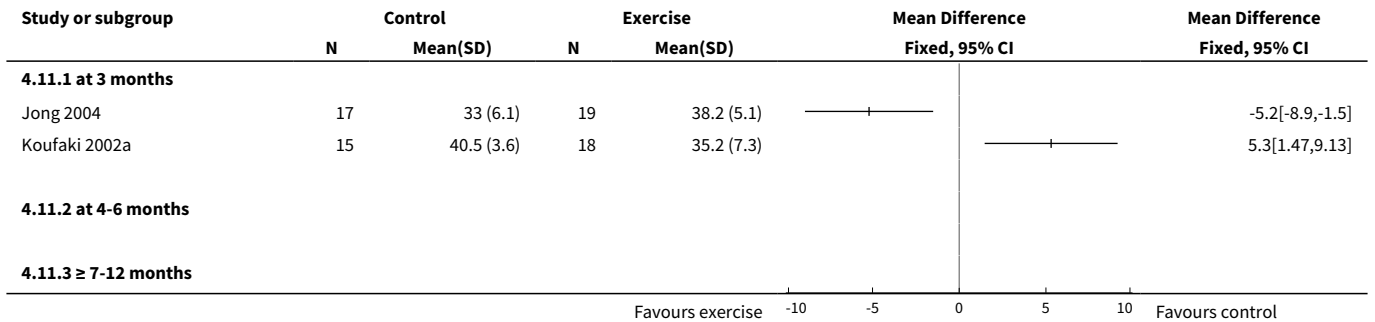


Analysis 4.10. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 10 Heart rate: resting.

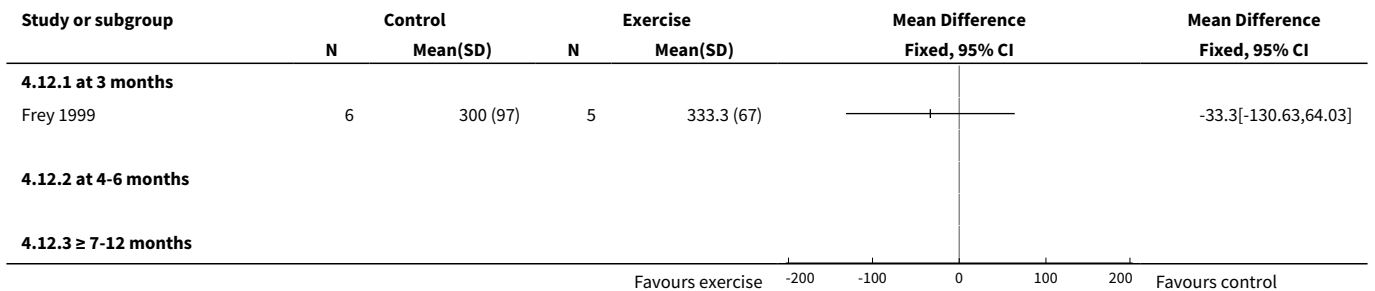




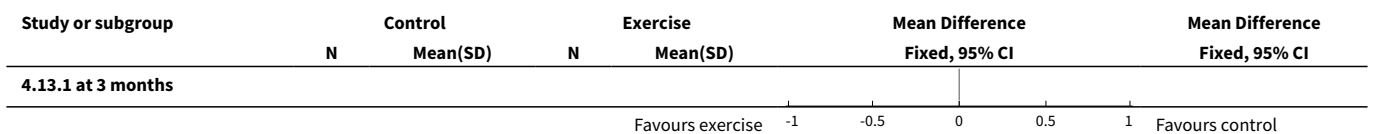
Analysis 4.11. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 11 Albumin.

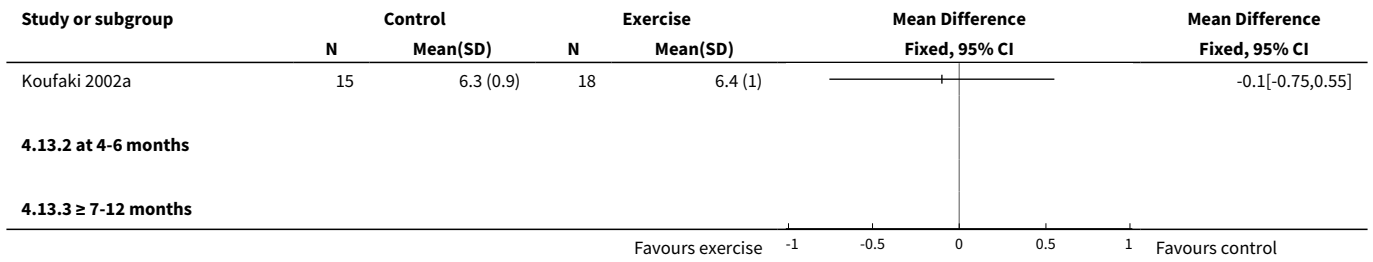


Analysis 4.12. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 12 Pre-albumin.

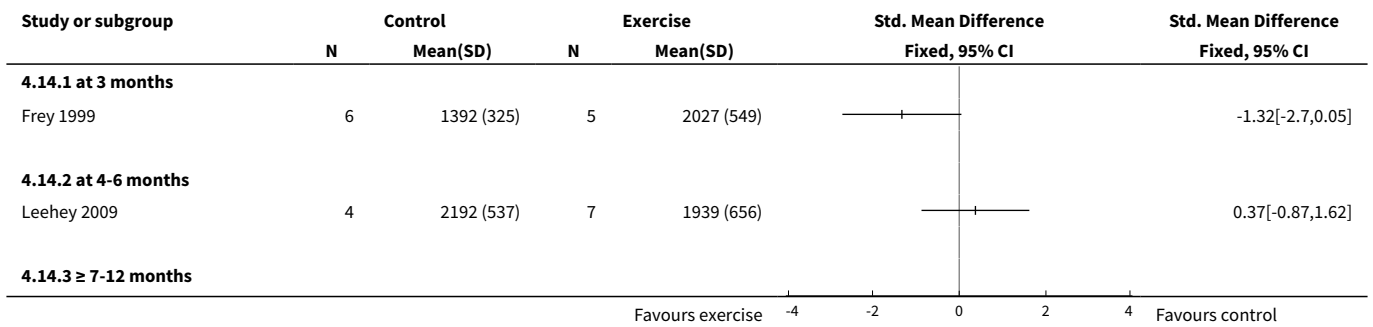


Analysis 4.13. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 13 SGA.

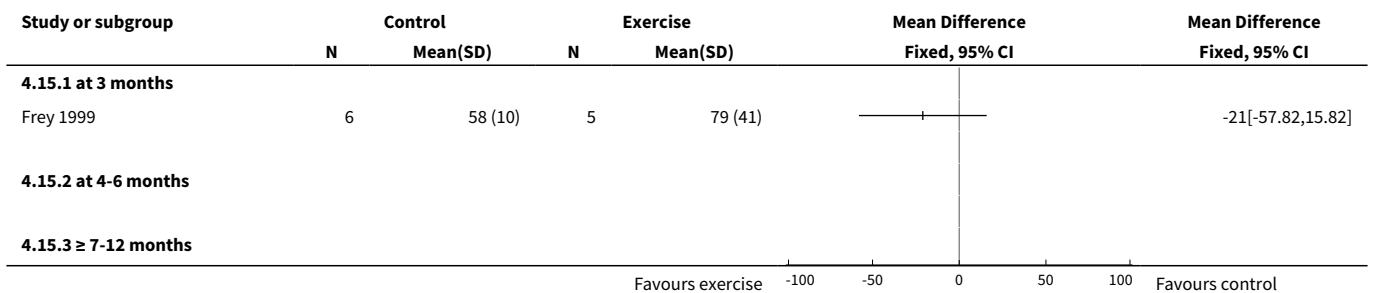




Analysis 4.14. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 14 Energy intake.



Analysis 4.15. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 15 Protein intake.



Analysis 4.16. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 16 Transferrin.



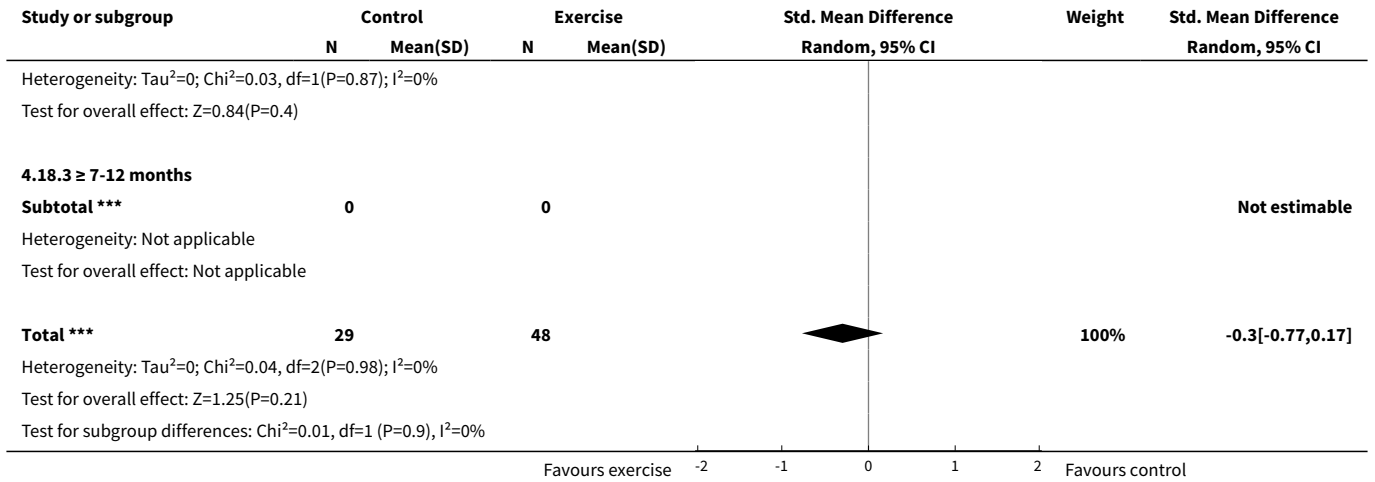
Study or subgroup	Control		Exercise		Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Mean Difference Fixed, 95% CI
4.16.3 ≥ 7-12 months						
Favours exercise -1 -0.5 0 0.5 1 Favours control						

Analysis 4.17. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 17 Fat mass.

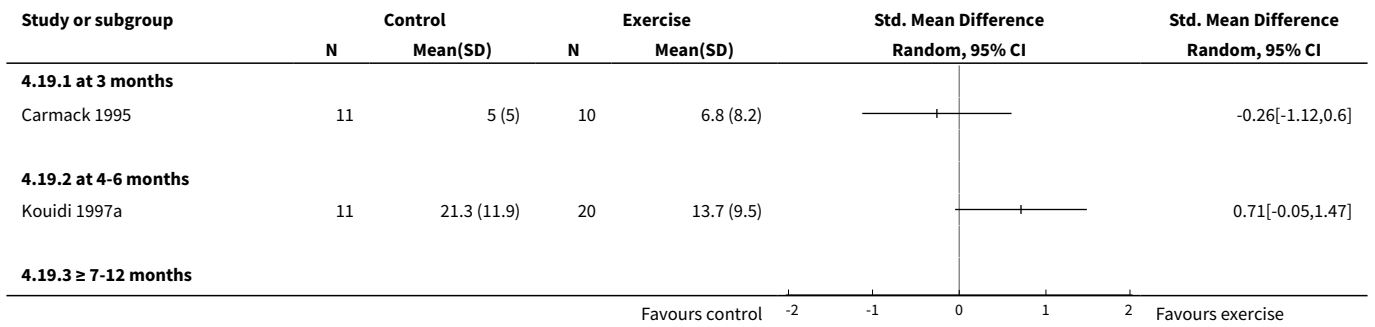
Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
4.17.1 at 3 months							
Subtotal ***	0		0				Not estimable
Heterogeneity: Not applicable Test for overall effect: Not applicable							
4.17.2 at 4-6 months							
Kopple 2007a	14	19.1 (2.4)	10	21.7 (2.8)	-0.98 [-1.84, -0.11]	17.08%	-0.98 [-1.84, -0.11]
Leehey 2009	4	50 (5)	7	40 (4)	2.1 [0.45, 3.74]	4.73%	2.1 [0.45, 3.74]
Subtotal ***	18		17		-0.31 [-1.08, 0.46]	21.81%	-0.31 [-1.08, 0.46]
Heterogeneity: Tau ² =0; Chi ² =10.5, df=1(P=0); I ² =90.48% Test for overall effect: Z=0.79(P=0.43)							
4.17.3 ≥ 7-12 months							
Painter 2002a	43	27.6 (10.5)	52	25.8 (10.8)	0.17 [-0.24, 0.57]	78.19%	0.17 [-0.24, 0.57]
Subtotal ***	43		52		0.17 [-0.24, 0.57]	78.19%	0.17 [-0.24, 0.57]
Heterogeneity: Not applicable Test for overall effect: Z=0.81(P=0.42)							
Total ***	61		69		0.06 [-0.29, 0.42]	100%	0.06 [-0.29, 0.42]
Heterogeneity: Tau ² =0; Chi ² =11.67, df=2(P=0); I ² =82.86% Test for overall effect: Z=0.35(P=0.73) Test for subgroup differences: Chi ² =1.16, df=1 (P=0.28), I ² =14.02%							
Favours control -4 -2 0 2 4 Favours exercise							

Analysis 4.18. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 18 Physical activity.

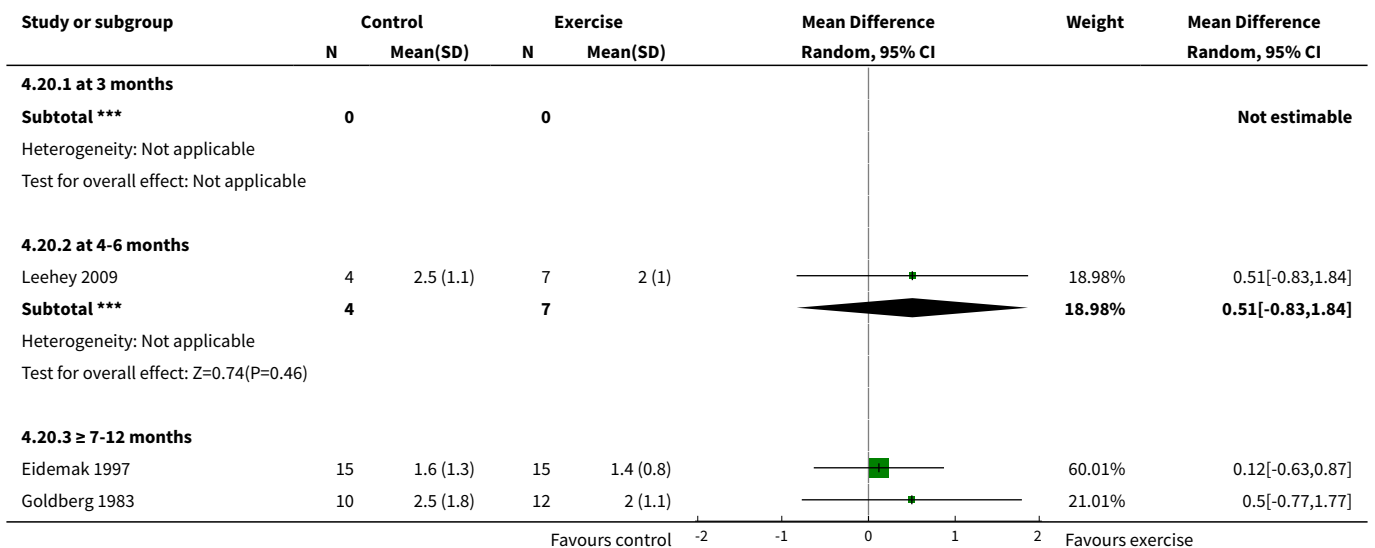
Study or subgroup	Control		Exercise		Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
4.18.1 at 3 months							
Koufaki 2002a	15	34.3 (1.7)	18	35.4 (4.1)	-0.33 [-1.02, 0.36]	46.02%	-0.33 [-1.02, 0.36]
Subtotal ***	15		18		-0.33 [-1.02, 0.36]	46.02%	-0.33 [-1.02, 0.36]
Heterogeneity: Not applicable Test for overall effect: Z=0.94(P=0.35)							
4.18.2 at 4-6 months							
Koh 2010a	7	943 (1701)	15	1920 (3273)	-0.32 [-1.23, 0.58]	26.89%	-0.32 [-1.23, 0.58]
Koh 2010b	7	943 (1701)	15	1712 (3868)	-0.22 [-1.12, 0.68]	27.09%	-0.22 [-1.12, 0.68]
Subtotal ***	14		30		-0.27 [-0.91, 0.37]	53.98%	-0.27 [-0.91, 0.37]
Favours exercise -2 -1 0 1 2 Favours control							

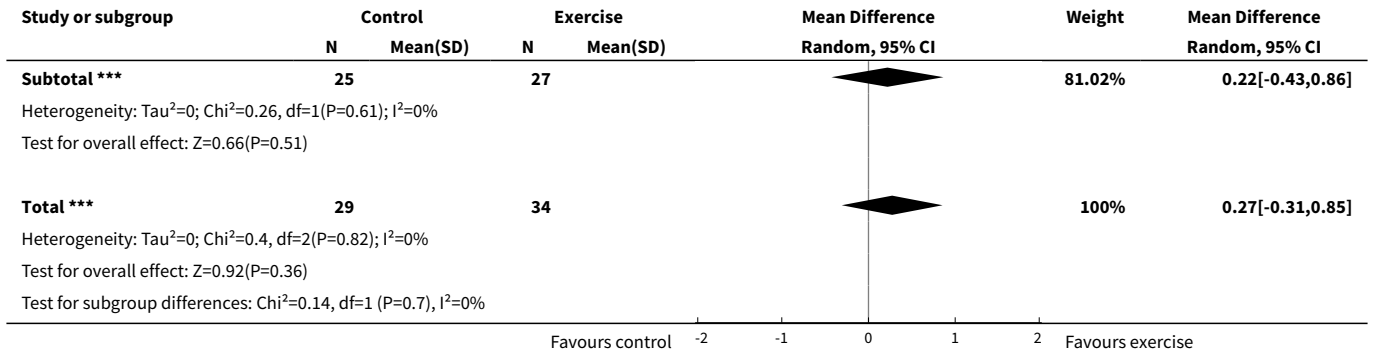


Analysis 4.19. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 19 Depression.

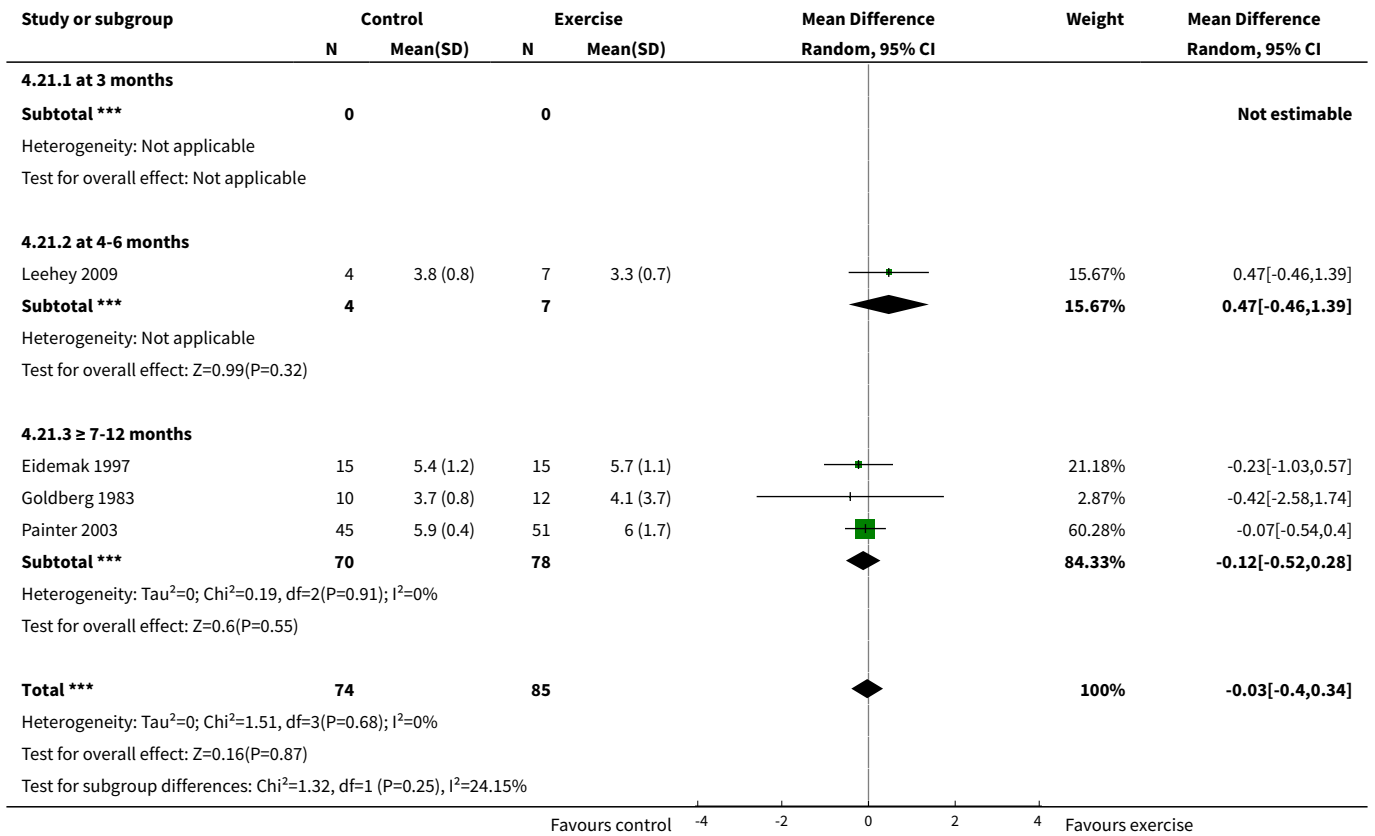


Analysis 4.20. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 20 Triglycerides.

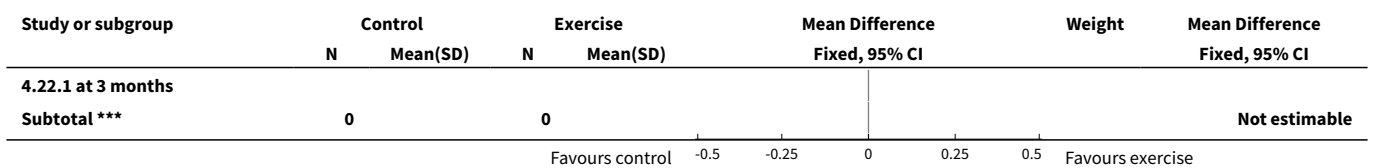


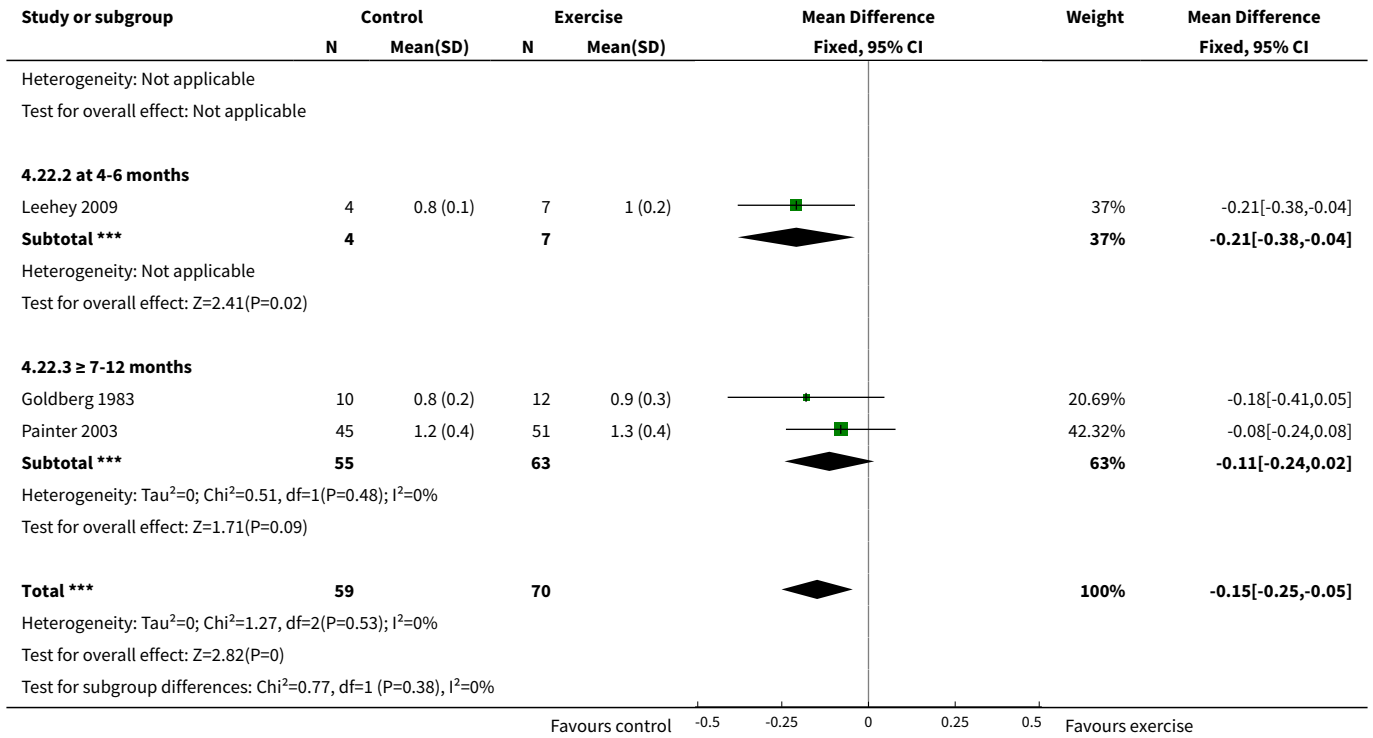


Analysis 4.21. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 21 Total cholesterol.



Analysis 4.22. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 22 HDL cholesterol.

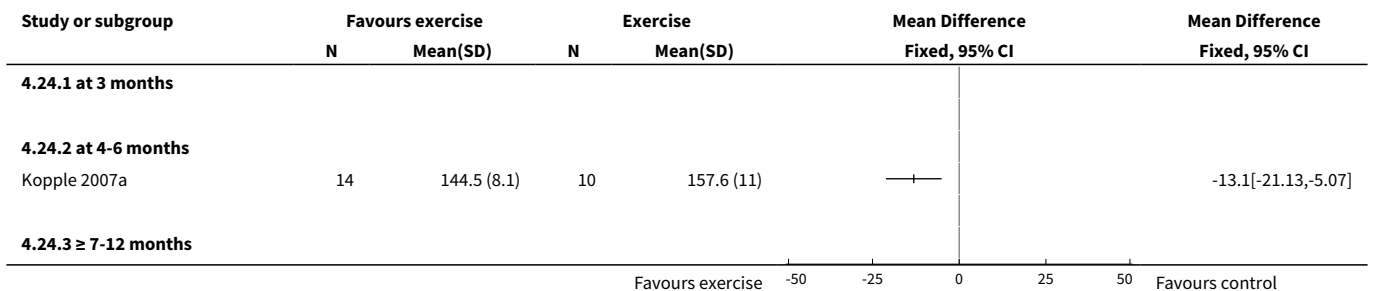




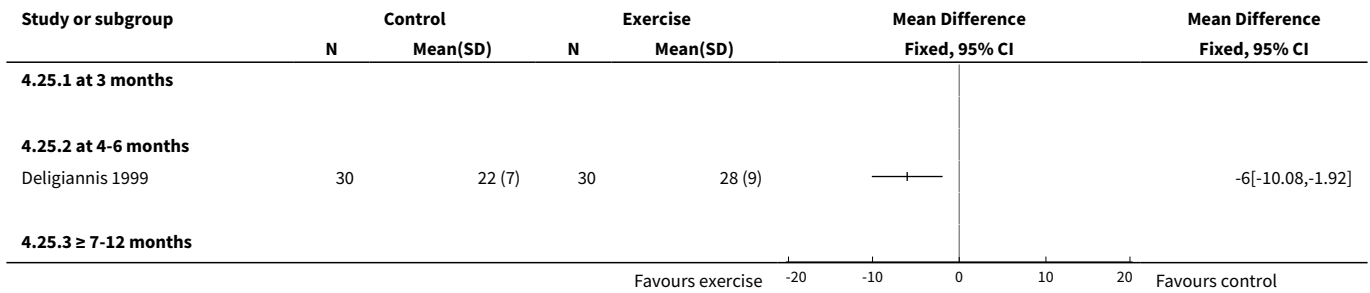
Analysis 4.23. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 23 LDL cholesterol.



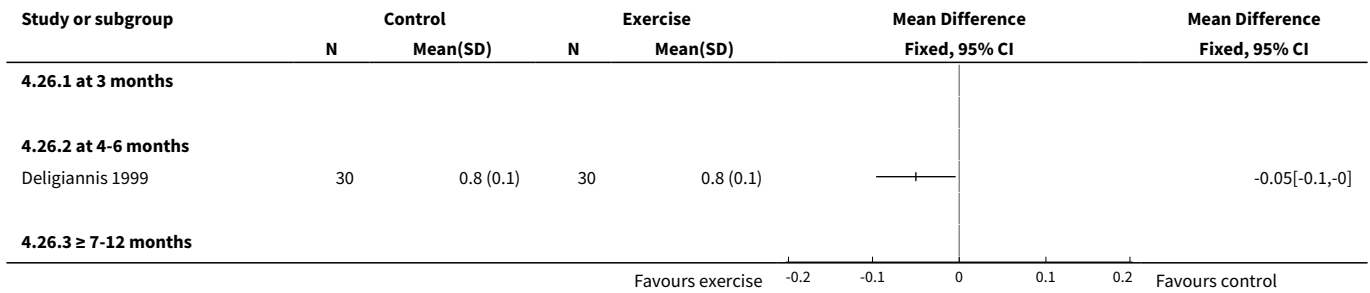
Analysis 4.24. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 24 Mid-thigh muscle area.



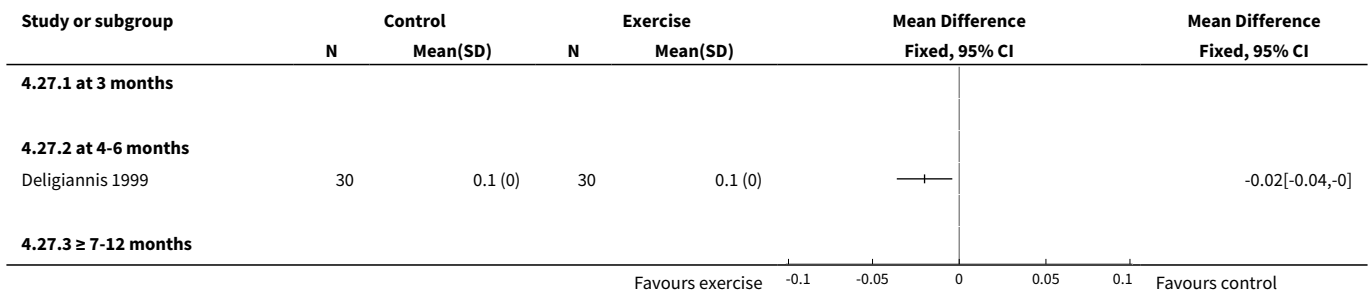
Analysis 4.25. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 25 HRV index.



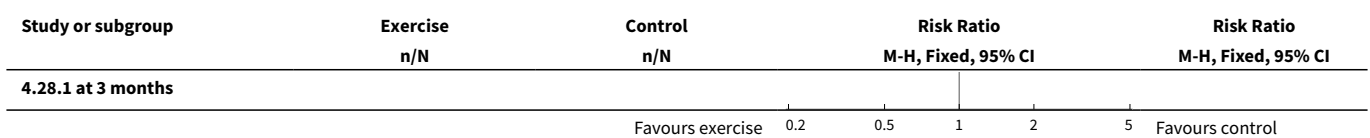
Analysis 4.26. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 26 Mean cardiac R-R interval.

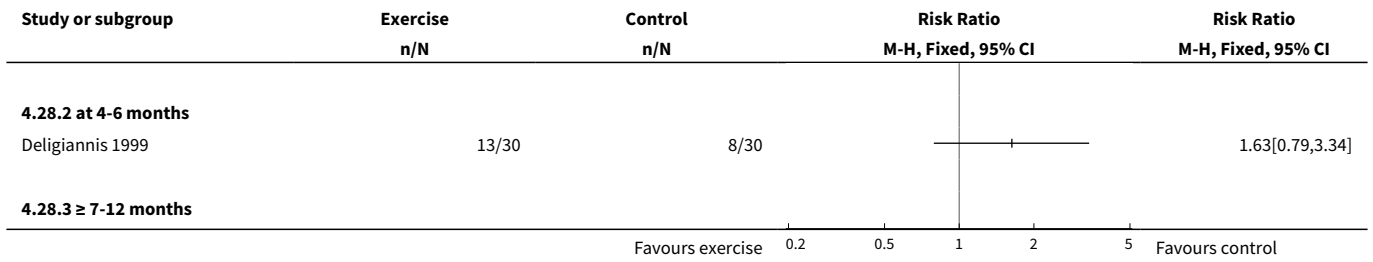


Analysis 4.27. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 27 SDNN.

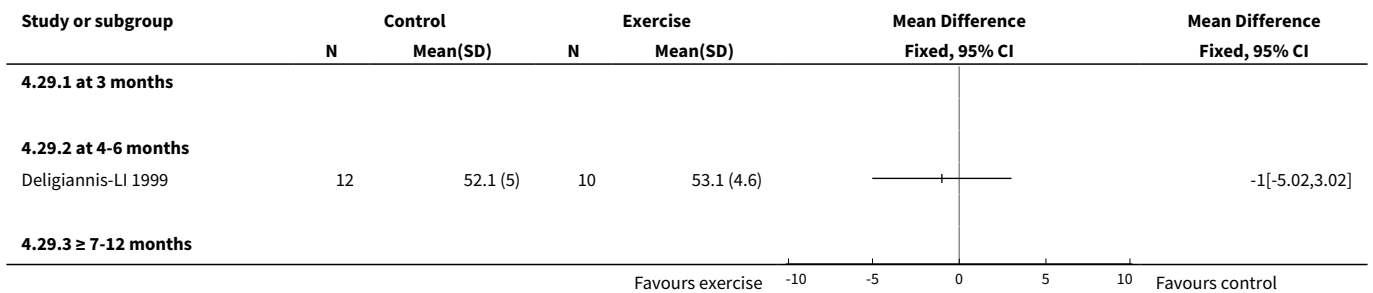


Analysis 4.28. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 28 Arrhythmias: Lown class > II (no).

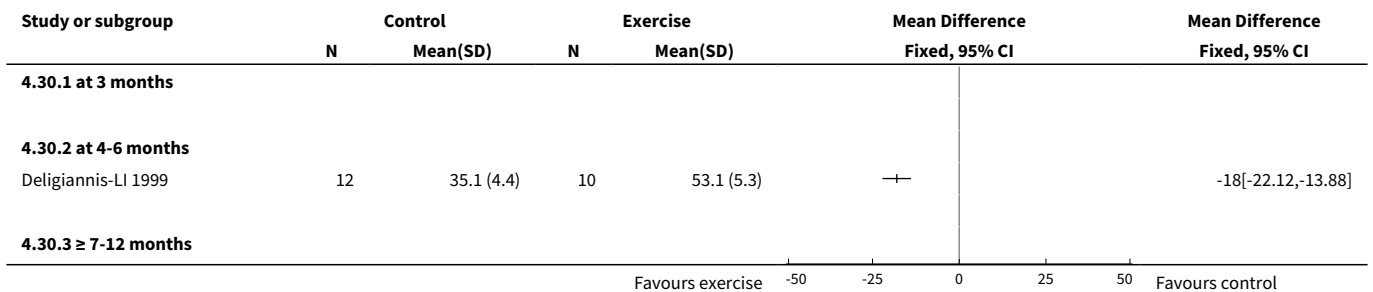




Analysis 4.29. Comparison 4 Cardiovascular exercise versus control (no exercise/ placebo exercise), Outcome 29 Left ventricular internal dimension at end-diastole.



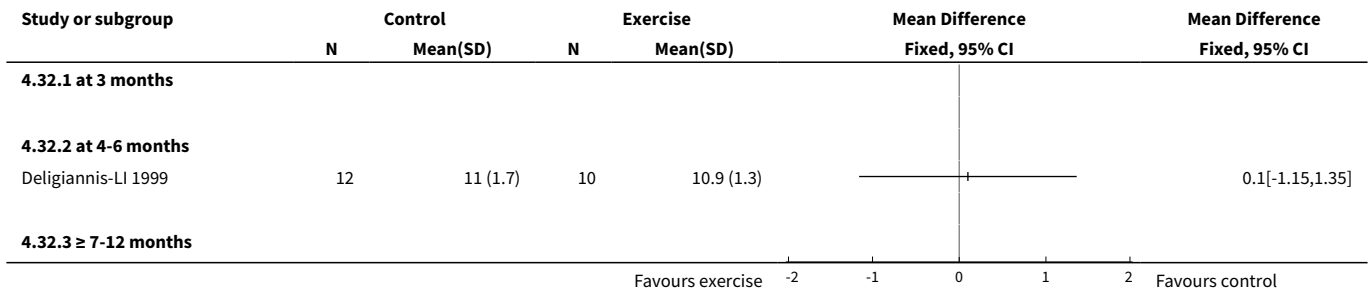
Analysis 4.30. Comparison 4 Cardiovascular exercise versus control (no exercise/ placebo exercise), Outcome 30 Left ventricular internal dimension at end-systole.



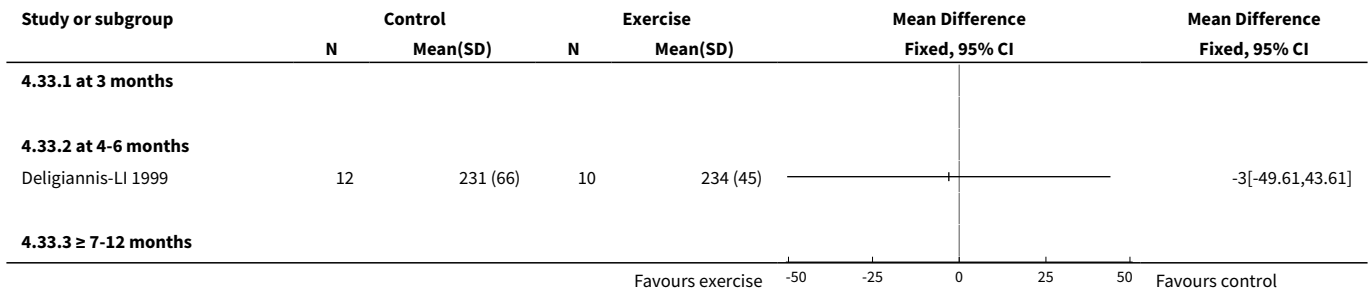
Analysis 4.31. Comparison 4 Cardiovascular exercise versus control (no exercise/ placebo exercise), Outcome 31 Intraventricular septal thickness at end-diastole.



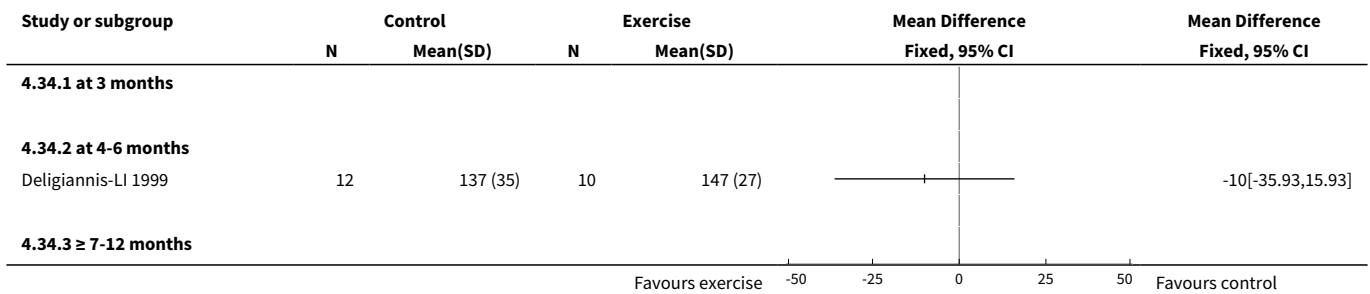
Analysis 4.32. Comparison 4 Cardiovascular exercise versus control (no exercise/ placebo exercise), Outcome 32 Left ventricular posterior wall thickness at end-diastole.



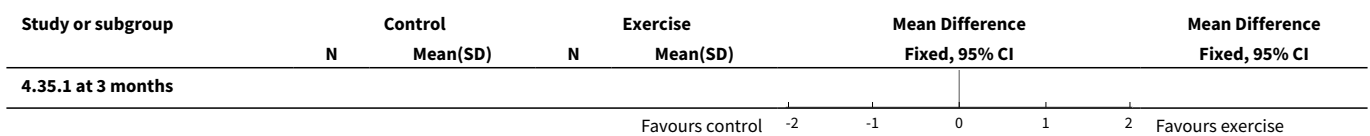
Analysis 4.33. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 33 Left ventricular mass.



Analysis 4.34. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 34 Left ventricular mass index.

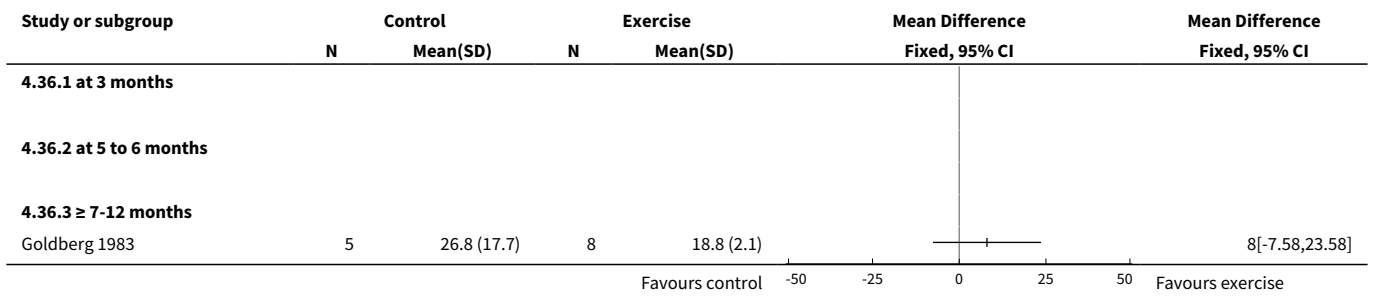


Analysis 4.35. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 35 Fasting plasma glucose.

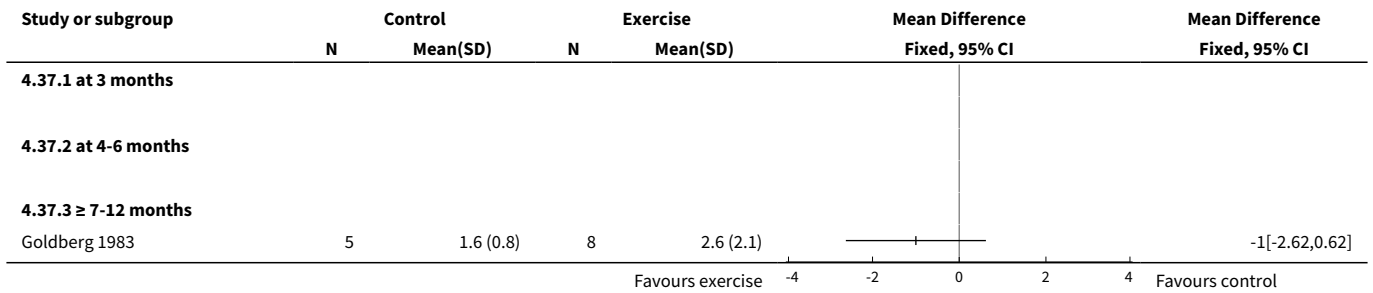




Analysis 4.36. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 36 Fasting plasma insulin.



Analysis 4.37. Comparison 4 Cardiovascular exercise versus control (no exercise/placebo exercise), Outcome 37 Glucose disappearance.



Comparison 5. Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	9	353	Std. Mean Difference (IV, Random, 95% CI)	-0.77 [-1.06, -0.48]
1.1 at 3 months	2	125	Std. Mean Difference (IV, Random, 95% CI)	-0.45 [-1.13, 0.22]
1.2 at 4-6 months	5	136	Std. Mean Difference (IV, Random, 95% CI)	-0.96 [-1.34, -0.59]

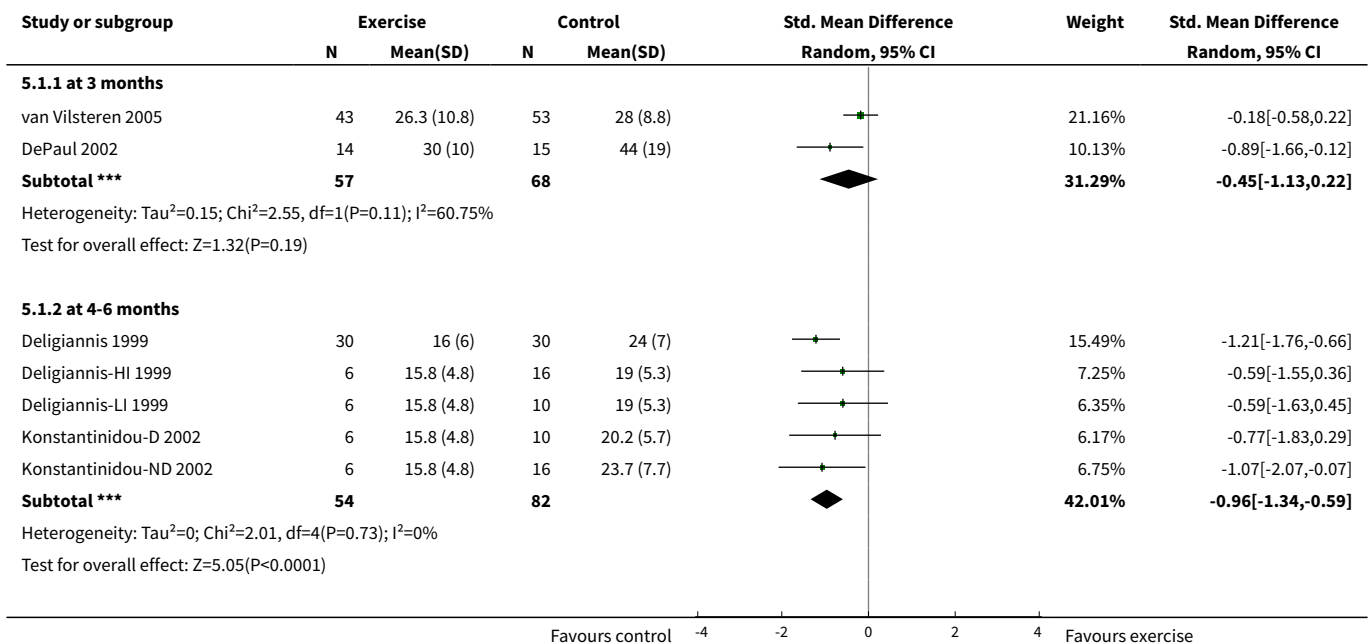
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 ≥ 7-12 months	2	92	Std. Mean Difference (IV, Random, 95% CI)	-0.93 [-1.36, -0.49]
2 Muscular strength	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
2.1 at 3 months	2		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 at 4-6 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Walking capacity	2		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 at 3 months	2	46	Std. Mean Difference (IV, Fixed, 95% CI)	-0.43 [-1.02, 0.16]
3.2 at 4-6 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 ADL capacity	0		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Diastolic blood pressure: resting	5	229	Mean Difference (IV, Fixed, 95% CI)	3.77 [1.61, 5.94]
5.1 at 3 months	2	125	Mean Difference (IV, Fixed, 95% CI)	0.52 [-3.85, 4.90]
5.2 at 4-6 months	1	28	Mean Difference (IV, Fixed, 95% CI)	3.0 [-1.27, 7.27]
5.3 ≥ 7-12 months	2	76	Mean Difference (IV, Fixed, 95% CI)	5.76 [2.70, 8.83]
6 Systolic blood pressure: resting	4	186	Mean Difference (IV, Fixed, 95% CI)	5.80 [1.19, 10.41]
6.1 at 3 months	2	125	Mean Difference (IV, Fixed, 95% CI)	6.38 [-1.99, 14.74]
6.2 at 4-6 months	1	28	Mean Difference (IV, Fixed, 95% CI)	8.0 [-0.89, 16.89]
6.3 ≥ 7-12 months	1	33	Mean Difference (IV, Fixed, 95% CI)	4.0 [-3.07, 11.07]
7 Heart rate: maximum	4	99	Mean Difference (IV, Fixed, 95% CI)	-5.38 [-10.33, -0.44]
7.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 at 4-6 months	3	66	Mean Difference (IV, Fixed, 95% CI)	-6.08 [-12.71, 0.54]

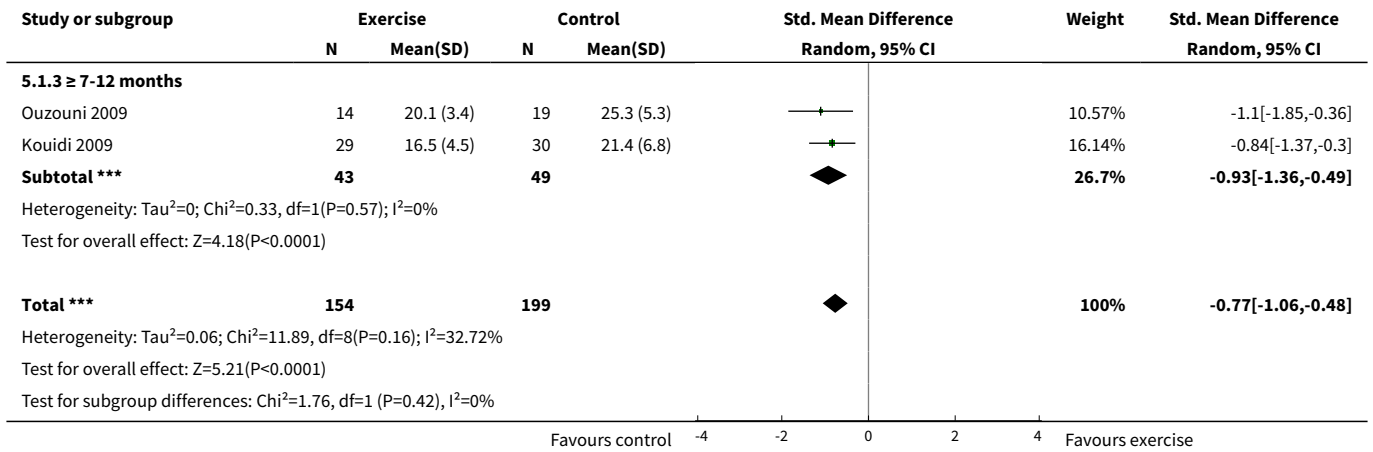
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.3 ≥ 7-12 months	1	33	Mean Difference (IV, Fixed, 95% CI)	-4.5 [-11.93, 2.93]
8 Heart rate: resting	3	104	Mean Difference (IV, Random, 95% CI)	4.94 [2.18, 7.70]
8.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 at 4-6 months	1	28	Mean Difference (IV, Random, 95% CI)	4.5 [-2.03, 11.03]
8.3 ≥ 7-12 months	2	76	Mean Difference (IV, Random, 95% CI)	4.81 [1.17, 8.46]
9 Fat mass	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Depression	2		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
10.1 at 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 at 4-6 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 ≥ 7-12 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Total cholesterol	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
11.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
11.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12 Mid-thigh muscle area	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
12.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 HRV index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
13.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Mean cardiac R-R interval	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 SDNN	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
15.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Arrhythmias: Low class > II (no)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
16.1 at 3 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.2 at 4-6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 ≥ 7-12 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Left ventricular inter- nal dimension at end- diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
17.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Left ventricular inter- nal dimension at end- systole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
18.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Intraventricular sep- tal thickness at end-di- astole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
19.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20 Left ventricular posterior wall thickness at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
20.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Left ventricular mass	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
21.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Left ventricular mass index	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
22.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 5.1. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.

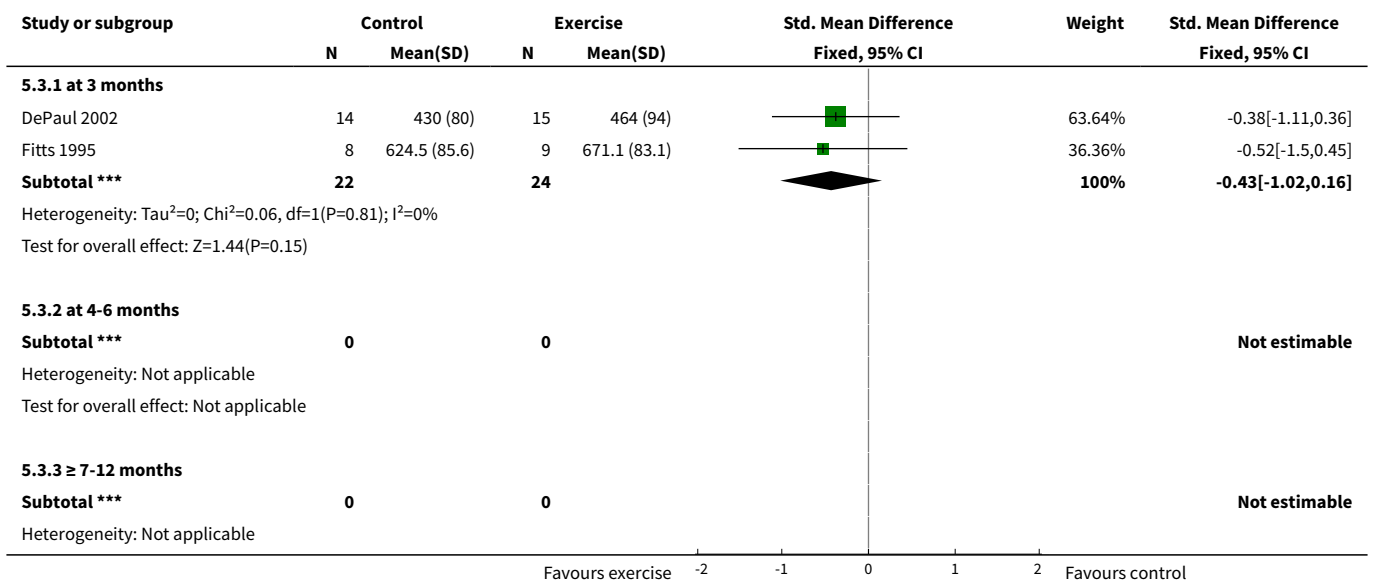




Analysis 5.2. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 2 Muscular strength.



Analysis 5.3. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 3 Walking capacity.



Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			

Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

Favours exercise -2 -1 0 1 2 Favours control

Analysis 5.5. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 5 Diastolic blood pressure: resting.

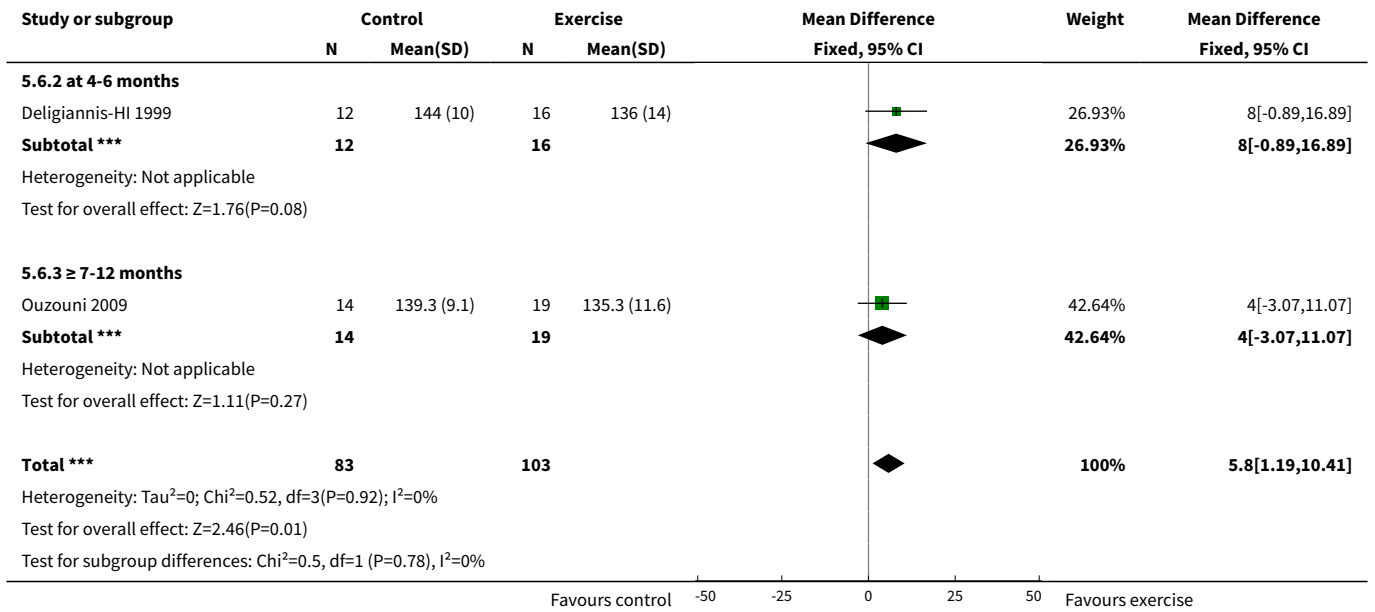
Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
5.5.1 at 3 months							
DePaul 2002	14	85.2 (11.7)	15	81.7 (8.6)		8.29%	3.5[-4.02,11.02]
van Vilsteren 2005	43	79 (12)	53	80 (14.9)		16.17%	-1[-6.38,4.38]
Subtotal ***	57		68			24.46%	0.52[-3.85,4.9]
Heterogeneity: Tau ² =0; Chi ² =0.91, df=1(P=0.34); I ² =0% Test for overall effect: Z=0.24(P=0.81)							
5.5.2 at 4-6 months							
Deligiannis-HI 1999	12	82 (3)	16	79 (8)		25.66%	3[-1.27,7.27]
Subtotal ***	12		16			25.66%	3[-1.27,7.27]
Heterogeneity: Not applicable Test for overall effect: Z=1.38(P=0.17)							
5.5.3 ≥ 7-12 months							
Kouidi 2009	21	82.4 (7)	22	76.9 (7.9)		23.57%	5.5[1.04,9.96]
Ouzouni 2009	14	85.2 (4.6)	19	79.2 (7.7)		26.31%	6[1.78,10.22]
Subtotal ***	35		41			49.89%	5.76[2.7,8.83]
Heterogeneity: Tau ² =0; Chi ² =0.03, df=1(P=0.87); I ² =0% Test for overall effect: Z=3.69(P=0)							
Total ***	104		125			100%	3.77[1.61,5.94]
Heterogeneity: Tau ² =0; Chi ² =4.8, df=4(P=0.31); I ² =16.68% Test for overall effect: Z=3.42(P=0) Test for subgroup differences: Chi ² =3.87, df=1 (P=0.14), I ² =48.25%							

Favours control -20 -10 0 10 20 Favours exercise

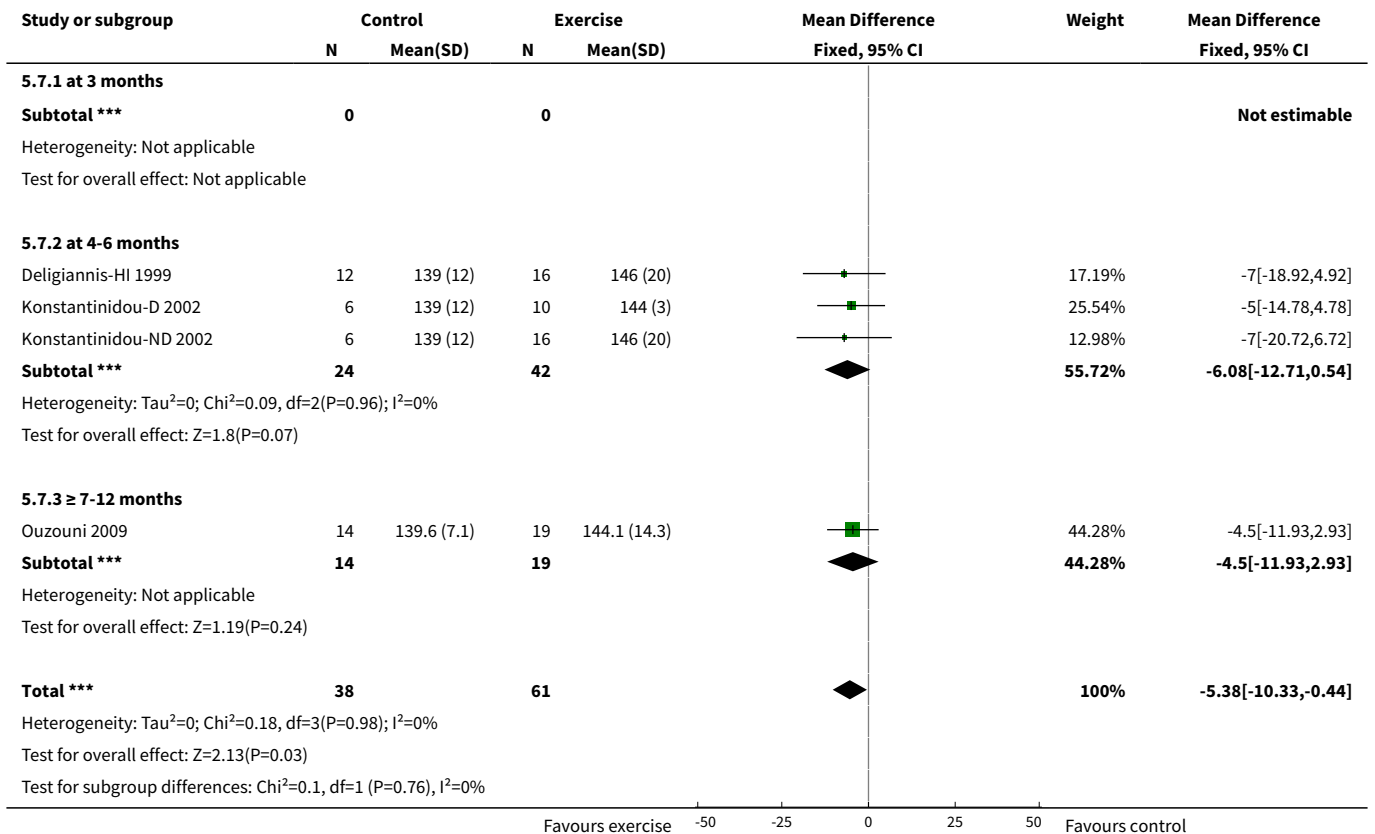
Analysis 5.6. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 6 Systolic blood pressure: resting.

Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
5.6.1 at 3 months							
DePaul 2002	14	153.1 (20.2)	15	146 (19)		10.42%	7.1[-7.2,21.4]
van Vilsteren 2005	43	146 (25)	53	140 (26.4)		20.02%	6[-4.31,16.31]
Subtotal ***	57		68			30.43%	6.38[-1.99,14.74]
Heterogeneity: Tau ² =0; Chi ² =0.01, df=1(P=0.9); I ² =0% Test for overall effect: Z=1.49(P=0.14)							

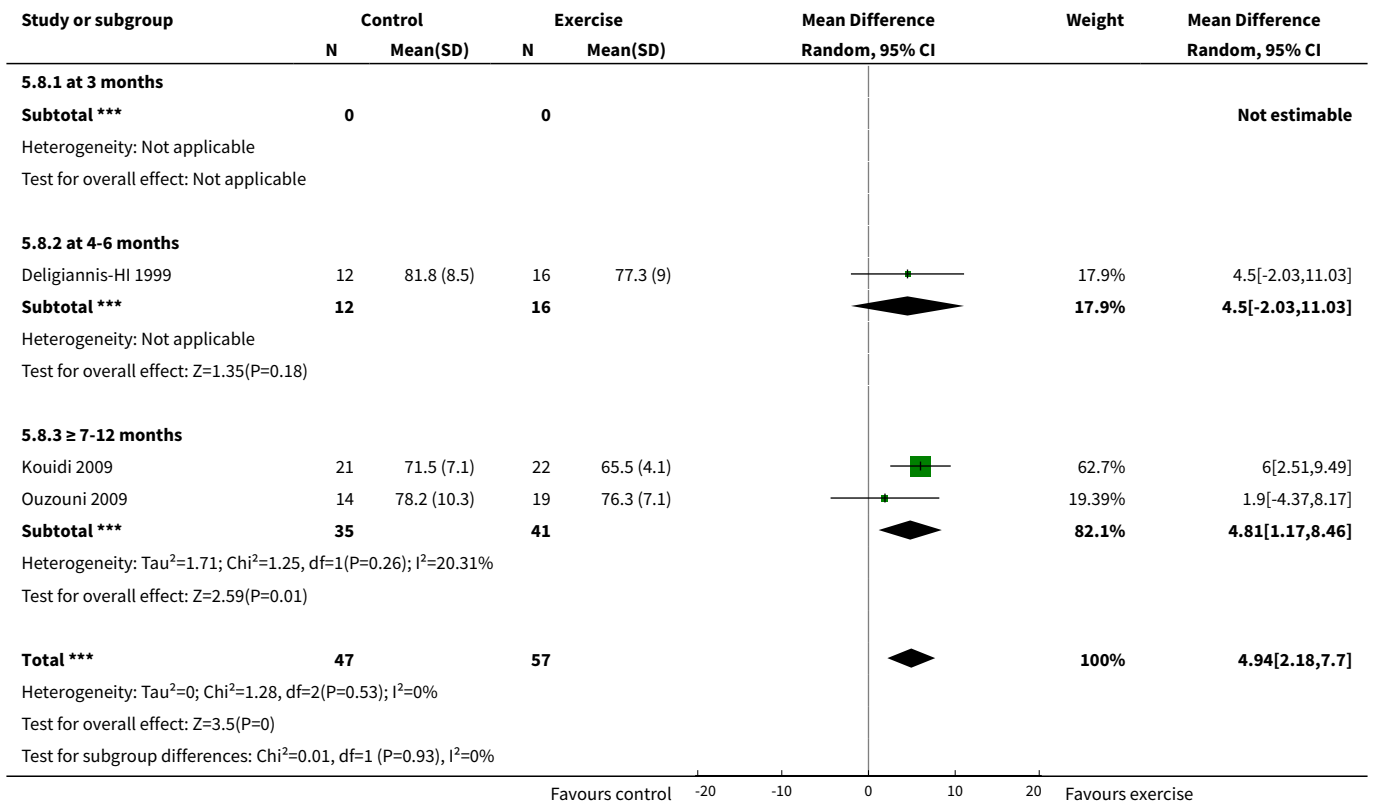
Favours control -50 -25 0 25 50 Favours exercise



Analysis 5.7. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 7 Heart rate: maximum.



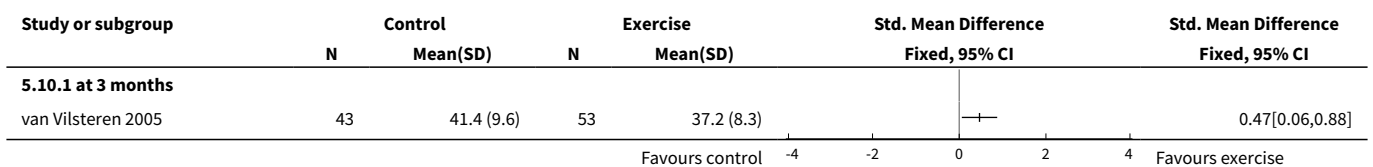
Analysis 5.8. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 8 Heart rate: resting.

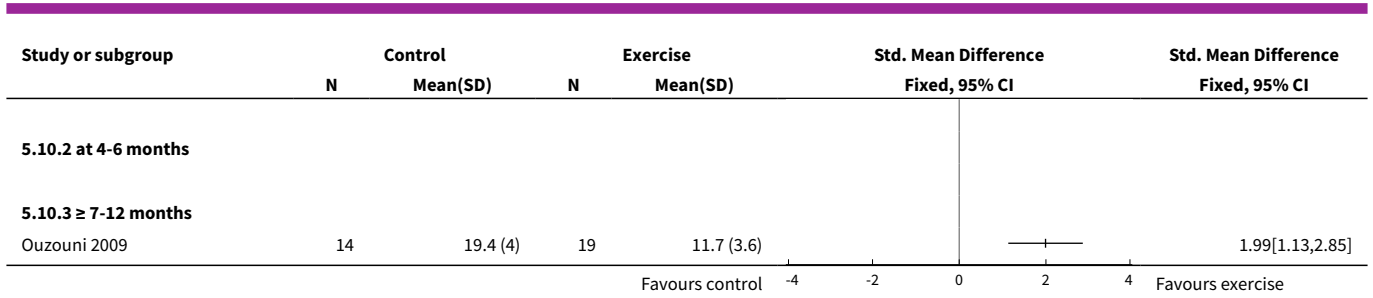


Analysis 5.9. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 9 Fat mass.

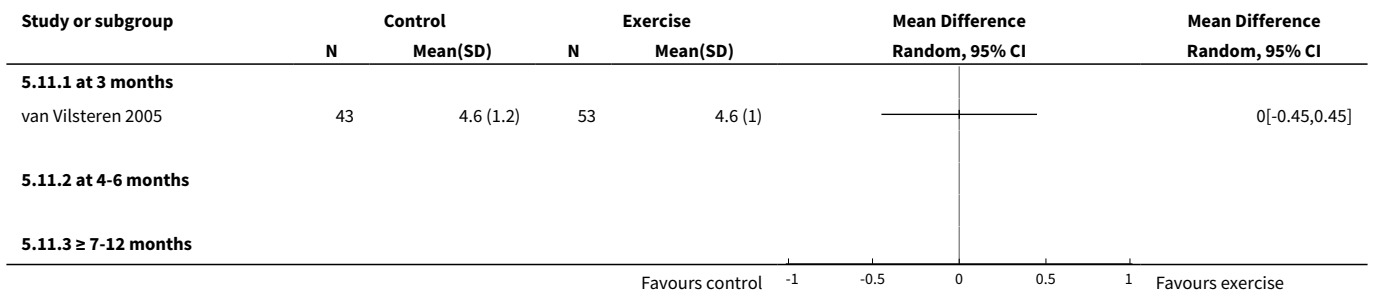


Analysis 5.10. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 10 Depression.

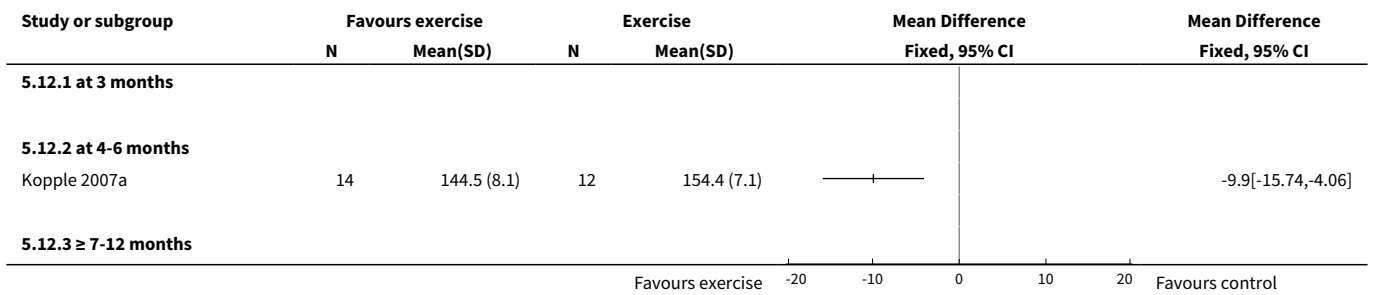




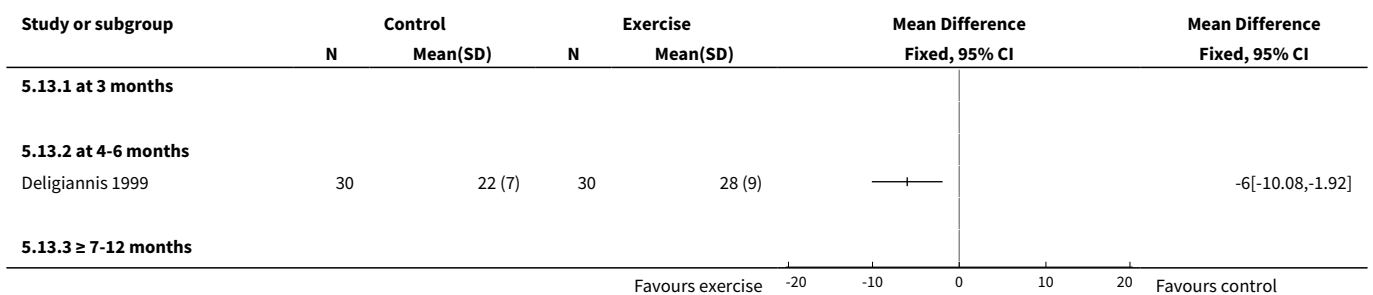
Analysis 5.11. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 11 Total cholesterol.



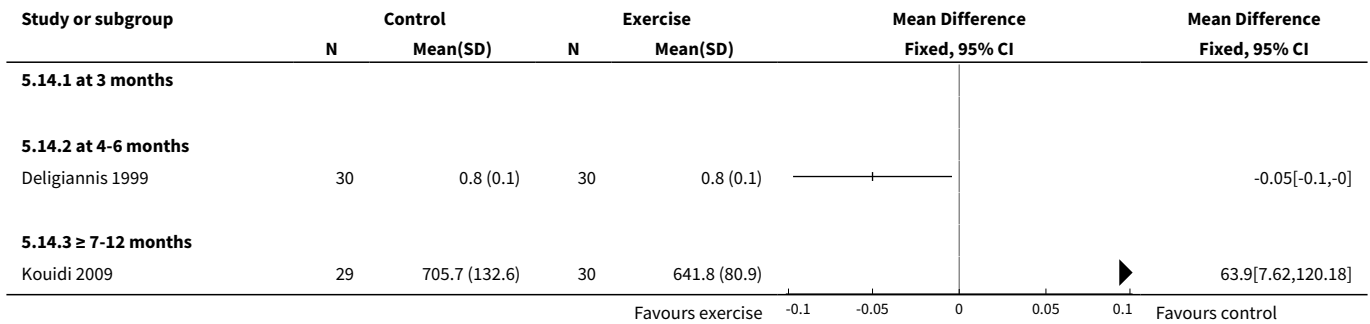
Analysis 5.12. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 12 Mid-thigh muscle area.



Analysis 5.13. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 13 HRV index.



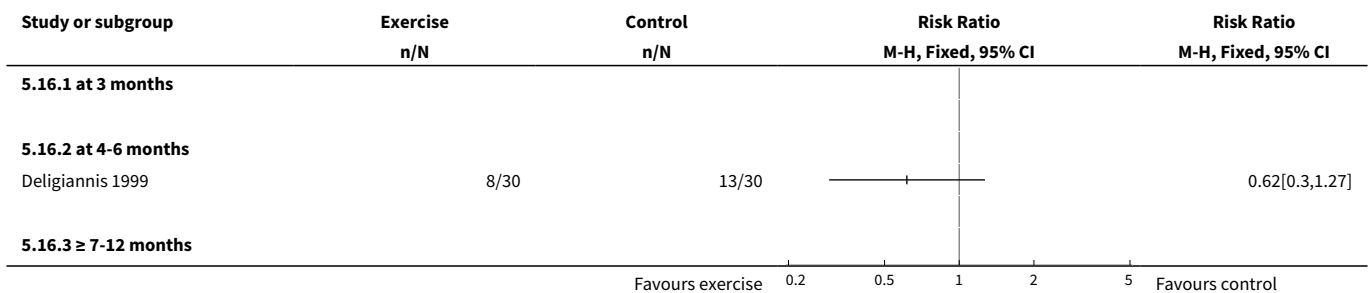
Analysis 5.14. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 14 Mean cardiac R-R interval.



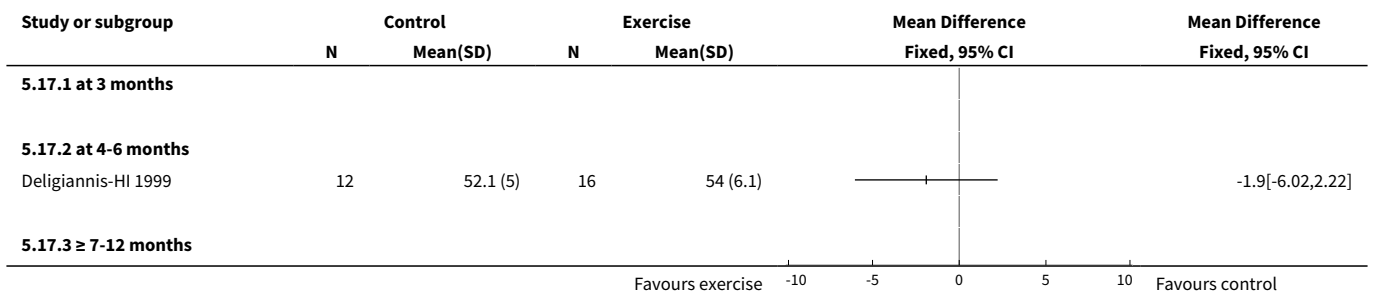
Analysis 5.15. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 15 SDNN.



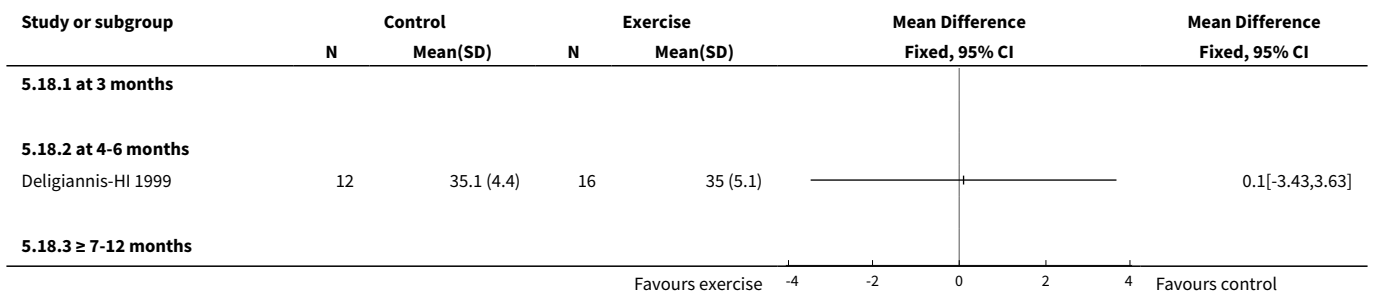
Analysis 5.16. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 16 Arrhythmias: Lown class > II (no).



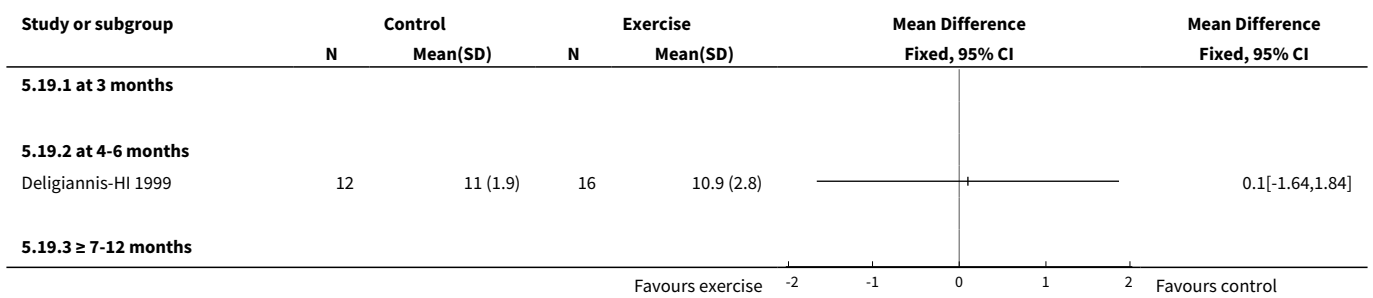
Analysis 5.17. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 17 Left ventricular internal dimension at end-diastole.



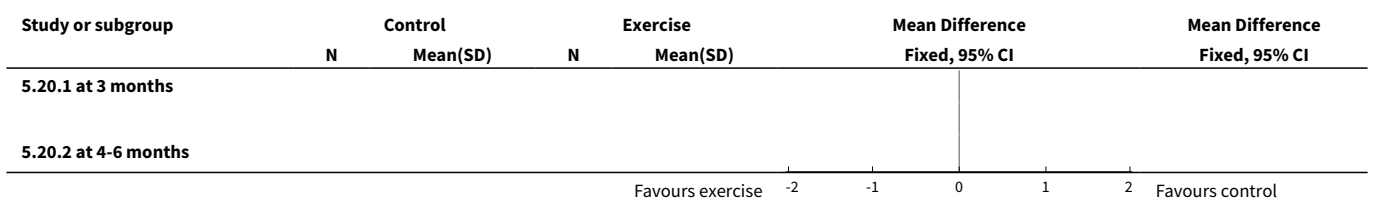
Analysis 5.18. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 18 Left ventricular internal dimension at end-systole.



Analysis 5.19. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 19 Intraventricular septal thickness at end-diastole.

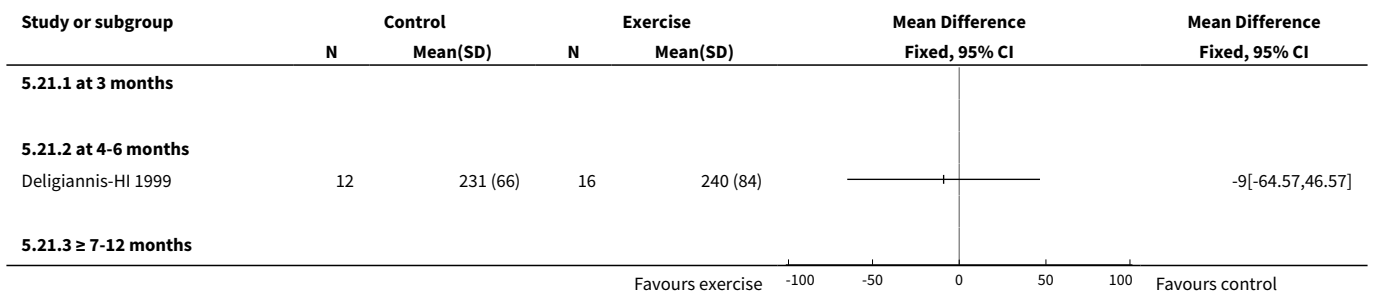


Analysis 5.20. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 20 Left ventricular posterior wall thickness at end-diastole.

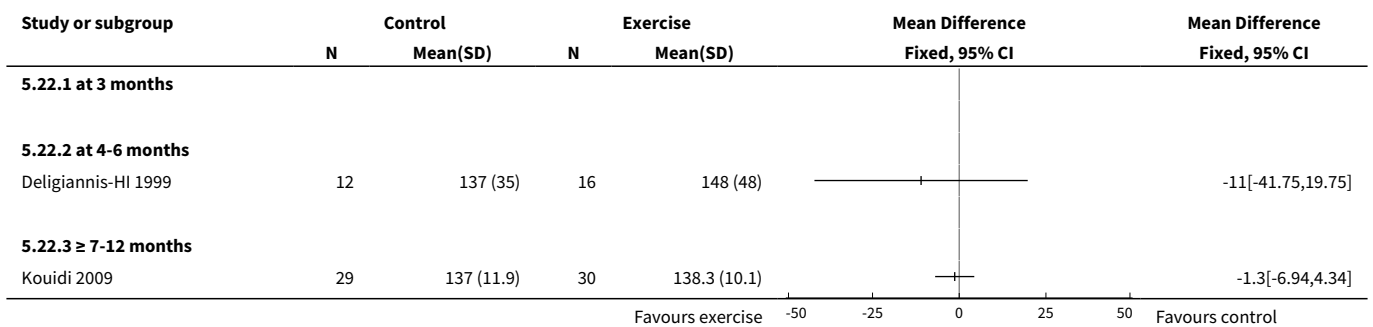




Analysis 5.21. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 21 Left ventricular mass.



Analysis 5.22. Comparison 5 Mixed cardiovascular and resistance exercise versus control (no exercise/placebo exercise), Outcome 22 Left ventricular mass index.



Comparison 6. Resistance training versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 at 3 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Muscular strength (high value = improved)	4	153	Std. Mean Difference (IV, Fixed, 95% CI)	-0.60 [-0.92, -0.27]
2.1 at 3 months	3	111	Std. Mean Difference (IV, Fixed, 95% CI)	-0.58 [-0.96, -0.19]
2.2 at 4-6 months	1	42	Std. Mean Difference (IV, Fixed, 95% CI)	-0.65 [-1.27, -0.03]
2.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Muscular strength (low value = improved)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 3 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Walking capacity	2		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 at 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Albumin	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 at 3 months	2	75	Mean Difference (IV, Fixed, 95% CI)	-1.46 [-2.89, -0.04]
6.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Pre-albumin	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 at 3 months	2	75	Mean Difference (IV, Fixed, 95% CI)	-45.24 [-73.90, -16.57]
7.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Energy intake	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 at 3 months	2	75	Mean Difference (IV, Fixed, 95% CI)	-3.70 [-7.46, 0.06]
8.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Protein intake	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Transferrin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
10.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Fat mass	2		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 at 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Waist circumference	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
12.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Mid-arm circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
13.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 9-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Mid-calf circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
14.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Mid-thigh circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
15.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Interleukin 6	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
16.1 at 3 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
16.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
16.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17 Lymphocytes (x 10⁹ L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
17.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Protein catabolic rate	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
18.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Physical activity	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
19.1 at 3 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Type I muscle fibre area	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
20.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21 Mid-thigh muscle area	4	135	Mean Difference (IV, Fixed, 95% CI)	-6.74 [-11.18, -2.30]
21.1 at 3 months	3	111	Mean Difference (IV, Fixed, 95% CI)	-3.22 [-9.67, 3.24]
21.2 at 4-6 months	1	24	Mean Difference (IV, Fixed, 95% CI)	-9.90 [-16.01, -3.79]
21.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Thigh muscle attenuation (Hounsfield units)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
22.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 6.1. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.

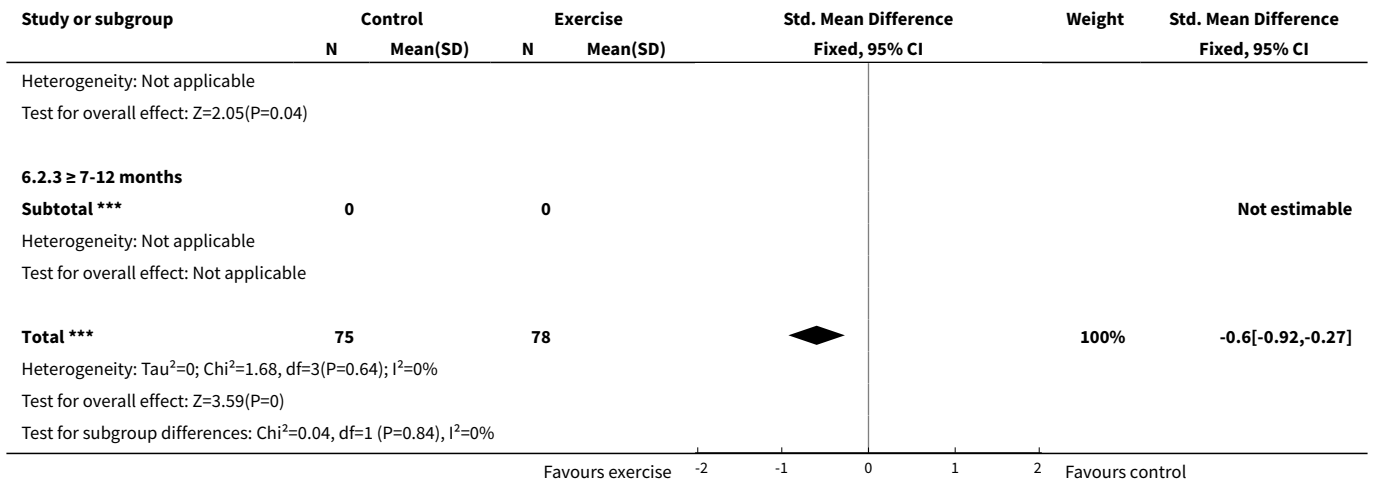
Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
6.1.1 at 3 months						
6.1.2 at 4-6 months						
Segura-Orti 2009	8	6.7 (3.1)	17	6.6 (2.7)		0.03[-0.81,0.87]
6.1.3 ≥ 7-12 months						

Favours treatment -2 -1 0 1 2 Favours control

Analysis 6.2. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 2 Muscular strength (high value = improved).

Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
6.2.1 at 3 months							
Castaneda 2001	12	38.8 (14)	14	55.9 (22.4)		16.09%	-0.87[-1.68,-0.06]
Johansen 2006	17	20 (9.1)	19	22.6 (11.6)		24.63%	-0.24[-0.9,0.41]
PEAK Study 2005	25	85.2 (34.3)	24	109.5 (35.1)		31.83%	-0.69[-1.27,-0.11]
Subtotal ***	54		57			72.55%	-0.58[-0.96,-0.19]
Heterogeneity: Tau ² =0; Chi ² =1.64, df=2(P=0.44); I ² =0%							
Test for overall effect: Z=2.96(P=0)							
6.2.2 at 4-6 months							
Chen 2010	21	12.1 (6.1)	21	15.8 (5)		27.45%	-0.65[-1.27,-0.03]
Subtotal ***	21		21			27.45%	-0.65[-1.27,-0.03]

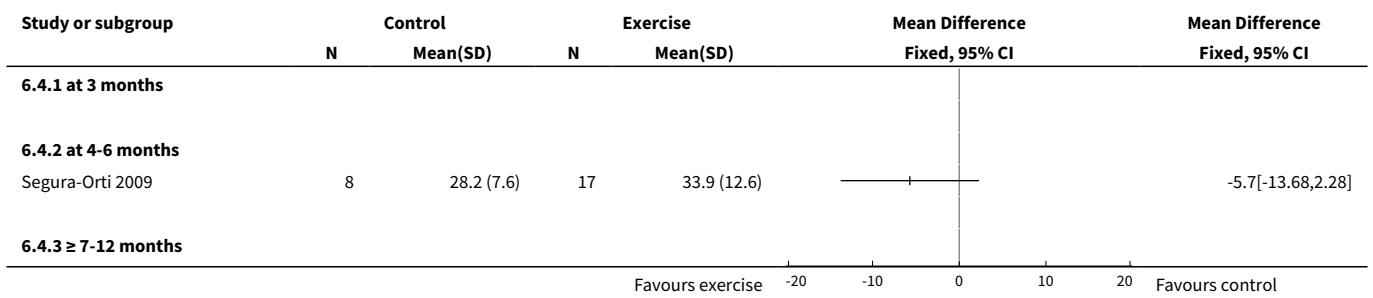
Favours exercise -2 -1 0 1 2 Favours control



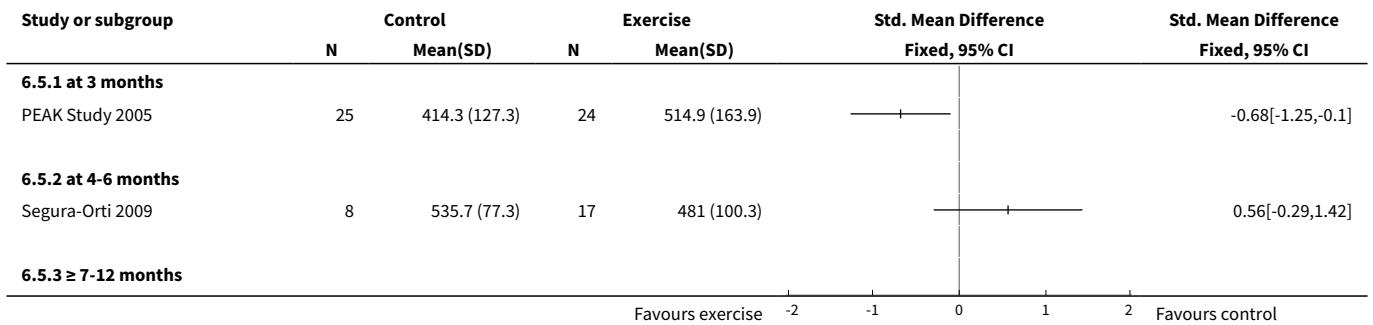
Analysis 6.3. Comparison 6 Resistance training versus control (no exercise/ placebo exercise), Outcome 3 Muscular strength (low value = improved).



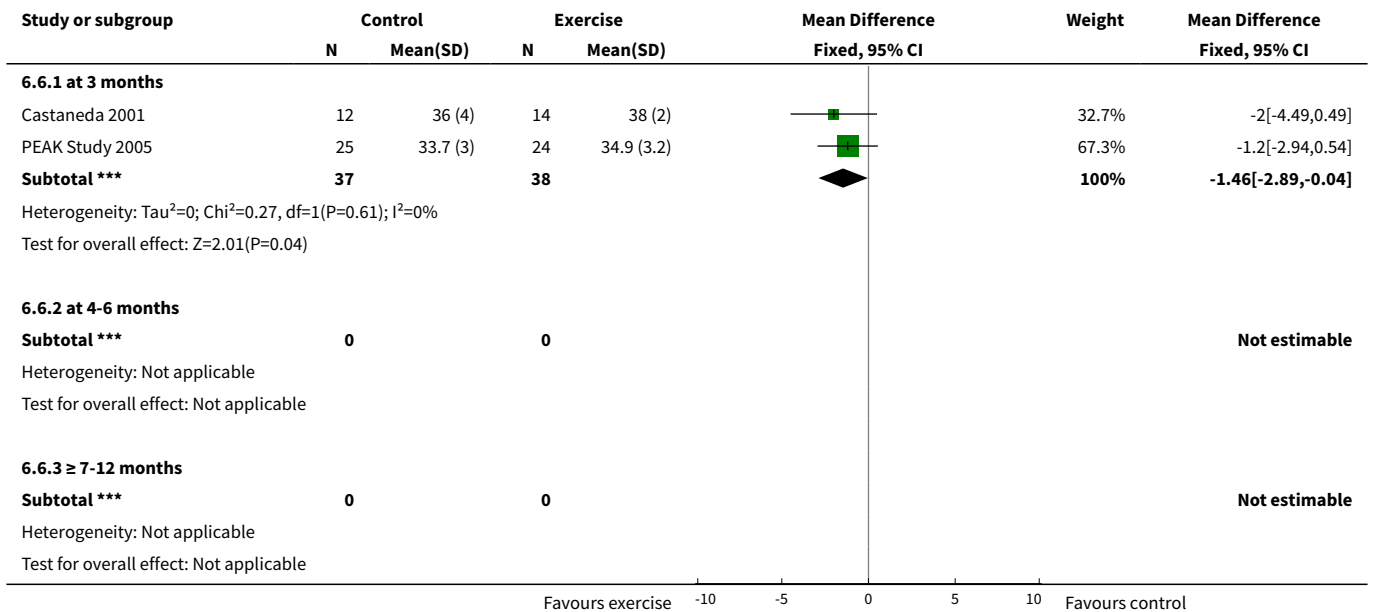
Analysis 6.4. Comparison 6 Resistance training versus control (no exercise/ placebo exercise), Outcome 4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60.



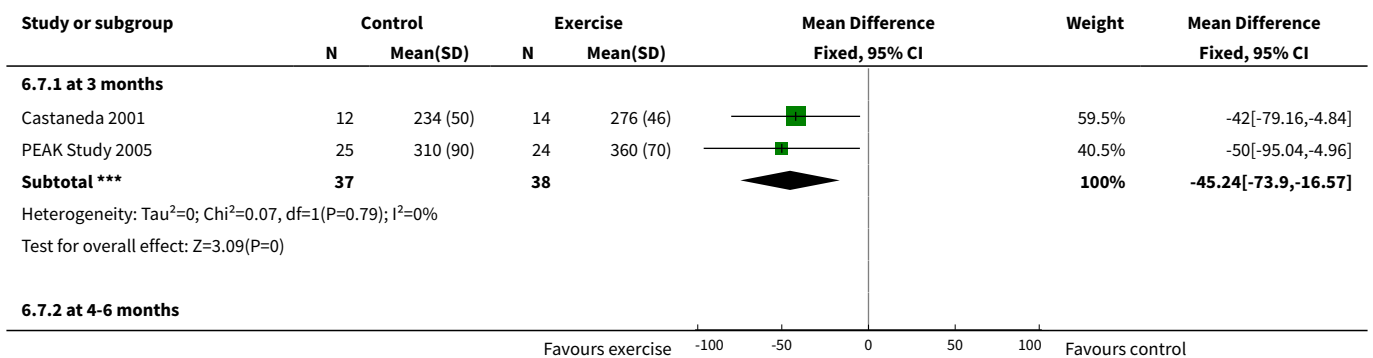
Analysis 6.5. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 5 Walking capacity.

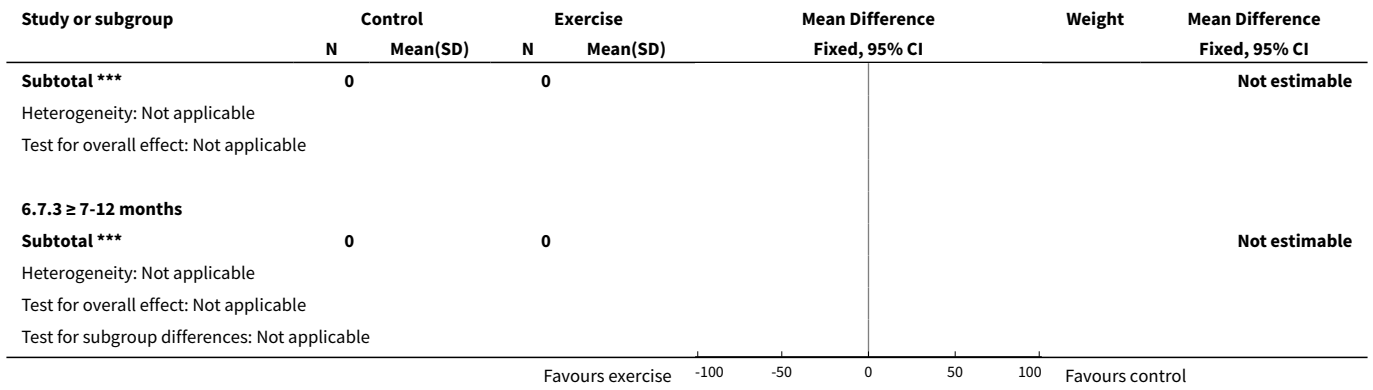


Analysis 6.6. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 6 Albumin.

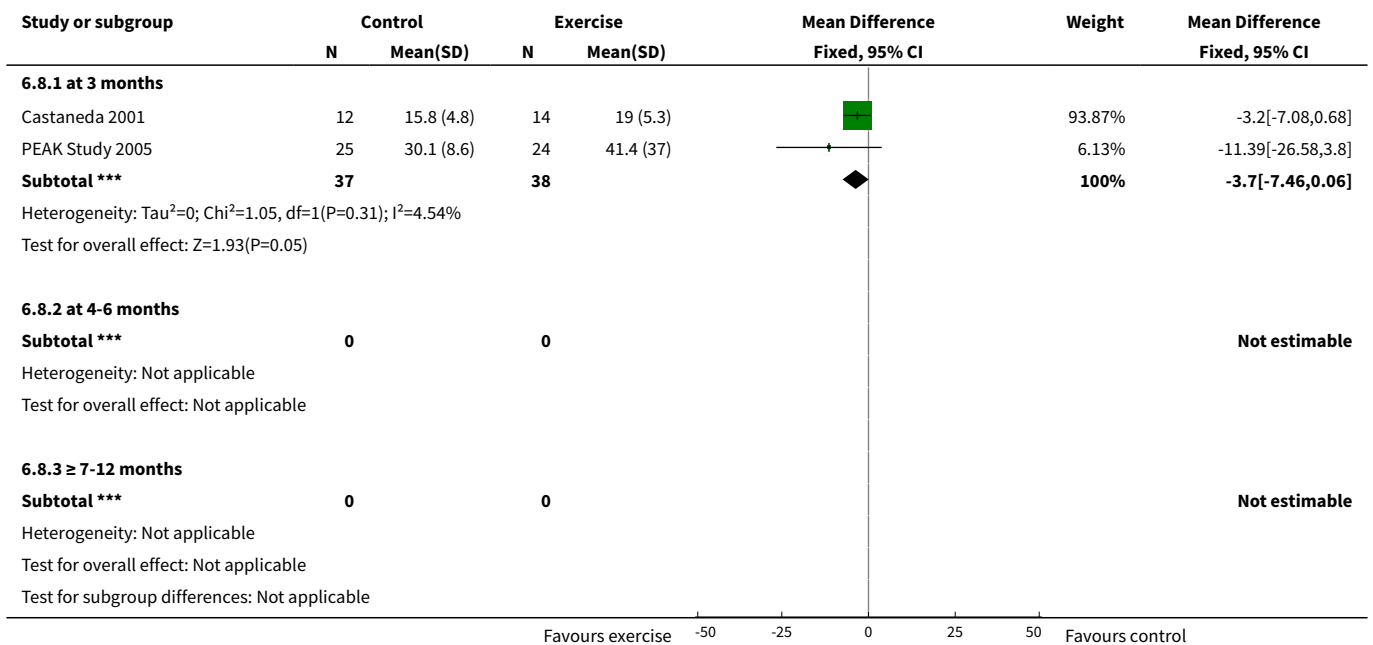


Analysis 6.7. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 7 Pre-albumin.

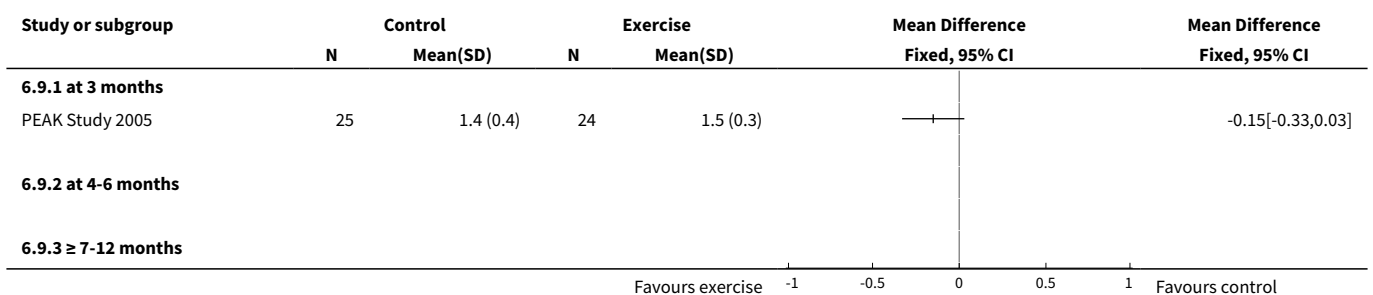




Analysis 6.8. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 8 Energy intake.



Analysis 6.9. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 9 Protein intake.



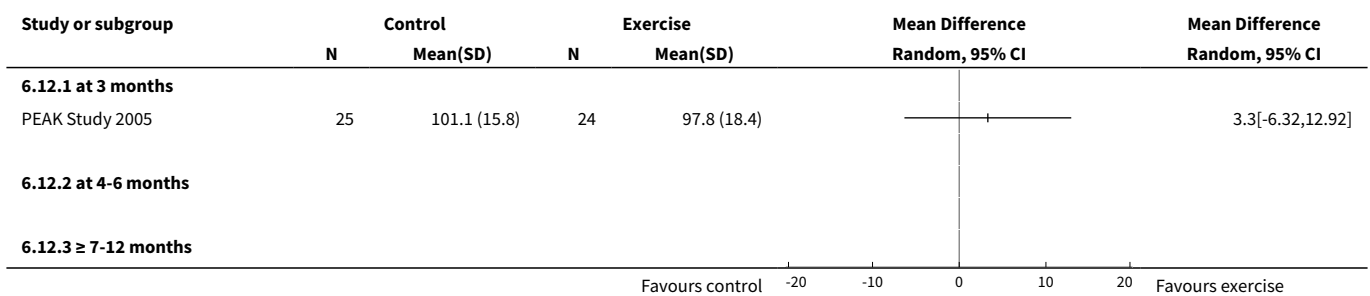
Analysis 6.10. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 10 Transferrin.



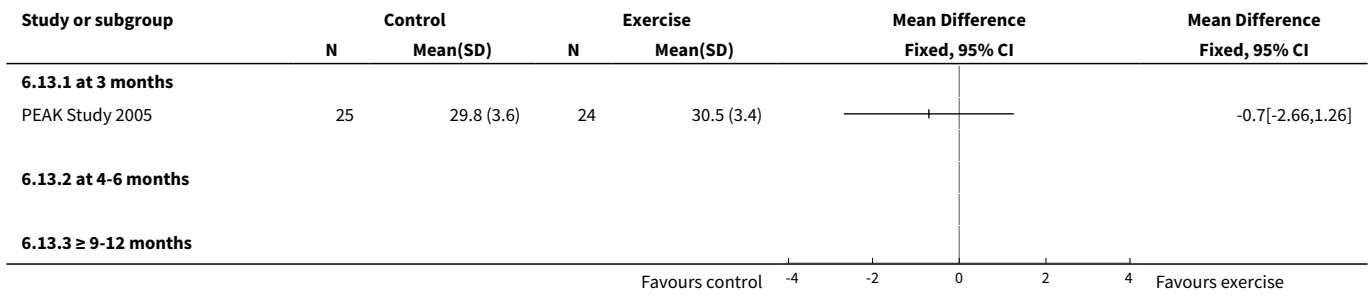
Analysis 6.11. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 11 Fat mass.



Analysis 6.12. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 12 Waist circumference.



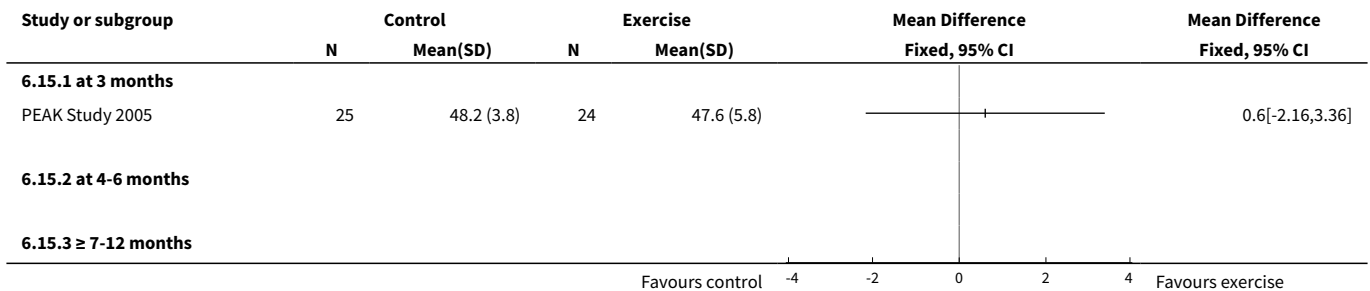
Analysis 6.13. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 13 Mid-arm circumference.



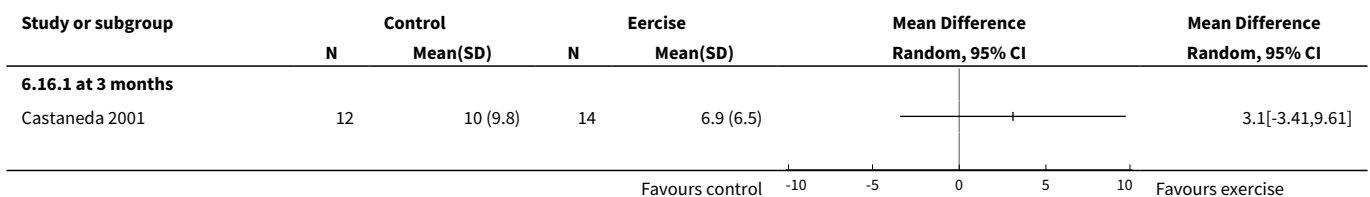
Analysis 6.14. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 14 Mid-calf circumference.

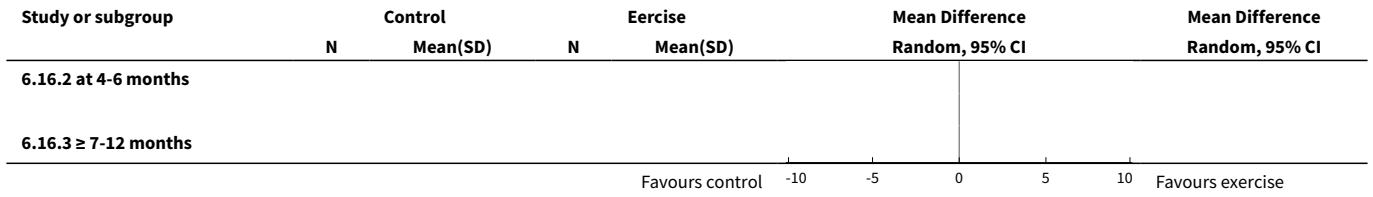


Analysis 6.15. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 15 Mid-thigh circumference.



Analysis 6.16. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 16 Interleukin 6.

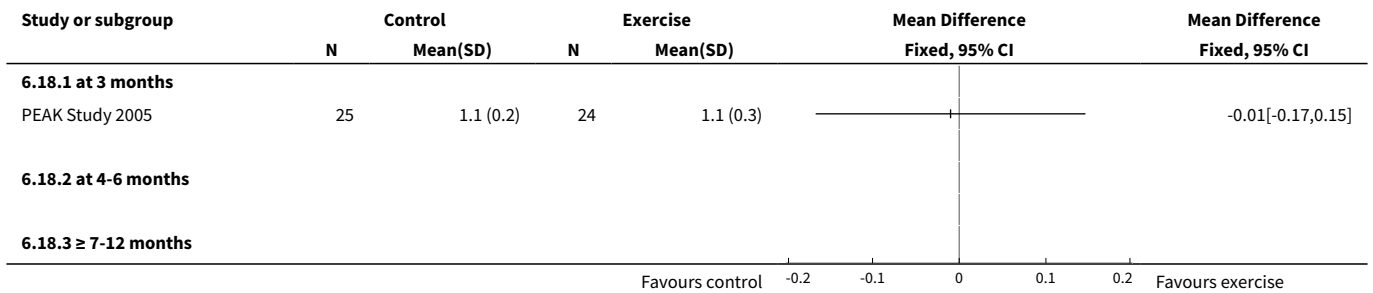




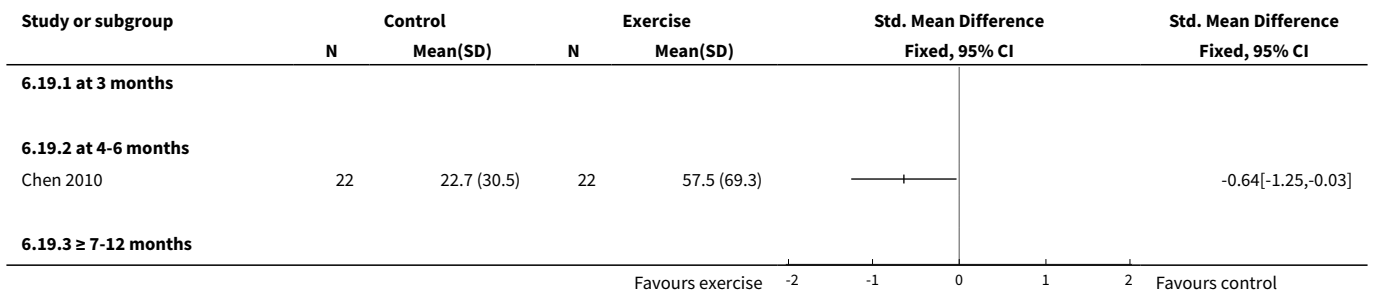
Analysis 6.17. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 17 Lymphocytes (x 10⁹ L).



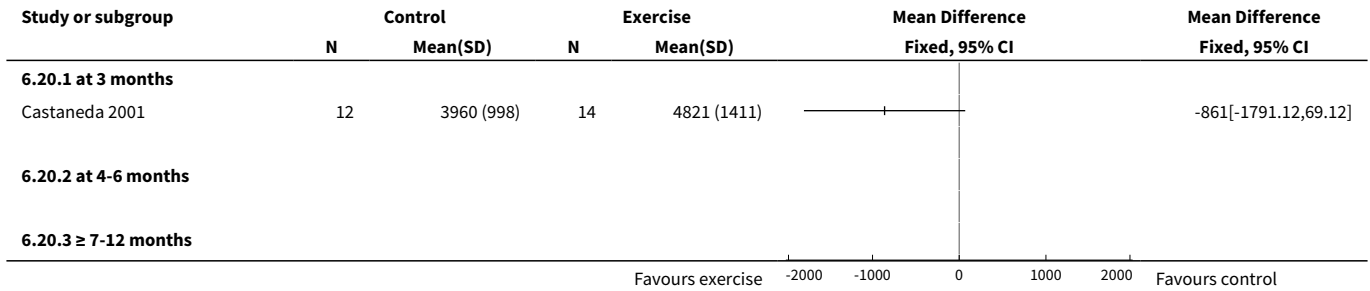
Analysis 6.18. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 18 Protein catabolic rate.



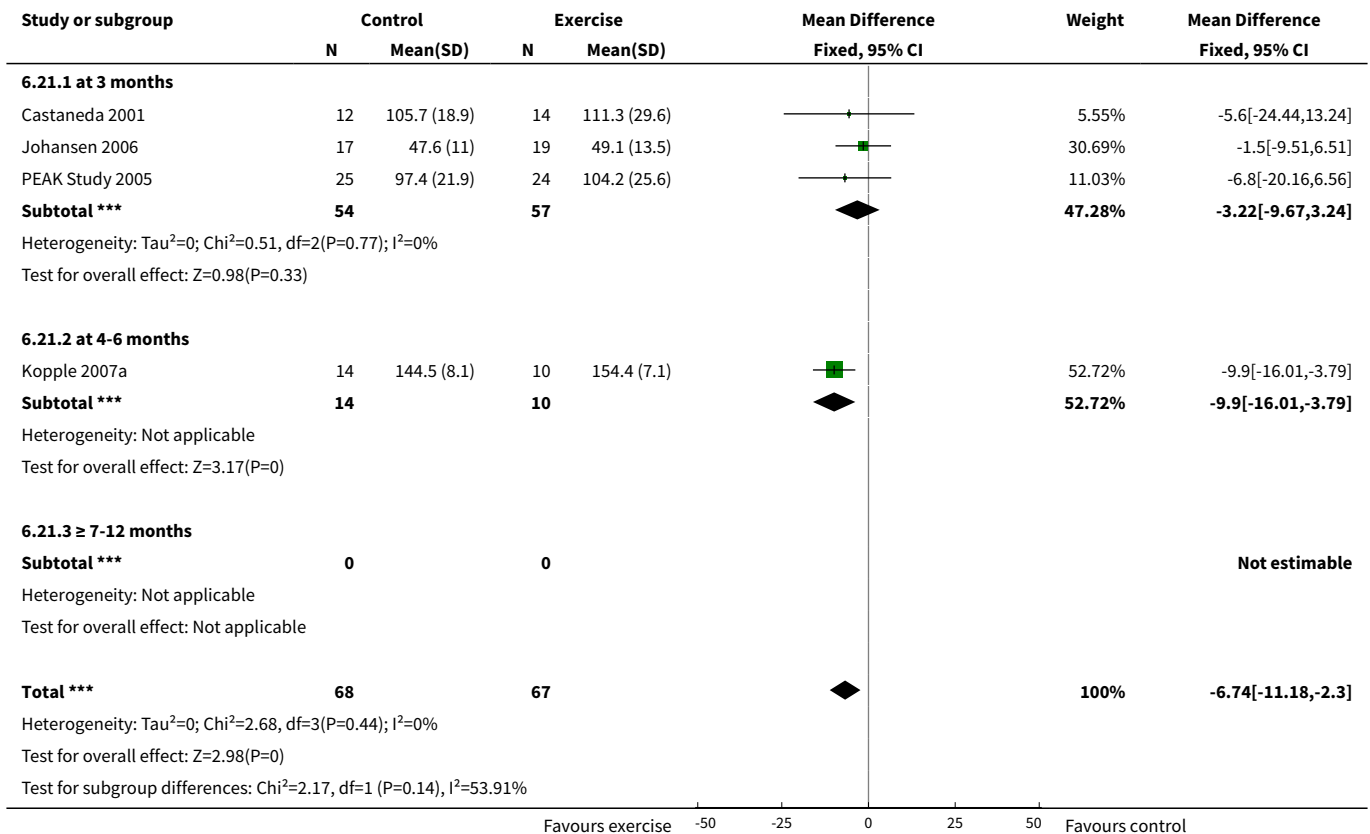
Analysis 6.19. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 19 Physical activity.



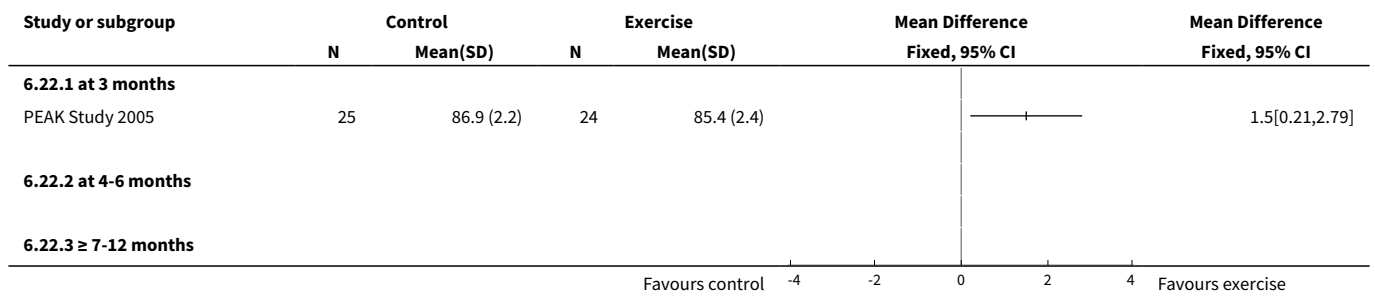
Analysis 6.20. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 20 Type I muscle fibre area.



Analysis 6.21. Comparison 6 Resistance training versus control (no exercise/placebo exercise), Outcome 21 Mid-thigh muscle area.



Analysis 6.22. Comparison 6 Resistance training versus control (no exercise/ placebo exercise), Outcome 22 Thigh muscle attenuation (Hounsfield units).



Comparison 7. Supervised exercise versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	16	538	Std. Mean Difference (IV, Fixed, 95% CI)	-0.65 [-0.83, -0.47]
1.1 at 3 months	5	184	Std. Mean Difference (IV, Fixed, 95% CI)	-0.32 [-0.62, -0.03]
1.2 at 4-6 months	8	237	Std. Mean Difference (IV, Fixed, 95% CI)	-0.83 [-1.11, -0.56]
1.3 ≥ 7-12 months	3	117	Std. Mean Difference (IV, Fixed, 95% CI)	-0.84 [-1.23, -0.46]
2 Muscular strength (high value = improved)	7	248	Std. Mean Difference (IV, Fixed, 95% CI)	-0.57 [-0.83, -0.32]
2.1 at 3 months	5	177	Std. Mean Difference (IV, Fixed, 95% CI)	-0.60 [-0.90, -0.29]
2.2 at 4-6 months	2	71	Std. Mean Difference (IV, Fixed, 95% CI)	-0.52 [-0.99, -0.05]
2.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Muscular strength (low value = improved)	3	148	Std. Mean Difference (IV, Fixed, 95% CI)	0.58 [0.25, 0.92]
3.1 at 3 months	2	123	Std. Mean Difference (IV, Fixed, 95% CI)	0.69 [0.32, 1.05]
3.2 at 4-6 months	1	25	Std. Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.80, 0.88]
3.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60	2	52	Mean Difference (IV, Fixed, 95% CI)	-3.64 [-7.93, 0.65]
4.1 at 3 months	1	27	Mean Difference (IV, Fixed, 95% CI)	-2.80 [-7.89, 2.29]
4.2 at 4-6 months	1	25	Mean Difference (IV, Fixed, 95% CI)	-5.70 [-13.68, 2.28]
4.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Walking capacity	5	160	Std. Mean Difference (IV, Fixed, 95% CI)	-0.36 [-0.68, -0.04]
5.1 at 3 months	3	105	Std. Mean Difference (IV, Fixed, 95% CI)	-0.49 [-0.88, -0.10]
5.2 at 4-6 months	2	55	Std. Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.65, 0.46]
5.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Stair climbing capacity: stair climb test (22 steps)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 ADL capacity	2		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 at 3 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 at 4-6 months	2		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 Diastolic blood pressure: resting	7	283	Mean Difference (IV, Fixed, 95% CI)	3.29 [1.21, 5.36]
8.1 at 3 months	2	125	Mean Difference (IV, Fixed, 95% CI)	0.52 [-3.85, 4.90]
8.2 at 4-6 months	2	57	Mean Difference (IV, Fixed, 95% CI)	1.39 [-2.52, 5.29]
8.3 ≥ 7-12 months	3	101	Mean Difference (IV, Fixed, 95% CI)	5.65 [2.69, 8.62]
9 Systolic blood pressure: resting	5	211	Mean Difference (IV, Random, 95% CI)	5.88 [1.42, 10.34]
9.1 at 3 months	2	125	Mean Difference (IV, Random, 95% CI)	6.38 [-1.99, 14.74]
9.2 at 4-6 months	1	28	Mean Difference (IV, Random, 95% CI)	8.0 [-0.89, 16.89]
9.3 ≥ 7-12 months	2	58	Mean Difference (IV, Random, 95% CI)	4.43 [-2.12, 10.97]
10 Heart rate: maximum	8	194	Mean Difference (IV, Fixed, 95% CI)	-6.62 [-11.00, -2.24]
10.1 at 3 months	2	46	Mean Difference (IV, Fixed, 95% CI)	-10.11 [-21.79, 1.57]
10.2 at 4-6 months	5	115	Mean Difference (IV, Fixed, 95% CI)	-7.11 [-13.23, -0.98]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.3 ≥ 7-12 months	1	33	Mean Difference (IV, Fixed, 95% CI)	-4.5 [-11.93, 2.93]
11 Heart rate: resting	5	158	Mean Difference (IV, Fixed, 95% CI)	4.14 [1.59, 6.70]
11.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	2	57	Mean Difference (IV, Fixed, 95% CI)	3.75 [-1.48, 8.98]
11.3 ≥ 7-12 months	3	101	Mean Difference (IV, Fixed, 95% CI)	4.27 [1.34, 7.20]
12 Albumin	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
12.1 at 3 months	2	75	Mean Difference (IV, Random, 95% CI)	-1.46 [-2.89, -0.04]
12.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
13 Pre-albumin	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.1 at 3 months	3	86	Mean Difference (IV, Fixed, 95% CI)	-44.02 [-71.52, -16.53]
13.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 SGA	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
14.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Energy intake	4	97	Std. Mean Difference (IV, Fixed, 95% CI)	-0.41 [-0.82, -0.01]
15.1 at 3 months	3	86	Std. Mean Difference (IV, Fixed, 95% CI)	-0.51 [-0.94, -0.08]
15.2 at 4-6 months	1	11	Std. Mean Difference (IV, Fixed, 95% CI)	0.37 [-0.87, 1.62]
15.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Protein intake	2		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
16.1 at 3 months	2	60	Std. Mean Difference (IV, Fixed, 95% CI)	-0.50 [-1.01, 0.02]
16.2 at 4-6 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Transferrin	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
17.1 at 3 months	2		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.2 at 4-6 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
17.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
18 Fat mass	3	91	Std. Mean Difference (IV, Fixed, 95% CI)	0.21 [-0.22, 0.63]
18.1 at 3 months	1	36	Std. Mean Difference (IV, Fixed, 95% CI)	-0.26 [-0.92, 0.40]
18.2 at 4-6 months	2	55	Std. Mean Difference (IV, Fixed, 95% CI)	0.55 [-0.01, 1.11]
18.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Waist circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
19.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Mid-arm circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
20.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Mid-calf circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
21.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Mid-thigh circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
22.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Interleukin 6	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
23.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
24 Lymphocytes (x 10⁹ L)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
24.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Protein catabolic rate	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
25.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Physical activity	2	63	Std. Mean Difference (IV, Fixed, 95% CI)	-0.35 [-0.85, 0.15]
26.1 at 3 months	1	33	Std. Mean Difference (IV, Fixed, 95% CI)	-0.33 [-1.02, 0.36]
26.2 at 4-6 months	1	30	Std. Mean Difference (IV, Fixed, 95% CI)	-0.36 [-1.09, 0.36]
26.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
27 Depression	3		Std. Mean Difference (IV, Random, 95% CI)	Totals not selected
27.1 at 3 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
27.2 at 4-6 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
27.3 ≥ 7-12 months	1		Std. Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
28 Triglycerides	3	89	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.25, 0.33]
28.1 at 3 months	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.32, 0.32]
28.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
28.3 ≥ 7-12 months	2	52	Mean Difference (IV, Fixed, 95% CI)	0.22 [-0.43, 0.86]
29 Total cholesterol	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
29.1 at 3 months	2	133	Mean Difference (IV, Random, 95% CI)	0.29 [-0.26, 0.83]
29.2 at 4-6 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
29.3 ≥ 7-12 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
30 HDL cholesterol	3	155	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.22, 0.01]
30.1 at 3 months	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.33, 0.19]
30.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
30.3 ≥ 7-12 months	2	118	Mean Difference (IV, Fixed, 95% CI)	-0.11 [-0.24, 0.02]
31 Type I muscle fibre area	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
31.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
31.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32 Mid-thigh muscle area	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
32.1 at 3 months	3	111	Mean Difference (IV, Fixed, 95% CI)	-3.22 [-9.67, 3.24]
32.2 at 4-6 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
32.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
33 Thigh muscle attenuation (Hounsfield units)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
33.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
33.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
33.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34 HRV index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
34.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
34.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35 Mean cardiac R-R interval	2	119	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.09, -0.02]
35.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
35.2 at 4-6 months	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.10, -0.00]
35.3 ≥ 7-12 months	1	59	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.12, -0.02]
36 SDNN	2	119	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.03, -0.01]

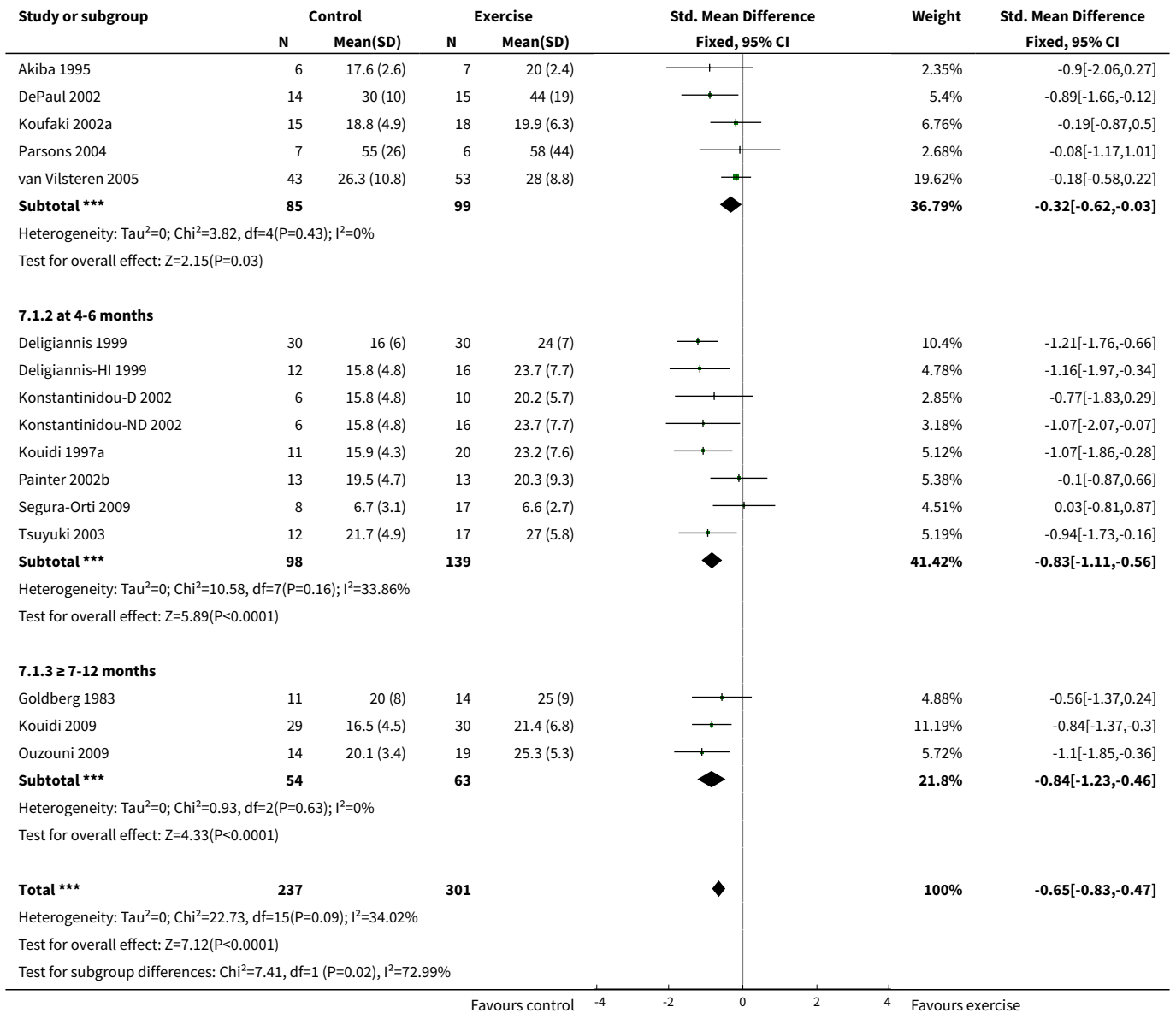
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
36.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
36.2 at 4-6 months	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.04, -0.00]
36.3 ≥ 7-12 months	1	59	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.03, -0.01]
37 Arrhythmias: Low class > II (no)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
37.1 at 3 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
37.2 at 4-6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
37.3 ≥ 7-12 months	0		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
38 Left ventricular inter- nal dimension at end- diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
38.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
38.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
38.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
39 Left ventricular inter- nal dimension at end- systole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
39.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
39.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
39.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
40 Intraventricular sep- tal thickness at end-di- astole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
40.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
40.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
40.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
41 Left ventricular pos- terior wall thickness at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
41.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
41.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
41.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
42 Left ventricular mass	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
42.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
42.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
42.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
43 Left ventricular mass index	2	87	Mean Difference (IV, Fixed, 95% CI)	-1.62 [-7.16, 3.93]
43.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
43.2 at 4-6 months	1	28	Mean Difference (IV, Fixed, 95% CI)	-11.0 [-41.75, 19.75]
43.3 ≥ 7-12 months	1	59	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-6.94, 4.34]
44 Fasting plasma glucose	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
44.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
44.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
44.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
45 Fasting plasma insulin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
45.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
45.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
45.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46 Glucose disappearance	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
46.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
46.3 ≥ 7-12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

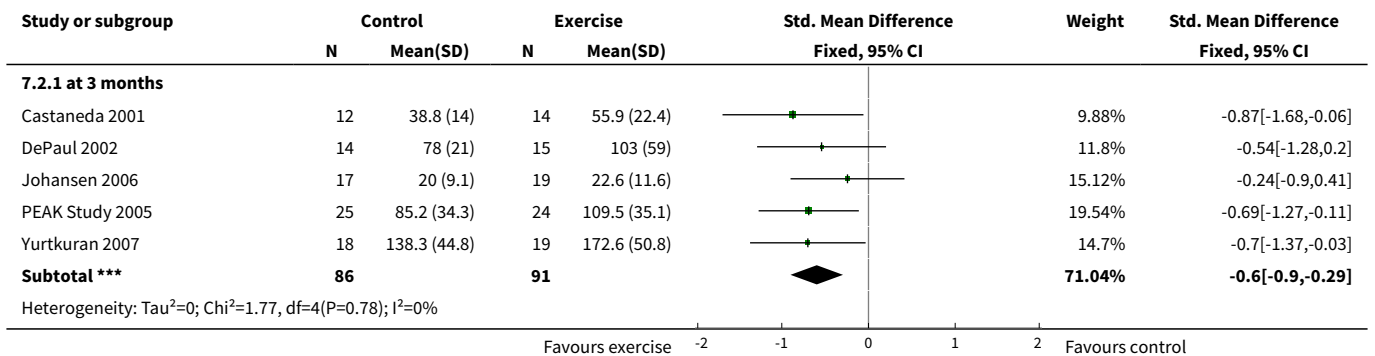
Analysis 7.1. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.

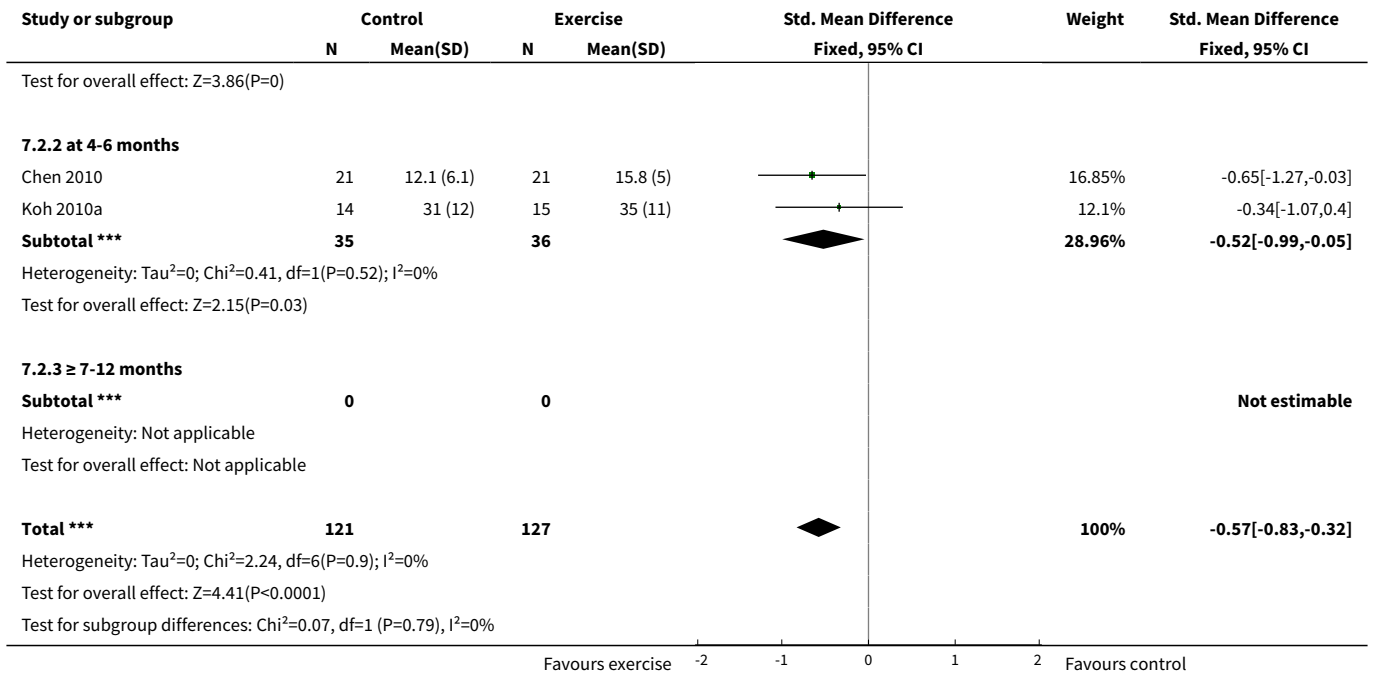
Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Weight	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
7.1.1 at 3 months							

Favours control -4 -2 0 2 4 Favours exercise

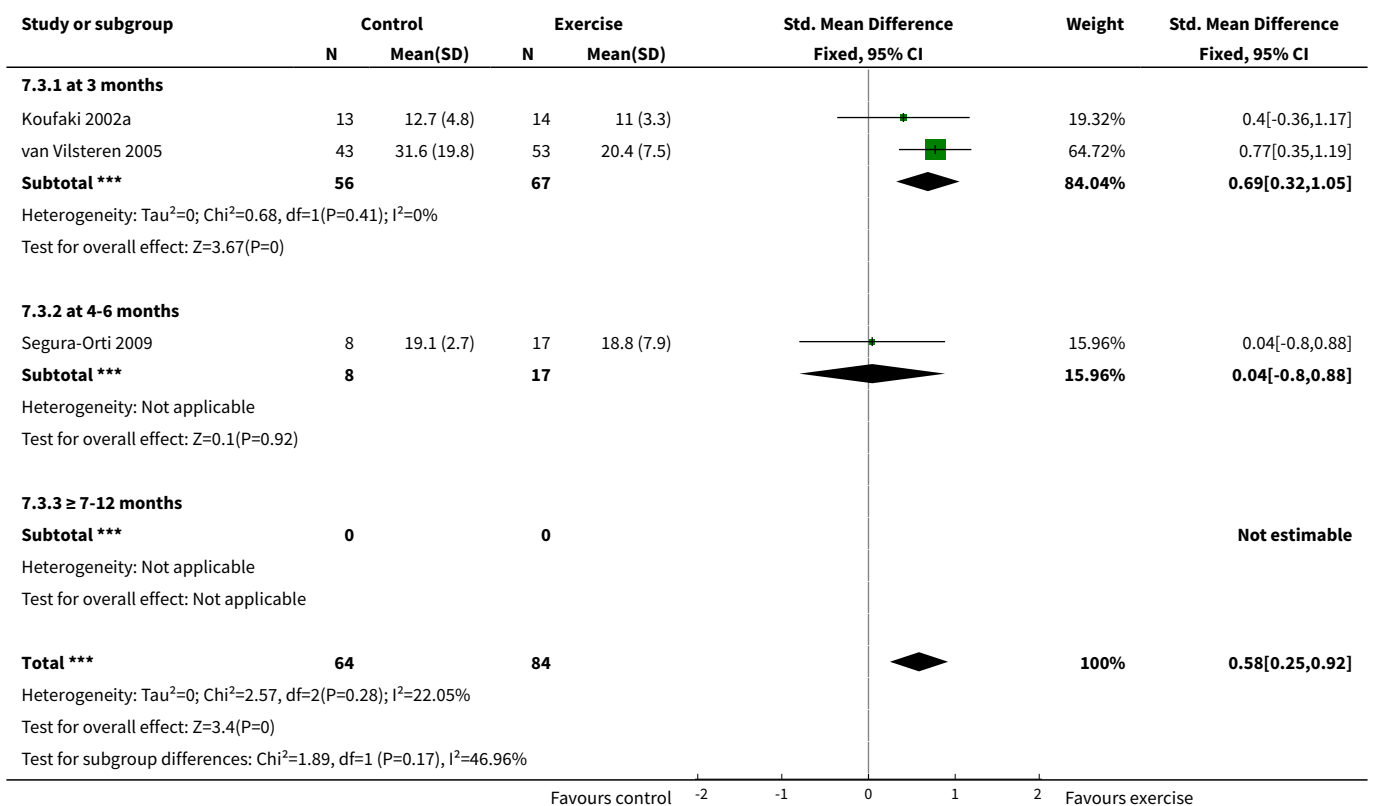


Analysis 7.2. Comparison 7 Supervised exercise versus control (no exercise/ placebo exercise), Outcome 2 Muscular strength (high value = improved).

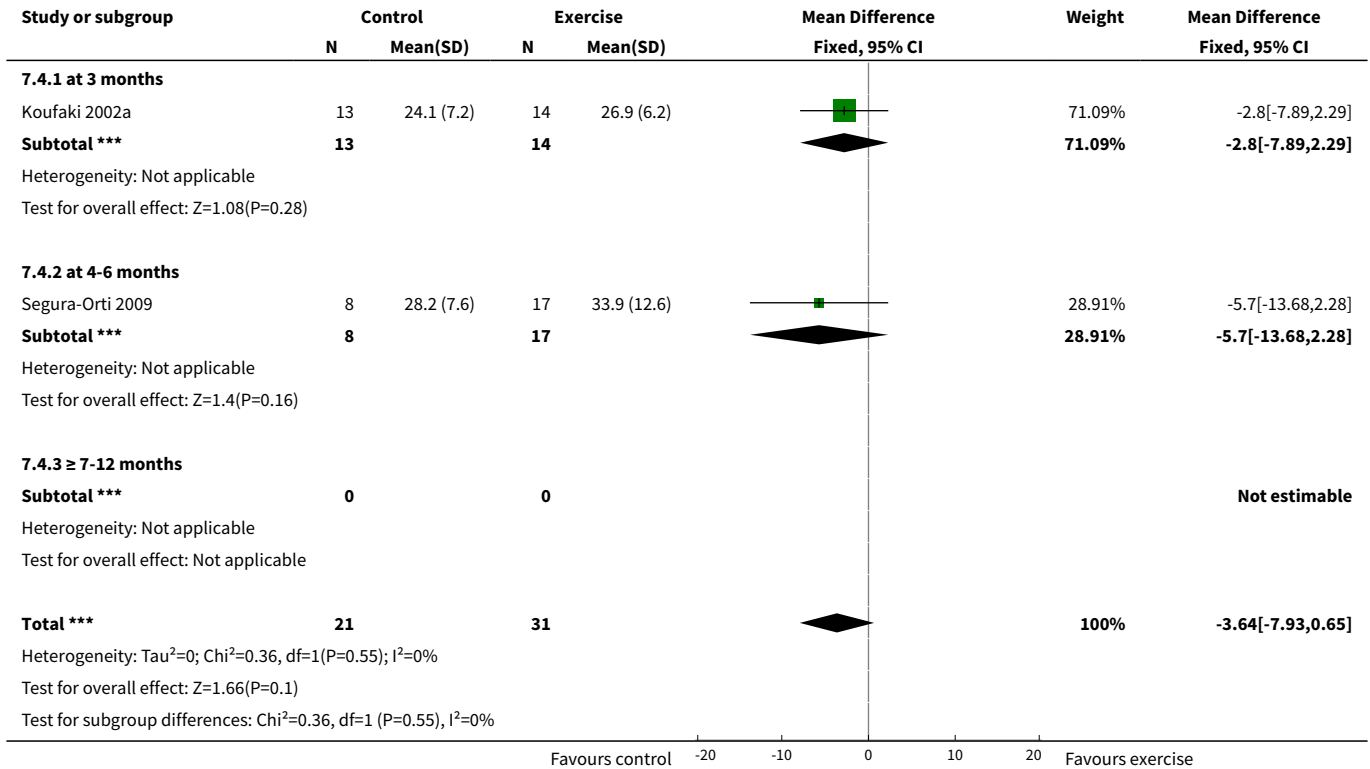




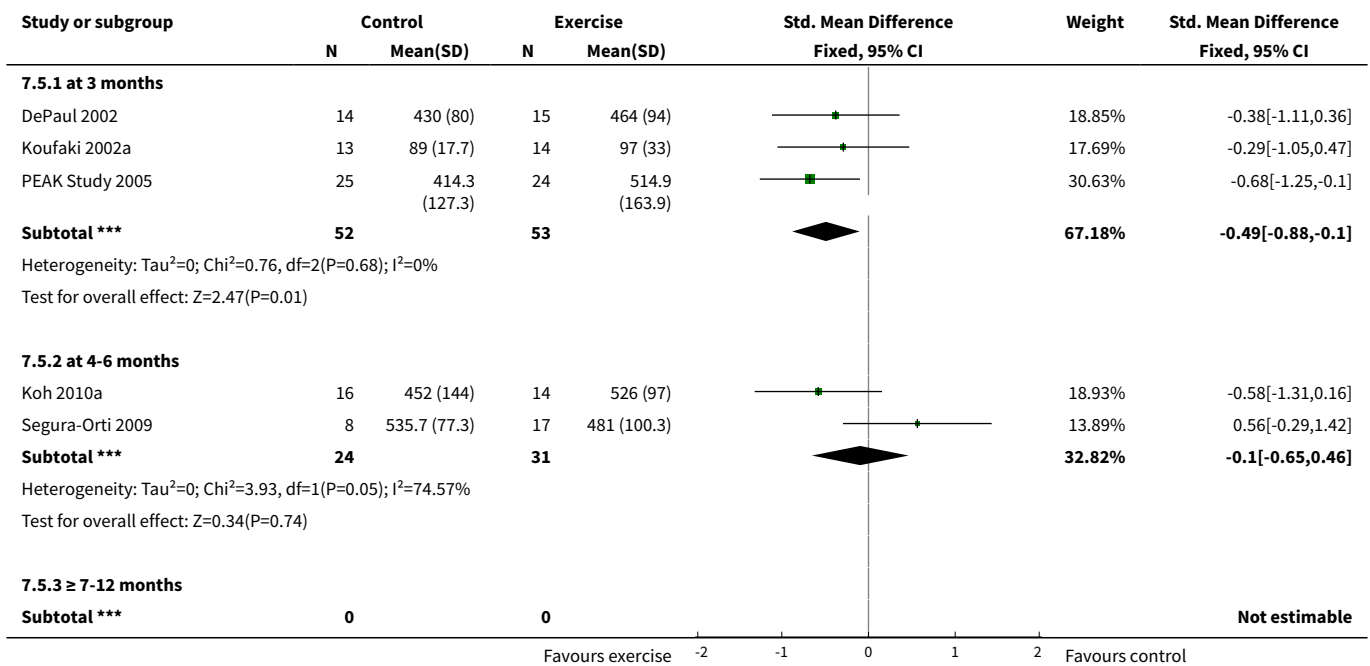
Analysis 7.3. Comparison 7 Supervised exercise versus control (no exercise/ placebo exercise), Outcome 3 Muscular strength (low value = improved).

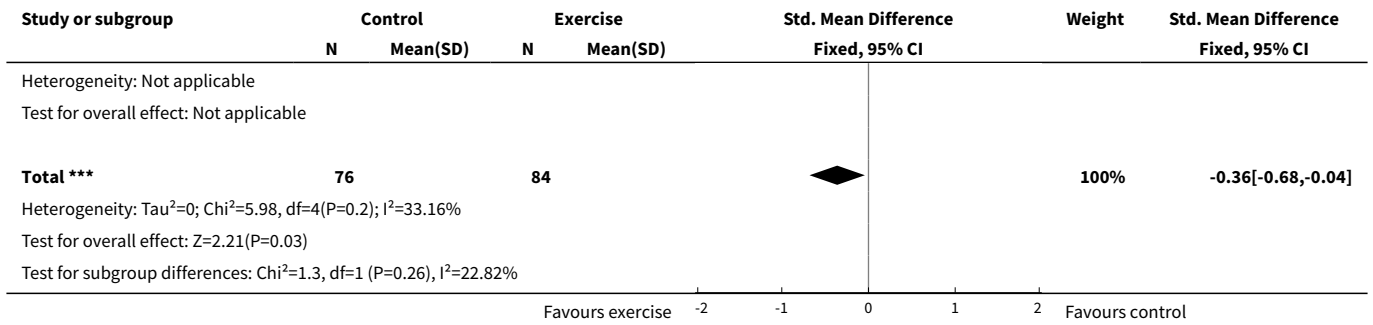


Analysis 7.4. Comparison 7 Supervised exercise versus control (no exercise/ placebo exercise), Outcome 4 Muscular endurance quadriceps: Sit-to-Stand-to-Sit-60.



Analysis 7.5. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 5 Walking capacity.

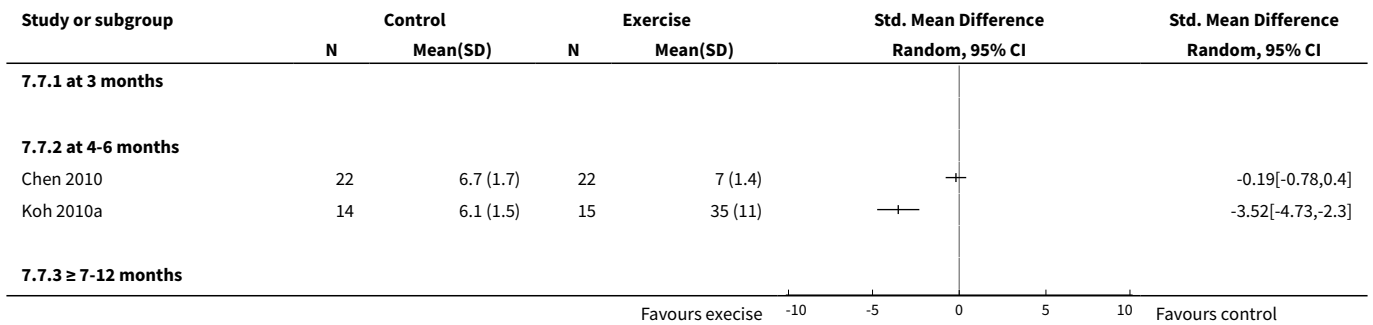




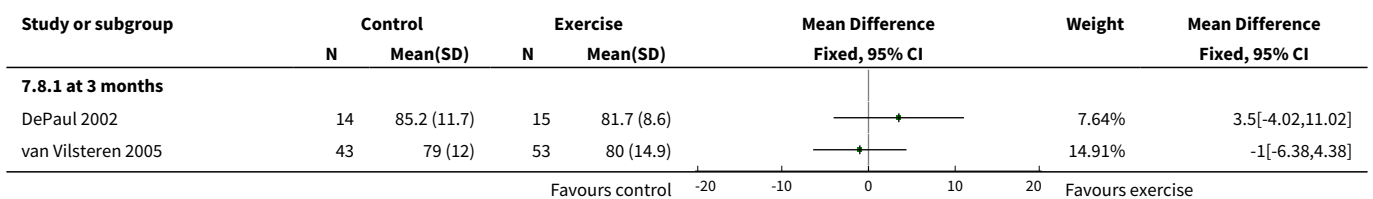
Analysis 7.6. Comparison 7 Supervised exercise versus control (no exercise/ placebo exercise), Outcome 6 Stair climbing capacity: stair climb test (22 steps).

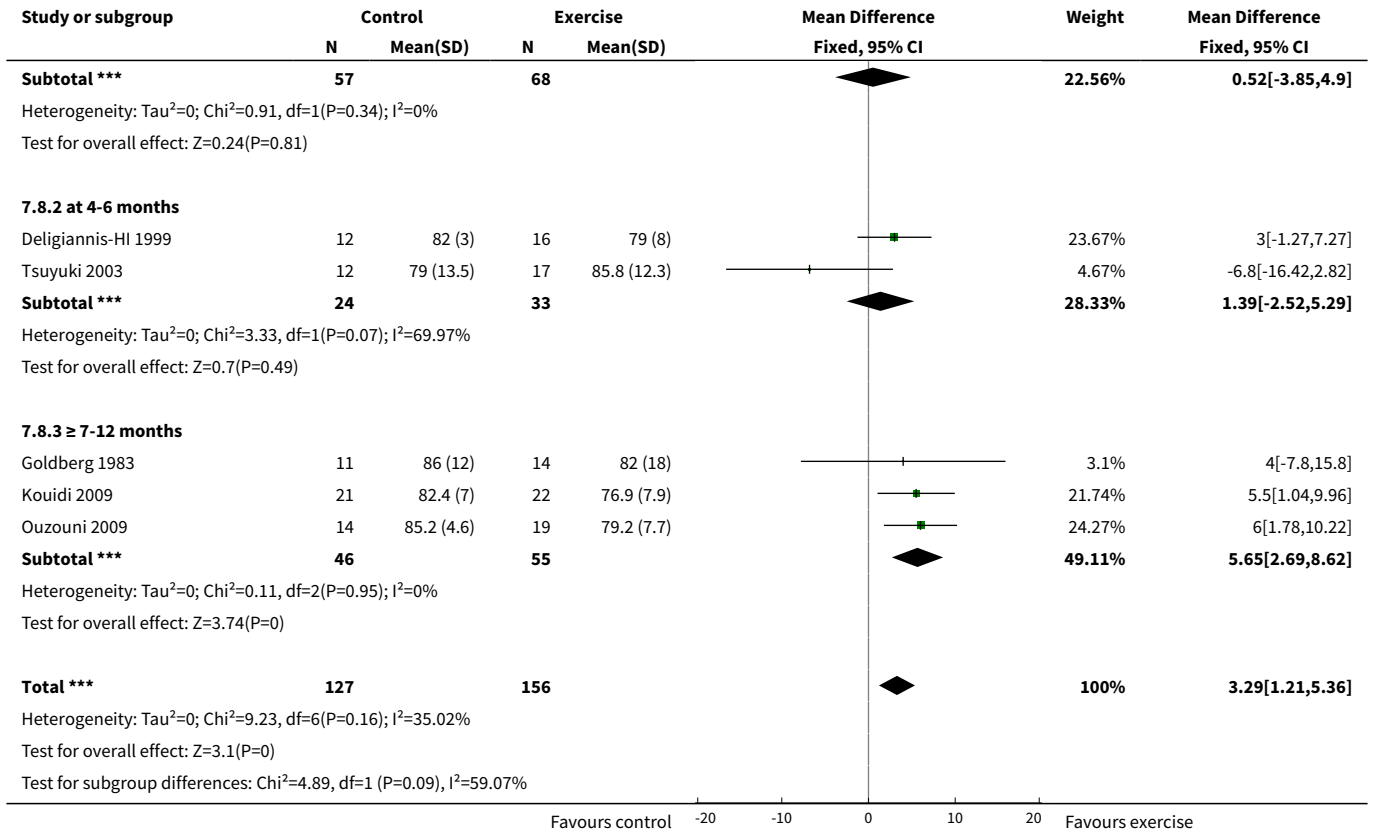


Analysis 7.7. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 7 ADL capacity.

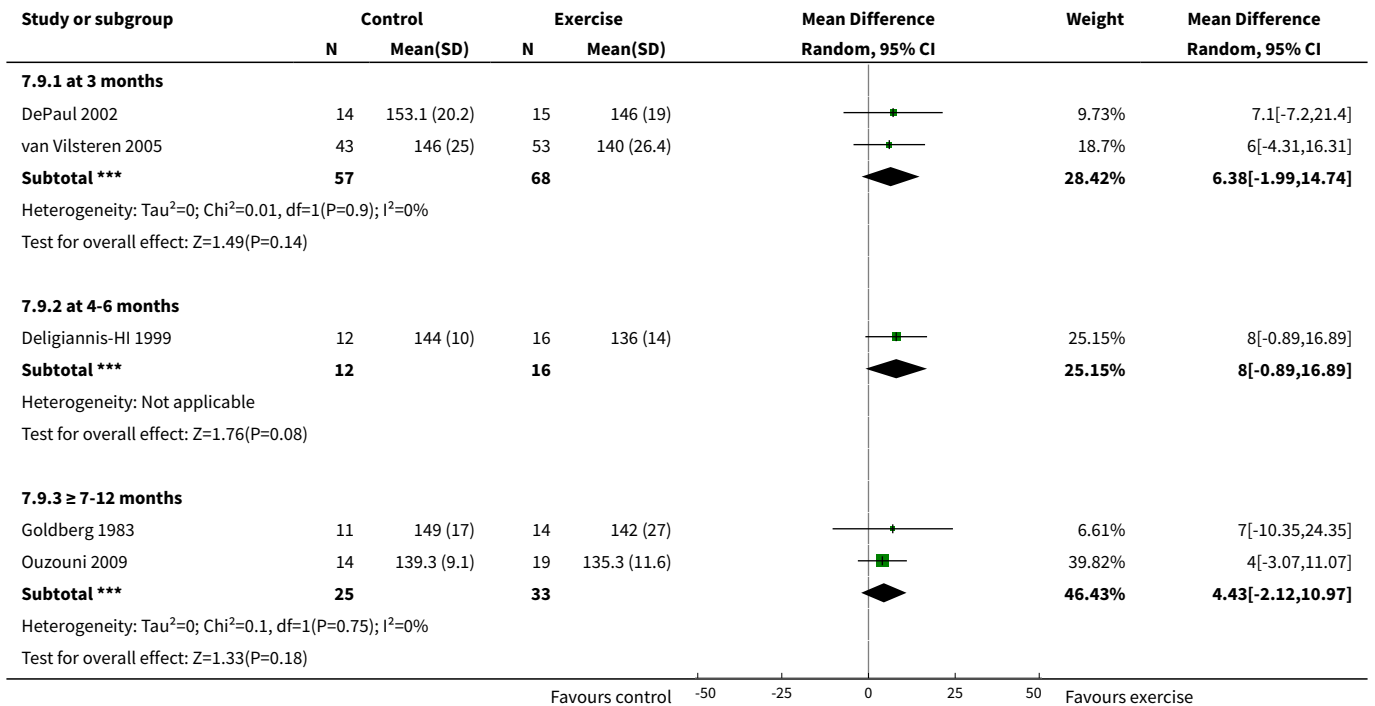


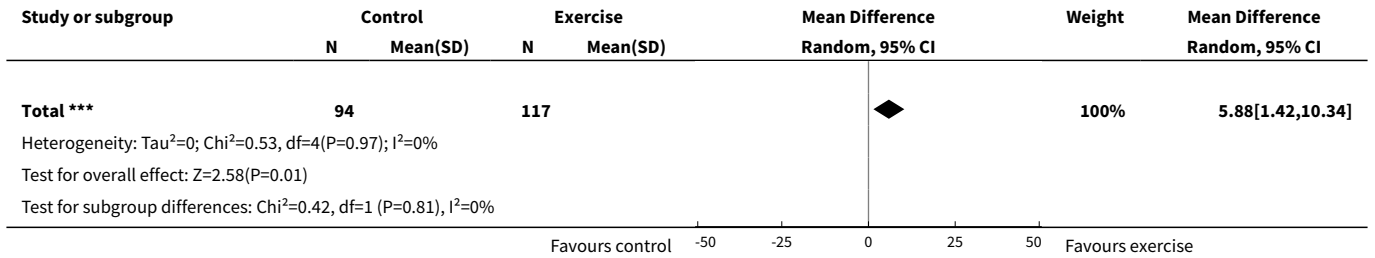
Analysis 7.8. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 8 Diastolic blood pressure: resting.



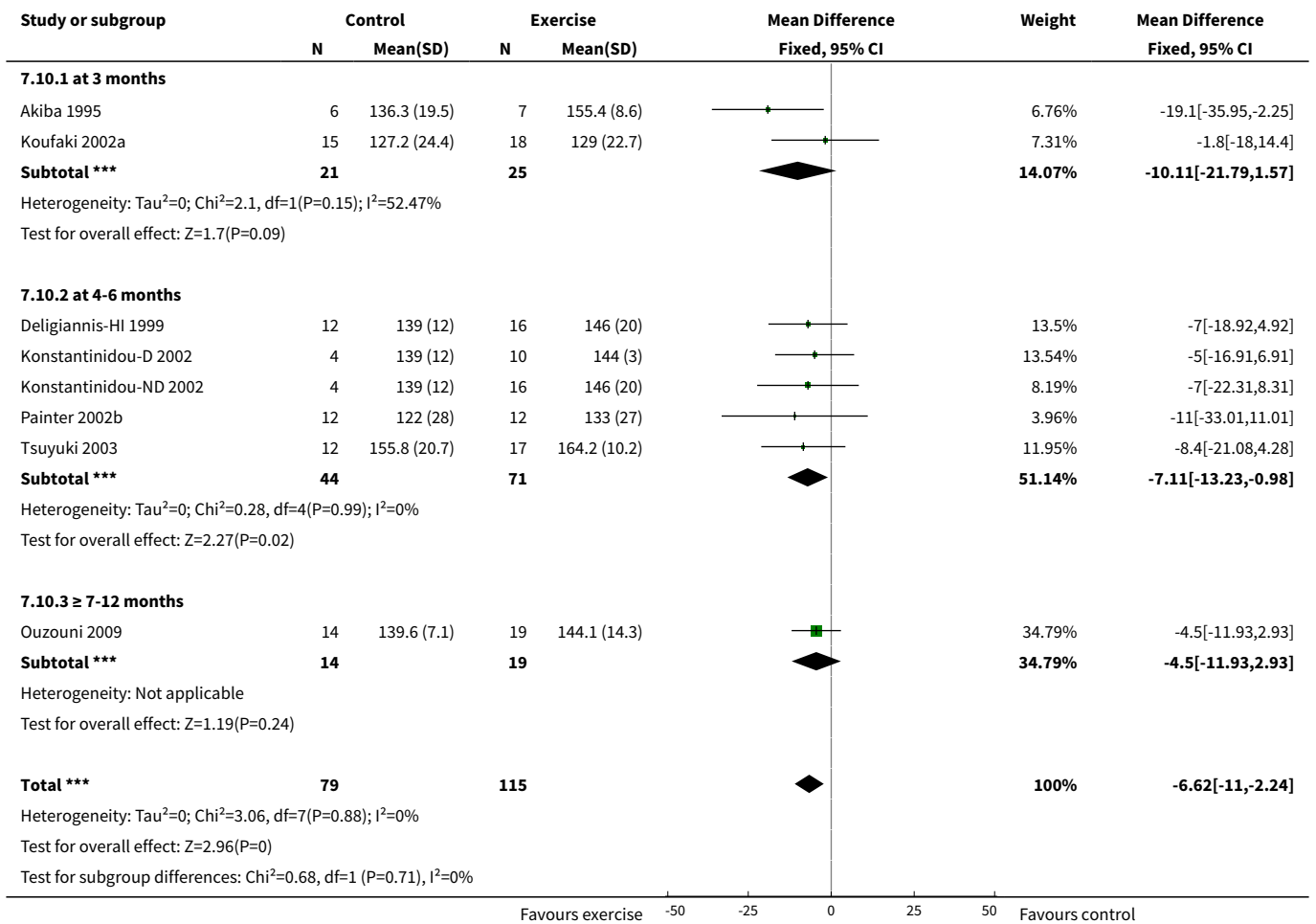


Analysis 7.9. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 9 Systolic blood pressure: resting.

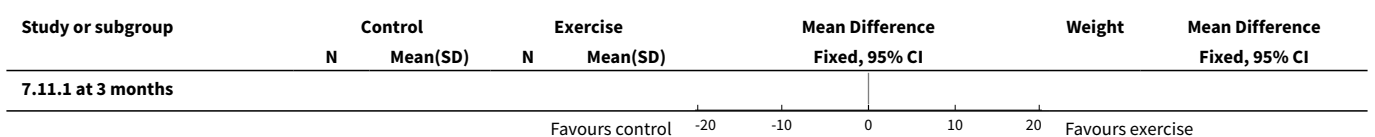


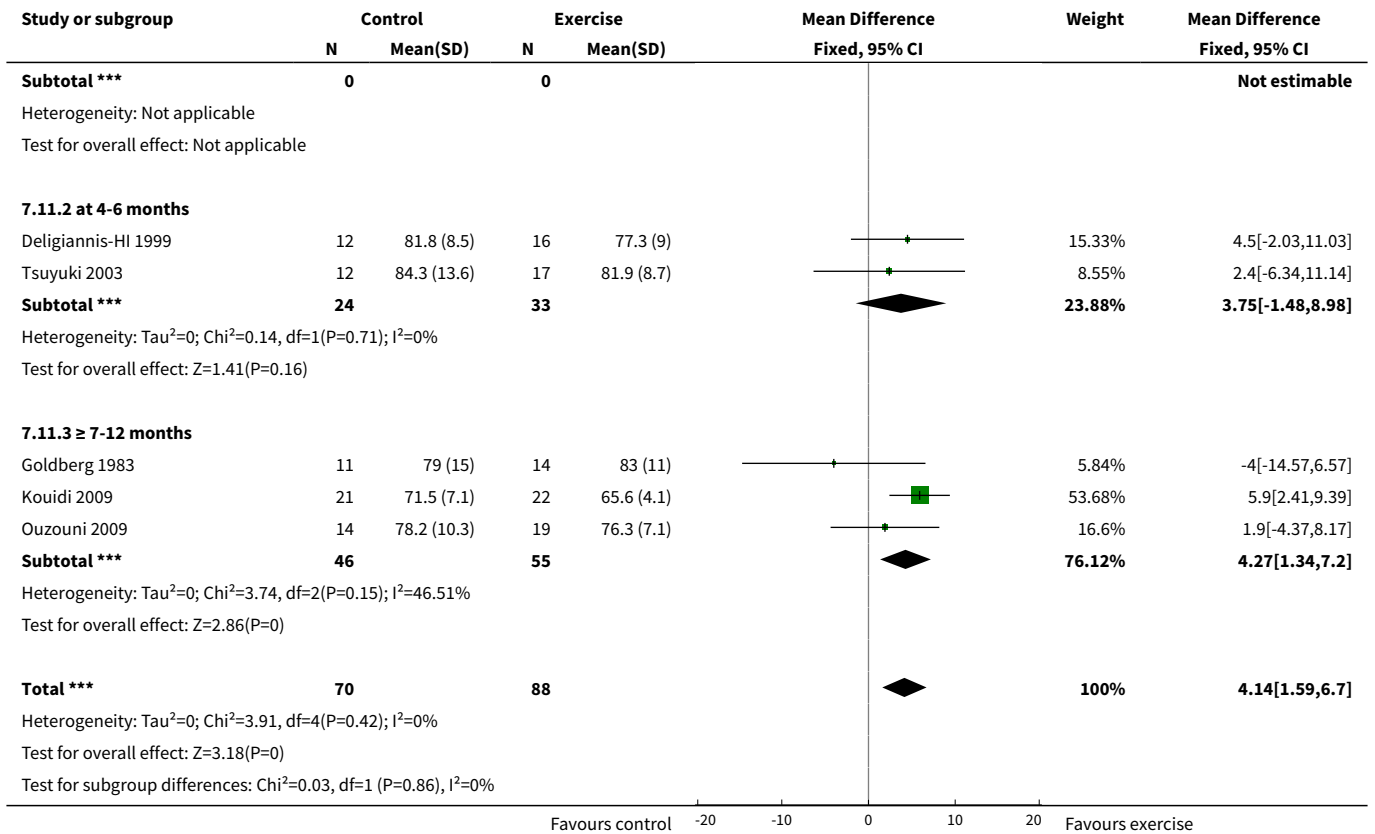


Analysis 7.10. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 10 Heart rate: maximum.

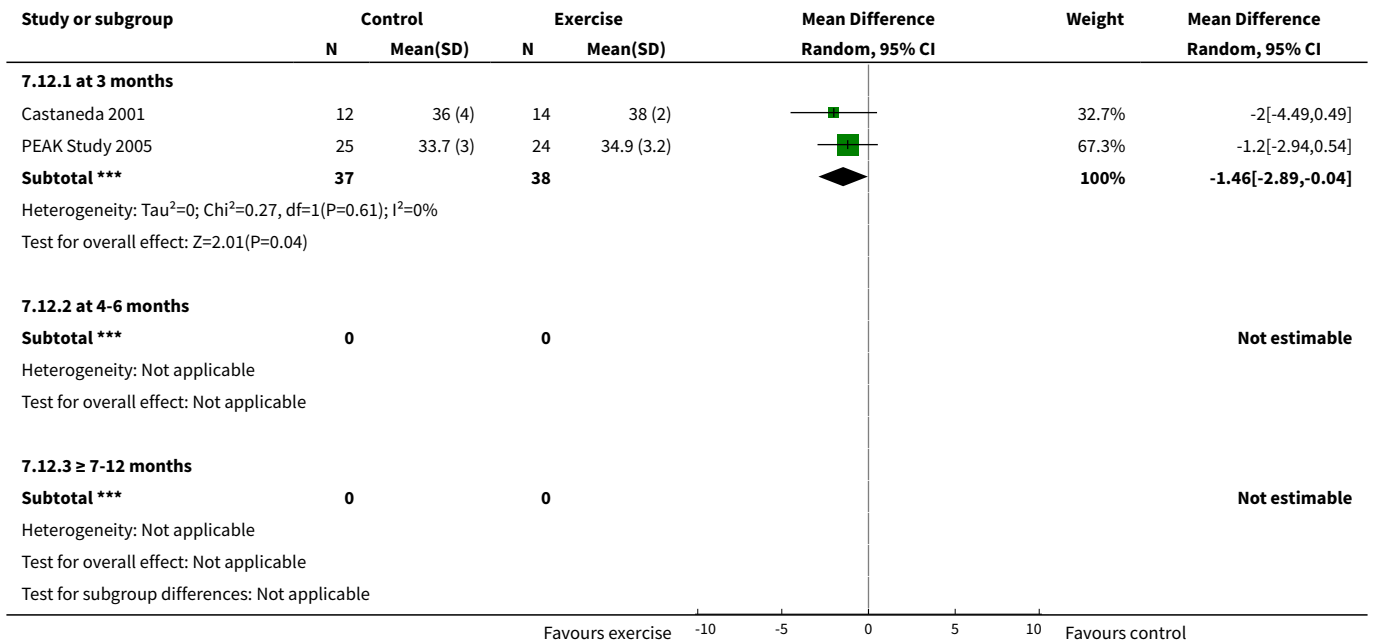


Analysis 7.11. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 11 Heart rate: resting.

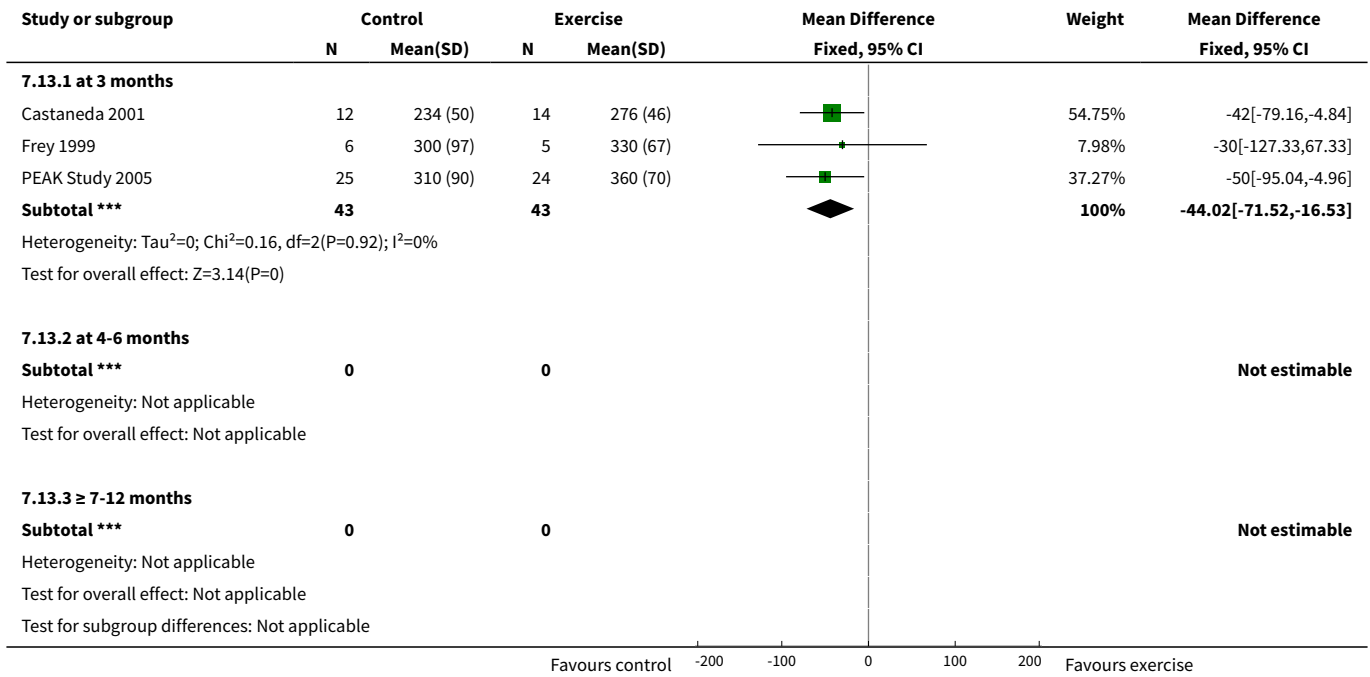




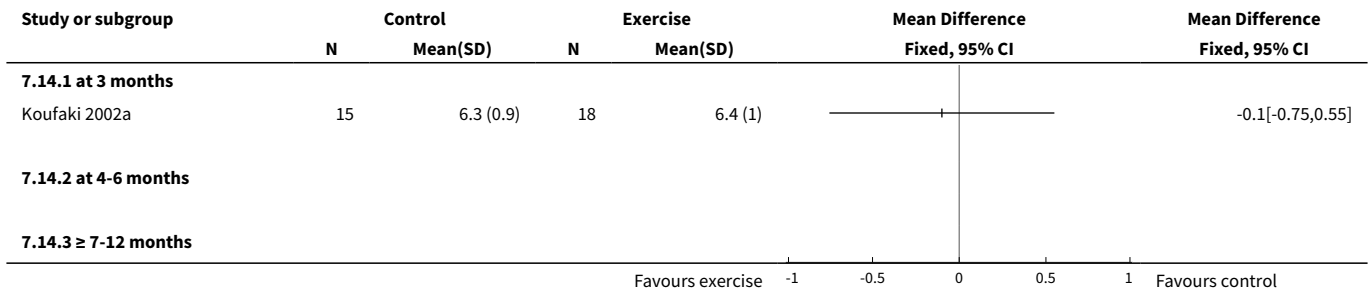
Analysis 7.12. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 12 Albumin.



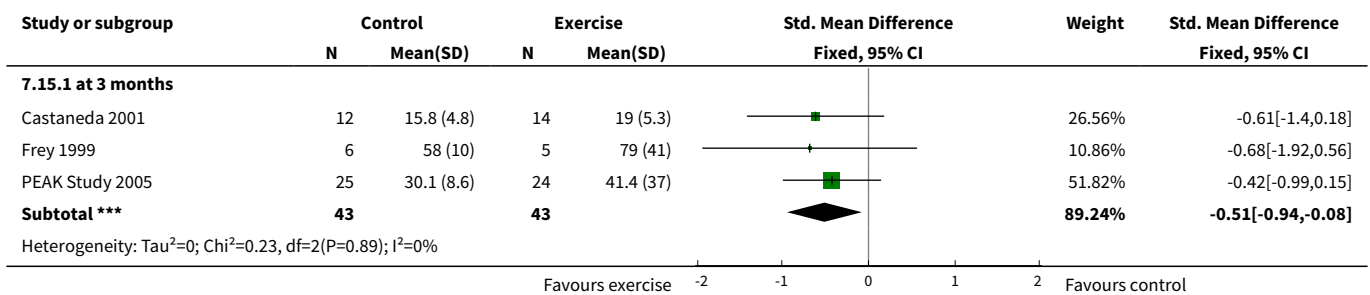
Analysis 7.13. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 13 Pre-albumin.

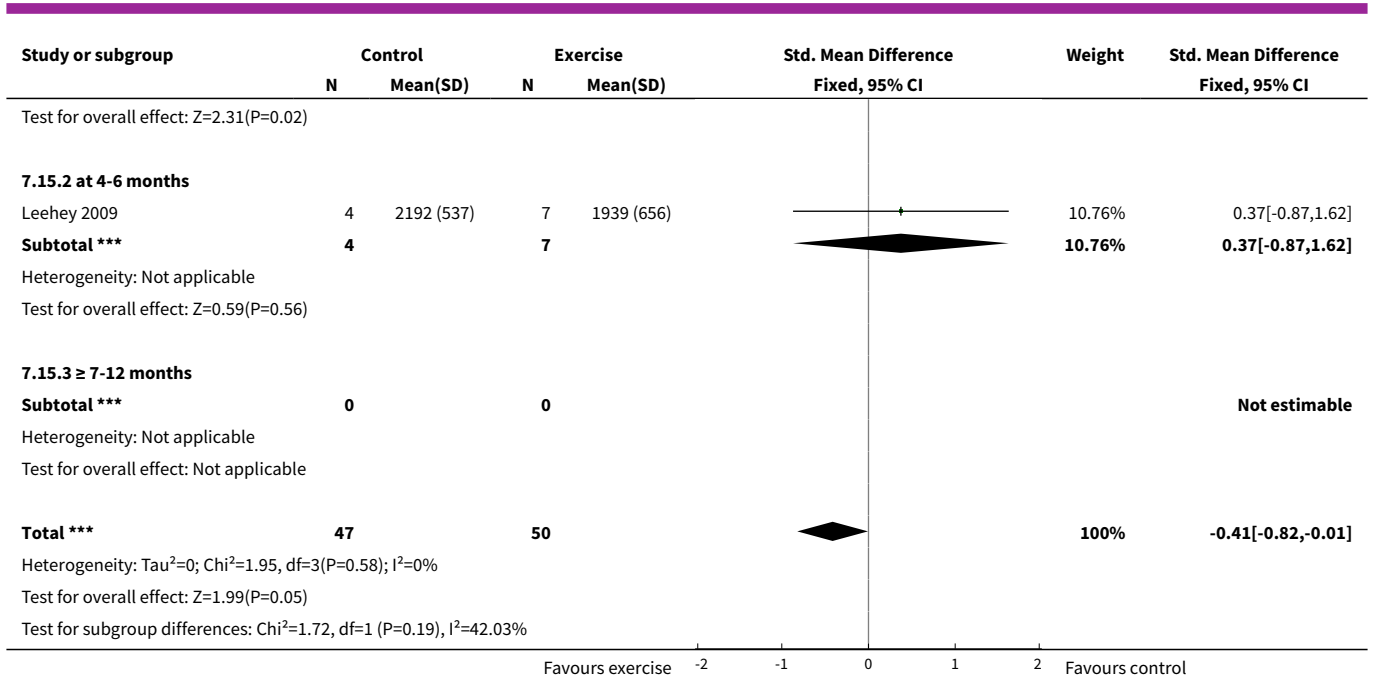


Analysis 7.14. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 14 SGA.

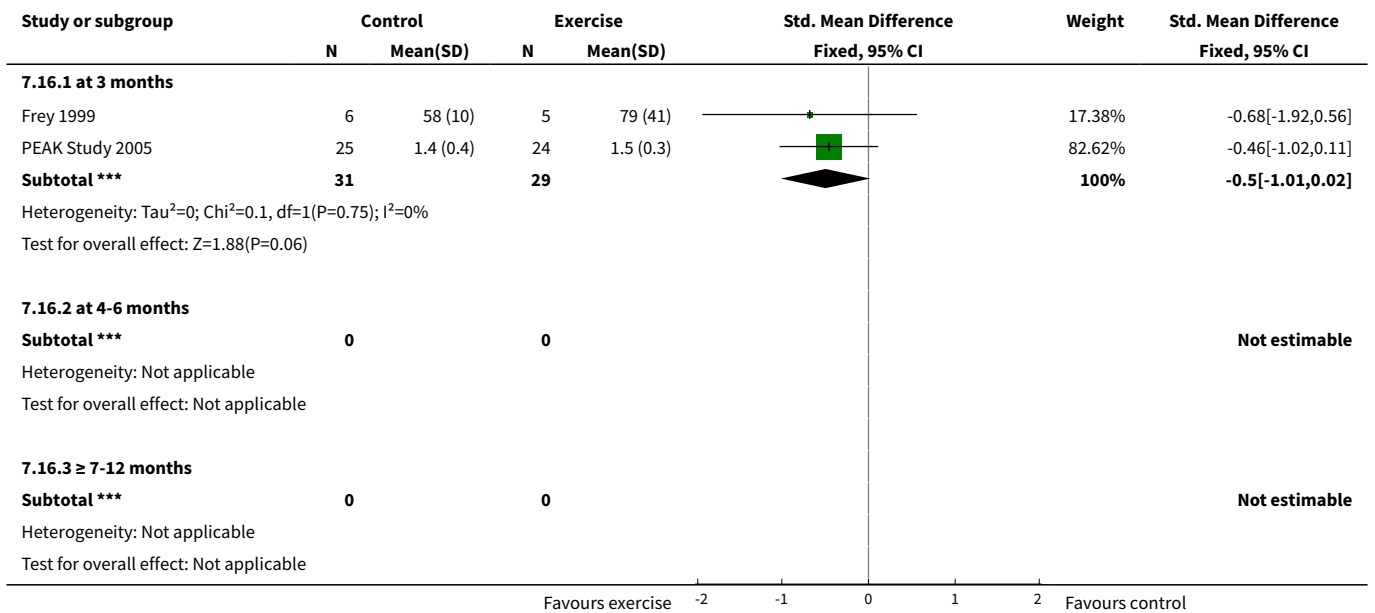


Analysis 7.15. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 15 Energy intake.

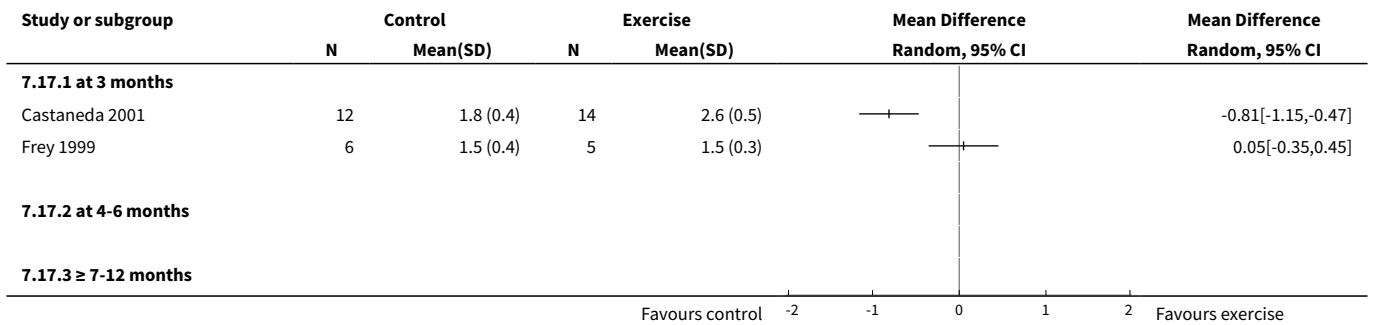




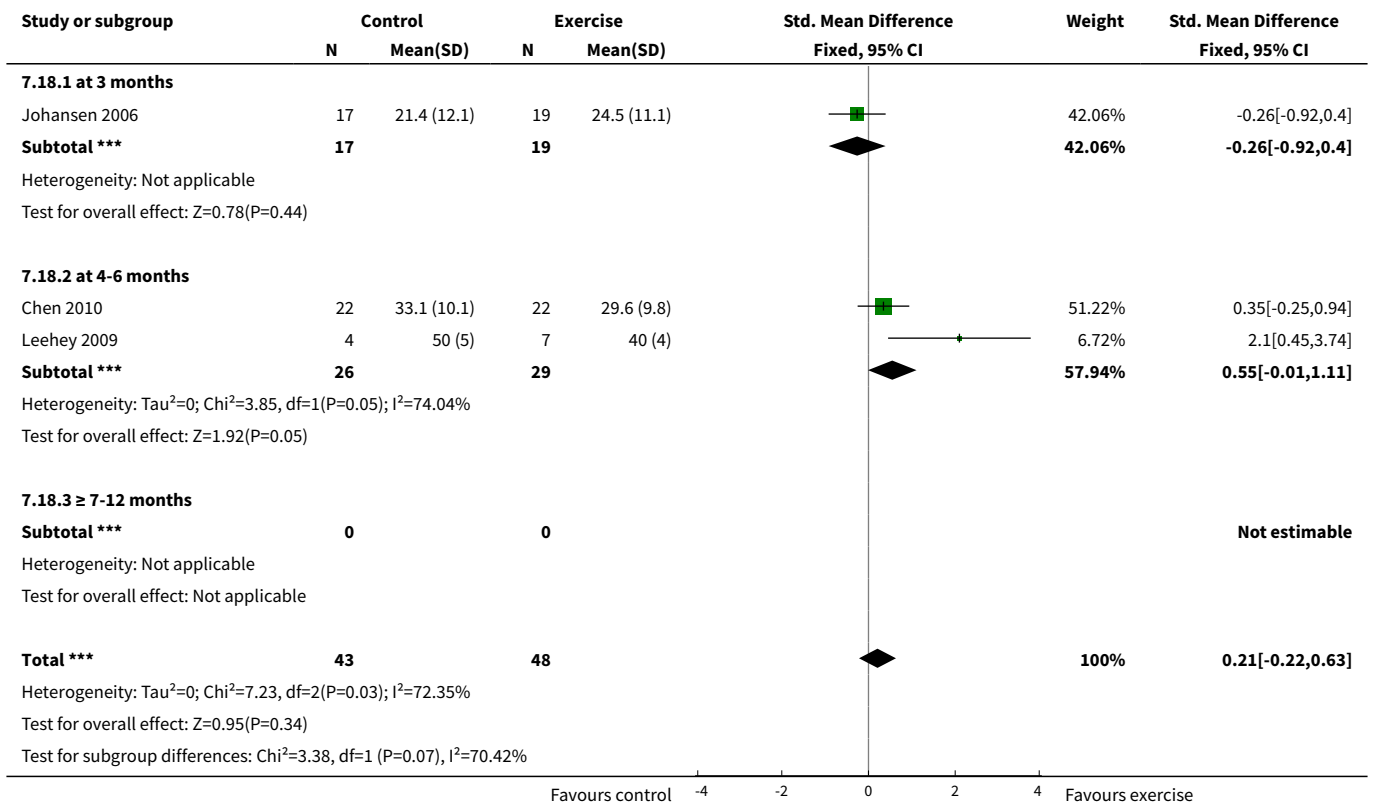
Analysis 7.16. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 16 Protein intake.



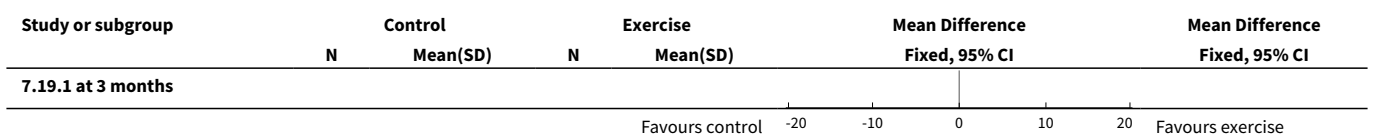
Analysis 7.17. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 17 Transferrin.

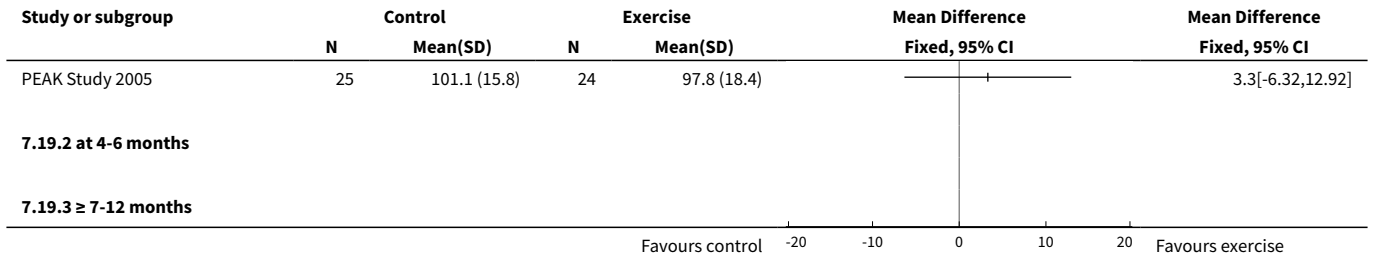


Analysis 7.18. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 18 Fat mass.

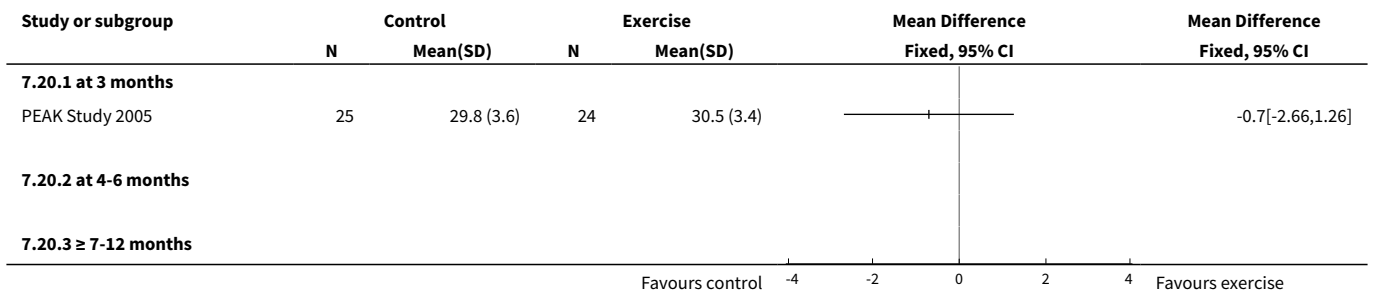


Analysis 7.19. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 19 Waist circumference.

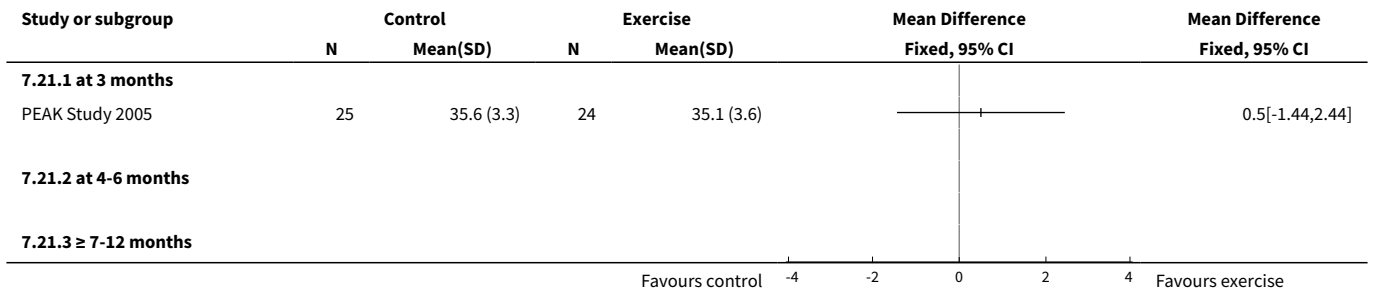




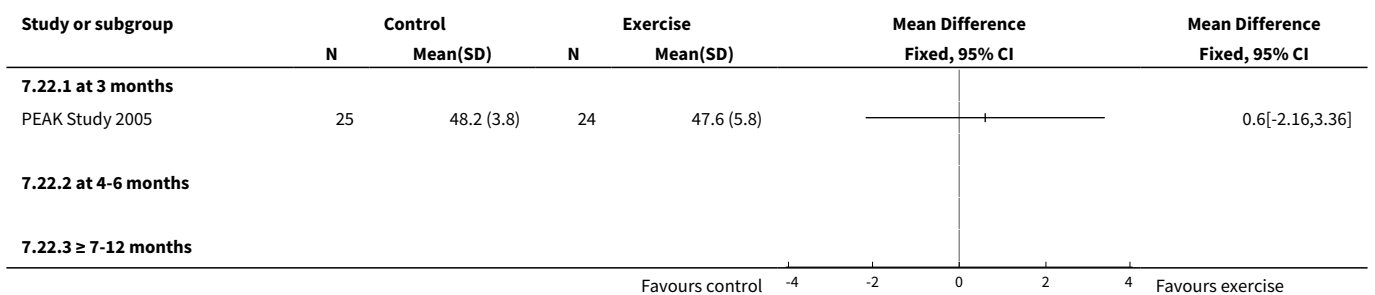
Analysis 7.20. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 20 Mid-arm circumference.



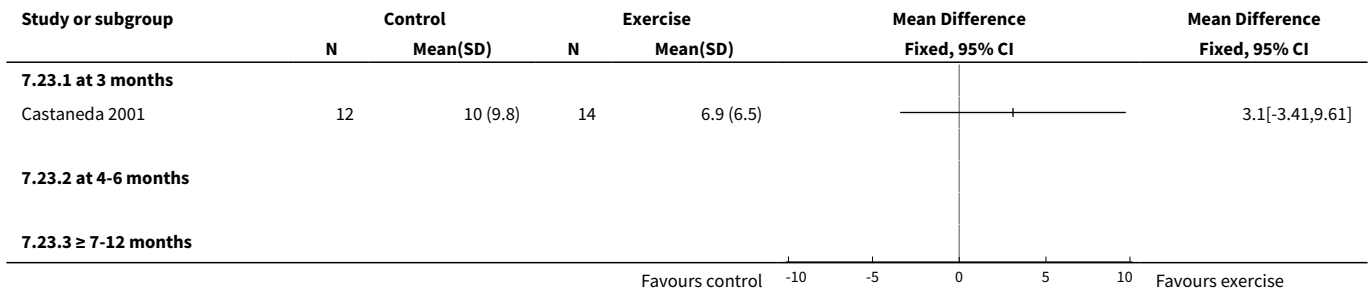
Analysis 7.21. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 21 Mid-calf circumference.



Analysis 7.22. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 22 Mid-thigh circumference.



Analysis 7.23. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 23 Interleukin 6.



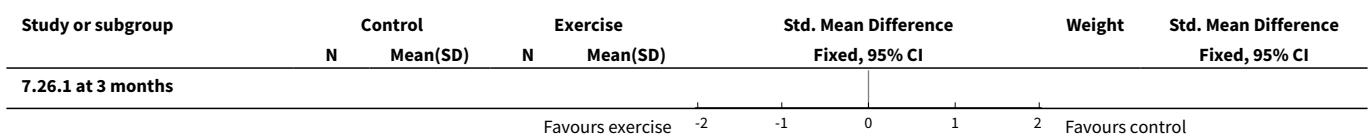
Analysis 7.24. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 24 Lymphocytes (x 10⁹ L).

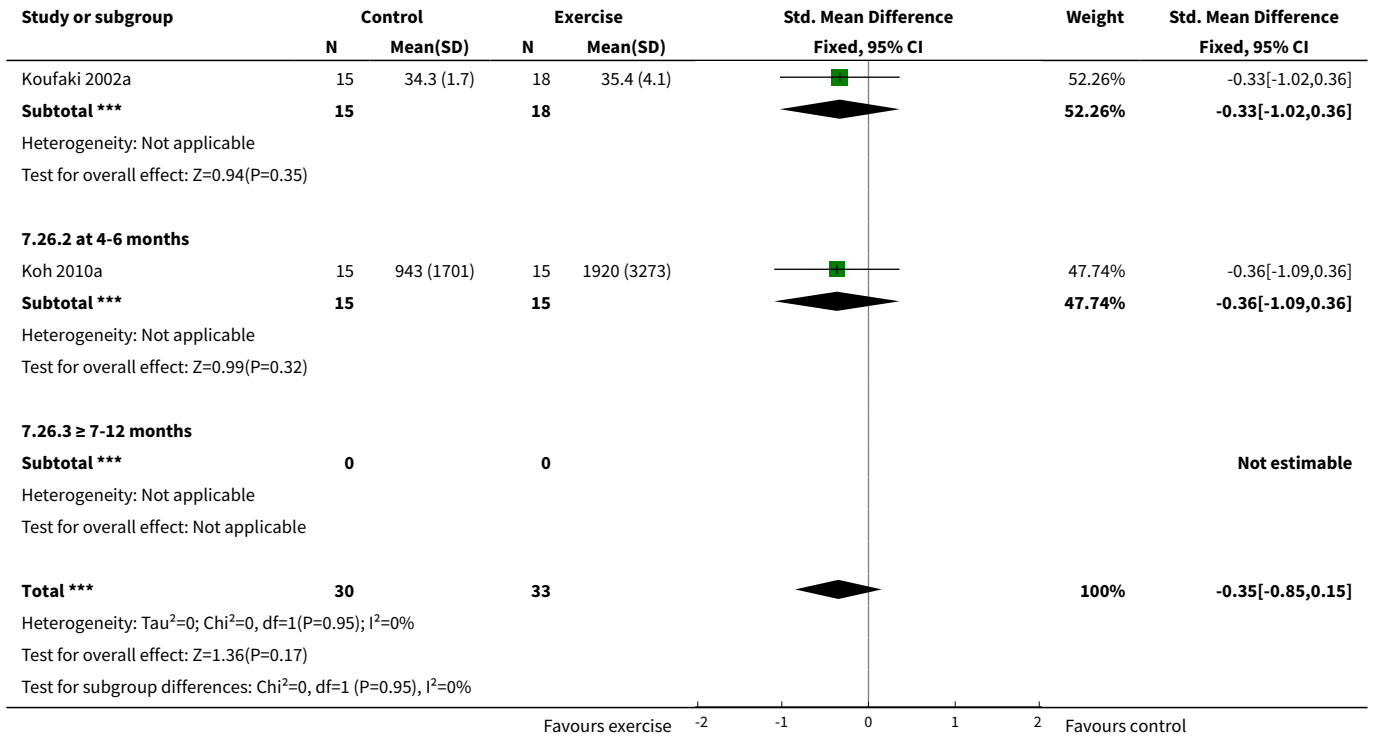


Analysis 7.25. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 25 Protein catabolic rate.

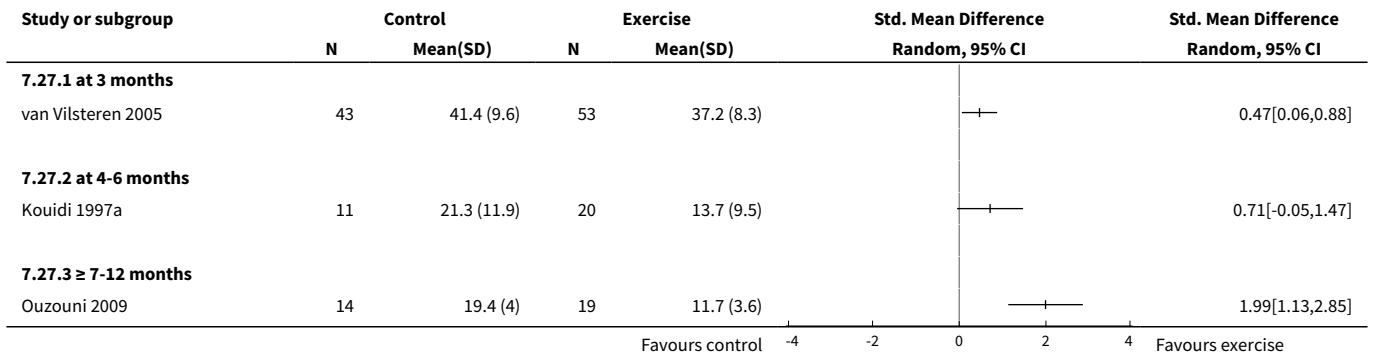


Analysis 7.26. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 26 Physical activity.

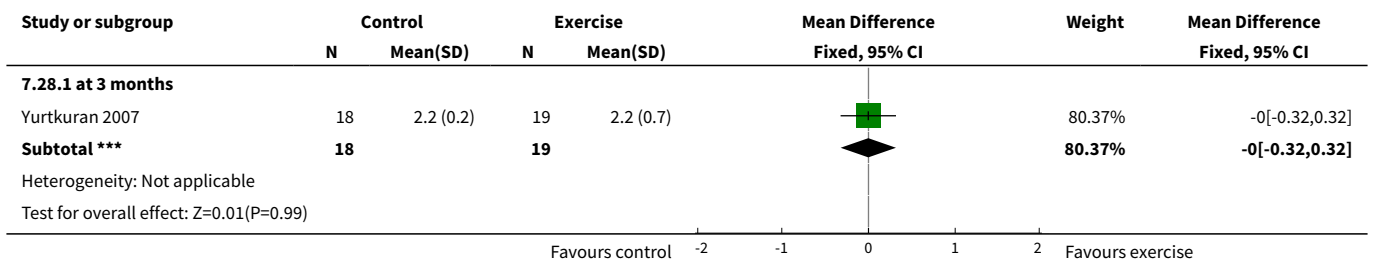


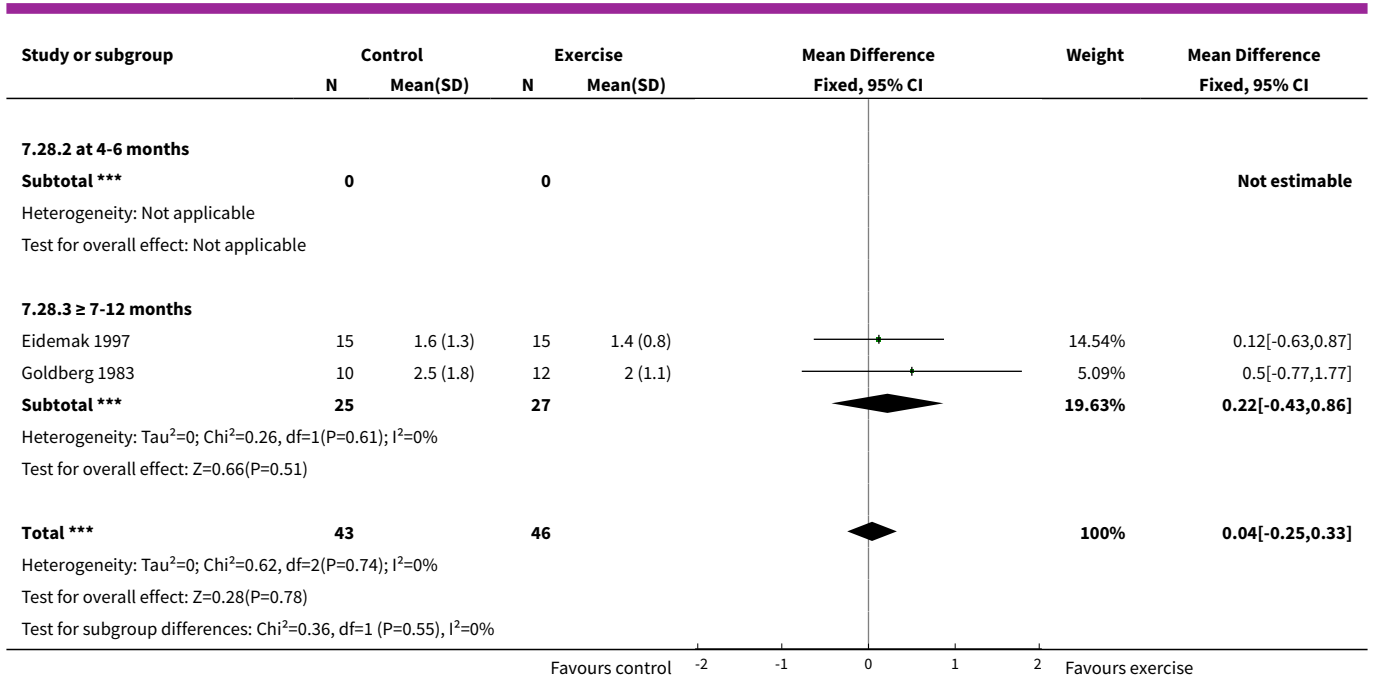


Analysis 7.27. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 27 Depression.

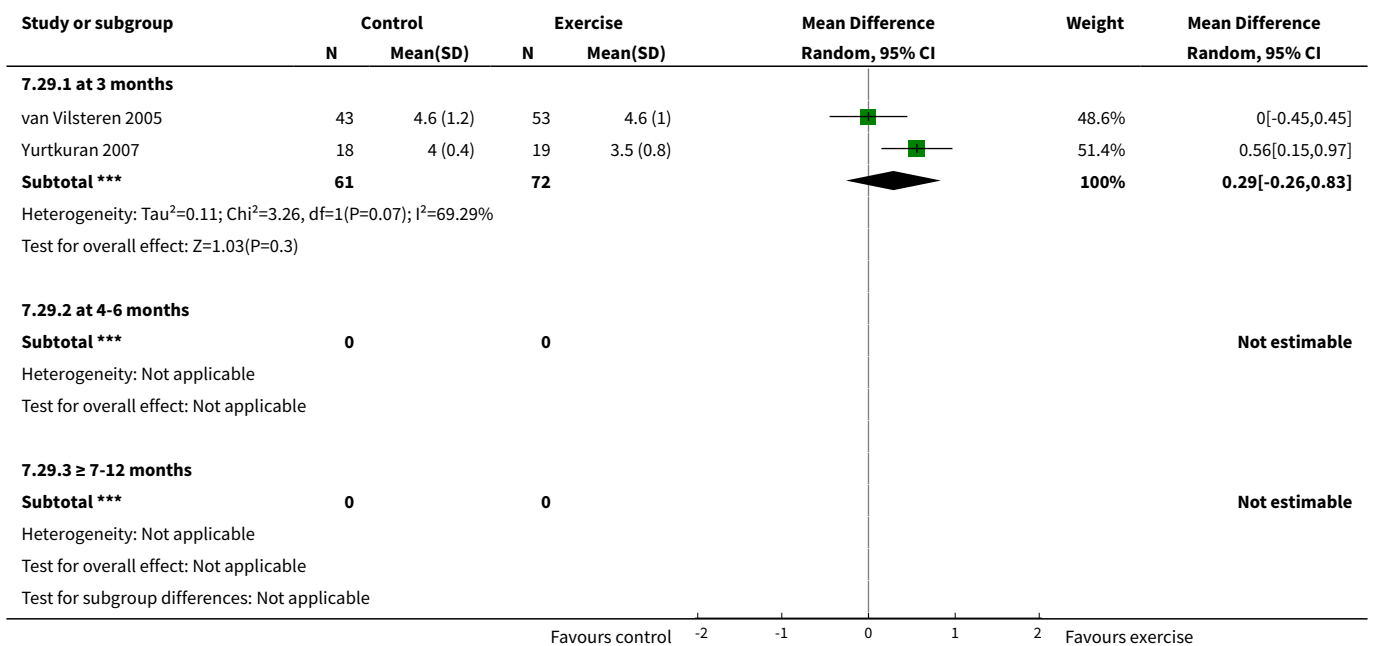


Analysis 7.28. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 28 Triglycerides.

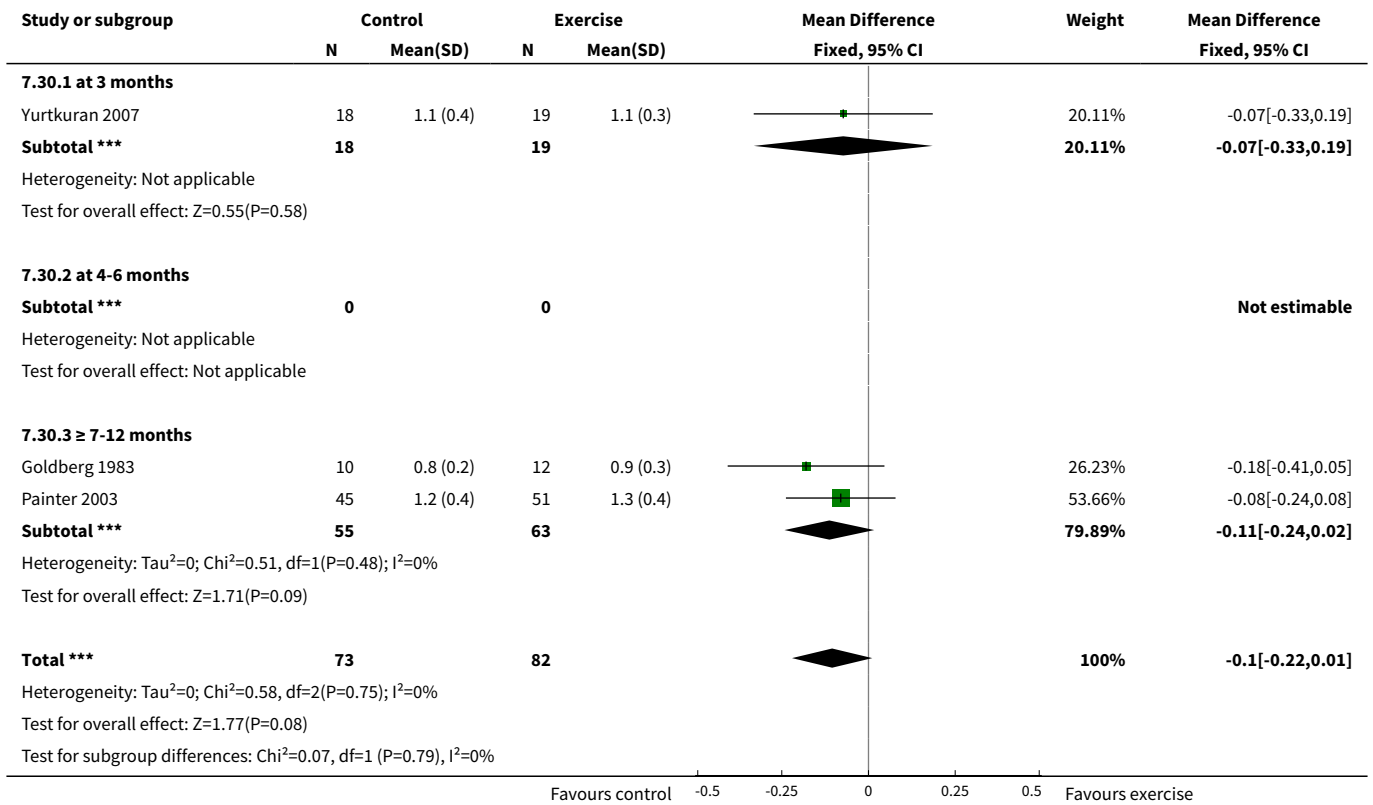




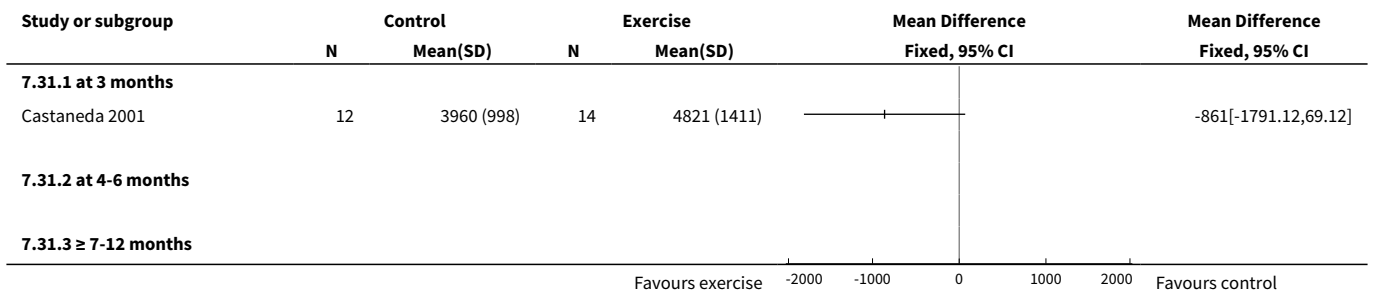
Analysis 7.29. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 29 Total cholesterol.



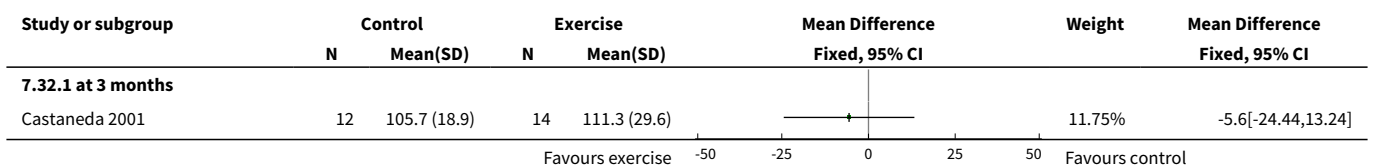
Analysis 7.30. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 30 HDL cholesterol.

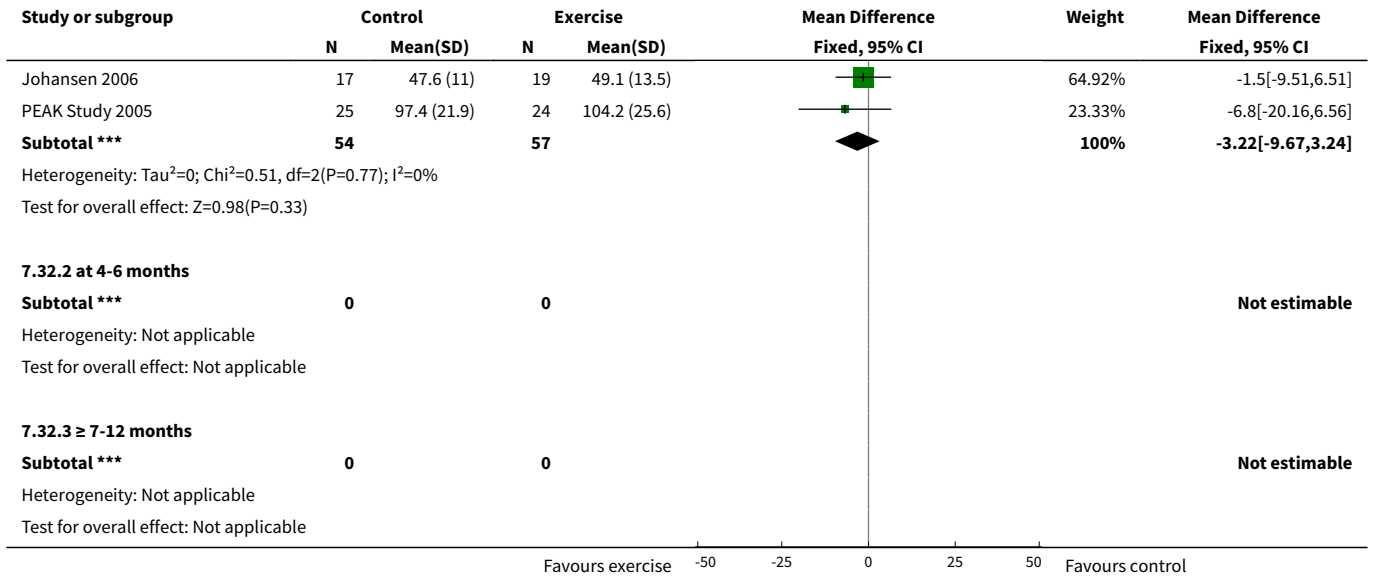


Analysis 7.31. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 31 Type I muscle fibre area.

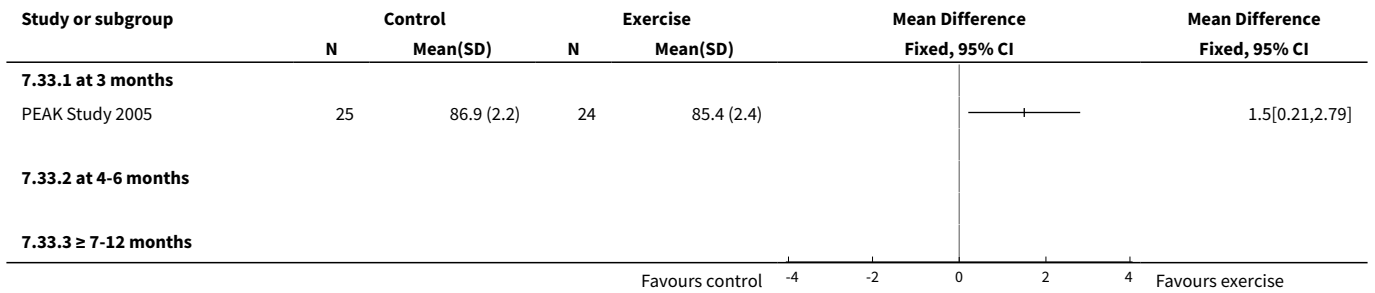


Analysis 7.32. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 32 Mid-thigh muscle area.





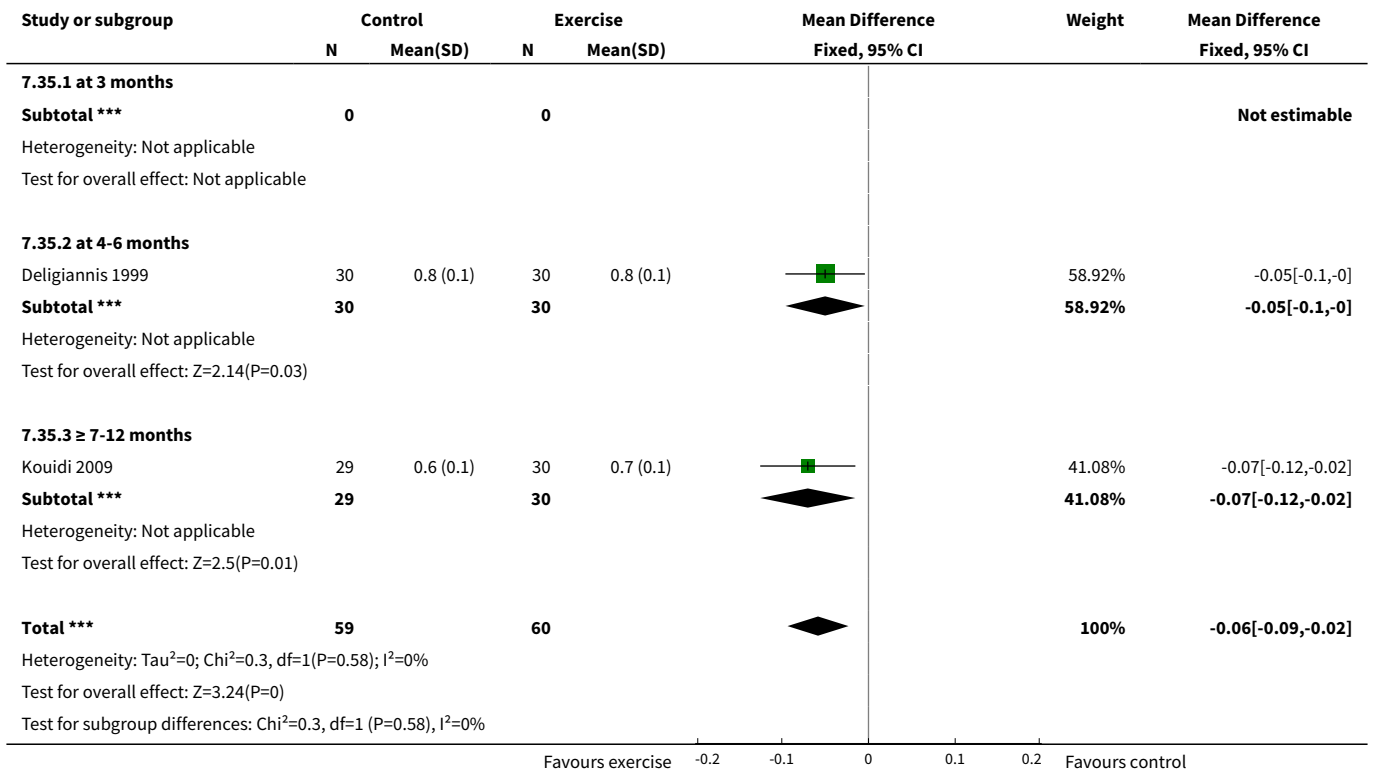
Analysis 7.33. Comparison 7 Supervised exercise versus control (no exercise/ placebo exercise), Outcome 33 Thigh muscle attenuation (Hounsfield units).



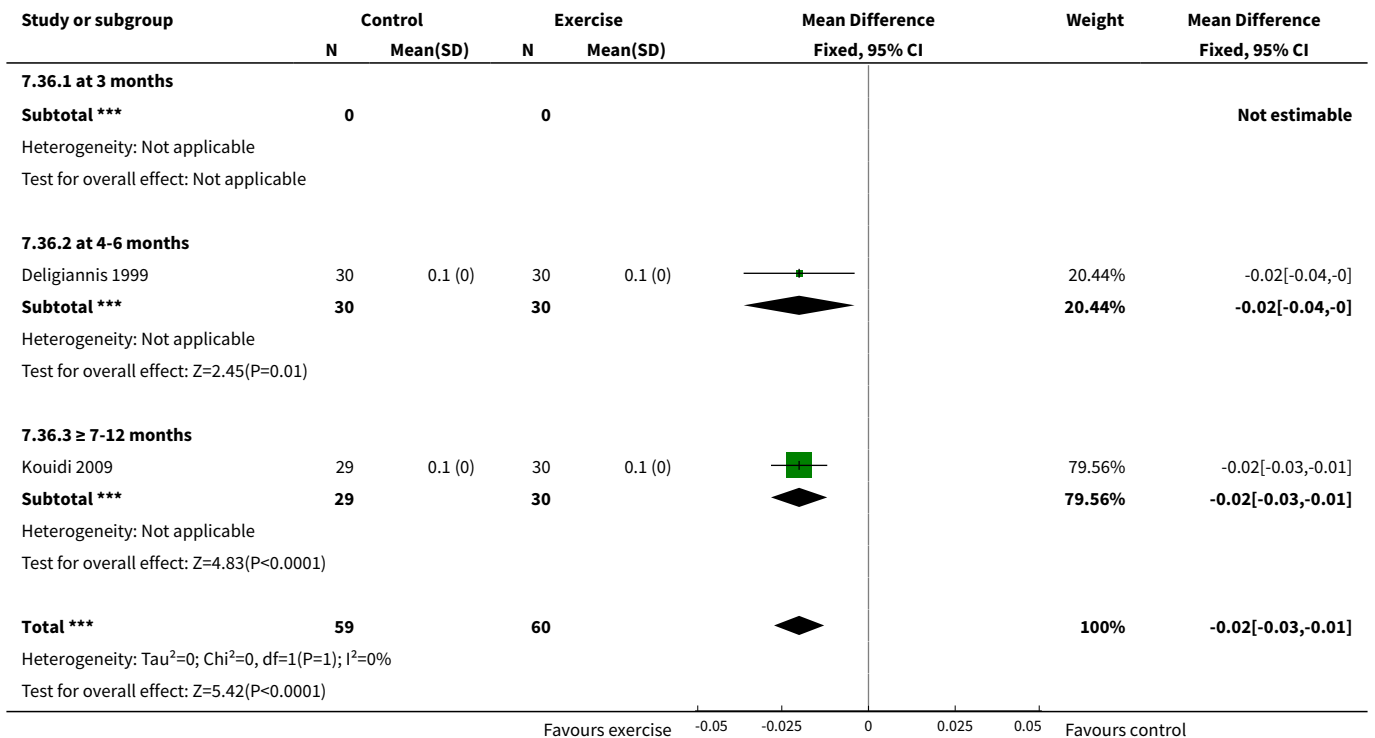
Analysis 7.34. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 34 HRV index.

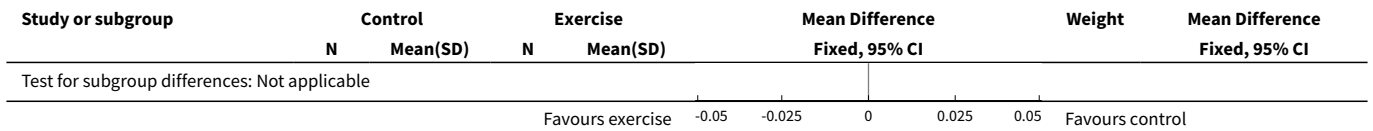


Analysis 7.35. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 35 Mean cardiac R-R interval.

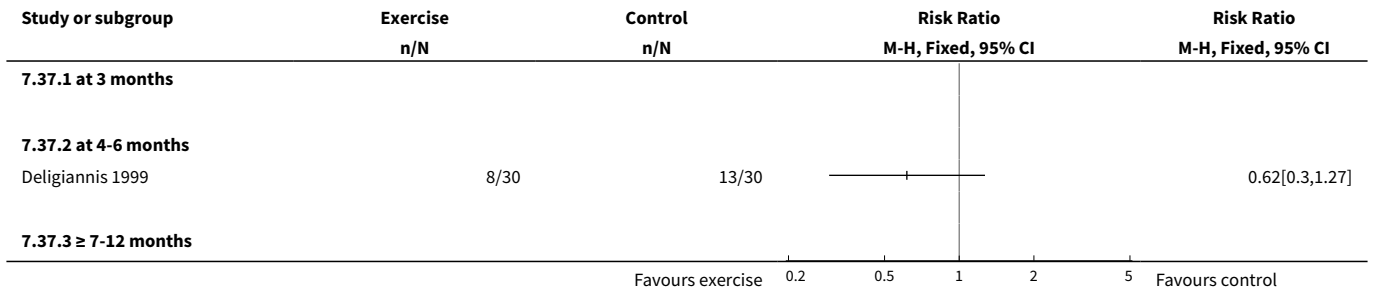


Analysis 7.36. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 36 SDNN.

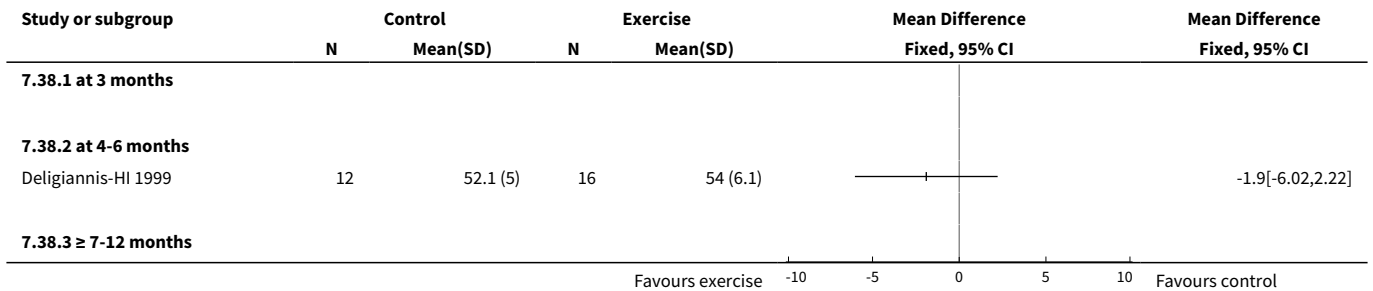




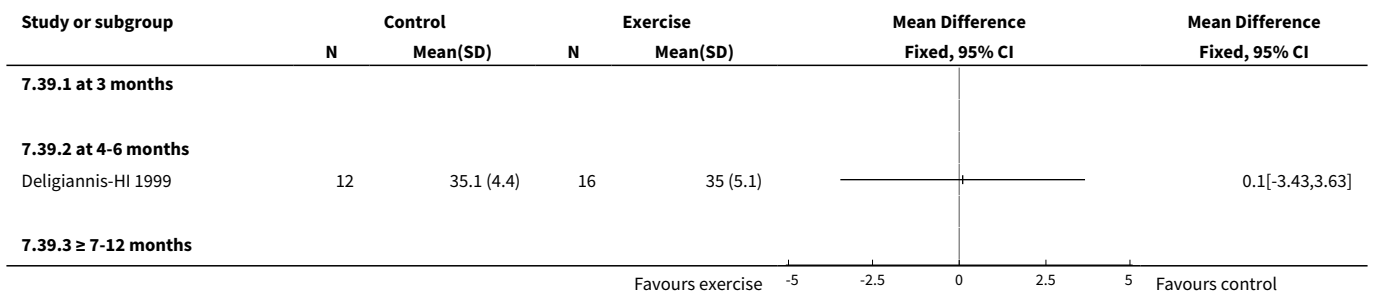
Analysis 7.37. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 37 Arrhythmias: Lown class > II (no).



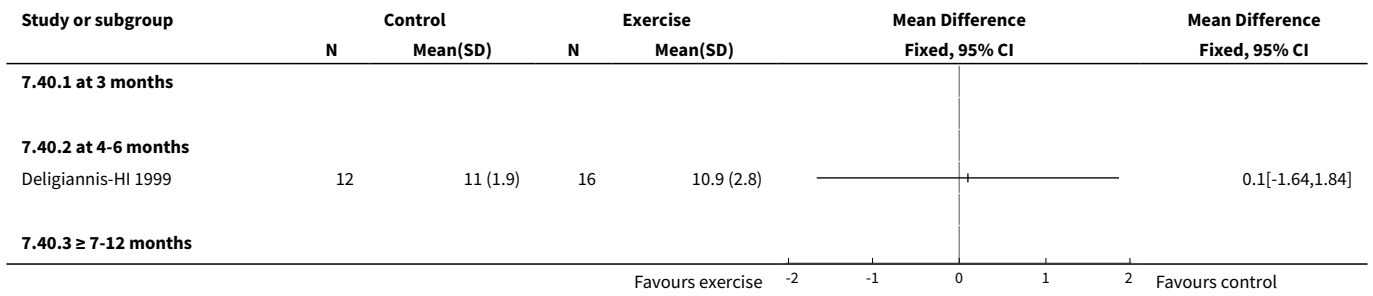
Analysis 7.38. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 38 Left ventricular internal dimension at end-diastole.



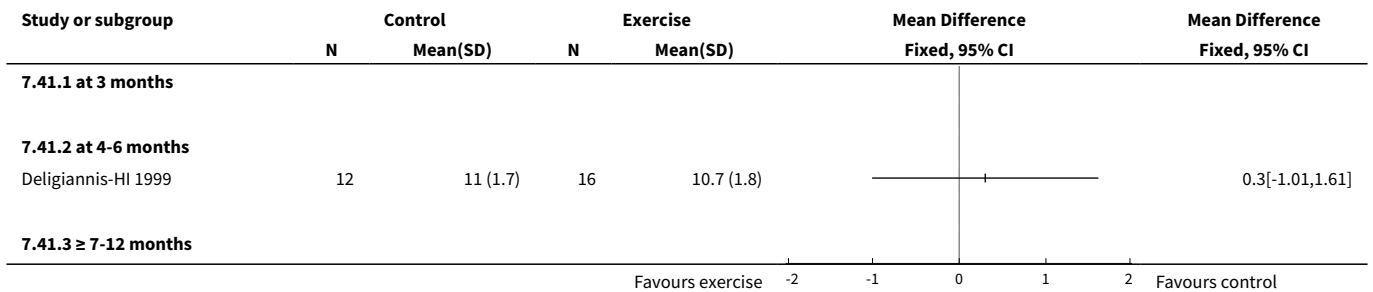
Analysis 7.39. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 39 Left ventricular internal dimension at end-systole.



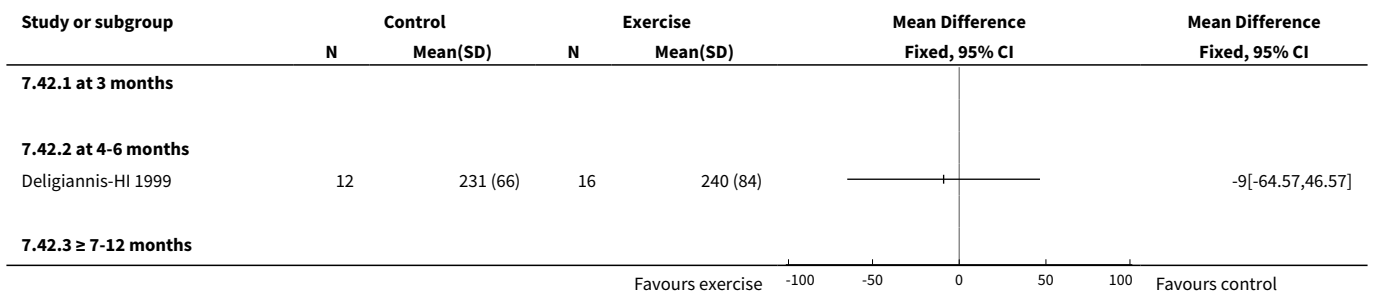
Analysis 7.40. Comparison 7 Supervised exercise versus control (no exercise/ placebo exercise), Outcome 40 Intraventricular septal thickness at end-diastole.



Analysis 7.41. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 41 Left ventricular posterior wall thickness at end-diastole.

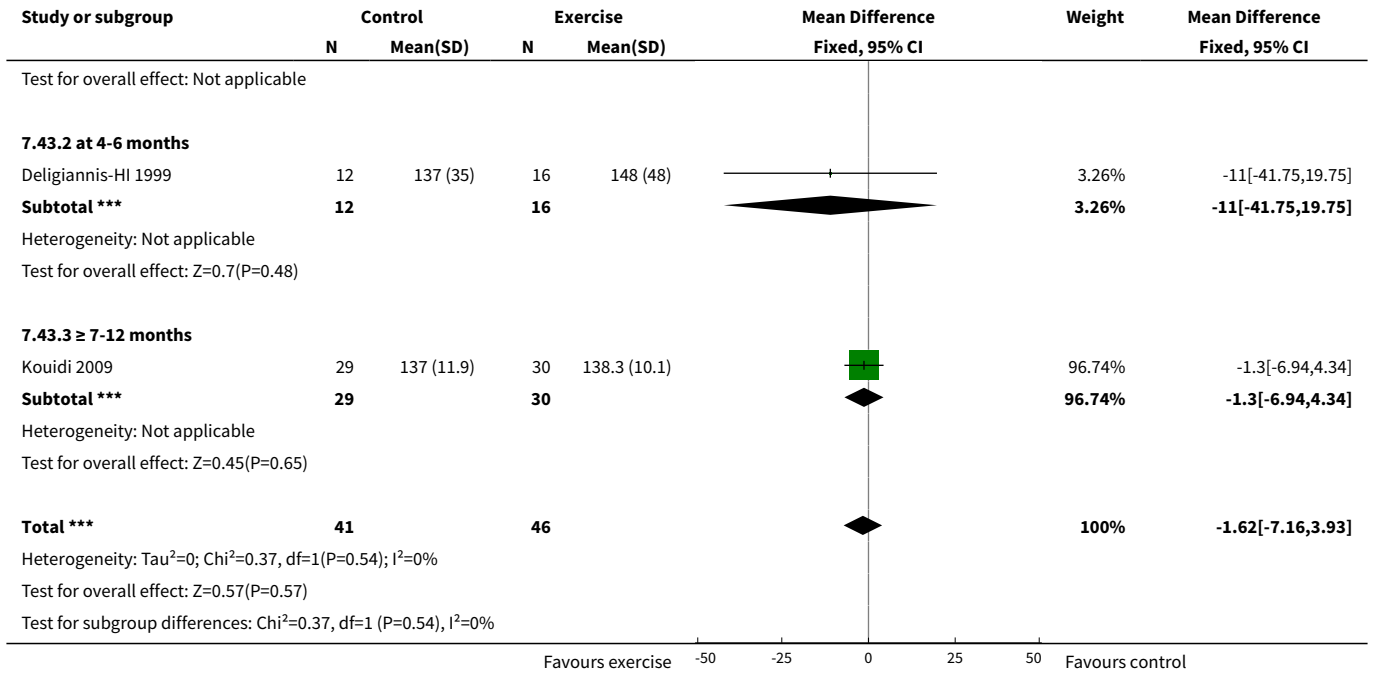


Analysis 7.42. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 42 Left ventricular mass.

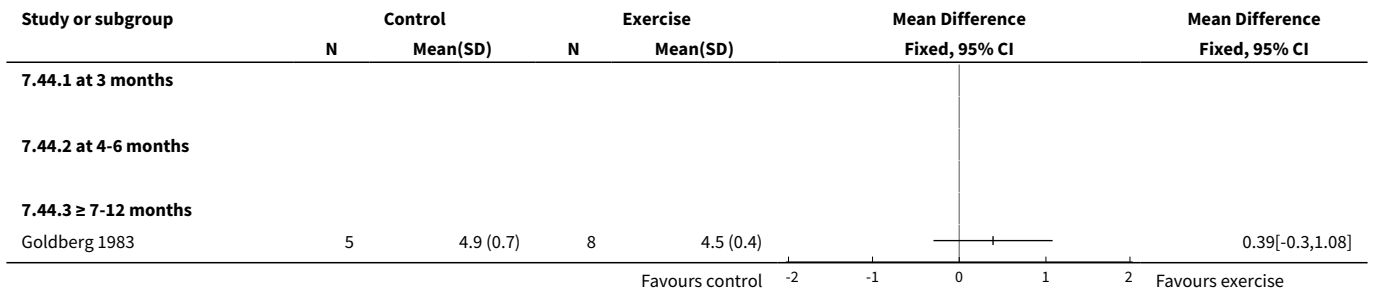


Analysis 7.43. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 43 Left ventricular mass index.





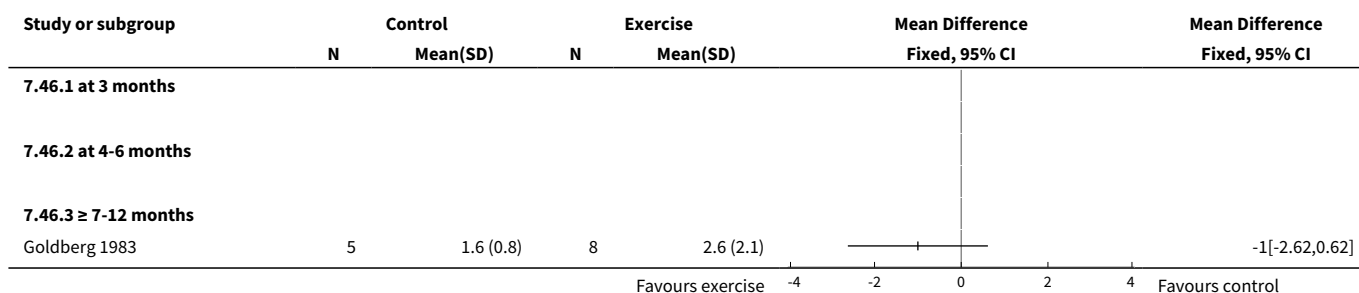
Analysis 7.44. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 44 Fasting plasma glucose.



Analysis 7.45. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 45 Fasting plasma insulin.



Analysis 7.46. Comparison 7 Supervised exercise versus control (no exercise/placebo exercise), Outcome 46 Glucose disappearance.



Comparison 8. Unsupervised exercise versus control (no exercise/placebo exercise)

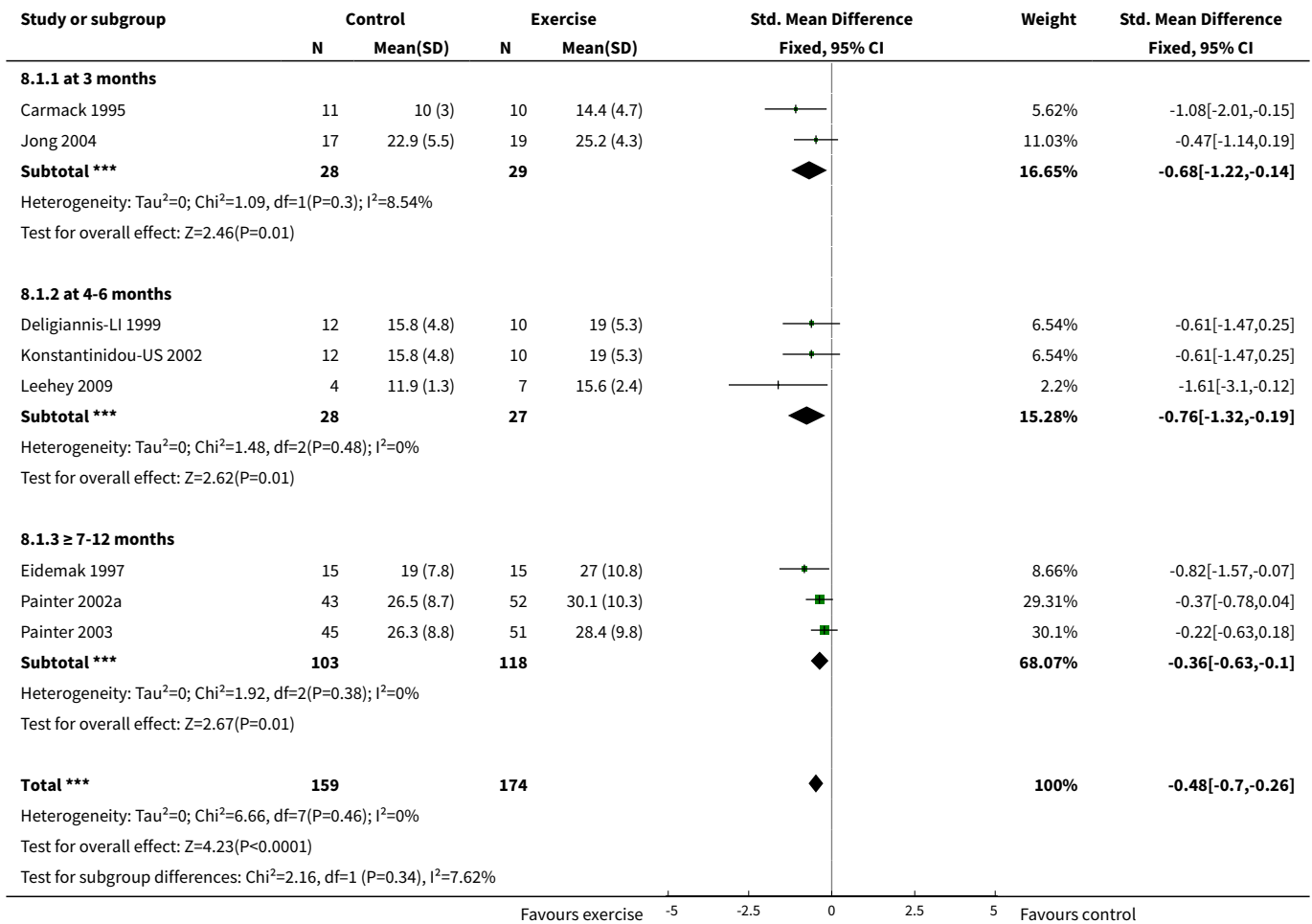
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic capacity	8	333	Std. Mean Difference (IV, Fixed, 95% CI)	-0.48 [-0.70, -0.26]
1.1 at 3 months	2	57	Std. Mean Difference (IV, Fixed, 95% CI)	-0.68 [-1.22, -0.14]
1.2 at 4-6 months	3	55	Std. Mean Difference (IV, Fixed, 95% CI)	-0.76 [-1.32, -0.19]
1.3 ≥ 7-12 months	3	221	Std. Mean Difference (IV, Fixed, 95% CI)	-0.36 [-0.63, -0.10]
2 Muscular strength	2	123	Std. Mean Difference (IV, Fixed, 95% CI)	-0.39 [-0.75, -0.03]
2.1 at 3 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 at 4-6 months	1	28	Std. Mean Difference (IV, Fixed, 95% CI)	-0.45 [-1.20, 0.30]
2.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.78, 0.04]
3 Walking capacity	2	47	Std. Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.94, 0.21]
3.1 at 3 months	1	17	Std. Mean Difference (IV, Fixed, 95% CI)	-0.52 [-1.50, 0.45]
3.2 at 4-6 months	1	30	Std. Mean Difference (IV, Fixed, 95% CI)	-0.28 [1.00, 0.44]
3.3 ≥ 7-12 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 ADL capacity	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Diastolic blood pressure: resting	4	148	Mean Difference (IV, Fixed, 95% CI)	0.27 [-2.72, 3.26]
5.1 at 3 months	1	19	Mean Difference (IV, Fixed, 95% CI)	-4.40 [-11.31, 2.51]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2 at 4-6 months	2	33	Mean Difference (IV, Fixed, 95% CI)	1.48 [-3.23, 6.20]
5.3 ≥ 7-12 months	1	96	Mean Difference (IV, Fixed, 95% CI)	1.20 [-3.45, 5.85]
6 Systolic blood pressure: resting	4	148	Mean Difference (IV, Fixed, 95% CI)	5.93 [0.32, 11.54]
6.1 at 3 months	1	19	Mean Difference (IV, Fixed, 95% CI)	6.40 [-10.11, 22.91]
6.2 at 4-6 months	2	33	Mean Difference (IV, Fixed, 95% CI)	11.23 [2.49, 19.98]
6.3 ≥ 7-12 months	1	96	Mean Difference (IV, Fixed, 95% CI)	1.20 [-6.96, 9.36]
7 Heart rate: maximum	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 at 4-6 months	3	55	Mean Difference (IV, Fixed, 95% CI)	-4.16 [-10.27, 1.95]
7.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Heart rate: resting	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 at 3 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 at 4-6 months	2	33	Mean Difference (IV, Fixed, 95% CI)	1.96 [-5.72, 9.63]
8.3 ≥ 7-12 months	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Albumin	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Energy intake	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
10.1 at 3 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Fat mass	2	106	Std. Mean Difference (IV, Fixed, 95% CI)	0.28 [-0.12, 0.67]
11.1 at 3 months	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 at 4-6 months	1	11	Std. Mean Difference (IV, Fixed, 95% CI)	2.10 [0.45, 3.74]
11.3 ≥ 7-12 months	1	95	Std. Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.24, 0.57]
12 Physical activity	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected

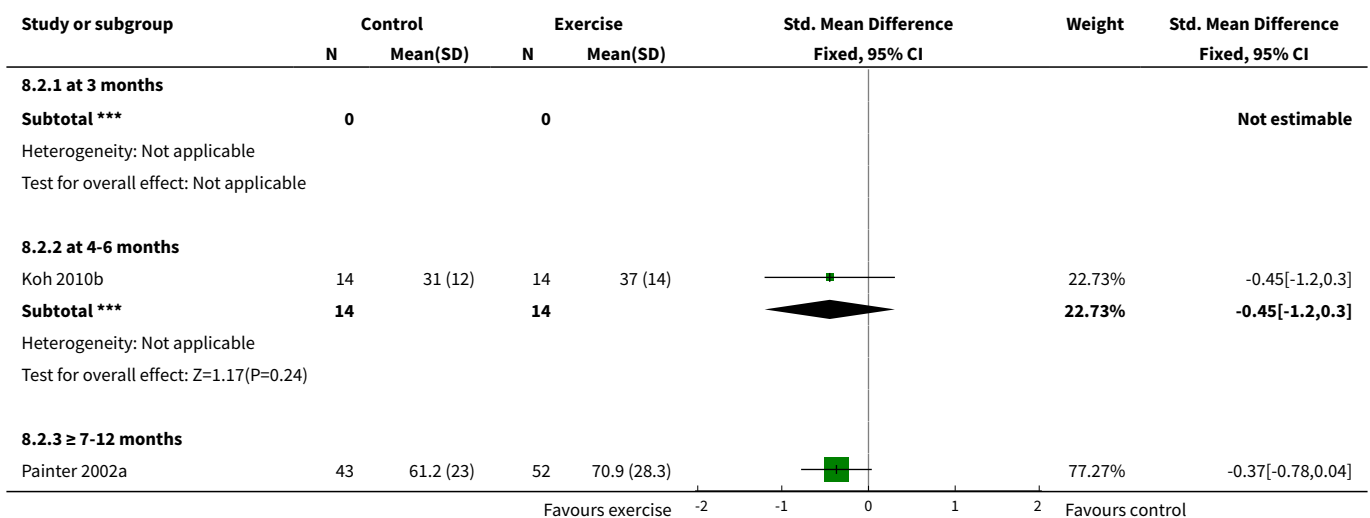
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 at 3 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 at 4-6 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Depression	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
13.1 at 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 at 4-6 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Triglycerides	2	41	Mean Difference (IV, Random, 95% CI)	0.21 [-0.44, 0.87]
14.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14.2 at 4-6 months	1	11	Mean Difference (IV, Random, 95% CI)	0.51 [-0.83, 1.84]
14.3 ≥ 7-12 months	1	30	Mean Difference (IV, Random, 95% CI)	0.12 [-0.63, 0.87]
15 Total cholesterol	3	137	Mean Difference (IV, Random, 95% CI)	0.00 [-0.42, 0.43]
15.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
15.2 at 4-6 months	1	11	Mean Difference (IV, Random, 95% CI)	0.47 [-0.46, 1.39]
15.3 ≥ 7-12 months	2	126	Mean Difference (IV, Random, 95% CI)	-0.12 [-0.61, 0.36]
16 HDL cholesterol	2	107	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.24, 0.07]
16.1 at 3 months	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
16.2 at 4-6 months	1	11	Mean Difference (IV, Random, 95% CI)	-0.21 [-1.34, 0.92]
16.3 ≥ 7-12 months	1	96	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.24, 0.08]
17 LDL cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
17.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Left ventricular internal dimension at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
18.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

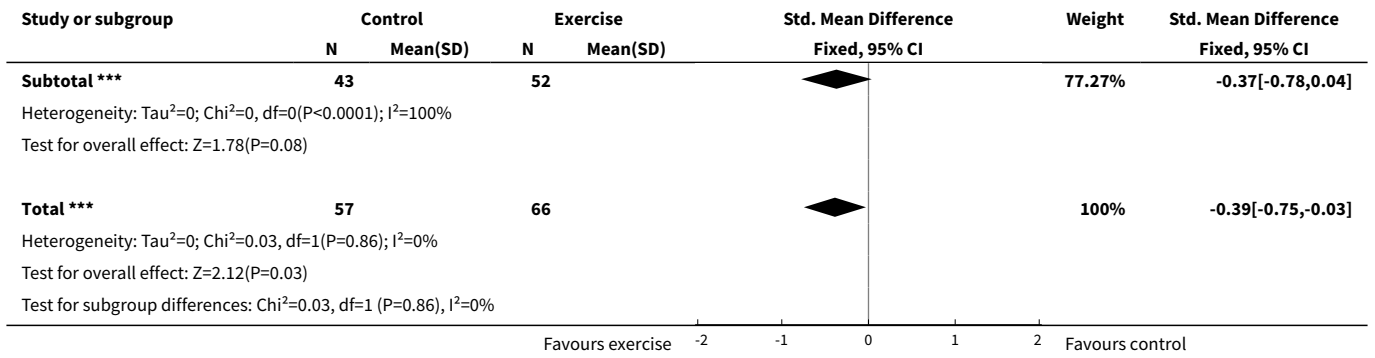
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
18.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Left ventricular internal dimension at end-systole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
19.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Intraventricular septal thickness at end-diastole	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
20.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Left ventricular posterior wall thickness at end-diastole	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
21.1 at 3 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
21.2 at 4-6 months	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
21.3 ≥ 7-12 months	0		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
22 Left ventricular mass	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
22.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Left ventricular mass index	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
23.1 at 3 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 at 4-6 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 ≥ 7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 8.1. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 1 Aerobic capacity.

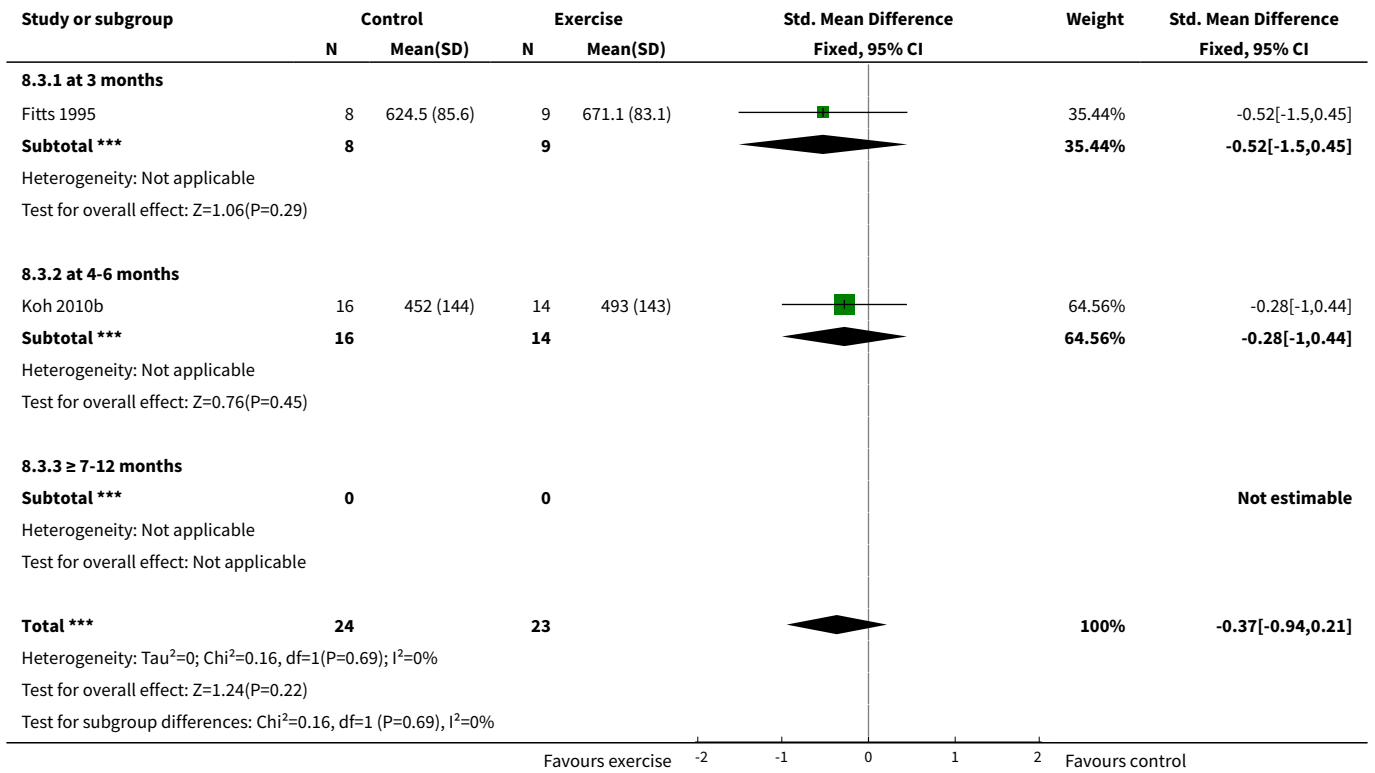


Analysis 8.2. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 2 Muscular strength.

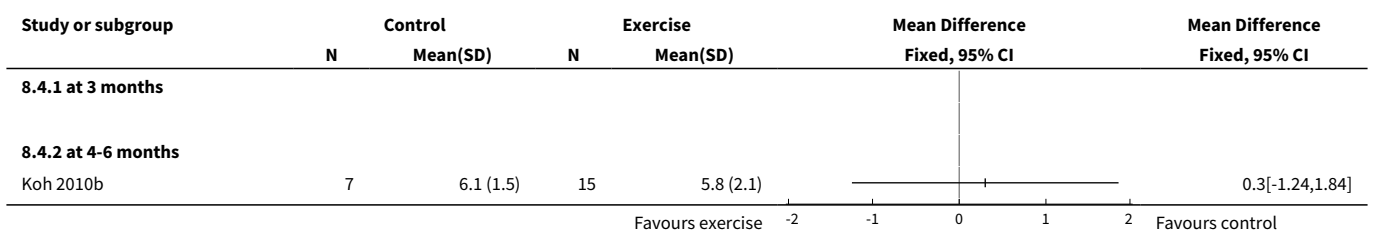




Analysis 8.3. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 3 Walking capacity.



Analysis 8.4. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 4 ADL capacity.



Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		

8.4.3 ≥ 7-12 months

Favours exercise -2 -1 0 1 2 Favours control

Analysis 8.5. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 5 Diastolic blood pressure: resting.

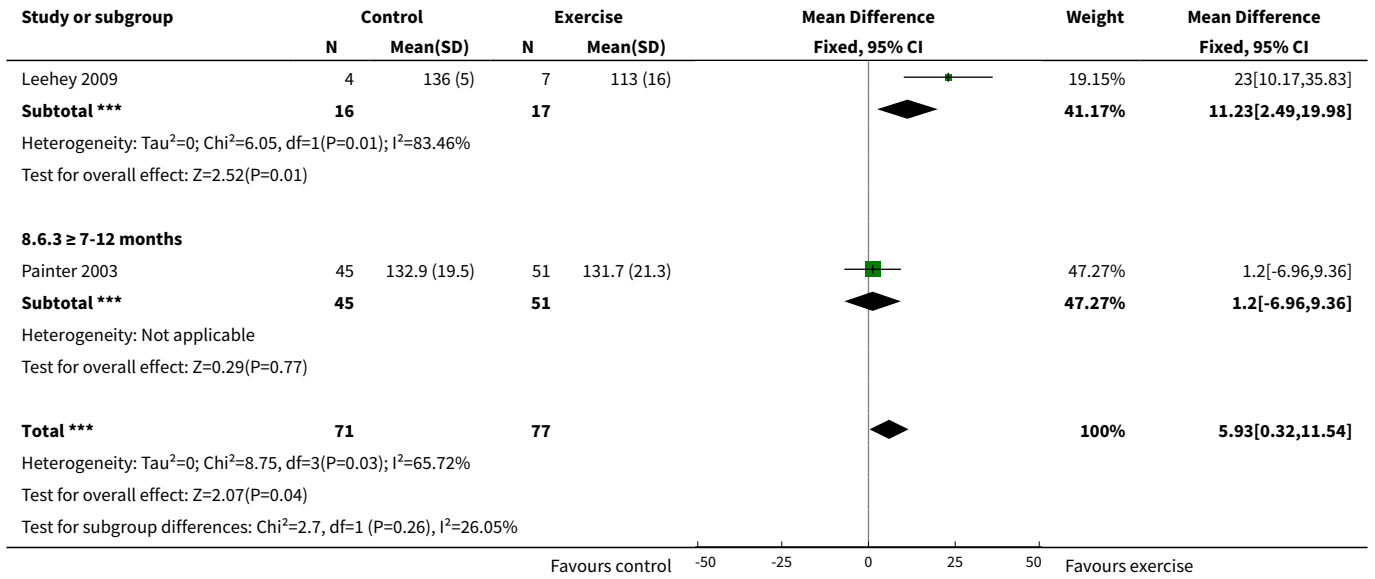
Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
8.5.1 at 3 months							
Toussaint 2008	10	72.8 (9.4)	9	77.2 (5.7)		18.65%	-4.4[-11.31,2.51]
Subtotal ***	10		9			18.65%	-4.4[-11.31,2.51]
Heterogeneity: Not applicable Test for overall effect: Z=1.25(P=0.21)							
8.5.2 at 4-6 months							
Deligiannis-LI 1999	12	82 (3)	10	83 (8)		32.46%	-1[-6.24,4.24]
Leehey 2009	4	77 (8)	7	65 (10)		7.66%	12[1.21,22.79]
Subtotal ***	16		17			40.12%	1.48[-3.23,6.2]
Heterogeneity: Tau ² =0; Chi ² =4.51, df=1(P=0.03); I ² =77.85% Test for overall effect: Z=0.62(P=0.54)							
8.5.3 ≥ 7-12 months							
Painter 2003	45	90.6 (11.6)	51	89.4 (11.6)		41.23%	1.2[-3.45,5.85]
Subtotal ***	45		51			41.23%	1.2[-3.45,5.85]
Heterogeneity: Not applicable Test for overall effect: Z=0.51(P=0.61)							
Total ***	71		77			100%	0.27[-2.72,3.26]
Heterogeneity: Tau ² =0; Chi ² =6.67, df=3(P=0.08); I ² =55.05% Test for overall effect: Z=0.18(P=0.86) Test for subgroup differences: Chi ² =2.16, df=1 (P=0.34), I ² =7.42%							

Favours control -50 -25 0 25 50 Favours exercise

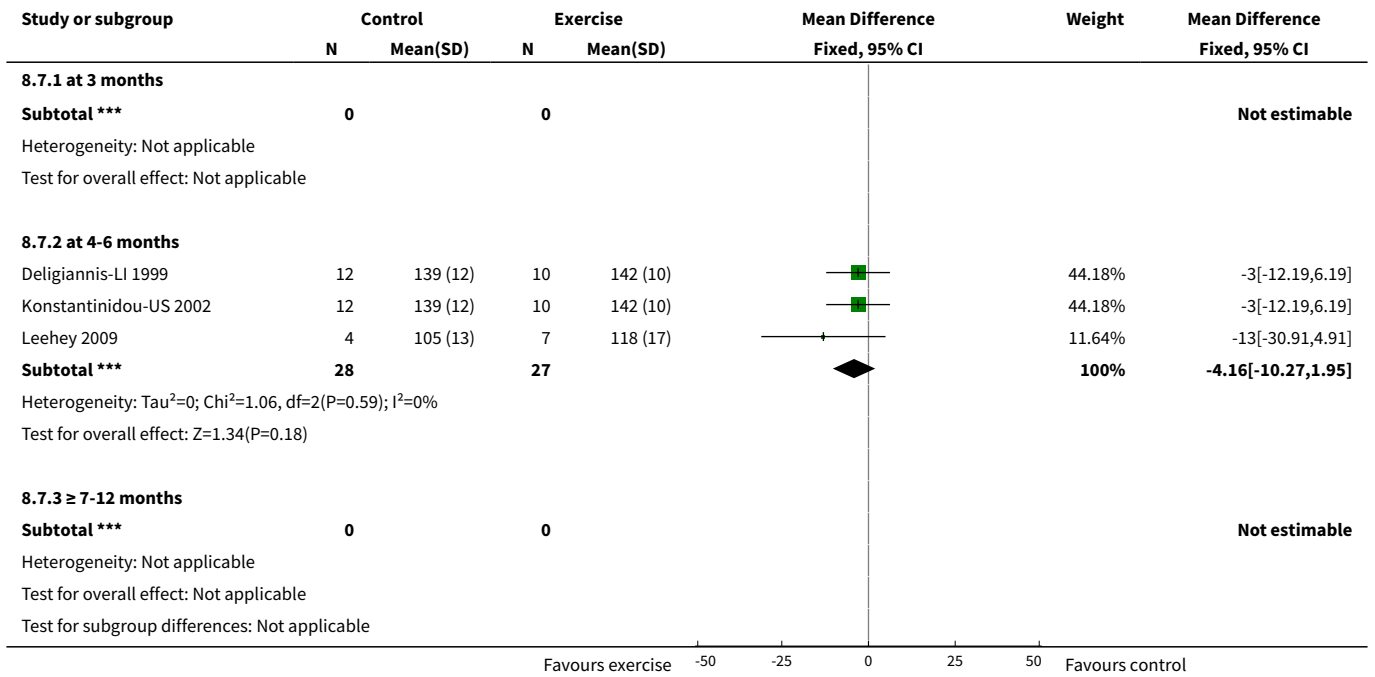
Analysis 8.6. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 6 Systolic blood pressure: resting.

Study or subgroup	Control		Exercise		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
8.6.1 at 3 months							
Toussaint 2008	10	147.8 (23.5)	9	141.4 (11.9)		11.56%	6.4[-10.11,22.91]
Subtotal ***	10		9			11.56%	6.4[-10.11,22.91]
Heterogeneity: Not applicable Test for overall effect: Z=0.76(P=0.45)							
8.6.2 at 4-6 months							
Deligiannis-LI 1999	12	144 (10)	10	143 (17)		22.02%	1[-10.96,12.96]

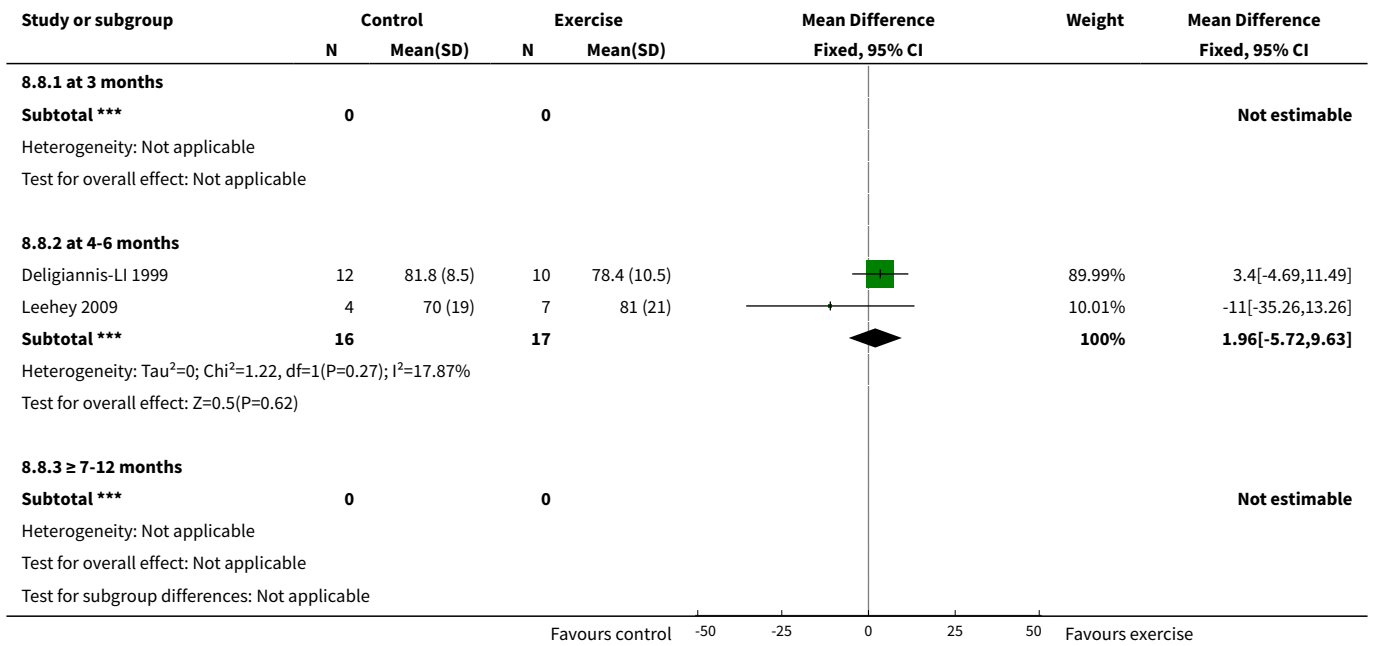
Favours control -50 -25 0 25 50 Favours exercise



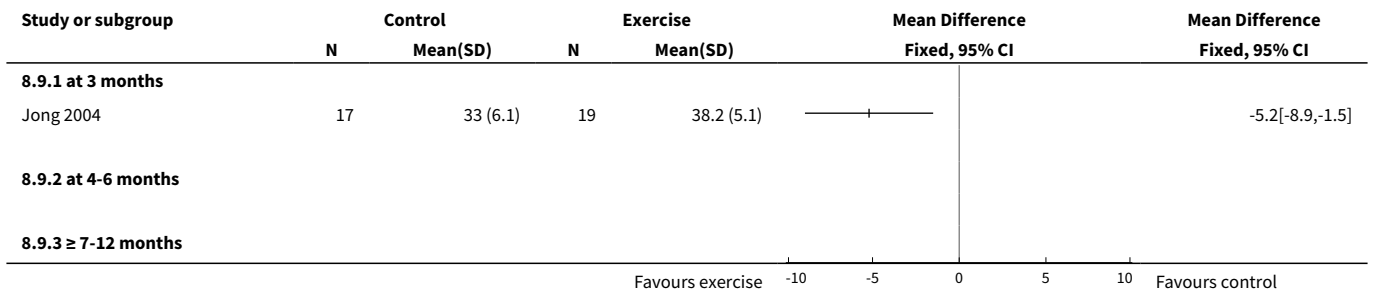
Analysis 8.7. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 7 Heart rate: maximum.



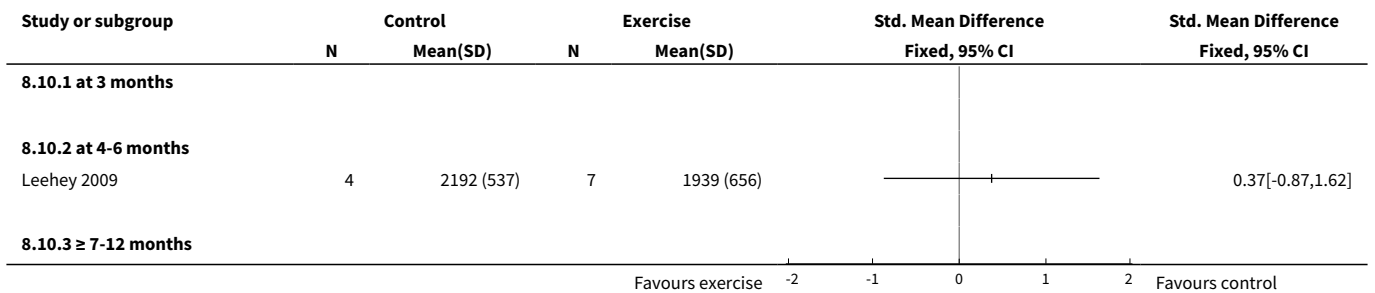
Analysis 8.8. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 8 Heart rate: resting.



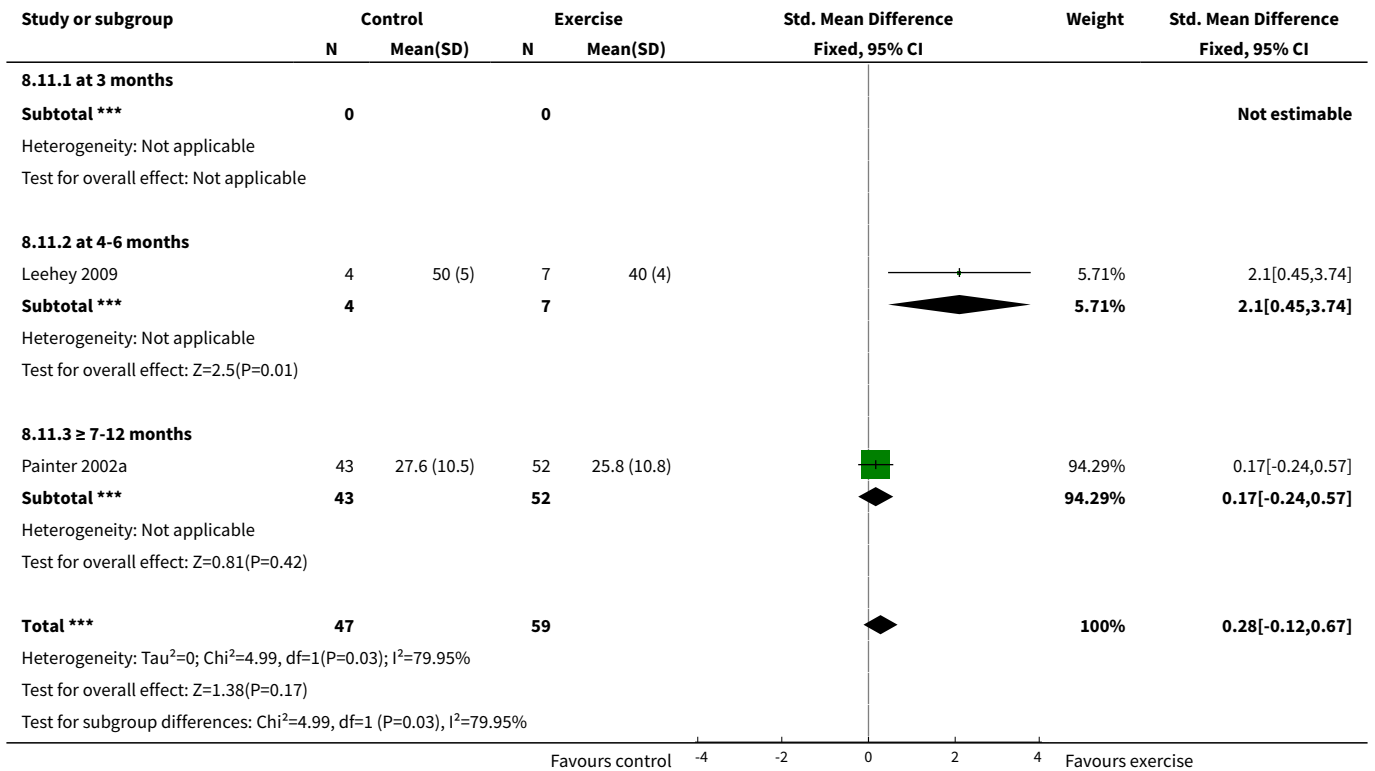
Analysis 8.9. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 9 Albumin.



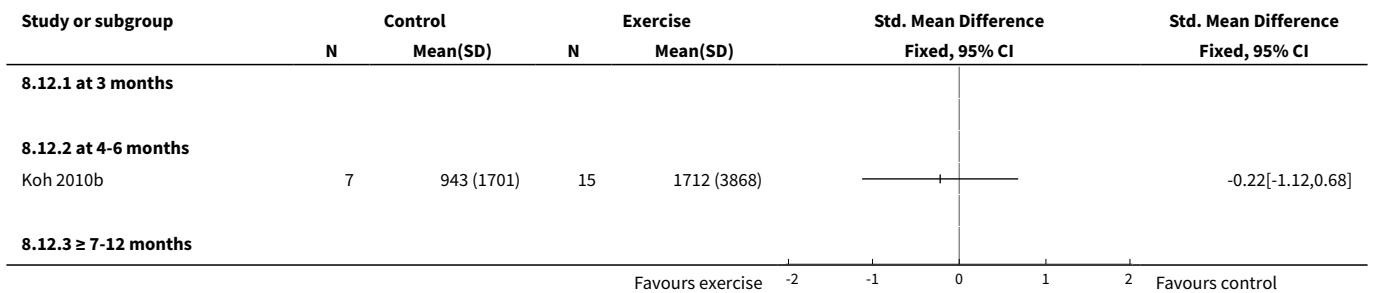
Analysis 8.10. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 10 Energy intake.



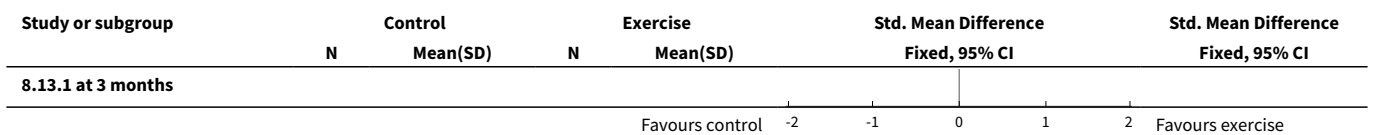
Analysis 8.11. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 11 Fat mass.

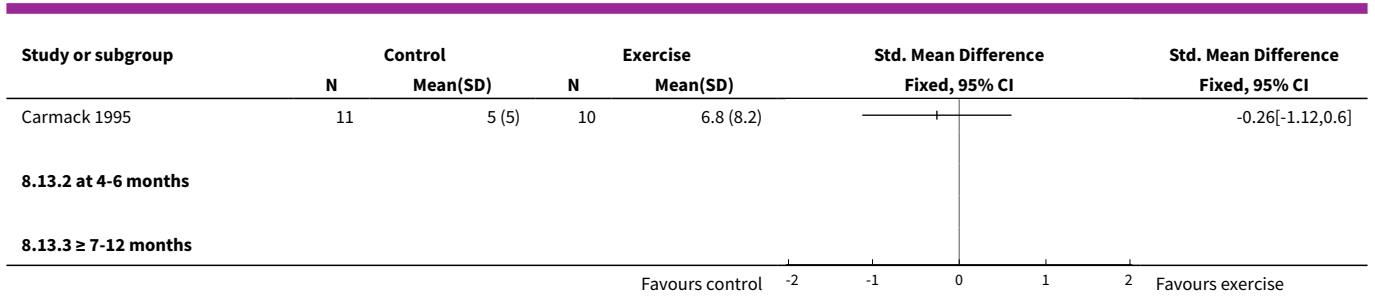


Analysis 8.12. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 12 Physical activity.

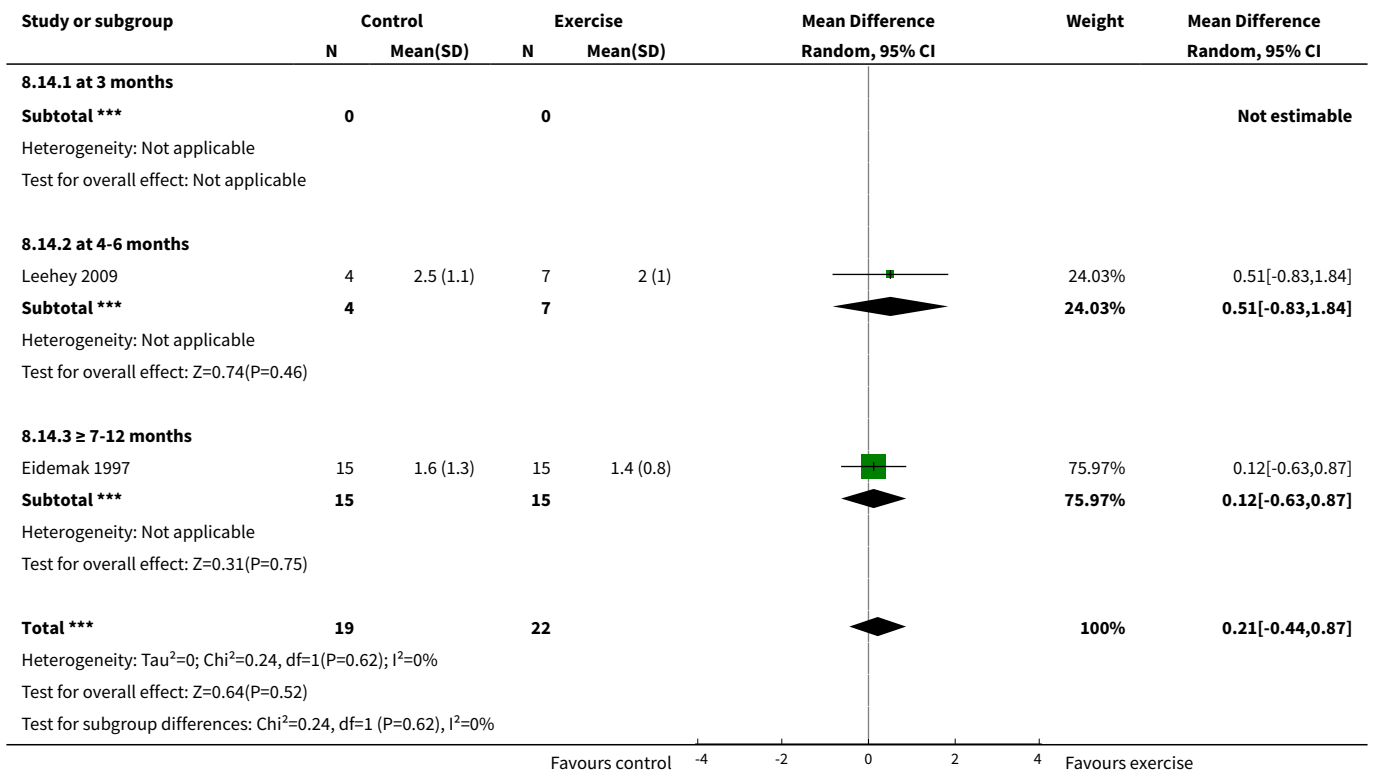


Analysis 8.13. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 13 Depression.

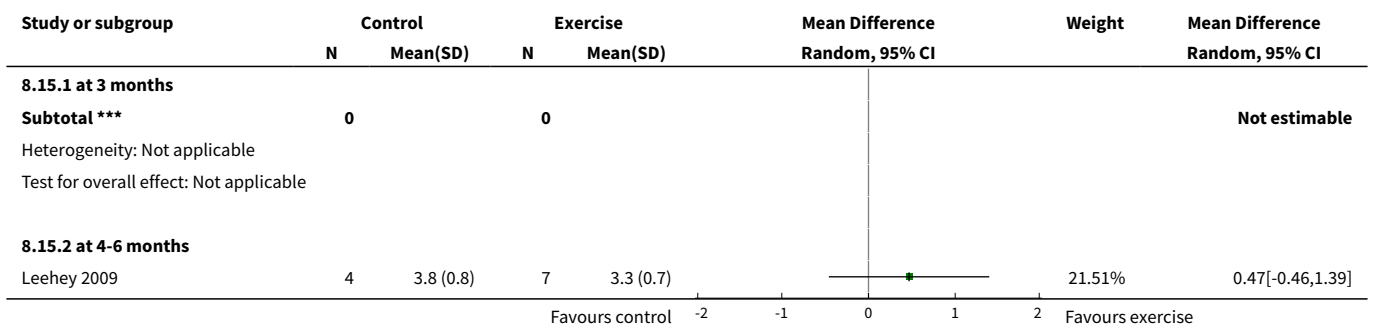


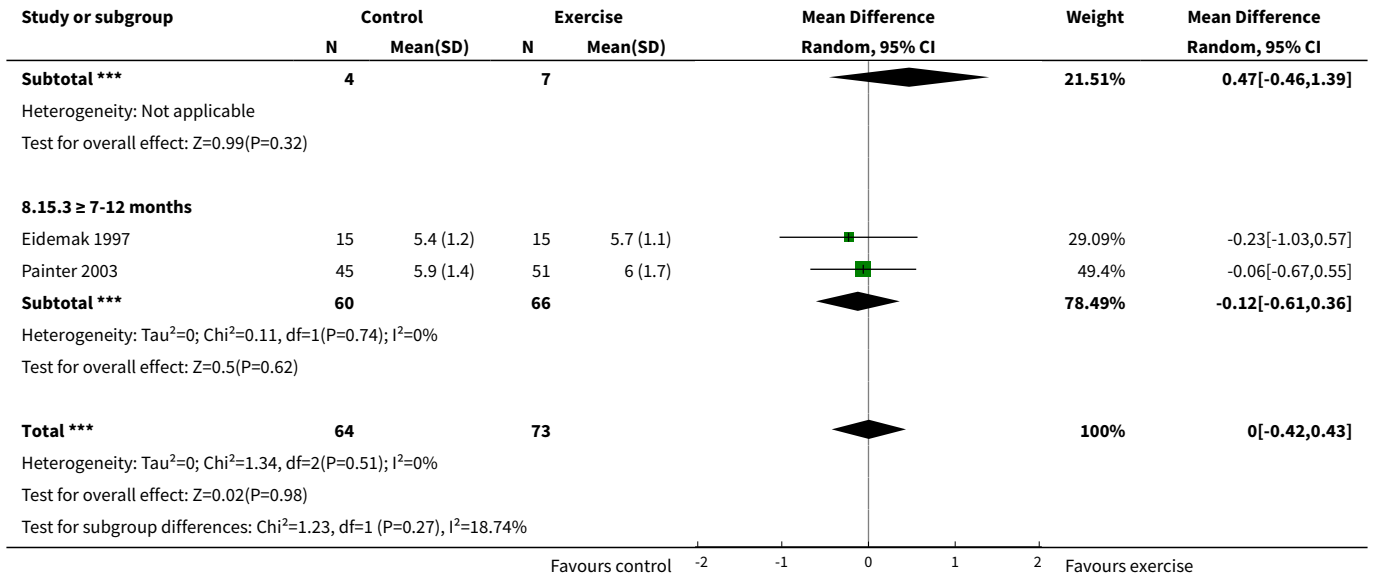


Analysis 8.14. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 14 Triglycerides.

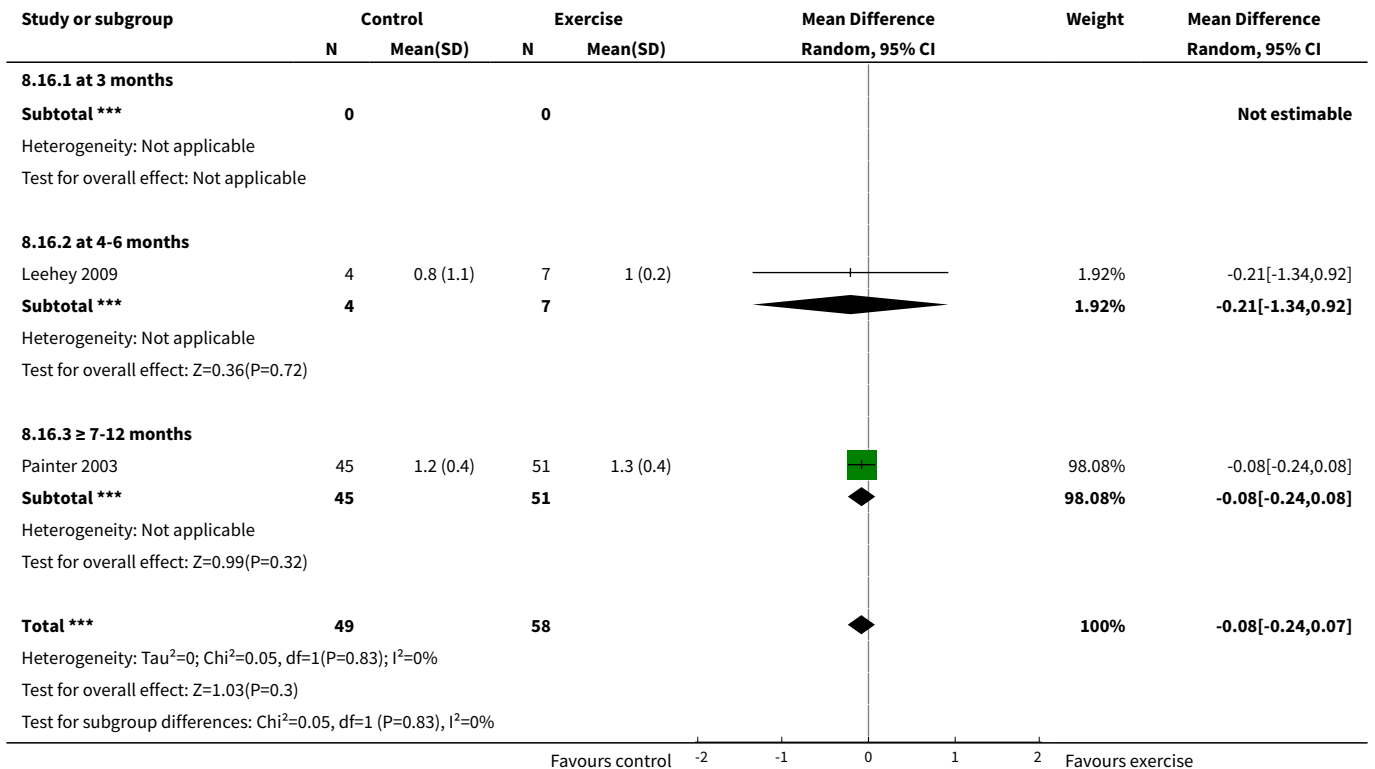


Analysis 8.15. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 15 Total cholesterol.

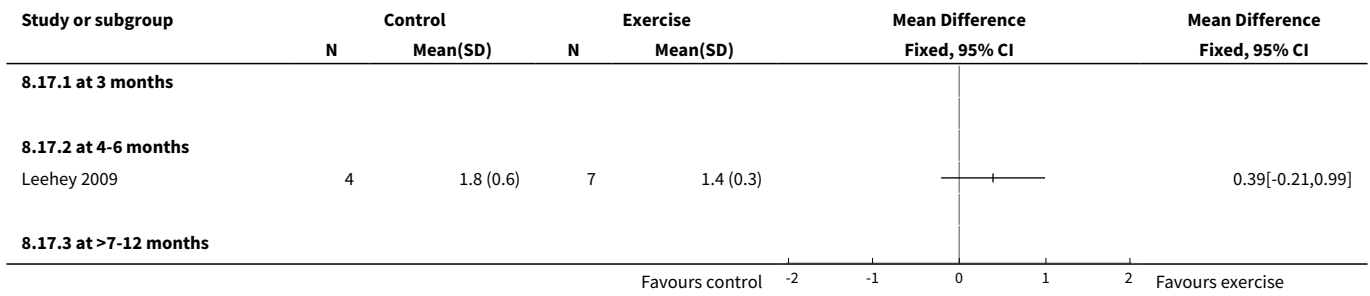




Analysis 8.16. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 16 HDL cholesterol.



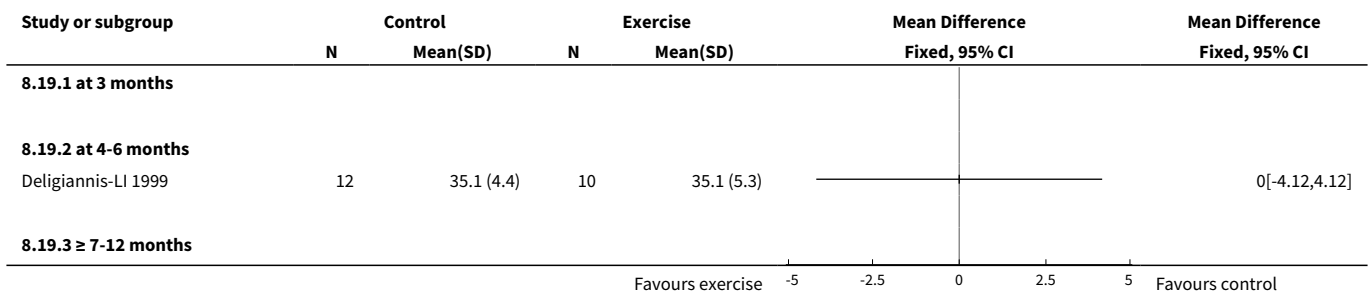
Analysis 8.17. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 17 LDL cholesterol.



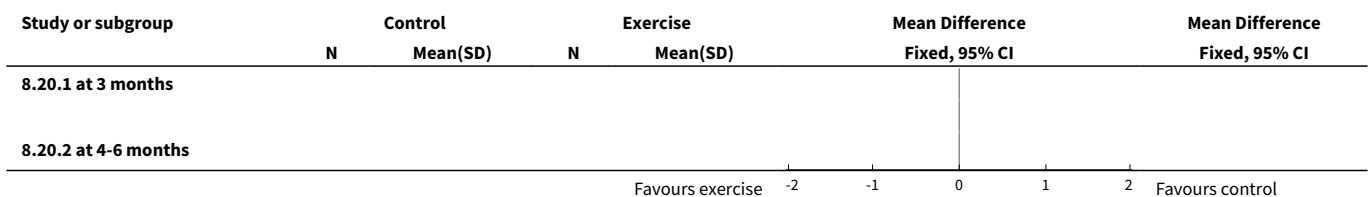
Analysis 8.18. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 18 Left ventricular internal dimension at end-diastole.

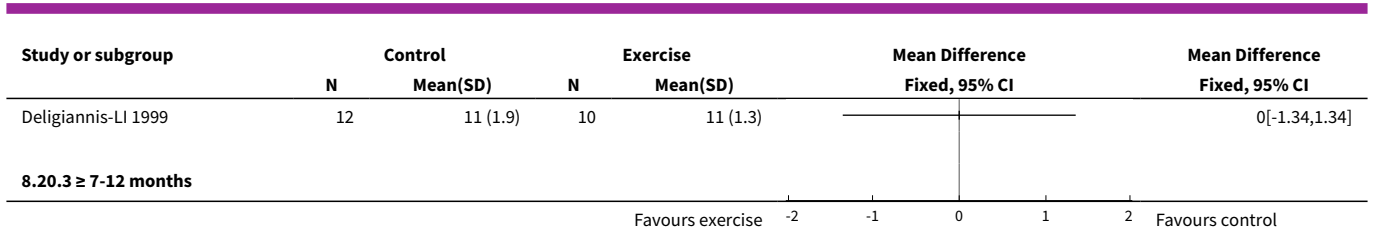


Analysis 8.19. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 19 Left ventricular internal dimension at end-systole.

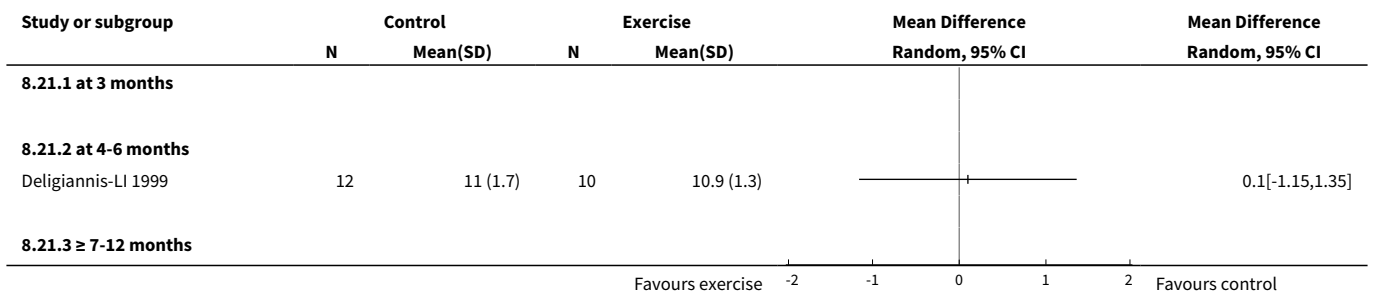


Analysis 8.20. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 20 Intraventricular septal thickness at end-diastole.

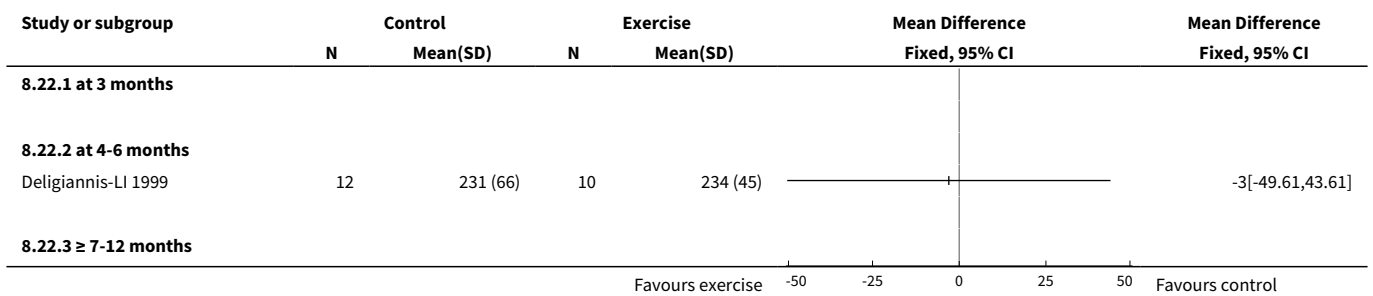




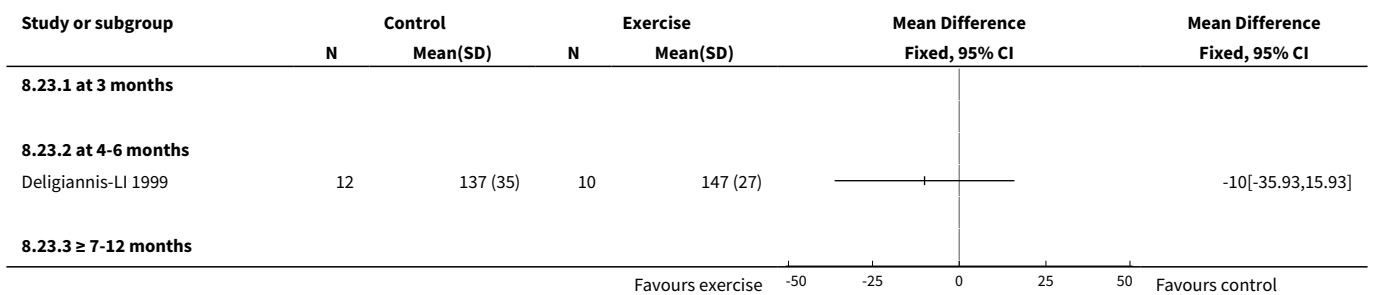
Analysis 8.21. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 21 Left ventricular posterior wall thickness at end-diastole.



Analysis 8.22. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 22 Left ventricular mass.



Analysis 8.23. Comparison 8 Unsupervised exercise versus control (no exercise/placebo exercise), Outcome 23 Left ventricular mass index.



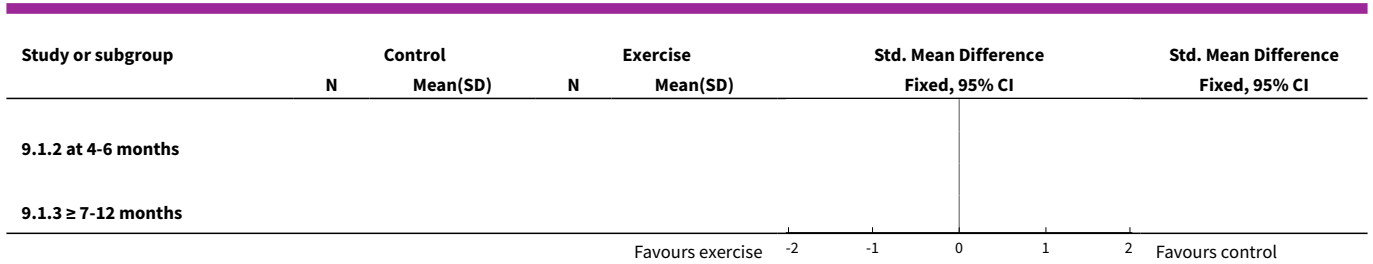
Comparison 9. Yoga exercise versus control (no exercise/placebo exercise)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Muscular strength (high value = improved)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 at 3 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 at 4-6 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 ≥ 7-12 months	0		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Grip strength	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Triglycerides	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Total cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 HDL cholesterol	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 at 3 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 at 4-6 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 at >7-12 months	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

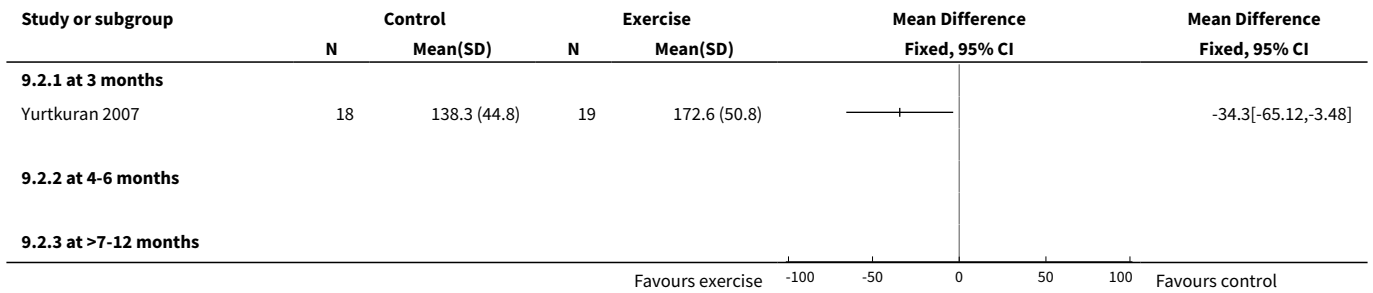
Analysis 9.1. Comparison 9 Yoga exercise versus control (no exercise/ placebo exercise), Outcome 1 Muscular strength (high value = improved).

Study or subgroup	Control		Exercise		Std. Mean Difference Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
9.1.1 at 3 months						
Yurtkuran 2007	18	138.3 (44.8)	19	172.6 (50.8)		-0.7[-1.37,-0.03]

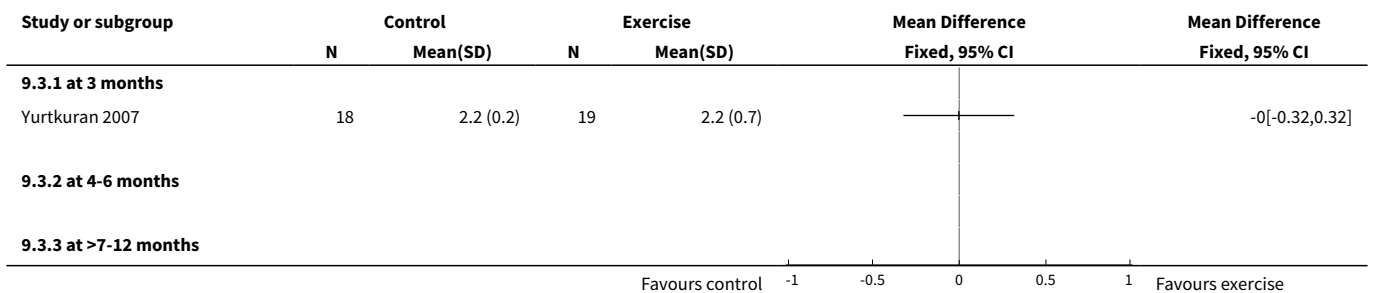
Favours exercise -2 -1 0 1 2 Favours control



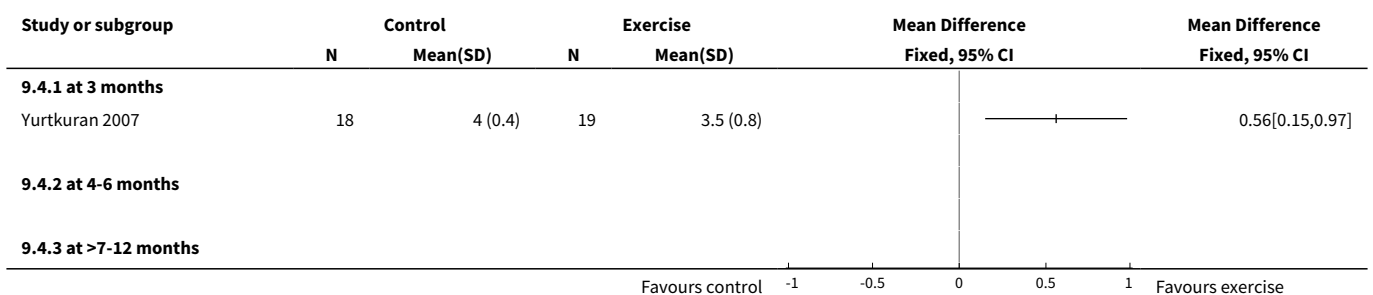
Analysis 9.2. Comparison 9 Yoga exercise versus control (no exercise/placebo exercise), Outcome 2 Grip strength.



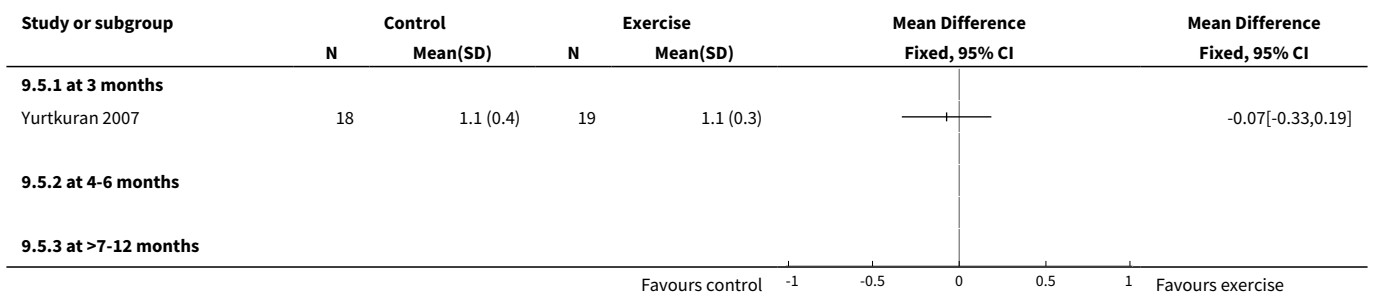
Analysis 9.3. Comparison 9 Yoga exercise versus control (no exercise/placebo exercise), Outcome 3 Triglycerides.



Analysis 9.4. Comparison 9 Yoga exercise versus control (no exercise/placebo exercise), Outcome 4 Total cholesterol.



Analysis 9.5. Comparison 9 Yoga exercise versus control (no exercise/placebo exercise), Outcome 5 HDL cholesterol.



APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	<ol style="list-style-type: none"> 1. MeSH descriptor Exertion explode all trees 2. MeSH descriptor Physical Education and Training, this term only 3. exercise:ti,ab,kw 4. (physical next (training or activity or fitness or rehabilitation)):ti,ab,kw 5. (resistance next (training or program*)):ti,ab,kw 6. (strength* and (muscle* or program* or training)):ti,ab,kw 7. kinesiotherapy:ti,ab,kw 8. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7) 9. (uremi* or uraemi*):ti,ab,kw 10.renal replacement therapy:ti,ab,kw 11.dialysis:ti,ab,kw 12.(hemodialysis or haemodialysis):ti,ab,kw 13.((kidney or renal) next (transplant* or graft*)):ti,ab,kw 14.(predialysis or pre-dialysis):ti,ab,kw 15.renal insufficiency:ti,ab,kw 16.MeSH descriptor Renal Insufficiency, Chronic explode all trees 17.((kidney or renal) next (failure or disease)):ti,ab,kw 18.(CKD or CKF or CRD or CRF or ESRD or ESKD or ESRF or ESKF):ti,ab,kw 19.(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18) 20.(#8 AND #19)
MEDLINE	<ol style="list-style-type: none"> 1. Treatment group Exertion/ 2. Treatment group Exercise Therapy/ 3. Exercise Test/ 4. "Physical Education and Training"/ 5. "Physical Fitness"/ 6. exercise.tw. 7. (resistance training or resistance program\$).tw. 8. (physical fitness or physical rehabilitation).tw. 9. (strength\$ and (muscle or program\$ or training)).tw. 10.or/1-9

(Continued)

- 11.Uremia/
- 12.ur?emi\$.tw.
- 13.or/11-12
- 14.Treatment group Renal Replacement Therapy/
- 15.(hemodialysis or haemodialysis or dialysis).tw.
- 16.(kidney transplant\$ or renal transplant\$ or kidney graft\$ or renal graft\$).tw.
- 17.Renal Insufficiency, Chronic/ or Kidney Failure, Chronic/
- 18.(kidney failure or renal failure).tw.
- 19.(kidney disease or renal disease).tw.
- 20.(CKF or CKD or CRF or CRD or ESRF or ESKF or ESKD or ESRD).tw.
- 21.or/14-20
- 22.13 or 21
- 23.and/10,22

EMBASE

1. Treatment group "Physical Activity Capacity and Performance"/
2. Treatment group Kinesiotherapy/
3. Exercise Test/
4. or/1-3
5. exercise.tw.
6. (resistance training or resistance program\$).tw.
7. (physical fitness or physical rehabilitation).tw.
8. (strength\$ and (muscle or program\$ or training)).tw.
9. or/5-8
- 10.or/4,9
- 11.Uremia/
- 12.ur?emi\$.tw.
- 13.or/11-12
- 14.Treatment group Hemodialysis/
- 15.Treatment group Kidney Transplantation/
- 16.Kidney Failure/
- 17.Chronic Kidney Failure/
- 18.or/14-17
- 19.(hemodialysis or haemodialysis).tw.
- 20.dialysis.tw.
- 21.(predialysis or pre-dialysis).tw.
- 22.(renal transplant\$ or kidney transplant\$).tw.
- 23.(renal failure or kidney failure).tw.
- 24.(renal disease or kidney disease).tw.
- 25.(CKD or CKF or CRD or CRF or ESKD or ESRD or ESKF or ESRF).tw.
- 26.or/19-25
- 27.or/13,18,26
- 28.10 and 27

CINAHL

1. Treatment group exertion/
2. Treatment group therapeutic exercise/
3. Treatment group exercise test/
4. physical fitness/
5. or/1-4
6. exercise.tw.
7. (resistance training or resistance program\$).tw.
8. (physical fitness or physical rehabilitation).tw.
9. (strength\$ and (muscle\$ or program\$ or training)).tw.

(Continued)

- 10.or/6-9
- 11.or/5,10
- 12.uremia/
- 13.ur?emia\$.tw.
- 14.12 or 13
- 15.(hemodialysis or haemodialysis).tw.
- 16.dialysis.tw.
- 17.Treatment group renal replacement therapy/
- 18.kidney failure chronic/
- 19.(kidney failure or renal failure or kidney disease or renal disease).tw.
- 20.(CKD or CKF or CRD or CRF or ESKD or ESKF or ESRD or ESRF).tw.
- 21.or/15-20
- 22.or/14,21
- 23.and/11,22

Webscience (Science citation index and Social science citation index)

1. (exertion OR exercise therapy OR physical education and training OR physical fitness OR exercise program* OR exercise training) AND (uremia OR ur?emia OR hemodialysis OR haemodialysis OR peritoneal dialysis OR renal* OR kidney*)
2. (exertion OR exercise* OR motion therapy* OR physical educ* OR physical train* OR physical fitness*) AND (uremia OR ur?emia OR hemodialysis OR haemodialysis OR peritoneal dialysis OR renal* OR kidney*) AND (controlled clinical trial* OR CCT OR clinical trial* OR CT OR Randomized controlled trial* OR RCT)

BIOSIS

1. exertion.mp.
2. exercise therapy.mp.
3. exercise test.mp.
4. (physical education and training).mp. [mp=title, book title (english), original language book title (non-english), abstract, concept codes, biosystematic codes, chemicals & biochemicals, diseases, major concepts, methods & equipment, organisms, parts, structures & systems of organisms, sequence data, super taxa, taxa notes, time, geopolitical locations, gene name, miscellaneous descriptors]
5. physical fitness.mp.
6. 1 or 2 or 3 or 4 or 5
7. exercise program\$.mp.
8. exercise training.mp.
9. 7 or 8
- 10.6 or 9
- 11.uremia.mp.
- 12.ur?emia.mp.
- 13.11 or 12
- 14.renal replacement therapy.mp.
- 15.haemodialysis.mp.
- 16.hemodialysis.mp.
- 17.renal transplant\$.mp.
- 18.peritoneal dialysis.mp.
- 19.14 or 15 or 16 or 17 or 18
- 20.kidney failure chronic.mp.
- 21.chronic kidney failure.mp.
- 22.chronic renal failure.mp.
- 23.20 or 21 or 22
- 24.13 or 19 or 23
- 25.10 and 24

(Continued)

PEDRO	<ol style="list-style-type: none"> 1. abstract & Title: renal 2. Therapy: fitness training
AMED	<ol style="list-style-type: none"> 1. Treatment group Exertion/ 2. exercise therapy.mp. or Treatment group Exercise therapy/ 3. Treatment group Exercise testing/ or exercise test.mp. 4. (physical education and training).mp. 5. Treatment group Physical fitness/ 6. 1 or 2 or 3 or 4 or 5 7. exercise program?.mp. 8. exercise training.mp. 9. 7 or 8 10.6 or 9 11.uremia.mp. 12.ur?emia.mp. 13.11 or 12 (9) 14.renal replacement therapy.mp. 15.haemodialysis.mp. 16.renal transplant?.mp. 17.peritoneal dialysis.mp. 18.hemodialysis.mp. or Treatment group Hemodialysis/ 19.14 or 15 or 16 or 17 or 18 20.Treatment group Kidney failure chronic/ 21.chronic kidney failure.mp. 22.chronic renal failure.mp. 23.20 or 21 or 22 24.13 or 19 or 23 25.10 and 24
PsycINFO	<ol style="list-style-type: none"> 1. Treatment group EXERCISE/ or Treatment group AEROBIC EXERCISE/ or exercise.mp. 2. Treatment group Dialysis/ or Treatment group Hemodialysis/ or Treatment group Kidney Diseases/ or Treatment group Organ Transplantation/ or Treatment group Kidneys/ 3. 1 AND 2 4. limit 3 to human
Ageline	<ol style="list-style-type: none"> 1. Exercise OR Exertion OR Fitness OR Training 2. uremia OR renal OR kidney OR hemodialysis OR peritoneal dialysis 3. Combine with AND 4. Limit to Research/Academic and Professional/Provider
KoreaMed	<ol style="list-style-type: none"> 1. exercise [ALL] AND nephrol [ALL] 2. exercise [ALL] AND kidney [ALL]

Appendix 2. Health-related quality of life assessment

Health-related quality of life assessment of adults with CKD enrolled in RCTs of regular exercise training versus control

Study ID	Scale or tool	Validated ¹	Time of assessment	Result
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(Continued)

High intensity cardiovascular exercise training

Dimeo 2007	The Medical Outcomes Short Form (SF-36) questionnaire	Yes	Baseline and end of treatment (2 months)	Significant increase in total score in the exercise group, whereas no change in neither total score in the control group.
Kouidi 1997a	The Quality of Life Index (QLI) – Spitzer Index ²	Yes	Baseline and end of treatment (6 months)	Significant increase in total score and in all sub-scores in the exercise group, whereas no change in neither total score nor sub-scores in the control group.
Matsumoto 2007	The Medical Outcomes Short Form (SF-36) questionnaire	Yes	Baseline and end of treatment (12 months)	Significant increase in total score and in the sub-scores RF, RP, VT and MH in the exercise group, whereas no change in neither total score nor sub-scores in the control group.
Painter 2002a	The Medical Outcomes Short Form (SF-36) questionnaire ³	Yes	Baseline, 6 months and end of treatment (in total 12 months)	No significant difference in any score between the exercise- and control group
Painter 2002b	The Medical Outcomes Short Form (SF-36) questionnaire ³	Yes	Baseline and end of treatment (5 months)	Significant increase of physical function score in the exercise group; no significant changes in other scores of the scale for neither the exercise- nor the control group.

Low intensity cardiovascular exercise training

Koh 2010a	The Medical Outcomes Short Form (SF-36) questionnaire	Yes	Baseline and end of treatment (6 months)	Significant increase in the sub-score PF but no other sub-score in the intra-dialytic exercise group; and no change in any sub-scores in the control group.
Koh 2010b	The Medical Outcomes Short Form (SF-36) questionnaire	Yes	Baseline and end of treatment (6 months)	No significant increase in any of the sub-scores in the home-based exercise group, and no change in any sub-scores in the control group.
Parsons 2004	The Medical Outcomes Short Form (SF-36) questionnaire ³	Yes	Baseline and end of treatment (2 months)	No significant difference in any score between the exercise- and control group or within a given group on any of the subscales.

Unknown intensity cardiovascular exercise training

Jong 2004	The Medical Outcomes Short Form (SF-36) questionnaire ³	Yes	Baseline and end of treatment (3 months)	Significant increase of physical function score in the exercise group; the remaining subscales were not used.
Kouidi 2005	The Quality of Life Index (QLI) ² Life Satisfactory Index, (LSI)	Yes Unclear	Baseline and end of treatment (10 months)	Significant increase in total score QLI and LSI in the exercise group, whereas no change in the control group. No change in mental sub-scores but a significant increase of physical function score (SF-36) in the exercise group; and no changes in the control group.

(Continued)

 The Medical Outcomes Short Form (SF-36) questionnaire³

Yes

High intensity resistance training

Chen 2010

The Medical Outcomes Short Form (SF-36) questionnaire

Baseline and end of treatment (6 months)

Significant increase of physical function scores in the exercise group. No significant change in the mental component. The remaining subscales were not used. No significant changes in the control group.

Johansen 2006

The Medical Outcomes Short Form (SF-36) questionnaire

Yes

Baseline and end of treatment (3 months)

 Significant increase in self-reported physical functioning on the PF-scale following 3 months regular exercise ($p=0.03$).

Segura-Orti 2009

The Medical Outcomes Short Form (SF-36) questionnaire

Yes

Baseline and end of treatment (6 months)

No significant change in any of the subscales neither in the exercise group nor the control group.

PEAK Study 2005

The Medical Outcomes Short Form (SF-36) questionnaire

Yes

Baseline and end of treatment (3 months)

Significant increase of physical function- and vitality scores in the exercise group. The remaining subscales were not used. No significant changes in the control group.

High intensity mixed cardiovascular and resistance training

DePaul 2002

The Medical Outcomes Short Form (SF-36) questionnaire

Yes

Baseline, end of treatment (3 months) and for an additional 5 months without intervention

No significant difference in any score between the exercise- and control group

Fitts 1999

Sickness Impact Profile (SIP)

Baseline, end of treatment (6 months) and for an additional 6 months without intervention

Significant increase of total score and physical score in pre-uraemic exercise group versus control group. No significant changes in psychosocial score. No change in total score or sub-scores in dialysis exercise- and control group.

Molsted 2004

The Medical Outcomes Short Form (SF-36) questionnaire

Yes

Baseline and end of treatment (5 months)

Significant improvement in physical function, bodily pain and physical component scale; no significant changes in the other scores of the scale in the exercise group. No changes in the control group.

Ouzouni 2009

The Medical Outcomes Short Form (SF-36) questionnaire

Yes

Baseline and end of treatment (10 months)

Significant improvement in physical component scale and mental component scale; no significant changes in the other scores of the scales in the exercise group. No changes in the control group.

Low intensity mixed cardiovascular and resistance training

(Continued)

van Vilsteren 2005	The Dutch Version of the MOS Short-Form General Health Survey (RAND-36)	Yes	Baseline and end of treatment (3 months)	Significant improvement in the sub-scores vitality, general health perception, and health change in the exercise group. No significant changes in the other scores of the scale. No changes in the control group.
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- ⁽¹⁾ A codified scale for standard assessment of health-related quality of life and whose validity has been tested in adults with CKD
- ⁽²⁾ A disease specific scale
- ⁽³⁾ A generic scale

CONTRIBUTIONS OF AUTHORS

- Susanne Heiwe: designed the systematic review and meta-analysis study, co-ordinated the review process, searched for studies, screened the search results, assessed the studies for quality, extracted data, analysed data, developed the systematic review and meta-analysis, and has had the primary role in writing the manuscript
- Stefan H Jacobson: screened search results, assessed the quality of studies, extracted data, and reviewed the final manuscript.

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