Physical activity for preventing and treating obesity-related dyslipoproteinemias

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Abstract


Purpose: The clinical trial data were reviewed on effects of physical activity on obesity-related dyslipoproteinemias (specifically low HDL-cholesterol (HDL-C), elevated triglycerides (TG), and high total and LDL-cholesterol (TC and LDL-C)) in adult men and women.

Methods: Effort was made to identify all randomized clinical trials (RCT), with exercise intervention programs of at least 4 months’ duration, which had lipoprotein outcomes. Those that had both an exercise only intervention and control groups or both a diet plus exercise and identical diet only intervention groups were reviewed. Tables were developed of baseline characteristics and weight and lipoprotein changes for aerobic exercise trials by body mass index: 1) < 25.0 kg·m⁻², 2) 25.0-29.9 kg·m⁻², and 3) ≥ 30.0 kg·m⁻² and for studies involving resistance exercise or increased energy expenditure from daily activities versus structured exercise programs.

Results: Very few RCT were found that specifically addressed the role of physical activity in preventing or treating obesity-related adverse lipoprotein levels. There was essentially no evidence found in lean or overweight men or women to support a specific role for exercise in improving undesirable lipoprotein levels; however, trial data strongly suggest that the addition of exercise to a hypocaloric, reduced-fat diet improves HDL-C and TG in men and women with generally desirable initial levels and reduces LDL-C in men and women with initially elevated LDL-C levels. The evidence is also reasonably strong that weight loss, including that achieved solely by exercise, improves HDL-C and TG in obese men, without reducing LDL-C, whereas it remains weak for women. There are also virtually no trial data to support a role for resistance exercise or an increase in daily living activities for improving obesity-related lipoproteins.

Conclusions: Current evidence from RCT is too limited to determine whether physical activity can raise low HDL-C or lower high TG or LDL-C levels in overweight and obese individuals.

The 1985 Panel for the National Institutes of Health (NIH) Consensus Development Conference on the Health Implications of Obesity recognized hypercholesterolemia as one of the adverse effects of obesity (18). In 1993, the second National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP-II) promoted weight loss to treat hyperlipidemia and low levels of high-density
lipoprotein cholesterol (HDL-C) in overweight patients (7). Subsequently, the Panel for the 1995 NIH Consensus Development Conference on Physical Activity and Cardiovascular Health concluded that exercise training of at least 12 wk duration results in beneficial changes in HDL-C (19) but stopped short of linking this to the loss of body fat that may accompany increased aerobic exercise. More recently, the Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity recommended weight loss to lower elevated levels of total cholesterol (TC), LDL-cholesterol (LDL-C), and triglycerides (TG), as well as to raise low levels of HDL-C, in overweight and obese persons with dyslipidemia (8). In addition, the Expert Panel concluded that physical activity, particularly when combined with dietary therapy, contributes to weight loss. The Expert Panel did not, however, evaluate the relationship between exercise-induced weight loss and lipoprotein changes or discuss a specific role for physical activity in preventing or treating lipoprotein disorders associated with obesity. The literature pertaining to these issues will be reviewed here.

Because of space limits, this review will be confined to randomized, controlled trials (RCT) that were designed to determine effects of increased physical activity on both weight and lipoproteins. This follows the evidence-based approach of the Expert Panel which recognized RCT as the best source of information (8). Therefore, the large number of epidemiological studies that have reported higher HDL-C and lower TG levels in individuals who self-selected a more physically active lifestyle, and who are generally much leaner than their sedentary counterparts (23,24,27,28,30), will not be discussed, nor will this paper review longitudinal studies which have reported significant relationships between physical activity level and weight and lipoprotein changes over time (16,23,24,30). Finally, this paper will not review the many elegantly designed metabolic and clinical studies designed to focus on the physiological effects of exercise on body composition and lipoprotein metabolism in highly controlled settings, which generally involve a small number of participants (22,24). An attempt is made to focus on RCT that are more likely to be generalizable to the millions of overweight and/or sedentary people who may be prescribed weight loss and/or increased physical activity to improve an adverse lipoprotein profile.

Tables 1-3 present RCT reporting both weight and lipoprotein effects of 4 months or longer of aerobic exercise training, with or without dietary change, in normal weight (mean body mass index (BMI) < 25.0 kg·m$^{-2}$ as the cut-point), overweight (BMI = 25.0-29.9 kg·m$^{-2}$), and obese (BMI > 30 kg·m$^{-2}$) individuals (8), respectively. Studies were included if they had an aerobic exercise and a control group or an aerobic exercise plus dietary change group and a group that made identical dietary changes, without the exercise component. The tables include the primary recruitment criteria, length of exercise training period, and mean baseline values for BMI (or weight, if neither BMI nor height were presented, using an estimated height of $\leq 178$ cm, for men, and $\leq 166$ cm, for women, to categorize such studies) and HDL-C, LDL-C, TG, and TC, generally estimated by averaging mean values for individual treatment groups, with an adjustment for number of subjects per group, and treatment group changes for HDL-C, LDL-C, TG, and TC, with statistical information on key between group comparisons. Despite an attempt to include all relevant trials, omissions are regrettably likely, and the reader should incorporate such trials into his/her perspective, as he/she becomes aware of them.
### Table 1. Randomized trials of lipoprotein effects of aerobic exercise in individuals with mean BMI < 25.0 kg·m⁻².

<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions: Treatment Groups</th>
<th>N post (baseline); Sex; Basic Key</th>
<th>Inclusion criteria</th>
<th>Training Duration</th>
<th>Weight Change (kg) (BMI)</th>
<th>HDL-C (mmol·L⁻¹)</th>
<th>LDL-C (mmol·L⁻¹)</th>
<th>TG (mmol·L⁻¹)</th>
<th>TC (mmol·L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huttunen et al., 1979 (11) 1: Aerobic exercise 2: Control</td>
<td>90 (100); male; age 40–45 yr</td>
<td>4 months</td>
<td>Wt: 79.2</td>
<td>1: 0.9</td>
<td>1: 0.14</td>
<td>1: 0.45</td>
<td>1: 0.24</td>
<td>1: 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>Wood et al., 1983 (29) 1: Aerobic exercise 2: Control</td>
<td>78 (81); male; age 30–55 yr; &lt;140% ideal wt; sedentary</td>
<td>9–12 months</td>
<td>BMI: 24.9</td>
<td>1: 1.9</td>
<td>1: 0.05</td>
<td>1: 0.13</td>
<td>1: 0.09</td>
<td>1: 0.13</td>
<td>NS</td>
</tr>
<tr>
<td>Leighton et al., 1990 (15) 1: Aerobic exercise + diet (counseling on low-fat) 2: Diet only (same)</td>
<td>51 (17 + 49); male and female; age ≥ 20 yr; high TC (&gt; age-spec. NIH, 1985)</td>
<td>26 wk</td>
<td>BMI: 23.7</td>
<td>1: 1.1</td>
<td>1: 0.06</td>
<td>1: 0.00</td>
<td>1: 0.11</td>
<td>1: 0.23</td>
<td>NS</td>
</tr>
<tr>
<td>Duncan et al., 1991 (5) 1: Aerobic walking (6.0 km·h⁻¹) 2: Brisk walking (6.4 km·h⁻¹) 3: Strolling (4.8 km·h⁻¹) 4: Control</td>
<td>50 (100); female; premenopausal; age 29–40 yr; sedentary</td>
<td>24 wk</td>
<td>BMI: 24.4</td>
<td>1: −0.5</td>
<td>1: 0.02</td>
<td>1: 0.65</td>
<td>1: 0.32</td>
<td>1: 0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Singh et al., 1990 (21) 1: Aerobic exercise + low-fat diet plus vegetables, fruits, and grains 2: Low-fat diet only</td>
<td>457 (419 + 44); male and female; age 25–65 yr; with ≥1 CHD risk factor (or &gt;110% sedentary, CHD)</td>
<td>24 wk</td>
<td>BMI: 24.3</td>
<td>1: −0.5</td>
<td>1: 0.02</td>
<td>1: 0.65</td>
<td>1: 0.32</td>
<td>1: 0.03</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Mean estimated from baseline means reported for individual treatment groups.  
* Data interpreted from graphs.  
* Values calculated from percent change from baseline.

Table 1. Randomized trials of lipoprotein effects of aerobic exercise in individuals with mean BMI < 25.0 kg·m⁻².  
* Mean estimated from baseline means reported for individual treatment groups.  
* Data interpreted from graphs.  
* Values calculated from percent change from baseline.
<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions: Treatment Groups</th>
<th>n (post (baseline); Sec. Baseline (key) Inclusion criteria)</th>
<th>Training Duration</th>
<th>Mean* Baseline BMI (Wt [BMI] and Lipids</th>
<th>Weight Change (kg) [BMI]</th>
<th>HDL-C (mmol-L(^{-1}))</th>
<th>LDL-C (mmol-L(^{-1}))</th>
<th>TG</th>
<th>TC</th>
</tr>
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<tbody>
<tr>
<td>Wood et al., 1991 (32)</td>
<td>1: Aerobic exercise + hypocaloric low-fat diet&lt;br&gt;2: Hypocaloric low-fat diet&lt;br&gt;3: Control</td>
<td>112 (132); female premenopausal age 25-49 yr BMI = 24-30 kg·m(^{-2})</td>
<td>9-12 months</td>
<td>BMI: 27.9</td>
<td>1: -5.1 1: +0.2 1: -0.29 1: -0.02 1: -0.28</td>
<td>HDL-C: 1.5 2: -4.1 2: -0.15 2: -0.28 2: +0.91 2: -0.39</td>
<td>LDL-C: 3.1 3: +1.3 3: -0.05 3: -0.63 3: +0.13 3: -0.03</td>
<td>TC: 5.0 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS</td>
<td>NS</td>
</tr>
<tr>
<td>King et al., 1991 (14)</td>
<td>1: Aerobic exercise-higher intensity, group-based&lt;br&gt;2: Aerobic exercise-higher intensity, home-based&lt;br&gt;3: Aerobic exercise-lower intensity, home-based&lt;br&gt;4: Control</td>
<td>167 (197); male age 55-65 yr sedentary</td>
<td>19-12 months</td>
<td>BMI: 29.6</td>
<td>1: -1.9 1: -0.1 1: -0.13 1: -0.06 1: -0.06</td>
<td>HLD L: 1.2 2: -0.2 2: 0.03 2: 0.19 2: -0.19</td>
<td>LDL L: 3.9 2: -0.9 2: 0.17 2: -0.16 2: 0.12</td>
<td>TC: 4.0 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Svendsen et al., 1993 (29)</td>
<td>1: Hypocaloric low-fat (NUT) diet + aerobic and anaerobic exercise&lt;br&gt;2: Hypocaloric NUT diet&lt;br&gt;3: Control</td>
<td>118 (121); female post-menopausal age 45-54 yr BMI = 25 kg·m(^{-2})</td>
<td>12 wk</td>
<td>BMI: 25.3</td>
<td>1: -1.0 1: -0.1 1: -0.04 1: -0.3 1: -0.13</td>
<td>HLD L: 1.4 2: -0.3 2: -0.1 2: -0.03 2: -0.10</td>
<td>LDL L: 4.3 2: +0.6 2: 0.17 2: 0.12 2: 0.06</td>
<td>TC: 6.3 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Holtmann et al., 1993 (10)</td>
<td>1: Aerobic exercise 2: Low-fat diet&lt;br&gt;3: Aerobic exercise + low-fat diet&lt;br&gt;4: Control</td>
<td>157 (158); male age 35-65 yr TC: 5.2-</td>
<td>6 months</td>
<td>BMI: 27.5</td>
<td>1: -0.1 1: +0.3 1: +0.01 1: -0.01 1: -0.12</td>
<td>HLD L: 1.4 2: -0.3 2: -0.1 2: -0.03 2: -0.10</td>
<td>LDL L: 4.3 2: +0.6 2: 0.17 2: 0.12 2: 0.06</td>
<td>TC: 5.3 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Andersen et al., 1995 (4)</td>
<td>1: Aerobic exercise&lt;br&gt;2: Hypocaloric diet&lt;br&gt;3: Aerobic exercise + diet&lt;br&gt;4: Control</td>
<td>209 (198 + 21); male and female; age 41-50 yr HLD L 2: 1.2 LDT L 3: 2.7-7.7 mmol·L(^{-1}) BMI = 24 kg·m(^{-2}), Hgb sedentary</td>
<td>12 months</td>
<td>BMI: 28.8</td>
<td>Mean BP tertiles* 1: -0.03 1: +0.03 1: +0.03 1: -0.03 1: +0.03</td>
<td>Mean BP tertiles vs control* 1: -0.03 1: +0.03 1: +0.03 1: -0.03 1: +0.03</td>
<td>TC: 6.3 1 vs 4 NS 1 vs 4 NS 1 vs 4 NS 1 vs 4 NS 1 vs 4 NS</td>
<td>NS</td>
<td></td>
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<tr>
<td>Stefanick et al., 1998 (25)</td>
<td>1: Aerobic exercise&lt;br&gt;2: Low-fat diet (NCEP Step II)&lt;br&gt;3: Aerobic exercise + low-fat (NCEP Step II)&lt;br&gt;4: Control</td>
<td>190 (197); male age 35-64 yr</td>
<td>9-12 months</td>
<td>BMI: 27.0</td>
<td>1: -0.6 1: +0.0 1: -0.09 1: -0.15 1: -0.13</td>
<td>HLD L: 1.4 2: -0.2 2: -0.07 2: -0.28 2: -0.07 2: -0.34</td>
<td>LDL L: 4.0 3: -0.2 3: -0.01 3: -0.52 3: -0.08 3: -0.30</td>
<td>TC: 6.1 1 vs 4 NS 1 vs 4 NS 1 vs 4 NS 1 vs 4 NS 1 vs 4 NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Mean estimated from baseline means reported for individual treatment groups. Overall mean calculated from net-differences between treatment group and control for each diastolic blood pressure tertile. Overall mean calculated from net-differences between treatment group and control for each diastolic blood pressure tertile. Overall mean calculated from net-differences between treatment group and control for each diastolic blood pressure tertile.
Table 3. Randomized trials of lipoprotein effects of aerobic exercise in individuals with BMI ≥30 kg·m⁻².

<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions; Treatment Groups</th>
<th>N post (baseline)</th>
<th>Sex, Basic (key) Inclusion criteria</th>
<th>Training Duration</th>
<th>Mean² Initial BMI and Lipids (kg·m⁻²)</th>
<th>Weight Change (kg)</th>
<th>HDL-C (mmol·L⁻¹)</th>
<th>LDL-C (mmol·L⁻¹)</th>
<th>TC (mmol·L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wood et al., 1988 (31)</td>
<td>1: Aerobic exercise 2: Hypocarotinic diet (no change in % fat calories) 3: Control</td>
<td>131 (155) male age 30-59 yr 120-160% &quot;ideal&quot; weight, sedentary</td>
<td>9-12 months</td>
<td>BMI: 30.7 1: -4.0 1: +0.11 1: +0.25 1: +0.16 1: -0.25</td>
<td>HDL: 1.1 2: -7.2 2: +0.12 2: -0.21 2: -0.27 2: -0.36</td>
<td>LDL: 3.8 3: -0.06 3: -0.02 3: +0.21 3: +0.08 3: -0.23</td>
<td>TC: 5.7 1: +0.5 2: vs 3 1: vs 5 NS 1: +0.2 3 1: vs 5 NS</td>
<td>P &lt; 0.001 P &lt; 0.01 P &lt; 0.001 1 vs 2 NS I vs 2</td>
<td></td>
</tr>
<tr>
<td>Wood et al., 1991 (32)</td>
<td>1: Aerobic exercise + hypocarotinic low-fat diet 2: Hypocarotinic low-fat diet 3: Control</td>
<td>119 (133) male age 25-49 yr BMI = 26-34 kg·m⁻²; sedentary</td>
<td>9-12 months</td>
<td>BMI: 30.7 1: -6.7 1: +0.18 1: -0.27 1: -0.48 1: -0.38</td>
<td>HDL: 1.1 2: -5.1 2: +0.02 2: -0.59 2: -0.12 2: -0.42</td>
<td>LDL: 3.6 3: -1.7 3: -0.05 3: -0.20 3: -0.19 3: -0.14</td>
<td>TC: 1.4 1 vs 2 1 vs 3 NS I vs 2 NS</td>
<td>P &lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Katz et al., 1995 (13)</td>
<td>1: Aerobic exercise without weight change 2: Hypocarotinic diet 3: Control</td>
<td>111 (170) male age 46-80 yr 120-160% &quot;ideal&quot; body weight, sedentary</td>
<td>9 months</td>
<td>BMI: 30.2 1: -0.5 1: +0.05 1: -0.12 1: -0.13 1: -0.09</td>
<td>HDL: 0.9 2: -0.5 2: +0.11 2: -0.13 2: -0.27 2: -0.18</td>
<td>LDL: 3.1 3: +0.2 3: +0.03 3: +0.15 3: +0.13 3: +0.29</td>
<td>TC: 1.5 1 vs 2 NS 1 vs 3 NS 1 vs 3 1 vs 3 NS 1 vs 3</td>
<td>P &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Ready et al., 1995 (20)</td>
<td>1: Aerobic exercise (walking) 2: Control</td>
<td>25 (40); female post-menopausal TC: 5.9-8.0 and TG &lt;4.2 mmol·L⁻¹ not active</td>
<td>6 months</td>
<td>BMI: 30.0 1: -1.9 1: 0.00 1: -0.19 1: -0.12 1: +0.30</td>
<td>HDL: 1.3 2: -0.6 2: -0.07 2: +0.08 2: +0.17 2: +0.01</td>
<td>LDL: 4.7 3: +0.0 3: +0.05 3: -0.15 3: +0.15 3: +0.15</td>
<td>TC: 1.8 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS 1 vs 2 NS</td>
<td>P &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Fox et al., 1996 (9)</td>
<td>1: Aerobic + resistance exercise (200 kcal·d⁻¹) + hypocarotinic diet (500 kcal·d⁻¹) 2: Hypocarotinic diet (500 kcal·d⁻¹) 3: Hypocarotinic diet (&lt;700 kcal·d⁻¹)</td>
<td>40 (46); female post-menopausal for &lt;5 yr age ≥50 yr 120-140% &quot;ideal&quot; weight</td>
<td>24 wk</td>
<td>BMI: 30.3 1: -7.1 1: -0.06 1: -0.11 1: -0.08</td>
<td>HDL: 1.6 2: -6.6 2: -0.15 2: +0.13 2: -0.12</td>
<td>LDL: 3.8 3: +0.8 3: -0.08 3: +0.06 3: -0.03</td>
<td>TC: 1.6 5: NS NS NS NS</td>
<td>P = 0.05</td>
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</table>

²Mean estimated form baseline means reported for individual treatment groups.

The tables are not segregated by lipoprotein profile; however, the reader should note that the NCEP-ATP II guidelines (2) for persons without coronary heart disease (CHD) specify the following levels for high-risk lipoproteins: TC ≥ 6.2 mmol·L⁻¹ (≥ 240 mg·dL⁻¹); LDL-C ≥ 0.9 mmol·L⁻¹ (<35 mg·dL⁻¹); and HDL-C ≥ 1.1 mmol·L⁻¹ (160 mg·dL⁻¹), for persons with fewer than two risk factors, and ≥ 3.4 mmol·L⁻¹ (130 mg·dL⁻¹), in the presence of two or more risk factors. Risk factors included in the 1993 NCEP algorithms were: age ≥ 45 for men and ≥ 55 for women; current smoking; blood pressure = 140/90 mm Hg; low HDL-C; diabetes mellitus; and family history of premature CHD in a first degree relative. Neither sedentary status nor obesity were included as risk factors in NCEP ATP-II. HDL-C ≥ 1.6 mmol·L⁻¹ (≥ 60 mg·dL⁻¹) is considered a negative risk factor. Triglycerides of 2.3-4.6 mmol (200-399 mg·dL⁻¹) are considered borderline high, with levels <2.3 being normal and >4.6 being high.

**RANDOMIZED TRIALS OF LIPOPROTEIN EFFECTS OF EXERCISE IN NORMAL WEIGHT INDIVIDUALS**

Table 1 presents five trials conducted in men (11,29), women (5) or both, combined (15,21), who spanned a range of body weights, from lean to obese, with a mean BMI falling in the normal weight range (<25 kg·m²). Three of the studies involved subjects with high-risk mean TC and LDL-C levels (11,15,21). Huttunen et al. (11) found no effect of 4 months of individualized aerobic exercise (walking, jogging, swimming, skiing, or cycling), compared with controls, on weight or TC or LDL-C.
in 90 men with high baseline TC and LDL-C levels; however, HDL-C was significantly increased and TG levels were decreased in the exercisers.

In contrast, Wood et al. (29) reported a significant, albeit modest, weight loss (2.5 kg; \(P < 0.01\)) and reduction in percent body fat by hydrostatic weighing (3.8%; \(P < 0.001\)), in exercisers versus controls, in a study of 78 predominantly normolipidemic men who were assigned to 9-12 months of either control (\(N = 32\)) or 3 d·wk\(^{-1}\) of supervised walking and jogging (\(N = 46\)), with three choices of training distance and intensity on any given day, based on selection of group leader. There were, however, no differences between groups in HDL-C or TG changes, nor in TC, LDL-C, and apolipoprotein AI, AIi, or B changes. Secondary analyses, which separated the exercisers into four treatment-dose groups (based on weekly mileage), found significant treatment effects for HDL-C and LDL-C. In exercisers who averaged at least 12.9 km (8 miles) per week, HDL-C increased by 0.11 mmol\(\cdot\)L\(^{-1}\) (4.4 mg\(\cdot\)dL\(^{-1}\); \(P < 0.05\)) compared with controls. Further exploratory analyses showed that the weekly mileage correlated significantly with body fat changes, which were also significantly related to HDL-C changes.

Leighton et al. (15) reported data from 51 of 17 men and 49 women with elevated TC levels who were randomized to 26 wk of diet counseling aimed at reducing total and saturated fat and cholesterol intake, with or without a supervised exercise program, which consisted of a variety of aerobic exercises at 80% heart rate reserve (stationary bicycling, walking, jogging, stair climbing, or rowing). Although exercising dieters lost 3 kg (\(P < 0.001\)) and controls did not change weight, differences between groups were not reported; however, it was reported that there were no differences in HDL-C, LDL-C, TG, or TC between groups.

Duncan et al. (5) reported results from 59 of 102 premenopausal women with low-risk lipoprotein profiles, who were assigned to no exercise or to 5 d·wk\(^{-1}\) of 4.8 km·d\(^{-1}\) of walking at one of three speeds, 4.8 km·h\(^{-1}\) (strollers, S), 6.4 km·h\(^{-1}\) (brisk walkers, BW), or 8.0 km·h\(^{-1}\) (aerobic walkers, AW). Maximal oxygen uptake increased significantly (\(P < 0.001\)) in walkers versus controls, and in a dose-response manner (AW > BW > S), with differences between aerobic walkers and strollers reaching significance (\(P < 0.001\)). Neither weight changes (gain) or HDL-C increases from baseline differed between any of the exercise groups and control or other walking groups, nor were there any significant differences between groups for LDL-C, TG, or TC.

Singh et al. (21) found significant reductions in TC and LDL-C in a study involving over 450 South Asian men (90% of sample) and women who were assigned to a reduced saturated fat and cholesterol diet and moderate exercise (brisk walking and spot running) compared to diet only. This study was confounded, however, by having additional dietary goals of decreasing total energy intake and increasing the intake of vegetables, fruits, grains, and nuts in the exercising diet group. There was significant weight loss and TG reduction in the exercise plus complex diet group versus diet only; however, HDL-C changes did not differ between groups (21).

In summary, only one of the five trials in normal weight individuals showed a significant improvement in HDL-C and TG with exercise training and these differences were in men with high TC and LDL-C, but normal HDL-C and TG levels (11). The only trial that showed an improvement in LDL-C or TC with exercise involved an additional dietary component that differed from the diet only comparison group (21).

Evidence statement. TOP

The evidence is weak to support a role for aerobic exercise training in improving an adverse lipoprotein profile in normal weight men or women, largely due to an absence of clinical trials in lean individuals with low HDL-C, high TG, and/or elevated LDL-C or total cholesterol (Category 2).
Table 2 presents six large trials conducted in men (3,10,13,25) and premenopausal (32) and postmenopausal (13,25,26) women with a mean BMI of 25.0-29.9 kg·m⁻². The 132 overweight, premenopausal women randomized into the second Stanford Weight Control Project had relatively low-risk lipoproteins, even though their percent body fat was 35.7%, based on hydrostatic weighing and their abdomen-to-hip ratio was 0.87 (32). In these women, aerobic exercise (brisk walking), combined with a hypocaloric, low-fat diet, did not result in greater weight loss than the diet alone, although weight loss was significant ($P < 0.001$) in both dieters (5.4 kg) and dieting exercises (6.4 kg) compared with controls, as was fat weight loss (4.5 kg and 6.0 kg, respectively), which was also not significantly different between intervention groups. HDL-C and HDL₂-C were, however, significantly increased in diet + exercise women versus diet only women (0.17 mmol·L⁻¹ and 0.19 mmol·L⁻¹, respectively; $P < 0.01$), partially due to a decrease in HDL-C in women assigned to the low-fat diet without exercise, compared with controls (-0.10 mmol·L⁻¹; NS), whereas HDL-C increased in diet + exercise women versus controls (0.7 mmol·L⁻¹; NS). Diet only women also decreased apolipoprotein A-I versus control (-8.8 mg·dL⁻¹; $P < 0.05$), whereas this was increased in diet + exercise (1.9 mg·dL⁻¹; NS). Diet + exercise women also decreased TG versus control (-0.15 mmol·L⁻¹; $P < 0.05$), but there were no significant differences between dieters and dieting exercisers in reductions in TC or LDL-C, which were significantly reduced in both groups, versus controls ($P < 0.05$), as was apolipoprotein B (-5.8 and -6.0 mg·dL⁻¹; $P < 0.01$). Neither the LDL-C to HDL-C nor apolipoprotein B to A-I ratios were improved in dieters compared with controls, whereas both ratios were reduced in dieting exercisers ($P < 0.05$). These results demonstrate that exercise can offset the HDL-C-lowering effect of a low-fat diet in overweight, premenopausal women who have low-risk lipoproteins; however, there seems to be no further benefit to the LDL-C- or TC-lowering effect of the low-fat diet in such women.

The Stanford-Sunnyvale Health Improvement Program (SSHIP) trial (13) randomly assigned 197 men and 160 postmenopausal women, aged 50-65 yr, to control or one of three 1-yr exercise groups: high-intensity, group-based aerobic exercise, involving three 40-min endurance training sessions per week at 73-88% of peak treadmill heart rate; high-intensity, home-based aerobic exercise, the same prescription, but performed by individuals from their home; and low-intensity, home-based aerobic exercise, five 30-min sessions per week at 60-73% maximum heart rate. The women had mean LDL-C levels of 4.3 mmol·L⁻¹, placing them at elevated CHD risk, whereas the men had LDL-C of 3.9 mmol·L⁻¹. Despite significant improvements in all three exercise groups in $\dot{V}O_{2max}$, averaging 5% increase compared with controls, there were no significant weight or body composition (by hydrostatic weighing) changes or changes in any of the lipid factors: HDL-C, LDL-C, TG or TC. At the end of the 1-yr, controlled trial, men and women in the three exercise groups were encouraged to continue their originally assigned exercise prescriptions for a 2nd yr; however, the controls were offered an exercise program and discontinued from the trial (14). At the end of this year, small, but significant HDL-C increases were reported within both home-based groups (sexes combined) compared with baseline values, particularly in the lower-intensity group, whose prescription required more frequent exercise sessions per week; however, there were no significant differences between groups. HDL-C increases were associated with decreases in waist-to-hip ratio, in both sexes ($P < 0.04$).

Svendsen et al. (26) randomized 121 postmenopausal women with a BMI ≥ 25 kg·m⁻² and a high mean TC and LDL-C levels at baseline who were recruited to control or to a special low-fat, hypocaloric formula diet with or without a 12-wk aerobic exercise program (bicycling, stair walking, or treadmill running) combined with resistance weight training. There were no significant differences in weight or lipid changes between women assigned to diet only versus diet plus exercise, although both intervention groups lost significant weight and improved LDL-C, TG, and TC compared with control. Neither group changed HDL-C compared with control.
Hellenius et al. (10) randomized 158 men with high initial TC levels to one of four groups: aerobic exercise (walking, jogging, etc.), a reduced-fat diet (NCEP Step 1, i.e., total fat < 30% of calories, saturated fat < 10%, monounsaturated fat 10-15%, complex carbohydrates, 50-60%, and cholesterol < 300 mg·d⁻¹; 7), aerobic exercise + the diet, or control for 6 months. All three intervention groups lost significant weight compared with control, but there were no differences among intervention groups; however, the dieting exercisers lost more fat weight (1.8 kg) than diet only, who, in turn, lost 1.2 kg lean weight, whereas dieting exercisers lost none (P < 0.05 vs dieters). Despite considerable weight loss in the diet and diet + exercise groups, HDL-C changes did not differ from controls; however, TG, TC, and LDL-C decreased in both dieters and dieting exercisers versus controls (P < 0.001) but did not differ between the weight loss groups. Therefore, the addition of aerobic and anaerobic exercise to a weight-reducing diet produced no greater lipoprotein changes than that seen with the diet alone.

The Oslo Diet and Exercise Study (ODES) was designed to investigate exercise and diet effects on blood pressure in normotensives and mild hypertensives (3). Weight changes are presented by diastolic blood pressure (DBP) tertiles (<84, 84-91, >91 mm Hg) for each treatment group, rather than by treatment assignment, requiring some manipulation of the data to estimate an overall mean for each treatment group. Weight loss, versus control, was significant for diet only and diet + aerobic exercise, but not for exercise only; and weight loss did not appear to differ between diet only and diet + exercise. The lipid data are presented as net differences between treatment group and control within each tertile, and significant net differences are represented by equal signs of confidence limits. Values presented in Table 2 were estimated by adding reported means for each DBP tertile within a treatment group and dividing by 3. Although triglycerides, HDL-C, and TC are reported to be significantly and favorably improved in all treatment groups, presumably versus control, there appear to be no differences between intervention groups.

The Stanford Diet and Exercise for Elevated Risk (DEER) trial (25) investigated the effects of aerobic exercise (walking, jogging), a reduced-fat diet (NCEP Step 2, i.e., total fat < 30% of calories, saturated fat < 7%, and cholesterol < 200 mg·d⁻¹; 7), aerobic exercise + the diet, or control for 9-12 months on the lipoprotein profile of 197 men and 180 postmenopausal women who were recruited to have both low HDL-C and elevated LDL-C levels. Total and fat weight losses were significant in dieters and dieting exercisers in both sexes compared with controls but did not differ between diet only and diet + exercise or between exercise only and control in either sex. In DEER men, dieters lost a mean of 3.3 kg (2.1 kg fat weight), and dieting exercisers lost 4.7 kg (3.5 kg fat weight) compared with controls (P < 0.001), whereas weight loss in exercisers (1.2 kg, 1.0 kg fat weight) was not significant. Lean mass loss did not differ between dieters or dieting exercisers and control men but was significantly greater in both dieting groups compared with exercise only (1.3 kg for both). In DEER women, dieters lost a mean of 3.5 kg and dieting exercisers lost 3.9 kg compared with controls, whereas weight loss in exercisers (1.2 kg) was not significant. Lean mass losses were minimal and did not differ between groups. It is worth noting that although changes in caloric intake did not differ between exercise only and control groups, both exercise men and women tended to increase daily intake by about 100 kcal·d⁻¹, based on multiple unannounced diet recalls, which totaled 700 kcal·wk⁻¹, during which they were expending approximately 900-1000 kcal·wk⁻¹ in walking and jogging.

HDL-C changes did not differ among DEER treatment groups in men or women (25); therefore, neither the modest weight loss achieved by the NCEP Step 2 diet, nor exercise, alone or combined with the diet, increased HDL-C in overweight men or women who would be encouraged to adopt these lifestyle changes to improve their lipoprotein profile. It is worth noting that HDL-C was more likely to be increased in the exercise only groups and that weight loss, particularly body fat loss, was strongly correlated with HDL-C increases in both exercise only men and women. In addition, there was a significant negative effect of assignment to the low-fat diet on HDL-C. Greater weight loss than that achieved in this study may be needed to overcome the HDL-C-lowering effect of the low-fat diet.
Compared with controls, LDL-C reductions were not significant in DEER men or women who adopted the NCEP Step 2 diet without increasing activity level or in men or women who increased their exercise level without altering their diet; however, significant LDL-C reductions were seen in both men and women assigned to the diet plus aerobic exercise (25). Whether slightly greater weight loss in the diet + exercise group played a role is unclear; however, this finding provides strong support for the addition of exercise, whatever its role on weight loss, for the management of lipoproteins.

In summary, none of these major trials of overweight men and women showed any benefit of aerobic exercise alone, compared with control, or of the addition of aerobic exercise to a low-fat diet, compared to the diet alone, on HDL-C, LDL-C, TG, or TC; however, the combination of diet and aerobic exercise resulted in significant lipoprotein improvements compared with controls in three of four trials that examined this question. Furthermore, a low-fat diet alone failed to reduce LDL-C in men (10,25) or postmenopausal women (25) who had high LDL-C levels; however, the addition of exercise to the diet was effective in lowering LDL-C in both sexes in a trial that involved men and women who also had low HDL-C (25). Finally, only one of these trials showed significant weight loss with aerobic exercise alone (10); none showed greater weight loss by adding exercise to diet versus diet only, whereas this combination resulted in significant weight loss versus control in all four trials which examined this question.

Evidence statement. TOP

Aerobic exercise training is unlikely to improve the lipoprotein profile in overweight men or women, unless it is combined with a hypocaloric diet; however, if the caloric reduction is achieved primarily by reducing saturated fat, benefits to HDL-C are likely to be reduced or eliminated, whereas improvements to LDL-C will be improved (Category 1). The addition of exercise to a weight-reducing and/or reduced-fat diet produces only a modest benefit to HDL-C, TG, and/or LDL-C compared with what is achieved by the diet alone (Category 1).

RANDOMIZED TRIALS OF LIPOPROTEIN EFFECTS OF EXERCISE IN OBESE (BMI ≥ 30 kg·m-2) MEN AND WOMEN TOP

Table 3 presents three relatively large exercise training trials of obese men (12,31,32), one of which involves men with low HDL-C, but who also have low-risk LDL-C and TC levels (12), and two medium-sized trials of obese postmenopausal women (9,20), one of which has women with high TC levels (20). No other major trials were found; therefore, data on the effects of exercise in obese individuals with adverse lipoproteins are extremely limited, particularly in premenopausal women.

The first Stanford Weight Control Project, SWCP-I (31), involving men recruited to be 20-60% above ideal body weight, was designed to test whether weight loss by aerobic exercise (walking, jogging), with diet composition and caloric intake held constant, differed from weight loss by caloric restriction, with no change in diet composition or activity level, in its effects on HDL-C and other lipoproteins. Compared with controls, total and fat weight losses were significantly greater (P < 0.001) in both dieters (-7.8 kg and -5.6 kg, respectively) and exercisers (-4.6 kg and -3.8 kg); whereas, lean mass loss was greater only in dieters (-2.1 kg; P < 0.001), who lost more lean weight than exercisers (-0.7 kg; P < 0.01). Fat weight loss did not differ between dieters and exercisers, whereas dieters lost significantly more total weight than exercisers (P < 0.05). HDL-C was elevated in both dieters (0.11 mmol·L-1) and exercisers (0.12 mmol·L-1) compared with controls (P < 0.01), whereas TG was reduced (-0.27 and -0.16 mmol·L-1; P < 0.05), but these changes did not differ between the two weight loss groups nor did LDL-C changes, which were no different from control for either weight loss group. Thus, weight loss achieved by caloric restriction alone, with no change in the percent of calories from fat, or by exercise with no dietary changes, improved HDL-C and TG levels but not LDL-C, and there was no difference with weight loss by exercise or caloric restriction. This study did demonstrate that exercise was effective in producing weight loss in obese men,
provided attention was given to preventing dietary changes (which was generally a plea to prevent increasing calories, as opposed to decreasing food intake) and that exercise-induced weight loss was effective in raising HDL-C and reducing TG in such men.

The second Stanford Weight Control Project, SWCP-II (32), compared aerobic exercise (walking, jogging) combined with a low-fat diet (NCEP Step 1; 7) with the diet only and controls in 132 men, aged 25-49 yr, who were recruited to have a BMI of 28-34 kg·m⁻². [These men had a mean of 28.2% body fat, by hydrostatic weighing compared with 35.7% body fat in SWCP-II women, who were recruited to have BMI of 24-30 kg·m⁻² and are described in the previous section. Both sexes had a mean fat mass of 27 kg.] In men, weight loss was significant in both diet only (-6.8 kg) and diet + exercise (-10.4 kg) compared with controls (P < 0.001), as was fat weight loss (-5.5 kg and -9.0 kg, respectively). Compared with men assigned to diet alone, dieting exercisers lost more total weight (-2.4 kg; P < 0.01) and fat weight (-3.5 kg; P < 0.001); in fact, the addition of exercise to the diet increased loss of body fat by 81%. Waist-to-hip girth was significantly reduced in both diet only and diet + exercise versus control (P < 0.001), but the decrease was significantly greater in dieting exercisers compared with diet only (P < 0.001).

Compared with controls, HDL-C was significantly increased in dieting exercisers (0.19 mmol·L⁻¹), as was apolipoprotein A-I (7.2 mg·dL⁻¹), whereas HDL-C was not significantly increased in dieters (0.7 mmol·L⁻¹); therefore, HDL-C increases in dieting exercisers were also significant compared with diet only (P < 0.01). Diet + exercise men decreased TG versus control (-0.66 mmol·L⁻¹; P < 0.001) and diet only men (-0.36 mmol·L⁻¹; P < 0.05). In contrast, LDL-C decreases were not significant in either dieters or dieting exercisers compared with controls; however, apolipoprotein B was reduced in both (-5.8 mg·dL⁻¹ and -6.0 mg·dL⁻¹; P < 0.01). Reductions in the LDL-C to HDL-C ratio were significant in both diet only and diet + exercise men versus control (P < 0.05) but did not differ between weight loss groups. There was also a significant reduction in the ratio of apolipoprotein B to apolipoprotein A-I in both dieting groups versus control (P < 0.001), and this reduction was greater in the diet plus exercise men versus diet only (P < 0.05).

Katzel and colleagues (12) specifically compared the effects of weight loss (achieved by diet, without a change in activity level) with aerobic exercise, without weight loss, in 111 of 170 obese (120-160% of ideal body weight) men, aged 46-80 yr, who were randomized to 9 months of control, weight loss by diet, or aerobic exercise, consisting of treadmill and cycle ergometer workouts. Before baseline testing, all three groups were instructed for 3 months on an isoenergetic reduced-fat (NCEP Step 1) diet, which may explain the low mean HDL-C, LDL-C, and TC levels in all men at baseline. Men in both the aerobic exercise and control groups were encouraged to continue a low-fat diet, without losing weight, throughout the trial; therefore, exercisers presumably increased their intake of low-fat foods. Men assigned to weight loss lost about 9.5 kg, 75% of which was fat mass, and did not change V̇O₂max, whereas exercisers did not change average weight but reduced percent body fat by 0.8% (P < 0.005). Compared with controls, HDL-C was significantly increased in the weight loss group (0.12 mmol·L⁻¹; P < 0.01) but not in the exercise group, whereas TG, TC and LDL-C were decreased (P < 0.05) in both the weight loss and exercise groups, and these changes did not differ between intervention groups. It is unclear whether the reduction in LDL-C and TC in exercisers was due to the increased exercise or increased intake of low-fat foods to maintain weight.

A comparison of the amount of weight lost by men in the two Stanford weight loss studies (31,32) and the Katzel study (12) raises some interesting issues. In SWCP-I (31), weight loss by reducing portion sizes without changing diet composition resulted in total and fat body weight losses of 7.8 and 6.2 kg, respectively, whereas those who lost weight by exercise only lost 4.6 kg and 4.4 kg. In SWCP-II (32), reducing calories by targeting dietary fat resulted in total and fat weight losses of 6.8 and 5.5 kg, and the addition of aerobic exercise increased this to 10.4 kg and 9.0 kg. Men who completed 1-yr tests in the weight loss group in the Katzel study (12) lost 9.5 kg and about 7 kg. HDL-C was similarly raised in SWCP-I by diet- and exercise-induced weight loss, even though weight loss was greater with diet. Weight loss accompanying the SWCP-II low-fat diet was similar in
magnitude to that from the SWCP-I diet and greater than that from the SWCP-I exercise, yet HDL-C was not elevated, unless exercise was added and/or greater weight loss was achieved, presumably because of a HDL-C-lowering effect of the low fat diet. Together, these studies suggest a HDL-C raising effect of weight loss and exercise, and a HDL-lowering effect of a low-fat diet, which interact to determine the HDL-C change. The greater weight loss achieved on the Katzel low-fat diet could explain the HDL-C increase in that study, or this may be due to the initiation of the low-fat diet 3 months before baseline measures and intervention. Similar issues are likely to exist for women; however, women may be more susceptible to the HDL-C-lowering effect of a low-fat and less responsive to the HDL-raising effect of weight loss or exercise, based on very limited data, such as from SWCP-II (32). Higher initial HDL-C levels may also contribute to sex differences in responses to exercise, as might sex differences in ability to lose weight with exercise (33).

Table 3 also presents two relatively small, 6-month exercise studies of obese postmenopausal women (9,20). [Studies with \( \leq 10 \) women per group were not included in this review.] In women with high LDL-C and TC, Ready et al. (20) reported greater, albeit modest, weight loss (-1.3 kg) in those assigned to walking (\( N = 15 \)) versus control (\( N = 10; P < 0.05 \)) and significant (\( P < 0.05 \)) decreases in TG and TC in walkers but no differences between groups in HDL-C or LDL-C changes. Fox et al. (9) found no weight loss or lipid change differences between women assigned to weight loss by either of two hypocaloric diets (-500 kcal·d\(^{-1}\) vs -700 kcal·d\(^{-1}\)) or by the -500 kcal·d\(^{-1}\) diet combined with a 200 kcal·d\(^{-1}\) energy deficit arising from a combination of aerobic exercise (1 h of walking 3 d·wk\(^{-1}\)) and resistance training (at 80% of one-repetition max capacity, 2 d·wk\(^{-1}\)).

In summary, three relatively large RCT of obese men have provided evidence that weight loss improves HDL-C and TG; however, none have been restricted to men with low HDL-C or elevated TG. One of these studies involved weight loss achieved solely by exercise with no dietary change (31). The only trial that showed LDL-C improvements with aerobic exercise required an increase in low-fat foods to maintain weight (12), whereas neither trial that promoted exercise-induced weight loss (31,32) provided evidence that weight loss or exercise reduce LDL-C. Evidence that weight loss and/or aerobic exercise improves dyslipoproteinemias in obese women is even weaker.

**Evidence statement.** Top

Weight loss achieved by exercise with no dietary change (or by caloric restriction with no exercise change) is likely to improve HDL-C and TG in obese men with normal lipoproteins, whereas the evidence that exercise or weight loss improve these lipids in men with dyslipidemias is weak (Category 1). Even less evidence exists to support a role for aerobic exercise in treating lipid disorders in obese women.

Table 4 presents three studies involving resistance exercise versus control, two in obese women (1,17) and one in normal weight women (4), none of which involved women with dyslipoproteinemias. [The author did not find RCT of lipoprotein effects of resistance training in lean or obese men, regardless of lipoprotein status.] Andersen et al. (1) randomized women who were consuming a hypocaloric (formula) diet to aerobic exercise, resistance training, the combination of these two modes of exercise, or no exercise. All four groups lost substantial weight, with mean total losses of 13-18 kg; however, there were no differences between groups in weight loss or HDL-C, LDL-C, TG, or TC changes. Manning et al. (17) also found no differences between obese women randomized to 12 wk of strength training versus control for weight gain (+1.4 vs 0.4) or lipid changes. On the other hand, Boyden et al. (4) reported significant reductions in LDL-C and TC in lean, premenopausal women with low-risk lipoproteins who were assigned to resistance training compared with controls; however, groups did not differ in weight changes or HDL-C or TG.
Evidence statement. TOP

There is essentially no data, especially in men, on effects of resistance exercise (strength training) on obesity-related dyslipoproteinemias.

LIFESTYLE (DAILY ENERGY EXPENDITURE) VERSUS STRUCTURED EXERCISE TOP

There has been considerable interest in recent years in the potential benefit of increasing energy expenditure through daily activities, rather than through a structured exercise program. Table 5 presents two randomized trials that compared these two exercise modes and reported weight and lipoprotein outcomes. Dunn et al. (6) combined results from 190 (of 116 plus 119) overweight men and women (mean = 28.2 kg·m⁻²) who were randomly assigned for 2 yr to lifestyle (accumulation of at least 30 min of moderate activity exercise, adapted to each individual, on most days of the week) or a structured aerobic exercise program at 50-85% of maximal aerobic power. The aerobic exercise group actually gained 0.7 kg over the 2-yr period, but this did not differ from controls (-0.1 kg). There were no differences between groups in HDL-C, LDL-C, or TC, which started at low-risk levels; however, TG increased in the structured exercise group (+0.07) and decreased in the lifestyle group (-0.11), resulting in a significant difference between groups (P < 0.05). Andersen et al. (2) randomized obese (≥ 15 plus kg ideal body weight) women to the same behavior + dietary weight loss program combined with either structured aerobic exercise or lifestyle for 4 months and found no differences between groups in weight or lipid changes.
Evidence statement. TOP

Effects of energy expenditure through daily activities on lipoproteins has not been shown to differ from effects of structured physical activity; however, the data are very limited at this time.

RESEARCH PRIORITIES TOP

To determine whether physical activity can prevent or treat lipoprotein disorders associated with obesity, studies need to be conducted in overweight and obese individuals who have specific adverse lipoprotein profiles. There are very few well-designed randomized clinical trials of exercise effects on lipoproteins in obese individuals, particularly in women, and those that exist are limited to the lower end of the class I obesity range, mean BMI < 31 kg·m⁻². Furthermore, despite a growing consensus that individuals with central obesity are more likely to have a higher prevalence of obesity-related CHD risk factors, no randomized, controlled trials were found which specifically evaluated the effect of physical activity on overweight or obese men or women with central obesity. This might be of particular importance in women, for whom most data are derived from women with the more common gynoid obesity pattern, who may differ in their ability to lose weight or improve lipoproteins versus those with android obesity.

REFERENCES TOP


27. Tran, Z. V., and A. Weltman. Differential effects of exercise on serum lipid and lipoprotein levels seen with changes in body weight. JAMA 254: 919-924, 1985. [Medline Link] [CrossRef] [Context Link]

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