Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis

CRD summary
This review found that regular aerobic exercise (900 kcal of energy expenditure or 120 minutes of exercise per week) increased high-density lipoprotein cholesterol (HDL-C) level. Exercise was more effective for those with initially high total cholesterol levels or a low body mass index. Whilst the overall conclusions are probably reliable, further research is needed to confirm findings on the influence of the patient or intervention characteristics on changes in HDL-C level.

Authors' objectives
To investigate the effect of exercise on serum high-density lipoprotein cholesterol (HDL-C) levels.

Searching
MEDLINE was searched from 1966 to 2005 for trials published in the English language. The search terms were briefly detailed in the paper. Reference lists of previous articles on the topic were also examined.

Study selection

Specific interventions included in the review
To be included, trials needed to compare aerobic exercise training of at least 8 weeks' duration with no exercise. Aerobic exercise was defined as rhythmic and repeated movements of the same large muscle groups (e.g. walking, cycling or continuous swimming) for at least 15 minutes. Studies including a cointervention such as a dietary intervention were excluded. The mean intervention duration in the included studies was 27.4 weeks.

Participants included in the review
To be included, trials needed to be of adults (mean age more than 20 years). Studies of participants with specific medical problems needing treatment with diet or drugs that would influence the effect of exercise were excluded. In the included studies the mean age, where reported, ranged from 23 to 75 years.

Outcomes assessed in the review
To be included, HDL-C measurements needed to be taken at baseline and at the end of the intervention. Exercise volume, in terms of weekly energy expenditure (EE) and weekly exercise length, needed to be calculable.

How were decisions on the relevance of primary studies made?
The authors did not state how the studies were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The methodological quality of each trial was assessed using the Jadad tool, which includes items on randomisation, blinding, withdrawals and drop-outs. Two reviewers appear to have examined each article and resolved any discrepancies with a third reviewer.

Data extraction
Two reviewers independently extracted the data from each article and resolved any discrepancies with a third reviewer.

The relative intensity of exercise (proportion of exercise intensity to maximal aerobic capacity) was extracted directly
from the studies, or estimated from the exercise heart rate reserve or a proportion of exercise heart rate to maximum according to a published formula. Absolute intensity of exercise, expressed in metabolic equivalents (METs), was calculated by multiplying the relative intensity by the maximal aerobic capacity, or estimated using linear regression analysis. Exercise volume was assessed using both total weekly exercise length and total weekly estimated EE. Weekly EE was calculated by multiplying exercise intensity by weekly exercise length and body mass. The mean difference in HDL-C (MDHC) change after training between exercise and non-exercise control groups was calculated. The standard error was extracted directly from the studies, or calculated from standard deviation (SD), confidence intervals (CIs) or p-values for HDL-C effects within groups.

Methods of synthesis
How were the studies combined?
The studies were combined using meta-analysis. Each MDHC was weighted according to the inverse variance method. Weighted MDHCs were pooled using a random-effects model. Publication bias was assessed both graphically and statistically using established methods.

How were differences between studies investigated?
Statistical heterogeneity was explored using chi-squared analyses. To assess the minimal volume of exercise necessary to raise HDL-C levels significantly, the trials were stratified into 4 intervals by weekly estimated EE or weekly exercise length, and the results standardised using a z score. Meta-regression analyses, weighted according to exercise group size, were undertaken to assess the influence of the patient or intervention characteristics on changes in HDL-C level. One outlier study was excluded from the subgroup analyses.

Results of the review
Thirty-five randomised controlled trials (1,404 participants) were included.

The mean quality score was 1.5 (SD=0.5) out of 5. Twelve of 25 trials reported withdrawals and the reasons for withdrawal. Where reported, drop-outs ranged from 4 to 39%. None of the trials reported methods of randomisation. Statistical tests showed no evidence of publication bias.

The mean estimated relative intensity of aerobic exercise was 64.8% of maximal aerobic capacity and the mean estimated absolute intensity was 5.3 METs. The mean estimated weekly EE was 1,019 kcal/week.

The net change in HDL-C was small but statistically significant: 2.53 mg/dL (95% CI: 1.36, 3.70), 0.065 mmol/L (95% CI: 0.035, 0.096), (z=4.23, p<0.001).

The pooled MDHC was statistically significant for 21 trials with a weekly estimated EE of greater than 900 kcal (z=5.16, p<0.001), but not for 13 trials which did not exceed 900 kcal/week. The pooled MDHC was also statistically significant for 25 trials in which exercise length was more than 120 minutes (z=3.60, p<0.001), but not for 9 trials where exercise did not exceed 120 minutes.

In univariate analyses, exercise duration was the strongest predictor of MDHC, and each 10-minute increase in exercise duration corresponded to a net increase in HDL-C level of 1.4 mg/dL when the duration ranged from 23 to 74 minutes per session. The pooled MDHC was not statistically significant when exercise duration was 30 minutes or less per session. In multivariate analyses, controlling for weekly EE or exercise length, exercise duration was positively associated with MDHC. The MDHC was not associated with other exercise parameters such as frequency or absolute or relative intensity. Participants with a mean total cholesterol (TC) level of 220 mg/dL or greater and a mean body mass index (BMI) less than 28 had, on average, a 2.1 mg/dL larger net increase in HDL-C level than when the mean TC was less than 220 mg/dL and the mean BMI was 28 or greater; participants who were less obese or had a higher TC level responded better to exercise training. Age, gender, HDL-C level and aerobic capacity were not significant predictors of MDHC.

Authors' conclusions
Regular aerobic exercise modestly increases HDL-C level, but there appears to be a minimum exercise volume to gain a
significant increase in HDL-C level. Exercise duration per session was the most important aspect of the intervention. Exercise was more effective for those with initially high TC levels or a low BMI.

**CRD commentary**

The review question was defined in terms of the participants, interventions, outcomes and study design. The authors made efforts to exclude studies using cointerventions which might confound the results of the exercise training. Although only published material was included, publication bias was assessed and found not to be significant by the tests used. The review process included attempts to minimise bias, such as the use of two independent reviewers to extract the data. However, there were a few methodological issues. Searching was limited to one database and the checking of references. This, together with the fact that only English language articles were eligible, might have led to studies being missed. Study quality was assessed but the results of this did not appear to inform any subgroup analyses.

The overall conclusions on the effectiveness of exercise for increasing HDL-C levels are probably reliable. However, the results of meta-regression analyses, such as those conducted to explore the influence of the patient or intervention characteristics on changes in HDL-C level, would generally need to be confirmed in direct comparisons and to this end the authors suggest areas of further research.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that additional research is needed to determine the minimal exercise frequency required to modify HDL-C levels. Further research is also needed to assess the relationship between baseline HDL-C level and response to exercise training; to compare the expected reduction of cardiovascular risk between elevation of HDL-C level and improvement of aerobic fitness; to investigate ethnic or gender differences in increases in HDL-C level through exercise; to review the effectiveness of resistance training on improving HDL-C level; and to clarify the mechanism for greater effectiveness of exercise in the less obese and those with a higher TC level.

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